Weight Gain During Pregnancy: Reexamining the Guidelines

Kathleen M. Rasmussen and Ann L. Yaktine, *Editors*

Committee to Reexamine IOM Pregnancy Weight Guidelines
Food and Nutrition Board and Board on Children, Youth, and Families

INSTITUTE OF MEDICINE *AND*
NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

PREPUBLICATION COPY: UNCORRECTED PROOFS

THE NATIONAL ACADEMIES PRESS   500 Fifth Street, N.W.   Washington, DC 20001

Additional copies of this report are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, http://www.nap.edu.

For more information about the Institute of Medicine, visit the IOM home page at: **www.iom.edu.**

The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

Suggested citation: IOM (Institute of Medicine). 2009. *Weight Gain During Pregnancy: Reexamining the Guidelines.* Washington, DC: The National Academies Press.

"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the Nation. Improving Health.

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Ralph J. Cicerone is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Charles M. Vest is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Ralph J. Cicerone and Dr. Charles M. Vest are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

COMMITTEE ON THE REEXAMINATION OF IOM PREGNANCY WEIGHT GUIDELINES

KATHLEEN M. RASMUSSEN (*Chair*), Professor of Nutrition, Division of Nutritional Sciences, Cornell University, Ithaca, NY
BARBARA ABRAMS, Professor, School of Public Health, University of California–Berkeley
LISA M. BODNAR, Assistant Professor, Department of Epidemiology, University of Pittsburgh, PA
CLAUDE BOUCHARD, Executive Director and George A. Bray Chair in Nutrition, Pennington Biomedical Research Center, Baton Rouge, LA
NANCY BUTTE, Professor of Pediatrics, Baylor College of Medicine, Houston, TX
PATRICK M. CATALANO, Chair, Department of Obstetrics and Gynecology, Case Western Reserve University, Cleveland, OH
MATTHEW GILLMAN, Professor, Department of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care, Boston, MA
FERNANDO A. GUERRA, Director of Health, San Antonio Metropolitan Health District, TX
PAULA A. JOHNSON, Executive Director, Connors Center for Women's Health and Gender Biology, Chief, Division of Women's Health, Brigham and Women's Hospital, Boston, MA
MICHAEL C. LU, Associate Professor of Obstetrics, Gynecology, and Public Health, Schools of Medicine and Public Health, University of California–Los Angeles
ELIZABETH R. McANARNEY, Professor and Chair Emerita, Department of Pediatrics, School of Medicine and Dentistry, University of Rochester, NY
RAFAEL PEREZ-ESCAMILLA, Professor of Nutritional Sciences & Public Health, Director, NIH EXPORT Center for Eliminating Health Disparities among Latinos, University of Connecticut, Storrs
DAVID A. SAVITZ, Charles W. Bluhdorn Professor of Community & Preventive Medicine, Director, Epidemiology, Biostatistics, and Disease Prevention Institute, Mount Sinai School of Medicine, New York, NY
ANNA MARIA SIEGA-RIZ, Associate Professor, Department of Epidemiology, School of Public Health, University of North Carolina–Chapel Hill

Study Staff

ANN L. YAKTINE, Senior Program Officer
HEATHER B. DEL VALLE, Research Associate
M. JENNIFER DATILES, Senior Program Assistant
ANTON BANDY, Financial Officer
GERALDINE KENNEDO, Administrative Assistant
LINDA D. MEYERS, Food and Nutrition Board Director
ROSEMARY CHALK, Director, Board on Children, Youth, and Families

Reviewers

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's (NRC's) Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

Haywood Brown, Department of Obstetrics and Gynecology, Duke University Medical Center, Durham, NC
Cutberto Garza, Boston College, MA
Susan Gennaro, William F. Connell School of Nursing, Boston College, MA
William Goodnight, Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, University of North Carolina–Chapel Hill School of Medicine
Erica P. Gunderson, Division of Research, Kaiser Permanente, Oakland, CA
Maxine Hayes, Department of Health, State of Washington, Tumwater
Lorraine V. Klerman, The Heller School for Social Policy and Management, Brandeis University, Waltham, MA
Kristine G. Koski, School of Dietetics and Human Nutrition, McGill University, Ste. Anne de Bellevue, Quebec, Canada
Charles Lockwood, Department of Obstetrics, Gynecology, and Reproductive Sciences, Yale University School of Medicine, New Haven, CT
Dawn Misra, Division of Epidemiology and Biostatistics, Department of Family Medicine and Public Health Sciences, Wayne State University School of Medicine, Detroit, MI
Jose M. Ordovas, Nutrition and Genomics Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA
Roy M. Pitkin, University of California–Los Angeles (Professor Emeritus)
David Rush, Friedman School of Nutrition Science and Policy (Professor Emeritus), Tufts University, Boston, MA
Jeanette South-Paul, Department of Family Medicine, University of Pittsburgh, PA

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **Neal A. Vanselow,** Tulane University, Professor Emeritus and **Nancy E. Adler,** Departments of Psychiatry and Pediatrics and Center for Health and Community, University of California–San Francisco.

Appointed by the NRC and Institute of Medicine, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

Preface

In the last century, many answers have been given by health professionals to the question "how much weight should I gain while I am pregnant?" In the early 1900's, the answer was often only 15-20 pounds. Between 1970 and 1990, the guideline for weight gain during pregnancy was higher, 20-25 pounds, and in 1990, with the publication of *Nutrition During Pregnancy*, it went higher still for some groups of women. This most recent guideline reflected new knowledge about the importance of maternal body fatness before conception, as measured by body mass index, for the outcome of pregnancy. It had become clear that heavier women could gain less weight and still deliver an infant of good size. Since that time, the obesity epidemic has not spared women of reproductive age. In our population today, more women of reproductive age are severely obese (obesity class III; 8 percent) than are underweight (3 percent) and their short- and long-term health has become a concern in addition to the size of the infant at birth. Clearly the time had come to reexamine the guidelines for weight gain during pregnancy.

To prepare for this possibility, the National Research Council and the Institute of Medicine held a workshop in 2006 to evaluate the availability of data that could be used reexamine the current guidelines. Based on the outcome of this workshop, numerous federal agencies (Department of Health and Human Services: Health Resources Services Administration; Centers for Disease Control and Prevention Division of Nutrition, Physical Activity, and Obesity; National Institutes of Health: The Eunice Kennedy Shriver National Institute of Child Health and Development; National Institute of Diabetes, Digestive and Kidney Diseases, Division of Nutrition Research Coordination Office on Women's Health; Office on Disease Prevention and Health Promotion; and Office on Minority Health; as well as the March of Dimes) agreed to sponsor the work of this committee.

The committee was asked to review the determinants and a wide range of short- and long-term consequences of variation in weight gain during pregnancy for both the mother and her infant. Based on the outcome of this review, the committee was asked to recommend revisions to the current guidelines if this was deemed to be necessary. In addition, the committee was asked to consider the approaches that might be necessary to promote appropriate weight gain and to identify gaps in knowledge and make recommendations about priorities for future research.

Although many studies relevant to the committee's charge have been published since 1990 and the Agency for Healthcare Research and Quality (AHRQ) completed their report *Outcomes of Maternal Weight Gain* while the committee was gathering data, many gaps in knowledge remained. To address this problem, the committee held a public session with project sponsors, and two workshops. We are grateful to those who participated in these sessions for sharing their experience and wisdom. We are also grateful to a number of individuals who supplied data to the committee: Aimin Chen, Amy Branum, Alan Ryan, Andrea Sharma, Joyce Martin, Sharon Kirmeyer, K.S. Joseph, Marie Cedergren, Raul Artal, and with special thanks to Patricia Dietz. The committee also commissioned additional analyses of data from both Denmark and the United States. We thank our consultants, Ellen Aagaard Nohr, Amy Herring, and Cheryl Stein

for these analyses and for their contributions to the committee's work. The committee also felt that it was important to understand what would be involved in analyzing the trade-off between mother and infant in risk of adverse outcomes of variation in weight gain during pregnancy. To accomplish this, we commissioned such an analysis based on the data at hand. We thank our consultant, James Hammitt, for conducting these analyses and for his contribution to the committee's work.

The committee's 14 members gave freely of their expertise and volunteered their time and energy in all aspects of the preparation of this report, from developing its intellectual framework, writing the text and deliberating about the recommendations and conclusions of the report. Their efforts merit our sincere gratitude.

The committee received excellent staff support from Ann Yaktine, Study Director, Heather Del Valle, Research Associate and Jennifer Datiles, Senior Program Assistant. Their effort on our behalf is sincerely appreciated. Both the Director of the Food and Nutrition Board, Linda Meyers, and the Director of the Board on Children, Youth and Families, Rosemary Chalk, contributed their wisdom and support to this effort and we thank them for it.

Kathleen M. Rasmussen, *Chair*
Committee to Reexamine IOM Pregnancy Weight Guidelines

Contents

*Appendixes A through G are not printed in this book, but can be found on the CD at the back of the report or online at http://www.nap.edu/catalog.php?record_id=12584.

Summary

Since 1990, the last time the Institute of Medicine (IOM) released guidelines for weight gain during pregnancy, many key aspects of the health of women of childbearing age have changed. This population now includes a higher proportion of women from racial/ethnic subgroups and prepregnancy body mass index (BMI) and gestational weight gain (GWG) have increased among all population subgroups. Moreover, high rates of overweight and obesity are common in the population subgroups that are at risk for poor maternal and child health outcomes. Finally, women are also becoming pregnant at an older age and, as a result, are entering pregnancy more commonly with chronic conditions such as hypertension or diabetes, which put them at risk for pregnancy complications and may lead to increased morbidity during their post-pregnancy years. These and other factors suggested a need to reexamine the IOM (1990) guidelines for weight gain during pregnancy and consider whether revision might be warranted.

In response to these concerns, sponsors[1] asked the Food and Nutrition Board of the IOM and the Board on Children, Youth, and Families in the Division of Behavioral and Social Sciences and Education of the National Research Council to review the IOM (1990) recommendations for weight gain during pregnancy. Specifically, the committee was asked to review evidence on relationships between weight gain patterns before, during, and after pregnancy, and maternal and child health outcomes; consider factors within a life-stage framework associated with outcomes such as lactation performance, postpartum weight retention, cardiovascular and other chronic diseases; and recommend revisions to existing guidelines where necessary. Finally, the committee was asked to recommend ways to encourage the adoption of the weight gain guidelines through consumer education, strategies to assist practitioners, and public health strategies.

GUIDELINES FOR WEIGHT GAIN DURING PREGNANCY

The new guidelines for GWG that are shown in Table S-1 are formulated as a range for each category of prepregnancy BMI. This approach reflects the imprecision of the estimates on which the recommendations are based, the reality that good outcomes are achieved within a range of weight gains, and the many additional factors that may need to be considered for an individual woman. It is important to note that these guidelines are intended for use among women in the United States. They may be applicable to women in other developed countries. However, they are not intended for use in areas of the world where women are substantially shorter or thinner than American women or where adequate obstetric services are unavailable.

The new guidelines differ from those issued in 1990 in two ways. First, they are based on the World Health Organization (WHO) cutoff points for the BMI categories instead of the previous ones, which were based on categories derived from the Metropolitan Life Insurance tables.

---

[1]Sponsors include: U.S. Department of Health and Human Services, Health Resources and Services Administration,; Centers for Disease Control and Prevention, Division of Nutrition, Physical Activity, and Obesity; National Institutes of Health, National Institute of Child Health and Human Development, National Institute of Diabetes and Digestive and Kidney Diseases; U.S. Department of Health and Human Services Office on Women's Health; U.S. Department of Health and Human Services Office on Disease Prevention and Health Promotion; and the March of Dimes. Additional support came from U.S. Department of Health and Human Services Office of Minority Health and the National Minority AIDS Council.

Second, and more importantly, the new guidelines include a specific, relatively narrow range of recommended gain for obese women.

TABLE S-1 New Recommendations for Total and Rate of Weight Gain during Pregnancy, by Prepregnancy BMI

Prepregnancy BMI	Total Weight Gain		Rates of Weight Gain* 2nd and 3rd Trimester	
	Range in kg	Range in lbs	Mean (range) in kg/week	Mean (range) in lbs/week
Underweight (< 18.5 kg/m^2)	12.5–18	28–40	0.51 (0.44–0.58)	1 (1–1.3)
Normal weight (18.5–24.9 kg/m^2)	11.5–16	25–35	0.42 (0.35–0.50)	1 (0.8–1)
Overweight (25.0–29.9 kg/m^2)	7–11.5	15–25	0.28 (0.23–0.33)	0.6 (0.5–0.7)
Obese (≥ 30.0 kg/m^2)	5–9	11–20	0.22 (0.17–0.27)	0.5 (0.4–0.6)

* Calculations assume a 0.5–2 kg (1.1– 4.4 lbs) weight gain in the first trimester (based on Siega-Riz et al., 1994; Abrams et al., 1995; Carmichael et al., 1997)

These new guidelines should be considered in the context of data on women's reported GWG. Data from several large groups of women indicate that the mean gains of underweight women fall within the new guidelines, but some normal weight women may exceed these new guidelines and a majority of overweight or obese women will likely exceed them. These data provide a strong reason to assume that interventions will be needed to assist women, particularly those who are overweight or obese at the time of conception, in meeting the guidelines. These interventions may need to occur at both the individual and community levels and may need to include components related to both improved dietary intake and increased physical activity.

The committee intends that the guidelines shown in Table S-1 be used in concert with good clinical judgment as well as a discussion between the woman and her care provider about diet and exercise. If a woman's GWG is not within the proposed guidelines, clinicians should consider other relevant clinical evidence, modifiable factors that might be causing excessive or inadequate gain, and information on the nature of excess GWG (e.g. fat or edema) as well as both the adequacy and consistency of fetal growth before suggesting that a woman modify her pattern of weight gain.

Special Populations

Women of Short Stature

The IOM (1990) report recommended that women of short stature (< 157 cm) gain at the lower end of the range for their prepregnant BMI. The committee was unable to identify evidence sufficient to continue to support a modification of GWG guidelines for women of short stature. Although women of short stature had an increased risk of emergency cesarean delivery, this risk was not modified by GWG. Women of short stature did not have an increased risk of having an small-for-gestational age (SGA) or large-for-gestational age (LGA) infant or of excessive postpartum weight retention over taller women.

Pregnant Adolescents

Evidence available since the IOM (1990) report is also insufficient to continue to support a modification of the GWG guidelines for adolescents (< 20 years old) during pregnancy. The committee also determined that prepregnancy BMI could be adequately categorized in adolescents by using the WHO cutoff points for adults, in part because of the impracticality of using pediatric growth charts in obstetric practices. Adolescents who follow adult BMI cutoff points will likely be categorized in a lighter group and thus advised to gain more; however, younger adolescents often need to gain more to improve birth outcomes.

Racial or Ethnic Groups

Although an increasing proportion of pregnant U.S. women are members of racial or ethnic minority groups, the limited data available to the committee from commissioned analyses suggested that membership in one of these groups did not modify the association between GWG and the outcome of pregnancy. As a result, the committee concluded that its recommendations should be generally applicable to the various racial or ethnic subgroups that make up the American population although additional research is needed to confirm this approach.

Women with Multiple Fetuses

Recent data suggest that the weight gain of women with twins who have good outcomes varies with prepregnancy BMI as is clearly the case for women with singleton fetuses. Inasmuch as the committee was unable to conduct the same kind of analysis for women with twins as it did for women with singletons, the committee offers the following provisional guidelines: normal weight women should gain 17-25 kg (37-54 pounds), overweight women, 14-23 kg (31-50 pounds) and obese women, 11-19 kg (25-42 pounds) at term. Insufficient information was available with which to develop even a provisional guideline for underweight women with multiple fetuses. These provisional guidelines reflect the interquartile (25th to 75th percentiles) range of cumulative weight gain among women who delivered their twins, who weighed ≥ 2,500 g on average, at 37-42 weeks of gestation.

DEVEOPMENT OF THE GUIDELINES FOR WEIGHT GAIN DURING PREGNANCY

The committee worked from the perspectives that the reproductive cycle begins before conception and continues through the first year postpartum and that maternal weight status throughout the entire cycle affects both the mother and her child. To inform its review of the literature and to guide the organization of its report, the committee reevaluated the conceptual framework that guided the development of the IOM (1990) report. To account for advances in our scientific understanding of the determinants and consequences of GWG, the committee developed a modified conceptual framework (Figure S-1). However, it retained the same scientific approach and epidemiologic conventions used previously and discussed in detail in the IOM (1990) report.
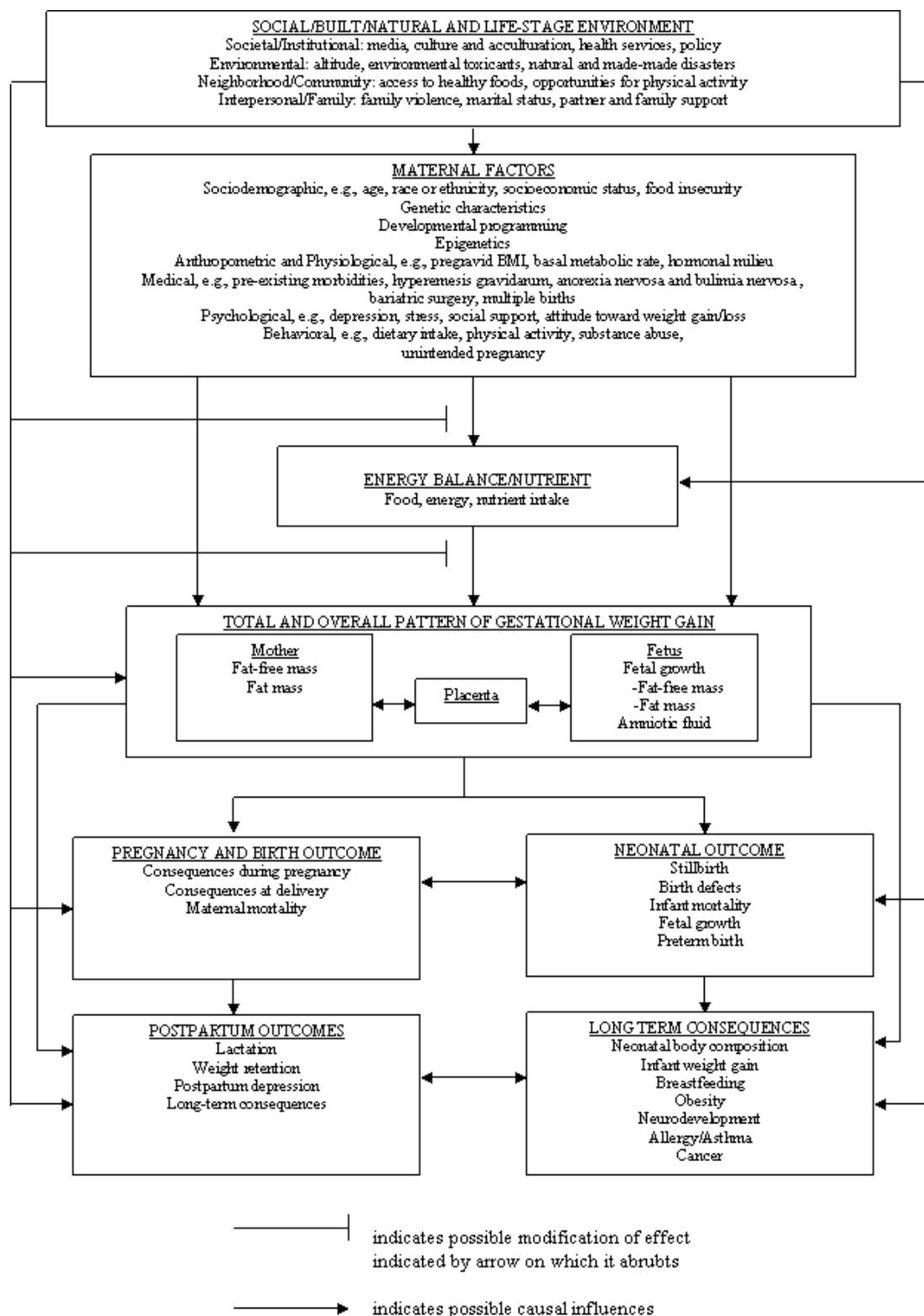
FIGURE S-1 Schematic summary of potential determinants and consequences for gestational weight gain.
SOURCE: Modified from IOM, 1990.

The committee began its work by considering appropriate BMI cutoff points and describing trends over time in maternal prepregnancy BMI and GWG among American women. In addition, data were sought on both the determinants and consequences of GWG. The search for such data revealed major gaps in data collection and analysis.

Key Finding S-1: The WHO cutoff points for categorizing BMI have been widely adopted and should be used for categorizing prepregnancy BMI as well.

Key Finding S-2: Currently available data sources are inadequate for studying national trends in GWG, or postpartum weight, or their determinants.

Action Recommendation S-1: The committee recommends that the Department of Health and Human Services conduct routine surveillance of GWG and postpartum weight retention on a nationally representative sample of women and report the results by prepregnancy BMI (including all classes of obesity), age, racial/ethnic group, and socioeconomic status.

Action Recommendation S-2: The committee recommends that all states adopt the revised version of the birth certificate, which includes fields for maternal prepregnancy weight, height, weight at delivery, and gestational age at the last measured weight. In addition, all states should strive for 100 percent completion of these fields on birth certificates and collaborate to share data, thereby allowing a complete national picture as well as regional snapshots.

Research Recommendation S-1: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies in large and diverse populations of women to understand how dietary intake, physical activity, dieting practices, food insecurity and, more broadly, the social, cultural and environmental context affect GWG.

In developing its recommendations, the committee identified a set of consequences for the short- or long-term health of the mother and the child that are potentially causally related to GWG. These consequences included those evaluated in a systematic review of outcomes of maternal weight gain prepared for the Agency for Healthcare Research and Quality (AHRQ) as well as others based on data from the literature outside the time window considered in that report. To address conflicts and gaps within the available literature, the committee commissioned four additional analyses from existing databases. The committee considered the results from these commissioned analyses in conjunction with evidence from published scientific literature.

Postpartum weight retention, cesarean delivery, gestational diabetes mellitus, and pregnancy-induced hypertension or preeclampsia emerged from this process as being the most important maternal health outcomes. The committee removed preeclampsia and gestational diabetes mellitus from consideration because of the lack of sufficient evidence that GWG was a cause of these conditions. Postpartum weight retention and, in particular, unscheduled primary cesarean delivery were retained for further consideration.

Measures of size at birth (e.g. SGA and LGA), preterm birth, and childhood obesity emerged from this process as being the most important infant health outcomes. The committee recognized that both SGA and LGA, when defined as < 10th percentile and > 90th percentile of weight-for-gestational age, respectively, represent a mix of individuals who are appropriately or inappropriately small or large. In addition, the committee recognized that being SGA was likely to be associated with deleterious outcomes for the infant but not the mother, while being LGA was likely to be associated with consequences for both the infant and the mother (e.g., cesarean delivery).

Key Finding S-3: Evidence from the scientific literature is remarkably clear that prepregnancy BMI is an independent predictor of many adverse outcomes of pregnancy. As a result women should enter pregnancy with a BMI in the normal weight category.

Key Finding S-4: Although a record-high proportion of American women of childbearing age have BMI values in obesity classes II and III, available evidence is insufficient to develop more specific recommendations for GWG among these women.

Research Recommendation S-2: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies in all classes of obese women, stratified by the severity of obesity, on the determinants and impact of GWG, pattern of weight gain, and its composition on maternal and child outcomes.

Key Finding S-5: There are only limited data available with which to link GWG to health outcomes of mothers and children that occur after the neonatal period.

Research Recommendation S-3: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies on the eating behaviors, patterns of dietary intake and physical activity, and metabolic profiles of pregnant women, especially obese women, who experience low gain or weight loss during pregnancy. In addition, the committee recommends that researchers conduct studies on the effects of weight loss or low GWG, including periods of prolonged fasting and the development of ketonuria/ketonemia during gestation, on growth and on development, and long-term neurocognitive function in the offspring.

Research Recommendation S-4: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct observational and experimental studies on the association between GWG and (a) glucose abnormalities and gestational hypertensive disorders that take into account the temporality of the diagnosis of the outcome, and (b) the development of glucose intolerance, hypertension and other cardiovascular risk factors as well as mental health and cancer later in a woman's life.

Research Recommendation S-5: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies that (a) explore mechanisms, including epigenetic mechanisms, that underlie effects of GWG on maternal and child outcomes and (b) address the extent to which optimal GWG differs not only by maternal prepregnancy BMI but also by other factors such as age (especially among adolescents), parity, racial/ethnic group, socioeconomic status, co-morbidities, and maternal/paternal/fetal genotype.

Research Recommendation S-6: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct observational and experimental studies to assess the impact of variation in GWG on a range of child outcomes, including duration of gestation, weight and body composition at birth, and neurodevelopment, obesity and related outcomes, and asthma later in childhood.

Based on the available published literature as well as the reports of its consultants, the committee ascertained the GWG value or range of values associated with lowest prevalence of the outcomes of greatest interest. When weighting the trade-off among these outcomes, the committee considered, within each category of prepregnant BMI (a) the incidence or prevalence of each of these outcomes, (b) whether the outcomes were permanent (e.g. neurocognitive deficits) or potentially modifiable (e.g. postpartum weight retention) and (c) the quality of the available data. The committee compared the resulting ranges with those developed in the

quantitative risk analysis conducted by its consultants. Finally, the committee considered how its possible recommendations might be accepted and used by clinicians and women.

Research Recommendation S-7: To permit the development of improved recommendations for GWG in the future, the committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to (a) conduct studies to assess utilities (values) associated with short- and long-term health outcomes associated with GWG for both mother and child and (b) include these values in studies that employ decision analytic frameworks to estimate optimal GWG according to category of maternal prepregnancy BMI and other subgroups.

APPROACHES TO ACHIEVING RECOMMENDED WEIGHT GAIN DURING PREGNANCY

To meet the recommendations of this report fully, two different challenges must be met. First, a higher proportion of American women should conceive at a weight within the range of normal BMI values. Meeting this first challenge requires preconceptional counseling and, for many women some weight loss. Such counseling may need to include additional contraceptive services as well as services directed toward helping women to improve the quality of their diets and increase their physical activity. Preconception counseling is an integral part of the recommendations from the Centers for Disease Control (Johnson et al., 2006). Practical guidelines for preconceptional care are provided in *Nutrition During Pregnancy and Lactation: An Implementation Guide* (IOM, 1992). The need to meet this challenge reinforces the importance of preconceptional counseling as the cornerstone for achieving optimal outcomes of pregnancy and improved health for mothers and their children.

Action Recommendation S-3: The committee recommends that appropriate federal, state and local agencies as well as health care providers inform women of the importance of conceiving at a normal BMI and that all those who provide health care or related services to women of childbearing age include preconceptional counseling in their care.

Second, a higher proportion of American women should limit their GWG to the range specified in these guidelines for their prepregnant BMI. Meeting this second challenge requires a different set of services**.** The first step in assisting women to gain within these guidelines is letting them know that they exist, which will require educating their healthcare providers as well as the women themselves.

Action Recommendation S-4: The committee recommends that relevant federal agencies, private voluntary organizations, and medical and public health organizations adopt these new guidelines for GWG and publicize them to their members and also to women of childbearing age.

Individualized attention is called for in the IOM (1990) guidelines and was an element in all of the interventions that have been successful in helping women to gain within their target range. Guidelines on providing such care are provided in *Nutrition During Pregnancy and Lactation: An Implementation Guide* (IOM, 1992). The increase in prevalence of obesity that has occurred since this report was written suggests that this recommendation has only become more important.

In offering women individualized attention, a number of kinds of services could be considered. Health care providers should chart women's weight gain and share the results with them so that they become aware of their progress toward their weight-gain goal. To assist healthcare providers in doing this, the committee has prepared charts that could be used as a

basis for this discussion with the pregnant woman. These charts are meant to be used as part of an assessment of the progress of pregnancy and a woman's weight gain, looking beyond the gain from one visit to the next and toward the overall pattern of weight gain. In addition, women should be provided with individualized advice about both diet and physical activity (ACOG, 2002). This may require referral to a dietitian as well as other appropriately qualified individuals, such as those who specialize in helping women to increase their physical activity. These services may need to continue into the postpartum period to give women the maximum support to return to their prepregnant weight within the first year and, thus, to have a better chance of returning to a normal BMI value at the time of a subsequent conception.

Individualized attention is likely to be necessary but not sufficient to enable most women to gain within the new guidelines. Family- and community-level factors must also be addressed if women are to succeed in gaining within these guidelines. Further research on these kinds of multilevel, ecological determinants of GWG is needed to guide the development of comprehensive and effective implementation strategies to achieve these guidelines. In addition, special attention should be given to low-income and minority women, who are at risk of being overweight or obese at the time of conception, consuming diets of lower nutritional value, and of performing less recreational physical activity.

Action Recommendation S-5: To assist women to gain within the guidelines, the committee recommends that those who provide prenatal care to women should offer them counseling, such as guidance on dietary intake and physical activity, that is tailored to their life circumstances.

Research Recommendation S-8: The committee recommends that the Department of Health and Human Services provide funding for research to aid providers and communities in assisting women to meet these guidelines, especially low-income and minority women. The committee also recommends that the Department of Health and Human Services provide funding for research to examine the cost-effectiveness (in terms of maternal and offspring outcomes) of interventions designed to assist women in meeting these guidelines.

CONCLUDING REMARKS

Although the guidelines developed as part of this committee process are not dramatically different from those published previously (IOM, 1990), fully implementing them would represent a radical change in the care provided to women of childbearing age. In particular, the committee recognizes that full implementation of these guidelines would mean:

- Offering preconceptional services, such as counseling on diet and physical activity as well as access to contraception, to all overweight or obese women to help them reach a healthy weight before conceiving. This may reduce their obstetric risk and normalize infant birth weight as well as improve their long-term health.
- Offering services, such as counseling on diet and physical activity, to all pregnant women to help them achieve the guidelines on GWG contained in this report. This may also reduce their obstetric risk, reduce postpartum weight retention, improve their long-term health, normalize infant birth weight and offer an additional tool to help reduce childhood obesity.
- Offering services, such as counseling on diet and physical activity, to all postpartum women. This may help them to eliminate postpartum weight retention and, thus, to be able to conceive again at a healthy weight as well as improve their long-term health.

The increase in overweight and obesity among American women of childbearing age and failure of many pregnant women to gain within the IOM (1990) guidelines alone justify this radical change in care as women clearly require assistance to achieve the recommendations in this report in the current environment. However, the reduction in future health problems among both women and their children that could possibly be achieved by meeting the guidelines in this report provide additional justification for the committee's recommendations.

These new guidelines are based on observational data, which consistently show that women who gained within the IOM (1990) guidelines experienced better outcomes of pregnancy than those who did not (see Chapters 5 and 6). Nonetheless, these new guidelines require validation from experimental studies. To be useful, however, such validation through intervention studies must have adequate statistical power not only to determine if a given intervention helps women to gain within the recommended range but also to determine if doing so improves their outcomes. In the future, it will be important to reexamine the trade-offs between women and their children in pregnancy outcomes related to prepregnancy BMI as well as GWG, and also to be able to estimate the cost-effectiveness of interventions designed to help women meet these recommendations.

REFERENCES

Abrams B., S. Carmichael and S. Selvin. 1995. Factors associated with the pattern of maternal weight gain during pregnancy. *Obstetrics and Gynecology* 86(2): 170-176.

ACOG (American College of Obstetricians and Gynecologists). 2002. ACOG committee opinion. Exercise during pregnancy and the postpartum period. Number 267, January 2002. American College of Obstetricians and Gynecologists. *International Journal of Gynaecology and Obstetrics* 77(1): 79-81.

Carmichael S., B. Abrams and S. Selvin. 1997. The pattern of maternal weight gain in women with good pregnancy outcomes. *American Journal of Public Health* 87(12): 1984-1988.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

IOM. 1992. *Nutrition During Pregnancy and Lactation: An Implementation Guide*. Washington, DC: National Academy Press.

Johnson K., S. F. Posner, J. Biermann, J. F. Cordero, H. K. Atrash, C. S. Parker, S. Boulet and M. G. Curtis. 2006. Recommendations to improve preconception health and health care--United States. A report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. *MMWR Recomm Rep* 55(RR-6): 1-23.

Siega-Riz A. M., L. S. Adair and C. J. Hobel. 1994. Institute of Medicine maternal weight gain recommendations and pregnancy outcome in a predominantly Hispanic population. *Obstetrics and Gynecology* 84(4): 565-573.

Setting the Stage for Revising Pregnancy Weight Guidelines: Conceptual Framework

BACKGROUND

Improvement of maternal, fetal, and child health are key public health goals. Over the past four decades, changes in public health trends have challenged the healthcare sector to provide optimal guidance to women before, during, and after pregnancy to achieve healthy outcomes for themselves and their newborns.

The report, *Maternal Nutrition and the Course of Pregnancy* (NRC, 1970) developed from concern about high neonatal and infant mortality rates in the United States compared to other developed countries. In that report, the Committee on Maternal Nutrition recognized the positive relationship between gestational weight gain (GWG) and birth weight. The committee also noted the positive association between prepregnancy maternal weight and birth weight and the fact that higher prepregnancy maternal weight reduced the impact of GWG on birth weight. The report advised an average gestational weight gain of 24 pounds (20-25-pound range) and advised against the then-current practice of limiting GWG to 10-14 pounds.

A subsequent Institute of Medicine (IOM) report *Nutrition During Pregnancy* (IOM, 1990) offered recommendations for weight gain during pregnancy based on prepregnancy maternal body mass index (BMI). The report also made specific weight gain recommendations for population subgroups, including adolescents, members of racial and ethnic groups, women of short stature, and women carrying twins. The report also details historic trends in weight gain recommendations and guidelines. These recommendations for weight gain during pregnancy have been adopted by or have been influential in many countries. Reviews of observational studies support that women who enter pregnancy at a normal BMI and gain within the ranges recommended in the IOM (1990) guidelines are more likely to have a good birth outcome than women who gain outside the recommended ranges (Taffel et al., 1993; Abrams et al., 2000; Gross, 2006).

In the years since the release of the weight gain recommendations from the IOM (1990) report, some dramatic shifts in the demographic and epidemiologic profile of the U.S. population have occurred. Notably, prepregnancy BMI and excess GWG have increased across all population groups, particularly minority groups (Yeh and Shelton, 2005; Kim et al., 2007). These and other factors suggested a need to consider whether a revision of the IOM (1990) pregnancy weight gain guidelines is needed.

RATIONALE FOR REVISING THE GUIDELINES

General Principles Framing the Guidelines

The IOM (1990) pregnancy weight guidelines were developed principally in response to concerns about low birth weight infants. Although adverse health outcomes for excess weight gain were considered in the IOM (1990) weight gain guidelines, these recommendations were derived largely from data collected in the 1980 National Natality Survey (Available: http://www.cdc.gov/nchs/about/major/nmihs/abnmihs.htm [accessed March 3, 2008]) and focused on preventing premature births and small-for-gestational age infants.

The IOM (1990) report and a subsequent report, *Nutrition During Pregnancy and Lactation* (IOM, 1992), identified specific actions practitioners could take to achieve the recommendations in working with patients. They also identified a series of research recommendations for epidemiologic, basic, and applied research to enable better estimates of GWG, prepregnancy weight for height, and gestational duration, which affect study design and interpretation.

INDICATORS FOR REVISING THE CONCEPTUAL FRAMEWORK OF THE GUIDELINES

In 1996 an expert work group was convened by the Maternal and Child Health Bureau of the Health Resources and Services Administration (HRSA), Department of Health and Human Services (HHS), to examine issues relating to maternal weight gain that had been published in the IOM (1990) report. The purpose of this group was to determine whether new research provided a basis for practitioners to change guidance for GWG, and to recommend future directions for research, training, and/or other programmatic initiatives. The group concluded that formal revision of the IOM (1990) weight gain recommendations was not yet warranted; however reservations were expressed that the recommendations for African-American women, young adolescents, and women of short stature were too specific (Suitor, 1997).

Since publication of the IOM reports *Nutrition During Pregnancy* (1990) and *Nutrition During Lactation* (1991) and the subsequent *Implementation Guide* (1992), the population of U.S. women of childbearing age has become more diverse. Although low birth weight remains a significant concern during pregnancy, new health concerns have emerged. These include the greater prevalence of women who are overweight or obese entering pregnancy, which puts them at high risk for pregnancy complications. For example, data from the 2003-2004 round of the National Health and Nutrition Examination Survey (NHANES) show that 28.9 percent of women of reproductive age (20-39 years old) were obese (BMI $\geq$ 30 kg/m^2) and 8.0 percent were extremely obese (BMI $\geq$ 40 kg/m^2) (Ogden et al., 2006). Women are becoming pregnant at an older age and enter pregnancy with chronic conditions such as type 2 diabetes, which also puts them at risk for pregnancy complications and may lead to increased morbidity during their post-pregnancy years (Cleary-Goldman et al., 2005; Joseph et al., 2005; Delpisheh et al., 2008).

EMERGING TRENDS FROM RESEARCH ON GESTATIONAL WEIGHT GAIN

Weight patterns (underweight and overweight) and GWG have short- and long-term consequences for the health of the mother. For example, prepregnancy BMI above normal values (19.8-26 kg/m^2) is associated with preeclampsia, gestational diabetes (GDM), cesarean delivery

(Doherty et al., 2006; Abenhaim et al., 2007), and failure to initiate and sustain breastfeeding (Hilson et al., 1997; Li et al., 2003; Kugyelka et al., 2004). Increased maternal BMI and GWG have also been associated with higher fat mass in infants and subsequent overweight in children (Hillier et al., 2007; Oken et al., 2007).

Collectively, these trends and newer research prompted concern about the appropriateness of existing guidelines for GWG to support optimal outcomes for mother, infant, and child. Specifically there were concerns about the implications of the recommendations for (1) the health of the mother, particularly for women who are overweight, underweight, older, adolescent, or short in stature; (2) for infant and child health; and (3) for other metabolic processes that may affect the in utero environment.

Another concern that has frequently been raised by researchers and practitioners is the difference between BMI categories used in the IOM (1990) report and those used in the report *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults* from the National Heart, Lung, and Blood Institute (NHLBI, 1998) in cooperation with the National Institute of Diabetes and Digestive and Kidney Diseases, which are based on a report from the World Health Organization (1995). This is a problem for practitioners as well as for researchers. Most importantly, despite the effort made to publicize the recommendations of the IOM (1990) report, including the development of a guide to assist the medical profession to implement these guidelines (IOM, 1992), many healthcare providers have not used these guidelines and many women have not followed them (Abrams et al., 2000).

SETTING THE STAGE FOR REVISING THE GUIDELINES

In response to such concerns, the Maternal and Child Health Bureau of HHS requested that the National Research Council and the IOM convene a workshop in May 2006. The purpose of this workshop was to review trends in maternal weight; explore emerging research findings related to the complex relationship of the biological, behavioral, psychological, and social interactions that affect maternal and pregnancy weight on maternal and child health outcomes and discuss interventions. The following specific questions were addressed by the workshop were:

- What research and databases describe the distribution of maternal weight (prior to, during, and after pregnancy) among different populations of women in the United States?
- What research and databases inform understanding of the effects of different weight patterns (including underweight and overweight) during pregnancy on maternal and child health outcomes?
- What research has been conducted to describe the individual, community, and healthcare system factors that impede or foster compliance with recommended GWG guidelines?
- What opportunities exist for Title V maternal and child health programs to build on this knowledge to help childbearing women achieve and maintain recommended weight?
- What future research and data collection efforts could improve the efforts of Title V programs to support women from different racial and ethnic backgrounds in their

efforts to comply with recommended weight guidelines and to improve their maternal health?

The workshop summary report, *Influence of Pregnancy Weight on Maternal and Child Health* (NRC-IOM, 2007), includes a review of U.S. trends in maternal weight (before, during, and after pregnancy) among different populations of women. The workshop report also includes a discussion of the determinants of GWG; the relationships among maternal weight, GWG, and the health of women and children; interventions in healthcare and community settings that help women achieve appropriate weight levels during and after pregnancy; and emerging themes that warrant further examination in future studies. Taken together, the workshop and its summary report reinforce the need to reexamine recommendations for GWG, especially in light of the current obesity epidemic, and to highlight ways to encourage their adoption.

THE COMMITTEE'S TASK

Sponsors[1] asked the IOM's Food and Nutrition Board and the Division of Behavioral and Social Sciences and Education Board on Children, Youth, and Families to review and update the IOM (1990) recommendations for weight gain during pregnancy and recommend ways to encourage their adoption through consumer education, strategies to assist practitioners, and public health strategies.

The committee was asked to address the following tasks:

1. Review evidence on the relationship between weight gain patterns before, during, and after pregnancy and maternal and child health outcomes, with particular attention to the prevalence of maternal obesity racial/ethnic and age differences, components of GWG, and implications of weight during pregnancy on postpartum weight retention and maternal and child obesity and later child health.
2. Within a life-stage framework consider factors in relation to GWG that are associated with maternal health outcomes such as lactation performance, postpartum weight retention, cardiovascular disease, metabolic processes including glucose and insulin-related issues, and risk of other chronic diseases; for infants and children, in addition to low birth weight, consider early developmental impacts and obesity related consequences (e.g., mental health, diabetes).
3. Recommend revisions to the existing guidelines, where necessary, including the need for specific pregnancy weight guidelines for underweight, normal weight, and overweight and obese women and adolescents and women carrying twins or higher-order multiples.
4. Consider a range of approaches to promote appropriate weight gain, including:

   - Individual (behavior), psychosocial, community, healthcare, and health systems;

---

[1] Sponsors include: U.S. Department of Health and Human Services, Health Resources and Services Administration,; Centers for Disease Control and Prevention, Division of Nutrition, Physical Activity, and Obesity; National Institutes of Health, National Institute of Child Health and Human Development, National Institute of Diabetes and Digestive and Kidney Diseases; U.S. Department of Health and Human Services Office on Women's Health; U.S. Department of Health and Human Services Office on Disease Prevention and Health Promotion; and the March of Dimes. Additional support came from U.S. Department of Health and Human Services Office of Minority Health and the National Minority AIDS Council.

- Timing and components of interventions; and
- Ways to enhance awareness and adoption of the guidelines, including interdisciplinary approaches, consumer education to men and women, strategies to assist practitioners to use the guidelines, and public health strategies; and

5. Identify gaps in knowledge and recommend research priorities.

Approach to the Task

The committee approached its task by gathering information from existing literature, which included a systematic review of the literature by the Agency for Healthcare Research and Quality (AHRQ) (Viswanathan et al., 2008) (see Appendix E for literature reviewed). The committee also gathered information from presentations by recognized experts in three workshops (see "Open Sessions"). It consulted with additional experts in relevant fields and commissioned new data analyses. Contributions made to the committee by consultants are noted throughout the report. The information-gathering activities laid the groundwork for the committee's work of deliberating on issues relevant to the task and formulating a strategy to address the scope of work. This task was not regarded by the committee as a formal systematic, evidence-based review as the full range of literature did not lend itself to this type of task. Rather, because of the wide-ranging and large literature on this subject, the committee relied on its collective expertise to determine how much weight to give to all of the sources of information at its disposal.

The committee worked from the perspective that pregnancy-related weight begins before conception and continues through the first year postpartum and affects both the mother and her child. In consideration of Task 1, given the magnitude and complexity of the task, the committee determined that it was unable to address maternal weight history before entering pregnancy other than to take prepregnant BMI into account. Whenever possible, the committee sought and presented data on outcomes associated with GWG by racial/ethnic groups. This was done in the spirit of documenting disparities across racial/ethnic groups that the committee anticipated would reflect the strong socio-economic differentials and not biological differences across these groups. This assumption is grounded in the fact that ethnicity is, by definition, a socio-cultural construct and race, the way it is defined in the U.S., has been shown to be a social and not a biological construct (Goodman, 2000).

It is noteworthy that the committee was not charged with evaluating either the safety or effectiveness of the IOM (1990) guidelines. However, observational studies clearly indicate that gaining within the 1990 guidelines is associated with better pregnancy outcomes (and, presumably, greater safety) than gaining outside of them (Taffel et al., 1993; Abrams et al, 2000; Gross, 2006). Moreover, safety and effectiveness of a set of guidelines is a function of many factors, including adoption and use of them by the health care team, acceptance and actual use of them by their target audience, any barriers the target audience might experience in achieving the guidelines and, finally, whether those who actually meet the guidelines have better outcomes.

ORGANIZATION OF THE REPORT

This report is organized into 8 chapters in which the committee describes what is known about GWG, with particular attention to demographic and other factors associated with GWG

that falls above or below recommended levels, identifies data gaps, and makes recommendations based on the committee's findings.

The report begins by introducing the reasoning for a reexamination of pregnancy weight guidelines, based on data that have been gathered since the publication of *Nutrition During Pregnancy* (IOM, 1990). To inform its review of the literature and to guide the organization of this report, the committee reevaluated the conceptual framework that guided the development of the IOM (1990) report. The committee developed a modified conceptual framework (see Figure 1-1) to account for advances in scientific understanding of the determinants and consequences of GWG. However, it retained the same scientific approach and epidemiologic conventions used previously and discussed in detail in the IOM (1990) report. Several changes in the conceptual framework are noteworthy. The committee chose to highlight the importance of numerous environmental factors as determinants of maternal factors that lead to GWG. It is recognized that some of these act through maternal factors to influence GWG and its consequences, while others may affect those consequences by other routes.

Trends in GWG are considered in Chapter 2, with particular attention to weight gain in racial or ethnic subgroups of the U.S. population. Composition and components of GWG are addressed in Chapter 3. Since the IOM (1990) report was prepared, the importance of the placenta in the dialogue between the mother and fetus has become more apparent and the physiology and metabolism of the components of weight gain, including the placenta, are also discussed in Chapter 3.

In consideration of the determinants of GWG, the committee chose to distinguish between maternal factors that are fixed at conception (e.g., age, racial or ethnic group, parity) and those that could potentially be modified during the gestation period (e.g., smoking, drug use, medical conditions that could be treated). These factors are discussed in Chapter 4.

The new conceptual framework draws attention to outcomes in the perinatal period as well as those that occur postpartum and also much later in the lives of mothers and their children. These consequences of GWG are discussed in Chapters 5 and 6. Recommendations for action and approaches to implementation are discussed in Chapters 7 and 8. Recommendations for research are presented at the end of each chapter. The data reviewed in the chapters is tabulated in accompanying appendixes.

SOCIAL/BUILT/NATURAL AND LIFE-STAGE ENVIRONMENT
Societal/Institutional: media, culture and acculturation, health services, policy
Environmental: altitude, environmental toxicants, natural and made-made disasters
Neighborhood/Community: access to healthy foods, opportunities for physical activity
Interpersonal/Family: family violence, marital status, partner and family support

MATERNAL FACTORS
Sociodemographic, e.g., age, race or ethnicity, socioeconomic status, food insecurity
Genetic characteristics
Developmental programming
Epigenetics
Anthropometric and Physiological, e.g., pregravid BMI, basal metabolic rate, hormonal milieu
Medical, e.g., pre-existing morbidities, hyperemesis gravidarum, anorexia nervosa and bulimia nervosa, bariatric surgery, multiple births
Psychological, e.g., depression, stress, social support, attitude toward weight gain/loss
Behavioral, e.g., dietary intake, physical activity, substance abuse, unintended pregnancy

ENERGY BALANCE/NUTRIENT
Food, energy, nutrient intake

TOTAL AND OVERALL PATTERN OF GESTATIONAL WEIGHT GAIN

Mother
Fat-free mass
Fat mass

Placenta

Fetus
Fetal growth
-Fat-free mass
-Fat mass
Amniotic fluid

PREGNANCY AND BIRTH OUTCOME
Consequences during pregnancy
Consequences at delivery
Maternal mortality

NEONATAL OUTCOME
Stillbirth
Birth defects
Infant mortality
Fetal growth
Preterm birth

POSTPARTUM OUTCOMES
Lactation
Weight retention
Postpartum depression
Long-term consequences

LONG TERM CONSEQUENCES
Neonatal body composition
Infant weight gain
Breastfeeding
Obesity
Neurodevelopment
Allergy/Asthma
Cancer

├── indicates possible modification of effect indicated by arrow on which it abrubts

───────► indicates possible causal influences

FIGURE 1-1 Schematic summary of potential determinants and consequences for gestational weight gain.
SOURCE: Modified from IOM, 1990.

REFERENCES

Abenhaim H. A., R. A. Kinch, L. Morin, A. Benjamin and R. Usher. 2007. Effect of prepregnancy body mass index categories on obstetrical and neonatal outcomes. *Archives of Gynecology and Obstetrics* 275(1): 39-43.

Abrams B., S. L. Altman and K. E. Pickett. 2000. Pregnancy weight gain: still controversial. *American Journal of Clinical Nutrition* 71(5 Suppl): 1233S-1241S.

Cleary-Goldman J., F. D. Malone, J. Vidaver, R. H. Ball, D. A. Nyberg, C. H. Comstock, G. R. Saade, K. A. Eddleman, S. Klugman, L. Dugoff, I. E. Timor-Tritsch, S. D. Craigo, S. R. Carr, H. M. Wolfe, D. W. Bianchi and M. D'Alton. 2005. Impact of maternal age on obstetric outcome. *Obstetrics and Gynecology* 105(5 Pt 1): 983-990.

Delpisheh A., L. Brabin, E. Attia and B. J. Brabin. 2008. Pregnancy late in life: a hospital-based study of birth outcomes. *Journal of Women's Health (Larchmt)* 17(6): 965-970.

Doherty D. A., E. F. Magann, J. Francis, J. C. Morrison and J. P. Newnham. 2006. Pre-pregnancy body mass index and pregnancy outcomes. *International Journal of Gynaecology and Obstetrics* 95(3): 242-247.

Hillier T. A., K. L. Pedula, M. M. Schmidt, J. A. Mullen, M. A. Charles and D. J. Pettitt. 2007. Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia. *Diabetes Care* 30(9): 2287-2292.

Hilson J. A., K. M. Rasmussen and C. L. Kjolhede. 1997. Maternal obesity and breast-feeding success in a rural population of white women. *American Journal of Clinical Nutrition* 66(6): 1371-1378.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

IOM. 1991. *Nutrition During Lactation*. Washington, DC: National Academy Press.

IOM. 1992. *Nutrition During Pregnancy and Lactation: An Implementation Guide*. Washington, DC: National Academy Press.

Joseph K. S., A. C. Allen, L. Dodds, L. A. Turner, H. Scott and R. Liston. 2005. The perinatal effects of delayed childbearing. *Obstetrics and Gynecology* 105(6): 1410-1418.

Kim S. Y., P. M. Dietz, L. England, B. Morrow and W. M. Callaghan. 2007. Trends in pre-pregnancy obesity in nine states, 1993-2003. *Obesity (Silver Spring)* 15(4): 986-993.

Kugyelka J. G., K. M. Rasmussen and E. A. Frongillo. 2004. Maternal obesity is negatively associated with breastfeeding success among Hispanic but not Black women. *Journal of Nutrition* 134(7): 1746-1753.

Li R., S. Jewell and L. Grummer-Strawn. 2003. Maternal obesity and breast-feeding practices. *American Journal of Clinical Nutrition* 77(4): 931-936.

NHLBI (National Heart, Lung, and Blood Institute). 1998. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. (National Institutes of Health Publication 98-4083). Washington, DC: National Institutes of Health.

NRC (National Research Council). 1970. *Maternal Nutrition and the Course of Pregnancy*. Washington, DC: National Academy Press.

NRC-IOM. 2007. *Influence of Pregnancy Weight on Maternal and Child Health. Workshop Report. Committee on the Impact of Pregnancy Weight on Maternal and Child Health. Board on Children, Youth, and Families, Division of Behavioral and Social Sciences and Education and Food and Nutrition Board, Institute of Medicine*. Washington, DC: The National Academies Press.

Ogden C. L., M. D. Carroll, L. R. Curtin, M. A. McDowell, C. J. Tabak and K. M. Flegal. 2006. Prevalence of overweight and obesity in the United States, 1999-2004. *Journal of the American Medical Association* 295(13): 1549-1555.

Oken E., E. M. Taveras, K. P. Kleinman, J. W. Rich-Edwards and M. W. Gillman. 2007. Gestational weight gain and child adiposity at age 3 years. *American Journal of Obstetrics and Gynecology* 196(4): 322 e321-328.

Suitor C. W. 1997. *Maternal Weight Gain: A Report of an Expert Work Group* Arlington, VA: National Center for Education in Maternal and Child Health.

Taffel S. M., K. G. Keppel and G. K. Jones. 1993. Medical advice on maternal weight gain and actual weight gain. Results from the 1988 National Maternal and Infant Health Survey. *Annals of the New York Academy of Sciences* 678: 293-305.

Viswanathan M., A. M. Siega-Riz, M.-K. Moos, A. Deierlein, S. Mumford, J. Knaack, P. Thieda, L. J. Lux and K. N. Lohr. 2008. *Outcomes of Maternal Weight Gain, Evidence Report/Technology Assessment No. 168. (Prepared by RTI International-University of North Carolina Evidence-based Practice Center under contract No. 290-02-0016.) AHRQ Publication No. 08-E-09.* Rockville, MD: Agency for Healthcare Research and Quality.

WHO (World Health Organization). 1995. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organization Technical Report Series* 854: 1-452.

Yeh J. and J. A. Shelton. 2005. Increasing prepregnancy body mass index: analysis of trends and contributing variables. *American Journal of Obstetrics and Gynecology* 193(6): 1994-1998.

Website:
http://www.cdc.gov/nchs/about/major/nmihs/abnmihs.htm

2

Descriptive Epidemiology and Trends

To reexamine recommendations for weight gain during pregnancy, it is important to evaluate trends since 1990 in maternal body mass index (BMI) before pregnancy as well as gestational weight gain (GWG). These are evaluated together because BMI before and after pregnancy and GWG are interrelated. It is also important to examine trends in key maternal characteristics and pregnancy outcomes that are related to maternal weight before pregnancy and also to GWG. This information provides a context for understanding the sociodemographic and behavioral environment that may influence successful promotion of healthy GWG and optimal pregnancy outcomes.

TRENDS IN MATERNAL WEIGHT AND GESTATIONAL WEIGHT GAIN

Maternal Body Mass Index

One of the most serious issues that practitioners and scientists have faced in the past 30 years is the increase in prevalence of overweight and obesity among American women of childbearing age (Flegal et al., 1998; Mokdad et al., 1999; IOM, 2005; Kim et al. 2007). The prevalence of obesity in women 12 to 44 years of age has more than doubled since 1976 (Table 2-1). Data collected by the National Center for Health Statistics (NCHS) in 1999-2004 showed that nearly two-thirds of women of childbearing age were classified as overweight (as defined by BMI $\geq$ 25 kg/m^2) and almost one-third were obese (BMI $\geq$ 30 kg/m^2) (personal communication, A. Branum, Centers for Disease Control and Prevention [CDC], December 2008). Obesity is far more common among racial or ethnic minority groups and increases in prevalence with advancing age.

Importantly, the prevalence of severe obesity, once a relatively rare condition, has increased dramatically among women of childbearing age (Table 2-1). Between 1979 and 2004, class I and II obesity doubled and class III obesity tripled. Trends are similar by age. The prevalence of all classes of obesity is lowest in white non-Hispanic women, and highest in non-Hispanic black women, where the prevalence of class I obesity approaches 25 percent, and the prevalence of class II and III obesity each exceeds 10 percent. Almost one-fifth of Hispanic women have class I obesity, with the proportions of class II and III obesity each approaching 10 percent.

TABLE 2-1 Distribution of BMI (World Health Organization categories) from 1976 to 2004 Among U.S. Nonpregnant Women 12 to 44 Years of Age by Race or Ethnicity and Age (percentage)

	1976-1980	1988-1994	1999-2004
Total (%)			
Underweight	6.0	4.4	3.5
Normal weight	62.1	53.4	41.1
Overweight	18.8	20.8	25.3
Class I obese	7.9	12.2	15.8
Class II obese	3.5	6.0	7.7
Class III obese	1.7	3.4	6.5
By Race or Ethnicity			
Non-Hispanic white (%)			
Underweight	6.3	4.7	4.3
Normal weight	64.2	58.3	46.4
Overweight	17.9	18.4	23.3
Class I obese	7.2	10.5	13.8
Class II obese	2.9	5.3	6.9
Class III obese	1.5	2.8	5.3
Non-Hispanic black (%)			
Underweight	3.9	2.7	—[a]
Normal weight	47.8	37.3	23.4
Overweight	24.4	27.7	25.7
Class I obese	13.3	15.8	23.7
Class II obese	7.3	9.7	12.2
Class III obese	—[a]	6.8	13.3
Mexican American (%)			
Underweight	—[b]	1.9	—[a]
Normal weight	—[b]	36.0	32.0
Overweight	—[b]	32.3	32.6
Class I obese	—[b]	18.1	19.6
Class II obese		6.9	7.9
Class III obese		4.7	6.7
By Age			
Age 20-34 (%)			
Underweight	7.1	5.1	4.6
Normal weight	64.9	58.3	44.2
Overweight	16.8	18.2	23.9
Class I obese	6.9	10.6	14.8
Class II obese	3.0	5.2	7.1
Class III obese	1.4	2.6	5.4
Age 35-44 (%)			
Underweight	3.8	3.3	2.1
Normal weight	55.7	46.8	37.3
Overweight	23.2	24.2	27.1
Class I obese	10.2	14.2	17.1
Class II obese	4.8	7.0	8.6
Class III obese	—[a]	4.4	7.9

NOTE: Underweight, < 18.5 kg/m^2; normal, 18.5 to < 25.0 kg/m^2; overweight, 25.0 to < 30.0 kg/m^2; class I obese, 30.0 to < 35.0 kg/m^2; class II obese, 35.0 to < 40 kg/m^2; class III obese, ≥ 40 kg/m^2.

[a] Insufficient unweighted data to make reliable estimates.

[b] Hispanic ethnicity not available in 1976-1980 National Health and Nutrition Examination Survey (NHANES).

SOURCE: Personal communication, A. Branum, CDC, Hyattsville, Md., December 2, 2008.

As a result, more women are already obese when they become pregnant. Based on data from the Pregnancy Risk Assessment Monitoring System (PRAMS), one-fifth of American women are obese (BMI > 29 kg/m^2) at the start of pregnancy, a figure that has risen 70 percent in the last decade (Kim et al., 2007) (Figure 2-1). Although the prevalence of overweight has increased slightly in the population as a whole and among black and white women, the prevalence of obesity doubled in white women and increased by 50 percent in black women. These statistics are based on data from only nine states; no nationally representative data are available from a modern cohort to provide trends in pregravid BMI values.
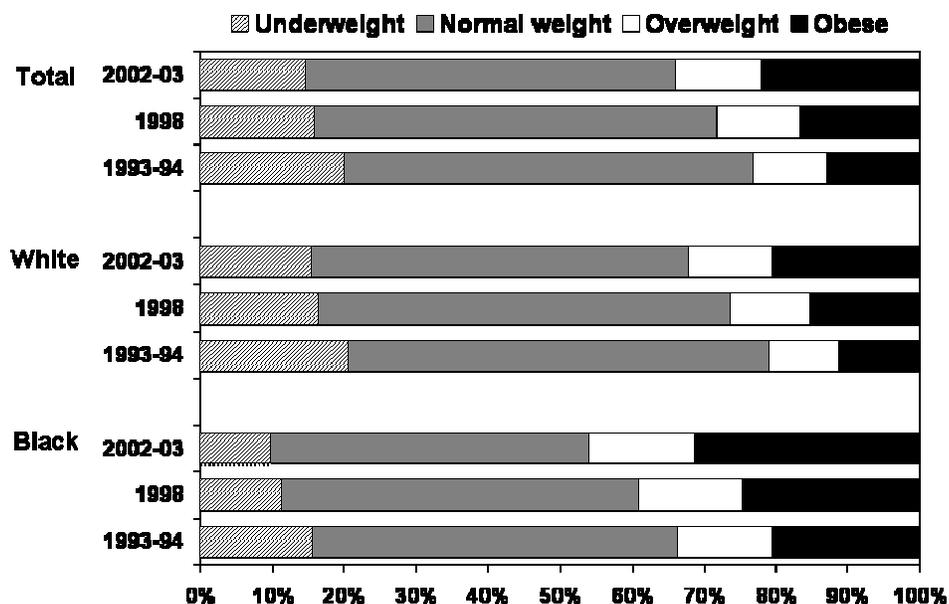

FIGURE 2-1 Trends in the distribution of BMI* from 1993 to 2003 among prepregnant U.S. women in the total population and by race or ethnicity.

*IOM BMI categories were used (underweight: < 19.8 kg/m^2; normal weight: 19.8-26.0 kg/m^2; overweight: 26.1- 29.0 kg/m^2; obese: > 29 kg/m^2).

SOURCE: Kim et al., 2007.

Body Mass Index Classification

The report *Nutrition During Pregnancy* (IOM, 1990) recommended the use of BMI to classify maternal prepregnancy weight. The four prepregnancy BMI categories used in that report were selected to be consistent with 90 percent, 120 percent, and 135 percent of the 1959 Metropolitan Life Insurance Company's ideal weight-for-height standards—the standard most commonly used in the United States when the report was written. Since then, the World Health Organization (WHO, 1998) has developed and the National Heart, Lung, and Blood Institute (NHLBI, 1998) has adopted the use of new BMI categories. The WHO BMI categories are based on different considerations and, as a result, are defined differently than those in the Institute of Medicine (1990) report. The WHO BMI categories also include several grades or categories of obesity (see Table 2-2).

The weight gain categories identified in IOM (1990) classify more women as underweight than the more stringent WHO cutoff point, while the WHO categories classify more women as overweight and fewer women as obese, with similar differences by race or ethnicity and age. In 1999-2004, with either the IOM or WHO cutoff points, about half of women are overweight (BMI > 26 with IOM cutoff point or > 25 with WHO cutoff point) (Figure 2-2). In addition, it is impractical to expect that pediatric growth charts are available in most obstetric practices. Adolescents that follow adult BMI cutoff points will likely be categorized in a lighter group and thus advised to gain more; however, young teens often need to gain more to improve birth weight outcomes.

TABLE 2-2 Comparison of Institute of Medicine (IOM) and World Health Organization (WHO) BMI Categories

| Category	IOM	WHO
Underweight	$< 19.8 \text{ kg/m}^2$	$< 18.5 \text{ kg/m}^2$
Normal weight	$19.8\text{-}26 \text{ kg/m}^2$	$18.5\text{-}24.9 \text{ kg/m}^2$
Overweight	$26.1\text{-}29 \text{ kg/m}^2$	$25.\text{-}29.9 \text{ kg/m}^2$
Obese Class I	$> 29 \text{ kg/m}^2$	$30\text{-}34.9 \text{ kg/m}^2$
Obese Class II	---	$35\text{-}39.9 \text{ kg/m}^2$
Obese Class III	---	$\geq 40 \text{ kg/m}^2$
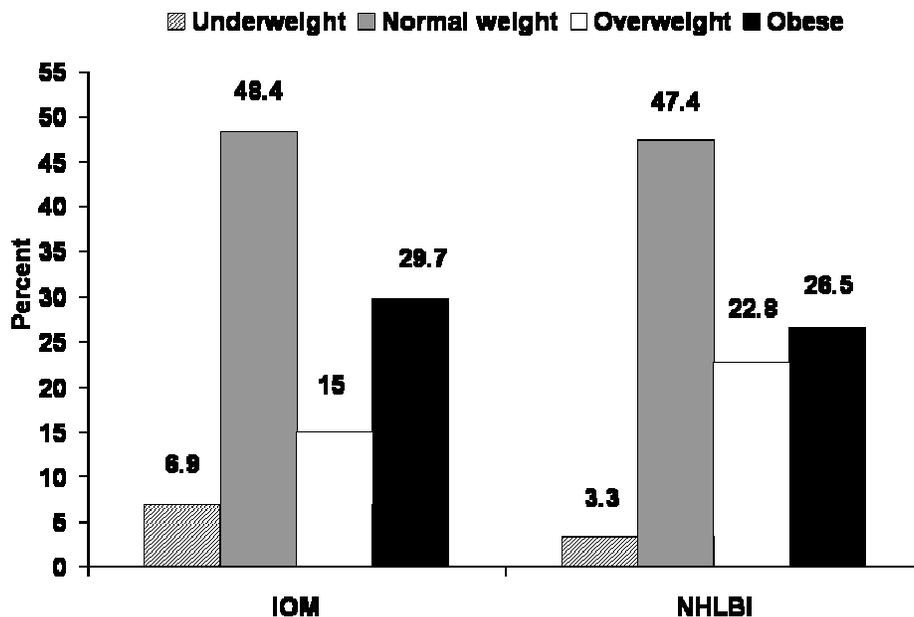
FIGURE 2-2 Distribution of BMI from 1999 to 2004 among U.S. nonpregnant women 12 to 44 years of age using the IOM* (1990) and the WHO** BMI cutoff points.

*IOM (1990) BMI categories are underweight, <19.8 kg/m^2; normal, 19.8-26.0 kg/m^2; overweight, 26.1-29.0 kg/m^2; obese, > 29 kg/m^2.
**WHO BMI categories are underweight, < 18.5 kg/m^2; normal, 18.5-24.9 kg/m^2; overweight, 25.0-29.9 kg/m^2; obese, ≥ 30 kg/m^2.

SOURCE: Personal communication, A. Branum, CDC, Hyattsville, Md., April 15, 2008.

Gestational Weight Gain

Assessment of both prepregnant BMI and GWG requires rigorous methods of data collection (see Table 2-3). Unfortunately, most of the data available to the committee were not collected with a high level of rigor, and most studies relied on recalled weight values (see Table 2-4). Although the IOM (1990) report called for collection of national data on GWG, prepregnancy height, and weight for proper surveillance, today there are still no nationally representative data with which to study trends in GWG in the United States.

TABLE 2-3 Data Required to Assess Trends in Pregnancy-Related Maternal Weight and the Ideal and Practical Methods of Measurement and Acquisition

Required Data	Method of Measurement and Acquisition	
	Ideal	**Practical**
Prepregnancy weight	Measured[a] at a preconceptional visit	Recalled at the first prenatal visit using a standardized question
Prepregnancy height	Measured[a] at the first prenatal visit	
Gestational weight gain	Total gain: last measured available weight abstracted from clinical records	Total gain: maternal recall of last available weight
	Pattern of gain: requires trimester-specific or midpregnancy weight abstractions	
Gestational age at last available weight[b]	Abstracted from clinical records	
Postpartum weight	Total retention: measured maternal weight abstracted from clinical records	Total retention: recalled maternal postpartum weight
	Measured longitudinally in nonpregnant women	Cross sectionally in nonpregnant women
	Time: serial measurements 3, 6, 9, 12, and 18 months after delivery	Time: 3, 6, 9, 12, or 18 months after delivery

[a]All weight and height measurements should be performed in light clothing without shoes.

[b]The gestational age at delivery may vary substantially from the gestational age at the last prenatal visit. Thus, misclassification may result if the gestational age at delivery is used in combination with weight at the last prenatal visit to determine weight gain adequacy.

TABLE 2-4 National Data Sources for Maternal Weight and Their Methods of Acquiring Key Variables

Data Source	Prepregnancy Weight	Prepregnancy Height	Gestational Weight Gain	Postpartum Weight	Data Coverage
Ideal	Recalled weight at first prenatal visit is abstracted from clinical records	Measured height at first prenatal visit is abstracted from clinical records	Last recorded weight is abstracted from clinical records	Measured weight at least once starting 3 months or more postpartum	50 states, little to no missing data
Standard U.S. birth certificate	Not available	Not available	Recalled at delivery	Not applicable	49 states (excludes California)
Revised 2003 U.S. birth certificate	Recalled at delivery	Recalled at delivery	Based on last recorded weight abstracted from the medical record	Not applicable	19 states in 2006
PRAMS	Recalled at 2-4 months postpartum	Recalled at 2-4 months postpartum	Obtained from birth certificates (recalled at delivery)	Not available	9 states
PNSS	Recalled at the prenatal visit or postpartum visit	Measured at the prenatal visit or postpartum visit	Recalled at the postpartum visit	Measured at WIC postpartum recertification visit	Low-income women in 26 states
IFPS II	Recalled in the postpartum period	Recalled in the postpartum period	Recalled in the postpartum period	Recalled at 3, 6, 9, and 12 months	Nationally distributed consumer opinion panel

NOTE: IFPS II = Infant Feeding Practices Study II; PNSS = Pregnancy Nutrition Surveillance System; WIC = Special Supplemental Nutrition Program for Women, Infants, and Children.

Trends in Gestational Weight Gain

The data obtained by standard U.S. birth certificates from 49 states illustrate that from 1990 to 2005 among mothers of term, singleton pregnancies, reported weight gains of < 16 pounds and > 40 pounds both increased (Figure 2-3). Weight gain within the broad recommended range (16 to 40 pounds) (IOM, 1990) declined slowly during this 15-year period. Unfortunately, the standard birth certificate lacks data on maternal prepregnancy weight and height. Thus, data from this source cannot provide information about GWG relative to prepregnant BMI category. In addition, the data on prepregnancy weight was self-report, which are more variable than clinical measures. The loss in precision and the degree of bias due to self report must be taken into account in interpreting self-reported data.

Important differences were found in low and high gains by maternal race or ethnicity and age. The greatest increase in the proportion of women with a weight gain > 40 pounds from 1990 to 2005 was among white women (Figure 2-4). In 2005, adolescents (< 20 years old) were more likely to gain excessive weight during pregnancy than women 35 years of age and older. Between 1990 and 2005, there was a 31 percent increase in GWG of at least 40 pounds in singleton pregnancies among adolescents (NCHS, 2007a). In 2005, weight gain of < 15 pounds was more common among black and Hispanic than among white women (Figure 2-5). Within each racial or ethnic group, the proportion of women with low gains increased with advancing age.
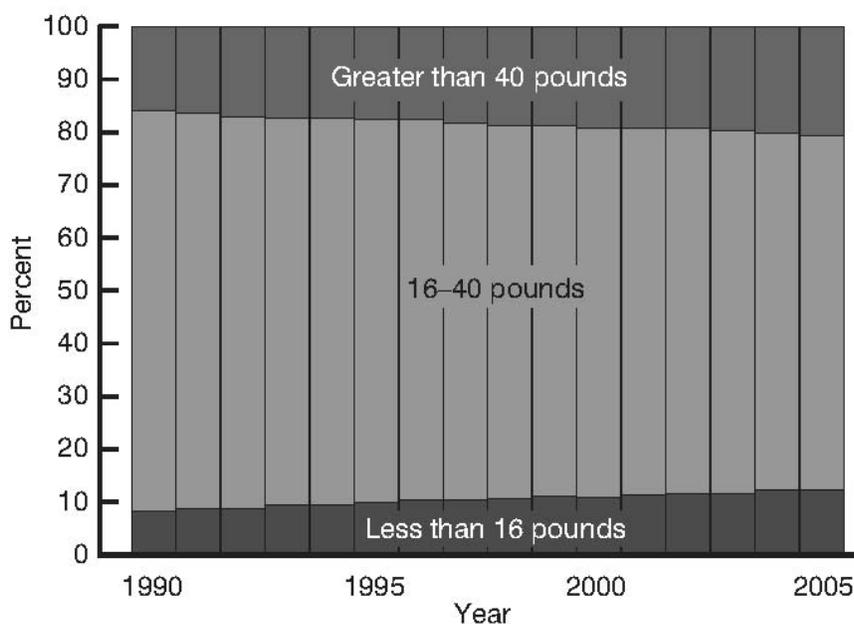

FIGURE 2-3 Weight gain during pregnancy for singleton term births in the United States, 1990-2005.
NOTES: California does not report weight gain in pregnancy. Term is ≥ 37 weeks' gestation.
SOURCE: NCHS, 2007a.
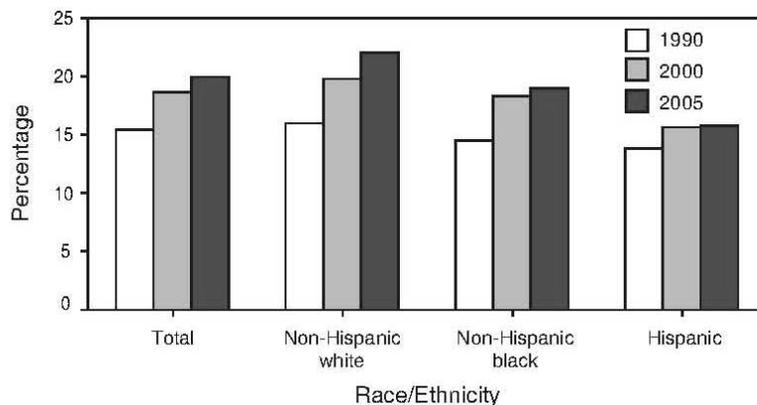
FIGURE 2-4 Percentage of women in the United States who gained more than 40 pounds during pregnancy, by race or ethnicity of the mother, 1990, 2000, and 2005.
NOTES: Includes only mothers with a singleton delivery and only non-Hispanic white, non-Hispanic black, and Hispanic mothers (who might be of any race). The total number of women who gained > 40 pounds was 456,678 in 1990, 588,253 in 2000, and 656,363 in 2005.
SOURCE: CDC, 2008a.
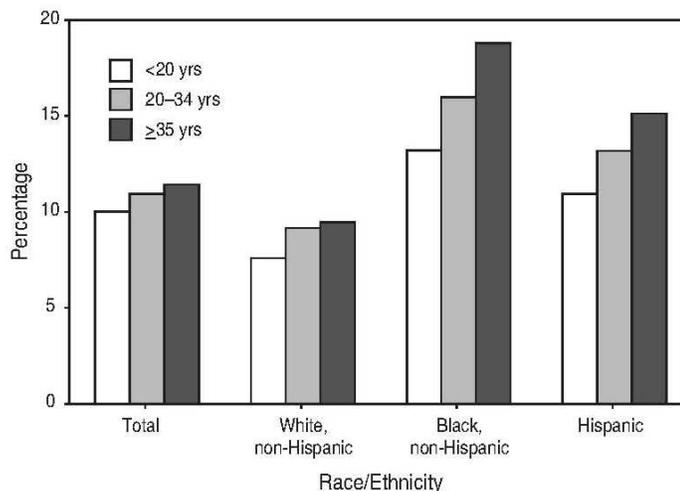
FIGURE 2-5 Percentage of women in the United States who gained less than 15 pounds during pregnancy by age and race or ethnicity of the mother, 2005.
NOTES: Includes only mothers with a term (≥ 37 weeks' gestation), singleton infant; excludes data for California.
SOURCE: CDC, 2008b.

Birth certificate data may yield more useful statistics for weight gain surveillance in the near future. After the IOM (1990) report called for collection of maternal prepregnancy weight and height, these fields were added to the 2003 revised U.S. birth certificate, and by 2006, 19 states were using the revised birth certificate.

At present, the two large surveillance systems collecting data on GWG and prepregnancy BMI in the United States, PRAMS and PNSS, (see Appendix A for descriptions) permit identification of trends in recommended weight gains, although neither system is nationally representative. For PRAMS, GWG is taken from the birth certificate and other data is either pulled from medical records or maternal recall.

PRAMS collects GWG data from birth certificates, and maternal prepregnancy height and weight are obtained from maternal interview in the postpartum period. Currently, 37 states, New York City and the Yankton Sioux Tribe (South Dakota) participate in PRAMS (Available online: http://www.cdc.gov/prams/ [accessed February 5, 2009]). For the analysis of trends in GWG reported here, data were limited to the eight PRAMS states with at least 70 percent response rates and to women with complete data on prepregnancy BMI and singleton, term pregnancies (Alabama, Arkansas, Florida, Maine, New York [excludes New York City], Oklahoma, South Carolina, and West Virginia). Limitations in the dataset, including self-reported weight, were considered.

In 2002-2003, PRAMS data indicate that the mean GWG was highest in underweight and normal weight women and declined in overweight and obese women among all racial/ethnic groups (Figure 2-6). The mean GWG among underweight and normal weight women in all racial/ethnic groups was within the recommended range, whereas it was higher than the recommendations for overweight women. For obese women, average weight gains were well above the 15-pound recommended minimum. Similar trends were observed in 1992-1993 and 1998 (data not shown).
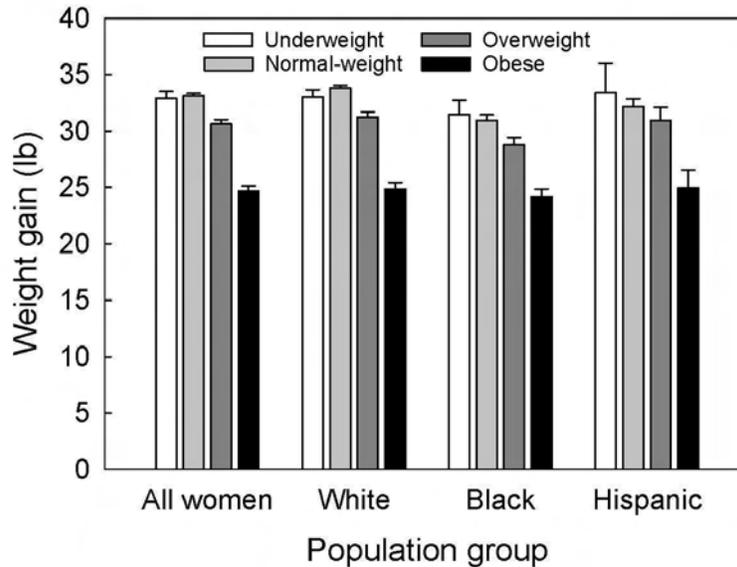
**FIGURE 2-6** Mean gestational weight gain by BMI category and race or ethnicity, Pregnancy Risk Assessment Monitoring System, 2002-2003.
NOTE: WHO BMI categories were used (underweight, < 18.5 kg/m^2; normal, 18.5-24.9 kg/m^2; overweight, 25.0-29.9 kg/m^2; obese, ≥ 30 kg/m^2).
SOURCE: Information contributed to the committee in consultation with P. Dietz, CDC, Atlanta, Ga., January 2009.

In 2002-2003, nearly half of underweight women represented in the PRAMS data gained within the range recommended by IOM (1990), while 30.6 percent and 19.5 percent gained below and above the recommendations, respectively (Figure 2-7). For normal weight women, GWG varied little over this 10-year period. There was a small decrease in the proportion of women gaining less than, while a larger proportion of women gained in excess of the IOM (1990) recommendations.

The majority of overweight women had weight gains greater than the recommended range (Figure 2-7). By 2002-2003, only about one-quarter of overweight women gained within the recommended range. For obese women, there was a modest rise in the prevalence of excessive weight gain from 1993-1994 to 2002-2003. By the end of the observation period, only one-third of obese women gained within the recommended range. Among women in all BMI categories, no more than 50 percent of women gained within the recommended range.
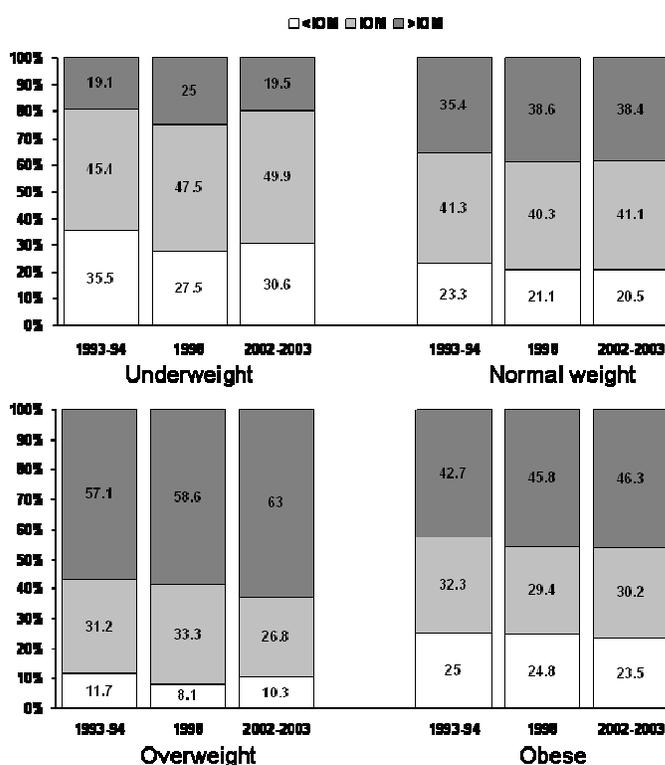
**FIGURE 2-7** Distribution of gestational weight gain by prepregnancy BMI category among singleton, term deliveries from 1993 to 2003.
NOTE: IOM BMI categories were used (underweight (lean), <19.8 kg/m^2; normal, 19.8 to 26.0 kg/m^2; overweight, 26.1 to 29.0 kg/m^2; obese, > 29 kg/m^2).
SOURCE: Information contributed to the committee in consultation with P. Dietz, CDC, Atlanta, Ga., January 2009.

The other large data source, the PNSS, collects data on low-income women participating in public health programs (predominantly Special Supplemental Nutrition Program for Women, Infants, and Children [WIC]) from 26 states, five tribal governments, and one U.S. territory. For the analyses described below, data on pregravid BMI were used to determine whether weight gains fell above, within, or below the ranges recommended by IOM (1990). In this analysis, the data also were not limited to singleton, term pregnancies. The data from the PNSS show that from 1997 to 2007 in the total population of participating women, the proportion who gained within the range recommended by IOM (1990) changed very little within BMI groups (Figure 2-8).

During the observed period, less than 30 percent of women with BMIs in the normal, overweight, and obese categories gained within the recommended ranges. The percentage of underweight women gaining within the recommended range rose slightly from nearly 36 percent in 1997 to just over 40 percent by 2007, while the percentage gaining below the recommended range declined from 41 percent to 32 percent. Furthermore, by the end of the observation period, approximately 46 percent of normal weight women, 46 percent of obese women, and 59 percent of overweight gained in excess of the recommendations (IOM, 1990).

Similar time trends were observed when the PNSS data were stratified by race or ethnicity. In all racial/ethnic groups, the rates of high weight gains increased, low weight gains decreased, and recommended weight gains varied little (Figure 2-9). Non-Hispanic black women and Hispanic women had similar rates of low weight gain and were more likely than non-Hispanic white women to gain less than the recommended levels. Non-Hispanic white women were most likely to gain weight above the recommendations (IOM, 1990).

Taken together, data from PRAMS and PNSS illustrate that less than half of the women in these populations met the IOM (1990) recommendations for GWG. Importantly, none of the data highlighted here provide information on pattern of weight gain.
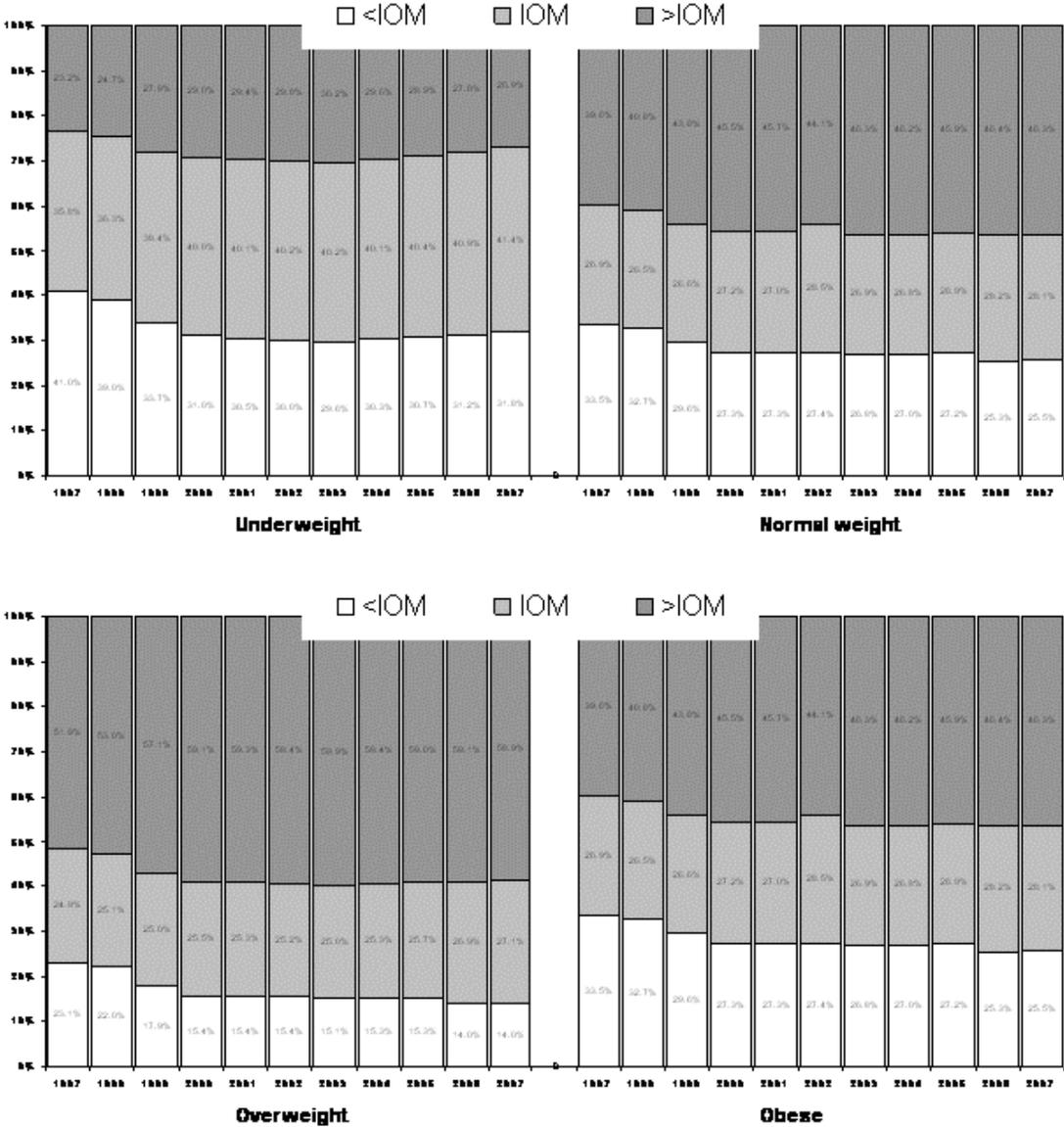
FIGURE 2-8 Distribution of gestational weight gain from 1997 to 2007 by pregravid BMI.
NOTE: BMI based on IOM categories
SOURCES: Personal communication, A. Sharma, CDC, Atlanta, Ga., December 2008; CDC, Pregnancy Nutrition Surveillance System. Available online at http://www.cdc.gov/PEDNSS/pnss_tables/pdf/national_table20.pdf [accessed February 12, 2009].
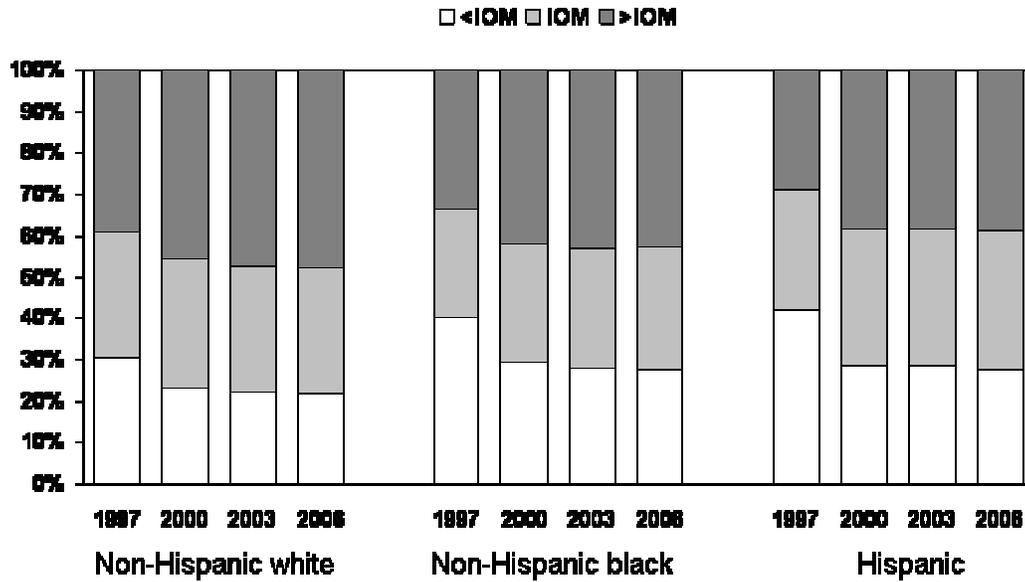
FIGURE 2-9 Distribution of gestational weight gain by race or ethnicity.
SOURCES: Personal communication, A. Sharma, CDC, Atlanta, Ga., December 2008; CDC, Pregnancy Nutrition Surveillance System. Available online at http://www.cdc.gov/PEDNSS/pnss_tables/pdf/national_table20.pdf [accessed February 12, 2009].

POSTPARTUM WEIGHT RETENTION

Postpartum weight status is usually determined by subtracting the prepregnancy weight from a weight obtained at a time after delivery. Postpartum weight status for a population can be represented in a variety of ways, including absolute weight change, percentage who retain a specific amount of weight over the prepregnancy weight (e.g., 10 or 20 pounds), or proportion of women whose BMI category changes from before to after pregnancy. Furthermore, it is important to assess postpartum weight retention according to both prepregnancy body size (e.g., BMI) and adequacy of GWG. Therefore, studies of population trends in maternal postpartum weight retention build upon and extend the data required to assess the adequacy of GWG. Unlike pregnancy, when maternal weight is monitored and routinely recorded in the clinical record, data on maternal postpartum weights are not widely available, particularly for times later in the year after birth.

In addition to the data on GWG provided by PNSS, this surveillance system also collects cross-sectional data on maternal weight at the mother's WIC recertification visit in the postpartum period. From 2004 to 2006, there were more than 1.4 million postpartum records with GWG and prepregnancy BMI in PNSS, but only about 49,000 of these occurred at 6 months postpartum or later and therefore provided useful information on postpartum weight retention in this low-income population sample (personal communication, A. Sharma, CDC, Atlanta, Ga., December 2008). Notably, PNSS data are not nationally representative and the women with postpartum records at > 24 weeks' postpartum were less likely to be non-Hispanic white and more likely to be Hispanic compared to the women with an early postpartum PNSS record.

These data suggest that at 6 months postpartum or later (median [SD], 30.6 [5.1] weeks), the mean postpartum weight retention was 11.8 (15.3) pounds. Approximately half of women retained more than 10 pounds, and one-quarter retained more than 20 pounds (personal

communication, A. Sharma, CDC, Atlanta, Ga., December 2008). In this sample, black women retained more weight postpartum than white or Hispanic women in every BMI and weight gain category (Figure 2-10). In all BMI categories and racial/ethnic groups, mean postpartum weight retention and the percentage of women retaining > 20 and > 10 pounds increased as GWG category increased (Figure 2-11). Among all women who gained above the range recommended by IOM (1990), mean postpartum weight retention was 15 to 20 pounds (Figure 2-10). When analyses were restricted to data collected at 24 weeks' postpartum or later, more than 60 percent of women in all racial/ethnic groups who gained above the range recommended by IOM (1990) retained > 10 pounds postpartum. More than 40 percent of women who gained excessively retained > 20 pounds (Figure 2-11).
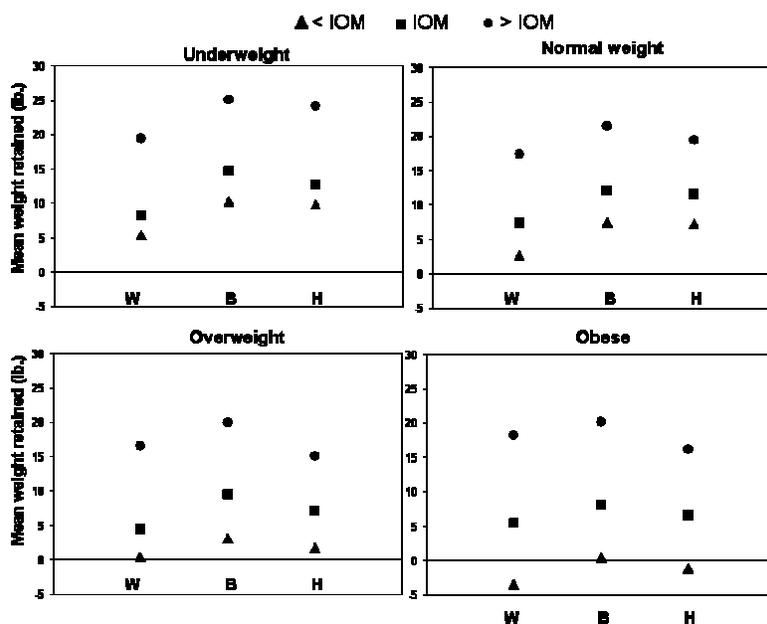
FIGURE 2-10 Mean postpartum weight retention at > 24 weeks' postpartum (mean 30.6 weeks' postpartum) by racial or ethnic group.
NOTE: W = non-Hispanic white; B = non-Hispanic black; H = Hispanic.
SOURCE: Personal communication, A. Sharma, CDC, Atlanta, Ga., December 2008.
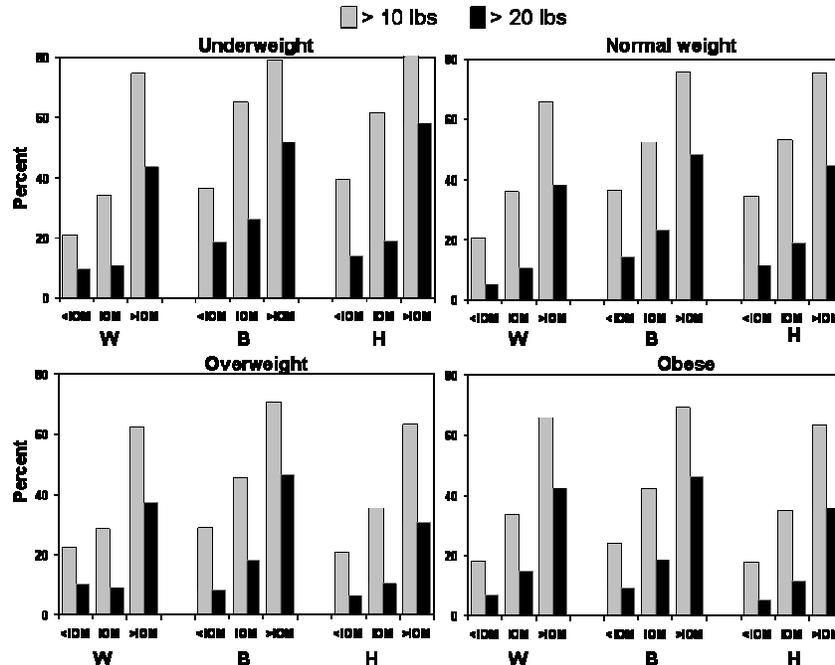
FIGURE 2-11 Percentage of women retaining more than 10 pounds and more than 20 pounds at >24 weeks' postpartum (mean 30.6 weeks' postpartum) by racial or ethnic group.
NOTE: W = non-Hispanic white; B = non-Hispanic black; H = Hispanic.
SOURCE: Personal communication, A. Sharma, CDC, Atlanta, Ga., December 2008.

The Infant Feeding Practices Study II (IFPS II) is a federally sponsored longitudinal study of approximately 4,000 mother-infant pairs that included questions about postpartum weight retention. Respondents were more likely to be non-Hispanic white and to have higher education and lower parity than the general U.S. population. At 2.0-4.9 months postpartum, one-third of women retained > 10 pounds and 12 percent retained > 20 pounds. At 11-13.9 months, only 24 percent of women retained > 10 pounds, but 12 percent still retained > 20 pounds (derived from IFPS II. Available online: http://www.cdc.gov/ifps/questionnaires.htm [accessed April 28, 2009]). In all BMI categories and at each postpartum visit, mean postpartum weight retention and the percentage of women retaining > 20 and > 10 pounds increased as GWG category increased (Figure 2-12). For normal weight and underweight women, weight retention decreased as time postpartum increased in all weight gain categories (classified according to IOM, 1990). Normal weight women who gained above the range recommended by IOM (1990), however, had a decrease in mean postpartum weight through 39 weeks' postpartum, but had an increase in their mean postpartum weight at 55 weeks (Figure 2-13). For overweight and obese women who gained above the recommended range, mean postpartum weight decreased as postpartum time increased, while obese women who gained less than the range recommended by IOM (1990) gained weight across the postpartum period. Importantly, obese women who gained within or less than the recommended range maintained a postpartum weight below their prepregnancy weight.
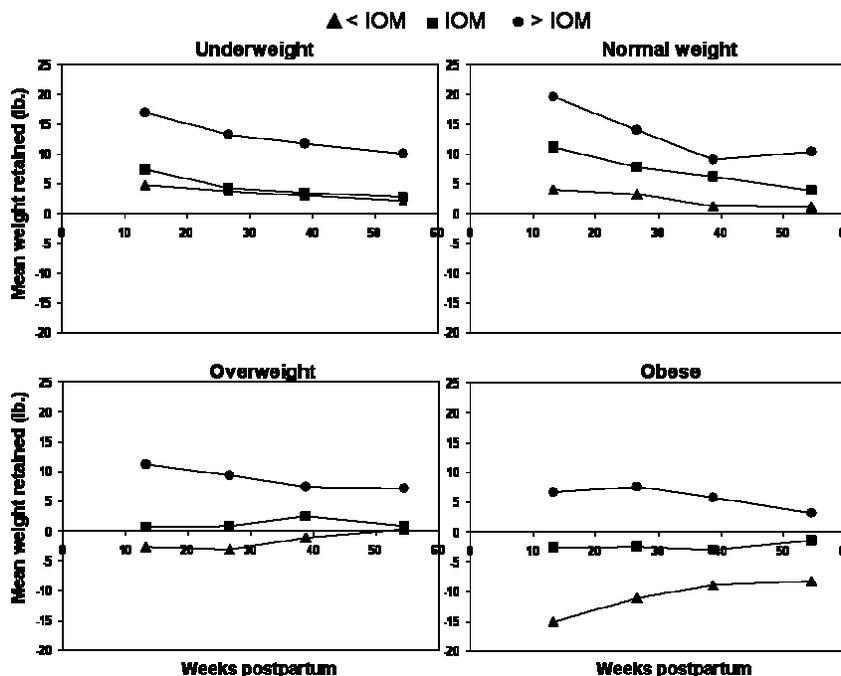
FIGURE 2-12 Mean postpartum weight retention by weight gain category (IOM, 1990) and prepregnancy BMI category across four postpartum visits in the IFPS II study.
SOURCE: Derived from IFPS II. Available online: http://www.cdc.gov/ifps/questionnaires.htm [accessed April 28, 2009].
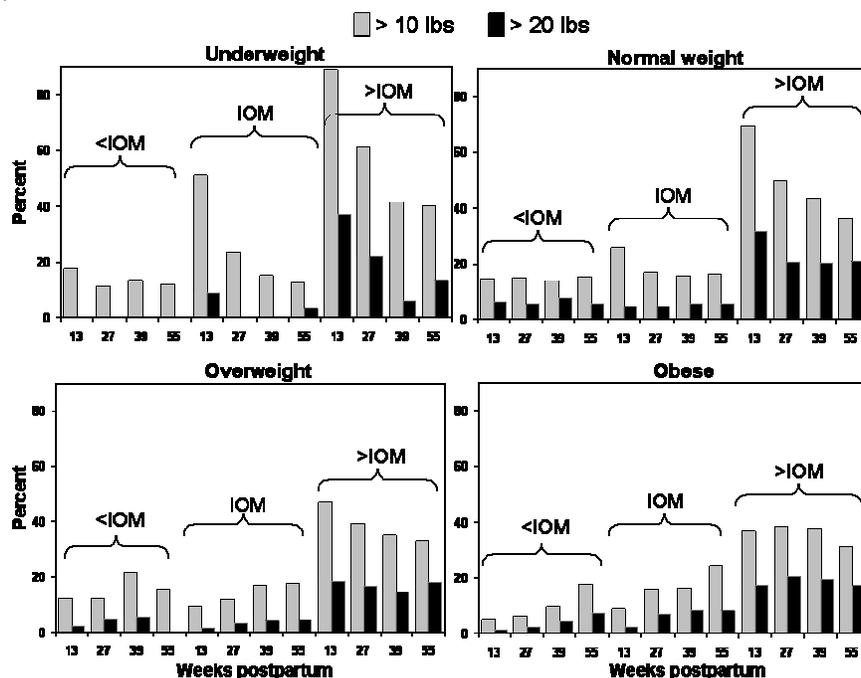
FIGURE 2-13 Percentage of women retaining greater than 10 pounds and greater than 20 pounds at 13 and 54 weeks' postpartum by weight gain category (IOM, 1990) and prepregnancy BMI category (IFPS II study).
SOURCE: Derived from IFPS II. Available online: http://www.cdc.gov/ifps/questionnaires.htm [accessed April 28, 2009].

In summary, taken together, data from both the PNSS and the IFPS II suggest that gaining above the range recommended by IOM (1990) is associated with excess maternal weight retention postpartum, regardless of prepregnancy BMI. The data from the IFPS II highlight that for most women, weight retention declines as time postpartum increases. However, postpartum weight retention remains a problem for a large proportion of mothers, even at one year after birth. These data also show that obese women who gained within or below the recommended ranges experienced a net loss in weight from their prepregnancy weight. However, for those who gained below their recommended range, the more time that passed after the birth, the more they experienced a net increase in weight and approached their prepregnancy weight. The racially diverse PNSS suggests that among low-income women, black women retain more weight than white or Hispanic women regardless of their prepregnancy weight or GWG category. Compared with the IFPS II, which is a higher-income sample, the low-income women in PNSS retained more weight.

SOCIODEMOGRAPHIC CHARACTERISTICS OF MOTHERS

Since 1990, there has been an increase in the racial and ethnic diversity of U.S. births (Table 2-5). A greater proportion of infants in 2005 were born to nonwhite mothers, with the largest increase in births from Hispanic mothers. Childbearing by unmarried mothers sharply increased in this 15-year period to a record high of 36.9 percent. More mothers attained high levels of education; in 2005, more than one-quarter of mothers had 16 years or more of education. The proportion of births for mothers 35 years and older also increased substantially in this interval. Although the teenage birth rate had been steadily declining since 1991, preliminary data from 2006 suggest that the overall birth rate for teenagers rose 3 percent to 41.9 births per 1,000 females 15-19 years of age. Teenage mothers 10-14 years of age were the only group that did not experience an increase in birth rate during this time. Finally, the proportion of mothers who reported any smoking during pregnancy declined by about 50 percent over the rates reported prior to 1990 (CDC, 2004).

TABLE 2-5 Distribution of Characteristics of Births in the United States, 1990 and 2005

	1990	2005
Maternal Race or Ethnicity (percentage of live births)[a]		
Non-Hispanic white	64.63	55.27
Non-Hispanic black	16.28	14.15
American Indian or Alaska Native	0.96	1.09
Asian or Pacific Islander	3.49	5.60
Hispanic	14.64	23.89
Total	100.00	100.00
Marital Status (percentage of live births)		
Married	71.98	63.10
Unmarried	28.02	36.90
Total	100.00	100.00
Education (percentage of live births)[b]		
0-8 years	6.39	6.19
9-11 years	17.44	14.74
12 years	38.37	29.80
13-15 years	20.32	21.47
16 years or more	17.48	27.80
Total	100.00	100.00
Maternal Age (percentage of live births)		
<15 years	0.28	0.16
15-17 years	4.41	3.22
18-19 years	8.14	6.80
20-24 years	26.30	25.14
25-29 years	30.71	27.34
30-34 years	21.31	22.97
35-39 years	7.64	11.68
40-44 years	1.17	2.53
45-49 years	0.04	0.15
50-54	NA	0.01
Total	100.00	100.00
Maternal Smoking (percentage of live births)	20.30	10.70

NOTE: NA = not available.

[a]Reflects percentage of total number of live births by race as presented in the table.
[b]Reflects percentage of total number of live births by education as presented in the table.

SOURCES: CDC, 2004; NCHS, 2007a; CDC/VitalStats, available online at http://www.cdc.gov/nchs/vitalstats.htm [accessed February 12, 2009].

Lifestyle Characteristics

Dietary Practices

Dietary intake No comprehensive national data is available on dietary intake practices of pregnant women. However, data from other surveys indicates that population-wide, less than 2 percent of females 14-30 years of age and less than 6 percent of females 31-50 years of age met

the recommended number of combined fruit and vegetable servings in 1999-2000 (Guenther et al., 2006) (Figure 2-14). Additionally, approximately two-thirds of women ages 14-50 years of age did not consume at least 5 servings of fruits and vegetables per day (BRFSS, 2007; Serdula et al., 2004). See Appendix B for additional information on nutritional intake.

No other nationally representative data on dietary intake among pregnant women or women of childbearing age are available. Among the population as a whole ages 19-39 years, total energy intake increased by 18 percent (1,856 to 2,198 kilocalories [kcal] per day) from 1977-1978 to 1994-1996. This included a sharp 58 percent increase in energy from snacks (244 to 387 kcal/d) as well as the proportion of total energy from fast foods and meals eaten at restaurants, including fast-food establishments (Nielsen et al., 2002). In addition, the proportion of energy from soft drinks nearly tripled; energy from fruit drinks doubled, while energy from milk decreased (Nielsen and Popkin, 2004).

From 1994-1996 to 1999-2000, there was little change in overall diet quality as measured by the Healthy Eating Index 2005 (Guenther et al., 2006). American's diets consistently met national recommendations for total grains and meat or beans, but were far below the recommendation for whole grains, dark-green and orange vegetables, and legumes. Intakes of sodium and energy from solid fats, alcoholic beverages, and added sugars were well above national recommendations.
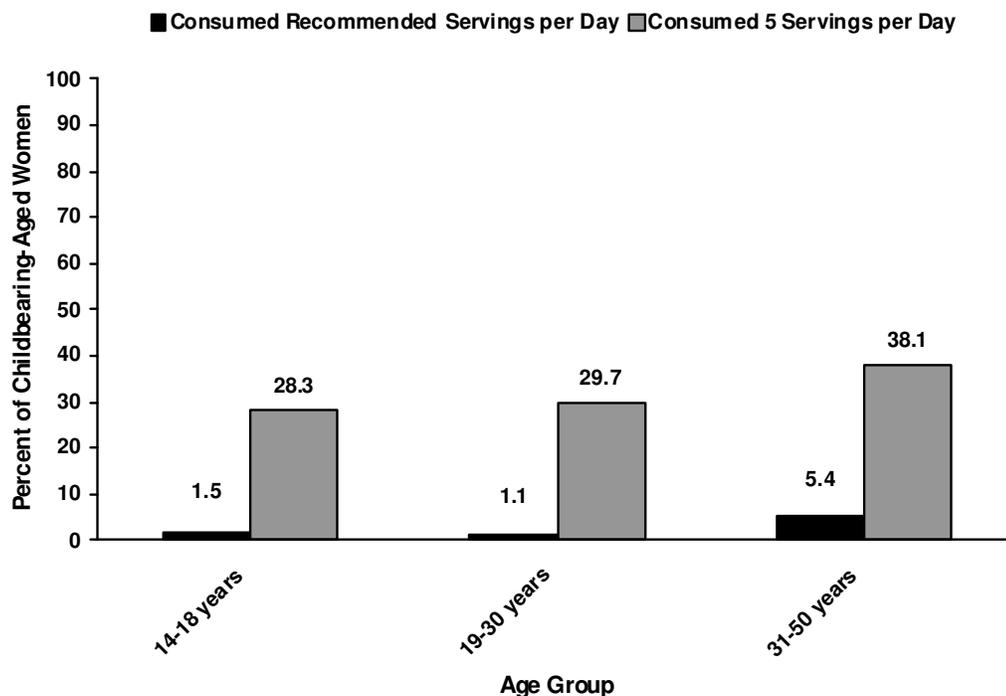
FIGURE 2-14 Percentage of U.S. childbearing-aged women who consumed the recommended number of servings of fruits and vegetables per day and five servings of fruits and vegetables per day.
NOTE: Recommended combined fruit and vegetable servings are eight servings for females age 14-18 and 31-50 and nine servings for females age 19-30.
SOURCE: Guenther et al., 2006.

Dieting There was a steady rise in the prevalence of attempted weight loss among women of childbearing age from 1989 to 2000 (Serdula et al., 1994, 1999; Bish et al., 2005). In 2000, 60 and 70 percent of overweight and obese women, respectively, were attempting to lose weight, while 29 percent of women whose BMI was < 25 kg/m^2 also were attempting to lose weight (Bish et al., 2005). Importantly, data from the Behavioral Risk Factors Surveillance System (BRFSS) also suggest an increase in the prevalence of attempted weight loss among women who reported being pregnant. In 1989, 3.6 percent of pregnant women who participated in the BRFSS said that they were attempting to lose weight (Cogswell et al., 1996). This figure doubled to 7.5 percent in 2003 (Bish et al., 2009). Furthermore, in 2003, 34.3 percent of women were trying to maintain their weight, that is, to keep from gaining weight (Bish et al., 2009).

Food insecurity Food insecurity is defined as "whenever the availability of nutritionally adequate and safe food or the ability to acquire acceptable foods in socially acceptable ways is limited or uncertain." In 2006, 10.9 percent of U.S. households (12.6 million) had either low food security (6.9 percent) or very low food security (4.0 percent). It is difficult to obtain a nutrient-dense diet in an environment of food insecurity, and this has important implications for GWG (USDA; available online at http://www.ers.usda.gov/Publications/ERR49/ERR49.pdf [accessed April 21, 2009]).

Pregnancy and lactation require modest increases in energy but greater increases in vitamin and mineral intake. For pregnant women to gain an appropriate amount of weight and meet their nutrient requirements, dietary changes to promote high nutrient density and appropriate energy intake is required. Unfortunately, the lack of nationally representative data on pregnant and postpartum women limits understanding of dietary trends among this important population subgroup.

Physical Activity

*Healthy People 2010 (*DHHS, 2000) and the 2008 Physical Activity Guidelines (DHHS, 2008) provide recommended levels of physical activity and emphasize that inactivity has adverse health consequences. Data from the BRFSS indicate that although the proportion of women of childbearing age who reported no recreational physical activity decreased between 1994 and 2004, one in five women aged 18-29 years of age and almost a quarter of those in their thirties and forties reported no physical activity in 2004 (Figure 2-15) (CDC, 2005). Similarly, barely half of women of childbearing age met the guideline in *Healthy People 2010* for aerobic activity in 2005, although the prevalence has increased significantly since 2001 (Figure 2-16) (CDC, 2007).
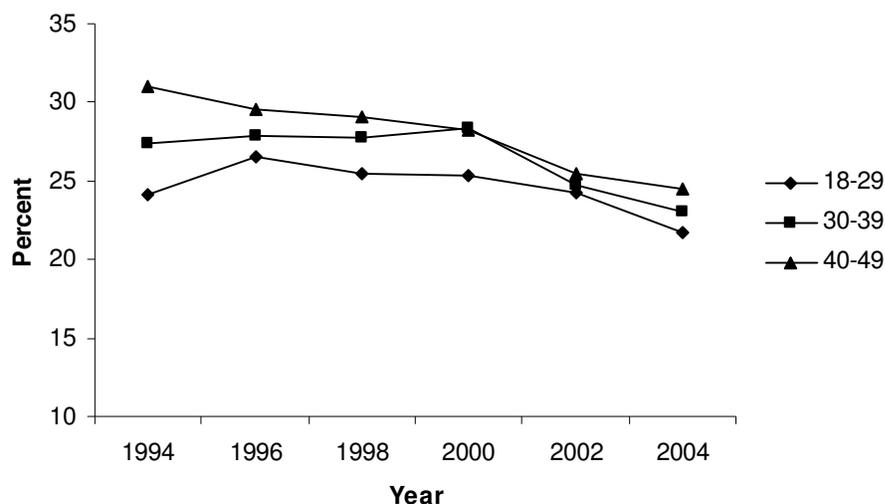
FIGURE 2-15 Trends in leisure-time physical inactivity for women of childbearing age, United States, 1994-2004.
NOTES: Leisure-time physical inactivity defined as a "no" response to the survey question, During the past month, other than your regular job, did you participate in any physical activities or exercise, such as running, calisthenics, golf, gardening, or walking for exercise? The reference time frame for the wording of this survey question was revised in 2001 to "During the past 30 days …" and was changed back to "During he past month …" in 2002. Also, in 2001, the phrase "other than your regular job" was added.
SOURCE: CDC, 2005.
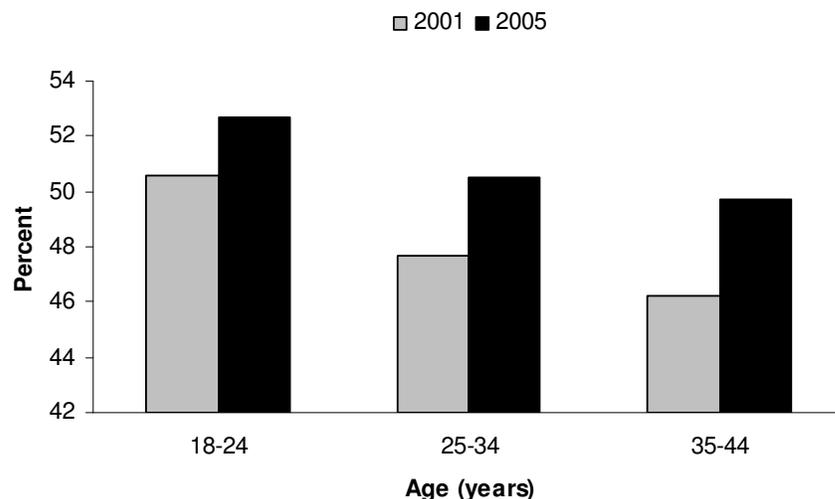
FIGURE 2-16 Trends in estimated percentage of women of childbearing age who reported meeting guidelines for regular physical activity
 NOTE: Physical activity is defined as at least 30 minutes of moderate-intensity activity per day on five or more days a week, or at least 20 minutes a day of vigorous-intensity activity on three or more days a week, or both, when not working; an exercise occurrence is defined as 10+ minutes.
SOURCE: CDC, 2007.

In 2000, 15.8 percent of pregnant women met minimum physical activity recommendations (Evenson et al., 2004) and only 6 percent of pregnant women met recommendations for vigorous

physical activity (Petersen et al., 2005). In these analyses, physical activity varied by maternal race/ethnicity, age, and education; and there was some evidence that physical activity was lower among women who worked outside the home. In 2005, almost half of white, non-Hispanic U.S. women of all ages met the *Healthy People 2010* objective for physical activity; only 36 percent of black, non-Hispanic women, 40 percent of Hispanic women, and 47 percent of other-race women did so (CDC, 2007). Physical activity increased with education, from 37 percent among women who did not graduate from high school to 53.3 percent among college graduates (CDC, 2007).

In summary, a high proportion of women of childbearing age fail to meet current guidelines for physical activity before or during pregnancy. The committee identified only limited data on physical activity or inactivity among pregnant women. The committee identified no data on postpartum mothers or physical activity according to BMI and weight change before, during, and after pregnancy.

Psychological Characteristics

Depression

Changes in appetite and weight are among the diagnostic criteria for major depression (American Psychiatric Association, 1994). In their meta-analysis, Gaynes et al. (2005) estimated that one in seven women will develop depression during pregnancy or after delivery. Although nationally representative data specific to women during and after pregnancy are not available, data for U.S. women of childbearing age illustrate striking increases in the prevalence of major depression from 1991-1992 to 2001-2002 in the total population and among white and black women (Figure 2-17) (Compton et al., 2006). Similar trends were observed among women 30 to 44 years of age, but the rates of major depression were lower than those of women age 18-29 years. Given that more than 10 percent of women of childbearing age may be depressed, screening and intervention for symptoms of depression during pregnancy may be required to achieve better GWG.
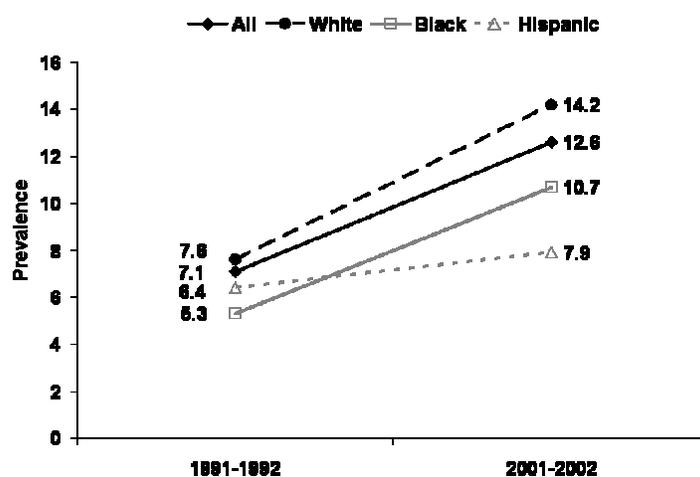
FIGURE 2-17 Prevalence of major depression among women 18-29 years of age in the United States by race or ethnicity, 1991-1992 and 2001-2002.
SOURCE: Compton et al., 2006.

Other Psychological Characteristics

Other psychological factors that may influence GWG include stress, social support, and attitude toward weight gain (see Chapter 4). The committee did not identify any nationally representative data specific to women during and after pregnancy that were indicative of trends or prevalence of these factors related to GWG.

PREGNANCY OUTCOMES RELATED TO GESTATIONAL WEIGHT GAIN

Gestational Diabetes

Data from birth certificates collected nationally illustrate that there has been a striking increase in the prevalence of diabetes in pregnancy in each age group (Figure 2-18), with the largest increase over time among women in the oldest age group (40 or more). However, the majority of birth certificates did not distinguish between pre-gestational diabetes (diagnosis before the index pregnancy) and gestational diabetes mellitus (GDM; diagnosis during the index pregnancy).

With data from the National Hospital Discharge Survey from 1989 to 2004, Getahun et al. (2008) determined trends in the prevalence of GDM among U.S. women 14 to 45 years of age. GDM increased by 122 percent, from 1.9 percent in 1989-1990 to 4.2 percent in 2003-2004. Furthermore, among women 35 years of age and older, the rate for GDM was highest among black women.
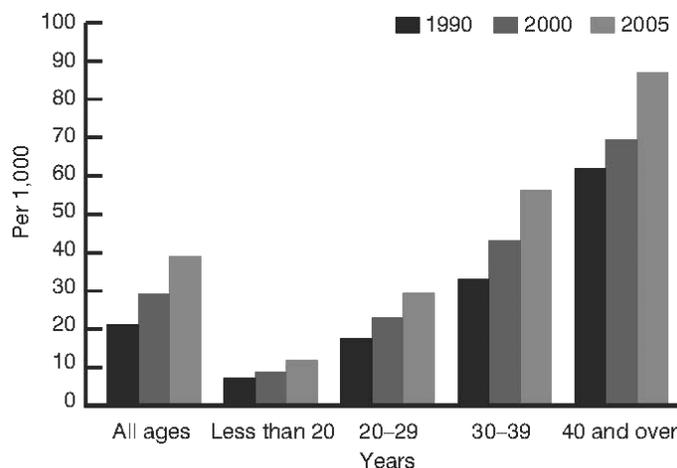
FIGURE 2-18 Diabetes rates by age of mother: United States, 1990, 2000, and 2005.
SOURCE: NCHS, 2007b.

Preeclampsia and Gestational Hypertension

Wallis et al. (2008) investigated population trends in the incidence rates of pregnancy-induced hypertension (preeclampsia and gestational hypertension [see Appendix A for definitions]) in the United States for 1987-2004 with data from the National Hospital Discharge Survey. The age-adjusted rate of preeclampsia increased 25 percent from 1987-1988 to 2003-2004. Gestational hypertension rates nearly tripled during the same period (Figure 2-19). The authors noted that clinical diagnostic criteria, revised in the 1990s, may have simultaneously caused an exaggerated rise in the rate of gestational hypertension and an attenuated increase in the rate of preeclampsia over the study period. They concluded that the small but consistent elevation in the rate of preeclampsia is a conservative estimate of the true population-level change.
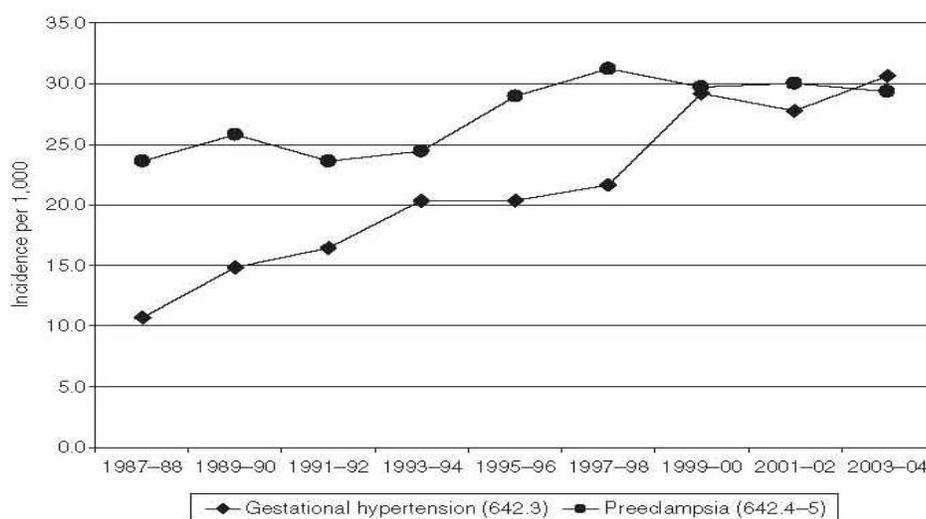
FIGURE 2-19 Age-adjusted incidence of preeclampsia and gestational hypertension per 1,000 deliveries in the United States, 1987-2004.
SOURCE: Wallis et al., 2008. Reprinted by permission from Macmillan Publishers Ltd: Wallis, A. B., A. F. Saftlas, J. Hsia, and H. K. Atrash. 2008. Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States, 1987-2004. *American Journal of Hypertension* 21(5): 521-526.

Cesarean Delivery

The rate of total cesarean deliveries in the United States increased almost fivefold between 1970 and 1988 and then declined to 20.7 percent in 1996 (Figure 2-20). Since then, the rate increased 50 percent to 31.1 percent—the highest rate ever recorded—in 2006 (Menacker et al., 2006; MacDorman et al., 2008). Primary cesareans (births to women with no previous cesarean delivery) mirror the pattern for total cesareans, while vaginal birth after a previous cesarean (VBAC) increased beginning in the mid-1980s, peaked in 1996, and then has declined since that time (MacDorman et al., 2008). An increase in primary cesarean deliveries appears to be the result of changes in obstetric practice rather than in medical risk profiles or maternal request (Menacker et al., 2006; MacDorman et al., 2008). However, a recent meta-analysis concluded that maternal obesity is associated with increased risk of cesarean delivery (Chu et al., 2007). The expanded availability of BMI data in U.S. birth certificates since 2003 will allow future researchers to more clearly understand relationships between maternal prepregnancy BMI, GWG, and cesarean deliveries in the United States.
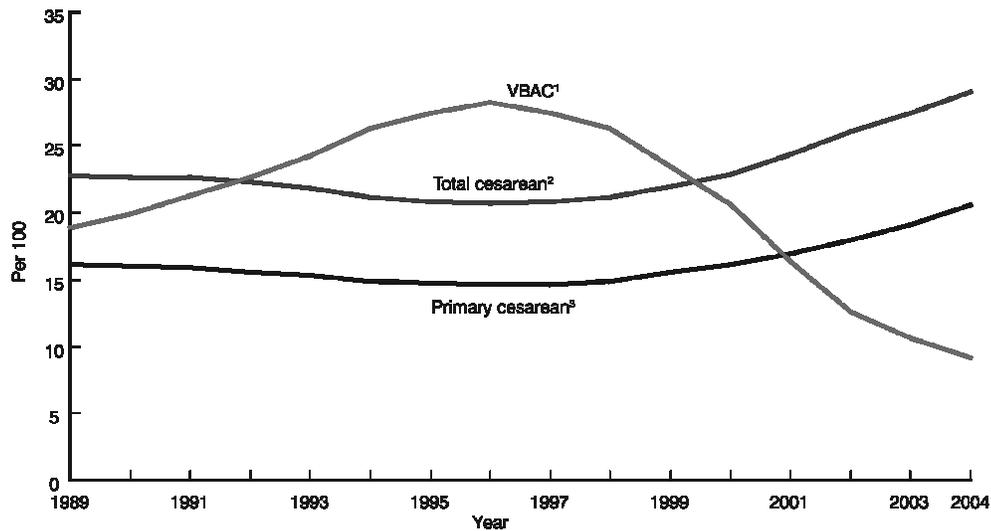
FIGURE 2-20 Total and primary cesarean rate, 1970-2004, and VBAC, 1985-2004.
SOURCE: NCHS, 2005.

Maternal Mortality

The crude maternal mortality rate (deaths per 100,000) steadily decreased in the United States from 83.3 in 1950 to 8.2 in 1990; increased rates since 2000 are believed to be due to changes in coding and increased surveillance (Hoyert, 2007; available online at http://mchb.hrsa.gov/whusa08/hstat/mh/pages/237mm.html [accessed January 14, 2009]). Nonetheless, in 2005, the age-adjusted maternal mortality rate was 9.6 for non-Hispanic white, 8.2 for Hispanic or Latina, and 31.7 for non-Hispanic black mothers, indicating an important disparity by race. Furthermore, among women 35 years and older the mortality rate in 2005 was 28.9 for white women and 112.8 for black women (NCHS, 2007b). A recent case-control study based on a statewide Pregnancy-Associated Mortality Review in Florida reported that maternal mortality was increased three-, four-, and fivefold with class I (BMI 30-34.9), class II (BMI 35-39.9), and class III obesity (BMI ≥ 40), respectively. Given the rising rates of obesity in the population, additional studies on obesity and maternal mortality are needed (Thompson et al., 2005).

Infant Mortality

The infant mortality rate (deaths of infants less than 1 year of age per 1,000 live births) in the United States was 6.71 in 2005 (MacDorman et al., 2008). The dramatic decrease in infant mortality that occurred during the last half of the twentieth century has slowed since 2000 (Figure 2-21), and the United States has fallen behind many other developed countries in infant survival (NCHS, 2007b). Trends are similar for other measures, including early and late neonatal mortality and post-neonatal mortality, although perinatal mortality has continued to decrease steadily since 1990 (Martin et al., 2008).

Disparities in infant mortality according to maternal racial or ethnic group continue (Figure 2-22). In 2005, the infant mortality rate for non-Hispanic black mothers was three times higher than for Cuban mothers, who had the lowest rate; Puerto Rican and American Indian or Alaskan Native mothers also had rates above the national average.
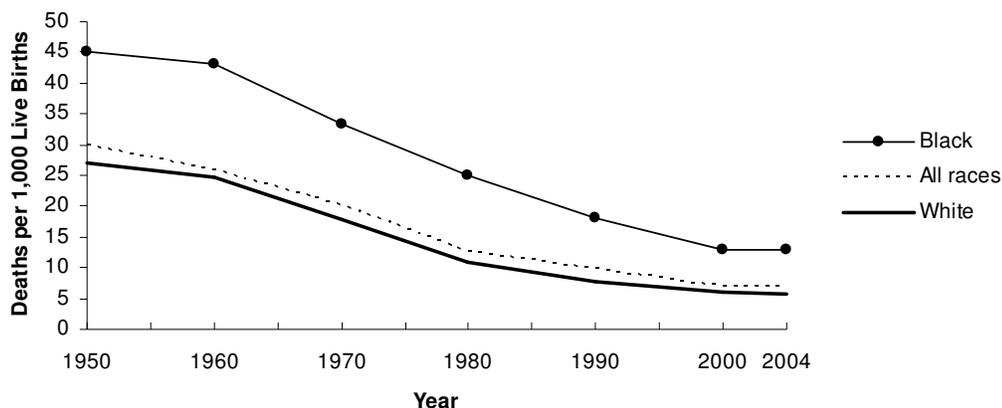
FIGURE 2-21 Infant mortality rates in the United States, 1950 through 2004, by race.
SOURCE: NCHS, 2007b.
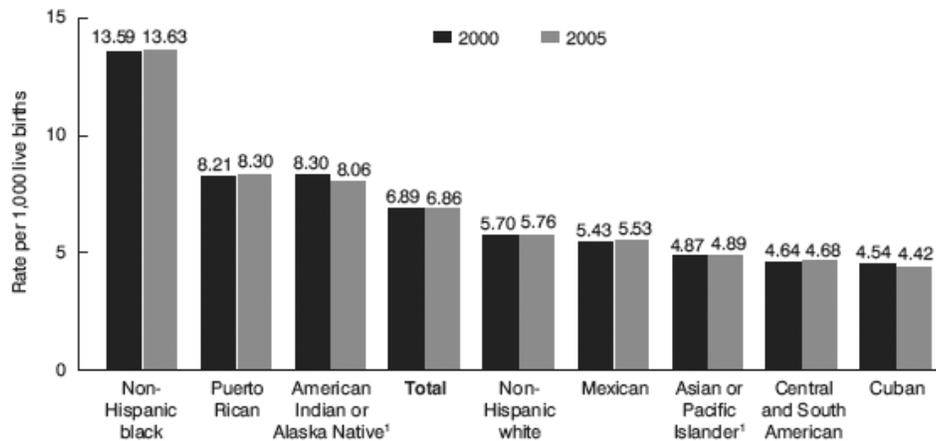
FIGURE 2-22 Infant mortality rates by race or ethnicity, 2000 and 2005.
SOURCE: NCHS, available online at http://www.cdc.gov/nchs/data/databriefs/db09.htm [accessed February 12, 2009].

Birth Weight

There is a strong association between very low birth weight (due to preterm delivery or extreme fetal growth restriction) and infant mortality that decreases as birth weight increases until it reaches about 4,500 g, when there is a slight increase in infant mortality due to problems associated with macrosomia (Mathews and MacDorman, 2007). Although rates of infant morality have decreased over time, the reverse J-shape of this relationship has not changed.

The proportion of small infants increased and large infants decreased among all reported births between 1990 and 2005 (Figure 2-23). This downward shift in the overall distribution of birth weight is attributable in part to an increase in multiple births, but the pattern is similar for singleton births. Other possible explanations for these trends in birth weight include a greater prevalence of older mothers, who tend to have more complications of pregnancy, as well as increased use of assisted reproductive technology and obstetrical procedures, including labor induction and elective cesarean deliveries.
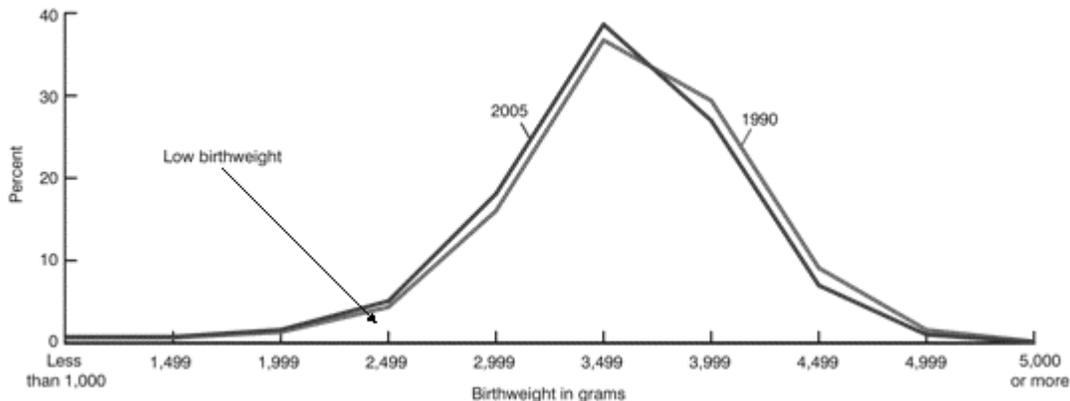
FIGURE 2-23 Percentage distribution of births by birth weight, United States, 1990 and 2005.
SOURCE: NCHS, 2007a.

Rates for low birth weight and very low birth weight increased in the United States between 1990 and 2005, when the overall rate of low birth weight among singletons was 6.41 percent and the overall rate of very low birth weight was 1.14 percent. The lowest rates of low birth weight are among Hispanics and white infants, the highest among black infants; Native American, and Asian-Pacific Islander infants fall in between (Figure 2-24). Low birth weight also varies by maternal age, with greater prevalence among women < 20 and > 40 years of age (Martin et al., 2008).
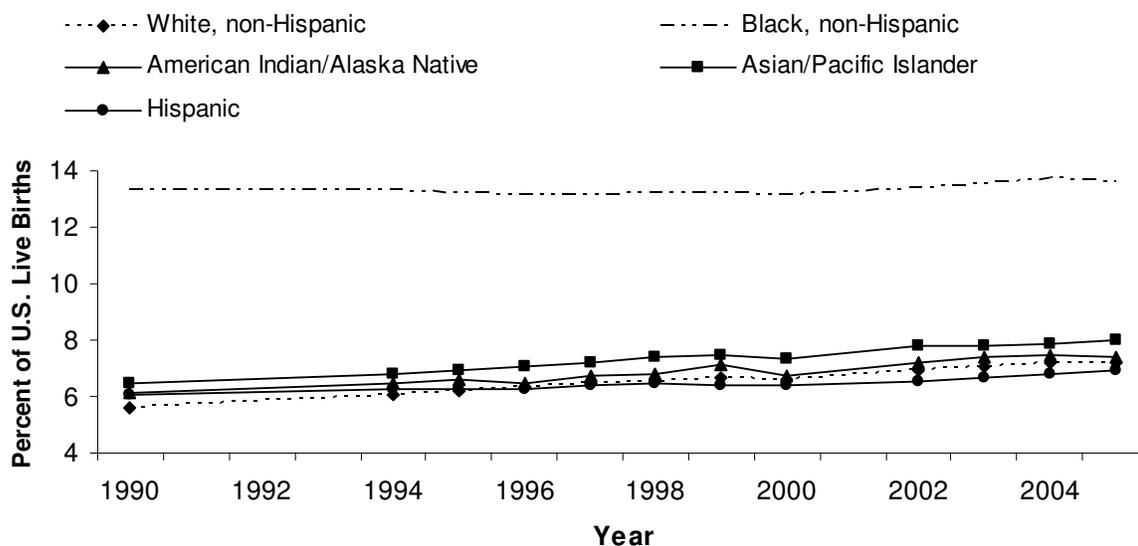
FIGURE 2-24 Trends in low birth weight of live-born singleton infants in the United States from 1990 through 2005, by race and ethnic background.
NOTE: Low birth weight is defined as less than 2,500 g.
SOURCES: NCHS, 2002; 2007a.

Small-for-Gestational Age Births

Small-for-gestational age (SGA) is used as a proxy to examine poor fetal growth (see Chapter 4) but can also include infants who are small but healthy due to their familial genetic background (Jaquet et al., 2005; Svensson et al, 2006). SGA rates for all groups decreased between 1990 and 2000 and then increased in 2005 (Table 2-6). Rates among non-Hispanic black infants were almost twice as high as those of white infants and were not appreciably different by gender. However, Hispanic and Asian female infants had lower SGA rates than males.

TABLE 2-6 Estimates of SGA by Sex, Race or Ethnicity, and Year: United States

	1990	1995	2000	2005
Males				
Total	10.5	10.5	10.2	10.7
Non-Hispanic white	8.7	8.8	8.4	8.7
Non-Hispanic black	17.1	16.9	16.3	16.8
Hispanic	10.7	10.6	10.4	10.7
White	9.1	9.2	8.9	9.3
Black	17.0	16.8	16.2	16.5
American Indian-Alaska Native	9.9	9.7	9.4	9.8
Asian-Pacific Islander	14.0	14.4	13.9	14.5
Females				
Total	10.7	10.5	10.1	10.5
Non-Hispanic white	9.0	8.9	8.4	8.8
Non-Hispanic black	17.3	16.9	16.2	16.7
Hispanic	10.4	10.2	9.8	10.1
White	9.3	9.2	8.7	9.1
Black	17.2	16.8	16.1	16.3
American Indian-Alaska Native	9.3	9.5	9.0	9.3
Asian-Pacific Islander	13.2	13.7	13.2	13.6

NOTE: Singleton births only.
SOURCE: CDC/NCHS, National Vital Statistics System, available online at http://www.cdc.gov/nchs/VitalStats.htm [accessed February 12, 2009].

Large-for-Gestational Age Birth

The proportion of infants born large-for-gestational age (LGA) decreased monotonically between 1990 and 2005 for males and females within all racial-ethnic groups, although American Indians-Alaska Natives had the highest rates (Table 2-7). Reasons for this decrease are not known but could include routine testing for GDM and increased cesarean deliveries performed at earlier gestational ages (Menacker et al., 2006).

TABLE 2-7 Estimates of LGA by Sex, Race or Ethnicity, and Year: United States

	1990	**1995**	**2000**	**2005**
Males				
Total	11.1	10.7	10.7	9.4
Non-Hispanic white	12.4	12.1	12.2	10.7
Non-Hispanic black	7.5	7.2	6.9	6.2
Hispanic	10.2	9.8	9.9	8.9
White	12.0	11.6	11.6	10.2
Black	7.5	7.2	7.0	6.4
American Indian-Alaska Native	13.8	13.6	13.2	12.0
Asian-Pacific Islander	6.5	6.2	6.1	5.4
Females				
Total	10.5	10.3	10.4	9.1
Non-Hispanic white	11.7	11.6	12.1	10.2
Non-Hispanic black	7.1	6.8	6.8	5.9
Hispanic	9.9	9.7	10.0	9.0
White	11.3	11.2	11.3	9.8
Black	7.1	6.8	6.8	6.1
American Indian-Alaska Native	14.3	13.5	13.5	12.8
Asian-Pacific Islander	6.8	6.6	6.4	5.7

NOTE: Singleton births only.
SOURCE: CDC/NCHS, National Vital Statistics System, available online at http://www.cdc.gov/nchs/VitalStats.htm [accessed February 12, 2009].

Preterm Birth

In 2005, 12.5 percent of all births were delivered preterm. The preterm birth rate has increased 20 percent since 1990 and 9 percent since 2000 (Figure 2-25). The greatest increase has been among late preterm births, those occurring at 34-36 weeks' gestation, which have climbed 25 percent since 1990. The preterm birth rate for singleton gestations increased 13 percent from 1990 to 2005, again with late preterm births accounting for a majority of the increase. An increase in the rates of cesarean deliveries and induced births contributes to but does not completely explain this trend in late preterm births (March of Dimes, available online at http://www.marchofdimes.com/files/MP_Late_Preterm_Birth-Every_Week_Matters_3-24-06.pdf [accessed January 14, 2009]).

There is a striking racial disparity in the rate of preterm birth (Figure 2-26). In the past 15 years, non-Hispanic black women were about twice as likely as non-Hispanic white women to deliver before 37 weeks' gestation. Since 1990, the preterm birth rate increased 38 percent for non-Hispanic whites and 10 percent for Hispanic births. There was a decrease in preterm births among non-Hispanic black mothers through most of the 1990s. However, the preterm birth rate is up 12 percent since 2000.
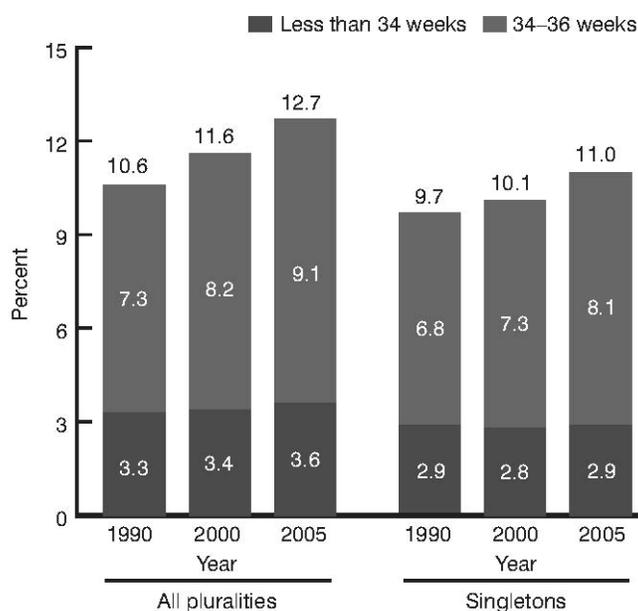
FIGURE 2-25 Preterm birth rates for all births and for singletons only: United States, 1990, 2000, and 2005
SOURCE: NCHS, 2007a.
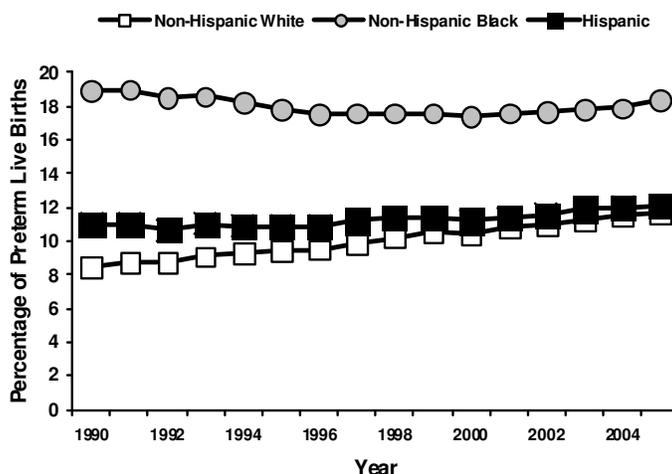
FIGURE 2-26 Trends in preterm live births in the United States by race, 1990 to 2005.
NOTE: Preterm is defined as an infant born before 37 weeks of gestation.
SOURCES: NCHS, 2007a.

Breastfeeding

Analysis of data from the Ross Laboratories Mothers Survey, a large, national survey (Ryan et al., 2002), shows that the rates of breastfeeding initiation (in-hospital) and breastfeeding at six months rose by 16 percent and 14 percent, respectively, in the 1990s. In 2001, rates were at their highest point in 40 years (Figures 2-27 and 2-28). Recent data from the National Immunization Survey, a population-based survey conducted by the CDC, shows that these rates continued to rise from 2000 to 2004.

There are remarkable disparities in rates of breastfeeding. Mothers who were white or Hispanic, older, college-educated, and not enrolled in WIC were significantly more likely to breastfeed and exclusively breastfeed in the hospital and at six months (Ryan et al., 2002).
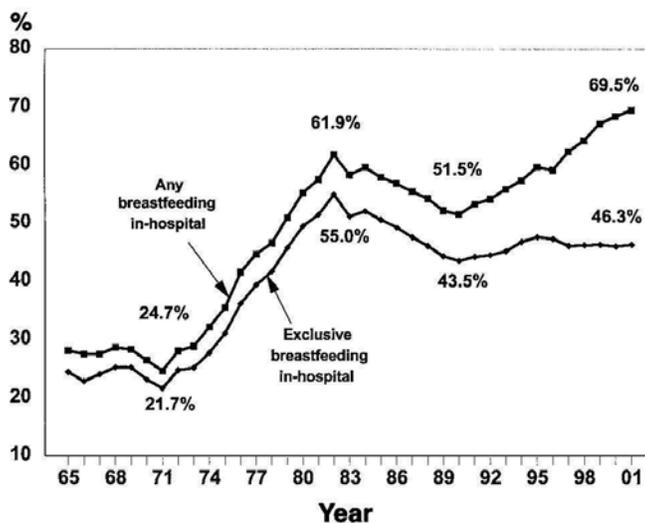
FIGURE 2-27 In-hospital breastfeeding and exclusive breastfeeding rates: 1965-2001.
SOURCE: Ryan et al., 2002. Reproduced with permission from *Pediatrics*, Vol. 110, pages 1103-1109. Copyright © 2002 by the AAP.
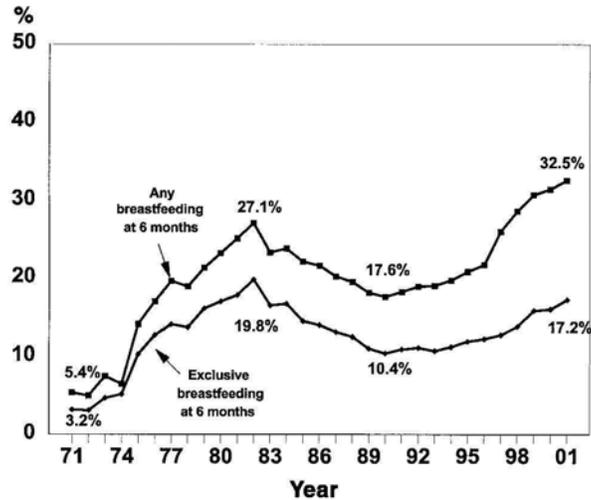
FIGURE 2-28 Breastfeeding and exclusive breastfeeding rates at 6 months of age: 1971-2001.
SOURCE: Ryan et al., 2002. Reproduced with permission from *Pediatrics*, Vol. 110, pages 1103-1109.
Copyright © 2002 by the AAP.

Childhood Obesity

Nationally representative data show continuous increases in obesity (BMI ≥ 95th percentile) among American school-aged children and adolescents from 1980 to the present (http://www.cdc.gov/nccdphp/dnpa/obesity/childhood/prevalence.htm; Accessed April 15, 2009) (Figure 2-29). Recent data suggest that this trend may be slowing (Ogden et al., 2008). Population estimates from 2003 through 2006 suggest that almost a third of 2-19 year olds were at or above the 85th BMI percentile for sex and age (Ogden et al., 2008). Of these, 16 percent were above the 95th percentile, well above the *Healthy People 2010* goal of 5 percent, and 11.3 percent were above 97th percentile (rates of high BMI varied by age and race-ethnicity). Non-Hispanic black adolescents have a dramatically greater prevalence of overweight compared to non-Hispanic whites; Mexican American girls also have somewhat higher rates (Table 2-8).
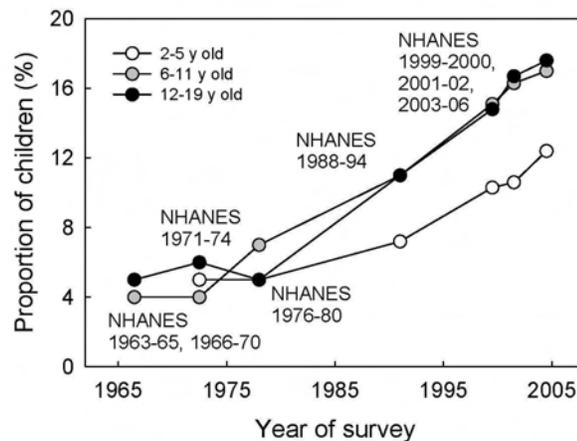
FIGURE 2-29 Prevalence of obesity (≥95th percentile) among children and adolescents, United States, 1963-2006.
SOURCES: Ogden et al., 2006; Ogden et al., 2008.

TABLE 2-8 Prevalence of High BMI by Age Among U.S. Adolescent Girls (12-19 years of age), 2003-2006

BMI Percentile of CDC Growth Charts	Non-Hispanic Black %(SE)	Mexican American %(SE)	Non-Hispanic White %(SE)
≥ 85th	44.5 (1.5)	37.1 (1.9)	31.7 (1.9)
≥ 95th	27.7 (1.9)	19.9 (1.4)	14.5 (2.0)
≥ 97th	19.6 (1.5)	14.1 (1.3)	9.1 (1.6)

SOURCE: Odgen et al., 2008.

FINDINGS AND RECOMMENDATIONS

Findings

1. Since the release of the weight gain recommendations of IOM (1990):

   - There has been a striking increase in the prevalence of maternal overweight and obesity, particularly among black, Hispanic, and older women;
   - There has been an increase in the racial and ethnic diversity of U.S. births, as well as a rise in the proportion of older and unmarried mothers and a decrease in the proportion of teenaged mothers; and
   - Low (< 16-pound) and high (> 40-pound) GWG has become more common.

2. American women of childbearing age are far from meeting national goals for dietary intake and physical activity, yet there is a dearth of nationally representative data on dietary intake, dieting practices and food insecurity, among women of childbearing age in general and among pregnant women in particular.

3. About half of reproductive-aged American women are trying to lose weight, and another one-third of pregnant women may be attempting to maintain their weight. The prevalence of attempted weight loss during pregnancy doubled in the past 20 years.

4. Rates of preterm birth, GDM, and hypertensive disorders of pregnancy are increasing. The rise in cesarean births and the decline in LGA births appear to result from medical practice patterns and social factors.

5. In the past 10 years, improvements that were observed during the twentieth century in maternal mortality and poor infant outcomes (mortality and low birth weight) have declined or ceased.

6. There are racial and ethnic disparities in nearly all weight-related predictors and outcomes reviewed.

7. Currently available data sources are inadequate for studying national trends in GWG. Even after the IOM (1990) report called for more sophisticated analyses, major gaps in GWG surveillance remain; specifically, data on prepregnancy weight and height, reliance on self-reported weight gain, and nationally representative sources are lacking.

8. Gestational weight gain in excess of the recommended range for BMI is associated with significant postpartum weight retention.

9. Major gaps in surveillance of postpartum weight exist. Notably, most national studies lack data on postpartum weight and/or the variables needed for its proper interpretation

(namely, prepregnancy height and weight, GWG, dietary intake, physical activity, and breastfeeding status).

Action Recommendations

Action Recommendation 2-1: The committee recommends that the Department of Health and Human Services conduct routine surveillance of GWG and postpartum weight retention on a nationally representative sample of women and report the results by prepregnancy BMI (including all classes of obesity), age, racial/ethnic group, and socioeconomic status.

Action Recommendation 2-2: The committee recommends that all states adopt the revised version of the birth certificate, which includes fields for maternal prepregnancy weight, height, weight at delivery, and gestational age at the last measured weight. In addition, all states should strive for 100 percent completion of these fields on birth certificates and collaborate to share data, thereby allowing a complete national picture as well as regional snapshots.

Supporting Actions

1. At the first prenatal visit, health care providers should record weight at last menstrual period and maternal height without shoes. Gestational weight gain should be based on measured weights (in light clothing and no shoes) abstracted from prenatal records. Gestational age at the last recorded weight should be documented, preferably through an early ultrasound, to properly evaluate adequacy of weight gain. To aid in data analysis, all data should be collected in a continuous form rather than categorically.

2. As part of maternal weight surveillance, health-care providers should document the prevalence of obesity grades I, II, and II rather than categorize women into one obesity group (BMI > 30 kg/m^2).

Areas for Additional Investigation

The committee identified the following areas for further investigation to support its research recommendations:

- The research community should conduct future monitoring of GWG; and
- Federal agencies should standardize the use of the WHO BMI cutoff points in all data collection relevant to monitoring weight gain in pregnancy.

REFERENCES

American Psychiatric Association. 1994. *Diagnostic and Statistical Manual of Mental Disorders*. Washington, DC: American Psychiatric Association.

Bish C. L., H. M. Blanck, M. K. Serdula, M. Marcus, H. W. Kohl, 3rd and L. K. Khan. 2005. Diet and physical activity behaviors among Americans trying to lose weight: 2000 Behavioral Risk Factor Surveillance System. *Obesity Research* 13(3): 596-607.

Bish C. L., S. Y. Chu, C. K. Shapiro-Mendoza, A. J. Sharma and H. M. Blanck. 2009. Trying to lose or maintain weight during pregnancy-United States, 2003. *Matern Child Health Journal* 13(2): 286-292.

CDC (Centers for Disease Control and Prevention). 2004. Smoking during pregnancy--United States, 1990-2002. *MMWR. Morbidity and Mortality Weekly Report* 53(39): 911-915.

CDC. 2005. Trends in leisure-time physical inactivity by age, sex, and race/ethnicity--United States, 1994-2004. *MMWR. Morbidity and Mortality Weekly Report* 54(39): 991-994.

CDC. 2007. Prevalence of regular physical activity among adults--United States, 2001 and 2005. *MMWR. Morbidity and Mortality Weekly Report* 56(46): 1209-1212.

CDC. 2008a. MMWR. Morbidity and Mortality Weekly Report. 57(5): 127.

CDC. 2008b. *MMWR. Morbidity and Mortality Weekly Report*. 57(11): 281-308.

Chu S. Y., S. Y. Kim, C. H. Schmid, P. M. Dietz, W. M. Callaghan, J. Lau and K. M. Curtis. 2007. Maternal obesity and risk of cesarean delivery: a meta-analysis. *Obes Rev* 8(5): 385-394.

Cogswell M. E., M. K. Serdula, A. H. Mokdad and D. F. Williamson. 1996. Attempted weight loss during pregnancy. *International Journal of Obesity and Related Metabolic Disorders* 20(4): 373-375.

Compton W. M., K. P. Conway, F. S. Stinson and B. F. Grant. 2006. Changes in the prevalence of major depression and comorbid substance use disorders in the United States between 1991-1992 and 2001-2002. *American Journal of Psychiatry* 163(12): 2141-2147.

DHHS (U.S. Department of Health and Human Services). 2000. *Healthy People 2010: Understanding and Improving Health, 2nd Ed*. Washington, DC: Government Printing Office.

DHHS. 2008. *Physical Activity Guidelines Advisory Committee Report*. Washington, DC.

Evenson K. R., D. A. Savitz and S. L. Huston. 2004. Leisure-time physical activity among pregnant women in the US. *Paediatric and Perinatal Epidemiology* 18(6): 400-407.

Flegal K. M., M. D. Carroll, R. J. Kuczmarski and C. L. Johnson. 1998. Overweight and obesity in the United States: prevalence and trends, 1960-1994. *International Journal of Obesity and Related Metabolic Disorders* 22(1): 39-47.

Gaynes B. N., N. Gavin, S. Meltzer-Brody, K. N. Lohr, T. Swinson, G. Gartlehner, S. Brody and W. C. Miller. 2005. Perinatal depression: prevalence, screening accuracy, and screening outcomes. *Evidence Report/Technology Assessessment (Summary)*(119): 1-8.

Getahun D., C. Nath, C. V. Ananth, M. R. Chavez and J. C. Smulian. 2008. Gestational diabetes in the United States: temporal trends 1989 through 2004. *American Journal of Obstetrics and Gynecology* 198(5): 525 e521-525.

Guenther P. M., K. W. Dodd, J. Reedy and S. M. Krebs-Smith. 2006. Most Americans eat much less than recommended amounts of fruits and vegetables. *Journal of the American Dietetic Association* 106(9): 1371-1379.

Hoyert D. L. 2007. Maternal mortality and related concepts. *Vital and Health Statistics. Series 3: Analytical Studies*(33): 1-13.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

IOM. 2005. *Preventing Childhood Obesity: Health in the Balance*. Washington, DC: The National Academies Press.

Jaquet D., S. Swaminathan, G. R. Alexander, P. Czernichow, D. Collin, H. M. Salihu, R. S. Kirby and C. Levy-Marchal. 2005. Significant paternal contribution to the risk of small for gestational age. *British Journal of Obstetrics and Gynaecology* 112(2): 153-159.

Kim S. Y., P. M. Dietz, L. England, B. Morrow and W. M. Callaghan. 2007. Trends in pre-pregnancy obesity in nine states, 1993-2003. *Obesity (Silver Spring)* 15(4): 986-993.

MacDorman M. F., F. Menacker and E. Declercq. 2008. Cesarean birth in the United States: epidemiology, trends, and outcomes. *Clinics in Perinatology* 35(2): 293-307, v.

Martin J. A., H. C. Kung, T. J. Mathews, D. L. Hoyert, D. M. Strobino, B. Guyer and S. R. Sutton. 2008. Annual summary of vital statistics: 2006. *Pediatrics* 121(4): 788-801.

Mathews T. J. and M. F. MacDorman. 2007. Infant mortality statistics from the 2004 period linked birth/infant death data set. *National Vital Statistics Reports* 55(14): 1-32.

Menacker F., E. Declercq and M. F. Macdorman. 2006. Cesarean delivery: background, trends, and epidemiology. *Seminars in Perinatology* 30(5): 235-241.

Mokdad A. H., M. K. Serdula, W. H. Dietz, B. A. Bowman, J. S. Marks and J. P. Koplan. 1999. The spread of the obesity epidemic in the United States, 1991-1998. *Journal of the American Medical Association* 282(16): 1519-1522.

NCHS (National Center for Health Statistics). 2002. Births: final data for 2001. *National Vital Statistics Reports* 51(2): 1-102.

NCHS. 2005. Births: preliminary data for 2004. *National Vital Statistics Reports* 54(8): 1-17.

NCHS. 2007a. Births: final data for 2005. *National Vital Statistics Reports* 56(6): 1-103.

NCHS. 2007b. *Health, United States, 2007*. Hyattsville, MD: Public Health Service.

NHLBI (National Heart, Lung, and Blood Institute). 1998. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. (National Institutes of Health Publication 98-4083). Washington, DC: National Institutes of Health.

Nielsen S. J., A. M. Siega-Riz and B. M. Popkin. 2002. Trends in energy intake in U.S. between 1977 and 1996: similar shifts seen across age groups. *Obesity Research* 10(5): 370-378.

Nielsen S. J. and B. M. Popkin. 2004. Changes in beverage intake between 1977 and 2001. *American Journal of Preventive Medicine* 27(3): 205-210.

Ogden C. L., M. D. Carroll, L. R. Curtin, M. A. McDowell, C. J. Tabak and K. M. Flegal. 2006. Prevalence of overweight and obesity in the United States, 1999-2004. *Journal of the American Medical Association* 295(13): 1549-1555.

Ogden C. L., M. D. Carroll and K. M. Flegal. 2008. High body mass index for age among US children and adolescents, 2003-2006. *Journal of the American Medical Association* 299(20): 2401-2405.

Petersen A. M., T. L. Leet and R. C. Brownson. 2005. Correlates of physical activity among pregnant women in the United States. *Medicine and Science in Sports and Exercise* 37(10): 1748-1753.

Ryan A. S., Z. Wenjun and A. Acosta. 2002. Breastfeeding continues to increase into the new millennium. *Pediatrics* 110(6): 1103-1109.

Serdula M. K., D. F. Williamson, R. F. Anda, A. Levy, A. Heaton and T. Byers. 1994. Weight control practices in adults: results of a multistate telephone survey. *American Journal of Public Health* 84(11): 1821-1824.

Serdula M. K., A. H. Mokdad, D. F. Williamson, D. A. Galuska, J. M. Mendlein and G. W. Heath. 1999. Prevalence of attempting weight loss and strategies for controlling weight. *Journal of the American Medical Association* 282(14): 1353-1358.

Svensson A. C., Y. Pawitan, S. Cnattingius, M. Reilly and P. Lichtenstein. 2006. Familial aggregation of small-for-gestational-age births: the importance of fetal genetic effects. *American Journal of Obstetrics and Gynecology* 194(2): 475-479.

Thompson D., Graham C., Burch D., Watson A. and Phelps A. 2005. *Pregnancy Related Mortaity Asociated with Obesity in Florida 1999 through 2002*. Tallahassee, FL: Florida Department of Health, Division of Family Health Services, Bureau of Family and Community Health.

Wallis A. B., A. F. Saftlas, J. Hsia and H. K. Atrash. 2008. Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States, 1987-2004. *American Journal of Hypertension* 21(5): 521-526.

WHO (World Health Organization). 1998. *Obesity—preventing and managing the global epidemic*. WHO Consultation on Obesity Report. Geneva.

Websites:
http://www.cdc.gov/prams/
http://www.cdc.gov/PEDNSS/pnss_tables/pdf/national_table20.pdf
http://www.cdc.gov/nchs/vitalstats.htm
http://www.ers.usda.gov/Publications/ERR49/ERR49.pdf
http://mchb.hrsa.gov/whusa08/hstat/mh/pages/237mm.html
http://www.cdc.gov/nchs/data/databriefs/db09.htm
http://www.marchofdimes.com/files/MP_Late_Preterm_Birth-Every_Week_Matters_3-24-06.pdf
http://www.cdc.gov/nchs

Composition and Components of Gestational Weight Gain: Physiology and Metabolism

Gestational weight gain (GWG) is a unique and complex biological phenomenon that supports the functions of growth and development of the fetus. Gestational weight gain is influenced not only by changes in maternal physiology and metabolism, but also by placental metabolism (Figure 3-1). The placenta functions as an endocrine organ, a barrier, and a transporter of substances between maternal and fetal circulation. Changes in maternal homeostasis can modify placental structure and function and thus impact fetal growth rate. Conversely, placental function may influence maternal metabolism through alterations in insulin sensitivity and systemic inflammation and, thus influence GWG.

This chapter provides relevant background material on normal physiologic and metabolic changes that occur during pregnancy and are related to GWG. The discussion begins with a review of total and pattern of GWG in singleton, twin, and triplet pregnancies. Next, the unique chemical composition and accretion rates of maternal, placental, and fetal components of GWG are presented, followed by discussions of fundamental biology of fetal and placental growth and fetal-placental physiology underlying GWG. Lastly, pathophysiologic conditions that may adversely affect GWG are reviewed to provide a foundation for understanding changes in body weight and composition during pregnancy.
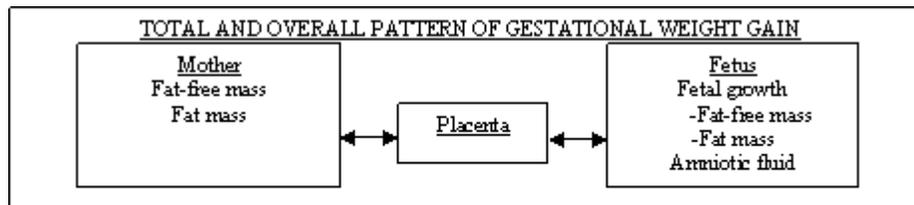
FIGURE 3-1 Schematic summary of components of gestational weight gain.

TOTAL AND PATTERN OF GESTATIONAL WEIGHT GAIN

Total Gestational Weight Gain

The total amount of weight gained in normal-term pregnancies varies considerably among women. Nevertheless, some generalizations can be made regarding tendencies and patterns of GWG in singleton and multiple pregnancies.

Singleton Pregnancies

An examination of studies published in the United States from 1985 to the present indicate that the mean total GWG of normal weight adult women giving birth to term infants ranged from a low of 10.0 to a high of 16.7 kg (Appendix C [Tables C-1A and C-1B] contains a tabular summary of the studies examined by the committee). Among adolescents, in general, GWG tended to be higher compared with adult women (means ranged from 14.6 to 18.0 kg in the studies examined). A consistent finding across studies was an inverse relationship between GWG and pregravid body mass index (BMI). Figure 3-2 illustrates a similar relationship with data derived from Abrams et al. (1986).

Since the release of the report, *Nutrition During Pregnancy* (IOM, 1990) and its guidelines for GWG, a number of studies have examined GWG among overweight and obese women. Bianco et al. (1998) found that the mean GWG for 613 obese (BMI > 35) women averaged 9.1 ± 7.4 kg. Thirteen percent of the women, however, gained more than 16 kg, and 9 percent either lost or failed to gain weight. In a cohort study using birth certificate data from 120,251 obese women in Missouri, 18, 30, and 40 percent of the women gained < 6.8 kg in obese classes I, II, and III, respectively. The amount of total gain associated with minimal risk for preeclampsia, caesarean delivery, large for gestational age (LGA), and small for gestational age (SGA) outcomes was 4.6-11.4, and 0-4.1 for class I and II obesity, respectively; and weight loss of 0-4.1 kg for class III obesity (Kiel et al., 2007) (see Chapter 2 for definition of obesity classes).

A prospective study of a cohort of 245,526 Swedish women confirmed that GWG among obese women (BMI = 30-34.9) and very obese women (BMI ≥ 35) was lower (11.1 and 8.7 kg, respectively) than among non-obese women (Cedergren, 2006). Low GWG (< 8 kg) occurred in 30.2 and 44.6 percent of the obese and very obese women, respectively. Among the 62,167 women in the Danish National Birth Cohort with data on GWG, about 36 percent of the obese women exhibited low rates of gain (0.28 kg per week). Fifty percent gained between 0.28 and 0.68 kg per week, and 14 percent gained > 0.68 kg per week (Nohr et al., 2007).

Obese women (BMI = 30-40) participating in a prenatal intervention gained less weight (adjusted GWG = 7.52 kg) than controls (adjusted GWG = 9.78 kg), and experienced no difference in pregnancy outcome (Claesson et al., 2008). In summary, from a population perspective, obese women as a group gain less weight than non-obese women, nevertheless GWG can vary widely.
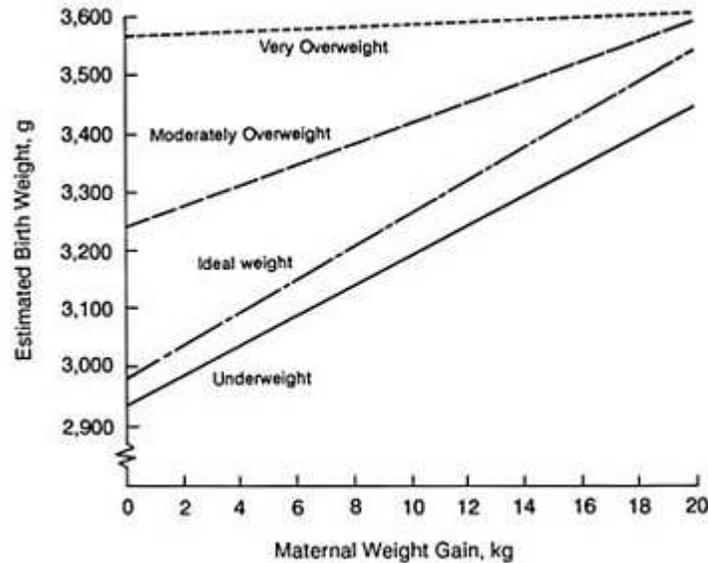
FIGURE 3-2 Birth weight as a function of maternal weight gain and prepregnancy weight for height. SOURCE: Modified from Abrams et al. (1986). This article was published in the *American Journal of Obstetrics and Gynecology*, 154(3), Prepregnancy weight, weight gain, and birth weight, pp. 503-509. Copyright Elsevier (1986).

Twin Pregnancies

Total GWG in twin pregnancies is generally higher than in singleton pregnancies; averaging from 15 to 22 kg (Appendix C, Table C-2). Outcomes associated with GWG in twin pregnancies, as with singleton pregnancies, are a function of pregravid BMI. Several studies have shown that, when stratified by pregravid BMI, increased GWG is associated with increased twin birth weight among underweight, normal weight, and overweight, but not obese, women (Brown and Schloesser, 1990; Luke et al., 1992; Lantz et al., 1996). Yeh and Shelton (2007) found that mean twin birth weights in the population studied increased incrementally from 2,237 g to 2,753 g for total GWG < 35, 35-45, 46-55, and > 55 pounds, respectively. The odds, however, of having a twin delivery at $\geq$ 36 weeks gestation and birth weight $\geq$ 2,500 g were significantly lower among women who gained < 35 pounds (AOR 0.49, 95% CI: 0.37-0.65) and significantly higher among women who gained > 55 pounds (AOR 2.24, 95% CI: 1.51-3.33) compared to those who gained 35-45 pounds. Interestingly, GWG > 55 pounds was associated with an approximate 1.5 times greater likelihood of having a maternal complication (cumulative of GDM, pregnancy-induced hypertension, preeclampsia, and anemia [AOR 1.63, 95% CI 1.02-2.60]) also of having a cesarean delivery [AOR 1.85, 95% CI 1.20-2.87]). The cumulative weight gain stratified by pregravid BMI for mothers of twins born at 37-42 weeks of gestation and with an average twin birth weight $\geq$ 2,500 g is shown in Table 3-1. Cumulative and rates of weight gain by trimester are presented in Appendix C, Tables C-3A and C-3B. In summary, GWG in twin gestations mirrors that in singleton pregnancies, i.e. there is an inverse relationship between maternal GWG and maternal pre-pregnancy BMI. These results suggest that a balance is needed between optimal GWG for maternal and twin outcomes.

TABLE 3-1 Summary of Adjusted and Unadjusted* Cumulative Weight Gain, by Pregravid BMI Status for Mothers of Twins at Gestational Ages 37-42 Wk, and with Average Twin Birth weight > 2,500 g

Pregravid BMI	Cumulative Weight Gain (To 37-42 weeks)		Interquartile 25th – 75th Percentile Ranges of Cumulative Weight Gain (To 37-42 weeks)	
	kg	lbs	kg	lbs
Normal Weight [a] (n = 409)	20.9 ± 0.3 (21.0 ± 6.1)*	45.9 ± 0.7 (46.2 ± 13.4)*	16.8 – 24.5	37 – 54
Overweight [b] (n= 154)	18.9 ± 0.5 (18.7 ± 7.0)*	41.6 ± 1.1 (41.1 ± 15.5)*	14.1 – 22.7	31 – 50
Obese [c] (n = 143)	15.7 ± 0.5 (15.4 ± 7.2)*	34.6 ± 1.2 (34.0 ± 15.9)*	11.4 – 19.1	25 – 42

NOTES: Results are presented as least square means ± SEM from models controlling for diabetes and gestational diabetes, preeclampsia, smoking during pregnancy, primiparity, and placental membranes (monochorionicity and missing chorionicity). Total cumulative gain is also adjusted for length of gestation. Results in parentheses are the unadjusted means ± SD (also see Appendix C, Tables C-3A through C-3D)

[a] BMI = 18.5-24.9 kg/m^2
[b] BMI = 25.0-29.9 kg/m^2
[c] BMI = ≥ 30 kg/m^2

SOURCE: Historical cohort of twin births delivered at John Hopkins Hospital, Baltimore, Jackson Memorial Hospital, Miami, Medical University of South Carolina, Charleston, and University of Michigan, Ann Arbor provided by Barbara Luke, Sc.D., M.P.H., R.D., and Mary L. Hediger, Ph.D. For more details on this historical cohort, see Luke et al. (2003).

Triplet and Quadruplet Pregnancies

Fewer studies are available on triplet and quadruplet pregnancies (Appendix C, Table C-2). In a large cohort study, GWG among mothers carrying triplets was found to range from 20.5 to 23.0 kg at 32-34 weeks and for quadruplets from 20.8 to 31.0 kg at 31-32 weeks (Luke, 1998). In the same cohort, the mean total GWG in 38 triplet pregnancies was found to be 20.2 kg at 33.4 weeks (Luke et al., 1995). The rate of gain before 24 weeks gestation was 0.48 kg per week and 0.96 kg per week after 24 weeks (Luke et al., 1995). In data from a different cohort, GWG was found to be a function of BMI category. Median GWG was 15.5, 21.8, and 15 kg for low-, normal-, and high-BMI categories, respectively (Eddib et al., 2007).

Pattern of Gestational Weight Gain

The pattern of GWG is most commonly described as sigmoidal (Hytten and Chamberlain, 1991), but linear, concave, and convex patterns of weight gain have been observed as well (Villamor et al., 1998).

Singleton Pregnancies

In the report *Nutrition During Pregnancy* (IOM, 1990) the average rates of GWG for well-nourished women with uncomplicated singleton pregnancies are reported as approximately 0.45 kg per week during the second trimester and 0.40 kg per week during the third trimester. Several studies, published since that report, indicate that higher rates of GWG in the second and third

trimesters are common among American women with normal range BMI values (Appendix C, Tables C-1A and C-1B).

The pattern of GWG by maternal BMI category was examined in a large cohort of women from University of California, San Francisco (Abrams, et al., 1995; Carmichael et al., 1997). Mean rate of gain was 0.169 kg per week in the first trimester. Mean weight gains were higher in the second (0.563 kg per week) than the third trimester (0.518 kg per week) in all groups except for obese women. The average gains in the second and third trimester were higher in underweight and normal weight women than in overweight and obese women. Birth weight was correlated most strongly with gain in the second trimester (32.8 g/kg GWG versus 18 and 17 g/kg in the first and third trimesters, respectively).

In another study, mean rates of GWG in non-obese, low-income black and white women were 2.48 kg in the first trimester and 0.49 and 0.45 kg per week in the second and third trimesters, respectively (Hickey et al., 1995). In contrast, rates of weight gain of predominantly Hispanic women (n = 7,589) participating in the Prematurity Prevention Project were similar in the second (0.52 kg per week) and third trimesters (0.53 kg per week) (Siega-Riz et al., 1996). In this study, the third-trimester gain was slightly lower in women who delivered preterm (0.50 vs. 0.53 kg per week). A similar pattern of GWG was found in adolescents, although the median gain and rate of gain were higher throughout gestation. From mid-pregnancy to term the rate of gain was 0.51 kg per week (Hediger et al., 1990). In summary, the pattern of GWG is generally higher in the second trimester and is related to maternal pregravid BMI. However, pattern of GWG can vary depending on maternal ethnicity and age.

Twin Pregnancies

A series of observational studies examined outcomes associated with the rate of GWG in women with twin pregnancies who delivered infants at 37-42 weeks gestation with mean birth weights exceeding 2,500 g. Luke et al. (1992) found that low rate of GWG, defined as < 1.0 pound/week, was associated with a significantly lower mean birth weight for twins compared to singletons (β, -0.137; p = 0.001). Significantly higher rates of GWG in the third trimester were observed among women whose mean birth weights for twins was $\geq$ 2,500 g compared to women with birth weights for twin that was < 2,500 g, regardless of BMI category. No significant differences were seen for first and second trimester GWG rates.

Among a large multiethnic population of 646 twin pregnancies at $\geq$ 28 weeks gestation, birth weight increased by 14, 20, and 17 g for each pound of weight gained between 0 and 20 weeks gestation, 20 and 28 weeks gestation, and 28 weeks to birth, respectively (Luke et al., 1997). Mean total GWG was 17.4 kg in a larger cohort of 1,564 twin births of > 28 weeks' gestation from the same population (Luke et al., 1998). In a another study from the same population database, Luke et al. (2003) found that rates of GWG associated with optimal outcomes were greater for underweight and normal weight women than for overweight and obese women. These results are similar to those of singleton pregnancies.

COMPONENTS OF GESTATIONAL WEIGHT GAIN

As pregnancy progresses, protein, fat, water, and minerals are deposited in the fetus, placenta, amniotic fluid, uterus, mammary gland, blood, and adipose tissue (Figure 3-3). The products of conception (placenta, fetus, amniotic fluid) comprise approximately 35 percent of the total GWG (Pitkin, 1976). The extent to which these changes in body composition are critical for

normal fetal development or are incidental to pregnancy is not completely understood.
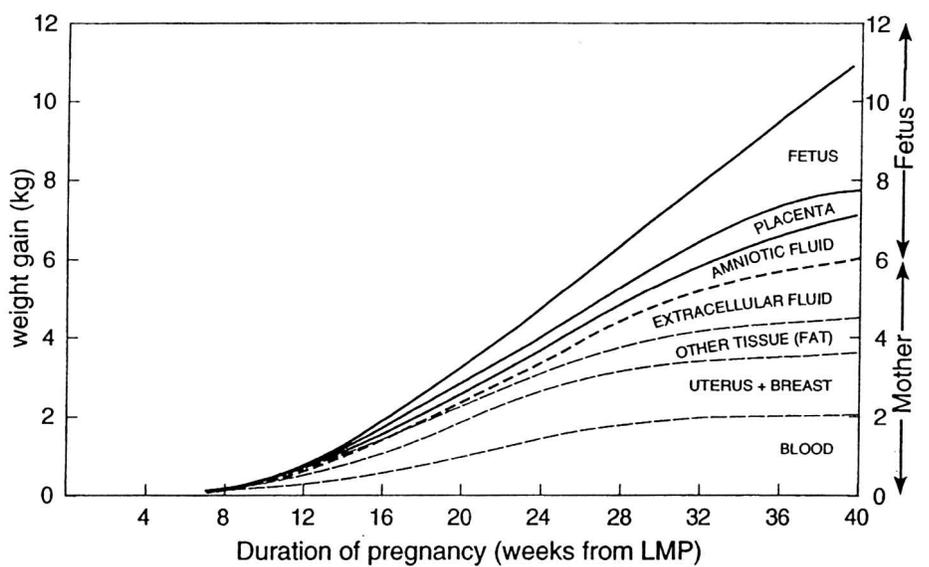
FIGURE 3-3 Components of gestational weight gain.
SOURCE: Pitkin, 1976. Nutritional support in obstetrics and gynecology. *Clinical Obstetrics and Gynecology* 19(3): 489-513. Reprinted with permission.

Maternal Components of Gestational Weight Gain

Total Body Water Accretion

Total body water (TBW) accretion is highly variable during pregnancy and largely under hormonal control. Across several studies, TBW accretion measured by deuterium or antipyrine tracers averaged about 7-8 liters (L) in healthy pregnancies (Hytten and Chamberlain, 1991). Expansion of the extracellular fluid (ECF) measured using the tracer sodium thiocyanate is estimated to be about 6-7 L. For a reference 12.5-kg GWG, total water gain at term is distributed in the fetus (2,414 g), placenta (540 g), amniotic fluid (792 g), blood-free uterus (800 g), mammary gland (304 g), blood (1,267 g), and extravascular-ECF (1,496 g) with no edema or leg edema, and ECF with generalized edema (4,697 g) (Hytten and Chamberlain, 1991). Maternal age, parity, and height did not affect the incidence of edema, but overweight women had greater generalized edema than underweight women. As pregnancy advances, plasma volume expansion measured using Evans blue dye increases up to 45 percent (Rosso, 1990). Maternal plasma volume expansion correlates positively with birth weight. Monthly bioimpedance analysis (BIA) measurements in 170 healthy pregnant women confirmed the progressive expansion of TBW, intracellular water (ICW), and ECF during pregnancy (Larciprete et al., 2003). Total body water accretion was positively correlated with birth weight, in agreement with other investigations (Langhoof-Roos et al., 1987; Lederman et al., 1997; Mardones-Santander et al., 1998; Butte et al., 2003).

Fat-Free Mass

Protein Accretion

Protein is accrued predominantly in the fetus (42 percent), but also in the uterus (17 percent), blood (14 percent), placenta (10 percent), and breasts (8 percent) (Hytten and Chamberlain, 1991). Protein accrual occurs predominantly in late pregnancy. Protein deposition has been estimated from measurements of total body potassium (TBK) accretion measured by whole-body counting in a number of studies of pregnant women (King et al., 1973; Emerson et al., 1975; Pipe et al., 1979; Forsum et al., 1988; Butte et al., 2003). King et al. (1973) observed a rate of TBK accretion of 24 milliequivalents (meq) per week between 26 and 40 weeks' gestation. Pipe et al. (1979) found a 312 meq potassium (K) increase. Lower increments of 110 and 187 meq at 36 weeks were found over pregravid values in two other studies (Forsum et al., 1988; Butte et al., 2003). Based on a potassium-nitrogen ratio in fetal tissues of 2.15 meq potassium/g nitrogen, the total protein deposition estimated from the longitudinal studies of King et al. (1973), Pipe et al. (1979), Forsum et al. (1988), and Butte et al. (2003) is 686 g. A study of 108 black adolescents, showed a mean rate of TBK accretion of 21 meq per week between 16 and 35 weeks' gestation, consistent with adult studies (Stevens-Simon et al., 1997). In summary, these recent studies suggest that protein accretion may be less than the approximate (~1 kg) estimates of the earlier findings of Hytten and Chamberlin (1991).

Fat Mass

Fat Accretion

The distribution of fat deposited during pregnancy is distinct to pregnancy. Figure 3-4 shows that, based on serial measurements of skinfold thickness at seven sites made in 84 healthy, pregnant women, fat appears to be deposited preferentially over the hips, back, and upper thighs up to about 30 weeks gestation (Taggart et al., 1967).
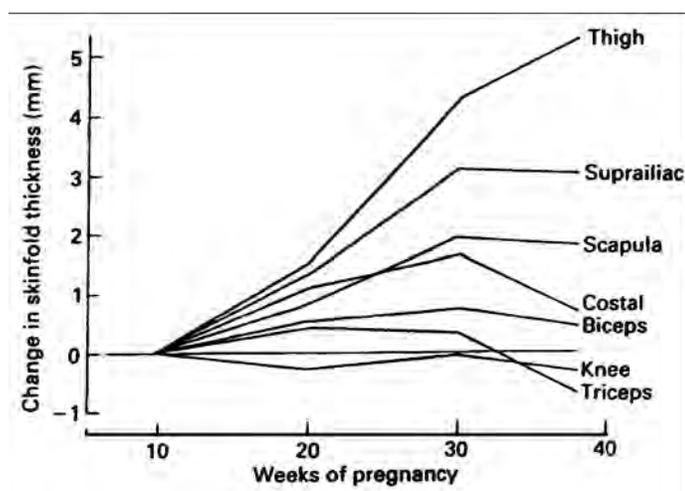
FIGURE 3-4 Longitudinal changes in skinfold thicknesses throughout pregnancy.
SOURCE: Taggart et al., 1967. Changes in skinfolds during pregnancy. *British Journal of Nutrition* 21(2): 439-451. Reprinted with the permission of Cambridge University Press.

Evidence using computer tomography in 14 women suggests that childbearing may be associated with preferential deposition of visceral fat (Gunderson et al., 2008). However, the majority of fat deposited during pregnancy is subcutaneous. Magnetic resonance imaging to assess fat deposition and distribution in 15 healthy women before and after pregnancy (Sohlstrom and Forsum, 1995) found that of the adipose tissue gained during pregnancy, 76 percent was deposited subcutaneously, similar to the fat distribution before pregnancy. Of the total fat deposition, 46 percent was in the lower trunk, 32 percent in the upper trunk, 16 percent in the thighs, 1 percent in the calves, 4 percent in the upper arms, and 1 percent in the forearms. Postpartum, fat was mobilized more completely from the thighs than the trunk and non-subcutaneous fat in the upper trunk actually increased postpartum.

Measurement of fat mass during pregnancy is technically challenging because the usual methodologies are imprecise, invalid, or not applicable to pregnancy. Skinfold measurements lack the precision necessary to estimate changes in fat mass accurately. Two-component body composition methods based on TBW, body density, and TBK, however, are invalid during pregnancy because of the increased hydration of fat-free mass (FFM) that occurs during pregnancy. The constants for hydration, density, and K content of FFM used in two-compartment models are not applicable to pregnant women and would lead to erroneous estimations of FFM and fat mass (FM). Corrected constants for the hydration, density, and K content of FFM in pregnancy have been determined (van Raaij et al., 1988; Hopkinson et al., 1997). Two-component models that use the corrected constants are satisfactory for use with pregnant women, as are three- or four-component models (Fuller et al., 1992) in which the hydration or density of FFM is measured.

Fat accretion models estimated in pregnant women using corrected two-component models, or three- and four-component body composition are summarized in Appendix C, Table C-4. Figure 3-5 shows a four-compartment body composition model of FM, TBW, protein, bone mineral, and non-osseous mineral measured by hydrodensitometry, deuterium dilution, and densitometry (dual energy X-ray absorptometry, DXA) (Lederman et al., 1997). When applied (after pregnancy) to 200 healthy women at 14 and 37 weeks of gestation the model showed that obese women gained significantly less fat than underweight and normal weight women (8.7 vs. 12.6 and 12.2 kg, respectively). There were no differences in the amount of TBW gained among the underweight, normal weight or obese women. The majority of women studied did not conform to the recommendations of IOM (1990). Sixty-seven percent of underweight, 61 percent of normal weight, 69 percent of overweight, and 78 percent of obese women gained outside the recommended ranges. Fat accretion paralleled GWG; FM gain was positively correlated with GWG ($r = 0.81$) and inversely correlated ($r = -0.25$) with pregravid weight. For those that gained within recommendations from IOM (1990), FM gain was highest among the underweight (6.0 kg), followed by the normal weight (3.8 kg), overweight (2.8 kg), and obese (–0.6 kg). For those who gained less than the recommendations, FM gain was 0.6 kg in the underweight, 1.3 kg in the normal weight, 0.3 kg in the overweight, and –5.2 kg in the obese. For those that gained more than the recommendations, FM was highest in the underweight (6.9 kg), followed by the normal weight (6.0 kg), overweight (4.2 kg), and obese (3.1 kg).
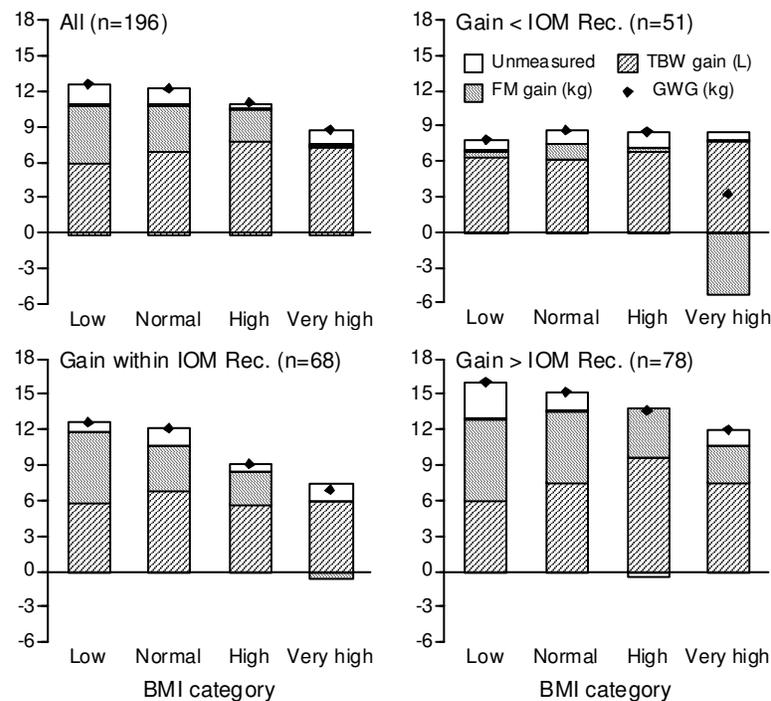
FIGURE 3-5 Body weight and composition changes in 196 women are presented by pregravid BMI category (low *n* = 21, normal *n* = 118, high *n* = 29, and very high *n* = 28). Gains in total body water and fat mass and gestational weight gain also are presented by compliance with the IOM 1990 recommendations for weight gain: women gaining less than (*n* = 51), within (*n* = 68), and more than (*n* = 78) the recommendations from IOM (1990).
SOURCE: Lederman et al., 1997.

Another four-compartment body composition model based on TBK, TBW, body volume, and bone mineral content measured by whole-body counting, deuterium dilution, hydrodensitometry, bone, and DXA (pre- and postgravid only) was used before pregnancy, at 9, 22, and 36 weeks of gestation; and at 2, 6, and 27 weeks after delivery (Butte et al., 2003) (see Figure 3-6). Protein accretion was measured by prompt-gamma activation measurements of total body nitrogen (TBN) taken before and after pregnancy. Total body K and TBN did not differ before and immediately after pregnancy, but did decline postpartum. On average, weight gain was 42 percent FM and 58 percent FFM. GWG was correlated linearly with gains in TBW ($r = 0.39$), TBK ($r = 0.49$), protein ($r = 0.49$), FFM ($r = 0.50$), and FM ($r = 0.76$). Gains in TBW, TBK, protein, and FFM did not differ among low-, normal- and high-BMI groups; only FM gain was higher in high-BMI group who also gained more weight. The body composition changes in those women who gained (mean 14.4 kg) within IOM (1990) recommendations were TBW (7.1 kg), TBK (5.0 g), protein (370 g), FFM (8.4 kg), and FM (4.1 kg). Postpartum weight retention positively correlated with GWG and FM gain, but not with total TBW, TBK, or FFM gain. Postpartum FM retention positively correlated with GWG and FM gain. FM retention at 27 weeks' postpartum was higher in those who gained above the recommendations (5.3 kg) than those that gained within (2.3 kg) and below (–0.5 kg) them. Birth weight was positively correlated with gains in weight, TBW, TBK, protein, and FFM, but not FM gain. Lederman et al. (1997) also found that maternal weight and FFM, but not FM, at term related to birth weight.

In summary, much of the variance in GWG is accounted for by the increase in fat mass, because that much of an increase in FFM also represents and increase in water. Similar to what was observed in GWG, the increase in fat mass during gestation in inversely proportional to pre-gravid obesity.

The relationships between accretion of maternal fat mass as a function of pre-gravid obesity may relate to pregravid maternal metabolic function. Sixteen healthy lean women were measured for body composition, basal oxygen consumption (VO_2), and insulin sensitivity before pregnancy and at 12-14 weeks and 34-36 weeks of gestation (Catalano et al., 1998). In early pregnancy, women with abnormal glucose tolerance had smaller increases in FM (1.3 kg) and percentage FM (1.6 percent) compared to those with normal glucose tolerance (2.0 kg, 3.6 percent). Fat accretion did not differ from early to late gestation but changes in maternal insulin sensitivity were inversely correlated with changes in energy expenditure and FM accretion in early but not late pregnancy.
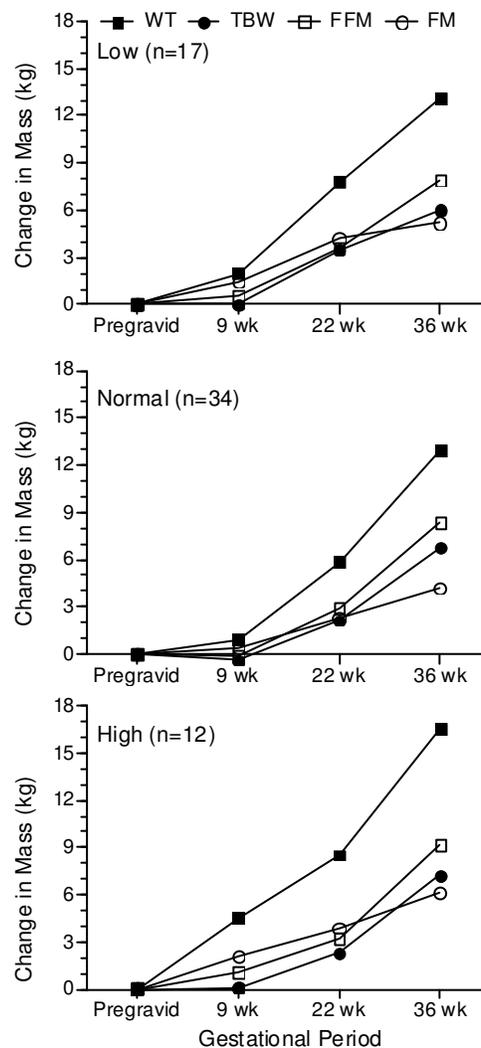
FIGURE 3-6 Changes in body weight and composition of 63 women (low pregravid BMI *n* = 17; normal pregravid BMI *n* = 34; high pregravid BMI *n* = 12) measured at 9, 22, and 36 weeks' gestation.
NOTE: WT = weight.
SOURCE: Butte et al., 2003.

Placenta

Placental Weight

There is a linear relationship between fetal growth and placental mass, fetal weight, and placental growth in both early and late gestation (Molteni et al., 1978). There is a significant increase in the mean placental weight and the fetal-placental weight ratio with advancing gestation in pregnancies that are appropriate-for-gestational age (AGA) and LGA.

In infants that were born SGA, placental weight showed no increase after 36 weeks, but the fetal-placental weight ratio continued to increase. Therefore, although there may be further growth of the fetus, albeit not optimal, there is a lack of placental growth commonly referred to as placental insufficiency. The basis for altered placental growth and function may be related to a variety of pathologies such as nutritional, vascular (e.g., hypertension, diabetic vasculopathy), or anatomic disorders.

There are a limited number of cases of higher-order placental weights in higher multiples, but Pinar et al. (2002) published a series of reference weights from triplet pregnancies. See Table C-5 in Appendix C for normative criteria for placental weight in singleton, twin, and triplet pregnancies.

Placental Growth

Normal placental growth using human tissue is difficult to ascertain because placentas obtained from early pregnancy are often the result of an abnormal pregnancy outcome. Prior to 20 weeks, most placentas are obtained at the time of either spontaneous or elective termination. In mid-pregnancy, placentas are obtained after either a preterm delivery or placental dysfunction such as placenta previa or abruptio placenta.

Placental Development

There are structural and functional changes in placental development with advancing gestation. Teasdale (1980) described these changes in placentas delivered in healthy pregnancies between 22 and 40 weeks' gestation. The first stage of placental growth lasting through 36 weeks is characterized by increases in the parenchymal and non-parenchymal tissue. The parenchyma is composed primarily of intravillous space, the trophoblast tissue (i.e., cytotrophoblast, syncytiotrophoblast), and fetal capillaries of peripheral and stem villi. The non-parenchymal tissue is composed of the decidual and chorionic plates, intercotyledonary septa, fetal vessels, connective tissue, and fibrin deposits. The second phase of placental development lasting from 36 weeks until term is the maturation phase. The maturation phase of placental growth is characterized by an increase in fetal growth but without an increase in placental functional or parenchymal tissue. During the maturation phase there is only an increase in non-parenchymal (i.e., nonfunctional) placental tissue. These relationships are all consistent with the importance of early placental growth and development needed to support the rapid fetal growth in the last trimester of pregnancy when fetal weight increases from a mean of 1,000 g to 3,400 g in the general U.S. population.

In addition to the weight and structural changes in placental development, there also may be differences in placental function as a consequence of a women's pregravid BMI. In general, obese women are more likely to have larger placentas and neonates in comparison to average-

weight women. As discussed previously the alterations in maternal metabolic function during pregnancy are most likely mediated through placental hormone and cytokine production, which in turn affect maternal fat accretion and nutrient availability necessary for fetal growth. Recently, Challier et al. (2008) reported that the placentas of obese women (pregravid BMI > 30 kg/m^2) had a two- to threefold increase in the number of macrophages in comparison with placentas of average-weight (pregravid BMI < 25 kg/m^2) women. There was also increased expression of the proinflammatory cytokines interleukin (IL-1), tumor necrosis factor-alpha (TNF-α), and IL-6. Hence, the chronic inflammation associated with obesity may affect placental growth and function, thereby altering maternal metabolic function and resulting in the women with pregravid obesity having decreased maternal pre-gravid maternal insulin resistance and decreased maternal fat accretion but increased placental and fetal growth.

Placental Growth

Because of the intrinsic problem of using cross-sectional data to determine normal placental growth, there developed an interest in the use of ultrasound to estimate placental growth using various volumetric measures. Bleker and Hoogland (1981) estimated placental volumes using longitudinal ultrasonographic techniques. Placental volume was 200 cm^2 at 21 weeks' gestation, 300 cm^2 at 28 weeks, and 500 cm^2 at term. The placental area was found to increase linearly until 24 weeks. There was a decreasing growth rate in the last trimester, although 15 percent of placentas showed a continuous increase through pregnancy. Abramovich (1969) was able to obtain placental weights at the time of abdominal hysterectomy with an intact amniotic sac. The average weight of the placenta at 10-12 weeks was 51 g, 12-14 weeks 66 g, 14-16 weeks 85 g, 16-18 weeks 110 g, and 18-20 weeks 141 g.

Placental Composition

The composition of the placenta varies with gestational age as well as maternal metabolic status. Approximately 88 percent of placental weight is water. In comparison, the fetus at term has approximately 80 percent water in its fat-free mass. In studies of Widdowson and Spray (1951), the composition of placentas ranging from 17 to 40 weeks' gestation was analyzed. The mean percentage of water was 88 percent, protein 11 percent, and fat 1 percent. Garrow and Hawes (1971) similarly reported that in more than 700 placentas, the blood-free placenta had approximately 10 percent protein. In a further analysis of the effect of maternal diabetes on placental composition, Diamant et al. (1982) described increased placental mass, amount of DNA, glycogen, and lipids in the placentas of women with diabetes compared to a normal glucose-tolerant control group. The relative changes in glycogen and fat exceeded the changes in weight and mg of DNA, suggesting that a true increase in glycogen and fat per placental cell may have occurred. The increase in lipids in the placenta of the women with diabetes consisted primarily of triglycerides and phospholipids but not cholesterol (See Table C-6 in Appendix C for placental lipid content).

Fetus

Patterns of Fetal Growth for Singletons, Twins, and Triplets

Singletons With the exception of longitudinal studies using methods such as ultrasound, all measures of fetal growth are cross-sectional by definition (i.e., each fetus having been measured only once) Hytten and Chamberlain, 1991). The criteria that are commonly used are to classify fetal growth (1) SGA (i.e., birth weight less than the 10th percentile for gestational age); (2) average (AGA; i.e., birth weight between the 10th and 90th percentile for gestational age); and (3) LGA (i.e., birth weight greater than the 90th percentile for gestational age). These criteria were arbitrarily chosen to help assess the neonatal risk for both short-term and, more recently, long-term morbidity. Since that time there have been numerous other publications relative to fetal growth rates.

For the fetus that is deemed viable, fetal weight, as a measure of fetal growth, is usually determined at the time of delivery. The gestational age of viability has decreased steadily over the years and the fetus is now considered potentially viable at 23-24 weeks. Therefore, most of the fetal growth curves relating to viable fetuses rely on clinical data starting from the mid-second trimester. Although the numbers are small, there appears to be minimal variation in fetal growth through 25 weeks' gestation (Archie et al., 2006).

Recently, Thomas et al. (2000) published data comparing gestation-specific growth parameters with those developed in the late 1960s using data from 85 nurseries including 27,229 neonates. For neonates at < 30 weeks' gestation, there were smaller variances and lower average weights, lengths, and head circumferences than previously published norms. For neonates > 36 weeks' gestation, the variance was similar, but the neonates were larger and heavier. The authors concluded that using older growth curves resulted in misclassification of gender- and race-specific criteria for SGA and LGA. Since then, many investigators have observed an increase in birth weight at term (Orskou et al., 2001; Ananth and Wen, 2002; Surkan, 2004; Catalano, 2007). Hence, the use of current birth weight curves is important in the assessment of fetal growth. Oken et al. (2003) published U.S. birth weight curves based on the 1999 and 2000 United States Natality datasets from 22 through 44 weeks gestation.

Although gestational age is an important factor related to fetal growth, other factors affect not only fetal growth but the pattern of growth. These include gender (Figure 3-7)—males grow more rapidly from the mid-third trimester through term. Other factors that can affect fetal growth include maternal age, height, weight, GWG, obesity, and parity (Catalano et al., 2007). Paternal factors can also affect fetal growth, although they explain much less of the variance than maternal factors (Klebanoff et al., 1998). High altitude results in decreased fetal growth as does maternal hypoxia. Maternal medical problems, e.g. hypertensive disorders, autoimmune disease, and smoking can also result in decreased fetal growth. In contrast, maternal diabetes without evidence of vascular involvement often results in increased fetal growth (see Chapter 4 for detailed discussion).
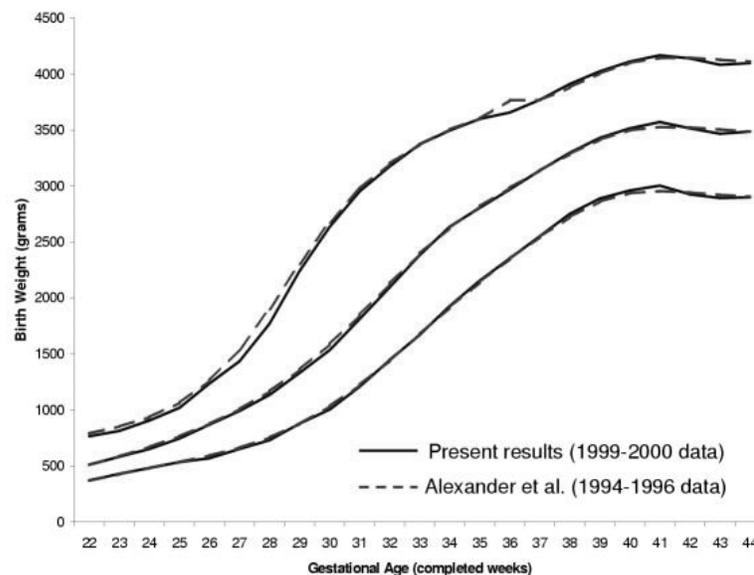
FIGURE 3-7 Select reference percentiles for birth weight at each gestational age from 22 to 44 completed weeks for all singleton infants. SOURCE: Oken E., K. P. Kleinman, J. Rich-Edwards, and M. W. Gillman. 2003. Reprinted with permission from *BMC Pediatrics* 3: 6, by BioMed Central.

The question of ethnic differences in fetal growth and implications for neonatal health has become more relevant recently. Kierans et al. (2008) evaluated all births in British Columbia from 1981 through 2000 and examined fetal growth and perinatal mortality in Chinese, South Asian, First Nation (Native American Indian), and other (primarily Caucasian) populations. They concluded that the ethnic differences in fetal growth rates were physiologic, not pathologic.

The rate of premature delivery (i.e., before 37 weeks' gestation) in the United States is approximately 12.5 percent. As such, birth weight tables that rely on actual neonatal weights for preterm infants represent a much smaller percentage of all births. Furthermore, there is evidence that infants born prematurely are smaller than infants of the same gestational age who remain in utero (Weiner et al., 1985).

In summary, normal fetal growth is relatively uniform until mid-second trimester. At term there is much greater variation in fetal weight as a result of varying determinants of GWG and other maternal factors (see Chapter 4 for complete discussion). Lastly, there has been an increase in term birth weight in developed countries over the last two decades, most likely because of the increased prevalence of obesity.

Twins and Triplets Fetal growth in multiple gestations can be considered very similar to singleton growth until the third trimester. Although there is a tendency to consider multiple gestations as being growth restricted, Blickstein (2002) described the fetal mass of a multiple pregnancy as "growth promoted" and the smaller size of the fetus as "growth adapted". In addition to previously discussed variables that may affect fetal growth such as gender and parity, in twin gestations, chorionicity may also affect fetal growth. Ananth et al. (1998) reported that

twins from monochorionic gestations weigh on average 66 g less than those from dichorionic gestations after correction for gestational age.

Gielen et al. (2007) reported on customized birth weight charts in more than 4,277 twin pairs in Flanders from 1964 through 2002. In their study, birth weight was affected by maternal parity and age. Zygosity, fetal gender, chorionicity, fusion of the placentas, placental weight, and site of umbilical cord insertion all influenced twin birth weights. These variables can account for as much as a 1,000 g difference in weight at term. After 40 weeks' gestation, there is a decrease in weight of twins with a monochorionic monozygotic placentation, while dichorionic dizygotic twins continue to grow. Min et al. (2000) estimated growth in 1,831 twin pregnancies using ultrasound at 2-week intervals from 20 through 40 weeks' gestation. The weight difference between twins and singleton pregnancies at their respective 50th percentiles was 147 g (10 percent) at 30 weeks' gestation, 242 g (14 percent) at 32 weeks' gestation, 347 g (17 percent) at 34 weeks' gestation, 450 g (19 percent) at 36 weeks' gestation, 579 g (22 percent) at 38 weeks' gestation, and 772 g (27 percent) at 40 weeks' gestation.

Lastly, Glinianaia et al. (2000) reported on 690 triplets born in Norway from 1967 through 1995. The birth weight by gestational age curves of the triplets were almost identical to those of singleton and twin gestations before 30 weeks. From 31 weeks of gestation onward, the median birth weight of triplets consistently diverged from that of twins. At 38 and 39 weeks' gestation the difference reached 478 and 541 g, respectively, with a weight difference between twins and triplets of 650 g in the 10th percentile at 39 weeks.

In summary, the growth rate in multiple gestations is similar to growth rate in singleton gestations up to approximately 30 weeks' gestation. In the third trimester, there is a decrease in individual fetal growth, more so in triplets than in twins and may be related to placental function.

Fetal Body Composition

The human fetus at term has a significantly different body composition than most other mammalian species. At birth the human fetus has approximately 12-16 percent body fat. In contrast, laboratory animals have 1-2 percent body fat at birth (Widdowson, 1950). Theoretically, the accrual of fetal fat has two possible sources: one is from the transfer of free fatty acids from the mother, and the second is *de novo* synthesis of fatty acids from substrates such as glucose, lactate, and acetate provided by the mother (Girard and Ferre, 1982). Regardless of the substrate source, fetal insulin is required for the fetus to increase adipose tissue stores.

The remaining tissue in the human fetus is lean body mass or FFM, which consists primarily of glycogen, protein, and water. At birth the human fetus has approximately 40 g of glycogen, primarily in muscle and liver tissue (Girard and Ferre, 1982). The protein content of the term fetus is approximately 12.8 percent of total body weight, or 15 percent of FFM (i.e., about 500 g; Fomon et al., 1982; Spady, 1989). The remainder is water. In the human fetus at term, approximately 80 percent of FFM is water (Fomon et al., 1982). Temporal changes in fetal growth and body composition have been characterized using ultrasound. The human fetus at 28 weeks weighs approximately 1 kg. Over the next 12 weeks the fetus gains approximately 2.5 kg. Fetal fat tissue begins to accrue in the mid-second trimester. Into the third trimester, however, there is a decrease in FFM as a percentage of total body weight. Bernstein et al. (1997) reported that, although the rate of fetal FFM accretion appeared linear when taken in aggregate, the compartments of FFM changed differentially. Peripheral muscle growth accelerated, and head circumference decelerated in late gestation. Fetal fat deposition accelerated as a quadratic

function. Hence, fetal growth of FM and FFM follow unique patterns and offer an additional means to assess normal and abnormal growth.

The gold standard for estimating body composition is carcass analysis. Sparks (1984), in his review of the data on 169 carcass analyses of fetuses, concluded that the differences in FFM are less variable at each gestational age than the fat content As with GWG, the variation in fetal growth may be related to the fat content of the fetus, which may reflect the intrauterine environment, while the FFM may be more representative of genetic factors.

Koo et al. (2000) using DXA, found that among the 214 singletons studied, neonates whose birth weight was < 2,500 g had 6 to 14 percent body fat. Neonates whose birth weight was > 2,500 g had 8 to 20 percent body fat. The mean percentage of body fat for a 3,500-g infant was 16.2 percent. Using total body electrical conductivity, Catalano et al. (2003) reported that body fat was 10.4 ± 4.6 percent in 220 term healthy singleton neonates. The difference in results between the two studies primarily represents differences in methodologies.

Birth weight and neonatal body composition are related to changes in maternal body composition. Butte et al. (2003) used DXA to assess body composition in 63 term infants at 2 weeks of age and related these data to changes in maternal body composition measured using a multi-component model. Birth weight correlated positively with prepregnancy weight ($r = 0.34$), prepregnancy FM ($r = 0.32$), GWG ($r = 0.35$), net GWG ($r = 0.26$), rate of weight gain ($r = 0.28$), and gestational age ($r = 0.49$). Birth weight was correlated significantly with gestational gains in TBW ($r = 0.37$), TBK ($r = 0.35$), and FFM ($r = 0.39$), but not FM. Maternal FFM gains in the first, second, and third trimesters were shown by multiple regression to make independent contributions to birth weight. Maternal TBW gains during the second and third trimesters and maternal TBK gain in the third trimester were independent predictors of birth weight. Infant body composition at 2 weeks of age (FFM, FM, or percent FM) was not correlated with maternal body composition before or after pregnancy or with maternal gains in TBW, TBK, FFM, and FM during pregnancy.

As is true for birth weight, multiple factors are associated with alterations in fetal body composition. Some of these factors are genetic. For example, at birth, male fetuses have greater lean body mass than females, and as a consequence, females have a higher percentage of body fat (Catalano et al., 1995; Ibanez et al., 2008). Maternal factors that have the strongest effect on fetal growth and primarily affect fetal fat accretion include parity, GWG, and medical problems. Maternal parity is positively correlated with neonatal adiposity (Harvey et al., 2007). Birth weight is significantly greater in neonates of overweight and obese women than underweight or normal weight women because of increased FM, not FFM (Sewell et al., 2006; Hull et al., 2008). Maternal weight gain is associated with both increased fetal FFM and increased FM and is related to maternal pregravid BMI (Catalano and Ehrenberg, 2006). Maternal medical problems, such as gestational diabetes mellitus, are associated with an increase in birth weight again because of increased FM, and in the macrosomic neonate a relative decrease in FFM (Catalano et al., 2003; Durnwald et al., 2004). Environmental factors also affect fetal body composition (see Chapter 4). Maternal smoking has a negative effect on fetal growth on the order of 150 g, which primarily decreases fetal FFM (Lindsay et al., 1997). Increased altitude has been reported to be associated with a 339-g decrease in birth weight. Crown-head length was shown to be reduced by 1 cm although the sum of five skinfolds was 5 mm greater, in those born at high altitude compared to those born at sea level (Ballew and Haas, 1986). In their study of > 400 newborns using total body electrical conductivity, Catalano and Ehrenberg (2006) found that maternal

pregravid BMI had the strongest correlation with maternal weight gain and GDM, as a factor associated with fetal adiposity.

In summary, the human fetus has a high percentage of body fat (12-16 percent) at birth compared to most mammalian species. Fetal fat mass contributes the greatest percentage of variance in birth weight, is affected by the in utero environment, and is more strongly correlated with maternal pre-gravid BMI than GWG.

Amniotic Fluid

Amniotic fluid has four major sources of volume flow into and out of the amniotic sac in late gestation (Ross and Brace, 2001). The two major inflow sources are fetal urine and lung liquid secretions. The two major outflows are fetal swallowing and intra-membranous absorption. Brace and Wolf (1989) reported on a series of 705 published amniotic fluid volumes based on either direct collection or dye dilution techniques. At 8 weeks of gestation the volume increases at a rate of 10 mL per week, and at 13 weeks the volume increases to 25 mL per week. The maximal increase in amniotic fluid of 60 mL per week occurs at 21 weeks' gestation. The weekly volume increment then decreases and reaches zero at 33 weeks' gestation (i.e., the time at which maximal volume is reached). There is wide variation in the amount of amniotic fluid in a normal pregnancy. Decreased amniotic fluid (i.e., oligohydramnios) occurs in approximately 8.2 percent of pregnancies, and increased amniotic fluid (i.e., polyhydramnios) occurs in approximately 1.6 percent of pregnancies (Ross and Brace, 2001). Oligohydramnios may occur as a consequence of fetal renal obstruction or dysplasia and may be associated with fetal growth restriction. Polyhydramnios is associated with various fetal structural anomalies such as congenital esophageal atresia, fetal anemia, congenital infections, and maternal diabetes. Given the wide range of normal amniotic fluid volume at term, this compartment may affect maternal GWG by as much as 1 kg. Therefore, amniotic fluid volume is an important component of maternal weight gain.

MATERNAL PHYSIOLOGY

The unique physiologic, metabolic, and endocrine milieu of the pregnant woman is crucial to understanding the mechanisms underlying GWG. The pregnant woman undergoes dramatic physiologic changes in anticipation and in support of fetal growth. Many of the obligatory components of GWG (for example, TBW) are directly related to the alterations in maternal physiology necessary to grow and develop a healthy fetus and placenta.

Cardiovascular Changes

In early pregnancy, cardiac output increases about 30-50 percent as a result of an increase in heart rate—primarily stroke volume—and remains elevated until term (Hytten and Chamberlain, 1991). As pregnancy progresses, blood flow increases to the uterus, kidney, skin, and probably the alimentary tract. Arterial blood pressure may decrease in mid-pregnancy. This is a result of increased peripheral vasodilatation and in order to maintain perfusion this results in an increase in cardiac output and relatively small decreases in mid-gestational blood pressure. Venous blood pressure rises in the lower limbs due to mechanical and hydrostatic pressure in the pelvis, causing edema in the lower limbs. Because of these cardiovascular changes, it is possible to have reduced exercise tolerance and dyspnea.

Physiological changes in circulation during pregnancy are marked and variable (Gabbe et al., 1991; Hytten and Chamberlain, 1991). Plasma volume increases progressively to 50 percent by

30-34 weeks of gestation. Importantly, plasma volume expansion is correlated with clinical performance and birth weight. Poor plasma volume expansion is associated with a poorly growing fetus and poor reproductive performance. The increases in maternal plasma volume account for a significant portion of the increase in total body water during pregnancy.

Red blood cell mass also increases about 18 percent by term without iron supplementation and 30 percent with iron supplementation. Minute ventilation increases 30-40 percent by late pregnancy due to increased tidal volume. Oxygen consumption increases only 15-20 percent, resulting in an increase in alveolar and arterial P_{AO2} (partial pressure of oxygen) and a fall in P_{ACO2} (partial pressure of carbon dioxide) levels (Gabbe et al., 1991).

Renal Changes

Renal plasma flow increases 70 percent over pregravid levels by 16 weeks of gestation and is maintained until late pregnancy when it falls slightly (Gabbe et al., 1991). Glomerular filtration rate (GFR) increases early in pregnancy, up to 50 percent by term. As a result of the increased GFR, serum levels of urea and creatinine decline. Plasma osmolarity declines early in pregnancy due to a reduction in serum sodium and associated anions. There is a net accumulation of approximately 900-1,000 meq of sodium in the fetus, placenta, and intravascular and interstitial fluids. There is a large increase in tubular sodium reabsorption during pregnancy, promoted by increased aldosterone, estrogen, and deoxycorticosterone. Plasma renin activity, renin substrate, and angiotensin levels increase five- to tenfold above the pregravid values. The adaptations in maternal renal physiology during gestation are among the primary mechanisms accounting for the increase in plasma volume and hence total body water during gestation.

Endocrine Changes

The plasma concentration of corticosteroid-binding globulin (CBG) increases significantly, reflecting increased hepatic synthesis (Gabbe et al., 1991). Estrogen-induced increases in CBG lead to elevated plasma cortisol concentration; with a three-fold increase occurring by the end of the third trimester. The concentration of the metabolically active free cortisol also progressively increases through gestation due to increased production and decreased clearance. Adrenocorticotropic hormone (ACTH) level is suppressed during pregnancy due to the action of estrogen and progesterone. The plasma concentration of dehydroepiandrosterone sulfate (DHEAS) declines during pregnancy due to an increase in metabolic clearance by the placenta and maternal liver.

The renin-angiotensin system changes dramatically during pregnancy. The adrenal gland remains responsive to the trophic action of angiotensin II, even though a refractory effect of pressors to angiotensin II develops early in pregnancy. This provides a probable explanation for the expansion of plasma volume during pregnancy. The secretion of prolactin from the pituitary and uterine decidua increases steadily during pregnancy. In contrast, luteinizing hormone and follicle-stimulating hormone are suppressed to levels similar to the luteal phase of ovulation. Growth hormone secretion is inhibited presumably by placental growth hormone production.

In normal pregnancy, thyroxine-binding globulin concentration is increased and the circulating pool of extrathyroidal iodide is decreased due to increased renal clearance. These changes cause the thyroid to enlarge and to synthesize and secrete the thyroid hormones T_4 (thyroxine) and T_3 (triiodothyronine) more actively. Despite elevated total T_4 and T_3, the concentrations of active hormones (free T_4 and free T_3) are unchanged during normal pregnancy,

with the exception of a transient increase in the first trimester in some women (Gabbe et al., 1991; Glinoer, 2004).

Adipose tissue produces an array of adipokines known to have profound effects on metabolism and fertility, but their role in reproductive performance is yet to be fully understood. In addition to adipose tissue, leptin and its receptor, TNF-α, and resistin also are expressed in the placenta (Mitchell et al., 2005). Serum adiponectin was found to be lower in the third trimester and this correlates with a decrease in insulin sensitivity (Catalano et al., 2006). Increases in maternal fat mass most likely are related to the decreases in circulating adiponectin concentrations.

Metabolic Changes

Many of the metabolic adjustments of pregnancy are well established in early pregnancy when fetal nutrient demands are still minor. Minimal nutrient balances are usually positive, reflecting the anabolic state of the fetus and the mother. In the absence of nausea or "morning sickness," most women experience an increase in appetite in the beginning of pregnancy (Gabbe et al., 1991). Several gastrointestinal changes occur during pregnancy, including decreased tone and motility of the stomach, reduced gastric acid secretion, delayed gastric emptying, and increased gastric mucous secretion as a function of increased progesterone. Motility of small intestine is also reduced during gestation; however, except for enhanced iron absorption, nutrient absorption is unchanged. These physiologic changes may affect the pattern of gestational weight gain in early gestation.

Changes in protein and nitrogen metabolism occur in early pregnancy, presumably in response to pregnancy-related hormones (Kalhan, 2000). Serum total α-amino nitrogen deceases, as does the rate of urea synthesis and the rate of transamination of branched-chain amino acids, which are aimed at conservation of nitrogen and protein accretion in pregnancy. Protein turnover on a weight basis, however, does not change (Kalhan, 2000). Serum total protein and albumin fall progressively and by term are 30 percent lower than non-pregnant values (Hytten and Chamberlain, 1991). The concentrations of binding proteins for corticosteroids, sex steroids, thyroid hormones, and vitamin D are also increased.

Changes in carbohydrate and lipid metabolism occur during pregnancy to ensure a continuous supply of nutrients to the growing fetus (Butte, 2000). In early pregnancy, glucose tolerance is normal or improved slightly, and peripheral (muscle) sensitivity to insulin and hepatic basal glucose production are normal or increase by as much as 15 percent (Catalano et al., 1991; 1992; 1993). As pregnancy advances, nutrient-stimulated insulin responses increase progressively despite only minor deterioration in glucose tolerance, which is consistent with progressive insulin resistance (Kühl, 1991). In late pregnancy, insulin action is 50-60 percent lower than in non-pregnant state (Ryan et al., 1985; Buchanan et al., 1990; Catalano et al., 1991; 1992; 1993). By the third trimester, basal and 24-hour mean insulin concentrations may double (Lesser and Carpenter, 1994). The first and second phases of insulin release are increased threefold by late pregnancy (Catalano et al., 1991). These alterations in maternal insulin sensitivity affect not only glucose metabolism but also lipid metabolism resulting in a decreased ability of insulin to suppress lipolysis (Catalano et al., 2002).

The return of normal physiologic function after delivery may occur rapidly over a matter of days—for example, an improvement in insulin sensitivity (Ryan et al., 1985)—or over a matter of weeks—for example, a return to a normal non-pregnant renal glomerular filtration rate (Sims and Krantz, 1958). The alterations in maternal physiology are mediated by placental factors as

evidenced by the significant increase in maternal insulin sensitivity within days after delivery of the fetus and placenta. The alterations in maternal metabolism have generally been ascribed to placental hormones such as hPL, progesterone, and estrogen (Kalkhoff et al., 1979; Ryan and Enns, 1988). Recently, Kirwan et al. (2002) have reported that circulating cytokines (i.e., TNF-α concentration) were inversely correlated with insulin sensitivity.

The metabolic changes in insulin sensitivity during pregnancy are modified by inflammatory factors (Friedman et al. 1999; 2008). In women with normal glucose tolerance during pregnancy who lose significant weight postpartum, there is a return to normal metabolic function. However, in women with GDM, particularly if there is no decrease in postpartum weight or adiposity, there remains a significant inflammatory milieu that results in chronic insulin resistance, increasing the risk of diabetes and the metabolic syndrome.

Depending on the pregravid insulin sensitivity status of the woman, insulin sensitivity may increase or decrease during early pregnancy. In the very insulin-sensitive woman, insulin sensitivity most often decreases and is accompanied by an increase in adipose tissue and basal metabolic rate (Catalano et al., 1998). In contrast, in the more insulin-resistant woman (e.g., those who are obese or have GDM), insulin sensitivity often increases and is accompanied by a decrease in basal metabolic rate and potential loss of adipose tissue (Okereke et al., 2004) (Figure 3-8). These physiologic changes may help to explain in part the relative decrease in weight gain in obese insulin-resistant women compared to the greater increases in weight in lean insulin-sensitive women in early gestation. The placental factors related to these alterations in insulin sensitivity, energy expenditure, and adipose tissue are not well understood relative to metabolic alterations in late pregnancy. Although there is a significant increase in maternal leptin concentrations in early pregnancy (Hauguel-de Mouzon et al., 2006), most likely related to placental production, the increased leptin concentrations do not appear to be associated differently with energy expenditure or fat accretion between lean and obese women.
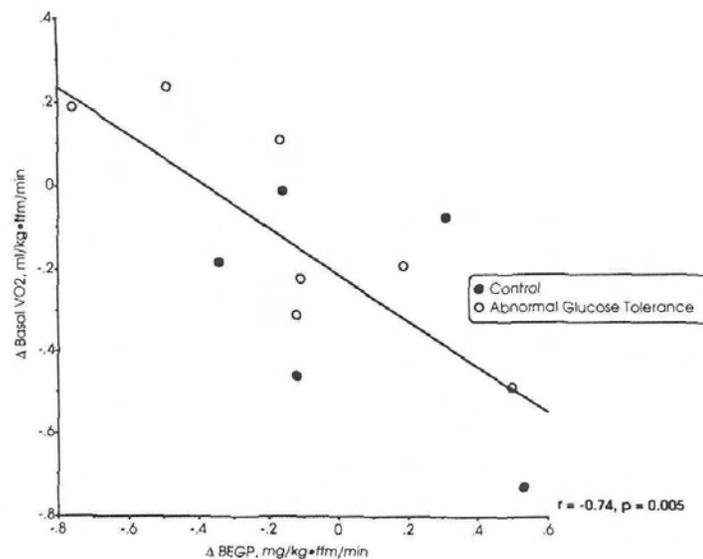
FIGURE 3-8 Alterations in basal VO_2 per kilogram of FFM per minute in relation to changes in basal endogenous glucose production
SOURCE: Catalano et al., 1998. Reprinted from *American Journal of Obstetrics and Gynecology*, Volume 179, Issue 1, Catalano P. M., N. M. Roman-Drago, S. B. Amini, and E. A. Sims, Longitudinal changes in body composition and energy balance in lean women with normal and abnormal glucose tolerance during pregnancy, pages 156-165. Copyright (2008), with permission from Elsevier.

FETAL-PLACENTAL PHYSIOLOGY

Transport Function

Three primary functions of the placenta are to serve as a barrier or filter, to transport substances between maternal and fetal circulation, and to cover a large spectrum of endocrine activity. Changes in fetal growth rate have been shown to result from effects related to maternal homeostasis and associated changes in placental structure or function in both normal and non-normal pregnancies (Thame et al., 2004; Desoye and Kaufman, 2005; MacLaughlin et al., 2005; Swanson and Bewtra, 2008). Changes in the maternal environment have been shown to have an impact on specific steps of placental transport of the major energy substrates (i.e., glucose, lipids, amino acids; Hauguel de-Mouzon and Shafrir, 2001). For example, maternal diabetes results in increased availability of glucose, which is transported directly across the placenta for fetal utilization (Baumann et al., 2002). In contrast to glucose, which is transported along a concentration gradient, regulation of lipid transfer from maternal to fetal circulation is more complex. The placenta has the capacity to regulate the uptake, storage, and release of maternal lipids through multiple regulatory mechanisms and thus control fetal plasma lipid composition (Haggarty, 2002). Changes in the maternal environment may also modify placental endocrine function. For example, changes in maternal circulating cholesterol affect lipid metabolism in human term placenta (Marseille-Tremblay et al., 2008). Higher cholesterol uptake may subsequently impact steroidogenesis because cholesterol is the primary precursor for progesterone synthesis (Pasqualini, 2005).

Interaction of Maternal and Placental Metabolism

The question of whether or how placental function(s) may have an impact on maternal metabolism has received little attention. Besides the uterus, the feto-placental unit, intra- and extravascular fluids, and mammary gland, most of the weight gain that occurs over the course of a pregnancy lies in changes in maternal adipose tissue mass. In this context, the placental contribution to weight changes through the action of systemic factors that control the pathways of lipid synthesis and storage within the adipocyte must be taken into consideration. The placenta does not release adipogenic substrates into the maternal circulation. Hence, the most probable routes by which placental function would alter the regulation of lipogenic pathways are modulation of maternal insulin sensitivity and inflammation, as discussed previously.

Placental Hormone Production

Sex steroids and hPL, which best reflect the endocrine function of the placenta, have been primary candidates for regulation of maternal insulin sensitivity (Leturque et al., 1989). Although estrogens certainly have insulin sensitizing properties, the action of progesterone is clearly linked to diminishing insulin sensitivity and weight gain (Kalkhoff, 1982; Gonzalez et al., 2000; Xiang et al., 2007). Hence, an imbalance in placental progesterone production may be a contributing factor to maternal weight regulation. Human placental lactogen is the most abundant polypeptide hormone produced by the placenta with strong anabolic and lipolytic properties. Inasmuch as hPL enhances maternal nitrogen accrual, this process could possibly contribute to weight regulation and that possibility has been the subject of speculation (Florini et al., 1966). However, the lipolytic action of hPL on adipose tissue has received more experimental support. One consequence of the lipolytic effect of hPL is the re-orientation of maternal metabolism

toward lipid rather than glucose utilization to favor glucose sparing for the fetus. Interestingly the ability of hPL to mediate pregnancy-induced insulin resistance, as suggested by Grumbach et al. (1968) was never fully established. Thus, the exact contribution of hPL to the regulation of maternal homeostasis remains to be established. Further, whether hPL synthesis is modified in pathologic pregnancies also has not been confirmed (Stewart et al., 1989). Just as occurs in white adipose tissue, the placenta synthesizes a large array of cytokines (Hauguel-de Mouzon and Guerre-Millo, 2006; Desoye and Hauguel-de Mouzon, 2007). All placenta-derived cytokines except leptin, which is released in large amounts in maternal circulation, likely act in either a paracrine or autocrine manner. Obesity and diabetes are associated with increased placental leptin production and maternal hyperleptinemia, but the consequences of high systemic leptin are unclear at this time (Hauguel-de Mouzon et al., 2006). Resistance to the central satiety effect of leptin during pregnancy as a possible consequence has been considered (Grattan et al., 2007).

Another potential contribution of the placenta to the regulation of maternal metabolism and subsequent alteration in maternal weight gain is systemic inflammatory priming by circulating syncytiotrophoblast microparticles (STBMs). Syncytiotrophoblast microparticles bind to monocytes and stimulate the production of inflammatory cytokines (Germain et al., 2007; Rovere-Querini et al., 2007). In addition to local placental inflammation, these microparticles are potential contributors to the altered systemic inflammatory response in pregnancy (Challier et al., 2008). Consequently, increased macrophage infiltration into maternal adipose tissue in combination with increased insulin resistance may contribute to the regulation of adipose mass during pregnancy (Xu et al., 2003).

Taken together there is little direct evidence that placental hormonal factors directly regulate maternal homeostasis and particularly quantitative changes in adipose tissue mass. The role of progesterone, hPL, and leptin in maternal insulin sensitivity and energy homeostasis remains to be established, but inflammatory mechanisms are novel potential regulatory pathways that will also have to be examined.

ABNORMAL MATERNAL METABOLISM

Weight Loss During Pregnancy

Weight loss or no GWG as a result of dietary caloric insufficiency will induce maternal hormonal and metabolic responses. Given the obligatory weight gain in the maternal tissues (uterus, breast, blood), and the fetal-placental unit, a weight gain less than ~7.5-8.5 kg would imply mobilization of maternal adipose tissue and possibly protein stores. Metabolic profile, dietary patterns, and eating behaviors of pregnant women undergoing weight loss or no weight gain have not been studied, but expected changes in fuel homeostasis can be deduced from studies conducted in pregnant women subjected to fasting.

Fasting in Pregnant Women

During 84 hours of fasting before elective termination of pregnancy at 16-20 weeks' gestation, ketonemia, increased urinary nitrogen excretion, and exaggerated reduction in gluconeogenic amino acids were detected in pregnant women (Felig, 1973). Glucose and insulin were lower, and acetoacetate and β-hydroxybutyrate were two to three times higher, in pregnant than non-pregnant women at 12-60 hours but not 84 hours (Felig and Lynch, 1970). Weight loss averaged 3.1 kg in non-pregnant women and 3.2 kg in pregnant women. Metzger et al. (1982)

subjected lean ($n = 11$) and obese ($n = 10$) pregnant women and lean ($n = 14$) and obese ($n = 13$) non-pregnant controls to an 18-hour fast. At 12 hours, there were no significant differences between groups, but by 16 and 18 hours, substantial increases in FFA and β-hydroxybutyrate (βHA), which were inversely correlated with glucose, were seen in the pregnant women. There was a significant difference in FFA concentrations between obese and lean pregnant women only at 16 hrs of fasting. In contrast there were no significant differences in BHA levels at any time point between lean and obese women.

Ketonuria and Ketonemia in Pregnancy

As first described by Freinkel (1980), pregnancy can be considered a condition of "accelerated starvation" because of the changes in maternal metabolism. The accelerated starvation occurs because of the increase in insulin resistance, particularly related to lipid metabolism, as discussed previously. As a result, there is an increased risk of developing ketonuria and ketonemia in pregnancy even among women with normal glucose tolerance. Chez and Curcio (1987) reported that eight of nine women with clinically normal pregnancies developed ketonuria at various times during their pregnancy. Gin et al. (2006) measured capillary blood ketones and βHA using a portable capillary meter in women with normal glucose tolerance (controls) and those with GDM three times a day from 25 to 37 weeks' gestation. Fasting ketonuria was strongly correlated with ketonemia in controls but not in women with GDM. There was a chronic increase in ketonemia levels in 12 percent of the controls and 47 percent of the women with GDM.

Pregnant women develop ketonemia much earlier than non-pregnant women during prolonged fasting because of the accelerated starvation. Felig (1973) studied women between 16 and 22 weeks' gestation who elected termination of pregnancy and were willing to undergo prolonged fasting and compared them with a non-pregnant control group. After an overnight fast of at least 12 hours and for the first 36 to 60 hours of starvation, blood βHA and acetoacetate concentrations were two- to threefold higher in the pregnant group than in the non-pregnant group. The increase in lipolysis among the pregnant women was attributed to increases in hPL. The ketone concentrations in maternal blood were equivalent to those in amniotic fluid and were fortyfold above levels in fed subjects. The assumption is that amniotic fluid levels represent maternal-to-fetal transport. Felig (1973) also hypothesized that ketones become an important metabolic fuel for the fetal brain once glucose concentrations decrease, because the human fetal brain has the enzymes necessary for ketone oxidation.

Coetzee et al. (1980) reported that 19 percent of obese, insulin-dependent diabetic women on 1,000-kilocalorie (kcal) diets developed ketonuria. In contrast, in diabetic women eating higher-energy diets, only 14 percent had ketonuria, and in pregnant non-diabetic women, only 7 percent developed ketonuria. Measurement of blood ketones was never positive if the urine measure was ≤ 2 plus and acetoacetate levels were always less than 1 mmol/L. There was no difference in neonatal outcomes among the three groups.

In summary, pregnant women are more likely to develop elevated measures of blood βHA and acetoacetate during prolonged fasting (after 12-18 hours) as a result of the metabolic and hormonal changes in pregnancy. Pregnant women with diabetes are more likely to develop elevated blood ketones than women with normal glucose tolerance. Nevertheless, a substantial proportion of pregnant women with normal glucose tolerance have elevated blood ketone levels some time during gestation. Although the evidence is based on associations and does not demonstrate causality, caution should be exercised regarding weight loss during pregnancy or no

GWG given the propensity to develop ketonemia, increased urinary nitrogen excretion, and decreased gluconeogenic amino acids and the potential to adversely impact the neurocognitive development of the offspring. There are significant consequences of caloric insufficiency, low GWG, and poorly controlled diabetes for the child and these are discussed in Chapter 6.

FINDINGS AND RECOMMENDATIONS

Findings

1. Total GWG in normal-term pregnancies displays considerable variability; nevertheless, some generalizations can be made regarding mean tendencies and patterns of GWG:

   a. A consistent inverse relationship is observed between GWG and pregravid BMI category;
   b. Mean GWG ranges from 10.0 to 16.7 kg in normal weight adults and 14.6 to 18.0 kg in adolescents giving birth to term infants;
   c. The pattern of GWG is most commonly described as sigmoidal, with mean weight gains higher in the second than the third trimester across BMI categories, except for obese women; and
   d. Lower GWGs, on the order of 11 kg and 9 kg, have been confirmed in large cohorts of obese women and very obese women, respectively.

2. The committee relied on observational GWG data of women giving birth to twins born at 37-42 weeks of gestation and with an average twin birth weight ≥ 2,500 g:

   a. Mean GWG of normal weight women with twin births ranged from 15.5 to 21.8 kg;
   b. GWG for triplets ranged from 20.5 to 23.0 kg at 32-34 weeks and for quadruplets from 20.8 to 31.0 kg at 31-32 weeks; and

3. When stratified by WHO prepregnancy BMI categories sample sizes from data on twins was insufficient to designate a value for underweight women with pregravid BMI <18.5 kg/m^2.
4. The extent to which fat mass accretion is critical rather than incidental to pregnancy is not clear, but unrestrained weight gain leads to postpartum weight retention.
5. Placental size is strongly correlated with fetal growth, averaging approximately 500 g in singleton pregnancies.
6. Amniotic fluid weight may affect maternal gestational weight gain by as much as 1 kg at term.
7. Gestational gains in weight, total body water, total body potassium, protein, and FFM, but not FM, are positively correlated with birth weight across all BMI categories.
8. Poor plasma volume expansion is associated with a poorly growing fetus and poor reproductive performance.
9. Pregnancy is a condition of systemic inflammation that also influences maternal and fetal nutrient utilization.
10. During prolonged fasting, i.e. 16-18 hours, pregnant women are more likely to develop

elevated measures of blood βHA and acetoacetate. In women with diabetes, plasma FFA and βHA were inversely associated with intellectual development of the offspring at 3-5 years of age. Therefore, caution is warranted regarding periods of prolonged fasting and weight loss during pregnancy and the development of ketonuria.

Research Recommendations

Research Recommendation 3-1: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies in all classes of obese women, stratified by the severity of obesity, on the determinants and impact of GWG, pattern of weight gain and its composition on maternal and child outcomes.

Research Recommendation 3-2: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies on the eating behaviors, patterns of dietary intake and physical activity, and metabolic profiles of pregnant women, especially obese women, who experience low gain or weight loss during pregnancy. In addition, the committee recommends that researchers conduct studies on the effects of weight loss or low GWG, including periods of prolonged fasting and the development of ketonuria/ketonemia during gestation, on growth and on development and long-term neurocognitive function in the offspring.

Areas for Additional Investigation

The committee identified the following areas for further investigation to support its research recommendation. The research community should conduct studies on:

- Potential effects of maternal weight loss on components of maternal body composition for both the mother and the fetus, particularly in obese women; and
- Mechanisms by which placental hormonal factors and systemic inflammation impact the regulation of maternal metabolism during pregnancy.

REFERENCES

Abramovich D. R. 1969. The weight of placenta and membranes in early pregnancy. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 76(6): 523-526.

Abrams B. F. and R. K. Laros, Jr. 1986. Prepregnancy weight, weight gain, and birth weight. *American Journal of Obstetrics and Gynecology* 154(3): 503-509.

Abrams B. and S. Selvin. 1995. Maternal weight gain pattern and birth weight. *Obstetrics and Gynecology* 86(2): 163-169.

Alexander G. 1962. Energy metabolism in the starved new-born lamb. *Australian Journal of Agricultural Research* 13(1): 144-164.

Ananth C. V., A. M. Vintzileos, S. Shen-Schwarz, J. C. Smulian and Y. L. Lai. 1998. Standards of birth weight in twin gestations stratified by placental chorionicity. *Obstetrics and Gynecology* 91(6): 917-924.

Ananth C. V. and S. W. Wen. 2002. Trends in fetal growth among singleton gestations in the United States and Canada, 1985 through 1998. *Seminars in Perinatology* 26(4): 260-267.

Archie J. G., J. S. Collins and R. R. Lebel. 2006. Quantitative standards for fetal and neonatal autopsy. *American Journal of Clinical Pathology* 126(2): 256-265.

Ausman L. M., E. M. Powell, D. L. Mercado, K. W. Samonds, M. Lozy and D. L. Gallina. 1982. Growth and developmental body composition of the cebus monkey. *American Journal of Primatology* 3(1-4): 211-227.

Ballew C. and J. D. Haas. 1986. Altitude differences in body composition among Bolivian newborns. *Human Biology* 58(6): 871-882.

Baumann M. U., S. Deborde and N. P. Illsley. 2002. Placental glucose transfer and fetal growth. *Endocrine* 19(1): 13-22.

Bernstein I. M., M. I. Goran, S. B. Amini and P. M. Catalano. 1997. Differential growth of fetal tissues during the second half of pregnancy. *American Journal of Obstetrics and Gynecology* 176(1 Pt 1): 28-32.

Bianco A. T., S. W. Smilen, Y. Davis, S. Lopez, R. Lapinski and C. J. Lockwood. 1998. Pregnancy outcome and weight gain recommendations for the morbidly obese woman. *Obstetrics and Gynecology* 91(1): 97-102.

Bleker O. P. and H. J. Hoogland. 1981. Short review: ultrasound in the estimation of human intrauterine placental growth. *Placenta* 2(3): 275-278.

Blickstein I. 2002. Normal and abnormal growth of multiples. *Seminars in Neonatology* 7(3): 177-185.

Brace R. A. and E. J. Wolf. 1989. Normal amniotic fluid volume changes throughout pregnancy. *American Journal of Obstetrics and Gynecology* 161(2): 382-388.

Brown J. E. and P. T. Schloesser. 1990. Prepregnancy weight status, prenatal weight gain, and the outcome of term twin gestations. *American Journal of Obstetrics and Gynecology* 162(1): 182-186.

Buchanan T. A., B. E. Metzger, N. Freinkel and R. N. Bergman. 1990. Insulin sensitivity and B-cell responsiveness to glucose during late pregnancy in lean and moderately obese women with normal glucose tolerance or mild gestational diabetes. *American Journal of Obstetrics and Gynecology* 162(4): 1008-1014.

Butte N. F. 2000. Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. *American Journal of Clinical Nutrition* 71(5 Suppl): 1256S-1261S.

Butte N. F., K. J. Ellis, W. W. Wong, J. M. Hopkinson and E. O. Smith. 2003. Composition of gestational weight gain impacts maternal fat retention and infant birth weight. *American Journal of Obstetrics and Gynecology* 189(5): 1423-1432.

Carmichael S., B. Abrams and S. Selvin. 1997. The association of pattern of maternal weight gain with length of gestation and risk of spontaneous preterm delivery. *Paediatric and Perinatal Epidemiology* 11(4): 392-406.

Catalano P. M., E. D. Tyzbir, N. M. Roman, S. B. Amini and E. A. Sims. 1991. Longitudinal changes in

insulin release and insulin resistance in nonobese pregnant women. *American Journal of Obstetrics and Gynecology* 165(6 Pt 1): 1667-1672.

Catalano P. M., E. D. Tyzbir, R. R. Wolfe, N. M. Roman, S. B. Amini and E. A. Sims. 1992. Longitudinal changes in basal hepatic glucose production and suppression during insulin infusion in normal pregnant women. *American Journal of Obstetrics and Gynecology* 167(4 Pt 1): 913-919.

Catalano P. M., E. D. Tyzbir, R. R. Wolfe, J. Calles, N. M. Roman, S. B. Amini and E. A. Sims. 1993. Carbohydrate metabolism during pregnancy in control subjects and women with gestational diabetes. *American Journal of Physiology* 264(1 Pt 1): E60-67.

Catalano P. M., N. M. Drago and S. B. Amini. 1995. Factors affecting fetal growth and body composition. *American Journal of Obstetrics and Gynecology* 172(5): 1459-1463.

Catalano P. M., N. M. Roman-Drago, S. B. Amini and E. A. Sims. 1998. Longitudinal changes in body composition and energy balance in lean women with normal and abnormal glucose tolerance during pregnancy. *American Journal of Obstetrics and Gynecology* 179(1): 156-165.

Catalano P. M., S. E. Nizielski, J. Shao, L. Preston, L. Qiao and J. E. Friedman. 2002. Downregulated IRS-1 and PPARgamma in obese women with gestational diabetes: relationship to FFA during pregnancy. *American Journal of Physiology Endocrinology and Metabolism* 282(3): E522-533.

Catalano P. M., A. Thomas, L. Huston-Presley and S. B. Amini. 2003. Increased fetal adiposity: a very sensitive marker of abnormal in utero development. *American Journal of Obstetrics and Gynecology* 189(6): 1698-1704.

Catalano P. M. and H. M. Ehrenberg. 2006. The short- and long-term implications of maternal obesity on the mother and her offspring. *British Journal of Obstetrics and Gynaecology* 113(10): 1126-1133.

Catalano P. M., M. Hoegh, J. Minium, L. Huston-Presley, S. Bernard, S. Kalhan and S. Hauguel-De Mouzon. 2006. Adiponectin in human pregnancy: implications for regulation of glucose and lipid metabolism. *Diabetologia* 49(7): 1677-1685.

Catalano P. M., A. Thomas, L. Huston-Presley and S. B. Amini. 2007. Phenotype of infants of mothers with gestational diabetes. *Diabetes Care* 30 Suppl 2: S156-160.

Cedergren M. 2006. Effects of gestational weight gain and body mass index on obstetric outcome in Sweden. *International Journal of Gynaecology and Obstetrics* 93(3): 269-274.

Challier J. C., S. Basu, T. Bintein, J. Minium, K. Hotmire, P. M. Catalano and S. Hauguel-de Mouzon. 2008. Obesity in pregnancy stimulates macrophage accumulation and inflammation in the placenta. *Placenta* 29(3): 274-281.

Chez R. A. and F. D. Curcio, 3rd. 1987. Ketonuria in normal pregnancy. *Obstetrics and Gynecology* 69(2): 272-274.

Claesson I. M., G. Sydsjo, J. Brynhildsen, M. Cedergren, A. Jeppsson, F. Nystrom, A. Sydsjo and A. Josefsson. 2008. Weight gain restriction for obese pregnant women: a case-control intervention study. *British Journal of Obstetrics and Gynaecology* 115(1): 44-50.

Coetzee E. J., W. P. Jackson and P. A. Berman. 1980. Ketonuria in pregnancy--with special reference to calorie-restricted food intake in obese diabetics. *Diabetes* 29(3): 177-181.

Desoye G. and P. Kaufman. 2005. The human placenta in diabetes. In *Diabetology of Pregnancy (Frontiers in Diabetes), Vol 17*. J. Djelmis, G. Desoye and M. Ivasinevic. Basel, Switzerland, Karger**:** Pp. 94-109.

Desoye G. and S. Hauguel-de Mouzon. 2007. The human placenta in gestational diabetes mellitus. The insulin and cytokine network. *Diabetes Care* 30 Suppl 2: S120-126.

Diamant Y. Z., B. E. Metzger, N. Freinkel and E. Shafrir. 1982. Placental lipid and glycogen content in human and experimental diabetes mellitus. *American Journal of Obstetrics and Gynecology* 144(1): 5-11.

Durnwald C., L. Huston-Presley, S. Amini and P. Catalano. 2004. Evaluation of body composition of large-for-gestational-age infants of women with gestational diabetes mellitus compared with women with normal glucose tolerance levels. *American Journal of Obstetrics and Gynecology* 191(3): 804-808.

Eddib A., J. Penvose-Yi, J. A. Shelton and J. Yeh. 2007. Triplet gestation outcomes in relation to maternal prepregnancy body mass index and weight gain. *Journal of Maternal-Fetal & Neonatal Medicine* 20(7): 515-519.

Emerson K., Jr., E. L. Poindexter and M. Kothari. 1975. Changes in total body composition during normal and diabetic pregnancy. Relation to oxygen consumption. *Obstetrics and Gynecology* 45(5): 505-511.

Felig P. and V. Lynch. 1970. [Starvation in human pregnancy: hypoglycemia, hypoinsulinemia, and hyperketonemia.]. *Science* 170(961): 990-992.

Felig P. 1973. Maternal and fetal fuel homeostasis in human pregnancy. *American Journal of Clinical Nutrition* 26(9): 998-1005.

Florini J. R., G. Tonelli, C. B. Breuer, J. Coppola, I. Ringler and P. H. Bell. 1966. Characterization and biological effects of purified placental protein (human). *Endocrinology* 79(4): 692-708.

Fomon S. J., F. Haschke, E. E. Ziegler and S. E. Nelson. 1982. Body composition of reference children from birth to age 10 years. *American Journal of Clinical Nutrition* 35(5 Suppl): 1169-1175.

Forsum E., A. Sadurskis and J. Wager. 1988. Resting metabolic rate and body composition of healthy Swedish women during pregnancy. *American Journal of Clinical Nutrition* 47(6): 942-947.

Freinkel N. 1980. Banting Lecture 1980. Of pregnancy and progeny. *Diabetes* 29(12): 1023-1035.

Friedman J. E., T. Ishizuka, J. Shao, L. Huston, T. Highman and P. Catalano. 1999. Impaired glucose transport and insulin receptor tyrosine phosphorylation in skeletal muscle from obese women with gestational diabetes. *Diabetes* 48(9): 1807-1814.

Friedman J. E., J. P. Kirwan, M. Jing, L. Presley and P. M. Catalano. 2008. Increased skeletal muscle tumor necrosis factor-alpha and impaired insulin signaling persist in obese women with gestational diabetes mellitus 1 year postpartum. *Diabetes* 57(3): 606-613.

Fuller N. J., S. A. Jebb, M. A. Laskey, W. A. Coward and M. Elia. 1992. Four-component model for the assessment of body composition in humans: comparison with alternative methods, and evaluation of the density and hydration of fat-free mass. *Clinical Science (London)* 82(6): 687-693.

Gabbe S., J. Niebyl and J. Simpson, Eds. (1991). *Obstetrics Normal & Problem Pregnancies*. New York, Churchill Livingstone.

Garrow J. S. and S. F. Hawes. 1971. The relationship of the size and composition of the human placenta to its functional capacity. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 78(1): 22-28.

Germain S. J., G. P. Sacks, S. R. Sooranna, I. L. Sargent and C. W. Redman. 2007. Systemic inflammatory priming in normal pregnancy and preeclampsia: the role of circulating syncytiotrophoblast microparticles. *Journal of Immunology* 178(9): 5949-5956.

Gielen M., P. J. Lindsey, C. Derom, R. J. Loos, R. Derom, J. G. Nijhuis and R. Vlietinck. 2007. Twin birth weight standards. *Neonatology* 92(3): 164-173.

Gin H., A. Vambergue, C. Vasseur, V. Rigalleau, P. Dufour, A. Roques, M. Romon, D. Millet, P. Hincker and P. Fontaine. 2006. Blood ketone monitoring: a comparison between gestational diabetes and non-diabetic pregnant women. *Diabetes and Metabolism* 32(6): 592-597.

Girard J. and P. Ferre. 1982. Metabolic and hormonal changes around birth. In *Biochemical Development of the Fetus and Neonate*. C. T. Jones. New York, Elsevier Biomedical Press**:** Pp. 517.

Glinianaia S. V., R. Skjaerven and P. Magnus. 2000. Birthweight percentiles by gestational age in multiple births. A population-based study of Norwegian twins and triplets. *Acta Obstetricia et Gynecologica Scandinavica* 79(6): 450-458.

Glinoer D. 2004. Increased TBG during pregnancy and increased hormonal requirements. *Thyroid* 14(6): 479-480; author reply 480-471.

Gonzalez C., A. Alonso, N. Alvarez, F. Diaz, M. Martinez, S. Fernandez and A. M. Patterson. 2000. Role of 17beta-estradiol and/or progesterone on insulin sensitivity in the rat: implications during pregnancy. *Journal of Endocrinology* 166(2): 283-291.

Grattan D. R., S. R. Ladyman and R. A. Augustine. 2007. Hormonal induction of leptin resistance during pregnancy. *Physiology & Behavior* 91(4): 366-374.

Grumbach M. M., S. L. Kaplan, J. J. Sciarra and I. M. Burr. 1968. Chorionic growth hormone-prolactin (CGP): secretion, disposition, biologic activity in man, and postulated function as the "growth hormone" of the 2d half of pregnancy. *Annals of the New York Academy of Sciences* 148(2): 501-531.

Gunderson E. P., B. Sternfeld, M. F. Wellons, R. A. Whitmer, V. Chiang, C. P. Quesenberry, Jr., C. E. Lewis and S. Sidney. 2008. Childbearing may increase visceral adipose tissue independent of overall increase in body fat. *Obesity (Silver Spring)* 16(5): 1078-1084.

Haggarty P. 2002. Placental regulation of fatty acid delivery and its effect on fetal growth--a review. *Placenta* 23 Suppl A: S28-38.

Harvey N. C., J. R. Poole, M. K. Javaid, E. M. Dennison, S. Robinson, H. M. Inskip, K. M. Godfrey, C. Cooper and A. A. Sayer. 2007. Parental determinants of neonatal body composition. *Journal of Clinical Endocrinology and Metabolism* 92(2): 523-526.

Hauguel-de Mouzon S. and E. Shafrir. 2001. Carbohydrate and fat metabolism and related hormonal regulation in normal and diabetic placenta. *Placenta* 22(7): 619-627.

Hauguel-de Mouzon S. and M. Guerre-Millo. 2006. The placenta cytokine network and inflammatory signals. *Placenta* 27(8): 794-798.

Hauguel-de Mouzon S., J. Lepercq and P. Catalano. 2006. The known and unknown of leptin in pregnancy. *American Journal of Obstetrics and Gynecology* 194(6): 1537-1545.

Hediger M. L., T. O. Scholl, I. G. Ances, D. H. Belsky and R. W. Salmon. 1990. Rate and amount of weight gain during adolescent pregnancy: associations with maternal weight-for-height and birth weight. *American Journal of Clinical Nutrition* 52(5): 793-799.

Hickey C. A., S. P. Cliver, S. F. McNeal, H. J. Hoffman and R. L. Goldenberg. 1995. Prenatal weight gain patterns and spontaneous preterm birth among nonobese black and white women. *Obstetrics and Gynecology* 85(6): 909-914.

Hopkinson J. M., N. F. Butte, K. J. Ellis, W. W. Wong, M. R. Puyau and E. O. Smith. 1997. Body fat estimation in late pregnancy and early postpartum: comparison of two-, three-, and four-component models. *American Journal of Clinical Nutrition* 65(2): 432-438.

Hull H. R., M. K. Dinger, A. W. Knehans, D. M. Thompson and D. A. Fields. 2008. Impact of maternal body mass index on neonate birthweight and body composition. *American Journal of Obstetrics and Gynecology* 198(4): 416 e411-416.

Hytten F. and G. Chamberlain. 1991. *Clinical Physiology in Obstetrics*. Oxford: Blackwell Scientific Publications.

Ibanez L., G. Sebastiani, A. Lopez-Bermejo, M. Diaz, M. D. Gomez-Roig and F. de Zegher. 2008. Gender specificity of body adiposity and circulating adiponectin, visfatin, insulin, and insulin growth factor-I at term birth: relation to prenatal growth. *Journal of Clinical Endocrinology and Metabolism* 93(7): 2774-2778.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

Kalhan S. C. 2000. Protein metabolism in pregnancy. *American Journal of Clinical Nutrition* 71(5 Suppl): 1249S-1255S.

Kalkhoff R., A. Kissebah and H. Kim. 1979. Carbohydrate and lipid metabolism during normal pregnancy: Relationship to gestational hormone action. In *The Diabetic Pregnancy: A Perinatal Perspective*. I. Merkatz and P. Adam. New York, Grune & Straton**:** Pp. Pp. 3-21.

Kalkhoff R. K. 1982. Metabolic effects of progesterone. *American Journal of Obstetrics and Gynecology* 142(6 Pt 2): 735-738.

Kiel D. W., E. A. Dodson, R. Artal, T. K. Boehmer and T. L. Leet. 2007. Gestational weight gain and pregnancy outcomes in obese women: how much is enough? *Obstetrics and Gynecology* 110(4): 752-758.

Kierans W. J., K. S. Joseph, Z. C. Luo, R. Platt, R. Wilkins and M. S. Kramer. 2008. Does one size fit all? The case for ethnic-specific standards of fetal growth. *BMC Pregnancy and Childbirth* 8(1): 1.

King J. C., D. H. Calloway and S. Margen. 1973. Nitrogen retention, total body 40 K and weight gain in

teenage pregnant girls. *Journal of Nutrition* 103(5): 772-785.

Kirwan J. P., S. Hauguel-De Mouzon, J. Lepercq, J. C. Challier, L. Huston-Presley, J. E. Friedman, S. C. Kalhan and P. M. Catalano. 2002. TNF-alpha is a predictor of insulin resistance in human pregnancy. *Diabetes* 51(7): 2207-2213.

Klebanoff M. A., B. R. Mednick, C. Schulsinger, N. J. Secher and P. H. Shiono. 1998. Father's effect on infant birth weight. *American Journal of Obstetrics and Gynecology* 178(5): 1022-1026.

Koo W. W., J. C. Walters and E. M. Hockman. 2000. Body composition in human infants at birth and postnatally. *Journal of Nutrition* 130(9): 2188-2194.

Kuhl C. 1991. Aetiology of gestational diabetes. *Baillieres Clinical Obstetrics and Gynaecology* 5(2): 279-292.

Langhoff-Roos J., G. Lindmark and M. Gebre-Medhin. 1987. Maternal fat stores and fat accretion during pregnancy in relation to infant birthweight. *British Journal of Obstetrics and Gynaecology* 94(12): 1170-1177.

Lantz M. E., R. A. Chez, A. Rodriguez and K. B. Porter. 1996. Maternal weight gain patterns and birth weight outcome in twin gestation. *Obstetrics and Gynecology* 87(4): 551-556.

Larciprete G., H. Valensise, B. Vasapollo, F. Altomare, R. Sorge, B. Casalino, A. De Lorenzo and D. Arduini. 2003. Body composition during normal pregnancy: reference ranges. *Acta Diabetologica* 40 Suppl 1: S225-232.

Lederman S. A., A. Paxton, S. B. Heymsfield, J. Wang, J. Thornton and R. N. Pierson, Jr. 1997. Body fat and water changes during pregnancy in women with different body weight and weight gain. *Obstetrics and Gynecology* 90(4 Pt 1): 483-488.

Lesser K. B. and M. W. Carpenter. 1994. Metabolic changes associated with normal pregnancy and pregnancy complicated by diabetes mellitus. *Seminars in Perinatology* 18(5): 399-406.

Leturque A., S. Hauguel, M. T. Sutter Dub, P. Maulard and J. Girard. 1989. Effects of placental lactogen and progesterone on insulin stimulated glucose metabolism in rat muscles in vitro. *Diabetes & Metabolism* 15(4): 176-181.

Lindsay C. A., A. J. Thomas and P. M. Catalano. 1997. The effect of smoking tobacco on neonatal body composition. *American Journal of Obstetrics and Gynecology* 177(5): 1124-1128.

Luke B., L. Keith and F. R. Witter. 1992. Theoretical Model for Reducing Neonatal Morbidity and Mortality and Associated Costs Among Twins. *The Journal of Maternal-Fetal Medicine* 1(1): 14-19.

Luke B., J. Minogue and H. Abbey. 1992. The association between maternal weight gain and the birth weight of twins. *The Journal of Maternal-Fetal Medicine* 1: 267-276.

Luke B., E. Bryan, C. Sweetland, S. Leurgans and L. Keith. 1995. Prenatal weight gain and the birthweight of triplets. *Acta Geneticae Medicae et Gemellologiae* 44(2): 93-101.

Luke B., B. Gillespie, S. J. Min, M. Avni, F. R. Witter and M. J. O'Sullivan. 1997. Critical periods of maternal weight gain: effect on twin birth weight. *American Journal of Obstetrics and Gynecology* 177(5): 1055-1062.

Luke B. 1998. What is the influence of maternal weight gain on the fetal growth of twins? *Clinical Obstetrics and Gynecology* 41(1): 56-64.

Luke B., S. J. Min, B. Gillespie, M. Avni, F. R. Witter, R. B. Newman, J. G. Mauldin, F. A. Salman and M. J. O'Sullivan. 1998. The importance of early weight gain in the intrauterine growth and birth weight of twins. *American Journal of Obstetrics and Gynecology* 179(5): 1155-1161.

Luke B., M. L. Hediger, C. Nugent, R. B. Newman, J. G. Mauldin, F. R. Witter and M. J. O'Sullivan. 2003. Body mass index--specific weight gains associated with optimal birth weights in twin pregnancies. *Journal of Reproductive Medicine* 48(4): 217-224.

MacLaughlin S. M., S. K. Walker, C. T. Roberts, D. O. Kleemann and I. C. McMillen. 2005. Periconceptional nutrition and the relationship between maternal body weight changes in the periconceptional period and feto-placental growth in the sheep. *The Journal of Physiology* 565(Pt 1): 111-124.

Mardones-Santander F., G. Salazar, P. Rosso and L. Villarroel. 1998. Maternal body composition near

term and birth weight. *Obstetrics and Gynecology* 91(6): 873-877.

Marseille-Tremblay C., M. Ethier-Chiasson, J. C. Forest, Y. Giguere, A. Masse, C. Mounier and J. Lafond. 2008. Impact of maternal circulating cholesterol and gestational diabetes mellitus on lipid metabolism in human term placenta. *Molecular Reproduction and Development* 75(6): 1054-1062.

Metzger B. E., V. Ravnikar, R. A. Vileisis and N. Freinkel. 1982. "Accelerated starvation" and the skipped breakfast in late normal pregnancy. *Lancet* 1(8272): 588-592.

Min S. J., B. Luke, B. Gillespie, L. Min, R. B. Newman, J. G. Mauldin, F. R. Witter, F. A. Salman and J. O'Sullivan M. 2000. Birth weight references for twins. *American Journal of Obstetrics and Gynecology* 182(5): 1250-1257.

Mitchell M., D. T. Armstrong, R. L. Robker and R. J. Norman. 2005. Adipokines: implications for female fertility and obesity. *Reproduction* 130(5): 583-597.

Molteni R. A., S. J. Stys and F. C. Battaglia. 1978. Relationship of fetal and placental weight in human beings: fetal/placental weight ratios at various gestational ages and birth weight distributions. *Journal of Reproductive Medicine* 21(5): 327-334.

Nohr E. A., B. H. Bech, M. Vaeth, K. M. Rasmussen, T. B. Henriksen and J. Olsen. 2007. Obesity, gestational weight gain and preterm birth: a study within the Danish National Birth Cohort. *Paediatric and Perinatal Epidemiology* 21(1): 5-14.

Oken E., K. P. Kleinman, J. Rich-Edwards and M. W. Gillman. 2003. A nearly continuous measure of birth weight for gestational age using a United States national reference. *BMC Pediatrics* 3: 6.

Okereke N. C., L. Huston-Presley, S. B. Amini, S. Kalhan and P. M. Catalano. 2004. Longitudinal changes in energy expenditure and body composition in obese women with normal and impaired glucose tolerance. *American Journal of Physiology Endocrinology and Metabolism* 287(3): E472-479.

Orskou J., U. Kesmodel, T. B. Henriksen and N. J. Secher. 2001. An increasing proportion of infants weigh more than 4000 grams at birth. *Acta Obstetricia et Gynecologica Scandinavica* 80(10): 931-936.

Pasqualini J. R. 2005. Enzymes involved in the formation and transformation of steroid hormones in the fetal and placental compartments. *Journal of Steroid Biochemistry and Molecular Biology* 97(5): 401-415.

Pinar H., M. Stephens, D. B. Singer, T. K. Boyd, S. M. Pflueger, D. L. Gang, D. J. Roberts and C. J. Sung. 2002. Triplet placentas: reference values for weights. *Pediatric and Developmental Pathology* 5(5): 495-498.

Pipe N. G., T. Smith, D. Halliday, C. J. Edmonds, C. Williams and T. M. Coltart. 1979. Changes in fat, fat-free mass and body water in human normal pregnancy. *British Journal of Obstetrics and Gynaecology* 86(12): 929-940.

Pitkin R. M. 1976. Nutritional support in obstetrics and gynecology. *Clinical Obstetrics and Gynecology* 19(3): 489-513.

Ross M. G. and R. A. Brace. 2001. National Institute of Child Health and Development Conference summary: amniotic fluid biology--basic and clinical aspects. *Journal of Maternal-Fetal Medicine* 10(1): 2-19.

Rosso P. 1990. *Nutrition and Metabolism in Pregnancy: Mother and Fetus*. New York: Oxford University Press.

Rovere-Querini P., M. T. Castiglioni, M. G. Sabbadini and A. A. Manfredi. 2007. Signals of cell death and tissue turnover during physiological pregnancy, pre-eclampsia, and autoimmunity. *Autoimmunity* 40(4): 290-294.

Russo A. R., L. M. Ausman, D. L. Gallina and D. M. Hegsted. 1980. Developmental body of composition of the squirrel monkey (Saimiri sciureus). *Growth* 44(4): 271-286.

Ryan E. A., M. J. O'Sullivan and J. S. Skyler. 1985. Insulin action during pregnancy. Studies with the euglycemic clamp technique. *Diabetes* 34(4): 380-389.

Ryan E. A. and L. Enns. 1988. Role of gestational hormones in the induction of insulin resistance.

Journal of Clinical Endocrinology and Metabolism 67(2): 341-347.

Sewell M. F., L. Huston-Presley, D. M. Super and P. Catalano. 2006. Increased neonatal fat mass, not lean body mass, is associated with maternal obesity. *American Journal of Obstetrics and Gynecology* 195(4): 1100-1103.

Siega-Riz A. M., L. S. Adair and C. J. Hobel. 1996. Maternal underweight status and inadequate rate of weight gain during the third trimester of pregnancy increases the risk of preterm delivery. *Journal of Nutrition* 126(1): 146-153.

Sims E. A. and K. E. Krantz. 1958. Serial studies of renal function during pregnancy and the puerperium in normal women. *Journal of Clinical Investigation* 37(12): 1764-1774.

Sohlstrom A. and E. Forsum. 1995. Changes in adipose tissue volume and distribution during reproduction in Swedish women as assessed by magnetic resonance imaging. *American Journal of Clinical Nutrition* 61(2): 287-295.

Spady D. W. 1989. Normal body composition of infants and children. In *Report of the 98th Ross Conference on Pediatric Research. Body composition measurements in infants and children*, Ross Laboratories**:** Pp. 67.

Sparks J. W. 1984. Human intrauterine growth and nutrient accretion. *Seminars in Perinatology* 8(2): 74-93.

Stevens-Simon C., E. R. McAnarney, K. J. Roghmann and G. B. Forbes. 1997. Composition of gestational weight gain in adolescent pregnancy. *Journal of Maternal-Fetal Medicine* 6(2): 79-86.

Stewart M. O., P. G. Whittaker, B. Persson, U. Hanson and T. Lind. 1989. A longitudinal study of circulating progesterone, oestradiol, hCG and hPL during pregnancy in type 1 diabetic mothers. *British Journal of Obstetrics and Gynaecology* 96(4): 415-423.

Surkan P. J., C. C. Hsieh, A. L. Johansson, P. W. Dickman and S. Cnattingius. 2004. Reasons for increasing trends in large for gestational age births. *Obstetrics and Gynecology* 104(4): 720-726.

Swanson L. D. and C. Bewtra. 2008. Increase in normal placental weights related to increase in maternal body mass index. *Journal of Maternal-Fetal & Neonatal Medicine* 21(2): 111-113.

Taggart N. R., R. M. Holliday, W. Z. Billewicz, F. E. Hytten and A. M. Thomson. 1967. Changes in skinfolds during pregnancy. *British Journal of Nutrition* 21(2): 439-451.

Teasdale F. 1980. Gestational changes in the functional structure of the human placenta in relation to fetal growth: a morphometric study. *American Journal of Obstetrics and Gynecology* 137(5): 560-568.

Thame M., C. Osmond, F. Bennett, R. Wilks and T. Forrester. 2004. Fetal growth is directly related to maternal anthropometry and placental volume. *European Journal of Clinical Nutrition* 58(6): 894-900.

Thomas P., J. Peabody, V. Turnier and R. H. Clark. 2000. A new look at intrauterine growth and the impact of race, altitude, and gender. *Pediatrics* 106(2): E21.

van Raaij J. M., M. E. Peek, S. H. Vermaat-Miedema, C. M. Schonk and J. G. Hautvast. 1988. New equations for estimating body fat mass in pregnancy from body density or total body water. *American Journal of Clinical Nutrition* 48(1): 24-29.

Villamor E., R. Gofin and B. Adler. 1998. Maternal anthropometry and pregnancy outcome among Jerusalem women. *Annals Of Human Biology* 25(4): 331-343.

Weiner C. P., R. E. Sabbagha, N. Vaisrub and R. Depp. 1985. A hypothetical model suggesting suboptimal intrauterine growth in infants delivered preterm. *Obstetrics and Gynecology* 65(3): 323-326.

Widdowson E. M. 1950. Chemical composition of newly born mammals. *Nature* 166(4224): 626-628.

Widdowson E. M. and C. M. Spray. 1951. Chemical development in utero. *Archives of Disease in Childhood* 26(127): 205-214.

Xiang A. H., M. Kawakubo, T. A. Buchanan and S. L. Kjos. 2007. A longitudinal study of lipids and blood pressure in relation to method of contraception in Latino women with prior gestational diabetes mellitus. *Diabetes Care* 30(8): 1952-1958.

Xu H., G. T. Barnes, Q. Yang, G. Tan, D. Yang, C. J. Chou, J. Sole, A. Nichols, J. S. Ross, L. A. Tartaglia and H. Chen. 2003. Chronic inflammation in fat plays a crucial role in the development

of obesity-related insulin resistance. *Journal of Clinical Investigation* 112(12): 1821-1830.

Yeh J. and J. A. Shelton. 2007. Association of pre-pregnancy maternal body mass and maternal weight gain to newborn outcomes in twin pregnancies. *Acta Obstetricia et Gynecologica Scandinavica* 86(9): 1051-1057.

4

Determinants of Gestational Weight Gain

The total amount of weight gain during pregnancy is determined by many factors. Aside from physiological factors (discussed in Chapter 2); psychological, behavioral, family, social, cultural, and environmental factors can also have an impact on gestational weight gain (GWG). Understanding these factors as determinants of GWG is an important component of revising weight gain guidelines for women during pregnancy.

Several conceptual models guided the committee's consideration of determinants of GWG. The ecological perspective recognizes that health behavior such as GWG is influenced at multiple levels. Brofenbrenner (1979) identified multiple levels of environmental influence on health behavior in general:

- The microsystem – face-to-face interactions in specific settings, such as family, school, or a peer group;
- The mesosystem (a system of microsystems) – the interrelations among the various settings in which the individual is involved, such as that between the family and the workplace;
- The exosystem – the larger social system in which the individual is embedded, such as the extended family or community; and
- The macrosystem – cultural values and beliefs, such as cultural beliefs about GWG.

Other models which recognize the multiple determinants of health behavior or outcome include the health field model, which identifies multiple domains including: the physical and social environments that exert influences on health behavior and outcome; and the epidemiological model which describes a triad of epidemiologic factors to model the complex and interrelated factors contributing to the increasing rate of obesity in the United States and other countries. One of the triad components describes an "obesogenic" environment as "the sum of influences that the surroundings, opportunities, or conditions of life have on promoting obesity in individuals or populations" (Swinburn and Egger, 2002). This obesogenic environment includes physical, economic, policy, and socio-cultural factors that can influence eating and physical activity behaviors.

Collectively, these models place emphasis on how the health of individuals is influenced by not only physiological functioning and genetic predisposition, but by a complex interplay of these biological determinants with social and familial relationships, environmental influences, and broader social and economic contexts over the life course. They further suggest that intervention efforts to change health behavior or outcome, such as GWG, should address not only "downstream" individual-level phenomena (e.g. physiologic pathways to disease, individual and lifestyle factors) and "mainstream" factors (e.g. population-based interventions), but also "upstream," societal-level phenomena (e.g. public policies) (IOM, 2000).

Another model, the life-course perspective (Kuh and Ben-Shlomo, 1997), perceives life not in disconnected stages, but as an integrated continuum; it recognizes that each stage of life is influenced by the life stages that precede it, and it, in turn, influences the life stages that follow (See Chapter 6 for detailed discussion).

Some of the most significant determinants of GWG at multiple levels (social/institutional, environmental, neighborhood/community, interpersonal/family, and individual levels) occur across the life course (Figure 4-1). The following discussion begins with a review of the evidence for a direct relationship between a given determinant (identified in the Conceptual Framework) and GWG. Where data are lacking, rationale are provided for why the committee thinks that it is potentially an important determinant which merits further research. The committee's review of evidence (tabulated in Appendix D) included both epidemiologic and clinical studies. Since this research discipline is focused largely on observational studies the committee recognized the need for proof of causality for determinants and outcomes significantly associated with GWG.
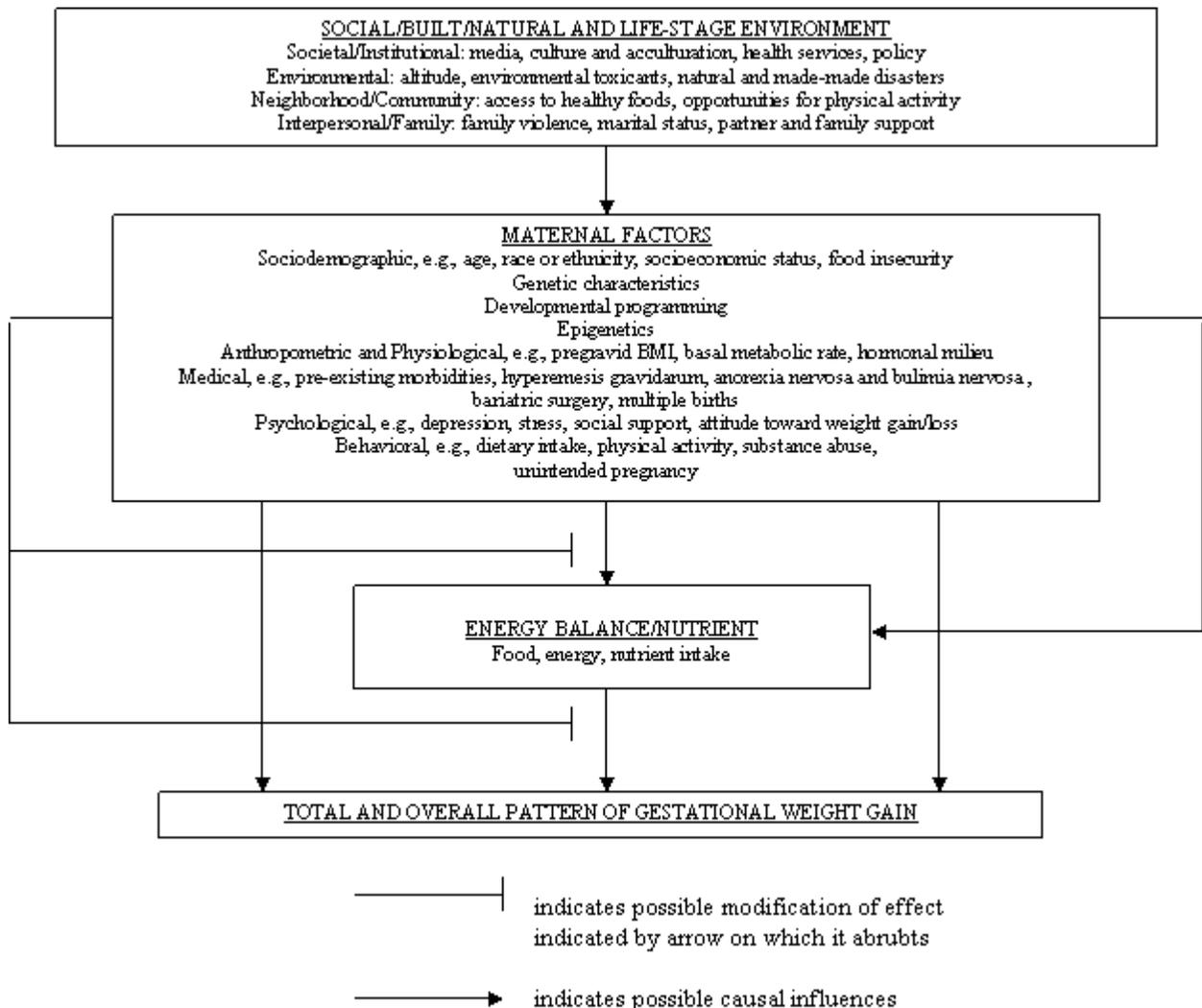
FIGURE 4-1 Schematic summary of determinants associated with GWG.

SOCIETAL/INSTITUTIONAL DETERMINANTS

Media

The committee was unable to identify studies that examined specifically the media's influence on GWG. From a life course perspective, however, it is plausible that the media may influence GWG by having an effect on eating and exercise habits that are established well before pregnancy. Several previous reports have documented the influence of advertising and marketing on children's food, beverage, and sedentary-pursuit choices that can adversely affect energy balance (Kunkel, 2001; IOM, 2006). An extensive systematic literature review concluded that food advertisements promote food purchase requests by children to parents, have an impact on children's product and brand preferences, and affect consumption behavior (Hastings et al., 2003). Other studies have shown that the media can encourage sedentary behaviors, such as television watching, that may adversely affect energy balance (Gortmaker et al., 1996; Gortmaker et al., 1999; Robinson, 1999; IOM, 2005; Epstein et al., 2008). Such eating habits and sedentary behaviors shaped during childhood and adolescence may be carried into young adulthood and continued into pregnancy and thus indirectly affect GWG. Moreover, by influencing energy balance over the long run these habits and behaviors may also have an impact on prepregnancy body mass index (BMI) as well as other biological determinants of GWG.

Not all media influences are negative, however. Media can be used to convey consumer information and public health messages, such as those regarding youth smoking, and seat belt and child car seat use. Social marketing programs that have used the media, either as focused efforts or as part of multi-component campaigns to promote physical activity or healthy diet in adults, have produced mixed results, often because discerning their impact is a challenge. The most successful social marketing programs have received more funding, been better sustained, and were shaped by formative research (IOM, 2006).

Taken together, available evidence is inconclusive about the media's influence on GWG. However, it is plausible that the media may exert its influence indirectly by affecting prepregnancy BMI and other biological determinants, as well as influencing eating habits and sedentary behaviors that are established well before pregnancy.

Culture and Acculturation

The committee was unable to identify studies that examined specifically the effects of culture and acculturation factors on GWG. However, cultural norms and beliefs may influence dietary behavior and physical activity, thereby affecting energy balance and, indirectly, GWG. For example, there is a belief among women of all ages, ethnic groups, and income and education levels that the consumption of certain foods marks a child before birth; which may then lead to certain food preferences and avoidances (IOM, 1992; King, 2000). There is also the belief that diet can influence ease of delivery. Most women know that low GWG will produce a small infant, which will be delivered more easily than a larger one. In some cultures this knowledge may encourage women to "eat down" in late pregnancy in order to avoid a difficult birth (King, 2000). Understanding these cultural norms and beliefs is important for effectively communicating recommendations for GWG.

Acculturation, the process in which members of one cultural group adopt the beliefs and behaviors of another, is often associated with adoption of unhealthy behaviors, including food choices. Using nativity or duration of residence in the U.S. as a proxy for acculturation, several

studies have found greater rates of overweight and obesity among children and non-pregnant adults who are more acculturated, compared to their less acculturated counterparts (Lizarzaburu and Palinkas, 2002; Hubert et al., 2005; Hernandez-Valero et al., 2007; Fuentes-Afflick and Hessol, 2008). A population-based study of 462 mothers in California found that in the three months before pregnancy, foreign-born Latinas had the lowest contribution of fat to total energy intake and the highest dietary intake of carbohydrate, cholesterol, fiber, grain products, protein foods, folate, vitamin C, iron, and zinc, compared to the dietary intake of white non-Latinas and U.S.-born Latinas (Schaffer et al., 1998). Other researchers have also documented increased risk for adverse birth outcomes, including preterm birth and low birth weight, among U.S.-born women compared to foreign-born women of the same ethnic origin (Ventura and Taffel, 1985; Scribner and Dwyer, 1989; Cabral et al., 1990; Kleinman et al., 1991; Rumbaut and Weeks, 1996; Singh and Yu, 1996; Fuentes-Afflick and Lurie, 1997; Jones and Bond, 1999; Callister and Birkhead, 2002; Baker and Hellerstedt, 2006). In these studies, however, GWG is usually not reported, and so the contribution of GWG to adverse outcomes is unclear. Taken together, there is indirect evidence that cultural and acculturation factors can influence GWG even though conclusive evidence for a direct effect is lacking.

Health Services

The U.S. Public Health Service Expert Panel on the Content of Prenatal Care recommended that pregnant women receive advice on gaining an appropriate amount of weight during pregnancy even though an influence of weight gain advice on GWG has not been conclusively demonstrated (DHHS, 1989). Several intervention studies have been conducted using nutrition advice alone (Orstead et al., 1985; Bruce and Tchabo, 1989) or such advice linked with home visits by nutritionists and supplemental food (Rush, 1981; Bruce and Tchabo, 1989), a nurse home visitation program (Olds et al., 1986), and the provision of prenatal care through multidisciplinary rather than traditional clinics (Morris et al., 1993). In three of the studies (Rush, 1981; Olds et al., 1986; Morris et al., 1993) the differences in mean GWG between intervention and control groups were not statistically significant. In two other studies (Orstead et al., 1985; Bruce and Tchabo, 1989) intervention groups gained significantly more weight than the control groups; however, the findings may be limited by gestational age bias. Additionally, only mean GWG was reported in the studies and no comparisons were made using different cutoff points based on pregravid BMI further limiting interpretation of the findings.

Brown et al. (1992) developed a prenatal weight gain intervention program based on social marketing methods. While circumstances arose that hampered full evaluation of the program, preliminary evidence suggests that GWG and birth weight of African Americans in the intervention group did not differ significantly from those of whites, whereas both weight gain and birth weight were significantly lower in African Americans than in whites in the control group.

Hickey (2000) identified several threats to the validity of previous studies on prenatal weight gain advice and actual GWG. These include, in addition to differences in pregravid nutritional status and BMI, issues such as self-selection bias, recall bias, differences in time during gestation when nutrition advice was given, variation in content and frequency of advice, the pairing of advice with other food or nonfood interventions, individual and social characteristics of the provider as contrasted with those of the pregnant woman, and racial-ethnic and socioeconomic disparities in weight gain advice given to women. Given all these threats, the evidence to evaluate the influence of prenatal weight gain advice on actual GWG is weak.

Policy

For the purpose of this report, policy is defined broadly to include principles, guidelines, or plans adopted by an organization to guide decisions, actions, and other matters. As an example of how policy can influence GWG, the weight gain recommendations from the report, *Nutrition During Pregnancy* (IOM, 1990) have been endorsed by obstetric organizations in the United States and many other countries. A 2005 cross-sectional survey mailed to 1,806 practicing members of the American College of Obstetricians and Gynecologists (ACOG) showed that more than 85 percent of the 900 respondents report counseling their patients about GWG often or most of the time (ACOG, 2005). The survey did not, however, assess the respondents' knowledge of the IOM (1990) guidelines or the content of counseling (Power et al., 2006).

The few studies that have examined the advice given for GWG, however, have shown that women often receive inconsistent or erroneous advice. Cogswell et al. (1999) found in a survey of approximately 2,300 women that they appear to be influenced by professional advice in the weight gain they believe is appropriate and the weight gain they actually achieve. Of the 1,643 women who recalled weight gain advice, 14 percent reported being advised to gain less than the recommended levels, and 22 percent were advised to gain more. Provider advice to gain below the recommended levels was associated with actual weight gain below the recommendations (an adjusted odds ratio of 3.6), and advice above the guidelines had the same odds ratio for higher rates of gain. Moreover, 27 percent of women reported receiving no advice about GWG; thus nearly two-thirds (63 percent) of women in this study reported receiving no advice or inappropriate advice from health professionals regarding GWG.

In a more recent study, Stotland et al. (2005) found that 79 percent of the nearly 1,200 women of all BMI ranges in the study reported a target GWG, or how much weight women think they should gain during pregnancy, within the IOM (1990) guidelines, as compared to only 59 percent reported in Cogswell et al. (1999). Given that the women in the Cogswell et al. cohort delivered in 1993, the authors speculated that the IOM (1990) guidelines are now more widely applied or accepted than they were in 1993. Still, Stotland et al. (2005) found that one-third (33 percent) of women received no advice from health professionals regarding GWG, and less than half (49 percent) reported receiving advice within guidelines. In sum, the IOM (1990) guidelines appear to influence what women believe to be appropriate weight gain during pregnancy, though their influence on actual GWG may be less, in part because many health professionals are providing no or inappropriate advice about GWG.

Another example of how policy can influence GWG is the Special Supplemental Food Program for Women, Infants and Children (WIC). Rush et al. (1988) conducted a national evaluation of WIC programs and found that a reversal of low weight gain in early pregnancy and greater total weight gain during pregnancy occurred among women who enrolled in WIC compared with controls. They also found greater intake of protein, iron, calcium, vitamin C, and energy among WIC participants. However, subsequent evaluations (Joyce et al., 2008) have challenged these earlier findings and found more limited associations between WIC participation and GWG. Nonetheless, it is possible that policy that increases food access would have an impact on dietary pattern and GWG.

Policy that does not directly affect pregnant women can also have an effect on GWG. Examples include policy recommendations to restrict food and beverage advertising and marketing to young children, to develop and implement nutritional standards for all competitive foods and beverages sold or served in schools, or to promote physical activity in schools (IOM,

2007). These policies can influence the development of children's eating and exercise habits, which will be important later in life.

ENVIRONMENTAL DETERMINANTS

Altitude

There is inconsistent evidence about the influence of altitude on GWG. Jensen and Moore (1997) examined the effect of high altitude on GWG and birth weight using Colorado birth certificates. They did not find any significant difference in GWG among women residing at 3,000 to 5,000 feet; 5,000 to 7,000 feet; 7,000 to 9,000 feet; and 9,000 to 11,000 feet. Mean birth weight, however, decreased and low birth weight rates increased with increasing altitude. The decline in birth weight associated with increase in altitude was found to be independent of and not interactive with gestational age, GWG, parity, maternal smoking, pregnancy-induced hypertension and other factors associated with birth weight (Jensen and Moore, 1997).

Environmental Toxicants

The committee was unable to identify studies that examined specifically the effects of exposures to environmental toxicants on GWG. There is some evidence linking environmental contaminants such as organophosphate and organochlorine compounds to fetal growth, but the evidence is inconsistent (Dar et al. 1992; Wolff et al., 2007). Additional research may better define the relationships among environmental exposures, GWG, and fetal growth.

Natural and Man-made Disasters

The committee was unable to identify studies that examined specifically the effects of natural or man-made disasters on GWG. However, it is plausible that disasters can affect GWG indirectly by influencing resource availability (including food supply), healthcare access, and stress levels (Callaghan et al., 2007). Several studies have documented the impact of disasters on pregnancy outcomes such as preterm birth (Weissman et al., 1989; Cordero, 1993; Glynn et al., 2001; Lederman et al., 2004) and fetal growth restriction (Eskenazi et al., 2007; Landrigan et al., 2008); however, it remains unclear whether these adverse outcomes were caused by low GWG.

NEIGHBORHOOD/COMMUNITY DETERMINANTS

Access to Healthy Foods

Evidence for a direct influence of neighborhood or community factors, such as access to healthy foods, on GWG is lacking. However, because appropriate nutrient intake and weight gain during pregnancy requires a safe and adequate food supply, it is likely women who live in areas where residents have poor accessibility to foods may be at increased risk for inadequate or inappropriate GWG and associated poor pregnancy outcomes (See Chapter 2 for trends in dietary practices and Appendix B for supplemental information). A study of urban retail food markets and birth weight outcomes in upstate New York found pregnant women who lived in proximity to urban retail corner markets without fresh produce, dairy, and other healthy foods had significantly more low birth weight infants compared to women who had access to supermarkets where healthy foods were available. These findings were independent of income level; however,

the study did not report on GWG (Lane et al., 2008). Laraia et al. (2004) investigated associations between the distance of a supermarket from home and diet quality of pregnant women, measured by a Diet Quality Index (DQI). They found that women who lived more than four miles from a supermarket had a two-fold greater risk of falling into the lowest DQI quartile compared to women who lived ≤ 2 miles from a supermarket, but the authors also did not report on GWG.

Opportunities for Physical Activity

While a growing body of evidence has demonstrated the role of the built environment for populations at high risk for obesity (See Chapter 2 for trends in physical activity), only one study was identified that examined the relationship between neighborhood contexts and GWG. Laraia et al. (2007) conducted a study of neighborhood factors associated with physical activity and weight gain during pregnancy. They found that social spaces, defined as the presence of parks, sidewalks, and porches as well as the presence of people, including nonresidential visitors, was associated with decreased odds for inadequate or excessive GWG. The social spaces scale was also associated with decreased odds of living greater than three miles from a supermarket. These findings suggest that neighborhood environments can influence GWG by providing access to healthy foods and opportunities for physical activities.

INTERPERSONAL/FAMILY DETERMINANTS

Family Violence

Several studies examined GWG in the context of family violence (Parker et al., 1994; McFarlane et al., 1996; Siega-Riz and Hobel, 1997; Moraes et al., 2006). Siega-Riz and Hobel (1997) found in a clinic sample of 4,791 Hispanic women in Los Angeles that physical abuse was associated with a greater than threefold risk for inadequate GWG among obese and overweight women. Moraes et al. (2006) found in a study of 394 pregnant women in Brazil that those with the highest physical abuse score gained, on average, 3 to 4 kg less than women unexposed to intimate partner violence. Boy and Salihu (2004) conducted a systematic review and found that abused pregnant women had less GWG than non-abused women. These studies suggest an association between intimate partner violence and insufficient GWG.

Marital Status

Several studies have examined the relationship between marital status and GWG. Kleinman et al. (1991) and Ventura (1994), who used 1992 U.S. national data, found that unmarried mothers were more likely than married mothers to gain less than 7.3 kg during pregnancy. Olsen and Strawderman (2003) found in a cohort of 622 healthy adult women that 38 percent of married women had gained above IOM (1990) guidelines, compared to 42 percent for women who were separated or divorced, and 48 percent for single women. They also found that 21 percent of married women had gained below IOM (1990) guidelines, compared to 23 percent for single women and 29 percent for women who were separated or divorced. Thus married women were more likely to gain within the IOM (1990) recommended weight gain range than single or separated/divorced women.

Partner and Family Support

Evidence to support a relationship between partner support and GWG is lacking at this time. Dipietro et al. (2003) found in a cross-sectional study of 130 women with low-risk pregnancies that partner support was associated with negative pregnancy body image, but not with attitudes or behaviors toward GWG. Siega-Riz and Hobel (1997) found that receiving financial support from the infant's father was significantly associated with decreased risk of poor GWG for overweight and obese women, but not for underweight or normal weight women.

Several studies have examined the influence of family support on GWG. Stevens-Simon et al. (1993) found in a sample of 99 pregnant adolescents that attitudes toward GWG were directly related to their perceived family support. Negative weight gain attitudes were most common among heavier adolescents, depressed adolescents, and adolescents who did not perceive their families as supportive. Gutierrez (1999) reported from a study of 46 pregnant Mexican American adolescents that the most powerful factors contributing to good food practices during pregnancy were maternal concern about the well-being of the infant, role of motherhood, and family support system; the contribution of family support to GWG attitudes or actual GWG was not reported in this study.

MATERNAL FACTORS

Sociodemographic Factors

Gestational Weight Gain in Adolescents

Adolescent pregnancy has been associated with increased risk of preterm delivery, low birth weight, SGA births, and increased risk of neonatal mortality, although reported risk associations vary (Chen et al., 2007). To reduce these risks, the IOM (1990) report recommended that pregnant adolescents gain weight within the ranges for adult women unless they were under 16 years of age or less than two years post-menarche. In either of these cases, adolescents were encouraged to gain at the upper limits of the GWG guidelines for their prepregnancy BMI category.

The youngest adolescents as well as somewhat older adolescents who conceive soon after menarche may still be growing themselves (Scholl and Hediger, 1993). Even girls who become pregnant for a second time during adolescence may still be growing. Scholl et al. (1990) showed that adolescents who were still growing during a first pregnancy delivered infants whose birth weight did not differ from those who were not growing. This was not true among adolescents who were still growing during a second pregnancy; their infants were significantly lighter at birth than those who were not growing themselves. The possibility of a competition for nutrients between the still-growing adolescent gravida and her fetus has been advanced as an argument for recommending relatively higher gains for at least some pregnant adolescents. What has been found instead is that still-growing adolescents are not mobilizing their fat gain during pregnancy to enhance fetal growth but, rather, are supporting the continued development of their own fat stores (Scholl et al., 1994).

In a retrospective review of natality data from 2000, Howie et al. (2003) reported an increased likelihood for excessive GWG among adolescents compared to older women. Other authors have corroborated that younger adolescents have a higher GWG compared to older

adolescents and adults, but whether the infant benefits from this greater weight-gain is not yet clear (Hediger et al. 1990; Scholl et al., 1990; Stevens-Simon et al., 1993). This is in part because—as is also the case for adult women—increases in GWG not only reduce the risk of delivering a low birth weight infant but also increases the risk of delivering a macrosomic infant (Scholl et al., 1988). Nielsen et al. (2006) showed that birth weight outcomes improved in all prepregnancy BMI groups when GWG increased from below to within the lower half of the weight gain recommended by IOM (1990) in a cohort of 815 pregnant African-American adolescents. Further gains were not beneficial, particularly for infants of adolescents with a high prepregnancy BMI.

The possibility that adolescents who gained at the upper end of the range for their BMI category might have an excess risk of postpartum weight retention or the later development of obesity was not considered in formulating the 1990 guidelines, but has long been recognized as a possible downside of recommending relatively high weight gains for them (McAnarney and Stevens-Simon, 1993). Adolescents who have given birth are heavier (Gigante et al., 2005) with more adipose tissue (Gunderson et al., 2009) than adolescents who have not. Gestational weight gain was a significant predictor of increase in BMI 6 and 9 years post delivery in all prepregnancy BMI categories among the 330 primiparous black adolescents studied by Groth (2008). In addition, those who gained above the IOM (1990) guidelines were more likely to have become obese by 9 years post delivery than those who gained within the guidelines.

In summary, the relationship of GWG to fetal and birth outcomes, postpartum weight retention, and risk for future overweight/obesity appears to be generally similar to that for adult women. However, information on these subjects is more limited for pregnancy among adolescents, particularly younger adolescents, than it is for adult women. Data generated since the IOM (1990) report, particularly related to the risk of developing postpartum weight retention and obesity in adult women who had been pregnant as young adolescents, support the recommendation that "…until more is known, adolescents less than two years post-menarche should be advised to stay within the IOM-recommended BMI-specific weight range without either restricting weight or encouraging weight gain at the upper end of the range" (Suitor, 1997).

Gestational Weight Gain in Older Women

Increased maternal age is significantly associated with risk for adverse pregnancy outcomes, including stillbirth (Fretts, 2005; Reddy et al., 2006), low birth weight, preterm birth, and SGA (Cnattingius et al., 1992; Delpisheh et al., 2008). In addition to poor outcomes, pregnancy in older women is also associated with increased risk for pregnancy complications, e.g. hypertension, diabetes, placenta previa, and placental abruption (Joseph et al., 2005).

Women who become pregnant after age 35 differ from their younger counterparts in several factors that can influence pregnancy outcome, including prepregnancy weight (or BMI) and GWG. In a study of obese and non-obese women who were pregnant, Gross et al. (1980) found that a greater proportion of obese subjects were older and of higher parity than non-obese subjects. The obese subjects also had higher rates of chronic hypertension, diabetes, and inadequate GWG. Prysak et al. (1995), in a retrospective comparison of pregnancy characteristics between older (≥ 35 years old) and younger (25-29 years old) nulliparous women, found that the older women had significantly lower mean GWG than the younger women. In addition, obesity was significantly greater in the older compared to the younger women.

Pregnant women over 35 years of age who were enrolled in the WIC program were evaluated by Endres et al. (1987) for nutrient intake, prepregnancy weight, and GWG compared to adolescents aged 15-18 years. Prepregnancy BMI was calculated for both groups and more than 50 percent of the older women were identified as obese prior to pregnancy. The study found no significant difference in total nutrient intake between the groups (neither met the RDAs), but the younger women had higher mean energy intakes ($P = 0.006$) and greater cumulative GWG in the third trimester (9.5 kg versus 7.6 kg) than the older women. In sum, several studies reported higher prepregnancy BMI and lower GWG among older women, compared to their younger counterparts. The contributions of GWG to birth outcomes, postpartum weight retention, and subsequent overweight/obesity among older women remain unclear.

Table 4-1 summarizes reports from the last three decades on GWG by age and racial/ethnic group.

TABLE 4-1 Effect of Chronological Maternal Age on GWG

Reference	Age (yrs)	Racial/Ethnic Group	Number in Sample	Weight Gain (kg)	Coefficient of Variation, %
Ancri et al.	12-17	Caucasian	26	13.4	26
(1977)	18-19	(one black woman)	22	12.4	31
	20-24		24	11.1	17
	25-32		26	10.7	18
Frisancho et al.	12-13	Latin-American	28	9.0	18
(1983)	14		104	9.8	22
	15		296	9.9	26
	16		565	9.7	25
	17		229	10.0	26
	18-25		46	9.7	16
Horon et al.	< 16	Black, White	422	12.5	NR [a]
(1983)	20-24		422	12.5	NR
Loris et al.	13-15.9	Mixed group	18	17.2	23
(1985)	16-17.9		84	17.1	40
	18-19.9		25	17.3	54
Meserole et al.	13-15	Mixed group	24	14.5	32
(1984)	16-17		25	17.9	35
Endres et al.	15-18	Mixed group	46	12.0	NR
(1985)	19-30		198	11.0	NR
Muscati et al.	14-17	NR	90	16.5	36
(1988)	18-19		135	15.1	36
	20-35		461	13.8	39
Scholl et al.	16.9 ± 1.3 [b]	Black, White, Hispanic	696	14.7	39
(1988)					
Haiek and Lederman	< 16	Black Americans, Black	90	14.6	NR
(1989)	19-30	Latin Americans, White Non-Latin Americans, White Latin Americans	90	16.9	NR
Hediger et al.	≤ 18	Puerto Rican	304	13.7	±5.6 [b]
(1990)		Black	501	13.8	±5.7 [b]
		White	514	15.9	±5.7 [b]
Stevens-Simon et al.	< 16		52	14.9	±5.9 [b]
(1993)	16-19	N/A	89	13.9	±6.0 [b]
Prysak et al.	25-29	White or other	1,054	15.0	±4.9 [b]
(1995)	≥ 35		890	14.2	±5.4 [b]
Gutierrez (1999)	13-18	Mexican-American	46	14.5	±4.5
Nielsen et al. (2006)	< 17	African-American	776	14.5	±6.9

[a]NR = Not reported.
[b]Standard deviation.

SOURCE: Modified from IOM, 1990.

Race or Ethnicity

Few studies have examined racial-ethnic differences in GWG, and even fewer studies have considered the influence of the many possible determinants of GWG among different racial/ethnic groups or alternatively, adjusted for race/ethnicity in their analyses. Caulfield et al.

(1996), for example, found that among 2617 black and 1253 white women delivering at a university hospital during 1987-1989 only 28.2 and 32.5 percent of black and white women, respectively gained within the ranges recommended by IOM (1990).

Black women are at increased risk for gaining less weight than recommended, when controlled for maternal pre-pregnancy BMI, height, parity, education, smoking, hypertension, duration of pregnancy, and fetal sex. Chu et al. (2009) assessed the amount of GWG among 52,988 underweight, normal weight, overweight, and obese U.S. women who delivered a singleton, full-term infant in 2004-2005 using PRAMS data (2004-2005). They found that black women were significantly more likely than white women to gain less than 15 pounds, but less likely than white women to gain more than 34 pounds. A review of birth records of 913,320 singleton births in New York City from 1995 to 2003 found that Asian and non-Hispanic black women were more likely to gain 0 to 9 kg, whereas Hispanic and non-Hispanic white women were more likely to gain 20+ kg during pregnancy (information contributed to the committee in consultation with Stein [see Appendix G, Part III). Table 4-2 presents GWG among women of different race and ethnicity in this study population.

Taken together, the limited data on the influence of race/ethnicity on GWG is suggestive of inadequate GWG among some racial/ethnic groups. However, the paucity of data on a national level and the lack of observational studies based on pre-pregnancy BMI preclude drawing any conclusions about the influence of race/ethnicity on GWG (see Chapter 2 and Figure 2-6 for trends in GWG for racial/ethnic groups by prepregnancy BMI).

TABLE 4-2 Bivariate Association between Gestational Weight Gain and Race or Ethnicity among Singleton Births, New York City, 1995–2003, $N = 913,320$

| | Gestational Weight Gain | | | |
	0 – 9 kg $N = 234,764$ N (percent)	10 – 14 kg $N = 333,968$ N (percent)	15 – 19 kg $N = 223,366$ N (percent)	20+ kg $N = 121,192$ N (percent)
Maternal race or ethnicity				
Non-Hispanic white	56,817 (20.3)	112,814 (40.4)	75,274 (26.9)	34,517 (12.3)
Non-Hispanic black	69,294 (29.2)	77,868 (32.8)	54,412 (22.9)	35,899 (15.1)
Hispanic	78,528 (26.9)	99,705 (34.1)	70,694 (24.2)	43,513 (14.9)
Asian	29,086 (29.0)	42,137 (41.9)	22,251 (22.1)	6,964 (6.9)
Other	1069 (30.1)	1,444 (40.7)	735 (20.7)	299 (8.4)

SOURCE: Information contributed to the committee in consultation with C. Stein (see Appendix G, Part III).

Socioeconomic Status

The committee found limited evidence for associations between GWG and socioeconomic status (SES), and few studies that considered the influence of the many possible determinants of GWG among different SES groups; or alternatively, adjusted for SES in their analyses (see Appendix D). Using 2004-2005 PRAMS data, Chu et al. (2009) found that women with less than 12 years of education were more likely to gain less than 15 pounds, and less likely to gain more than 34 pounds, compared to women with more than 12 years of education (Table 4-3). This analysis, however, did not control for pre-pregnancy BMI or other factors that could potentially influenced GWG.

TABLE 4-3 Gestational Weight Gain (pounds) by Selected Characteristics among Women Delivering Full-term, Singleton Births (Underweight Women Excluded), PRAMS, 2004-2005

Characteristic	≤ 14 (n = 8091)[a]		15-24 (n = 9970)[a]		25-34 (n = 14,545)[a]		35-44 (n = 10,311)[a]		≥ 45 (n = 7112)[a]	
	Percent[b]	SE[b]	Percent[b]	SE[b]	Percent[b]	SE[b]	Percent[b]	SE[b]	Percent[b]	SE[b]
Age, y (n)[a]										
14-19 (5249)	15.4	0.8	16.9	0.8	25.7	0.9	20.4	0.9	21.7	0.9
20-24 (12,477)	15.3	0.5	19.3	0.5	26.7	0.6	20.3	0.5	18.4	0.5
25-29 (13,483)	15.8	0.5	18.6	0.5	28.5	0.6	22.2	0.5	15.0	0.5
30-34 (11,169)	15.1	0.5	18.6	0.5	30.8	0.6	22.1	0.6	13.4	0.5
≥ 35 (7651)	15.9	0.6	19.8	0.7	32.2	0.8	20.8	0.7	11.2	0.6
Race/ethnicity										
White (27,393)	13.3	0.3	17.4	0.3	30.0	0.4	22.7	0.4	16.6	0.3
Black (7790)	21.7	0.7	21.1	0.6	23.9	0.7	18.2	0.6	15.1	0.6
Hispanic (7428)	17.3	0.7	21.2	0.7	29.3	0.8	20.1	0.7	12.1	0.6
Other (7221)	16.4	0.8	19.9	0.9	30.6	1.1	19.8	0.9	13.5	0.8
Education, y (n)										
< 12 (8154)	19.6	0.7	21.1	0.7	25.7	0.8	18.0	0.7	15.7	0.7
12 (15,550)	17.3	0.5	19.4	0.5	26.0	0.5	19.9	0.5	17.4	0.5
> 12 (25,667)	12.7	0.3	17.8	0.3	31.7	0.4	23.3	0.4	14.5	0.3
Parity (n)										
0 (20,782)	11.5	0.3	15.9	0.4	28.3	0.5	24.3	0.4	20.1	0.4
1-2 (23,911)	16.8	0.4	20.5	0.4	29.8	0.4	20.3	0.4	12.7	0.3
≥ 3 (5100)	23.2	0.9	22.9	0.9	28.3	0.9	14.8	0.7	10.8	0.7
Total (50,029)	15.5	0.2	18.8	0.3	28.9	0.3	21.4	0.3	15.5	0.2

x^2 test used for difference in gestational weight gain by maternal age, race/ethnicity, educational level, and parity were all statistically significant ($P < .001$)

[a] Based on unweighted data.
[b] Based on weighted data

SOURCE: Reprinted from Chu S. Y., W. M. Callaghan, C. L. Bish and D. D'Angelo. Gestational weight gain by body mass index among US women delivering live births, 2004-2005: fueling future obesity. *American Journal of Obstetrics and Gynecology*. Copyright (2009), with permission from Elsevier.

Food Insecurity

Food insecurity is closely tied to socioeconomic status and thus, it is included in the discussion even though it is arguably a modifiable factor. Several studies have identified a relationship between food insecurity, defined as "whenever the availability of nutritionally adequate and safe food or the ability to acquire acceptable foods in socially acceptable ways is limited or uncertain" and overweight/obesity (Anderson, 1990). These studies have shown a higher prevalence of overweight and obesity among women living in food insecure households compared to women living in food secure households (Frongillo et al., 1997; Olson, 1999; Townsend et al., 2001; Adams et al., 2003; Basiotis and Lino, 2003; CDC, 2003; Crawford et al., 2004). The mechanisms mediating this association are not well understood, but reports in the literature addressing eating patterns support the idea that food deprivation can result in overeating (Olson and Strawderman, 2008). Polivy (1996) found that food restriction or deprivation, whether voluntary or involuntary, results in a variety of changes including the preoccupation with food and eating. It has also been suggested that food-insecure households tend to purchase calorie-dense foods that are often high in fats and added sugars as an adaptative response to food insecurity (Drewnowski and Darmon, 2005).

More recently, Jones and Frongillo (2007) found food insecurity without hunger to be associated with risk for overweight/obesity, but not with subsequent weight gain in women of all racial/ethnic groups. Wilde and Peterman (2006) examined the relationship between food insecurity and change in self-reported weight over 12 months in a national sample of non-pregnant women. These investigators found that women in households that were marginally food secure were significantly more likely to gain 4.54 kg (10 pounds) or more in a year compared to women in food secure households.

While food insecurity and obesity have been shown to be positively associated in women, little is known about the direction of causality between food insecurity and obesity. Olson and Strawderman (2008) found in a cohort of 622 healthy adult women from rural areas followed from early pregnancy until two years postpartum that food insecurity in early pregnancy was not associated with increased risk of obesity at two years postpartum. However, obesity in early pregnancy was significantly associated with increased risk of food insecurity at two years postpartum, suggesting that the causal direction of the relationship between food insecurity and obesity likely goes from obesity to food insecurity. Moreover, they found that women who were both obese and food insecure in early pregnancy were at greatest risk of major gestational and postpartum weight gain, suggesting that food insecurity may play a role in GWG (trends in food insecurity are shown in Chapter 2).

Genetic Characteristics

The role of DNA sequence variation in the regulation of body weight is being investigated in many laboratories around the world. However, the role of genetic factors in the modulation of weight gain during pregnancy has not received much attention to date. The committee was unable to identify studies dealing with familial aggregation or heritability of GWG. The only evidence comes from a small number of reports focusing on the contribution of single nucleotide polymorphisms (SNPs) in specific genes on GWG. At present no study has considered the important issue of nutrition or physical activity interactions with genes on GWG.

Several studies have considered the effect of the Trp64Arg allelic substitution in the beta 3 adrenergic receptor gene (ADRβ3) on weight gain during pregnancy (Festa et al., 1999; Yanagisawa et al., 1999; Alevizaki et al., 2000; Tsai et al., 2004; Fallucca et al., 2006). The

homozygotes for the 64Arg allele were found to have gained more weight from baseline to gestational weeks 20 to 31 than heterozygotes in Austrian mothers (Festa et al., 1999). In pregnant women with type 2 diabetes, a gain in BMI of more than 5 units was found to have a prevalence of 12.2 percent in homozygotes for the Trp allele, 19.2 percent for the heterozygotes and 28.6 percent for the Arg allele homozygotes (Yanagisawa et al., 1999). However, in the latter study from Japan, there were no differences among the three genotypes for GWG. In a study from Greece, no differences among the ADRB3 genotypes were found for the rate of weight gain (g/day) calculated from the difference between the prepregnancy reported body weight and the weight measured between weeks 28 and 36 of gestation (Alevizaki et al., 2000). Similarly, no differences were observed among genotypes in a Taiwanese population for weight gain at 24 to 31 weeks of gestation (Tsai et al., 2004). In the largest study to date, 627 pregnant women from Italy were studied and no effect of the ADRB3 polymorphism on GWG was found (Fallucca et al., 2006). In the same study, a marker in the insulin receptor substrate 1 (IRS-1) gene was also not associated with GWG.

The Pro12Ala polymorphism in the peroxisome proliferator-activated receptor gamma 2 (PPARδ2) was typed in pregnant Turkish women (Tok et al., 2006). Among 62 women who had gestational diabetes (GDM), those with the Ala allele gained more weight during pregnancy but this was not observed in 100 non-diabetic pregnant women. The 825 cytosine/thymidine (C/T) base substitutions, a common polymorphism of the G-protein beta-3 subunit gene, was studied in 294 women with uncomplicated, singleton pregnancies with term deliveries ranging from 37 to 40 weeks (Dishy et al., 2003). Pregnant women homozygous for the T allele (17.4 ± 0.9 kg) gained significantly more weight than the C allele carriers (15.1 ± 0.4 kg). However, the sample was composed of women from various ethnic ancestries which may have affected the results in an undetermined manner.

From this small body of data, it is not possible to conclude whether there is a role for specific genes and alleles in GWG. None of the studies reported to date were based on sufficiently large sample sizes to ensure that adequate statistical power was available to identify the effects of alleles or genotypes with a small effect size. Studies conducted on large samples of ethnically homogeneous pregnant women will be needed to be able to understand the contribution of specific genes and sequence variants to GWG.

Genetics and Birth Weight

Gestational weight gain is associated with the weight of the infant at birth even though there may not always be a cause and effect relationship and despite the fact that reverse causation often cannot be excluded. In this context, it is useful to consider the role that genetic factors may play in the variation of birth weight. In particular, it is important to understand the potential role of risk alleles at specific genes on risk for SGA and LGA.

The topic of the heritability of birth weight has been addressed for more than 50 years in the scientific literature. The evidence up to the late 1970s was reviewed (Robson, 1978) in a three volume treatise on Human Growth. The conclusion was that the fetal genotype played a small role on birth weight, probably of the order of 10 percent, while the maternal genotype accounted for about 24 percent of the total variance. These estimates were derived from data on full siblings, half-siblings, first cousins, mother-child, father-child, and monozygotic and dizygotic twins.

Recent twin studies have consistently generated slightly higher significant genetic components for birth weight in the range of 20 percent to 40 percent (Vlietinck et al., 1989;

Whitfield et al., 2001; Dubois et al., 2007). A recent report from Norway on birth weight was obtained in the mother, father, and up to three singleton offspring (included data from 101,748 families) (Lunde et al., 2007). It concluded that the fetal genetic component of birth weight adjusted for birth order, sex and generation reached 31 percent. The heritability estimates reached 31 percent for birth length and 11 percent for variation in gestational age. Given the ample statistical power of the latter study, 31 percent represents the most valid and reliable heritability estimate to date of the contribution of the fetal genes to birth weight (Beaty, 2007). The latter is concordant with the 25 percent value reported in another large Norwegian study of trios composed of mother-father-firstborn child (Magnus et al., 2001).

Importantly, variation in birth weight is influenced by a number of other factors besides the genetic makeup of the newborn. Several studies have found a role for the maternal genotype on the weight of the newborn. In the large Norwegian study cited above, maternal genetic factors accounted for 22 percent of the variation in birth weight (Lunde et al., 2007). Of particular interest is whether there is a paternal genetic component to birth weight.

In a study of 6,811 white singletons and their natural parents, the effect of parental height and weight on the length and weight at birth of an offspring was evaluated (Griffiths et al., 2007). It was observed that the effects of parental height on birth weight are similar for the two parents. However, the influence of the mother's weight on the infant's birth weight was stronger than that of the father. In a report on parental role in the familial aggregation of SGA based on 256 cases, it was found that both parents contributed almost equally to the risk (Jaquet et al., 2005). The risk of SGA for an infant at birth was 4.7 times greater for mothers and 3.5 times for fathers who were themselves SGA compared to those who were of average weight for gestational age. The risk of a SGA infant was however 16 times higher when both parents had been SGA (Jaquet et al., 2005). The most compelling data for a role of paternal birth weight on weight of the offspring at birth comes once again from a Norwegian study. A total of 67,795 trios of father-mother-firstborn child were used to plot the birth weight of infants against paternal birth weight by classes of maternal birth weight (Magnus et al., 2001). The regression of a child's birth weight on the father's birth weight was 0.137 while that on the mother's birth weight reached 0.252. The effect of paternal birth weight was about the same within each category of maternal birth weight, with no significant interaction effects between parental birth weight levels.

Evidence for a role of specific genes with a focus on their implications for diabetes on birth weight is limited (McCarthy and Hattersley, 2008). Glucokinase encoded by the *GCK* gene is an enzyme that phosphorylates glucose to glucose-6-phosphate in the pancreas, where it serves as a glucose sensor and is the rate limiting step in glucose metabolism. A defect in the pancreatic glucose sensing mechanisms of the fetus could potentially reduce weight at birth and have profound effects on the regulation of glucose and insulin later in life. Mutations altering highly conserved amino acids in *GCK* were genotyped in 58 offspring and their mothers from the UK (Hattersley et al., 1998). When a mutation was present in the fetus but not carried by the mother, weight at birth was diminished by more than 500 g. A concordant observation was that in 19 pairs of siblings discordant for a *GCK* mutation, the infant with the mutation weighed about 500 g less at birth than the other sibling (See Figure 4-2). When a mutation was absent in the fetus but present in the mother, mean birth weight was higher by about 600 g. When the mutation was present in both mother and fetus, body weight at birth was normal. The low and high birth weights associated with a number of *GCK* missense mutations are thought to reflect variation in fetal insulin secretion resulting from the *GCK* fetal genotype and indirectly from the fetal response to maternal hyperglycemia (Hattersley et al., 1998). This may represent an explanation

for some of the fetal programming cases in which there is an association between low birth weight and later insulin resistance and type 2 diabetes.

In a short report of four cases from Italy exhibiting different *GCK* mutations, three had substantially lower than average birth weight (Prisco et al., 2000). One recent study focused on the effect of the adenosine (A) allele (SNP at position -30) at the *GCK* gene on birth weight (Weedon et al., 2005). Using data from 2,689 mother-child pairs, the A allele in the mother was associated with a 64 g increase in the offspring birth weight. There was no effect of the offspring *GCK* genotype at this particular mutation on birth weight.

Hepatocyte nuclear factor 1 beta (HNF1β) is a transcription factor, encoded by the *HNF1β* gene, critical for the development of the pancreas. Birth weight was studied in 21 patients with *HNF1β* mutations (Edghill et al., 2006). Weight at birth was low in all cases, with a median weight of 2.7 kg. In 13 of these patients born to unaffected mothers, 69 percent were SGA at birth, with a median percentile weight of 3 (Figure 4-2).

Another transcription factor, hepatocyte nuclear factor 4 alpha (HNF4α) is involved in the regulation of pancreatic insulin secretion. The *HNF4α* gene is responsible for MODY-1 and accounts for about 4 percent of all maturity-onset diabetes in the young (MODY) cases (McCarthy and Hattersley, 2008). Mutations in *HNF4α* also associate with type 2 diabetes. Weight at birth was studied in 108 infants from families with *HNF4α* mutations (Pearson et al., 2007). Birth weight was increased by 790 g in *HNF4α* mutation carriers compared to non-mutated family members (Figure 4-2). Fifty-four percent of mutation carriers were macrosomic compared with 13 percent for non-mutation family members.
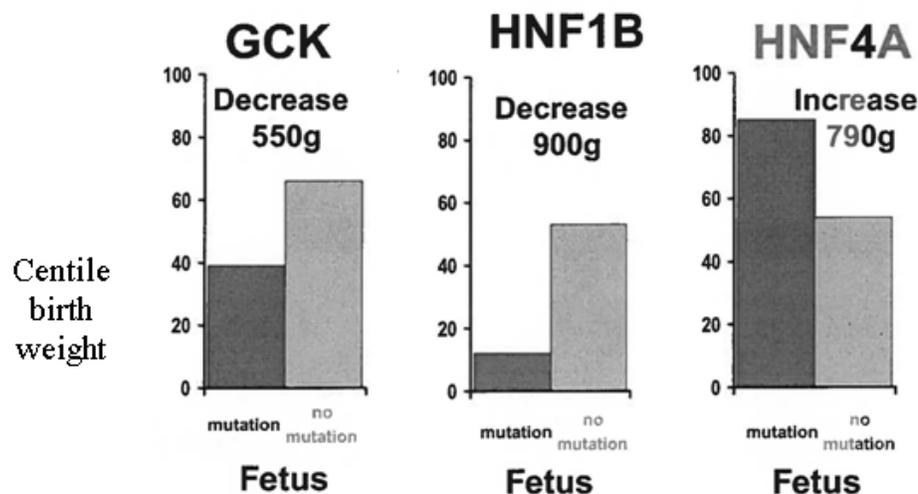
FIGURE 4-2 The impact on birth weight of a fetus inheriting three common maturity-onset diabetes in the young (MODY) gene mutations. Birth weight is presented in centile birth weight with the fetus inheriting the mutation in black and in comparison a fetus without the mutation in gray.
SOURCE: Modified from McCarthy and Hattersley, 2008. Copyright © 2008 American Diabetes Association From Diabetes®, Vol. 57, 2008; 2889-2898. Modified with permission from *The American Diabetes Association.*

In another candidate gene study, a common SNP in the fat mass and obesity associated gene (*FTO)* was investigated for its relationship to weight at birth in 234 full-term, healthy newborns (Lopez-Bermejo et al., 2008). An allelic variant known to influence body weight and fat mass in children and adults was not associated with birth weight but an association became evident after about two weeks postnatally.

Another line of evidence for a role of genes on birth weight and thus perhaps on GWG comes from scanning the whole genome. Three studies have dealt with genome-wide linkages using panels of highly polymorphic markers and birth weight. The first was based on 269 Pima Indians from 92 families and 503 autosomal microsatellite markers (Lindsay et al., 2002). A quantitative trait locus (QTL) was identified on chromosome 11 (logarithmic odds [LOD] for an imprinted locus = 3.4), suggesting that a paternally imprinted gene at map position 88 cM was influencing birth weight in this population (Lindsay et al., 2002). Subsequently, a QTL on chromosome 6q was shown to be linked to birth weight in Mexican-Americans from the San Antonio Family Birth Weight Study (LOD = 3.7) and partially replicated in a European-American population (LOD = 2.3) (Arya et al., 2006). The latest study using this approach was also on Hispanic newborns from Texas (Cai et al., 2007). Birth weight was available from birth certificates for 629 children from 319 families. Birth weight was highly heritable in this population and a QTL was identified on 10q22 with a LOD score of 2.6.

From this body of data, one can draw the preliminary conclusion that: (a) there is a fetal genotype effect on weight at birth (about 30 percent of the adjusted variance), (b) both parents' genes influence birth weight with a stronger effect for maternal genes, (c) specific allelic variants have been associated with weight at birth, (d) mutations in *GCK* and *HNF1β* are associated with low birth weight, (e) mutations in *HNF4α* are associated with high birth weight, and (f) a few quantitative trait loci on chromosomes 6, 10, and 11 have been uncovered from genome-wide linkage scans. None of the high risk alleles identified thus far have been studied for their potential contributions to GWG with or without control for the weight of the infant. The issue of the contribution of specific genes and variants to human variation in birth weight would greatly benefit from a number of genome-wide association studies with comprehensive panels of markers, particularly in cohorts with large sample size and substantial numbers of small- and large-for-gestational age infants. It will also be critical in the future to design studies that will make it possible to define the maternal and fetal alleles at key genes which associate with increased risk for GWG outside recommended ranges in the context of maternal dietary and physical activity habits.

Developmental Programming

Among the multitude of factors influencing GWG, early developmental programming may increase risk for GWG above recommended ranges. Developmental programming (physiological, metabolic or behavioral adaptation resulting from exposure or lack thereof to hormones, nutrients, stress and other agents at critical periods during embryonic or fetal development) suggests that exposures and experiences during sensitive developmental periods in utero, and possibly early postnatal life may encode the functions of organs or systems that become manifest as risk factors for disease later in life (Barker, 1998; Seckl, 1998).

One example to illustrate how developmental programming may influence maternal GWG is the suggestion that developmental programming could influence the ability to respond to and cope with repeated exposure to stress. This could in turn, provide a mechanism by which some women may be at greater risk for excessive GWG. Animals and humans subjected to chronic and

repeated stress exhibit elevated basal glucocorticoid levels and exaggerated hypothalamic-pituitary-adrenal (HPA) response to natural or experimental stressors (Sapolsky, 1995). Epidemiologic evidence suggests there may be a relationship between elevated glucocorticoid levels and physiologic changes consistent with metabolic syndrome, including increased adiposity (Pasquali et al, 2006; Barat et al., 2007). Hyperactivity of the HPA axis has been hypothesized to play a role in development of abdominal obesity and insulin resistance (Bjorntorp, 1993, 1996; Bjorntorp and Rosmond, 2000). A potential mechanism for HPA hyperactivity is through diminished feedback inhibition of pituitary activity resulting from down-regulation of glucocorticoid receptors in the brain (Vicennati and Pasquali, 2000). Over time HPA hyperactivity and excess glucocorticoid secretion can lead to both hyperinsulinemia and insulin resistance with subsequent increased risk of type II diabetes (Vicennati and Pasquali, 2000). These observations suggest that GWG could be influenced by not only factors that arise in pregnancy, but also by in utero developmental events that may predispose the mother to HPA dysregulation.

Even though the evidence for a role of developmental programming during fetal life on the risk of obesity and late-onset metabolic diseases is growing, the committee was unable to identify studies that directly examined the influences of programming on GWG in the mother. Consequences of high GWG to the child that may be related to developmental programming are discussed in Chapter 6.

Epigenetics

In addition to developmental programming, another line of evidence suggests that modifications in DNA and histone proteins could translate into phenotypic differences that often mimic those associated with DNA sequence variants. Such DNA and nucleoprotein alterations have been collectively referred to as "epigenetic events". Epigenetic events begin to occur early after fertilization, are typically stable, and influence gene expression. There is already compelling evidence to suggest that nutritional factors can entrain DNA methylation and modifications in histone proteins (Waterland and Jirtle, 2003); some of which occur at the embryonic stage in key tissues (Sinclair et al., 2007; Waterland et al., 2008). Such events are known to lead to the silencing (or switching off) of genes particularly when they occur in their promoter regions. Cytosine residue (in CpG islands) and histone (H3 and H4) methylation, acetylation or other chemical modifications occurring during early fetal life provide a mechanism, although it is not the only one, by which programming of the developing organism beyond the blueprint specified in the genomic DNA may occur.

However, it is important to recognize that epigenetic events can occur throughout life and may thus account for some of the phenotypic variation observed among adults. In this regard, the observation that the pattern of DNA methylation in monozygotic twins diverges more as they become older is of great interest (Fraga et al., 2005). It reinforces the view of those who believe that considerable phenotypic differences can arise among individuals with the same genotype. Such phenotypic variations in physiology and behavior have been observed before in inbred rodent strains but no satisfactory explanations have been provided thus far for them.

Future progress in understanding the role of programming and epigenetic factors on GWG will require increased attention not only to the role of DNA sequence variation but also to the potential influence of early programming and epigenetic events and their lasting impact on pregnant women.

Anthropometric and Physiological Factors

Pregravid BMI in concert with physiological changes in a woman's basal energy expenditure and hormonal milieu that occur during pregnancy can influence her GWG and may predict both maternal and fetal outcomes.

Pregravid BMI

Epidemiological studies, based largely on self-reported data, suggest that GWG is influenced by maternal BMI and is an important determinant of both maternal and neonatal health. In the United States, Chu et al. (2009) assessed PRAMS data for GWG by prepregnancy BMI among 52,988 women delivering full-term singleton infants from 2004-2005 (Table 4-4). This analysis found that GWG decreased as BMI increased, however, even though obese women gained less than normal or overweight women; about one-fourth of them still gained 35 pounds or more. Using a multivariable regression model, they showed that maternal prepregnancy obesity was the strongest predictor of low GWG, followed by higher parity, African American or Hispanic racial identity, and higher maternal age. In Germany, Voigt et al. (2007) analyzed perinatal statistics from over 2.3 million singleton deliveries from 1995-2000. This analysis concluded that overall, relatively short and heavy women had lower GWGs than tall and thin women.

Although pregravid BMI can predict GWG there are also metabolic changes in pregnancy, i.e. basal metabolic rate (BMR), total energy expenditure (TEE), and hormonal changes that are independent of BMI which can influence GWG.

TABLE 4-4 Gestational weight gain (pounds) by prepregnancy BMI among mothers delivering full-term, singleton births, PRAMS, 2004-2005

BMI Group	≤ 14 (n = 8442)[a]		15-24 (n = 10,583)[a]		25-34 (n = 15,477)[a]		35-44 (n = 10,942)[a]		≥ 45 (n = 7544)[a]	
	Percent[b]	SE[b]	Percent[b]	SE[b]	Percent[b]	SE[b]	Percent[b]	SE[b]	Percent[b]	SE[b]
Underweight (BMI, < 18.5 kg/m2)	10.5	0.9	17.7	1.1	34.4	1.5	23.2	1.3	14.2	1.0
Normal (BMI, 18.5-24.9 kg/m2)	10.4	0.3	16.1	0.3	31.8	0.4	24.7	0.4	17.1	0.3
Overweight (BMI, 25.0-29.9 kg/m2)	15.7	0.5	20.3	0.5	27.5	0.6	20.5	0.5	16.1	0.5
Obese (BMI, ≥ 30.0 kg/m2)	29.8	0.7	24.4	0.6	22.1	0.6	13.1	0.5	10.7	0.5
Total	15.3	0.2	18.7	0.3	29.1	0.3	21.4	0.3	15.5	0.2

χ^2 test for the difference in gestational weight gain by body mass index (BMI) group was statistically significant ($P < .001$).

[a] Based on unweighted data.

[b] Based on weighted data; percentages were age adjusted.

SOURCE: Reprinted from Chu S. Y., W. M. Callaghan, C. L. Bish and D. D'Angelo. Gestational weight gain by body mass index among US women delivering live births, 2004-2005: fueling future obesity. *American Journal of Obstetrics and Gynecology*. Copyright (2009), with permission from Elsevier. Insulin, Leptin, and Hormonal Milieu

Basal Metabolic Rate

The metabolic response to pregnancy varies widely among women. Prentice et al. (1989) reported on longitudinal changes from pre-conception through 36 weeks gestation in eight healthy well nourished women. The mean GWG at 38 weeks gestation was 14.4 ± 4.1 kg. Lean body mass increased linearly to a mean of 6.7 ± 1.6 kg by 36 weeks gestation. Measured BMR varied from 8.6 to 35.4 percent above pregravid BMR, although some obese subjects showed significant decreases in BMR up to 24 weeks gestation ($r = 0.84$). In pregnant women, the relative cost of exercise for 120 minutes was approximately 10 percent of total energy expenditure. The authors concluded from finding a small range for energy savings from either minor physical activity or thermogenesis along with high variability in BMR during pregnancy, that offering prescriptive energy intake recommendations would be impractical because it is impossible to know how an individual woman's metabolism will respond.

Durnin (1991) reported on longitudinal changes in energy expenditure during pregnancy among Scottish and Dutch women. Among this cohort, an increase in BMR was not seen until 16 weeks gestation and was followed by a mean increase of 400 kcal/day over pregravid BMI. The total energy cost of pregnancy was estimated at 69,000 kcal. Adjusting for dietary energy intake (~22,000 kcal) the authors estimated that decreased physical activity or increased efficiency of work accounted for an additional savings of ~47,000 kcal. Similarly Forsum et al. (1985) found an increase in BMR throughout gestation in a study of Swedish women.

Lawrence et al. (1985), studied how women in a developing country responded to increasing food intake during pregnancy. Pregnant women in the Gambia who followed their normal dietary pattern experienced energy sparing of 11,000 kcal with no increase in BMR above pregravid BMI until 30 weeks gestation. Further, the women showed a mean GWG of 6 kg with no increase in adipose tissue mass. When their baseline diet was supplemented with 723 kcal/day in additional food, BMR increased by approximately 1,000 kcal over pregravid BMI. Women whose diets were supplemented with additional food had a mean 8 kg increase in GWG and a 2 kg increase in fat mass. Food supplementation had no effect, however, on the energy cost of activity and did not result in increased birth weight when physical work was decreased.

Goldberg et al. (1993) used the doubly labeled water method (International Dietary Energy Consulting Group, 1990) to assess BMR, energy intake, and body composition in 12 affluent women at pre-conception and at 6 week intervals from 6 through 36 weeks gestation. Estimated changes in BMR, total energy expenditure (TEE) and fat deposition were 112 ± 104 MJ, 243 ± 279 MJ, and 132 ± 127 MJ, respectively. The mean total energy cost of pregnancy calculated from BMR, TEE, and energy deposited as fat was 418 ± 348 MJ. The women's self-reported energy intake however was only 208 ± 272 MJ, a significant underestimate of the calculated additional energy cost of pregnancy. Again, the variability in the individual biological response shown in this study supports the impracticality of prescriptive recommendations for energy intake during pregnancy.

A similar prospective study by Butte et al. (2004) of measured energy expenditure in women by prepregnant BMI showed that women in the highest BMI group accumulated greater fat mass (8.4 kg) compared to those in the low BMI group (5.3 kg). The increase in fat mass accounted for most of the variance in total weight gain among BMI groups. In both the low and high BMI groups mean TEE decreased in the second trimester but increased in the third trimester. When adjusted for fat free mass (FFM), TEE decreased in all BMI groups toward the end of gestation. Using multiple regression analysis, the change in TEE throughout the course of gestation was

related to prepregnancy BMI and percent body fat as well as weight gain and increase in FFM. These variables accounted for 33 percent of the variance in 24 hour TEE, primarily from change in BMR. Physical activity accounted for very little net increase in TEE and actually decreased in all groups with advancing gestation.

Hormonal Milieu

Maternal pregravid insulin sensitivity may vary up to 2- to 3-fold, depending on factors such as obesity, level of fitness and genetic make-up. Over the course of pregnancy a 40-60 percent decrease in insulin sensitivity occurs, depending on pregravid metabolic status (Catalano et al., 1993; Catalano et al., 1999). For example, a 50 percent decrease in insulin sensitivity in both a thin athletic woman and an obese sedentary woman with type 2 diabetes may represent a 2-fold or greater quantitative change in insulin sensitivity between them by the end of gestation. In the last 12 weeks of pregnancy, when fetal weight increases on the average from 1.0 kg to 3.5 kg, decreased insulin sensitivity increases the availability of energy to support fetal growth (Hytten and Chamberlain, 1991).

These changes in insulin sensitivity occur over a matter of months whereas in a non-pregnant individual they may occur over many years. Swinburn et al. (1991) in a longitudinal study (3.5 years) showed that, in Pima Indians, those that were insulin resistant gained less weight over time than insulin sensitive subjects (3.1 versus 7.6 kg, $p = 0.0001$). The percent change in weight per year was correlated with glucose utilization ($r = 0.34$, $p = 0.0001$). Whether similar physiologic relationships also apply to decreased GWG in obese women is not known. Swinburn et al. (1991) may not have had sufficient power to account for the greater inter-individual variability that was observed. There is, however, preliminary data showing that at least in early pregnancy changes in maternal BMR and fat accretion are inversely related to the changes in insulin sensitivity in a small number of subjects (Catalano et al., 1998). Whether increased energy intake in obese insulin-resistant women during pregnancy has a greater effect on maternal and fetal fat accretion than in non-obese women remains to be determined.

Cytokines

Both leptin and adiponectin are two adipocytokines related to fat accretion that have been examined in pregnancy. Leptin is produced in relatively large quantities by the placenta and is transferred primarily into the maternal circulation (Hauguel-deMouzon et al., 2006). Maternal leptin concentrations increase by 12 weeks gestation and have a significant positive correlation with both maternal body fat and basal metabolic rate in both early and late gestation (Highman et al., 1998). Using a stepwise regression analysis, Kirwan et al. (2002) showed that leptin made a significant contribution to changes in insulin sensitivity during gestation. A possible role for leptin in maternal metabolic adaptations to pregnancy may be found in the relationship between circulating leptin and increased maternal fat oxidation (Okereke et al., 2004).

Adiponectin is a unique circulating cytokine that is positively correlated with insulin sensitivity and negatively correlated with adiposity (Cnop et al., 2003). In contrast to leptin and other cytokines, adiponectin is made exclusively in the maternal and fetal compartments, and not in the placenta (Pinar et al., 2008). There is no transfer of leptin from mother to fetus or vice versa. Lower adiponectin concentrations have been reported in women with previous GDM (Winzer et al., 2004) and leptin was shown to decrease over the course of pregnancy in women

with GDM compared to women with normal glucose tolerance (Retnarkaran et al., 2004; Williams et al., 2004).

In summary both leptin and adiponectin are correlated with various components of maternal metabolism such as energy expenditure and adiposity. However, there are no direct mechanistic effects relating to the changes in maternal weight gain described in human pregnancy. Indirectly these cytokines through their effects on maternal insulin sensitivity may represent markers of other mechanisms effecting gestational weight changes.

Medical Factors

Pre-Existing Morbidities

The committee was unable to identify studies that directly examined pre-existing morbidities as determinants of GWG. However, in general the pre-conceptional health status of a woman is important for optimal pregnancy outcome. This is particularly true for chronic diseases such as inflammatory bowel disease and systemic lupus erythematosus. In women with inflammatory bowel disease, and in particular Crohn's disease, the level of disease activity during pregnancy is related to disease activity at conception. Fonager et al. (1998) reported a decrease in birth weight and increased preterm delivery in women with active Crohn's disease at conception. Similarly in women with lupus complicating pregnancy, pregnancy outcomes are improved if lupus has been quiescent for at least six months before conception (Cunningham et al., 2005).

Hyperemesis Gravidarum

Although as many as 70-85 percent of pregnant women will have nausea and occasional vomiting in pregnancy (Jewell and Young, 2003), this often resolves by the second trimester. There are usually no long-term sequelae and treatment is mostly symptomatic including avoidance of certain foods and small frequent meals. However, approximately 0.5-2.0 percent of pregnant women will develop hyperemesis gravidarum (ACOG, 2004). The most commonly cited criteria for hyperemesis gravidarum include: persistent vomiting unrelated to other medical conditions, ketonuria, and weight loss of 5 percent or greater of prepregnancy weight at < 16 weeks' gestation (Goodwin et al., 1992). Other associated findings include dehydration, ketonuria, and electrolyte imbalance. The underlying etiology of this disorder is not known with certainty but rapid increases in circulating human chorionic gonadotropin (HCG) and estrogen in early pregnancy have been associated with the condition (Furneaux et al., 2001; Goodwin, 2002).

In mild cases of nausea and vomiting there appears to be no adverse effect on maternal weight gain or pregnancy outcome. However, among women with hyperemesis gravidarum there is evidence of decreased GWG and a higher risk of low birth weight. Gross et al. (1989) reported on 64 women with a diagnosis of hyperemesis gravidarum. In the women who lost > 5 percent of their prepregnancy body weight, total GWG was lower (9.6 ± 2.4 versus 13.7 ± 3.2 kg, $p < 0.05$), and fetal growth was compromised, i.e. smaller percent weight for gestational age (38 percentile versus 72 percentile, $p < 0.025$) and increased growth restriction (30 percent versus 6 percent, $p < 0.01$) compared to women with a similar diagnosis that lost < 5 percent of their prepregnancy weight. Vilming and Nesheim (2000) and Bailit (2005) also reported that women with hyperemesis gravidarum had overall lower GWG and birth weight in comparison with a control group. Evidence for long-term outcomes on infant growth was not found.

Anorexia Nervosa and Bulimia Nervosa

Anorexia nervosa and bulimia nervosa are frequently encountered in young women of reproductive age. Anorexia is defined as body weight less than 85 percent of expected for age and height. The prevalence in women of reproductive age is between 0.5-1.0 percent. Whereas bulimia is defined as weight at the minimally normal range but where the individual employs binge eating and subsequent compensatory methods such as self-induced vomiting, laxative or diuretic medications to avoid appropriate weight gain. Bulimia occurs in 1-3 percent of young women. A dysfunctional perception of body weight and shape is common to both disorders (Wisner et al., 2007).

Sollid et al. (2004) in a Danish register-based follow-up study reported the results of 302 women with eating disorders before pregnancy and who were delivered 504 children and were compared with 900 control subjects who were delivered 1,552 children. There was almost a two-fold increased risk of preterm delivery and SGA. (Unfortunately the investigators were not able to obtain any information on prepregnancy BMI or GWG. In a smaller study from Sweden, Kouba et al. (2005) reported that among 49 women with previously diagnosed eating disorders 22 percent had a relapse of their eating disorder in pregnancy. The women with either a past or current eating disorder were at significantly increased risk of hyperemesis, and delivered children with significantly lower birth weight and head circumference as compared with a control group. Although there were no significant differences in GWG between the groups, the anorectic women ($n = 24$) gained less weight than women with previous history of eating disorders (10.4 ± 3.9 versus 12.1 ± 2.6 kg, $p < 0.05$). The authors speculated that potential causes for the decreased fetal growth in the women with a history of eating disorders include their inability to achieve the recommended weight gain of 11.5-16.0 kg during pregnancy. There was no significant difference in intake of folate, protein or total caloric intake between the two groups. Bulik et al. (2008) found among a cohort of 35,929 pregnant Norwegian women, that 35 reported broad anorexia nervosa, 304 bulimia nervosa, 1,812 binge eating disorder, and 36 eating disorder not otherwise specified (EDNOS)-purging type in the six months before or during pregnancy. Prepregnancy BMI was lower in anorexia, and higher in binge eating disorder than the referent group, and anorexia, bulimia, and binge eating disordered mothers reported greater GWG.

Bariatric Surgery

Parallel to the trend of increasing prevalence of obesity in the U.S., is an increase in the number of bariatric surgeries performed as treatment. The reported total number of bariatric surgical procedures performed in the U.S. increased from approximately 13,365 in 1998 to approximately 72,177 in 2002 (Santry et al., 2005; Davis et al., 2006). Furthermore, most of the procedures were performed on women; 81 percent in 1998 and 84 percent in 2002.

The American College of Obstetricians and Gynecologists (ACOG) published a Committee Opinion on Obesity and Pregnancy addressing the issue of bariatric surgery and pregnancy (ACOG, 2005). ACOG recommends that obese women who have undergone bariatric surgery receive the following counseling before and during pregnancy:

- Patients with adjustable gastric banding should be advised that they are at risk of becoming pregnant unexpectedly after weight loss following surgery.

- All patients are advised to delay pregnancy for 12-18 months after surgery to avoid pregnancy during the rapid weight loss phase.
- Women with gastric banding should be monitored by their general surgeons during pregnancy because adjustments of the band may be necessary.
- Patients should be evaluated for nutritional deficiencies, including iron, B12, folate, vitamin D and calcium, and supplemented with vitamins as necessary.

With respect to GWG, three studies reported a decrease in weight gain during a subsequent pregnancy in women who had bariatric surgery (Skull et al., 2004; Dixon et al., 2005; Ducarme et al., 2007). Nutritional complications during pregnancy, such as folate and B_{12} deficiencies, are also associated with bariatric surgery (Gurewitsch et al., 1996).

No prospective randomized trials of pregnancy outcome in obese women treated by bariatric surgery were identified. However, there have been reports using the patient as her own control i.e. a pregnancy outcome before bariatric surgery and a subsequent pregnancy outcome after having a bariatric procedure (Marceau et al., 2004; Skull et al., 2004; Dixon et al., 2005) or retrospective case controlled studies (Ducarme et al., 2007). Incidence of GDM and hypertensive disorders were found to be decreased in the studies of Skull et al. (2004), Dixon et al. (2005), and Ducarme et al. (2007). The effect of bariatric surgery on the risk of fetal macrosomia and birth weight are inconclusive. Marceau et al. (2004) and Ducarme et al. (2007) reported a decreased risk of macrosomia in women following bariatric surgery. In contrast, neither Dixon et al. (2005) nor Skull et al. (2004) reported a decrease in macrosomia. Care must be taken in the interpretation of these studies because of their retrospective nature and use of various definitions of outcome measures.

Twins and Higher Order Pregnancy

The presence of multiple fetuses in a pregnancy has an influence on total GWG. In comparison to singleton birth the additional components of the products of a twin gestation (fetus, placenta and amniotic fluid) account for up to two additional kilograms in GWG (See discussion in Chapter 3). The effects of GWG on maternal and child health outcomes for multiple births are discussed in Chapters 5 and 6, respectively.

Psychological Factors

Depression

Several investigators have reported positive associations between GWG and depressive symptoms. Bodnar et al. (in press) followed a sample of 242 mostly well-educated white women through pregnancy and assessed clinical depression through structured interviews at 20, 30, and 36 weeks gestation. The study found that all women with GWG below the ranges recommended by IOM (1990) had an elevated prevalence of major depression, regardless of their pregravid BMI (Bodnar et al., in press). Hickey et al. (1995) conducted a prospective study of depressive symptoms at 24-26 weeks and inadequate GWG in a large cohort of low-income, non-obese black and white women. The authors reported that white women in the highest quartile of depressive symptom score were three times as likely as women in the lowest quartile to have weight gain below the ranges recommended by IOM (1990). No relationship was found,

however, between depression and low weight gain in black women (Hickey et al., 1995). In a cohort of over 4,000 Hispanic women, self-reported feelings of depression during the pregnancy were found to be negatively associated with GWG (Siega-Riz and Hobel, 1997).

In a recent study, pregnant women who gained in excess of the ranges recommended by IOM (1990) were more likely to have high depressive symptoms than women who met the weight gain recommendations (Webb et al., 2009). Casanueva et al. (2000) used a case-control study to test for associations between maternal depressive symptoms and fat deposition among pregnant adolescents in Mexico City. Body weight and anthropometric measures of skinfold thickness were used to determine fat deposition beginning at 20 weeks gestation through four weeks postpartum. The results of this study indicated an association between depressive symptoms and excessive fat deposition in Mexican adolescents. In cross-sectional studies, high depressive symptoms have been linked with negative attitudes about GWG (Stevens-Simon et al., 1993; Dipietro et al., 2003). Women who are concerned before and during pregnancy about their weight gain have higher depressive scores in the week following delivery (Abraham et al., 2001).

Cameron et al. (1996) studied a biracial sample of 132 women in mid-gestation and found that GWG had no association with depressive symptoms in the second trimester. Third-trimester weight was negatively correlated with depression score, but only among white women with low self-esteem. A positive association between GWG and depression score was found for white women with high self-esteem, whereas GWG had no effect on depression in black women (Cameron et al., 1996). Walker and Kim (2002) used data from a longitudinal study of postpartum weight patterns in low income women to test for relationships between depressive symptoms and GWG and birth weight. Regression analyses found that depressive symptoms were not significantly associated with GWG. Collectively, the majority of studies indicate that low and high GWG may be a marker of depression during pregnancy. Trends in depression among women of child-bearing age are shown in Chapter 2.

Stress

Among studies that evaluate stress, social support, or depression and its relationship to postpartum weight retention there is no consistent evidence in support of a relationship between stress and GWG or increased postpartum weight retention. The impact, however, of psychosocial factors such as stress on GWG and postpartum weight retention may be underestimated as a result of the limitations in measurement and data analysis in observational studies. An additional confounding factor is that stress can have different kinds of effects depending on how an individual responds.

The influence of psychological stress as a factor in GWG and pregnancy outcome was examined in a controlled prospective study of a group of 60 women utilizing an urban prenatal clinic (Picone et al., 1982). Psychological stress was assessed using a social readjustment rating scale from the Holmes-Rahe life events questionnaire. This study found a correlation between higher stress scores and lower GWG, independent of nutrient or caloric intake. This finding suggests that stress did not affect food intake in these subjects, rather the utilization of calories and nutrients from the foods consumed to support pregnancy was impacted.

A robust association between the appraisals of stress and sufficiency of coping resources and adequacy of GWG in crude or adjusted models was not identified. However, when evaluating the risk ratio differences observed between women who gained inadequate or excessive weight (relative to women who gained adequate weight), the former tended to have a stronger, albeit modest, link to perceived stress than the latter. This distinction is comparable to a pattern also

cited previously in another investigation (Brawarsky et al., 2005). In that study, women who reported high stress during pregnancy tended to gain weight below clinical guidelines in contrast to those who did not report significant prenatal stress. This relationship failed to emerge among those who gained weight in excess of clinical advice. This finding is also consistent with earlier work that typically reported higher stress in relation to insufficient GWG (Orr et al., 1996).

Social Support

There is inconclusive evidence for a role of social support as a determinant of GWG. In a prospective study of 806 low-income, non-obese pregnant women, Hickey et al. (1995) found that the levels of social support did not predict low GWG for either black or white women. Casanueva et al. (1994) reported on the impact of psychological support, given to a group of adolescents during pregnancy, on GWG. Adolescents who received additional psychological support by a psychotherapy team gained, on average, 2.8 kg more than adolescents who did not receive support. More recently, Olson and Strawderman (2003) found the effect of social support on GWG varied significantly by BMI group. Low social support among low, normal, and obese women was associated with significantly more weight gain than that of their counterparts with average or high social support. However, obese women who had low social support gained significantly less weight relative to those with average or high social support.

Attitudes Toward Weight Gain or Weight Loss

Several studies have examined the relationship between maternal attitude toward weight gain during pregnancy and actual GWG. Palmer et al. (1985) developed an 18-item scale measuring pregnant women's attitude toward their own weight gain and found among 29 white, middle-class women that positive attitude was significantly associated with higher actual weight gain. Steven-Simon et al. (1993) found, in a study of 99 pregnant adolescents, that weight gain was significantly related to 4 of 18 scale items but not the total attitude scale score. However, Copper et al. (1995) found in a sample of 1,000 black and white low-income women that the attitude score was not significantly related to GWG. Maternal attitude toward weight gain was found to be influenced by prepregnancy BMI; thin women tended to have positive attitudes and obese women tended to have negative attitudes about GWG (Copper et al., 1995). Taken together, the evidence is inconclusive regarding the influence of maternal attitude on actual GWG.

For the majority of women, weight loss during pregnancy is discouraged. However, a small percentage (8.1) of women reported in the Behavioral Risk Factor Surveillance Survey (BRFSS) that they attempted to lose weight during pregnancy (CDC, 1989; 1991). Another survey of women who reported being pregnant and also trying to lose weight indicated that prevalence of weight loss behavior during pregnancy occurred among those who reported drinking and smoking (12.7 percent), women in the first trimester of pregnancy (9.4 percent), those who were diabetic (9 percent), and those with very high BMIs (6.9 percent) (Cogswell et al., 1996). Cohen and Kim (2009) reviewed aggregated multiple year data between 1996 and 2003 from the BRFSS (1989) and found weight loss attempts during pregnancy were more frequent among women over 34 years of age (6.2 percent) and Hispanic women (13.1 percent). Carmichael et al. (2003) reported in a population-based case control study of 538 cased and 539 control infants that restricted food intake or fad dieting by the mother during the first trimester of pregnancy was associated with significant risk for neural tube defect among both food restrictors (OR = 2.1 [95% CI: 1.1-4.1]) and dieters (OR = 5.8 [95% CI: 1.7-10]) compared to controls. Interestingly,

no significant increased risk for neural tube defect was detected for dieting behaviors during the three months prior to conception.

Behavioral Factors

The issue of energy balance is central relative to the evaluation of GWG, regardless of whether it is in gravid or pregravid women.

Dietary Intake

Dietary factors may influence GWG however, a significant difference in GWG from balanced energy/protein supplementation in normal weight women was not supported in a systematic review of 10 trials (Kramer and Kakuma, 2003). Two trials reviewed in Kramer and Kakuma (2003) among women who were obese (Campbell, 1983) or had high GWG (Campbell and MacGillivray, 1975) showed energy/protein restriction was associated with a significant reduction in weekly maternal weight gain (weighted mean difference of 255 [95% CI= -436.56 to -73.0] g/week).

Several observational studies have also examined the relationship between prepregnancy BMI, caloric intake, and GWG. Bergmann et al. (1997) reported on data in 156 healthy German women. The authors defined maternal weight gain as "net weight gain", i.e. the weight gain of the mother from the end of the third trimester minus the measured weight in the first trimester, excluding the weight of the fetus and placenta. The authors defined high BMI as > 24. Net weight gain was related to both maternal pregravid BMI and energy intake. There was a decrease in net weight gain in the high BMI group (4.2 kg) as compared to the medium BMI group (6.2 kg) and low BMI group (5.9 kg). In the high BMI group, parity was a significant co-variable. The lower weight gain was confined to the multigravid women, whereas the primigravid high BMI group actually had greater net weight gain. These associations did not appreciably change when adjusted for energy intake, which did not vary during the course of pregnancy. Neither maternal BMI nor energy intake was related to birth weight.

Olson and Strawderman (2003) used a proxy measure for energy intake by questioning women about changes in the amount of food eaten prior to and during pregnancy. They found in a clinic sample of 622 healthy pregnant women that consuming either "much more" or "much less" food during rather than prior to pregnancy was associated with greater (3.67 pounds; $P < 0.001$) and less (-3.16 pounds; $P < 0.05$) GWG, respectively, compared with maintaining similar levels of food intake. Their multivariable model found that women who ate "much more" during rather than before their pregnancy had an adjusted odds ratio of 2.35 for excessive GWG. Lagiou et al. (2004) found in a clinic sample of 224 pregnant women that increased GWG by the end of the second trimester of pregnancy was associated with higher total energy intake as well as a higher proportion of protein and lipids of animal origin and lower proportion of carbohydrates.

More recently, Olafsdottir et al. (2006) reported on the relationship of dietary factors relating to GWG in 495 healthy Icelandic women using food frequency questionnaires. Optimal weight gain in normal weight women was defined as between 12-18 kg and for overweight women between 7-12 kg. Eleven percent of overweight women had inadequate weight gain (≤ 7 kg). Additionally, 55 percent of overweight women gained excessive weight (>12 kg) and 20 percent of normal weight women gained excessive weight (>18 kg). A "suboptimal" weight gain resulted in a mean birth weight of 3,591 ± 447 g while excessive weight gain resulted in a mean weight of 3,872 ± 471 g.

Analyses from the Pregnancy, Infection, and Nutrition Study (Deierlein et al., 2008) showed that compared to women consuming diets within the lowest quartile for energy density (defined as the number of calories/g of food consumed) during the second trimester, women consuming diets with energy density values in the third and highest quartiles gained a significant excess of over 1 kg in total GWG.

Beyond general food intake, several studies have also examined consumption of different types of food as well as macronutrient and micronutrient intake. Steven-Simon and McAnarney (1992) showed in a study of adolescents that those who consumed fewer than three snacks a day had slower weight gains during pregnancy. Olson and Strawderman (2003) found women who consumed three or more servings of fruits and vegetables per day gained 1.81 pounds less than those who consumed fewer servings during pregnancy. Olafsdottir et al. (2006) found that among women in Iceland, the percentage of energy intake from various macronutrients is an important predictor of weight gain only among overweight women and late in pregnancy. Compared with women gaining suboptimal weight, the diet of overweight women gaining excessive weight had higher energy percentage from fat and lower energy percentage from carbohydrates. They also found that consumption of dairy products and sweets in late pregnancy was associated with a decreased risk of inadequate gain and an increased risk of excessive gain during pregnancy.

In a small randomized clinical trial of a low-glycemic versus a high-glycemic diet, Clapp (2002) found that the women on the low-glycemic diet gained less weight during pregnancy (22.9 compared with 40.9 pounds). The mechanisms involved were thought to include changes in: daily digestible energy requirements (i.e. metabolic efficiency), substrate utilization (glucose oxidation versus lipid oxidation), and insulin resistance and sensitivity (Clapp, 2002). However, Deierlein et al. (2008) reported no statistical effect of glycemic load alone on total GWG or weight gain ratio. Their findings suggest that race/ethnicity may interact with glycemic processes, such that white women with glycemic load increases were more sensitive to increased weight gain during pregnancy; this was not true for black women

Altogether several studies have demonstrated a relationship between energy intake and GWG. Additional evidence suggests that dietary intake may also influence GWG however the evidence is insufficient to draw a conclusion.

Physical Activity

The American College of Obstetricians and Gynecologists (ACOG) took the position in 2002 that, in the absence of either medical or obstetric complications, 30 minutes or more of moderate exercise a day on most, if not all, days was recommended for pregnant women (ACOG, 2002). The ACOG report emphasized that participation in a wide range of recreational activities appears to be safe for pregnant women. Participation in activities with a high potential for trauma to the woman or fetus, however, should be avoided.

Published reviews on exercise and pregnancy concluded that the balance of evidence suggests a benefit of exercise during pregnancy, especially for maternal outcomes (Morris and Johnson, 2005; Gavard and Artal, 2008). Moderate exercise during a low risk pregnancy was found to be safe for both the mother and fetus and to improve overall maternal fitness and well-being as well as maternal and fetal outcomes (Morris and Johnson, 2005).

The report of the Physical Activity Guidelines Advisory Committee (DHHS, 2008) concluded that:

a) Moderate-intensity leisure time physical activity is not associated with an increased risk of low birth weight, preterm delivery, or early pregnancy loss; and

b) Participation in vigorous activities has been associated with small reductions in birth weight compared to less active women (Hegaard et al., 2007; Leet and Flick, 2003) but not with gestational age at birth or birth weight (Evenson et al., 2002; Duncombe et al., 2006).

Gavard and Artal (2008) concurred with the latter findings however a Cochrane Review (Kramer and McDonald, 2006) concluded that the evidence was insufficient to evaluate the risks or benefits of exercise in pregnant women for infant outcomes.

Several studies have examined the effects of regular physical activity on GWG (Abrams et al., 2000; Siega-Riz et al., 2004). Based on theoretical energy calculation alone, it appears that regular physical activity has the potential to prevent excessive GWG. The main issue then becomes whether it can be shown to work in practice. A number of observational studies but few randomized controlled trials have been reported on this topic. A small number of reports have addressed the issue of the prevalence of physical activity behavior in pregnant women. A cross sectional survey of pregnant women found that about 48 percent reported some exercise participation during pregnancy (Hinton and Olson, 2001). The most common activities were walking, swimming and aerobics. In general, the proportion of exercising pregnant women declines across trimesters of pregnancy. In one study of 388 pregnant women, 41 percent were active before pregnancy (Ohlin and Rossner, 1994). By the third trimester, only 14 percent of the women continued to participate in aerobic exercise.

Two meta-analyses and several reviews have concluded that the level of physical activity in pregnant women did not have an influence on GWG (Lokey et al., 1991; Sternfeld et al., 1995; Stevenson, 1997; Kramer and Kakuma, 2003; Morris and Johnson, 2005). However, the meta-analyses did not take into account a number of key factors, including the most critical one: the level of physical activity-related energy expenditure. If the energy cost of the exercise program is very low, it should not be surprising that its influences on GWG cannot be shown.

Some observational studies suggest that maintaining an active lifestyle or adding physical activity to the normal daily schedule of the pregnant woman may attenuate GWG. Clapp and Little (1995) compared exercising women who became pregnant and who continued to exercise at least three times per week to a group of women who stopped exercising once they became pregnant. The rate of GWG and of subcutaneous fat accretion (determined by skinfold thickness) was similar between the two groups during the first and second trimesters but the exercising women gained significantly less body weight and skinfold thickness during the third trimester. On average, the pregnant women who continued to exercise gained about 3 kg less. These observations were from a Norwegian study of 467 pregnant women who answered a questionnaire on physical activity level in week 36 of their pregnancy (Haakstad et al., 2007). Women who exercised regularly had significantly lower weight gain than inactive women in the third trimester only.

In a study of 96 obese women with GDM self-enrolled in either a diet ($n = 57$) or an exercise plus diet ($n = 39$) program during the last two months of pregnancy, the mean weight gain per week was less in the exercise plus diet group (0.1 ± 0.4 kg versus 0.3 ± 0.4 kg) (Artal et al., 2007). The exercise session consisted of walking on the treadmill or cycling in a semi-recumbent position once a week followed by unsupervised exercise at home for the remaining six days. The

exercise plus diet group exercised for 153 ± 91 min per week. Complications, infant birth weight, and the proportion of cesarean deliveries were comparable between the two groups.

Based on the limited available evidence, the Physical Activity Guidelines Advisory Committee concluded that "unless there are medical reasons to the contrary, a pregnant woman can begin or continue a regular physical activity program throughout gestation, adjusting the frequency, intensity, and time as her condition warrants" (DHHS, 2008). The committee added that "in the absence of data, it is reasonable for women during pregnancy and the postpartum period to follow the moderate-intensity recommendations set for adults unless specific medical concerns warrant a reduction in activity". It is commonly recognized however that adequately powered randomized, controlled intervention studies on the potential benefits and risks of regular physical activity at various dose levels in pregnant women are needed.

Physical activity, such as work, spontaneous activity, fidgeting, and personal chores as well as exercise account for a widely variable fraction of total energy expenditure. In some, this may reach only about 15 percent of daily energy expenditure while in others it may be as high as 50 percent (Hill et al., 2004). Most recently, Lof et al. (2008) assessed the effects of maternal physical activity level (PAL) and BMI on GWG in 223 healthy Swedish women. Pregravid PAL was related to decreased weight gain in the third trimester, about 0.10 kg/week less in the high PAL than in the low or medium PAL groups. Maternal BMI was inversely associated with weight gain in the second trimester but there was a positive association between maternal BMI and GWG in the third trimester. However, maternal smoking, parity, education, age, pre-gravid PAL explained only four percent of the variance in maternal weight gain and PAL was not related to birth weight.

In sum, several studies have demonstrated an inverse relationship between the level of physical activity and GWG. Based on energetic fundamentals alone, maintaining a reasonable level of exercise-related energy expenditure during pregnancy should moderate GWG. Energy requirements based on PAL are provided in Appendix B.

Substance Abuse

Cigarette smoking Taken together, early studies examining associations between decreasing GWG and amount of reported smoking show inconclusive results. Rush (1974) found a strong relationship between amount of smoking and decreasing GWG ($p < 0.01$) while Garn et al. (1979) found no association between smoking and non-smoking mothers and GWG. Several investigators examined whether smoking had a negative effect on caloric intake as a causative factor for higher incidence of SGA in smoking mothers. Haworth et al. (1980) found that women who smoked during pregnancy actually had higher mean caloric intakes with no difference in GWG; but a greater number of low birth weight infants than non-smokers. Similarly, Papoz et al. (1982) found higher mean caloric intake and lower birth weight in women who smoked during pregnancy. More recently, Furuno et al. (2004) found no significant difference in mean GWG between smoking and non-smoking mothers but did find a slightly increased (1.3-fold) risk for low GWG among smokers.

Although there is limited evidence that cigarette smoking may be inversely associated with GWG there is a preponderance of evidence that supports an independent effect of smoking on birth weight (Muscati et al., 1988; Wolff et al., 1993; Adriananse et al., 1996). Seckler-Walker and Vacek (2003) examined the effect of smoking on birth weight independent of GWG and found that gains in infant birth weight among mothers who stopped smoking during pregnancy were not related to GWG, but rather to the independent effect of smoking on birth weight.

Alcohol use Little information is available about effects of alcohol consumption on GWG. Wells et al. (2006) assessed biological, psychological and behavioral characteristics to determine associations with inadequate or excessive GWG. This analysis found no significant association between smoking and drinking and GWG outside the IOM (1990) guidelines. Little et al., (1986) found no difference in GWG between infrequent (< 7.5 g/day), occasional (7.5-15 g/day), and regular (≥ 15g/day) alcohol consumers during pregnancy. In a study of determinants of GWG in poor black adolescent mothers, Stevens-Simon and McAnarney (1992) found that alcohol use was more frequent among mothers who experienced rapid GWG. Alcohol, however, is a potent teratogen and its effects on pregnancy outcome are independent of GWG (Hanson et al., 1978; Little et al., 1986; Jacobsen et al., 1994; Bagheri et al., 1998). Thus, any impact of alcohol consumption on GWG is of little relevance compared to its teratogenic effects.

Drug use Amphetamines are anorectic drugs and their use during pregnancy would be expected to result in low GWG. Smith et al. (2006) assessed a cohort of 1,618 pregnant women that included 84 methamphetamine users. Analysis of GWG in the methamphetamine exposed group showed that those who used the drug in the first two trimesters but ceased use by the third trimester gained significantly more weight than either women who used throughout pregnancy or non-exposed women, suggesting the anorexic effects of methamphetamine are limited to continuous use, and there may be a rebound in weight gain if the mother stops use. Nevertheless, this study found exposure to methamphetamines increased the incidence of SGA births 3.5 times over the non-exposed group. Graham et al. (1992) conducted a prospective study with 30 women who were social users of cocaine during the first trimester of pregnancy. No significant differences were found between the drug users and non-users for GWG, delivery complications, birth weight, and other adverse outcomes. Chronic use of cocaine, however, has been shown to be associated with adverse maternal and fetal consequences (Wagner et al., 1998; Ogunyemi and Hernandez-Loera, 2004).

Unintended Pregnancy

Evidence for an effect of unintended pregnancy on GWG appears to be conflicting. Hickey et al. (1997) found that mistimed or unplanned pregnancy was associated with an increased risk for insufficient GWG among black but not among white women. In a study by Siega-Riz and Hobel (1997), planned pregnancy was associated with a marginally statistically significant decreased risk for insufficient GWG, but only among the low and normal weight subjects in a Hispanic cohort. Using data from the National Longitudinal Survey of Labor Market Experiences of Youth, Marsiglio and Mott (1988) found in a cohort of 6,015 primiparous women that not desiring a pregnancy was not a significant predictor of very low prenatal weight gain. Several large population-based surveys have not found an association between GWG and planned pregnancy (Kost et al., 1998; Wells et al., 2006).

VULNERABLE POPULATIONS

Seasonal Migrant Workers

The actual number of migrant farm workers currently in the U.S. in not known, but estimates are that at least 3-5 million migrant and seasonal workers come to the U.S. each year (CDC, 1997). Further, approximately 16 percent of migrant workers are women. Data about GWG among migrant women in four states was obtained through the Pregnancy Nutrition Surveillance

System (PNSS). Analysis of the data collected showed that about 52 percent of migrant women gained less than the range recommended by IOM (1990) compared to 32 percent of non-migrant women. Mean weight gain was also lower for migrant women (22.9 pounds) compared to non-migrant women (29.7 pounds). However, even though migrant women had lower GWG than non-migrant women, the prevalence for adverse birth outcomes (low birth weight, very low birth weight, preterm birth, and small for gestational age) was similar for both groups (CDC, 1997). Similarly, Reed et al. (2005) found that migrant women had higher rates of pregnancy-related risk factors but lower rates of adverse birth outcomes compared to non-migrant women.

Military

The committee was unable to identify studies that specifically examined GWG among women in military service. Several studies found women in active-duty experience greater stress but less job control, as well as higher rates of depression, compared to a parity-matched control group of dependent military wives (Magann and Nolan, 1991; O'Boyle et al., 2005), but it is unclear how these factors might influence GWG. One study surveyed pregnant women with deployed partners (Haas and Pazdernik, 2006). Women whose partners were deployed showed a greater tendency to deliver a large infant and reported more stress and changed eating habits, compared to women whose partners were not deployed; however, the results were not statistically significant. No difference was seen in the gestational age at delivery, percentage with vaginal delivery, average number of children at home, self-reported stress, or reported GWG.

Women Incarcerated During Pregnancy

The U.S. Department of Justice estimates that women offenders account for about 16 percent of the total corrections population (Bureau of Justice Statistics, 1999). Recent estimates show that the number of women under the jurisdiction of State or Federal prison authorities increased 1.2 percent from year-end 2007, reaching 115,779 (Available: http://www.ojp.usdoj.gov/bjs/prisons.htm. Accessed April 13, 2009). Of women who are incarcerated, most are of child-bearing age and approximately 6 percent are pregnant (Bureau of Justice Statistics, 1994; Safyer and Richmond, 1995).

While there are no studies that have examined the direct effect of incarceration on GWG *per se*, several studies (Martin et al., 1997a, 1997b; Bell et al., 2004) have examined its effect on birth weight. Martin et al. (1997a) found that a higher number of pregnancy days spent incarcerated was found to be associated with higher infant birth weight. Furthermore, Martin et al. (1997b) also found that infant birth weights among women incarcerated during pregnancy were not significantly different from women never incarcerated; however, infant birth weights were significantly worse among women incarcerated at a time other than during pregnancy than among never-incarcerated women and women incarcerated during pregnancy, suggesting certain aspects of the prison environment, such as shelters and regular meals, may be protective particularly for high-risk pregnant women.

FINDINGS AND RECOMMENDATIONS

Findings

1. There is a lack of evidence on societal/institutional (media, culture/acculturation, health services, policy), environmental (altitude, exposures to environmental toxicants, disasters), and neighborhood determinants (access to healthy foods, opportunities for physical activities) of GWG.

    a. Few of the studies reviewed considered the influence of the many possible determinants of GWG among women of different racial/ethnic and socioeconomic groups, or alternatively, adjusted for race/ethnicity or SES in their analyses.
    b. There is insufficient evidence to evaluate the influences of psychological factors such as depression, stress, social support, or attitude toward GWG on actual GWG.
    c. There remains a lack of information to relate dietary intake or physical activity to GWG even though they are primary determinants of weight gain in non-pregnant individuals.

2. Married women are more likely to have appropriate GWG than unmarried women. Intimate partner violence is associated with insufficient GWG. There is a paucity of studies examining the influence of partner/family support on GWG.
3. GWG is generally higher among adolescents and lower among women > 35 years of age, although the relationship of GWG among these groups to birth outcomes, post-partum weight retention, and subsequent risk for overweight/obesity remains unclear.
4. There is a lack of evidence on GWG among vulnerable populations, specifically, seasonal migrant workers, women in military service, and women incarcerated during pregnancy.
5. The IOM (1990) GWG guidelines appear to influence what women believe to be appropriate weight gain during pregnancy, though their influence on actual GWG is less clear in part because many health professionals are providing no or inappropriate advice about weight gain during pregnancy.
6. There is growing evidence suggesting that specific fetal and maternal genes and alleles can influence GWG, though both parental genotypes appear to affect birth weight. The effect of developmental programming and epigenetic events on GWG is strongly suspected but direct evidence is still lacking. Leptin and adiponectin may represent markers of insulin sensitivity or other mechanisms affecting gestational weight changes.

Research Recommendation

Research Recommendation 4-1: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies in large and diverse populations of women to understand how dietary intake, physical activity, dieting practices, food insecurity and, more broadly, the social, cultural and environmental context affect GWG.

Areas for Additional Investigation

The committee identified the following areas for further investigation to support its research recommendations. The research community should conduct studies on:

- social, cultural, and environmental contexts of GWG. Findings from these studies should help guide the development of implementation strategies for GWG recommendations;
- healthcare providers' knowledge, attitude, and behavior with respect to GWG recommendations. These studies should identify facilitators and barriers to adoption of GWG recommendations by healthcare providers in their clinical practice;
- partner and family influences on GWG;
- influences of genetic factors, epigenetic events, and developmental programming on GWG;
- how GWG affect birth outcomes, postpartum weight retention, and overweight and obesity in later life among adolescents and older women. Findings from these studies should be used to reevaluate the appropriateness of GWG recommendations for these women.
- determining whether maternal biomarkers such as leptin, adiponectin, and other markers of insulin sensitivity can be used to enhance clinical prediction of adverse birth outcomes and guide further interventions for women with GWG outside the recommended ranges. Data on relevant biomarkers should be made available through databases such as the Federal Human Nutrition Research and Information Management (HNRIM) System Database; and
- influences of psychological factors, such as depression, stress, social support, and attitude toward GWG on actual GWG.

The Department of Health and Human Services (HHS) or other appropriate federal agencies should:

- track racial-ethnic and socioeconomic disparities in GWG and that the research community conduct studies on how GWG affect birth outcomes, postpartum weight retention, and overweight and obesity in later life among women of different racial-ethnic and socioeconomic groups;
- collect nationally representative data on dietary intake, physical activity, and food insecurity among prepregnant, pregnant and postpartum women, and report these data by prepregnancy body mass index (including all classes of obesity), age, racial/ethnic group, and socioeconomic status; and
- collect data on GWG among vulnerable populations.

REFERENCES

Abraham S., A. Taylor and J. Conti. 2001. Postnatal depression, eating, exercise, and vomiting before and during pregnancy. *International Journal of Eating Disorders* 29(4): 482-487.

Abrams B., S. L. Altman and K. E. Pickett. 2000. Pregnancy weight gain: still controversial. *American Journal of Clinical Nutrition* 71(5 Suppl): 1233S-1241S.

ACOG (American College of Obstetricians and Gynecologists). 2002. ACOG committee opinion. Exercise during pregnancy and the postpartum period. Number 267, January 2002. American College of Obstetricians and Gynecologists. *International Journal of Gynaecology and Obstetrics* 77(1): 79-81.

ACOG. 2004. Nausea and vomiting of pregnancy. *Practice Bulletin No. 52* 103: 803-814.

ACOG. 2005. Committee Opinion number 315, September 2005. Obesity in pregnancy. *Obstetrics and Gynecology* 106(3): 671-675.

Adams E. J., L. Grummer-Strawn and G. Chavez. 2003. Food insecurity is associated with increased risk of obesity in California women. *Journal of Nutrition* 133(4): 1070-1074.

Adriaanse H. P., J. A. Knottnerus, L. R. Delgado, H. H. Cox and G. G. Essed. 1996. Smoking in Dutch pregnant women and birth weight. *Patient Education and Counseling* 28(1): 25-30.

Alevizaki M., L. Thalassinou, S. I. Grigorakis, G. Philippou, K. Lili, A. Souvatzoglou and E. Anastasiou. 2000. Study of the Trp64Arg polymorphism of the beta3-adrenergic receptor in Greek women with gestational diabetes. *Diabetes Care* 23(8): 1079-1083.

Ancri G., E. H. Morse and R. P. Clarke. 1977. Comparison of the nutritional status of pregnant adolescents with adult pregnant women. III. Maternal protein and calorie intake and weight gain in relation to size of infant at birth. *American Journal of Clinical Nutrition* 30(4): 568-572.

Anderson S. A. 1990. Core Indicators of Nutritional State for Difficult-to-Sample Populations. *Journal of Nutrition* 120(11_Suppl): 1555-1600.

Artal R., R. B. Catanzaro, J. A. Gavard, D. J. Mostello and J. C. Friganza. 2007. A lifestyle intervention of weight-gain restriction: diet and exercise in obese women with gestational diabetes mellitus. *Applied Physiology, Nutrition, and Metabolism* 32(3): 596-601.

Arya R., E. Demerath, C. P. Jenkinson, H. H. Goring, S. Puppala, V. Farook, S. Fowler, J. Schneider, R. Granato, R. G. Resendez, T. D. Dyer, S. A. Cole, L. Almasy, A. G. Comuzzie, R. M. Siervogel, B. Bradshaw, R. A. DeFronzo, J. MacCluer, M. P. Stern, B. Towne, J. Blangero and R. Duggirala. 2006. A quantitative trait locus (QTL) on chromosome 6q influences birth weight in two independent family studies. *Human Molecular Genetics* 15(10): 1569-1579.

Bagheri M. M., L. Burd, J. T. Martsolf and M. G. Klug. 1998. Fetal alcohol syndrome: maternal and neonatal characteristics. *Journal of Perinatal Medicine* 26(4): 263-269.

Bailit J. L. 2005. Hyperemesis gravidarium: Epidemiologic findings from a large cohort. *American Journal of Obstetrics and Gynecology* 193(3 Pt 1): 811-814.

Baker A. N. and W. L. Hellerstedt. 2006. Residential racial concentration and birth outcomes by nativity: do neighbors matter? *Journal of the National Medical Association* 98(2): 172-180.

Barat P., M. Gayard-Cros, R. Andrew, J. B. Corcuff, B. Jouret, N. Barthe, P. Perez, C. Germain, M. Tauber, B. R. Walker, P. Mormede and M. Duclos. 2007. Truncal distribution of fat mass, metabolic profile and hypothalamic-pituitary adrenal axis activity in prepubertal obese children. *Journal of Pediatrics* 150(5): 535-539, 539 e531.

Barker D. J. 1998. In utero programming of chronic disease. *Clinical Science (London)* 95(2): 115-128.

Basiotis P. P. and M. Lino. 2003. Food Insufficiency and Prevalence of Overweight Among Adult Women. *Family Economics & Nutrition Review* 15(2): 55-57.

Beaty T. H. 2007. Invited commentary: two studies of genetic control of birth weight where large data sets were available. *American Journal of Epidemiology* 165(7): 753-755.

Bell J. F., F. J. Zimmerman, M. L. Cawthon, C. E. Huebner, D. H. Ward and C. A. Schroeder. 2004. Jail incarceration and birth outcomes. *Journal of Urban Health* 81(4): 630-644.

Bergmann M. M., E. W. Flagg, H. L. Miracle-McMahill and H. Boeing. 1997. Energy intake and net

weight gain in pregnant women according to body mass index (BMI) status. *International Journal of Obesity and Related Metabolic Disorders* 21(11): 1010-1017.

Bjorntorp P. 1993. Visceral obesity: a "civilization syndrome". *Obesity Research* 1(3): 206-222.

Bjorntorp P. 1996. The origins and consequences of obesity. Diabetes. *Ciba Foundation Symposium* 201: 68-80; discussion 80-69, 188-193.

Bjorntorp P. and R. Rosmond. 2000. The metabolic syndrome--a neuroendocrine disorder? *British Journal of Nutrition* 83 Suppl 1: S49-57.

Bodnar L. M., K. L. Wisner, E. Moses-Kolko, D. K. Sit and B. H. Hanusa. In press. Prepregnancy body mass index, gestational weight gain and the likelihood of major depression during pregnancy. *Journal of Clinical Psychiatry*.

Boy A. and H. M. Salihu. 2004. Intimate partner violence and birth outcomes: a systematic review. *International Journal of Fertility and Womens Medicine* 49(4): 159-164.

Brawarsky P., N. E. Stotland, R. A. Jackson, E. Fuentes-Afflick, G. J. Escobar, N. Rubashkin and J. S. Haas. 2005. Pre-pregnancy and pregnancy-related factors and the risk of excessive or inadequate gestational weight gain. *International Journal of Gynaecology and Obstetrics* 91(2): 125-131.

Brofenbrenner U. 1979. *The ecology of human development: experiments by nature and design.* Cambridge, MA: Harvard University Press.

Brown J. E., T. M. Tharp and C. McKay. 1992. Development of a prenatal weight gain intervention program using social marketing methods. *Journal of Nutrition Education* 24: 21-28.

Bruce L. and J. G. Tchabo. 1989. Nutrition intervention program in a prenatal clinic. *Obstetrics and Gynecology* 74(3 Pt 1): 310-312.

Bulik C. M., A. Von Holle, A. M. Siega-Riz, L. Torgersen, K. K. Lie, R. M. Hamer, C. K. Berg, P. Sullivan and T. Reichborn-Kjennerud. 2008. Birth outcomes in women with eating disorders in the Norwegian Mother and Child cohort study (MoBa). *International Journal of Eating Disorders*.

Bureau of Justice Statistics. 1994. *Women in Prison*. Washington, DC: Government Printing Office.

Bureau of Justice Statistics. 1999. *Women Offenders*. Washington, DC: Government Printing Office.

Butte N. F., W. W. Wong, M. S. Treuth, K. J. Ellis and E. O'Brian Smith. 2004. Energy requirements during pregnancy based on total energy expenditure and energy deposition. *American Journal of Clinical Nutrition* 79(6): 1078-1087.

Cabral H., L. E. Fried, S. Levenson, H. Amaro and B. Zuckerman. 1990. Foreign-born and US-born black women: differences in health behaviors and birth outcomes. *American Journal of Public Health* 80(1): 70-72.

Cai G., S. A. Cole, K. Haack, N. F. Butte and A. G. Comuzzie. 2007. Bivariate linkage confirms genetic contribution to fetal origins of childhood growth and cardiovascular disease risk in Hispanic children. *Human Genetics* 121(6): 737-744.

Callaghan W. M., S. A. Rasmussen, D. J. Jamieson, S. J. Ventura, S. L. Farr, P. D. Sutton, T. J. Mathews, B. E. Hamilton, K. R. Shealy, D. Brantley and S. F. Posner. 2007. Health concerns of women and infants in times of natural disasters: lessons learned from Hurricane Katrina. *Maternal and Child Health Journal* 11(4): 307-311.

Callister L. C. and A. Birkhead. 2002. Acculturation and perinatal outcomes in Mexican immigrant childbearing women: an integrative review. *Journal of Perinatal and Neonatal Nursing* 16(3): 22-38.

Cameron R. P., C. M. Grabill, S. E. Hobfoll, J. H. Crowther, C. Ritter and J. Lavin. 1996. Weight, self-esteem, ethnicity, and depressive symptomatology during pregnancy among inner-city women. *Health Psychology* 15(4): 293-297.

Campbell D. M. and I. MacGillivray. 1975. The effect of a low calorie diet or a thiazide diuretic on the incidence of pre-eclampsia and on birth weight. *British Journal of Obstetrics and Gynaecology* 82(7): 572-577.

Campbell D. 1983. Dietary restriction in obesity and its effect on neonatal outcome. In *Nutrition in pregnancy. Proceedings of 10th Study Group of the RCOG*. Campbell DM and G. MDG. London,

RCOG: Pp. 85-98.

Carmichael S. L., G. M. Shaw, D. M. Schaffer, C. Laurent and S. Selvin. 2003. Dieting behaviors and risk of neural tube defects. *American Journal of Epidemiology* 158(12): 1127-1131.

Casanueva E., D. Legarreta, M. Diaz-Barriga, Y. Soberanis, T. Cardenas, A. Iturriaga, T. Lartigue and J. Vives. 1994. Weight gain during pregnancy in adolescents: evaluation of a non-nutritional intervention. *Revista de Investigacion Clinica* 46(2): 157-161.

Casanueva E., J. Labastida, C. Sanz and F. Morales-Carmona. 2000. Depression and body fat deposition in Mexican pregnant adolescents. *Archives of Medical Research* 31(1): 48-52.

Catalano P. M., E. D. Tyzbir, R. R. Wolfe, J. Calles, N. M. Roman, S. B. Amini and E. A. Sims. 1993. Carbohydrate metabolism during pregnancy in control subjects and women with gestational diabetes. *American Journal of Physiology* 264(1 Pt 1): E60-67.

Catalano P. M., N. M. Roman-Drago, S. B. Amini and E. A. Sims. 1998. Longitudinal changes in body composition and energy balance in lean women with normal and abnormal glucose tolerance during pregnancy. *American Journal of Obstetrics and Gynecology* 179(1): 156-165.

Catalano P. M., L. Huston, S. B. Amini and S. C. Kalhan. 1999. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. *American Journal of Obstetrics and Gynecology* 180(4): 903-916.

Caulfield L. E., F. R. Witter and R. J. Stoltzfus. 1996. Determinants of gestational weight gain outside the recommended ranges among black and white women. *Obstetrics and Gynecology* 87(5 Pt 1): 760-766.

CDC (Centers for Disease Control and Prevention). 1989. *Behavioral Risk Factor Surveillance System Survey Data*. Atlanta, Ga.: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

CDC. 1991. *Behavioral Risk Factor Surveillance System Survey Data.* Atlanta, Ga: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

CDC. 1997. Pregnancy-related behaviors among migrant farm workers--four states, 1989-1993. *MMWR. Morbidity and Mortality Weekly Report* 46(13): 283-286.

CDC. 2003. Self-reported concern about food security associated with obesity--Washington, 1995-1999. *MMWR. Morbidity and Mortality Weekly Report* 52(35): 840-842.

Chen X. K., S. W. Wen, N. Fleming, K. Demissie, G. G. Rhoads and M. Walker. 2007. Teenage pregnancy and adverse birth outcomes: a large population based retrospective cohort study. *International Journal of Epidemiology* 36(2): 368-373.

Chu S. Y., W. M. Callaghan, C. L. Bish and D. D'Angelo. 2009. Gestational weight gain by body mass index among US women delivering live births, 2004-2005: fueling future obesity. *American Journal of Obstetrics and Gynecology* 200(3): 271 e271-277.

Clapp J. F., 3rd and K. D. Little. 1995. Effect of recreational exercise on pregnancy weight gain and subcutaneous fat deposition. *Medicine and Science in Sports and Exercise* 27(2): 170-177.

Clapp J. F., III. 2002. Maternal carbohydrate intake and pregnancy outcome. *Proceedings of the Nutrition Society* 61(1): 45-50.

Cnattingius S., M. R. Forman, H. W. Berendes and L. Isotalo. 1992. Delayed childbearing and risk of adverse perinatal outcome. A population-based study. *Journal of the American Medical Association* 268(7): 886-890.

Cnop M., P. J. Havel, K. M. Utzschneider, D. B. Carr, M. K. Sinha, E. J. Boyko, B. M. Retzlaff, R. H. Knopp, J. D. Brunzell and S. E. Kahn. 2003. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. *Diabetologia* 46(4): 459-469.

Cogswell M. E., M. K. Serdula, A. H. Mokdad and D. F. Williamson. 1996. Attempted weight loss during pregnancy. *International Journal of Obesity and Related Metabolic Disorders* 20(4): 373-375.

Cogswell M. E., K. S. Scanlon, S. B. Fein and L. A. Schieve. 1999. Medically advised, mother's personal target, and actual weight gain during pregnancy. *Obstetrics and Gynecology* 94(4): 616-622.

Cohen J. H. and H. Kim. 2009. Sociodemographic and health characteristics associated with attempting

weight loss during pregnancy. *Preventing Chronic Disease* 6(1): A07.

Copper R. L., M. B. DuBard, R. L. Goldenberg and A. I. Oweis. 1995. The relationship of maternal attitude toward weight gain to weight gain during pregnancy and low birth weight. *Obstetrics and Gynecology* 85(4): 590-595.

Cordero J. F. 1993. The epidemiology of disasters and adverse reproductive outcomes: lessons learned. *Environmental Health Perspectives* 101 Suppl 2: 131-136.

Crawford P. B., M. S. Townsend and D. L. Metz. 2004. How can Californians be overweight and hungry? *California Agriculture* 58(1): 12-17.

Cunningham F. G., J. C. Hauth, K. J. Leveno, L. Gilstrap III, S. L. Bloom and K. D. Wenstrom, Eds. (2005). *Williams Obstetrics 22nd Edition*. New York, NY, McGraw-Hill Medical Publishing Division.

Dar E., M. S. Kanarek, H. A. Anderson and W. C. Sonzogni. 1992. Fish consumption and reproductive outcomes in Green Bay, Wisconsin. *Environmental Research* 59(1): 189-201.

Davis M. M., K. Slish, C. Chao and M. D. Cabana. 2006. National trends in bariatric surgery, 1996-2002. *Archives of Surgery* 141(1): 71-74; discussion 75.

Deierlein A. L., A. M. Siega-Riz and A. Herring. 2008. Dietary energy density but not glycemic load is associated with gestational weight gain. *American Journal of Clinical Nutrition* 88(3): 693-699.

Delpisheh A., L. Brabin, E. Attia and B. J. Brabin. 2008. Pregnancy late in life: a hospital-based study of birth outcomes. *Journal of Women's Health (Larchmt)* 17(6): 965-970.

DHHS (U.S. Department of Health and Human Services). 1989. *Caring for Our Future: The Content of Prenatal Care*. A Report of the Public Health Service Expert Panel on the Content of Prenatal Care. Washington, DC.

DHHS. 2008. *Physical Activity Guidelines Advisory Committee Report*. Washington, DC.

Dipietro J. A., S. Millet, K. A. Costigan, E. Gurewitsch and L. E. Caulfield. 2003. Psychosocial influences on weight gain attitudes and behaviors during pregnancy. *Journal of the American Dietetic Association* 103(10): 1314-1319.

Dishy V., S. Gupta, R. Landau, H. G. Xie, R. B. Kim, R. M. Smiley, D. W. Byrne, A. J. Wood and C. M. Stein. 2003. G-protein beta(3) subunit 825 C/T polymorphism is associated with weight gain during pregnancy. *Pharmacogenetics* 13(4): 241-242.

Dixon J. B., M. E. Dixon and P. E. O'Brien. 2005. Birth outcomes in obese women after laparoscopic adjustable gastric banding. *Obstetrics and Gynecology* 106(5 Pt 1): 965-972.

Dominguez T. P., C. D. Schetter, R. Mancuso, C. M. Rini and C. Hobel. 2005. Stress in African American pregnancies: testing the roles of various stress concepts in prediction of birth outcomes. *Annals of Behavioral Medicine* 29(1): 12-21.

Drewnowski A. and N. Darmon. 2005. Food choices and diet costs: an economic analysis. *Journal of Nutrition* 135(4): 900-904.

Dubois L., M. Girard, A. Girard, R. Tremblay, M. Boivin and D. Perusse. 2007. Genetic and environmental influences on body size in early childhood: a twin birth-cohort study. *Twin Research and Human Genetics* 10(3): 479-485.

Ducarme G., A. Revaux, A. Rodrigues, F. Aissaoui, I. Pharisien and M. Uzan. 2007. Obstetric outcome following laparoscopic adjustable gastric banding. *International Journal of Gynaecology and Obstetrics* 98(3): 244-247.

Duncombe D., H. Skouteris, E. H. Wertheim, L. Kelly, V. Fraser and S. J. Paxton. 2006. Vigorous exercise and birth outcomes in a sample of recreational exercisers: a prospective study across pregnancy. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 46(4): 288-292.

Durnin J. V. 1991. Energy requirements of pregnancy. *Diabetes* 40 Suppl 2: 152-156.

Edghill E. L., C. Bingham, A. S. Slingerland, J. A. Minton, C. Noordam, S. Ellard and A. T. Hattersley. 2006. Hepatocyte nuclear factor-1 beta mutations cause neonatal diabetes and intrauterine growth retardation: support for a critical role of HNF-1beta in human pancreatic development. *Diabetic Medicine* 23(12): 1301-1306.

Endres J. M., K. Poell-Odenwald, M. Sawicki and P. Welch. 1985. Dietary assessment of pregnant

adolescents participating in a supplemental-food program. *Journal of Reproductive Medicine* 30(1): 10-17.

Endres J., S. Dunning, S. W. Poon, P. Welch and H. Duncan. 1987. Older pregnant women and adolescents: nutrition data after enrollment in WIC. *Journal of the American Dietetic Association* 87(8): 1011-1016, 1019.

Epstein L. H., J. N. Roemmich, J. L. Robinson, R. A. Paluch, D. D. Winiewicz, J. H. Fuerch and T. N. Robinson. 2008. A randomized trial of the effects of reducing television viewing and computer use on body mass index in young children. *Archives of Pediatrics and Adolescent Medicine* 162(3): 239-245.

Eskenazi B., A. R. Marks, R. Catalano, T. Bruckner and P. G. Toniolo. 2007. Low birthweight in New York City and upstate New York following the events of September 11th. *Human Reproduction* 22(11): 3013-3020.

Evenson K. R., A. M. Siega-Riz, D. A. Savitz, J. A. Leiferman and J. M. Thorp, Jr. 2002. Vigorous leisure activity and pregnancy outcome. *Epidemiology* 13(6): 653-659.

Fallucca F., M. G. Dalfra, E. Sciullo, M. Masin, A. M. Buongiorno, A. Napoli, D. Fedele and A. Lapolla. 2006. Polymorphisms of insulin receptor substrate 1 and beta3-adrenergic receptor genes in gestational diabetes and normal pregnancy. *Metabolism* 55(11): 1451-1456.

Festa A., W. Krugluger, N. Shnawa, P. Hopmeier, S. M. Haffner and G. Schernthaner. 1999. Trp64Arg polymorphism of the beta3-adrenergic receptor gene in pregnancy: association with mild gestational diabetes mellitus. *Journal of Clinical Endocrinology and Metabolism* 84(5): 1695-1699.

Fonager K., H. T. Sorensen, J. Olsen, J. F. Dahlerup and S. N. Rasmussen. 1998. Pregnancy outcome for women with Crohn's disease: a follow-up study based on linkage between national registries. *American Journal of Gastroenterology* 93(12): 2426-2430.

Forsum E., A. Sadurskis and J. Wager. 1985. Energy maintenance cost during pregnancy in healthy Swedish women. *Lancet* 1(8420): 107-108.

Fraga M. F., E. Ballestar, M. F. Paz, S. Ropero, F. Setien, M. L. Ballestar, D. Heine-Suner, J. C. Cigudosa, M. Urioste, J. Benitez, M. Boix-Chornet, A. Sanchez-Aguilera, C. Ling, E. Carlsson, P. Poulsen, A. Vaag, Z. Stephan, T. D. Spector, Y. Z. Wu, C. Plass and M. Esteller. 2005. Epigenetic differences arise during the lifetime of monozygotic twins. *Proceedings of the National Academy of Sciences of the United States of America* 102(30): 10604-10609.

Fretts R. C. 2005. Etiology and prevention of stillbirth. *American Journal of Obstetrics and Gynecology* 193(6): 1923-1935.

Frisancho A. R., J. Matos and P. Flegel. 1983. Maternal nutritional status and adolescent pregnancy outcome. *American Journal of Clinical Nutrition* 38(5): 739-746.

Frongillo E. A., Jr., B. S. Rauschenbach, C. M. Olson, A. Kendall and A. G. Colmenares. 1997. Questionnaire-based measures are valid for the identification of rural households with hunger and food insecurity. *Journal of Nutrition* 127(5): 699-705.

Fuentes-Afflick E. and P. Lurie. 1997. Low birth weight and Latino ethnicity. Examining the epidemiologic paradox. *Archives of Pediatrics and Adolescent Medicine* 151(7): 665-674.

Fuentes-Afflick E. and N. A. Hessol. 2008. Acculturation and Body Mass among Latina Women. *Journal of Women's Health (Larchmt)* 17(1): 67-73.

Furneaux E. C., A. J. Langley-Evans and S. C. Langley-Evans. 2001. Nausea and vomiting of pregnancy: endocrine basis and contribution to pregnancy outcome. *Obstetrical and Gynecological Survey* 56(12): 775-782.

Furuno J. P., L. Gallicchio and M. Sexton. 2004. Cigarette smoking and low maternal weight gain in Medicaid-eligible pregnant women. *Journal of Women's Health (Larchmt)* 13(7): 770-777.

Garn S. M., K. Hoff and K. D. McCabe. 1979. Is there nutritional mediation of the "smoking effect" on the fetus. *American Journal of Clinical Nutrition* 32(6): 1181-1184.

Gavard J. A. and R. Artal. 2008. Effect of exercise on pregnancy outcome. *Clinical Obstetrics and Gynecology* 51(2): 467-480.

Gigante D. P., K. M. Rasmussen and C. G. Victora. 2005. Pregnancy increases BMI in adolescents of a population-based birth cohort. *Journal of Nutrition* 135(1): 74-80.

Glynn L. M., P. D. Wadhwa, C. Dunkel-Schetter, A. Chicz-Demet and C. A. Sandman. 2001. When stress happens matters: effects of earthquake timing on stress responsivity in pregnancy. *American Journal of Obstetrics and Gynecology* 184(4): 637-642.

Goldberg G. R., A. M. Prentice, W. A. Coward, H. L. Davies, P. R. Murgatroyd, C. Wensing, A. E. Black, M. Harding and M. Sawyer. 1993. Longitudinal assessment of energy expenditure in pregnancy by the doubly labeled water method. *American Journal of Clinical Nutrition* 57(4): 494-505.

Goodwin T. M., M. Montoro and J. H. Mestman. 1992. Transient hyperthyroidism and hyperemesis gravidarum: clinical aspects. *American Journal of Obstetrics and Gynecology* 167(3): 648-652.

Goodwin T. M. 2002. Nausea and vomiting of pregnancy: an obstetric syndrome. *American Journal of Obstetrics and Gynecology* 186(5 Suppl Understanding): S184-189.

Gortmaker S. L., A. Must, A. M. Sobol, K. Peterson, G. A. Colditz and W. H. Dietz. 1996. Television viewing as a cause of increasing obesity among children in the United States, 1986-1990. *Archives of Pediatrics and Adolescent Medicine* 150(4): 356-362.

Gortmaker S. L., K. Peterson, J. Wiecha, A. M. Sobol, S. Dixit, M. K. Fox and N. Laird. 1999. Reducing obesity via a school-based interdisciplinary intervention among youth: Planet Health. *Archives of Pediatrics and Adolescent Medicine* 153(4): 409-418.

Graham K., A. Feigenbaum, A. Pastuszak, I. Nulman, R. Weksberg, T. Einarson, S. Goldberg, S. Ashby and G. Koren. 1992. Pregnancy outcome and infant development following gestational cocaine use by social cocaine users in Toronto, Canada. *Clinical and Investigative Medicine. Medecine Clinique et Experimentale* 15(4): 384-394.

Griffiths L. J., C. Dezateux and T. J. Cole. 2007. Differential parental weight and height contributions to offspring birthweight and weight gain in infancy. *International Journal of Epidemiology* 36(1): 104-107.

Gross T., R. J. Sokol and K. C. King. 1980. Obesity in pregnancy: risks and outcome. *Obstetrics and Gynecology* 56(4): 446-450.

Gross S., C. Librach and A. Cecutti. 1989. Maternal weight loss associated with hyperemesis gravidarum: a predictor of fetal outcome. *American Journal of Obstetrics and Gynecology* 160(4): 906-909.

Groth S. 2007. Are the Institute of Medicine recommendations for gestational weight gain appropriate for adolescents? *Journal of Obstetric, Gynecologic, and Neonatal Nursing* 36(1): 21-27.

Groth S. W. 2008. The long-term impact of adolescent gestational weight gain. *Research in Nursing and Health* 31(2): 108-118.

Gunderson E. P., R. Striegel-Moore, G. Schreiber, M. Hudes, F. Biro, S. Daniels and P. B. Crawford. 2009. Longitudinal Study of Growth and Adiposity in Parous Compared With Nulligravid Adolescents. *Archives of Pediatrics and Adolescent Medicine* 163(4): 349-356.

Gurewitsch E. D., M. Smith-Levitin and J. Mack. 1996. Pregnancy following gastric bypass surgery for morbid obesity. *Obstetrics and Gynecology* 88(4 Pt 2): 658-661.

Gutierrez Y. M. 1999. Cultural factors affecting diet and pregnancy outcome of Mexican American adolescents. *Journal of Adolescent Health* 25(3): 227-237.

Haakstad L. A., N. Voldner, T. Henriksen and K. Bo. 2007. Physical activity level and weight gain in a cohort of pregnant Norwegian women. *Acta Obstetricia et Gynecologica Scandinavica* 86(5): 559-564.

Haas D. M. and L. A. Pazdernik. 2006. A cross-sectional survey of stressors for postpartum women during wartime in a military medical facility. *Military Medicine* 171(10): 1020-1023.

Haiek L. and S. A. Lederman. 1989. The relationship between maternal weight for height and term birth weight in teens and adult women. *Journal of Adolescent Health Care* 10(1): 16-22.

Hanson J. W., A. P. Streissguth and D. W. Smith. 1978. The effects of moderate alcohol consumption during pregnancy on fetal growth and morphogenesis. *Journal of Pediatrics* 92(3): 457-460.

Hastings G., M. Stead, L. McDermot, A. Forsyth, A. MacKintosh, M. Rayner, C. Godfrey, M. Caraher

and K. Angus. 2003. *Review of Research on the Effects of Food Promotion to Children*. Glasgow, UK: Centre for Social Marketing.

Hattersley A. T., F. Beards, E. Ballantyne, M. Appleton, R. Harvey and S. Ellard. 1998. Mutations in the glucokinase gene of the fetus result in reduced birth weight. *Nature Genetics* 19(3): 268-270.

Hauguel-de Mouzon S., J. Lepercq and P. Catalano. 2006. The known and unknown of leptin in pregnancy. *American Journal of Obstetrics and Gynecology* 194(6): 1537-1545.

Haworth J. C., J. J. Ellestad-Sayed, J. King and L. A. Dilling. 1980. Relation of maternal cigarette smoking, obesity, and energy consumption to infant size. *American Journal of Obstetrics and Gynecology* 138(8): 1185-1189.

Hediger M. L., T. O. Scholl, I. G. Ances, D. H. Belsky and R. W. Salmon. 1990. Rate and amount of weight gain during adolescent pregnancy: associations with maternal weight-for-height and birth weight. *American Journal of Clinical Nutrition* 52(5): 793-799.

Hegaard H. K., B. K. Pedersen, B. B. Nielsen and P. Damm. 2007. Leisure time physical activity during pregnancy and impact on gestational diabetes mellitus, pre-eclampsia, preterm delivery and birth weight: a review. *Acta Obstetricia et Gynecologica Scandinavica* 86(11): 1290-1296.

Hernandez-Valero M. A., A. V. Wilkinson, M. R. Forman, C. J. Etzel, Y. Cao, C. H. Barcenas, S. S. Strom, M. R. Spitz and M. L. Bondy. 2007. Maternal BMI and country of birth as indicators of childhood obesity in children of Mexican origin. *Obesity (Silver Spring)* 15(10): 2512-2519.

Hickey C. A., S. P. Cliver, R. L. Goldenberg, S. F. McNeal and H. J. Hoffman. 1995. Relationship of psychosocial status to low prenatal weight gain among nonobese black and white women delivering at term. *Obstetrics and Gynecology* 86(2): 177-183.

Hickey C. A., S. P. Cliver, R. L. Goldenberg, S. F. McNeal and H. J. Hoffman. 1997. Low prenatal weight gain among low-income women: what are the risk factors? *Birth* 24(2): 102-108.

Hickey C. A. 2000. Sociocultural and behavioral influences on weight gain during pregnancy. *American Journal of Clinical Nutrition* 71(5 Suppl): 1364S-1370S.

Highman T. J., J. E. Friedman, L. P. Huston, W. W. Wong and P. M. Catalano. 1998. Longitudinal changes in maternal serum leptin concentrations, body composition, and resting metabolic rate in pregnancy. *American Journal of Obstetrics and Gynecology* 178(5): 1010-1015.

Hill J. O., W. H. Saris and J. A. Levine. 2004. Energy Expenditure in Physical Activity. In *Handbook of Obesity: Etiology and Pathophysiology, Second Edition*. G. A. Bray and C. Bouchard. New York, Marcel Dekker Inc**:** Pp.

Hinton P. S. and C. M. Olson. 2001. Predictors of pregnancy-associated change in physical activity in a rural white population. *Maternal and Child Health Journal* 5(1): 7-14.

Horon I. L., D. M. Strobino and H. M. MacDonald. 1983. Birth weights among infants born to adolescent and young adult women. *American Journal of Obstetrics and Gynecology* 146(4): 444-449.

Howie L. D., J. D. Parker and K. C. Schoendorf. 2003. Excessive maternal weight gain patterns in adolescents. *Journal of the American Dietetic Association* 103(12): 1653-1657.

Hubert H. B., J. Snider and M. A. Winkleby. 2005. Health status, health behaviors, and acculturation factors associated with overweight and obesity in Latinos from a community and agricultural labor camp survey. *Preventive Medicine* 40(6): 642-651.

Hytten F. and G. Chamberlain. 1991. *Clinical Physiology in Obstetrics*. Oxford: Blackwell Scientific Publications.

International Dietary Energy Consulting Group. 1990. *The doubly-labeled water method for measuring energy expenditure: technical recommendations for use in humans*. Vienna: NAHRES-4 International Atomic Energy Agency.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

IOM. 1992. *Nutrition During Pregnancy and Lactation: An Implementation Guide*. Washington, DC: National Academy Press.

IOM. 2000. *Promoting Health: Intervention Strategies from Social and Behavioral Sciences*. Washington, DC: National Academy Press.

IOM. 2005. *Preventing Childhood Obesity: Health in the Balance*. Washington, DC: The National Academies Press.

IOM. 2006. *Food Marketing to Children and Youth*. Washington, DC: The National Acadmies Press.

IOM. 2007. *Nutrition Standards for Foods in Schools: Leading the Way Toward Healthier Youth*. Washington, DC: The National Academies Press.

Jacobson J. L., S. W. Jacobson, R. J. Sokol, S. S. Martier, J. W. Ager and S. Shankaran. 1994. Effects of alcohol use, smoking, and illicit drug use on fetal growth in black infants. *Journal of Pediatrics* 124(5 Pt 1): 757-764.

Jaquet D., S. Swaminathan, G. R. Alexander, P. Czernichow, D. Collin, H. M. Salihu, R. S. Kirby and C. Levy-Marchal. 2005. Significant paternal contribution to the risk of small for gestational age. *British Journal of Obstetrics and Gynaecology* 112(2): 153-159.

Jensen G. M. and L. G. Moore. 1997. The effect of high altitude and other risk factors on birthweight: independent or interactive effects? *American Journal of Public Health* 87(6): 1003-1007.

Jewell D. and G. Young. 2003. *Interventions for nausea and vomiting in early pregnancy*. Chichester, UK: John Wiley & Sons, Ltd.

Jones M. E. and M. L. Bond. 1999. Predictors of birth outcome among Hispanic immigrant women. *Journal of Nursing Care Quality* 14(1): 56-62.

Jones S. J. and E. A. Frongillo. 2007. Food insecurity and subsequent weight gain in women. *Public Health Nutrition* 10(2): 145-151.

Joseph K. S., A. C. Allen, L. Dodds, L. A. Turner, H. Scott and R. Liston. 2005. The perinatal effects of delayed childbearing. *Obstetrics and Gynecology* 105(6): 1410-1418.

Joyce T., A. Racine and C. Yunzal-Butler. 2008. Reassessing the WIC effect: evidence from the Pregnancy Nutrition Surveillance System. *Journal of Policy Analysis and Management* 27(2): 277-303.

King J. C. 2000. Physiology of pregnancy and nutrient metabolism. *American Journal of Clinical Nutrition* 71(5 Suppl): 1218S-1225S.

Kirwan J. P., S. Hauguel-De Mouzon, J. Lepercq, J. C. Challier, L. Huston-Presley, J. E. Friedman, S. C. Kalhan and P. M. Catalano. 2002. TNF-alpha is a predictor of insulin resistance in human pregnancy. *Diabetes* 51(7): 2207-2213.

Kleinman J. C., L. A. Fingerhut and K. Prager. 1991. Differences in infant mortality by race, nativity status, and other maternal characteristics. *American Journal of Diseases of Children* 145(2): 194-199.

Kost K., D. J. Landry and J. E. Darroch. 1998. The effects of pregnancy planning status on birth outcomes and infant care. *Family Planning Perspectives* 30(5): 223-230.

Kouba S., T. Hallstrom, C. Lindholm and A. L. Hirschberg. 2005. Pregnancy and neonatal outcomes in women with eating disorders. *Obstetrics and Gynecology* 105(2): 255-260.

Kramer M. S. and R. Kakuma. 2003. Energy and protein intake in pregnancy. *Cochrane Database Syst Rev*(4): CD000032.

Kramer M. S. and S. W. McDonald. 2006. Aerobic exercise for women during pregnancy. *Cochrane Database Syst Rev* 3: CD000180.

Kuh D. and Y. Ben-Shlomo. 1997. *A Life Course Approach to Chronic Disease Epidemiology: Tracing the Origins of Ill-health from early to Adult Life*. Oxford: Oxford University Press.

Kunkel K. 2001. Children and Television Advertising. In *Hanbook of Children and the Media*. D. Singer and J. Singer. Thousand Oaks, CA, Sage Publishing**:** Pp.

Lagiou P., R. M. Tamimi, L. A. Mucci, H. O. Adami, C. C. Hsieh and D. Trichopoulos. 2004. Diet during pregnancy in relation to maternal weight gain and birth size. *European Journal of Clinical Nutrition* 58(2): 231-237.

Landrigan P. J., J. Forman, M. Galvez, B. Newman, S. M. Engel and C. Chemtob. 2008. Impact of september 11 World Trade Center disaster on children and pregnant women. *Mount Sinai Journal of Medicine* 75(2): 129-134.

Lane S. D., R. H. Keefe, R. Rubinstein, B. A. Levandowski, N. Webster, D. A. Cibula, A. K. Boahene, O.

Dele-Michael, D. Carter, T. Jones, M. Wojtowycz and J. Brill. 2008. Structural violence, urban retail food markets, and low birth weight. *Health & Place* 14(3): 415-423.

Laraia B. A., A. M. Siega-Riz, J. S. Kaufman and S. J. Jones. 2004. Proximity of supermarkets is positively associated with diet quality index for pregnancy. *Preventive Medicine* 39(5): 869-875.

Laraia B., L. Messer, K. Evenson and J. S. Kaufman. 2007. Neighborhood factors associated with physical activity and adequacy of weight gain during pregnancy. *Journal of Urban Health* 84(6): 793-806.

Lawrence M., J. Singh, F. Lawrence and R. G. Whitehead. 1985. The energy cost of common daily activities in African women: increased expenditure in pregnancy? *American Journal of Clinical Nutrition* 42(5): 753-763.

Lederman S. A., V. Rauh, L. Weiss, J. L. Stein, L. A. Hoepner, M. Becker and F. P. Perera. 2004. The effects of the World Trade Center event on birth outcomes among term deliveries at three lower Manhattan hospitals. *Environmental Health Perspectives* 112(17): 1772-1778.

Leet T. and L. Flick. 2003. Effect of exercise on birthweight. *Clinical Obstetrics and Gynecology* 46(2): 423-431.

Lindsay R. S., S. Kobes, W. C. Knowler and R. L. Hanson. 2002. Genome-wide linkage analysis assessing parent-of-origin effects in the inheritance of birth weight. *Human Genetics* 110(5): 503-509.

Little R. E., R. L. Asker, P. D. Sampson and J. H. Renwick. 1986. Fetal growth and moderate drinking in early pregnancy. *American Journal of Epidemiology* 123(2): 270-278.

Lizarzaburu J. L. and L. A. Palinkas. 2002. Immigration, acculturation, and risk factors for obesity and cardiovascular disease: a comparison between Latinos of Peruvian descent in Peru and in the United States. *Ethnicity and Disease* 12(3): 342-352.

Lof M., L. Hilakivi-Clarke, S. Sandin and E. Weiderpass. 2008. Effects of pre-pregnancy physical activity and maternal BMI on gestational weight gain and birth weight. *Acta Obstetricia et Gynecologica Scandinavica* 87(5): 524-530.

Lokey E. A., Z. V. Tran, C. L. Wells, B. C. Myers and A. C. Tran. 1991. Effects of physical exercise on pregnancy outcomes: a meta-analytic review. *Medicine and Science in Sports and Exercise* 23(11): 1234-1239.

Lopez-Bermejo A., C. J. Petry, M. Diaz, G. Sebastiani, F. de Zegher, D. B. Dunger and L. Ibanez. 2008. The association between the FTO gene and fat mass in humans develops by the postnatal age of two weeks. *Journal of Clinical Endocrinology and Metabolism* 93(4): 1501-1505.

Loris P., K. G. Dewey and K. Poirier-Brode. 1985. Weight gain and dietary intake of pregnant teenagers. *Journal of the American Dietetic Association* 85(10): 1296-1305.

Luke B., J. Minogue and H. Abbey. 1992. The association between maternal weight gain and the birth weight of twins. *The Journal of Maternal-Fetal Medicine* 1: 267-276.

Lunde A., K. K. Melve, H. K. Gjessing, R. Skjaerven and L. M. Irgens. 2007. Genetic and environmental influences on birth weight, birth length, head circumference, and gestational age by use of population-based parent-offspring data. *American Journal of Epidemiology* 165(7): 734-741.

Magann E. F. and T. E. Nolan. 1991. Pregnancy outcome in an active-duty population. *Obstetrics and Gynecology* 78(3 Pt 1): 391-393.

Magnus P., H. K. Gjessing, A. Skrondal and R. Skjaerven. 2001. Paternal contribution to birth weight. *Journal of Epidemiology and Community Health* 55(12): 873-877.

Marceau P., D. Kaufman, S. Biron, F. S. Hould, S. Lebel, S. Marceau and J. G. Kral. 2004. Outcome of pregnancies after biliopancreatic diversion. *Obesity Surgery* 14(3): 318-324.

Marsiglio W. and F. L. Mott. 1988. Does Wanting to Become Pregnant with a First Child Affect Subsequent Maternal Behaviors and Infant Birth Weight? *Journal of Marriage and the Family* 50(4): 1023-1036.

Martin S. L., H. Kim, L. L. Kupper, R. E. Meyer and M. Hays. 1997a. Is incarceration during pregnancy associated with infant birthweight? *American Journal of Public Health* 87(9): 1526-1531.

Martin S. L., R. H. Rieger, L. L. Kupper, R. E. Meyer and B. F. Qaqish. 1997b. The effect of

incarceration during pregnancy on birth outcomes. *Public Health Reports* 112(4): 340-346.

McAnarney E. R. and C. Stevens-Simon. 1993. First, do no harm. Low birth weight and adolescent obesity. *American Journal of Diseases of Children* 147(9): 983-985.

McCarthy M. I. and A. T. Hattersley. 2008. Learning from molecular genetics: novel insights arising from the definition of genes for monogenic and type 2 diabetes. *Diabetes* 57(11): 2889-2898.

McFarlane J., B. Parker and K. Soeken. 1996. Abuse during pregnancy: associations with maternal health and infant birth weight. *Nursing Research* 45(1): 37-42.

Meserole L. P., B. S. Worthington-Roberts, J. M. Rees and L. S. Wright. 1984. Prenatal weight gain and postpartum weight loss patterns in adolescents. *Journal of Adolescent Health Care* 5(1): 21-27.

Moraes C. L., A. R. Amorim and M. E. Reichenheim. 2006. Gestational weight gain differentials in the presence of intimate partner violence. *International Journal of Gynaecology and Obstetrics* 95(3): 254-260.

Morris D. L., A. B. Berenson, J. Lawson and C. M. Wiemann. 1993. Comparison of adolescent pregnancy outcomes by prenatal care source. *Journal of Reproductive Medicine* 38(5): 375-380.

Morris S. N. and N. R. Johnson. 2005. Exercise during pregnancy: a critical appraisal of the literature. *Journal of Reproductive Medicine* 50(3): 181-188.

Muscati S., M. Mackey and B. Newsome. 1988. The influence of smoking and stress on prenatal weight gain and infant birth weight of teenage mothers. *Journal of Nutrition Education* 20: 299-302.

Nielsen J. N., K. O. O'Brien, F. R. Witter, S. C. Chang, J. Mancini, M. S. Nathanson and L. E. Caulfield. 2006. High gestational weight gain does not improve birth weight in a cohort of African American adolescents. *American Journal of Clinical Nutrition* 84(1): 183-189.

O'Boyle A. L., E. F. Magann, R. E. Ricks, Jr., M. Doyle and J. C. Morrison. 2005. Depression screening in the pregnant soldier wellness program. *Southern Medical Journal* 98(4): 416-418.

Ogunyemi D. and G. E. Hernandez-Loera. 2004. The impact of antenatal cocaine use on maternal characteristics and neonatal outcomes. *Journal of Maternal-Fetal & Neonatal Medicine* 15(4): 253-259.

Ohlin A. and S. Rossner. 1994. Trends in eating patterns, physical activity and socio-demographic factors in relation to postpartum body weight development. *British Journal of Nutrition* 71(4): 457-470.

Okereke N. C., L. Huston-Presley, S. B. Amini, S. Kalhan and P. M. Catalano. 2004. Longitudinal changes in energy expenditure and body composition in obese women with normal and impaired glucose tolerance. *American Journal of Physiology Endocrinology and Metabolism* 287(3): E472-479.

Olafsdottir A. S., G. V. Skuladottir, I. Thorsdottir, A. Hauksson and L. Steingrimsdottir. 2006. Maternal diet in early and late pregnancy in relation to weight gain. *International Journal of Obesity (London)* 30(3): 492-499.

Olds D. L., C. R. Henderson, Jr., R. Tatelbaum and R. Chamberlin. 1986. Improving the delivery of prenatal care and outcomes of pregnancy: a randomized trial of nurse home visitation. *Pediatrics* 77(1): 16-28.

Olson C. M. 1999. Nutrition and health outcomes associated with food insecurity and hunger. *Journal of Nutrition* 129(2S Suppl): 521S-524S.

Olson C. M. and M. S. Strawderman. 2003. Modifiable behavioral factors in a biopsychosocial model predict inadequate and excessive gestational weight gain. *Journal of the American Dietetic Association* 103(1): 48-54.

Olson C. M. and M. S. Strawderman. 2008. The relationship between food insecurity and obesity in rural childbearing women. *Journal of Rural Health* 24(1): 60-66.

Orr S. T., S. A. James, C. A. Miller, B. Barakat, N. Daikoku, M. Pupkin, K. Engstrom and G. Huggins. 1996. Psychosocial stressors and low birthweight in an urban population. *American Journal of Preventive Medicine* 12(6): 459-466.

Orstead C., D. Arrington, S. K. Kamath, R. Olson and M. B. Kohrs. 1985. Efficacy of prenatal nutrition counseling: weight gain, infant birth weight, and cost-effectiveness. *Journal of the American Dietetic Association* 85(1): 40-45.

Palmer J. L., G. E. Jennings and L. Massey. 1985. Development of an assessment form: attitude toward weight gain during pregnancy. *Journal of the American Dietetic Association* 85(8): 946-949.

Papoz L., E. Eschwege, G. Pequignot, J. Barrat and D. Schwartz. 1982. Maternal smoking and birth weight in relation to dietary habits. *American Journal of Obstetrics and Gynecology* 142(7): 870-876.

Parker B., J. McFarlane and K. Soeken. 1994. Abuse during pregnancy: effects on maternal complications and birth weight in adult and teenage women. *Obstetrics and Gynecology* 84(3): 323-328.

Pasquali R., V. Vicennati, M. Cacciari and U. Pagotto. 2006. The hypothalamic-pituitary-adrenal axis activity in obesity and the metabolic syndrome. *Annals of the New York Academy of Sciences* 1083: 111-128.

Pearson E. R., S. F. Boj, A. M. Steele, T. Barrett, K. Stals, J. P. Shield, S. Ellard, J. Ferrer and A. T. Hattersley. 2007. Macrosomia and hyperinsulinaemic hypoglycaemia in patients with heterozygous mutations in the HNF4A gene. *Public Library of Science Medicine* 4(4): e118.

Picone T. A., L. H. Allen, M. M. Schramm and P. N. Olsen. 1982. Pregnancy outcome in North American women. I. Effects of diet, cigarette smoking, and psychological stress on maternal weight gain. *American Journal of Clinical Nutrition* 36(6): 1205-1213.

Pinar H., S. Basu, K. Hotmire, L. Laffineuse, L. Presley, M. Carpenter, P. M. Catalano and S. Hauguel-de Mouzon. 2008. High molecular mass multimer complexes and vascular expression contribute to high adiponectin in the fetus. *Journal of Clinical Endocrinology and Metabolism* 93(7): 2885-2890.

Polivy J. 1996. Psychological consequences of food restriction. *Journal of the American Dietetic Association* 96(6): 589-592; quiz 593-584.

Power M. L., M. E. Cogswell and J. Schulkin. 2006. Obesity prevention and treatment practices of U.S. obstetrician-gynecologists. *Obstetrics and Gynecology* 108(4): 961-968.

Prentice A. M., R. G. Whitehead, M. Watkinson, W. H. Lamb and T. J. Cole. 1983. Prenatal dietary supplementation of African women and birth-weight. *Lancet* 1(8323): 489-492.

Prentice A. M., G. R. Goldberg, H. L. Davies, P. R. Murgatroyd and W. Scott. 1989. Energy-sparing adaptations in human pregnancy assessed by whole-body calorimetry. *British Journal of Nutrition* 62(1): 5-22.

Prisco F., D. Iafusco, A. Franzese, N. Sulli and F. Barbetti. 2000. MODY 2 presenting as neonatal hyperglycaemia: a need to reshape the definition of "neonatal diabetes"? *Diabetologia* 43(10): 1331-1332.

Prysak M., R. P. Lorenz and A. Kisly. 1995. Pregnancy outcome in nulliparous women 35 years and older. *Obstetrics and Gynecology* 85(1): 65-70.

Reddy U. M., C. W. Ko and M. Willinger. 2006. Maternal age and the risk of stillbirth throughout pregnancy in the United States. *American Journal of Obstetrics and Gynecology* 195(3): 764-770.

Reed M. M., J. M. Westfall, C. Bublitz, C. Battaglia and A. Fickenscher. 2005. Birth outcomes in Colorado's undocumented immigrant population. *BMC Public Health* 5: 100.

Retnakaran R., A. J. Hanley, N. Raif, P. W. Connelly, M. Sermer and B. Zinman. 2004. Reduced adiponectin concentration in women with gestational diabetes: a potential factor in progression to type 2 diabetes. *Diabetes Care* 27(3): 799-800.

Robinson T. N. 1999. Reducing children's television viewing to prevent obesity: a randomized controlled trial. *Journal of the American Medical Association* 282(16): 1561-1567.

Robson E. 1978. The Genetics of Birth Weight. In *Human Growth, Volume 1 Principles and Prenatal Growth*. F. Falkner and J. Tanner. London, Baillière Tindall**:** Pp. 285-297.

Rondo P. H., R. F. Ferreira, F. Nogueira, M. C. Ribeiro, H. Lobert and R. Artes. 2003. Maternal psychological stress and distress as predictors of low birth weight, prematurity and intrauterine growth retardation. *European Journal of Clinical Nutrition* 57(2): 266-272.

Rumbaut R. G. and J. R. Weeks. 1996. Unraveling a Public Health Enigma: Why do Immigrants Experience Superior Perinatal Health Outcomes? *Research in the Sociology of Health Care* 13: 335-388.

Rush D. 1974. Examination of the relationship between birthweight, cigarette smoking during pregnancy and maternal weight gain. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 81(10): 746-752.

Rush D. 1981. Nutritional services during pregnancy and birthweight: a retrospective matched pair analysis. *Canadian Medical Association Journal* 125(6): 567-576.

Rush D., D. G. Horvitz, W. B. Seaver, J. Leighton, N. L. Sloan, S. S. Johnson, R. A. Kulka, J. W. Devore, M. Holt, J. T. Lynch and et al. 1988. The National WIC Evaluation: evaluation of the Special Supplemental Food Program for Women, Infants, and Children. IV. Study methodology and sample characteristics in the longitudinal study of pregnant women, the study of children, and the food expenditures study. *American Journal of Clinical Nutrition* 48(2 Suppl): 429-438.

Safyer S. M. and L. Richmond. 1995. Pregnancy behind bars. *Seminars in Perinatology* 19(4): 314-322.

Santry H. P., D. L. Gillen and D. S. Lauderdale. 2005. Trends in bariatric surgical procedures. *Journal of the American Medical Association* 294(15): 1909-1917.

Sapolsky R. M. 1995. Social subordinance as a marker of hypercortisolism. Some unexpected subtleties. *Annals of the New York Academy of Sciences* 771: 626-639.

Schaffer D. M., E. M. Velie, G. M. Shaw and K. P. Todoroff. 1998. Energy and nutrient intakes and health practices of Latinas and white non-Latinas in the 3 months before pregnancy. *Journal of the American Dietetic Association* 98(8): 876-884.

Scholl T. O., R. W. Salmon, L. K. Miller, P. Vasilenko, 3rd, C. H. Furey and M. Christine. 1988. Weight gain during adolescent pregnancy. Associated maternal characteristics and effects on birth weight. *Journal of Adolescent Health Care* 9(4): 286-290.

Scholl T. O., M. L. Hediger, I. G. Ances, D. H. Belsky and R. W. Salmon. 1990. Weight gain during pregnancy in adolescence: predictive ability of early weight gain. *Obstetrics and Gynecology* 75(6): 948-953.

Scholl T. O. and M. L. Hediger. 1993. A review of the epidemiology of nutrition and adolescent pregnancy: maternal growth during pregnancy and its effect on the fetus. *Journal of the American College of Nutrition* 12(2): 101-107.

Scholl T. O., M. L. Hediger, J. I. Schall, C. S. Khoo and R. L. Fischer. 1994. Maternal growth during pregnancy and the competition for nutrients. *American Journal of Clinical Nutrition* 60(2): 183-188.

Scribner R. and J. H. Dwyer. 1989. Acculturation and low birthweight among Latinos in the Hispanic HANES. *American Journal of Public Health* 79(9): 1263-1267.

Secker-Walker R. H. and P. M. Vacek. 2003. Relationships between cigarette smoking during pregnancy, gestational age, maternal weight gain, and infant birthweight. *Addictive Behaviors* 28(1): 55-66.

Seckl J. R. 1998. Physiologic programming of the fetus. *Clinics in Perinatology* 25(4): 939-962, vii.

Siega-Riz A. M. and C. J. Hobel. 1997. Predictors of poor maternal weight gain from baseline anthropometric, psychosocial, and demographic information in a Hispanic population. *Journal of the American Dietetic Association* 97(11): 1264-1268.

Siega-Riz A. M., K. R. Evenson and N. Dole. 2004. Pregnancy-related weight gain--a link to obesity? *Nutrition Reviews* 62(7 Pt 2): S105-111.

Sinclair K. D., R. G. Lea, W. D. Rees and L. E. Young. 2007. The developmental origins of health and disease: current theories and epigenetic mechanisms. *Society of Reproduction and Fertility Supplement* 64: 425-443.

Singh G. K. and S. M. Yu. 1996. Adverse pregnancy outcomes: differences between US- and foreign-born women in major US racial and ethnic groups. *American Journal of Public Health* 86(6): 837-843.

Skull A. J., G. H. Slater, J. E. Duncombe and G. A. Fielding. 2004. Laparoscopic adjustable banding in pregnancy: safety, patient tolerance and effect on obesity-related pregnancy outcomes. *Obesity Surgery* 14(2): 230-235.

Smith L. M., L. L. LaGasse, C. Derauf, P. Grant, R. Shah, A. Arria, M. Huestis, W. Haning, A. Strauss, S. Della Grotta, J. Liu and B. M. Lester. 2006. The infant development, environment, and lifestyle

study: effects of prenatal methamphetamine exposure, polydrug exposure, and poverty on intrauterine growth. *Pediatrics* 118(3): 1149-1156.

Sollid C. P., K. Wisborg, J. Hjort and N. J. Secher. 2004. Eating disorder that was diagnosed before pregnancy and pregnancy outcome. *American Journal of Obstetrics and Gynecology* 190(1): 206-210.

Sternfeld B., C. P. Quesenberry, Jr., B. Eskenazi and L. A. Newman. 1995. Exercise during pregnancy and pregnancy outcome. *Medicine and Science in Sports and Exercise* 27(5): 634-640.

Stevenson L. 1997. Exercise in pregnancy. Part 1: Update on pathophysiology. *Canadian Family Physician* 43: 97-104.

Stevens-Simon C. and E. R. McAnarney. 1992. Determinants of weight gain in pregnant adolescents. *Journal of the American Dietetic Association* 92(11): 1348-1351.

Stevens-Simon C., E. R. McAnarney and K. J. Roghmann. 1993. Adolescent gestational weight gain and birth weight. *Pediatrics* 92(6): 805-809.

Stevens-Simon C., I. Nakashima and D. Andrews. 1993. Weight gain attitudes among pregnant adolescents. *Journal of Adolescent Health* 14(5): 369-372.

Stotland N. E., J. S. Haas, P. Brawarsky, R. A. Jackson, E. Fuentes-Afflick and G. J. Escobar. 2005. Body mass index, provider advice, and target gestational weight gain. *Obstetrics and Gynecology* 105(3): 633-638.

Suitor C. W. 1997. *Maternal Weight Gain: A Report of an Expert Work Group* Arlington, VA: National Center for Education in Maternal and Child Health.

Swinburn B. A., B. L. Nyomba, M. F. Saad, F. Zurlo, I. Raz, W. C. Knowler, S. Lillioja, C. Bogardus and E. Ravussin. 1991. Insulin resistance associated with lower rates of weight gain in Pima Indians. *Journal of Clinical Investigation* 88(1): 168-173.

Swinburn B. and G. Egger. 2002. Preventive strategies against weight gain and obesity. *Obesity Reviews* 3(4): 289-301.

Tok E. C., D. Ertunc, O. Bilgin, E. M. Erdal, M. Kaplanoglu and S. Dilek. 2006. PPAR-gamma2 Pro12Ala polymorphism is associated with weight gain in women with gestational diabetes mellitus. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 129(1): 25-30.

Townsend M. S., J. Peerson, B. Love, C. Achterberg and S. P. Murphy. 2001. Food insecurity is positively related to overweight in women. *Journal of Nutrition* 131(6): 1738-1745.

Tsai P. J., S. C. Ho, L. P. Tsai, Y. H. Lee, S. P. Hsu, S. P. Yang, C. H. Chu and C. H. Yu. 2004. Lack of relationship between beta3-adrenergic receptor gene polymorphism and gestational diabetes mellitus in a Taiwanese population. *Metabolism* 53(9): 1136-1139.

Ventura S. J. and S. M. Taffel. 1985. Childbearing characteristics of U.S.- and foreign-born Hispanic mothers. *Public Health Reports* 100(6): 647-652.

Ventura S. J. 1994. Recent trends in teenage childbearing in the United States. *Statistical Bulletin / Metropolitan Insurance Companies* 75(4): 10-17.

Vicennati V. and R. Pasquali. 2000. Abnormalities of the hypothalamic-pituitary-adrenal axis in nondepressed women with abdominal obesity and relations with insulin resistance: evidence for a central and a peripheral alteration. *Journal of Clinical Endocrinology and Metabolism* 85(11): 4093-4098.

Vilming B. and B. I. Nesheim. 2000. Hyperemesis gravidarum in a contemporary population in Oslo. *Acta Obstetricia et Gynecologica Scandinavica* 79(8): 640-643.

Vlietinck R., R. Derom, M. C. Neale, H. Maes, H. van Loon, C. Derom and M. Thiery. 1989. Genetic and environmental variation in the birth weight of twins. *Behavior Genetics* 19(1): 151-161.

Voigt M., S. Straube, P. Schmidt, S. Pildner von Steinburg and K. T. Schneider. 2007. [Standard values for the weight gain in pregnancy according to maternal height and weight]. *Zeitschrift fur Geburtshilfe und Neonatologie* 211(5): 191-203.

Wagner C. L., L. D. Katikaneni, T. H. Cox and R. M. Ryan. 1998. The impact of prenatal drug exposure on the neonate. *Obstetrics and Gynecology Clinics of North America* 25(1): 169-194.

Walker L. O. and M. Kim. 2002. Psychosocial thriving during late pregnancy: relationship to ethnicity,

gestational weight gain, and birth weight. *Journal of Obstetric, Gynecologic, and Neonatal Nursing* 31(3): 263-274.

Waterland R. A. and R. L. Jirtle. 2003. Transposable elements: targets for early nutritional effects on epigenetic gene regulation. *Molecular and Cellular Biology* 23(15): 5293-5300.

Waterland R. A., M. Travisano, K. G. Tahiliani, M. T. Rached and S. Mirza. 2008. Methyl donor supplementation prevents transgenerational amplification of obesity. *International Journal of Obesity (London)*.

Webb J. B., A. M. Siega-Riz and N. Dole. 2009. Psychosocial determinants of adequacy of gestational weight gain. *Obesity (Silver Spring)* 17(2): 300-309.

Weedon M. N., T. M. Frayling, B. Shields, B. Knight, T. Turner, B. S. Metcalf, L. Voss, T. J. Wilkin, A. McCarthy, Y. Ben-Shlomo, G. Davey Smith, S. Ring, R. Jones, J. Golding, L. Byberg, V. Mann, T. Axelsson, A. C. Syvanen, D. Leon and A. T. Hattersley. 2005. Genetic regulation of birth weight and fasting glucose by a common polymorphism in the islet cell promoter of the glucokinase gene. *Diabetes* 54(2): 576-581.

Weissman A., E. Siegler, R. Neiger, P. Jakobi and E. Z. Zimmer. 1989. The influence of increased seismic activity on pregnancy outcome. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 31(3): 233-236.

Wells C. S., R. Schwalberg, G. Noonan and V. Gabor. 2006. Factors influencing inadequate and excessive weight gain in pregnancy: Colorado, 2000-2002. *Matern Child Health J* 10(1): 55-62.

Whitfield J. B., S. A. Treloar, G. Zhu and N. G. Martin. 2001. Genetic and non-genetic factors affecting birth-weight and adult Body Mass Index. *Twin Research* 4(5): 365-370.

Wilde P. E. and J. N. Peterman. 2006. Individual weight change is associated with household food security status. *Journal of Nutrition* 136(5): 1395-1400.

Williams M. A., C. Qiu, M. Muy-Rivera, S. Vadachkoria, T. Song and D. A. Luthy. 2004. Plasma adiponectin concentrations in early pregnancy and subsequent risk of gestational diabetes mellitus. *Journal of Clinical Endocrinology and Metabolism* 89(5): 2306-2311.

Winzer C., O. Wagner, A. Festa, B. Schneider, M. Roden, D. Bancher-Todesca, G. Pacini, T. Funahashi and A. Kautzky-Willer. 2004. Plasma adiponectin, insulin sensitivity, and subclinical inflammation in women with prior gestational diabetes mellitus. *Diabetes Care* 27(7): 1721-1727.

Wisner K., D. Sit and S. Reynolds. 2007. Psychiatric Disorders. In *Obstetrics Normal and Problems Pregnancies Fifth Edition*. S. Gabbe, J. Niebyl and J. Simpson. Philadelphia, PA, Churchill Livingstone**:** Pp. Pp. 1249-1279.

Wolff C. B., M. Portis and H. Wolff. 1993. Birth weight and smoking practices during pregnancy among Mexican-American women. *Health Care for Women International* 14(3): 271-279.

Wolff M. S., S. Engel, G. Berkowitz, S. Teitelbaum, J. Siskind, D. B. Barr and J. Wetmur. 2007. Prenatal pesticide and PCB exposures and birth outcomes. *Pediatric Research* 61(2): 243-250.

Yanagisawa K., N. Iwasaki, M. Sanaka, S. Minei, M. Kanamori, Y. Omori and Y. Iwamoto. 1999. Polymorphism of the beta3-adrenergic receptor gene and weight gain in pregnant diabetic women. *Diabetes Research and Clinical Practice* 44(1): 41-47.

Websites:
http://www.ojp.usdoj.gov/bjs/prisons.htm
http://cdc.gov/yrbss

5

Consequences of Gestational Weight Gain for the Mother

Women whose weight gain during pregnancy is outside of the recommended ranges may experience various adverse maternal outcomes, which may include increased risk for pregnancy-associated hypertension, gestational diabetes (GDM), complications during labor and delivery, and postpartum weight retention and subsequent maternal obesity as well as an increased risk for unsuccessful breastfeeding. As noted in Chapter 1 and discussed in detail in Chapter 2, there is an increased prevalence in the United States of women who are overweight or obese entering pregnancy, also putting them at greater risk for several of these same adverse pregnancy outcomes. Additionally, more women are becoming pregnant at an older age and are thus entering pregnancy with chronic conditions, such as type 2 diabetes that could contribute to increased morbidity during both the prenatal and postpartum periods.

To review the evidence on outcomes related to gestational weight gain (GWG) within or outside the 1990 Institute of Medicine (IOM) guidelines, the Agency for Healthcare Research and Quality (AHRQ) commissioned a comprehensive, systematic evidence-based review of the literature since the release of the IOM (1990) report *Nutrition During Pregnancy.* This review included evidence on the consequences of GWG for both the mother and infant (Viswananthan et al., 2008). The committee used this review as a foundation for discussion of the state of the science for GWG and maternal outcomes in this chapter as well as for infant outcomes in Chapter 6. It is important to note that research since 1990 has focused on the consequences of gains *above* the IOM (1990) recommendations—to the exclusion of gains *below* those recommendations—on maternal and infant outcomes. The reader is referred to IOM (1990) for a discussion of the consequences of gaining too little weight gain during pregnancy.

The following briefly reviews the state of the science before the IOM (1990) report then summarizes findings from the recently published AHRQ evidence-based review on outcomes of gestational weight gain (GWG) (Viswanathan et al., 2008). These discussions also include articles published since the AHRQ report in which associations between GWG and maternal outcomes are examined (see Appendix F for summary data tables).

To interpret the rating scales from the AHRQ report, the committee indicates how the articles were rated and how the strength of the evidence was determined. The methodological approach and system of rating articles used in the AHRQ review is provided in Appendix E.

CONCEPTUAL FRAMEWORK: CONSEQUENCES OF GESTATIONAL WEIGHT GAIN FOR THE MOTHER

The committee's conceptual framework (see Chapter 1) illustrates a model for maternal and child outcomes consequent to GWG outside the ranges recommended by the IOM (1990) report (Figure 5-1). There are numerous potential causal factors, including environmental factors, that can influence the determinants of GWG and its consequences and others that may affect those

consequences by other routes. These consequences, i.e. adverse health outcomes to the mother, can arise in the prenatal and/or postpartum periods. Among the well-studied prenatal maternal outcomes that result from excessive GWG are pregnancy-associated hypertension (including preeclampsia and eclampsia) and risk of complications in labor and delivery. In the postpartum period, weight retention can lead to higher weight status in subsequent pregnancies as well as weight retention and other long-term maternal health consequences such as increased risk for type 2 diabetes and cardiovascular disease. Unfortunately the literature in this area does not allow inference of causality because it is based solely on observational studies.
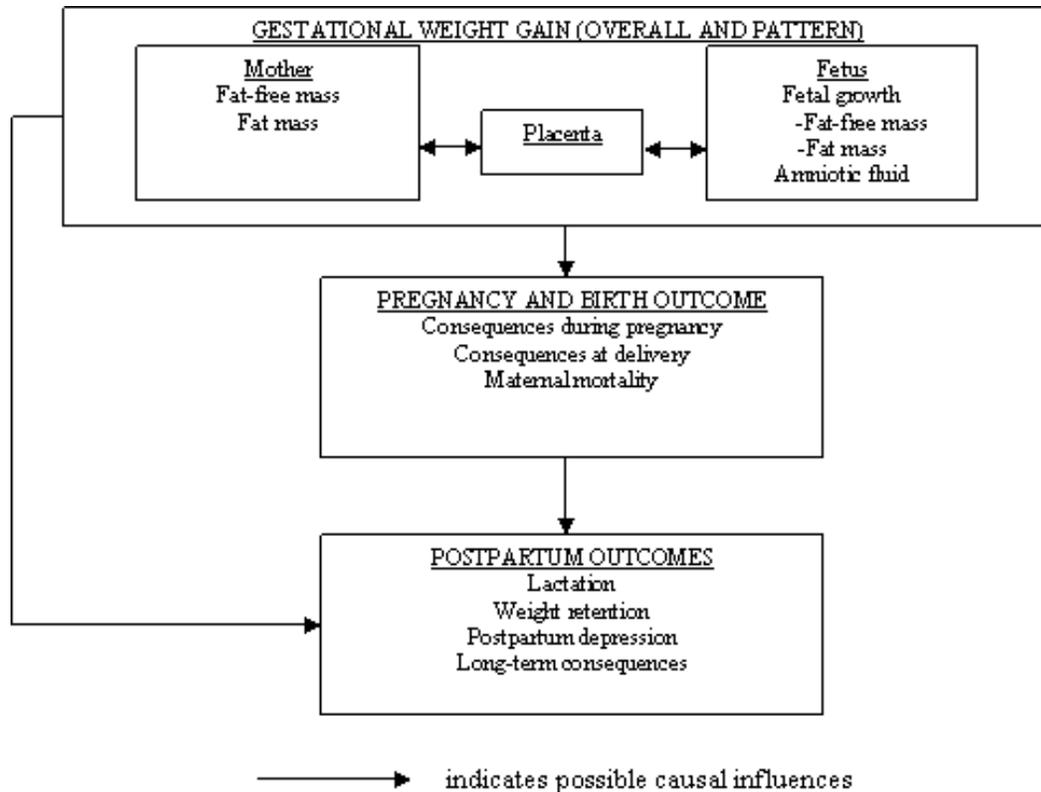
FIGURE 5-1 Schematic summary of maternal consequences associated with gestational weight gain.

CONSEQUENCES DURING PREGNANCY

Gestational Diabetes and Impaired Glucose Tolerance

Pregnancy is frequently accompanied by a pronounced physiological decrease in peripheral insulin sensitivity (reviewed in Chapter 3). Gestational diabetes, the development of abnormal glucose tolerance only during pregnancy, generally arises from the combination of decreased peripheral insulin sensitivity and beta-cell dysfunction. It is well established that women who are obese when they enter pregnancy tend to develop a more pronounced insulin resistance and are at greater risk for GDM than are non-obese women (Dahlgren, 2006; Chu et al., 2007). The incidence of GDM has increased dramatically in recent decades (See Chapter 2). From 1989 to 2004 there was a relative increase in prevalence of GDM of 122 percent for the U.S. population as a whole; and 260 percent among African American women (Getahun et al., 2008).

Most women with normal glucose tolerance develop elevated blood ketones with ketonuria at various times during pregnancy (Chez and Curcio, 1987). Pregnant women with diabetes, on the other hand, are more likely to develop sustained elevated blood ketones and ketonuria than women with normal glucose tolerance in pregnancy. Gin et al. (2006), who measured capillary blood ketones and beta-hydroxybutyrate in women with normal glucose tolerance (controls) and those with GDM three times a day between 25 and 37 weeks gestation, found that fasting ketonuria was strongly correlated with ketonemia in controls but not women with GDM. Maternal ketonuria or acetonuria during pregnancy is a concern because it can result in neonatal or childhood neurocognitive dysfunction (see discussion in Chapters 3 and 6).

As described in the AHRQ review (Viswanathan et al., 2008), the literature since 1990 includes 11 published articles that together provide weak evidence in support of an association between GWG and development of abnormal glucose metabolism (either GDM or impaired glucose tolerance). Four of the studies reported that GWG above the range recommended in the IOM (1990) report was positively associated with abnormal glucose tolerance (Edwards et al., 1996; Kieffer et al., 2001; Kabiru and Raynor, 2004; Saldana et al., 2006). Three studies reported that women whose GWG was below the recommended range had a higher likelihood of GDM (Thorsdottir et al., 2002; Brennand et al., 2005; Kieffer et al., 2006) and four studies found no significant association between GWG and glucose tolerance (Bianco et al., 1998; Murakami et al., 2005; Seghieri et al., 2005; Hackmon et al., 2007). All but one study (Saldana et al., 2006) were limited by the use of total GWG as the exposure variable rather than weight gain until the time of diagnosis. This is problematic because management of GDM includes dietary counseling and efforts to control weight gain.

Catalano et al. (1993) reported that weight gain in women who developed GDM was less than in women with normal glucose tolerance primarily as a result of their greater pregravid weight. When GWG was assessed separately for early, mid- and late gestation in women with GDM, there was a significantly decreased rate of weight gain in overweight women with GDM, although only from 30 weeks gestation until delivery. There is biologic plausibility for an effect of GWG on the development of glucose tolerance: higher GWG could result in greater fat deposition, which could then influence insulin sensitivity. The body of evidence to date, however, is weak in support of such an association.

Hypertensive Disorders

Hypertensive disorders during pregnancy include pregnancy-induced hypertension, pre-eclampsia, and eclampsia. The risk for pregnancy-induced hypertension is greater among women who enter pregnancy overweight or obese. Thadhani et al (1999) examined the relationship between pre-gravid BMI, elevated cholesterol, and the development of hypertensive disorders of pregnancy among 15,262 women. The age-adjusted relative risk for developing gestational hypertension was 1.7 and 2.2 for women with BMI values of 25-29.9 and $\geq$ 30 kg/m^2, respectively, compared to women with BMI values < 21 kg/m^2.

Preeclampsia is about twice as prevalent among overweight and about three times as prevalent among obese women as it is among normal weight women (Sibai et al., 1997; Catalano et al., 2007). Furthermore, the severity of the disease increases as BMI increases (Bodnar et al., 2007). The IOM (1990) report described the relationship between GWG and hypertensive conditions as being unclear because of limited and inclusive data. Since that report was published, 12 studies were examined in the AHRQ review (Viswanathan et al., 2008). Out of five studies (two rated fair and the rest rated poor) that examined the outcome of pregnancy-induced hypertension (Edwards et al., 1996; Bianco et al., 1998; Thorsdottir et al., 2002; Brennand et al., 2005; Jensen et al., 2005), an association between higher GWG and pregnancy-induced hypertension was found in only two of them (Thorsdottir et al., 2002; Jensen et al., 2005). The studies, however, differed in control for confounding. Thorsdottir et al. (2002) adjusted for age, parity, height, and gestational age. Jensen et al (2005) adjusted for 2-hour oral glucose tolerance test (OGTT) result, maternal age, prepregnancy BMI, gestational age (continuous variables), parity, smoking, and ethnic background. As a result, the relationship between increased GWG and onset of hypertension continues to remain unclear.

The outcome of preeclampsia has been examined in a total of 10 studies (Edwards et al., 1996; Ogunyemi et al., 1998; Thorsdottir et al., 2002; Kabiru and Raynor, 2004; Brennand et al., 2005; Murakami et al., 2005; Cedergen, 2006; Wataba et al., 2006; DeVader et al., 2007; Kiel et al., 2007), of which seven were rated fair and the rest were rated of poor quality. Overall, an association between higher total GWG and higher risk of pre-eclampsia was found in six of these studies (Edwards et al., 1996; Ogunyemi et al., 1998; Brennand et al., 2005; Cedergen, 2006; DeVader et al., 2007; Kiel et al., 2007). Lower total weight gains were found to be protective in four studies (Brennand et al., 2005; Cedergren, 2006; DeVader et al., 2007; Kiel et al., 2007). Those studies that did not find an association for high total GWG (Thorsdottir et al., 2002; Kabiru and Raynor, 2004; Murakami et al., 2005; Wataba et al., 2006) were primarily conducted in women who were not overweight or obese (two were conducted in Japan). Two studies not included in the AHRQ review using birth certificate data from the state of Missouri (Kiel et al., 2007 and DeVader et al., 2007), showed similar results, namely that GWG above the recommended range leads to higher risk of preeclampsia among overweight women (Langford et al., 2008). These studies were also limited by methodological problems associated with the use of total weight gain as the exposure as opposed to a weight gain before the diagnosis of preeclampsia. There was also a lack of a consistent definition for preeclampsia across these studies, which makes it difficult to compare them.

Preeclampsia is a condition noted for a decrease in the normal (50-60 percent) expansion in maternal intravascular (plasma) volume. The condition may also affect weight gain in early gestation. In addition, increased vascular permeability and decreased plasma oncotic pressure, caused by preeclampsia, can lead to increased edema and excessive weight gain in late gestation. Hence placental dysfunction in early gestation may effect both early and late weight gain—albeit

in opposite directions. These physiologic parameters preclude the use of total weight as a measure of GWG in preeclampsia.

Other Quality of Life Measures

As noted in Chapter 4, the influence of psychosocial status on GWG has been examined in several studies. However, there was no evidence available about possible effects of GWG on a woman's mental health during pregnancy and there was no information in the IOM (1990) report related to other measures of quality of life.

There are eight studies covered in AHRQ review (Viswanathan et al., 2008) on other antepartum outcomes. Topics include a composite outcome for discomfort in general (Rodriguez et al., 2001), physical energy and fatigue (Tulman et al., 1998), stretch marks (Madlon-Kay, 1993; Atwal et al., 2006), heartburn (Marrero et al., 1992), gallstones (Lindseth and Bird-Baker, 2004; Ko, 2006), and hyperemesis (Dodds et al., 2006). Three of these studies were rated as fair (Tulman et al., 1998; Rodriguez et al., 2001; Ko, 2006) and five as poor-quality (Marrero et al., 1992; Madlon-Kay, 1993; Lindseth and Bird-Baker, 2004; Atwal et al., 2006; Dodds et al., 2006). Overall, there was no association between higher GWG and the outcomes of interest except for the two studies in which stretch marks were examined (Madlon-Kay, 1993; Atwal et al., 2006). This association was weak because of the small sample size, study design (one was a cross-sectional study), and the lack of adjustment for confounding factors. In the one study in which hyperemesis was examined, women who gained a total of < 7 kg had an increased likelihood of more antenatal admissions for this outcome (Dodds et al., 2006). For this outcome in particular, GWG was not a causal factor but was more likely the result of having had hyperemesis during the pregnancy.

In summary, evidence for an association between GWG and pregnancy complications such as GDM and gestational hypertensive disorders is inconclusive because of inconsistent results and methodological flaws. The evidence for the outcome of mental health during pregnancy is understudied.

CONSEQUENCES AT DELIVERY

In IOM (1990), the link between GWG and complications during labor and delivery was viewed as a consequence of delivering a large-for-gestational age (LGA) infant. This report concluded that the contribution of GWG to these outcomes was quite small. Since then, the literature has grown and the outcomes related to delivery have been subdivided so as to understand the process of labor more fully.

Induction of Labor

In the AHRQ review (Viswanathan et al., 2008) five studies were reviewed related to an association between GWG and induction of labor (Ekblad and Grenman 1992; Kabiru and Raynor 2004; Jensen et al., 2005; Graves et al., 2006; DeVader et al., 2007.) The strength of the evidence from these studies was rated weak for an association between high GWG and labor induction or failure of labor induction. A statistically significant increase in the outcomes associated with high GWG was found in all of the studies. Comparisons across studies however were not meaningful because of differences in the definition of high GWG and a lack of control for confounding factors.

Length of Labor

Three studies in the AHRQ review (Viswanathan et al., 2008) examined associations between GWG and length of labor (Ekblad and Grenman, 1992; Johnson et al., 1992; Purfield and Morin, 1995). The evidence was rated weak for an association between higher GWG and longer duration of labor. Two of the three studies found a significant increase in the length of labor with higher weight gains, but both lacked control for confounding factors (Ekblad and Grenman, 1992; Purfield and Morin, 1995).

Mode of Delivery

The association between GWG and mode of delivery has been examined in many studies. A total of 21 studies reviewed in the AHRQ review (Viswanathan et al., 2008) examined this association using GWG as a continuous or categorical variable unrelated to the IOM (1990) guidelines (Ekbald and Grenman, 1992; Johnson et al., 1992; Purfield and Morin, 1995; Witter et al., 1995; Bianco et al., 1998; Shepard et al., 1998; Young and Woodmansee, 2002; Joseph et al., 2003; Chen et al., 2004; Kabiru and Raynor, 2004; Brennand et al., 2005; Jensen et al., 2005; Murakami et al., 2005; Rosenberg et al., 2005; Cedergren, 2006; Graves et al., 2006; Wataba et al., 2006; DeVader et al., 2007; Jain et al., 2007; Kiel et al., 2007; Sherrard et al., 2007). Overall, these studies provided moderate evidence of an association between high GWG and cesarean delivery; only four studies failed to find an association (Bianco et al., 1998; Brennand et al., 2005; Murakami et al., 2005; Graves et al., 2006). An important factor to consider in this literature is the route of previous delivery for multiparous women. Only half of the studies reviewed adjusted for this and, among those that did, five also adjusted for co-morbidities that could also have contributed to the route of delivery (e.g. GDM and preeclampsia) (Witter et al., 1995; Shepard et al., 1998; Joseph et al., 2003; Rosenberg et al., 2005; Sherrard et al., 2007). Higher weight gains were associated with instrumental deliveries in three (Purfield and Morin, 1995; Kabiru and Raynor, 2004; Cedergren, 2006) studies but not in two others (Ekblad and Grenman, 1992; DeVader et al., 2007).

When GWG was categorized according to the ranges recommended in the IOM (1990) report, the body of research provided moderate evidence that weight gain above the recommended ranges was associated with cesarean delivery among normal- and underweight women. In contrast, the evidence among obese and morbidly obese women was rated as weak (Parker and Abrams, 1992; Edwards et al., 1996; Bianco et al., 1998; Thorsdottir et al., 2002; Stotland et al., 2004; Hilakivi-Clarke et al., 2005; DeVader et al., 2007; Kiel et al., 2007).

There was a consistent observation (noted in 10 studies) that women who were overweight or obese before pregnancy were at higher risk of cesarean delivery compared to women who entered pregnancy at a lower BMI (Johnson et al., 1992; Witter et al., 1995; Shepard et al., 1998; Joseph et al., 2003; Chen et al., 2004; Murakami et al., 2005; Rosenberg et al., 2005; Graves et al., 2006; Jain et al., 2007; Sherrard et al., 2007).

Maternal Mortality

Both the IOM (1990) report and the AHRQ review (Viswanathan et al., 2008) concluded that there was no information on the relationship between GWG and maternal mortality. From a theoretical perspective, if GWG above recommended ranges is associated with LGA infants and shoulder dystocia in settings that do not allow for immediate cesarean delivery or attendance by a trained clinician, the mother could die during childbirth. In such an event, the immediate cause

of death would be attributed to the size of the infant and associated labor and delivery complications. This impedes the study of consequences of GWG on maternal mortality. In summary, current evidence supports a strong association between GWG above recommended ranges and increased risk of cesarean delivery. There is no evidence, however, to support an association of GWG with maternal mortality in countries where women have ready access to obstetric care.

POSTPARTUM CONSEQUENCES

Lactation

IOM (1990) reported only one study that examined the relationship between GWG and milk quality and quantity (Butte et al., 1984). There was no relationship between GWG and these outcomes in this study.

The AHRQ review (Viswanathan et al., 2008) includes four studies on the association of GWG, categorized according to the recommendations of IOM (1990), with lactation performance (Rasmussen et al., 2002; Li et al., 2003; Hilson et al., 2006; Baker et al., 2007). These studies provide evidence rated moderate that low weight gain is associated with decreased initiation of breastfeeding, and weak for any association between GWG and duration of exclusive or any breastfeeding. Three of the studies reviewed showed that obese women had a shorter duration of breastfeeding (both exclusive and any breastfeeding) regardless of GWG (Rasmussen et al., 2002; Hilson et al., 2006; Baker et al., 2007). Subsequently, Manios et al. (2008), in a cross-sectional study done in Greece, found results similar to those in the AHRQ review (Viswanathan et al., 2008). This study found that women with higher prepregnancy BMI were less likely to initiate breastfeeding and that GWG had no effect on either initiation or duration of breastfeeding.

Postpartum Weight Retention

A woman's weight immediately after delivery of the fetus, placenta, and amniotic fluid is termed her postpartum weight. In the subsequent days to weeks, the increase in the woman's extracellular and extravascular water that occurred during pregnancy is lost and her plasma volume returns to prepregnancy values. The amount of weight that remains then minus her pregravid weight is termed postpartum weight retention. It reflects the increased breast tissue being used for lactation as well as any remaining fat mass that was gained during pregnancy.

IOM (1990) stated that women with GWG well beyond the recommended ranges are more likely to retain weight postpartum and are at increased risk for subsequent obesity. The emphasis of the IOM (1990) guidelines, however, was on infant outcomes rather than maternal postpartum weight retention in an effort to optimize birth weight.

The AHRQ review only included studies that directly examined associations between GWG and postpartum weight retention and did not include those that used parity or childbearing as a proxy for GWG. The report only found two studies that examined differences in the amount of fat retained in the postpartum period for GWG according to IOM (1990) categories (Butte et al., 2003; Lederman et al., 1997). Butte et al. (2003) examined a convenience sample of non-smoking women aged 18-40 from Houston (17 underweight, 34 normal weight, 12 overweigh/obese). Body composition was measured using dual-energy x-ray absorptiometry (DXA) before and after pregnancy and weight was obtained before pregnancy, during pregnancy,

and after pregnancy. Results showed that maternal fat retention was significantly higher among women who gained above (5.3 kg) compared to those who gained within (2.3 kg) or below (-0.5 kg) the IOM (1990) guidelines.

Lederman et al. (1997) studied 196 non-smoking women aged 18-36 years, recruited from 3 prenatal clinics in New York City. Women who gained below the IOM (1990) recommendations had the lowest fat gain from 14 to 37 weeks of gestation compared to those with an intermediate and those with the highest fat gain. In addition the study found that, among obese women who gained within the IOM (1990) guidelines, the amount of body fat change (-0.6 kg) was significantly lower than among women in the other BMI groups who also gained within the recommendations (6.0 for underweight, 3.8 for normal, and 2.8 kg for overweight women). Unfortunately no test of significance was conducted. These data suggest, however, that higher GWG results in higher maternal fat gains, although the evidence for this is weak because of the limited number of studies and small sample sizes.

The AHRQ review (Viswanathan et al., 2008) separated the studies on postpartum weight retention into three categories according to the time postpartum when weight retention was assessed: short-term, less than 11 weeks; intermediate, 3 months to 3 years, and long-term, greater than 3 years. Within the short-term (≤ 11 weeks) studies, there was weak evidence for a relationship between GWG as a continuous variable and postpartum weight retention (Muscati et al., 1996). However, when GWG was categorized according to IOM (1990), there was a moderate, consistent relationship. Four studies showed that GWG exceeding the IOM (1990) guidelines was associated with higher postpartum weight retention (Stevens-Simon and McAnarney, 1992; Scholl et al., 1995; Luke et al., 1996; Walker et al., 2004). This observation was consistent for women irrespective of age.

In the intermediate-term (3 months to 3 years), one study rated good (Harris et al., 1999), three studies rated fair (Ohlin and Rossner, 1990; Soltani and Fraser, 2000; Walker et al., 2004), and one study rated poor (Parham et al., 1990) showed moderate evidence for a relationship between GWG above recommended ranges and greater postpartum weight retention. The strength of the evidence was the same for subjects who gained above the IOM (1990) prepregnancy guidelines as for those who stayed within the guidelines, based on five studies rated fair (Scholl et al., 1995; Walker, 1996; Rooney and Schauberger, 2002; Olson et al., 2003; Amorim et al., 2007) and one study rated poor (Keppel and Taffel, 1993). Thus, overall, higher GWG is associated with greater postpartum weight retention measured at 3 to 36 months postpartum. The authors noted, however, that the data should be interpreted cautiously because of a lack of consistent adjustment for covariates such as nutrition and exercise. In interpreting these data, it is important to note that the relationship between GWG and postpartum weight retention depends not only on dietary intake and physical exercise, but also on breastfeeding behavior. In the only available study that considered prepregnancy BMI, GWG, and breastfeeding simultaneously, Baker et al. (2008) showed that women from the Danish National Birth Cohort with reasonable weight gains (e.g. ~12 kg) and exclusively breastfed for 6 months as currently recommended would have no weight retention at 6 months postpartum. For racial/ethnic groups, only one study was available. Keppel and Taffel (1993) used a nationally representative database to show that black women retained more weight than white women regardless of GWG.

In the long-term (> 3 years), the evidence is less conclusive for a relationship between GWG and postpartum weight retention. One study rated good, Callaway et al. (2007) found a weak association between GWG and weight of the mother 21 years after the pregnancy, while in

another study rated fair, Linne et al. (2003) found that women who became overweight after 15 years had higher GWG in the index pregnancy compared to women who remained within a normal weight range (although no adjustment was made for confounding). In the latter study, the authors also concluded that women who began pregnancy at a higher BMI tended to stay on the same weight trajectory later in life (Linne et al., 2004). There was moderate evidence in support of a relationship between gaining above the IOM (1990) guidelines and greater postpartum weight retention based on findings from three studies rated as fair (Rooney and Schauberger, 2002; Rooney et al., 2005; Amorim et al., 2007); however the amount of weight retained was small.

Studies by Gunderson (2004) and Rosenberg et al. (2003), although not included in the AHRQ review, provide information that is consistent with its conclusions. The work of Nohr et al. (2008) also largely corroborates these earlier findings and strengthens the evidence for an association between GWG and postpartum weight retention in the intermediate period. Nohr et al. (2008) gathered data from 60,892 women with term pregnancies in the Danish National Birth Cohort. They linked these data to birth and hospital-discharge registers. After adjustment for multiple confounding factors, they reported that women who gained 16-19 kg or $\geq$ 20 kg were at 2.3- and 6.2-fold higher odds of retaining $\geq$ 5 kg at 6 months postpartum than women who gained only 10-15 kg. The study results were attenuated for the measurements obtained at 18 months postpartum, which was only based on approximately one-half of the original study cohort.

A major concern with postpartum weight retention is that a woman may move into a higher BMI category than she was in before pregnancy. Being in this higher category is then associated with a greater risk of pregnancy complications and adverse birth outcomes in a subsequent pregnancy. Scholl et al. (1995) calculated that adolescent women (12-29 years old) had a 2.8-fold higher risk of becoming overweight at 6 months postpartum if their rate of weight gain during pregnancy was > 0.68 kg per week than women with lower gains. Gunderson et al. (2000) observed a similar magnitude of effect in adults when she calculated the risk of becoming overweight at the start of the second pregnancy with weight gains above the IOM (1990) recommendations in the first. Nohr et al. (2008) also showed that with GWG between 16-19 kg, 12 to 14 percent of women with pregravid BMIs > 18.5 kg/m^2 move up one category of weight status at 6 months postpartum and that this increases to 25 percent with weight gains > 20 kg.

Overall the evidence suggests that low GWG is moderately associated with initiation of breastfeeding and that there is a strong association between higher GWG and postpartum weight retention (3 months to 3 years). The outcome of mental health is understudied and worthy of exploration.

Postpartum Depression

There were no data on the relationship of GWG and postpartum depression in the IOM (1990) report. The AHRQ review (Viswanathan et al., 2008) does not include data on this relationship. The committee was unable to identify new data on this possible relationship.

LONG-TERM CONSEQUENCES

The IOM (1990) report did not address long-term maternal outcomes of GWG. Excess postpartum weight retention could exacerbate these problems (see discussion above) and contribute to the development of chronic conditions that include diabetes, hypertension, and other cardiovascular risk factors (Arendas et al., 2008).

Type 2 Diabetes/Metabolic Disorders

The committee was unable to identify published studies that examined the possible association between GWG and the development of metabolic disorders later in a woman's life. Such an association is biologically plausible because of the link between GWG and postpartum weight retention. Gunderson et al. (2008) showed that childbearing was associated with increased visceral fat postpartum, but their study did not include data on GWG. Berg and Scherer (2005) reviewed evidence on the role of adipose tissue in systemic inflammation and determined that the distribution of fat is important as well as the amount. Visceral fat in obese subjects was shown to be more strongly associated with insulin resistance than visceral fat in lean subjects.. Lim et al. (2007) identified a relationship between abnormal glucose tolerance at one year post-partum and increased visceral fat in women who had GDM that was independent of maternal age and BMI.

Cardiovascular Disorders

The committee was also unable to identify any published studies that examined a direct association between GWG and the development of cardiovascular disorders later on in life. However, obesity, preeclampsia, or toxemia of pregnancy is linked to long-term sequelae that include cardiovascular disease (Bellamy et al., 2007; Zhang et al., 2008).

Other Adverse Health Outcomes

Mental Health

The topic of mental health of the mother is not addressed in the AHRQ review (Viswanathan et al., 2008). Two small studies (Jenkin and Tiggemann, 1997; Walker, 1997) provide weak evidence regarding the connection between post-partum weight retention up to one year post-delivery and self-esteem/depression. These studies did not control for prepregnancy BMI.

Cancer

There is weak evidence for an association of GWG with risk of breast cancer. One retrospective cohort study of 2,089 Finnish women showed a positive relationship between weight gain in the upper tertile (> 15 kg) and post-menopausal breast cancer risk, after adjustment for prepregnancy BMI (RR = 1.62, 95% CI: 1.03-2.53) (Kinnunen et al., 2004). In a nested case-control study of 65 cases of breast cancer in this cohort, the BMI at the time of diagnosis did not change the findings. Although there was a relationship between increased weight gain and an increased risk of post-menopausal breast cancer in this cohort, in another population of Finnish women weight gain of > 16 kg during pregnancy and increased BMI during adult life was associated with a reduced risk of pre-menopausal breast cancer (Hilakivi-Clarke et al., 2005).

Overall there is insufficient evidence to link GWG to long-term health consequences of the mother as a result of the lack of studies in this area.

CONCLUDING REMARKS

There is a general lack of research that relates GWG to maternal outcomes beyond the first year postpartum other than for postpartum weight retention and subsequent obesity. This is understandable because most of the outcomes that are of the greatest interest, such as cardiovascular disease, cancer, and depression take longer to study because they occur later in the woman's life. It is well established however that obesity is associated with increased morbidity and mortality (hypertension, dyslipidemia, diabetes mellitus, cholelithiasis, coronary heart disease, osteoarthritis, sleep apnea, stroke, and certain cancers) (Must et al., 1992; Troiano et al., 1996; Allison et al., 1999; Calle et al., 2003; Gregg et al., 2005). Furthermore, for subsequent pregnancies, maternal overweight and obesity are associated with higher rates of cesarean delivery, GDM, preeclampsia and pregnancy-induced hypertension as well as postpartum anemia (Bodnar et al., 2004).

Overall, the consequences for the mother of GWG above recommended ranges appear to be well-substantiated for outcomes such as cesarean delivery and postpartum weight retention. The studies that have examined glucose abnormalities and hypertensive disorders of pregnancy have been methodologically flawed and thus do not provide sufficient evidence to support or refute a possible association. For GWG below recommended ranges, the only outcome for which there is any substantial evidence is initiation of breastfeeding. There are no available studies of a relationship between low GWG and increased maternal mortality among American women.

FINDINGS AND RECOMMENDATIONS

Findings

1. The literature related to GWG and maternal outcomes does not allow inference of causality since it is based solely on observational studies.
2. Evidence for an association between GWG and pregnancy complications such as glucose abnormalities and gestational hypertension disorders is inconclusive and problematic due to methodological flaws and that the outcome of mental health during pregnancy is understudied.
3. There is a strong association between higher GWG and increased risk of cesarean delivery.
4. There is no research on the effect of GWG on maternal mortality from which they could make any conclusions.
5. Low GWG is moderately associated with failure to initiate breastfeeding.
6. There is a strong association between higher GWG and postpartum weight retention in the immediate postpartum period (three months to three years).
7. The outcome of mental health is understudied.
8. There is insufficient evidence to link GWG to long-term health consequences of the mother due to the lack of studies in this area.
9. Maternal prepregnancy weight status is an important independent predictor of maternal short and long term outcomes.

Recommendations for Action and Research

Action Recommendation 5-1: The committee recommends that appropriate federal, state and local agencies as well as health care providers inform women of the importance of

conceiving at a normal BMI and that all those who provide health care or related services to women of childbearing age include preconceptional counseling in their care.

Research Recommendation 5-1: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to researchers to conduct observational and experimental studies on the association between GWG and (a) glucose abnormalities and gestational hypertensive disorders that take into account the temporality of the diagnosis of the outcome, and (b) the development of glucose intolerance, hypertension and other CVD risk factors as well as mental health and cancer later in a woman's life.

Research Recommendation 5-2: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies that (a) explore mechanisms, including epigenetic mechanisms, that underlie effects of GWG on maternal and child outcomes and (b) address the extent to which optimal GWG differs not only by maternal prepregnancy BMI but also by other factors such as age (especially among adolescents), parity, racial/ethnic group, socioeconomic status, co-morbidities, and maternal/paternal/fetal genotype.

Areas for Additional Investigation

The committee identified the following areas for further investigation to aid in future revisions of GWG recommendations. The research community should conduct studies on:

- Associations between gestational weight gain and maternal mortality;
- Effects of GWG on maternal mental status during pregnancy, in the postpartum period and in long-term.
- The causal nature of how gestational weight gain leads to short and long term maternal outcomes.

REFERENCES

Amorim A. R., S. Rossner, M. Neovius, P. M. Lourenco and Y. Linne. 2007. Does excess pregnancy weight gain constitute a major risk for increasing long-term BMI? *Obesity (Silver Spring)* 15(5): 1278-1286.

Arendas K., Q. Qiu and A. Gruslin. 2008. Obesity in pregnancy: pre-conceptional to postpartum consequences. *Journal of Obstetrics and Gynaecology Canada* 30(6): 477-488.

Atwal G. S., L. K. Manku, C. E. Griffiths and D. W. Polson. 2006. Striae gravidarum in primiparae. *British Journal of Dermatology* 155(5): 965-969.

Baker J. L., K. F. Michaelsen, T. I. Sorensen and K. M. Rasmussen. 2007. High prepregnant body mass index is associated with early termination of full and any breastfeeding in Danish women. *American Journal of Clinical Nutrition* 86(2): 404-411.

Baker J. L., M. Gamborg, B. L. Heitmann, L. Lissner, T. I. Sorensen and K. M. Rasmussen. 2008. Breastfeeding reduces postpartum weight retention. *American Journal of Clinical Nutrition* 88(6): 1543-1551.

Bellamy L., J. P. Casas, A. D. Hingorani and D. J. Williams. 2007. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. *British Medical Journal* 335(7627): 974.

Berg A. H. and P. E. Scherer. 2005. Adipose tissue, inflammation, and cardiovascular disease. *Circulation Research* 96(9): 939-949.

Bianco A. T., S. W. Smilen, Y. Davis, S. Lopez, R. Lapinski and C. J. Lockwood. 1998. Pregnancy outcome and weight gain recommendations for the morbidly obese woman. *Obstetrics and Gynecology* 91(1): 97-102.

Bodnar L. M., J. M. Catov, M. A. Klebanoff, R. B. Ness and J. M. Roberts. 2007. Prepregnancy body mass index and the occurrence of severe hypertensive disorders of pregnancy. *Epidemiology* 18(2): 234-239.

Brennand E. A., D. Dannenbaum and N. D. Willows. 2005. Pregnancy outcomes of First Nations women in relation to pregravid weight and pregnancy weight gain. *Journal of Obstetrics and Gynaecology Canada* 27(10): 936-944.

Butte N. F., C. Garza, J. E. Stuff, E. O. Smith and B. L. Nichols. 1984. Effect of maternal diet and body composition on lactational performance. *American Journal of Clinical Nutrition* 39(2): 296-306.

Butte N. F., K. J. Ellis, W. W. Wong, J. M. Hopkinson and E. O. Smith. 2003. Composition of gestational weight gain impacts maternal fat retention and infant birth weight. *American Journal of Obstetrics and Gynecology* 189(5): 1423-1432.

Callaway L. K., H. D. McIntyre, M. O'Callaghan, G. M. Williams, J. M. Najman and D. A. Lawlor. 2007. The association of hypertensive disorders of pregnancy with weight gain over the subsequent 21 years: findings from a prospective cohort study. *American Journal of Epidemiology* 166(4): 421-428.

Catalano P. M., N. M. Roman, E. D. Tyzbir, A. O. Merritt, P. Driscoll and S. B. Amini. 1993. Weight gain in women with gestational diabetes. *Obstetrics and Gynecology* 81(4): 523-528.

Catalano P. M. 2007. Increasing maternal obesity and weight gain during pregnancy: the obstetric problems of plentitude. *Obstetrics and Gynecology* 110(4): 743-744.

Cedergren M. 2006. Effects of gestational weight gain and body mass index on obstetric outcome in Sweden. *International Journal of Gynaecology and Obstetrics* 93(3): 269-274.

Chen G., S. Uryasev and T. K. Young. 2004. On prediction of the cesarean delivery risk in a large private practice. *American Journal of Obstetrics and Gynecology* 191(2): 616-624; discussion 624-615.

Chez R. A. and F. D. Curcio, 3rd. 1987. Ketonuria in normal pregnancy. *Obstetrics and Gynecology* 69(2): 272-274.

Chu S. Y., W. M. Callaghan, S. Y. Kim, C. H. Schmid, J. Lau, L. J. England and P. M. Dietz. 2007. Maternal obesity and risk of gestational diabetes mellitus. *Diabetes Care* 30(8): 2070-2076.

Dahlgren J. 2006. Pregnancy and insulin resistance. *Metabolic Syndrome and Related Disorders* 4(2): 149-152.

DeVader S. R., H. L. Neeley, T. D. Myles and T. L. Leet. 2007. Evaluation of gestational weight gain guidelines for women with normal prepregnancy body mass index. *Obstetrics and Gynecology* 110(4): 745-751.

Dodds L., D. B. Fell, K. S. Joseph, V. M. Allen and B. Butler. 2006. Outcomes of pregnancies complicated by hyperemesis gravidarum. *Obstetrics and Gynecology* 107(2 Pt 1): 285-292.

Edwards L. E., W. L. Hellerstedt, I. R. Alton, M. Story and J. H. Himes. 1996. Pregnancy complications and birth outcomes in obese and normal-weight women: effects of gestational weight change. *Obstetrics and Gynecology* 87(3): 389-394.

Ekblad U. and S. Grenman. 1992. Maternal weight, weight gain during pregnancy and pregnancy outcome. *International Journal of Gynaecology and Obstetrics* 39(4): 277-283.

Getahun D., C. Nath, C. V. Ananth, M. R. Chavez and J. C. Smulian. 2008. Gestational diabetes in the United States: temporal trends 1989 through 2004. *American Journal of Obstetrics and Gynecology* 198(5): 525 e521-525.

Gin H., A. Vambergue, C. Vasseur, V. Rigalleau, P. Dufour, A. Roques, M. Romon, D. Millet, P. Hincker and P. Fontaine. 2006. Blood ketone monitoring: a comparison between gestational diabetes and non-diabetic pregnant women. *Diabetes and Metabolism* 32(6): 592-597.

Graves B. W., S. A. DeJoy, A. Heath and P. Pekow. 2006. Maternal body mass index, delivery route, and induction of labor in a midwifery caseload. *Journal of Midwifery and Women's Health* 51(4): 254-259.

Gunderson E. P., B. Abrams and S. Selvin. 2000. The relative importance of gestational gain and maternal characteristics associated with the risk of becoming overweight after pregnancy. *International Journal of Obesity and Related Metabolic Disorders* 24(12): 1660-1668.

Gunderson E. P., B. Sternfeld, M. F. Wellons, R. A. Whitmer, V. Chiang, C. P. Quesenberry, Jr., C. E. Lewis and S. Sidney. 2008. Childbearing may increase visceral adipose tissue independent of overall increase in body fat. *Obesity (Silver Spring)* 16(5): 1078-1084.

Hackmon R., R. James, C. O'Reilly Green, A. Ferber, Y. Barnhard and M. Divon. 2007. The impact of maternal age, body mass index and maternal weight gain on the glucose challenge test in pregnancy. *Journal of Maternal-Fetal & Neonatal Medicine* 20(3): 253-257.

Hilakivi-Clarke L., R. Luoto, T. Huttunen and M. Koskenvuo. 2005. Pregnancy weight gain and premenopausal breast cancer risk. *Journal of Reproductive Medicine* 50(11): 811-816.

Hilson J. A., K. M. Rasmussen and C. L. Kjolhede. 2006. Excessive weight gain during pregnancy is associated with earlier termination of breast-feeding among White women. *Journal of Nutrition* 136(1): 140-146.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

Jain N. J., C. E. Denk, L. K. Kruse and V. Dandolu. 2007. Maternal obesity: can pregnancy weight gain modify risk of selected adverse pregnancy outcomes? *American Journal of Perinatology* 24(5): 291-298.

Jenkin W. and M. Tiggemann. 1997. Psychological effects of weight retained after pregnancy. *Women & Health* 25(1): 89-98.

Jensen D. M., P. Ovesen, H. Beck-Nielsen, L. Molsted-Pedersen, B. Sorensen, C. Vinter and P. Damm. 2005. Gestational weight gain and pregnancy outcomes in 481 obese glucose-tolerant women. *Diabetes Care* 28(9): 2118-2122.

Johnson J. W., J. A. Longmate and B. Frentzen. 1992. Excessive maternal weight and pregnancy outcome. *American Journal of Obstetrics and Gynecology* 167(2): 353-370; discussion 370-352.

Joseph K. S., D. C. Young, L. Dodds, C. M. O'Connell, V. M. Allen, S. Chandra and A. C. Allen. 2003. Changes in maternal characteristics and obstetric practice and recent increases in primary cesarean delivery. *Obstetrics and Gynecology* 102(4): 791-800.

Kabiru W. and B. D. Raynor. 2004. Obstetric outcomes associated with increase in BMI category during

pregnancy. *American Journal of Obstetrics and Gynecology* 191(3): 928-932.

Keppel K. G. and S. M. Taffel. 1993. Pregnancy-related weight gain and retention: implications of the 1990 Institute of Medicine guidelines. *American Journal of Public Health* 83(8): 1100-1103.

Kieffer E. C., W. J. Carman, B. W. Gillespie, G. H. Nolan, S. E. Worley and J. R. Guzman. 2001. Obesity and gestational diabetes among African-American women and Latinas in Detroit: implications for disparities in women's health. *Journal of the American Medical Women's Association* 56(4): 181-187, 196.

Kieffer E. C., B. P. Tabaei, W. J. Carman, G. H. Nolan, J. R. Guzman and W. H. Herman. 2006. The influence of maternal weight and glucose tolerance on infant birthweight in Latino mother-infant pairs. *American Journal of Public Health* 96(12): 2201-2208.

Kiel D. W., E. A. Dodson, R. Artal, T. K. Boehmer and T. L. Leet. 2007. Gestational weight gain and pregnancy outcomes in obese women: how much is enough? *Obstetrics and Gynecology* 110(4): 752-758.

Kinnunen T. I., R. Luoto, M. Gissler, E. Hemminki and L. Hilakivi-Clarke. 2004. Pregnancy weight gain and breast cancer risk. *BMC Women's Health* 4(1): 7.

Ko C. W. 2006. Risk factors for gallstone-related hospitalization during pregnancy and the postpartum. *American Journal of Gastroenterology* 101(10): 2263-2268.

Langford A., C. Joshu, J. J. Chang, T. Myles and T. Leet. 2008. Does Gestational Weight Gain Affect the Risk of Adverse Maternal and Infant Outcomes in Overweight Women? *Maternal and Child Health Journal*.

Lederman S. A., A. Paxton, S. B. Heymsfield, J. Wang, J. Thornton and R. N. Pierson, Jr. 1997. Body fat and water changes during pregnancy in women with different body weight and weight gain. *Obstetrics and Gynecology* 90(4 Pt 1): 483-488.

Li R., S. Jewell and L. Grummer-Strawn. 2003. Maternal obesity and breast-feeding practices. *American Journal of Clinical Nutrition* 77(4): 931-936.

Lim S., S. H. Choi, Y. J. Park, K. S. Park, H. K. Lee, H. C. Jang, N. H. Cho and B. E. Metzger. 2007. Visceral fatness and insulin sensitivity in women with a previous history of gestational diabetes mellitus. *Diabetes Care* 30(2): 348-353.

Lindseth G. and M. Y. Bird-Baker. 2004. Risk factors for cholelithiasis in pregnancy. *Research in Nursing and Health* 27(6): 382-391.

Linne Y., L. Dye, B. Barkeling and S. Rossner. 2003. Weight development over time in parous women-- the SPAWN study--15 years follow-up. *International Journal of Obesity and Related Metabolic Disorders* 27(12): 1516-1522.

Linne Y., L. Dye, B. Barkeling and S. Rossner. 2004. Long-term weight development in women: a 15-year follow-up of the effects of pregnancy. *Obesity Research* 12(7): 1166-1178.

Luke B., M. L. Hediger and T. O. Scholl. 1996. Point of diminishing returns: when does gestational weight gain cease benefiting birthweight and begin adding to maternal obesity? *Journal of Maternal-Fetal Medicine* 5(4): 168-173.

Madlon-Kay D. J. 1993. Striae gravidarum. Folklore and fact. *Archives of Family Medicine* 2(5): 507-511.

Manios Y., E. Grammatikaki, K. Kondaki, E. Ioannou, A. Anastasiadou and M. Birbilis. 2008. The effect of maternal obesity on initiation and duration of breast-feeding in Greece: the GENESIS study. *Public Health Nutrition*: 1-8.

Marrero J. M., P. M. Goggin, J. S. de Caestecker, J. M. Pearce and J. D. Maxwell. 1992. Determinants of pregnancy heartburn. *British Journal of Obstetrics and Gynaecology* 99(9): 731-734.

Murakami M., M. Ohmichi, T. Takahashi, A. Shibata, A. Fukao, N. Morisaki and H. Kurachi. 2005. Prepregnancy body mass index as an important predictor of perinatal outcomes in Japanese. *Archives of Gynecology and Obstetrics* 271(4): 311-315.

Muscati S. K., K. Gray-Donald and K. G. Koski. 1996. Timing of weight gain during pregnancy: promoting fetal growth and minimizing maternal weight retention. *International Journal of Obesity and Related Metabolic Disorders* 20(6): 526-532.

Nohr E. A., M. Vaeth, J. L. Baker, T. Sorensen, J. Olsen and K. M. Rasmussen. 2008. Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy. *American Journal of Clinical Nutrition* 87(6): 1750-1759.

Ogunyemi D., S. Hullett, J. Leeper and A. Risk. 1998. Prepregnancy body mass index, weight gain during pregnancy, and perinatal outcome in a rural black population. *Journal of Maternal-Fetal Medicine* 7(4): 190-193.

Parker J. D. and B. Abrams. 1992. Prenatal weight gain advice: an examination of the recent prenatal weight gain recommendations of the Institute of Medicine. *Obstetrics and Gynecology* 79(5 (Pt 1)): 664-669.

Purfield P. and K. Morin. 1995. Excessive weight gain in primigravidas with low-risk pregnancy: selected obstetric consequences. *Journal of Obstetric, Gynecologic, and Neonatal Nursing* 24(5): 434-439.

Rasmussen K. M., J. A. Hilson and C. L. Kjolhede. 2002. Obesity as a risk factor for failure to initiate and sustain lactation. *Advances in Experimental Medicine and Biology* 503: 217-222.

Rodriguez A., G. Bohlin and G. Lindmark. 2001. Symptoms across pregnancy in relation to psychosocial and biomedical factors. *Acta Obstetricia et Gynecologica Scandinavica* 80(3): 213-223.

Rooney B. L. and C. W. Schauberger. 2002. Excess pregnancy weight gain and long-term obesity: one decade later. *Obstetrics and Gynecology* 100(2): 245-252.

Rooney B. L., C. W. Schauberger and M. A. Mathiason. 2005. Impact of perinatal weight change on long-term obesity and obesity-related illnesses. *Obstetrics and Gynecology* 106(6): 1349-1356.

Rosenberg T. J., S. Garbers, H. Lipkind and M. A. Chiasson. 2005. Maternal obesity and diabetes as risk factors for adverse pregnancy outcomes: differences among 4 racial/ethnic groups. *American Journal of Public Health* 95(9): 1545-1551.

Saldana T. M., A. M. Siega-Riz, L. S. Adair and C. Suchindran. 2006. The relationship between pregnancy weight gain and glucose tolerance status among black and white women in central North Carolina. *American Journal of Obstetrics and Gynecology* 195(6): 1629-1635.

Scholl T. O., M. L. Hediger, J. I. Schall, I. G. Ances and W. K. Smith. 1995. Gestational weight gain, pregnancy outcome, and postpartum weight retention. *Obstetrics and Gynecology* 86(3): 423-427.

Seghieri G., A. De Bellis, R. Anichini, L. Alviggi, F. Franconi and M. C. Breschi. 2005. Does parity increase insulin resistance during pregnancy? *Diabetic Medicine* 22(11): 1574-1580.

Shepard M. J., A. F. Saftlas, L. Leo-Summers and M. B. Bracken. 1998. Maternal anthropometric factors and risk of primary cesarean delivery. *American Journal of Public Health* 88(10): 1534-1538.

Sherrard A., R. W. Platt, D. Vallerand, R. H. Usher, X. Zhang and M. S. Kramer. 2007. Maternal anthropometric risk factors for caesarean delivery before or after onset of labour. *British Journal of Obstetrics and Gynaecology* 114(9): 1088-1096.

Sibai B. M., M. Ewell, R. J. Levine, M. A. Klebanoff, J. Esterlitz, P. M. Catalano, R. L. Goldenberg and G. Joffe. 1997. Risk factors associated with preeclampsia in healthy nulliparous women. The Calcium for Preeclampsia Prevention (CPEP) Study Group. *American Journal of Obstetrics and Gynecology* 177(5): 1003-1010.

Stevens-Simon C. and E. R. McAnarney. 1992. Adolescent pregnancy. Gestational weight gain and maternal and infant outcomes. *American Journal of Diseases of Children* 146(11): 1359-1364.

Stotland N. E., L. M. Hopkins and A. B. Caughey. 2004. Gestational weight gain, macrosomia, and risk of cesarean birth in nondiabetic nulliparas. *Obstetrics and Gynecology* 104(4): 671-677.

Thadhani R., M. J. Stampfer, D. J. Hunter, J. E. Manson, C. G. Solomon and G. C. Curhan. 1999. High body mass index and hypercholesterolemia: risk of hypertensive disorders of pregnancy. *Obstetrics and Gynecology* 94(4): 543-550.

Thorsdottir I., J. E. Torfadottir, B. E. Birgisdottir and R. T. Geirsson. 2002. Weight gain in women of normal weight before pregnancy: complications in pregnancy or delivery and birth outcome. *Obstetrics and Gynecology* 99(5 Pt 1): 799-806.

Tulman L., K. H. Morin and J. Fawcett. 1998. Prepregnant weight and weight gain during pregnancy: relationship to functional status, symptoms, and energy. *Journal of Obstetric, Gynecologic, and Neonatal Nursing* 27(6): 629-634.

Viswanathan M., A. M. Siega-Riz, M.-K. Moos, A. Deierlein, S. Mumford, J. Knaack, P. Thieda, L. J. Lux and K. N. Lohr. 2008. *Outcomes of Maternal Weight Gain, Evidence Report/Technology Assessment No. 168. (Prepared by RTI International-University of North Carolina Evidence-based Practice Center under contract No. 290-02-0016.) AHRQ Publication No. 08-E-09.* Rockville, MD: Agency for Healthcare Research and Quality.

Walker L. O. 1997. Weight and weight-related distress after childbirth: relationships to stress, social support, and depressive symptoms. *Journal of Holistic Nursing* 15(4): 389-405.

Walker L., J. H. Freeland-Graves, T. Milani, G. George, H. Hanss-Nuss, M. Kim, B. S. Sterling, G. M. Timmerman, S. Wilkinson, K. L. Arheart and A. Stuifbergen. 2004. Weight and behavioral and psychosocial factors among ethnically diverse, low-income women after childbirth: II. Trends and correlates. *Women & Health* 40(2): 19-34.

Wataba K., T. Mizutani, K. Wasada, M. Morine, T. Sugiyama and N. Suehara. 2006. Impact of prepregnant body mass index and maternal weight gain on the risk of pregnancy complications in Japanese women. *Acta Obstetricia et Gynecologica Scandinavica* 85(3): 269-276.

Witter F. R., L. E. Caulfield and R. J. Stoltzfus. 1995. Influence of maternal anthropometric status and birth weight on the risk of cesarean delivery. *Obstetrics and Gynecology* 85(6): 947-951.

Young T. K. and B. Woodmansee. 2002. Factors that are associated with cesarean delivery in a large private practice: the importance of prepregnancy body mass index and weight gain. *American Journal of Obstetrics and Gynecology* 187(2): 312-318; discussion 318-320.

Zhang C., K. M. Rexrode, R. M. van Dam, T. Y. Li and F. B. Hu. 2008. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in US women. *Circulation* 117(13): 1658-1667.

6

Consequences of Gestational Weight Gain for the Child

The authors of the report, *Nutrition During Pregnancy* (IOM, 1990) emphasized short-term outcomes in developing guidelines for recommended gestational weight gain (GWG) ranges. This resulted from a lack of data on long-term outcomes and the fact that the research community was only beginning to understand the importance of the intrauterine environment for long-term health. In the interim, the literature on the topic has expanded, and more information is now available on neonatal as well as long-term consequences of both inadequate and excessive GWG during pregnancy.

Only by knowing the magnitude of causal relationships can one say with confidence that recommending a certain amount of GWG will result in altered frequency of adverse child health outcomes. The limited experimental data from randomized controlled trials in humans, however, impedes efforts to determine how much of any observed association is causal. It is possible that associations of GWG with outcomes do not result from GWG itself, but rather to underlying factors that influence both weight gain and the outcomes (e.g. maternal diet composition or physical activity level). In particular, it is important to determine whether these relationships are independent of prepregnancy body mass index (BMI) or if they differ by prepregnancy BMI. This is because observational studies are often limited by mixing effects of confounding factors with the predictor of real interest.

Although reverse causality is less of a problem in cohort than in cross-sectional studies, confounding is not readily controlled in any observational study. Only with large, well-designed and carefully controlled randomized studies can causal relationships be inferred with a high degree of confidence. Otherwise, inferences must be made using the best data available in consideration of plausible biologic mechanisms, confounding and other aspects of the study methodology, and the patterns of results.

The following reviews the current evidence and strives to quantify, wherever possible, causal relationships between GWG and childhood outcomes.

GENERAL CONCEPTS

Causal Concepts

The committee generated a general conceptual causal model of determinants (see Chapter 1) for maternal and child outcomes that may result from excessive or inadequate GWG (Figure 6-1). This model fits well with two paradigms that offer useful conceptual frameworks for considering long-term effects on the offspring. One, termed the life course approach to chronic disease, invokes two axes (Kuh and Ben-Shlomo, 2004). The first is time. Factors may act in the pre-conceptional through the prenatal period, into infancy, childhood, and beyond to determine

risk of chronic disease. The second is hierarchical: these factors can range from the social/built/natural environment (macro) through behavior, physiology, and genetics (micro) (See Chapter 4). Factors interact with each other over the life course, with different determinants being more or less important at different life stages.

The other paradigm, called developmental origins of health and disease, focuses primarily on the prenatal and early postnatal periods, because they are the periods of most rapid somatic growth and organ development (Gillman, 2005; Sinclair et al., 2007; Hanson and Gluckman, 2008). Both of these frameworks invoke the concept of programming, which refers to perturbations or events that occur at early, plastic, and perhaps critical phases of development that can have long-lasting, sometimes irreversible, health consequences. The period of plasticity may vary for different organs and systems (Gluckman and Hanson, 2006). The model predicts that adult risk factors can only partially modify the trajectories of health and disease patterns established in earlier life (Barker et al., 2002; Ben-Shlomo and Kuh, 2002; McMillen and Robinson, 2005; Sullivan et al., 2008).
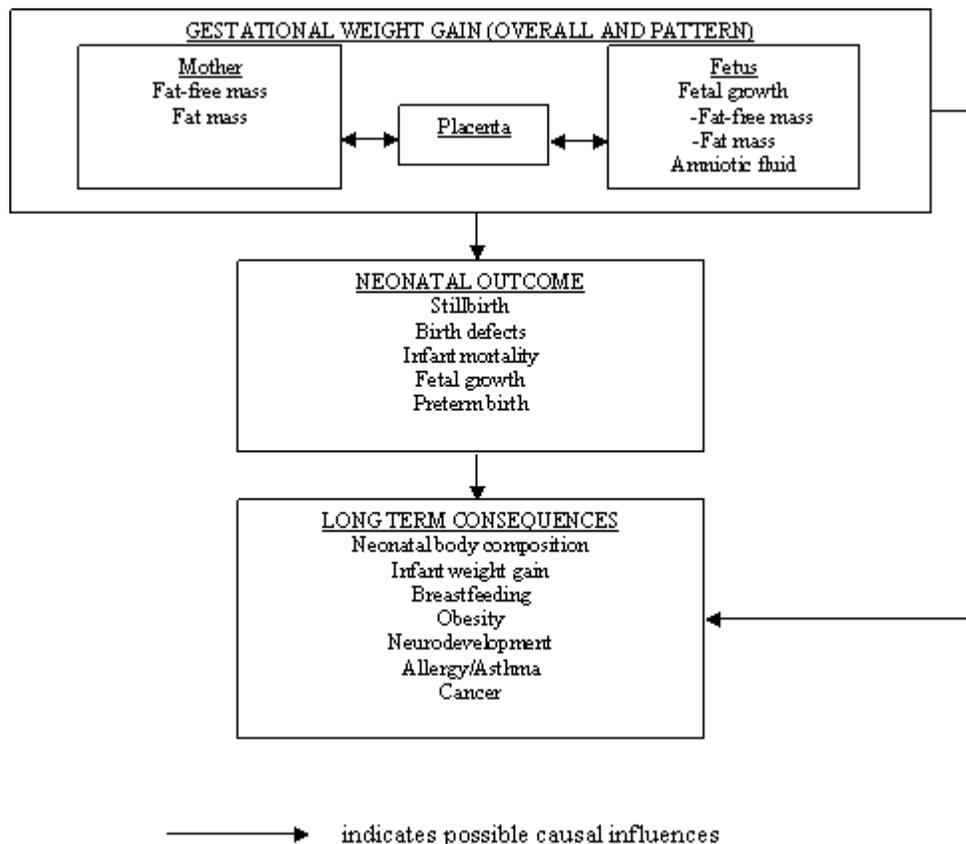

FIGURE 6-1 Schematic summary of neonatal, infant, and child consequences of GWG.

Developmental programming, including the possible role of epigenetics as potential determinants of GWG, is discussed in Chapter 4. In this chapter, the role of developmental programming as a mechanism for some of the effects of GWG on postnatal outcomes is discussed. Many animal models have demonstrated that altering the environment in utero can have lifelong consequences. Perturbations of the maternal diet during pregnancy (typically by severe energy or protein restriction; administering hormones such as glucocorticoids; mechanical means, such as ligation of the uterine artery; or inducing anemia or hypoxia) have postnatal consequences on a number of metabolic and behavioral traits. Effects are inducible in rodents and in mammals, including non-human primates. Inasmuch as humans differ from other animal species in duration of pregnancy, placentation, and other important factors, the importance of the findings from animal studies lies not in the specific interventions but rather in the general principle that altering the supply of nutrients, hormones, and oxygen to the growing embryo and fetus or exposing them to stressors and toxicants can have long-term effects. Much of this animal research has focused on obesity-related outcomes such as adiposity, fat distribution, sarcopenia, insulin sensitivity, glucose intolerance, and blood pressure. These are leading causes of morbidity—and ultimately, mortality—in the U.S. and, as discussed below, GWG appears to be related to offspring obesity. The ways in which GWG could influence a number of child health outcomes through developmental programming is also discussed below.

Until recently, most of the research in animal models has concentrated on the long-term effects of interventions that cause offspring to be born small, typically small-for-gestational age (SGA) rather than early. Such work has been a good companion to a series of epidemiologic observations made within the last two decades that lower birth weight, apparently resulting from both reduced fetal growth and reduced length of gestation, is associated with higher risks of central obesity, insulin resistance, the metabolic syndrome, type 2 diabetes, hypertension, and coronary heart disease. These associations are potentiated by rapid weight gain in childhood (Bhargava et al., 2004; Barker et al., 2005).

It is important to note, however, that in recent years researchers have recognized that higher birth weight is also associated with later obesity and its consequences. Given that greater GWG is associated with increased weight at birth (reviewed below) and that total GWG and excessive gain—which are based on total GWG and prepregnancy BMI—appear to be rising over time (see Chapter 2), these observations regarding higher birth weights raise questions about the long-term adverse effects of higher weight gains in pregnancy. Accompanying these observations are newer animal experiments that involve "overnutrition" of the mother during pregnancy, which are also discussed briefly below.

In addition, it is critical to recognize that effects of GWG, or indeed any factor that alters the in utero environment, may have long-term effects on the offspring without any alterations of fetal growth or length of gestation. Thus the most important epidemiologic evidence for long-term effects of GWG does not depend on birth weight, gestational age or birth weight-for-gestational-age as exposures or outcomes, but rather provides data on the direct associations of GWG with various health outcomes in the offspring.

With these distinctions in mind, the committee considered "fetal growth" outcomes, including small-for-gestational age (SGA) and large-for-gestational age (LGA), and preterm birth as short-term outcomes. These measures have demonstrable and substantial associations with neonatal morbidity and mortality. Other short-term outcomes include stillbirth and birth defects.

In contrast, neonatal body composition is included in the discussion of long-term outcomes because of the hypothesis (still unproven, however) that relative amounts of adiposity and lean mass—and their physiologic consequences—in fetal and neonatal life are important in setting long-term cardio-metabolic trajectories.

It also bears noting that this report focuses primarily on GWG, rather than prepregnancy BMI. Nevertheless, because the two factors are closely linked, one must account for confounding and effect modification by BMI in addressing offspring effects of GWG. Also it is possible that factors in infancy or childhood (e.g., growth in stature, adiposity, and infant feeding) could mediate effects of GWG on long-term child health.

Potential Mechanisms Linking Gestational Weight Gain to Long-Term Offspring Health

The existence of plausible biological mechanisms is one criterion for establishing causal relationships between GWG and child health outcomes. The following discussion focuses primarily on potential mechanisms linking GWG to offspring obesity and its consequences. Gestational weight gain is clearly about weight, so it is appropriate to address weight-related outcomes. Also most of the emerging evidence on long-term outcomes is based on these endpoints. The epidemiologic evidence for effects of GWG on other important child health outcomes are addressed later this chapter.

Although the following discussion focuses primarily on long-term child outcomes, similar mechanisms may also underlie associations of GWG with fetal growth. One issue that hampers inferences regarding fetal growth is that it is usually characterized by (gestational-age-specific) weight at birth, with less consideration of trajectory of weight from conception, body length or body composition (see Chapters 3 and 4 for a review of existing studies that address these issues). In contrast to the prenatal period, serial measurement of length/height and weight is common, even though data on body composition are relatively scarce.

Insulin resistance and glucose intolerance during pregnancy may mediate effects of GWG on long-term child outcomes. Weight gain in pregnancy is partly a gain in adiposity, which is accompanied by a state of relative insulin resistance starting in mid-pregnancy, among other metabolic alterations (Reece et al., 1994; Williams, 2003; Catalano et al., 2006; King, 2006; Hwang et al., 2007) (also see Chapter 3). This is an adaptive response, as it allows more efficient transfer of fuels across the placenta to the growing fetus (King, 2006). In overweight and obese pregnant women, these changes are magnified. For example, insulin resistance is more severe than in normal weight women, substantially raising the risk of impaired glucose tolerance and frank gestational diabetes (GDM).

In pregnant women who have hyperglycemia, the fetus also experiences hyperglycemia, as glucose freely crosses the placenta. In a sequence that Freinkel et al. (1986) termed "fuel-mediated teratogenesis" nearly 30 years ago, fetal hyperglycemia causes fetal hyperinsulinemia, leading to increased adiposity in the fetus. This increase is reflected in larger size at birth, which translates to higher rates of LGA and lower rates of SGA newborns (see discussion below and Chapter 3). Presumably through programming mechanisms, the increased fetal adiposity also results in increased adiposity in the growing child.

Other fuels besides glucose may also be involved. Increased fetal production of anabolic hormones and growth factors in combination with the increased levels of glucose, lipids, and amino acids that occurs in GDM result in fetal macrosomia and increase the risk for neonatal complications (Catalano et al., 2003). Crowther et al. (2005) and Pirc et al. (2007) showed that

diet and insulin therapy along with blood glucose monitoring in pregnant women with mild GDM could lower plasma insulin and leptin (but not glucose) concentrations in cord blood as well as major adverse birth outcomes. This intervention more than halved the risk of macrosomia (birth weight > 4,500 g) (Crowther et al., 2005).

This physiologic milieu may also increase the risk for long-term complications, particularly obesity. But long-term follow-up of children from this and similar randomized trials is necessary to determine if treatment of GDM or impaired glucose intolerance during pregnancy can reduce adiposity and related physiology. Results from observational studies, however, suggest this possibility. Among 5-7 year-old children in two American health plans, Hillier et al. (2007) showed that risk of high weight-for-age was lower among those whose mothers had been treated for GDM than those who had not been treated. The weight status of the "treated" offspring was similar to those whose mothers had normal glucose tolerance.

The Freinkel hypothesis is supported by animal experiments, such as those of van Assche and colleagues (1979) and more recently Plagemann and colleagues (1998), who have pharmacologically induced GDM in rats. They observe fetal hyperglycemia and hyperinsulinemia, as hypothesized, as well as changes in the hypothalamus that give rise to hyperphagia, overweight, and impaired glucose tolerance in the offspring as they mature.

Another way to induce offspring metabolic derangement in rats is through over-feeding the pregnant dam. Samuelsson et al. (2008) found that maternal diet-induced obesity resulted in increased adult adiposity and evidence of cardiovascular and metabolic dysfunction compared to the offspring of lean dams. Earlier work by Dorner et al. (1988) and Diaz and Taylor (1998) showed that a period of overfeeding or GDM in the pregnant dam during a developmentally sensitive period in gestation could change the metabolic phenotype of the immediate offspring that would then persist over two succeeding generations. In their review of animal studies, Aerts and Van Assche (2003) demonstrate that these intergenerational physiologic effects are maternally transmitted, most likely through epigenetic processes.

Seemingly paradoxically, in animal experiments it is also possible to produce offspring insulin resistance, features of the metabolic syndrome, and diabetes, including GDM, by reducing energy or macronutrient intake of the mother during pregnancy. This situation can also result in intergenerational amplification of obesity and its consequences. For example, glucose metabolism is altered in the grand-offspring of female rats who had been protein restricted during pregnancy and lactation (Benyshek et al., 2006).

Overall, animal experiments show that offspring obesity and related metabolic sequelae can result from maternal over- or underfeeding during pregnancy, from experimental manipulation like pharmacologic induction of GDM, or from mechanical means like uterine artery ligation. Epigenetic modifications likely explain many of these phenomena (Simmons, 2007). A human counterpart to the animal experimental work is epidemiologic studies showing that higher birth weight is related to later obesity and type 2 diabetes, while lower birth weight is associated with central obesity, the metabolic syndrome, and indeed, type 2 diabetes as well (Gillman, 2005). In other words, a U-shape relationship exists between birth weight and obesity-related health outcomes.

The extent to which these observations have relevance for GWG guidelines is still unclear. Few animal studies directly assess the influence of GWG on short- or long-term offspring outcomes. Animal experimentalists typically do not measure weight gain during pregnancy, and it is not clear whether appropriate animal models exist to study GWG and obesity-related outcomes in the offspring. Neither is it clear that models of either diet-induced obesity or GDM

are instructive for assessing effects of GWG. Similarly, human population studies that rely on birth weight or its components, duration of gestation, and size at birth as predictors of later outcomes (e.g., Hofman et al., 2004; Hovi et al., 2007) do not directly assess GWG.

Further, intervention studies to treat GDM do not in themselves provide evidence for making recommendations for appropriate GWG. Only randomized trials that alter weight gain during pregnancy can address that goal directly. Recently Wolff and colleagues (2008) analyzed results from 50 participants in a randomized controlled trial of reducing weight gain among obese pregnant women. The intervention was successful in restricting GWG: mean weight gain in the intervention group was 6.6 kg (± 5.5 kg) v. 13.3 kg (± 7.5 kg) in the control group a mean difference of 6.7 kg (95% CI: 2.6-10.8 [$p = 0.002$]). Insulin and leptin concentrations were also reduced, although glucose values were hardly altered.

Overall this small trial, along with other data from experimental animals and human subjects, raises the possibility that moderating GWG among obese pregnant women may reduce the risk of insulin resistance and glucose intolerance during gestation and, in turn, childhood obesity, but larger and longer-term studies are needed to address this question directly.

EFFECTS ON NEONATAL MORBIDITY AND MORTALITY

Although there is a substantial literature on prepregnancy BMI and neonatal morbidity and mortality, the literature on GWG in relation to these outcomes remains more limited, with the exception of its influence on fetal growth (Cedergren, 2006; Kiel et al., 2007). Infant mortality is strongly associated with maternal prepregnancy BMI as are a number of other clinically important outcomes, including stillbirth and preterm birth (Figure 6-2). Given that GWG, which is lower on average for heavier women, differs in relation to prepregnancy BMI, studies that examine GWG without stratifying by prepregnancy BMI are subject to confounding. These component relationships (prepregnancy BMI and GWG, and prepregnancy BMI and health outcome), as seen in Figure 6-2, are sufficiently strong that studies of GWG and neonatal outcomes that fail to account for prepregnancy BMI are of limited value in addressing the independent effects of GWG.
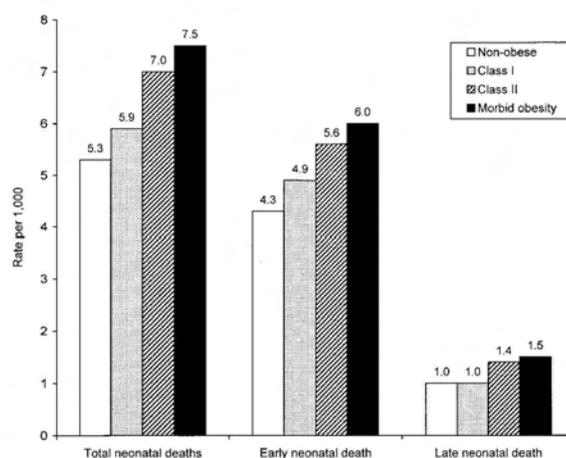

FIGURE 6-2 Rate of neonatal, early, and late neonatal death by obesity subclass.
SOURCE: Salihu et al., 2008. Obesity and extreme obesity: new insights into the black-white disparity in neonatal mortality. *Obstetrics and Gynecology* 111(6): 1410-1416. Reprinted with permission.

Stillbirth

Inadequate or excessive GWG has the potential to affect fetal viability in later pregnancy, specifically risk of stillbirth (defined as pregnancy loss after 20 weeks' gestation). Both Naeye (1979) and NCHS (1986) showed that women with low prepregnancy BMI tended to have elevated risk of fetal or perinatal mortality (a combination of stillbirth and neonatal mortality) when combined with low GWG, but women with elevated prepregnancy BMI experienced increased risk of adverse outcomes when combined with excessive GWG. In an analysis from the California Child Health and Development Studies of the School of Public Health, University of California, Berkeley, Tavris and Read (1982) found a strong inverse association between total GWG and fetal death but it was eliminated by restriction to births of greater then 35 weeks' gestation. Thus, the association was an artifact of using cumulative weight gain as the predictor, strongly related to duration of gestation with stillbirths of notably shorter gestational duration than live births. A case-control study of stillbirths in Sweden reported a strong positive association between prepregnancy BMI and stillbirth, with odds ratios approaching 3.0 for obese women, but the authors reported no effect of GWG measured in either early or late pregnancy among term births (Stephansson et al., 2001). The large size of the study (649 cases and 690 controls) is notable as well as the ability to consider an array of covariates, but the results for total GWG were not presented in the publication.

In summary, the research on GWG and stillbirth remains quite limited in quantity and quality. In addition to considering prepregnancy BMI, there is a need to avoid the error of comparing total GWG in pregnancies resulting in stillbirths with those resulting in live births because of the time in pregnancy when stillbirth is likely to occur. Although early studies suggested adverse effects of low GWG among women with low prepregnancy BMI and also of high GWG among women with elevated prepregnancy BMI, more detailed studies have not been done to corroborate or refute this pattern. Recent, better studies largely do not support an association between GWG and stillbirth.

Birth Defects

The authors of the IOM (1990) report found no studies of GWG associations with birth defects and recognized that the etiologic period for congenital defects is so early in pregnancy that the issue of weight gain was not likely to be relevant. Although there is a growing literature on prepregnancy BMI and congenital defects which suggests that there is an increased risk of birth defects with increasing BMI (Watkins et al., 2003; Anderson et al., 2005; Villamor et al., 2008), only one recent study addressed GWG in relation to birth defects directly. Infants born to mothers who gained less than 5 kg or less than 10 kg during pregnancy were at increased risk of neural tube defects (Shaw, 2001). In addition, one report indicated that dieting to lose weight during pregnancy was associated with an increased risk of neural tube defects (Carmichael et al., 2003). Although there are several pathways by which GWG and birth defects may be related, including a shared influence of diet on both high and low weight gain related to an abnormally developing fetus, a direct causal effect of GWG on risk of birth defects is precluded by the timing of these events during gestation.

Infant Mortality

Infant mortality is obviously of great clinical and public health importance and is often used as a summary indicator of a population's reproductive health status. Concern with fetal growth

and preterm birth as health outcomes is based largely on their known relationships with mortality (as well as morbidity). As a result, studies that directly address mortality as the outcome are of particular relevance and can help to interpret the patterns seen for the studies of intermediate outcomes such as preterm birth or growth restriction.

Only limited research exists in which an association between GWG and infant mortality is assessed. Perinatal mortality was examined in only one study (NCHS, 1986) noted in the IOM (1990) report. Recently, Chen et al. (2009) examined maternal prepregnancy BMI and GWG in the National Maternal and Infant Health Survey (NMIHS) and considered 4,265 infant deaths and 7,293 controls. Among underweight and normal-weight women, low GWG was associated with a marked increase in infant mortality, with relative risks on the order of 3-4 compared to those with the highest GWG. Among overweight and obese women, there were more modest effects of GWG, but both lower and higher GWG were associated with approximately 2-fold increases in risk of infant mortality. In all cases, the patterns were stronger for neonatal deaths (in the first 30 days of life) than for postneonatal deaths (those occurring after one month but before the completion of one year). As seen in Table 6-1 within BMI strata, the relative risk for neonatal death was 3.6 for the lowest weight gain group among underweight women, 3.1 among normal weight women, 2.0 among overweight women, and 1.2 among obese women, showing a diminishing effect of low GWG with increasing BMI. At high GWG, the relative risks for neonatal mortality for underweight, normal weight, overweight, and obese women were 1.0, 1.2, 1.4, and 1.8, respectively, which showed the exact opposite tendency. Here excessive GWG was more strongly associated with neonatal death with increasing BMI. Maternal age at delivery did not affect neonatal mortality. After adjusting for gestational age at delivery, no association was found between teenage pregnancy and neonatal mortality. The same general pattern was seen for post neonatal deaths; but was less pronounced (Table 6-1).

More studies of infant mortality are needed, but the evidence from Chen et al. (2009) warrants serious consideration not only because of the importance of the outcome but also because of the implications for the more voluminous literature on fetal growth and preterm birth. Although this study did not link GWG to those intermediate outcomes and the intermediate outcomes to mortality, the strength of the patterns and their parallels with studies of fetal growth add credibility to the presumption that a causal chain from GWG to adverse birth outcomes to death is operative. Based on a limited volume of research, but in one well done study, the evidence for a link to infant mortality can be considered moderate.

TABLE 6-1 Maternal Prepregnancy BMI and Gestational Weight Gain of Infant Deaths and Controls (1988 National Maternal and Infant Health Survey [NMIHS])

Maternal Prepregnancy BMI (kg/m²)	Total Weight Gain During Pregnancy [a] (kg)	Neonatal Death OR[b] (95% CI)	Postneonatal Death OR[b] (95% CI)	Infant Death OR[b] (95% CI)
< 18.5	< 6.0	3.55 (1.92-6.54)	2.96 (1.42-6.15)	3.26 (1.86-5.72)
	6.0 – 11.6	1.35 (0.88-2.06)	1.34 (0.83-2.14)	1.34 (0.93-1.92)
	12.0 – 17.6 [c]	1.00	1.00	1.00
	≥ 18.0	0.99 (0.63-1.54)	0.55 (0.32-0.95)	0.79 (0.53-1.17)
18.5 – 24.9	< 6.0	3.07 (2.45-3.85)	1.96 (1.51-2.55)	2.58 (2.12-3.14)
	6.0 – 11.6	1.41(1.19-1.68)	1.12 (0.92-1.36)	1.29 (1.11-1.49)
	12.0 – 17.6 [c]	1.00	1.00	1.00
	≥ 18.0	1.15 (0.96-1.37)	0.94 (0.77-1.15)	1.06 (0.91-1.23)
25 – 29.9	< 6.0	1.98 (1.34-2.92)	0.81 (0.51-1.29)	1.42 (1.02-1.99)
	6.0 – 11.6	1.20 (0.85-1.68)	0.64 (0.43-0.95)	0.94 (0.71-1.25)
	12.0 – 17.6 [c]	1.00	1.00	1.00
	≥ 18.0	1.41(1.00-2.00)	0.87(0.58-1.31)	1.16 (0.87-1.56)
≥ 30	< 6.0	1.19 (0.69-2.06)	0.81 (0.40-1.62)	1.04 (0.64-1.70)
	6.0 – 11.6	0.67 (0.39-1.17)	0.91 (0.47-1.78)	0.78 (0.48-1.26)
	12.0 – 17.6 [c]	1.00	1.00	1.00
	≥ 18.0	1.78 (0.96-3.33)	1.29 (0.58-2.84)	1.61 (0.92-2.81)

NOTE: Midpoint and range values for outcomes (neonatal death, postnatal death, infant death) are derived using a separate reference group for each BMI category.

[a] Weight gain during pregnancy projected to 40 weeks' gestation.
[b] Adjusted for race, maternal age at pregnancy, maternal education, maternal smoking during pregnancy, child's sex, live birth order, and plurality
[c] Referent group for comparisons within BMI stratum

SOURCE: Modified from Chen et al. (2009).

Fetal Growth

The relationship of GWG to fetal growth was considered in some detail in the IOM (1990) report. Much of the literature on consequences of fetal size fails to separate preterm delivery from fetal growth restriction, which is problematic for the purposes of this report. As noted in IOM (1990) and by others, smaller size at birth is associated with increased fetal and infant mortality, cerebral palsy, hypoglycemia, hypocalcemia, polycythemia and birth asphyxia, persistent deficits in size, and persistent deficits in neurocognitive performance (Pryor et al., 1995; Goldenberg et al., 1998). Health consequences of small size at birth tend to follow a dose-response relationship with elevated relative risks at the lowest weights. Large size causes delivery complications, including shoulder dystocia and other forms of birth injury, as well as cesarean delivery, maternal death, and fistulae (IOM, 1990).

Birth weight combines duration of gestation with rate of fetal growth. Infants on a given growth trajectory who are born earlier will weigh less than infants on the same growth trajectory who are born later. To isolate fetal growth, studies often use SGA and LGA, which compare the infant's weight to the distribution of birth weight of all infants in the same week of gestation.

Most commonly, those infants in the lowest and highest 10th percentiles are classified as SGA and LGA, respectively, but some use the more extreme values of the 5th percentile or two standard deviations or more below or above the mean. The cutoff points for those percentiles may be specific to gender, race/ethnicity, and/or parity in addition to week of gestation. There is some controversy about the use of racial/ethnic-specific norms, in particular because their biological meaning is in doubt. Black infants in the U.S. have a markedly different weight distribution than non-black infants (of varying race/ethnicity). Identification of deviations from group-specific norms is a useful means of predicting mortality; although separate group-specific norms could be interpreted as acceptance of differences in birth outcome by race/ethnicity as absolute. Such differences are not absolute, however, because health disparities are strongly influenced by social and behavioral factors. The term intrauterine growth restriction (IUGR) is generally applied to births that are designated as a lower weight than would have been attained had the pregnancy been a "normal" one. Obviously the definition of "normal" or "expected" is problematic because it is not known what would have happened had conditions been different—only what did happen. Thus results may not be comparable across studies when different indices are used.

At the time of the IOM (1990) report, the evidence for an effect of GWG on fetal growth was viewed as "quite convincing." Increased GWG was related to increased birth weight, and the report noted that the strength of that relationship varied as a function of prepregnancy BMI. The lower the prepregnancy BMI, the stronger the association between increased GWG and increased birth weight. Among obese women, the association between increased GWG and increased birth weight was questionable. The patterns of influence of GWG on fetal growth were evident both for mean birth weight and for the tails of the distribution, usually described as IUGR or macrosomia (variably defined as > 90th percentile of birth weight for gestational age or > 4,000 grams).

In addition to the consistent observational data that linked inadequate GWG, especially in underweight and normal weight women, with increased risk for SGA, and the evidence that linked excessive weight gain, especially in overweight and obese women, with increased risk of LGA and its sequelae, there is some evidence from randomized trials in women that is important. A series of early randomized trials of dietary supplements, carefully reviewed by Susser (1991), provides very little support for the argument that increased energy or protein intake during pregnancy enhances fetal growth in general. Only for women who were near starvation was the evidence linking improved nutrition to GWG to fetal growth supportive of a causal relationship. For other groups of pregnant women, there was no benefit and some indication of possible harm from ingesting supplements with high protein concentrations. In contrast, results from a Cochrane systematic review suggested a consistent benefit of supplementation in reducing risk of SGA, though this does not necessarily mean that such benefits were mediated by GWG (Kramer and Kakuma, 2003).

Recent randomized trials have focused directly on the impact of *limiting* GWG to determine whether this results in short-term metabolic effects or improved clinical outcomes. Polley et al. (2002) randomized normal weight and overweight women (~ 30 in each class and arm of the trial) to assess the impact of a multifaceted program designed to maintain GWG within recommended guidelines. The intervention yielded benefits in preventing excessive GWG only among normal weight women. Women whose GWG was moderated had infants that weighed 93 g less on average than controls. Fewer of the treated number developed GDM or had cesarean deliveries.

In summary, the issue of whether the association between GWG and fetal growth is causal cannot be answered with certainty based on the available evidence. Observational data provide replicated indications of a strong association between GWG and increased risk of SGA, especially in underweight and normal-weight women, and between higher GWG and increased risk of LGA, particularly among overweight and obese women. Randomized trials are either only indirectly applicable (because they are from less-relevant populations and time periods) or are too small to provide strong evidence. Biological considerations also need to be taken into account in judging the likelihood that associations from observational studies are causal.

There are several possible explanations for the associations between GWG and fetal growth that have been reported: GWG is causally related to fetal growth, both GWG and fetal growth are independently affected by maternal diet and/or physical activity, and both GWG and fetal growth have shared genetic or other intrinsic biological determinants. If the non-causal explanations are correct, then manipulating GWG will not affect fetal growth directly. However, if the same behavioral changes that produce a more optimal GWG also happen to result in a more optimal fetal growth, then there would be a benefit realized. If there is a shared, intrinsic biological basis for a link between GWG and fetal growth, genetic or otherwise, modification of GWG would not affect fetal growth. In the absence of clear evidence on the causal pathway, the committee presumes that the relationship between GWG and fetal growth was causal in an effort to ensure that the guidelines are protective of the health of the fetus and infant.

The Agency for Healthcare Research and Quality (AHRQ) evidence-based review on outcomes of GWG (Viswanathan et al., 2008) provides a thorough summary of the literature on GWG and birth outcomes. That report included studies published between 1990 and 2007, so that it supplements the IOM (1990) report; and the committee expanded on the AHRQ review by considering studies published subsequently (see Chapter 5 and Appendix F). The committee did not exhaustively review the studies from before 1990 given the thorough work of the IOM (1990) committee. Earlier studies are mentioned only when the information they provide affects the overall conclusions.

The AHRQ review (Viswanathan et al., 2008) considered 25 studies of variable quality that addressed GWG and birth weight as a continuous measure. Every one of those studies demonstrated an association between higher GWG and higher infant birth weight. Although there was substantial variability in magnitude of effect across studies, in general differences were on the order of 300 g in birth weight from lowest to highest GWG categories. Among the stronger studies, the AHRQ review found that for each 1 kg increase in GWG, birth weight rose 16.7-22.6 g. Fewer studies considered weight gain by trimester, and they tended to show a lower increase in birth weight per unit increase in GWG in the third than in the first or second trimester.

A smaller but still sizable number of studies (13) examined the relationship of GWG to risk of low birth weight (LBW, defined as < 2,500 g). These studies showed that risk of LBW diminishes as GWG increases, particularly as total gain exceeds 25-30 pounds. Although the magnitude of association varied substantially across studies, in general the highest GWG category had roughly half the risk of a LBW infant compared to the lowest GWG category. At the other end of the birth weight spectrum, 12 studies considered infant macrosomia, defined as birth weight > 4,000 or > 4,500 grams. Recognizing the variability in definitions of macrosomia and GWG categories, the committee found that the studies showed a consistent trend for increased risk of macrosomia with increasing GWG. Relative risks were 2-3 for macrosomia in the highest compared to the lowest GWG category. These results consistently indicate that the

relationship of GWG to birth weight applies across the full range of weights and is not limited to the low or high end of the distribution. However, because birth weight is a combination of fetal growth and length of gestation, studies that separate these two components are more informative.

The AHRQ review (Viswanathan et al., 2008) also considered studies of SGA that did not stratify by prepregnancy BMI and identified 15 of them that showed a consistent pattern of diminishing risk of SGA with increasing GWG. It is difficult to provide quantitative estimates of the magnitude of this effect given variable study methods and results, but as for LBW, relative risks on the order of 2-3 across extreme GWG categories are typical. The six studies that stratified by prepregnancy BMI similarly found lower GWG was associated with increased risk of SGA births. While methods and results were again variable, the studies did not strongly suggest that prepregnancy BMI modified the relationship between GWG and SGA, in contrast to the interpretation in the IOM (1990) report.

In the 10 studies in which GWG and LGA were considered, there was reasonably consistent support for a positive association. For each 1 kg increment in GWG, the relative risk of LGA increased by approximately a factor of 1.1, and comparing the highest to lowest categories of GWG yielded relative risks on the order of 2. The studies that stratified by prepregnancy BMI did not show notable differences in the GWG–LGA association across BMI categories, with only a modest tendency towards a stronger association among women with lower prepregnancy BMI.

Three additional studies that addressed GWG and birth weight appeared after the period covered by the AHRQ review (Viswanathan et al., 2008). Lof et al. (2008), whose focus was on the role of physical activity in relation to GWG and pregnancy outcome, noted that GWG during weeks 12-33 (unadjusted for prepregnancy BMI) was modestly correlated with increased birth weight, $r = 0.13$ (P = 0.05), stronger than the relationship for GWG during weeks 12-25 or 25-33 alone. Segal et al. (2008) found similar results in a study of obesity and family history of diabetes in relation to pregnancy outcome, with an adjusted correlation coefficient of 0.19 (P = 0.09) between weight gain before the oral glucose tolerance test and birth weight, accounting for prepregnancy BMI in the analysis.

Nohr et al. (2008) conducted the most informative analysis of the independent effects of prepregnancy BMI and GWG among over 60,000 births from the Danish National Birth Cohort. The authors considered the relationship of GWG with SGA and LGA as well as the interaction of prepregnancy BMI and GWG in relation to birth weight. They report statistically significant but generally modest indications of an interaction between prepregnancy BMI and GWG with the exception of a stronger association of low GWG with SGA among underweight women.

Subsequent analyses of this data (information contributed to the committee in consultation with Nohr) revealed that the relative risk of SGA associated with lower (< 10 kg) versus medium GWG (10-15 kg) among underweight women was 2.1, while it was 1.7 for normal weight women, 1.6 for overweight women, and 1.3 for obese women. The increased risk of LGA associated with very high GWG (≥ 20 kg) versus medium GWG (10-15 kg) was 3.7 for underweight women, 2.6 for normal weight women, 2.0 for overweight women, and 1.8 for obese women, again suggesting that the effect of GWG is dampened with increasing prepregnancy BMI. This analysis is an important contribution to quantifying the magnitude of effect of GWG on birth weight, consistent with the large body of previous studies and demonstrating an overall shift of less SGA and more LGA (and higher mean birth weight) with increasing GWG (see Appendix G, Part I).

Dietz et al. (in press) provided analyses from the Pregnancy Risk Assessment Monitoring System (PRAMS) in which they considered estimated associations between GWG and delivery

of a SGA infant using three definitions of SGA: > two standard deviations below the mean birth weight for gestational age, a customized measure, < 10th percentile of expected birth weight for gestational age; and < 10th percentile of birth weight for gestational age using a population-based reference. Population-based information about 104,980 singleton term births in 2000-2005 from 29 states participating in PRAMS provided the basis of the analysis. Risk of LGA births or births > 4,500 g yielded clear and similar findings; with increasing weight gain, there was a markedly increased risk of LGA births, present among all BMI groups, but most pronounced on a relative scale among the women with the lowest BMI. The magnitudes of association were striking, with more than a 10-fold gradient in risk from lowest to highest weight gain categories for underweight women, and a 3- to 4-fold gradient in risk for women in the other BMI categories (Table 6-2).

In summary, the evidence that GWG is related to birth weight-for-gestational age is quite strong and the magnitude of that association is large, with relative risks of SGA with low GWG on the order of 2-3. It appears that the entire birth weight distribution is shifted upward with increased GWG, reducing the risk of SGA and increasing the risk of LGA as the mean birth weight rises. The evidence that this pattern is enhanced among women with low prepregnancy BMI is moderately strong as well. The IOM (1990) report suggested consideration of a different relationship between GWG and fetal growth among young mothers. As they noted, however, it was unclear whether this pattern was reflective of a different causal process, and the subsequent literature has not strengthened the support for differential effects by maternal age group. Only limited research is available on the potential for different effects of GWG on fetal growth by ethnicity, smoking status, or other maternal attributes, and the results that are summarized in the AHRQ review are inconsistent. There is moderate support for a stronger effect of GWG that occurs during the first or second trimester on birth weight-for-gain than there is for third trimester GWG (Viswanathan et al., 2008).

TABLE 6-2 Adjusted* Odds Ratios for Association of Total GWG with SGA Stratified by Prepregnancy BMI

	Prepregnancy BMI			
	Lean	**Normal**	**Overweight**	**Obese**
Total GWG (kg)	**AOR (95% CI)**	**AOR (95% CI)**	**AOR (95% CI)**	**AOR (95% CI)**
0.4-6.7	1.0 (0.7, 1.3)	1.3 (1.1, 1.5)	1.0 (0.7, 1.4)	1.5 (1.2, 1.8)
6.8-11.7	Ref	Ref	Ref	Ref
11.8-16.3	0.6 (0.5, 0.7)	0.6 (0.5, 0.7)	0.7 (0.5, 0.7)	0.6 (0.5, 0.7)
16.4-20.8	0.4 (0.3, 0.5)	0.5 (0.4, 0.5)	0.5 (0.3, 0.6)	0.4 (0.3, 0.5)
≥20.9	0.3 (0.2, 0.3)	0.2 (0.2, 0.3)	0.3 (0.2, 0.5)	0.3 (0.2, 0.5)

NOTES: Adjusted for infant gender and gestational age; and maternal race/ethnicity, age, marital status, education, Medicaid recipient, parity, and smoking during pregnancy. Lean BMI = < 19.8 kg/m^2; Normal BMI = 19.8-26 kg/m^2; Overweight BMI = 26.1-28.9 kg/m^2; Obese BMI = > 29 kg/m^2
SOURCE: Dietz et al. (in press). This article will be published in the *American Journal of Obstetrics and Gynecology*, Copyright Elsevier (2009).

Preterm Birth

Preterm birth (< 37 weeks' completed gestation) is a critical indicator of maturity. Although defined dichotomously, risks of death and morbidity are a direct function of the degree of prematurity, with births at the margins, 33-36 weeks' gestation, most common and at modestly increased risk of health problems. In contrast, earlier births, < 33 weeks' gestation, are rarer events but at much greater risk. The spectrum of health consequences of preterm birth includes acute respiratory, central nervous system, and gastrointestinal disorders, and long-term deficits in neurobehavioral development (IOM, 2007) and possibly adverse cardiometabolic outcomes (Hofman et al., 2004; Hovi et al., 2007). An early delivery may well reflect the better alternative as compared to an intrauterine death, whether resulting from clinical intervention (an increasingly common "cause" of preterm birth) or natural processes. Nonetheless, the high and growing frequency of preterm birth in the U.S. makes this a critical endpoint to consider in relation to GWG.

At the time of the IOM (1990) report, the volume and quality of literature on preterm birth was quite limited. Several studies suggested that low GWG was associated with increased risk of preterm birth, but as they demonstrated, much of that may have resulted from the simple error of failing to recognize that the shortened period of pregnancy (i.e., preterm birth) limits the duration of time over which weight can be gained. Comparing term and preterm births on total weight gain is meaningless for that reason. Data generated on behalf of this committee (information contributed to the committee in consultation with: Herring [see Appendix G, Part II] and Stein [see Appendix G, Part III]) provided some of the first information on GWG and preterm birth to consider prepregnancy BMI, which is predictive of both preterm birth (higher risk with lower BMI) and GWG (higher GWG with lower BMI). The results of that effort suggested little effect of rate of net weight gain (the only proper measure to compare pregnancies of varying duration) on risk of preterm birth.

The AHRQ review (Viswanathan et al., 2008) included a detailed summary of the findings of 12 more recent studies that considered the relationship of rate of GWG to preterm birth. Using rate of weight gain rather than total amount gained takes into account the truncated period of pregnancy—and thus truncated opportunity to gain weight—for women who give birth before term. There was a consistently increased risk of preterm birth in both the lowest and highest GWG categories. It is difficult to summarize the quantitative impact because the studies used varying definitions of high and low rates of weight gain and different analytic methods to characterize the relationship with preterm birth. In studies that provided relative risks comparing higher and lower GWG to the middle range of GWG, the relative risks were on the order of 1.5-2.5 for both the higher and lower GWG groups, with greater consistency for the influence of lower GWG on preterm birth.

A number of these studies examined effect modification by prepregnancy BMI (Siega-Riz et al., 1996; Spinillo et al., 1998; Schieve et al., 1999; Dietz et al., 2006; Nohr et al., 2007), and those reports were consistent in finding a stronger effect of a lower rate of GWG on preterm delivery among underweight women. As prepregnancy BMI increased, the magnitude of increased risk associated with a lower rate of GWG diminished. There was some evidence that the increased risk of preterm birth associated with a higher rate of GWG was greater with increasing BMI, so that the optimal GWG shifted downward with higher prepregnancy BMI. Four studies applied the IOM (1990) guidelines to define adequacy of GWG, and all of these

reported increased risk of preterm birth associated with inadequate GWG among underweight and normal-weight women.

Some studies considered the clinical presentation of preterm birth (Siega-Riz et al., 1996; Spinillo et al., 1998; Nohr et al., 2007), and some considered severity of prematurity (Dietz et al., 2006; Stotland et al., 2006) in their analyses. Though limited in quantity, the results of these studies do not provide a clear suggestion that the association between GWG and preterm birth differs by clinical presentation or severity. More recently, Rudra et al. (2008) considered preterm birth subtypes in relation to prepregnancy BMI and GWG. They reported that greater GWG during gestational weeks 18-22 was weakly associated with lower risk of spontaneous preterm birth and higher risk of medically indicated preterm birth, with some variation in these patterns in relation to prepregnancy BMI.

Biological Plausibility

The pathogenesis of spontaneous preterm delivery has not been clearly elucidated but may involve five or more primary pathogenic mechanisms: activation of the maternal or fetal hypothalamic-pituitary-adrenal (HPA) axis, amniochorionic-decidual or systemic inflammation, uteroplacental thrombosis and intrauterine vascular lesions, pathologic distention of the myometrium, and cervical insufficiency (IOM, 2007). The committee found no studies that directly linked GWG to activation of the maternal or fetal HPA axis; however, several animal studies have linked periconceptional undernutrition to accelerated maturation of fetal HPA axis resulting in preterm delivery (Bloomfield et al., 2003; Bloomfield et al., 2004; Kumarasamy et al., 2005).

With respect to amniochorionic-decidual or systemic inflammation, the committee also found no direct link to GWG. However, it is plausible that maternal undernutrition may increase the risk of preterm delivery by suppressing immune functions or increasing oxidative stress. Macro- or micronutrient deficiencies can adversely affect maternal immune functions. For example, iron-deficiency anemia can alter the proliferation of T- and B-cells, reduce the killing activity of phagocytes and neutrophils, and lower bactericidal and natural killer cell activity, thereby increasing maternal susceptibility to infections (Allen, 2001). Furthermore, protein and/or micronutrient deficiencies may impair cellular antioxidant capacities because proteins provide amino acids needed for synthesis of antioxidant defense enzymes, such as glutathione and albumin (reactive oxygen species scavengers), and many micronutrients themselves are antioxidants. Increase in reactive oxygen species, such as oxidized low-density lipoprotein and F2-isoprostanes (lipid peroxidation products), may contribute to cellular toxicity, inflammation, vasoconstriction, platelet aggregation, vascular apoptosis and endothelial cell dysfunction (Luo et al., 2006), which may also activate the pathway to preterm delivery involving uteroplacental thrombosis and intrauterine vascular lesions.

The committee cannot establish a causal relationship between GWG and preterm delivery based on available evidence. Although there are intriguing data linking macro- and/or micronutrient deficiencies to accelerated maturation of fetal HPA axis and altered immune functions and/or increased oxidative stress that suggest biological plausibility, important questions regarding timing, threshold, content, and interactions remain unanswered. These uncertainties about a direct causal relationship between GWG and preterm delivery guided the committee's approach to decision analysis in Chapter 7, which weighed the trade-offs of GWG with and without taking into account preterm delivery as an outcome.

In summary, there is strong evidence for a U-shaped association between lower GWG and preterm birth among normal weight and underweight women, and moderate evidence for an association of higher GWG and preterm birth. The magnitude of the association is fairly strong, with relative risks on the order of two, but difficult to summarize because of variability in the definitions of higher and lower rates of weight gain. In addition, as noted in the chapter introduction, the lack of strong biological plausibility between GWG and preterm birth calls into question the causal relationship between the two. There is no empirical basis for suggesting modifiers of this relationship other than prepregnancy BMI, for which the data are clear in showing that associations of low GWG with preterm birth are stronger among underweight women.

LONG-TERM CONSEQUENCES

The IOM (1990) report recommendations for GWG were focused largely on avoiding inadequate weight gain and thus the short-term consequences of low fetal growth and prematurity (see Chapter 1). Since its publication, the emergence of epidemic obesity in the American population has raised the possibility that excessive GWG may also be harmful. A small number of studies now address the associations of GWG with adiposity at birth and with markers of childhood obesity and its cardiometabolic sequelae.

Neonatal Body Composition

As reviewed above, GWG is directly associated with fetal growth as measured by birth weight for gestational age. For outcomes related to long-term adiposity, however, it is important to measure not only weight (and length) at birth, but also body composition. Catalano and colleagues performed a series of studies relating maternal characteristics to neonatal body composition measured by total body electrical conductivity, a method no longer in use. One set of studies compared infants who were born at term to overweight/obese women (pregravid BMI > 25 kg/m^2; $n = 76$) with those born to lean/average weight women ($n = 144$) (Sewell et al., 2006). As expected, GWG was higher among lean/average (mean 15.2 kg) than overweight/obese (13.8 kg) women. Among the overweight/obese women, stepwise regression analyses that included pregravid weight as a covariate revealed that the higher the GWG, the higher the newborn fat mass. The authors did not report the correlation among the lean women, presumably because the associated p-value exceeded 0.05. In another study, however, which combined diabetic and non-diabetic pregnant women (total $n = 415$), Catalano and Ehrenberg (2006) found that GWG was directly associated with birth weight, including both lean and fat mass. These results are consistent with those of Udal et al. (1978), who found a direct association between GWG and sum of eight neonatal skinfold measurements among 109 non-diabetic mothers who delivered term infants, an association that was independent of prepregnancy weight, gestational age, smoking and family history of diabetes.

The findings of these studies raise the possibility that higher GWG may lead to long-lasting adiposity in the offspring. Studies that link GWG with body composition from birth onwards in populations from developed countries would be quite informative but are presently unavailable.

Infant Weight Gain

Rapid weight gain during infancy is associated with obesity later in life (Baird et al., 2005; Monteiro and Victoria, 2005; Gillman, 2008). It is unclear whether this pattern is particularly an

issue among infants who are born SGA (Ong and Loos, 2006; Taveras et al., 2009). Therefore, infant weight gain may serve as a surrogate, or intermediate marker, of later adiposity. Although it may be more feasible to obtain intermediate markers than ultimate health outcomes, they are rarely perfect surrogates and are sometimes misleading. Therefore, one should view any associations of GWG with surrogate outcomes—even in randomized trials—with caution, and only as suggestive of effects on actual health outcomes. Also, this line of evidence would be strengthened by studies with serial measures of body composition, not just weight (with or without length) from birth onwards.

Only one study was identified that addressed GWG and infant weight gain, and it was not the primary goal of the study. Ong et al. (2000) conducted a prospective study of 848 term infants born in the UK who had weight measured at birth and at two and five years of age. The 30.7 percent of children who gained more than 0.67 weight standard deviations in the first two years of life had more adiposity at age five than the other children, but they also had been lighter, shorter, and thinner at birth. The mothers of these children were not more likely to have had a higher prepregnancy BMI or to have gained more weight during pregnancy.

Breastfeeding Initiation and Maintenance

Breastfeeding Outcomes

Breastfeeding is an important outcome to study not only because it may be associated with reduced obesity, and is therefore an intermediate like infant weight gain, but also because it predicts other health outcomes such as reduced otitis media and gastrointestinal illness and better cognition. Observational studies (see Chapter 5) have documented a relationship between excessive weight gain during pregnancy and poor breastfeeding outcomes.

Long-term Effects on Obesity

Despite the importance of this issue, high-quality studies that link GWG with obesity and related health outcomes in childhood are only beginning to be published. The AHRQ review (Viswanathan et al., 2008) identified only one cohort study that examined childhood obesity in relation to weight gain according to the IOM (1990) guidelines. Oken et al. (2007) analyzed data from Project Viva, a prospective study of predominantly non-low-income pregnant women and their children in Massachusetts (Table 6-3). Among the sample of 1,044 mothers included in this analysis, 51 percent gained excessive, 35 percent adequate, and 14 percent inadequate weight during pregnancy. Compared with inadequate GWG, adequate and excessive gains were associated with odds ratios of 3.77 (95% CI: 1.38, 10.27) and 4.35 (1.69, 11.24), respectively, for obesity at 3 years of age (BMI > 95th percentile versus < 50th percentile) in analyses adjusted for key covariates. In addition, the authors found higher BMI z-score, sum of triceps and subscapular skinfold thicknesses, and systolic blood pressure for each 5-kg increment in total GWG.

The AHRQ review (Viswanathan et al., 2008) found three other studies that assessed total GWG and childhood adiposity. One of these studies (Ong et al., 2000) examined weight gain from birth to two years as an outcome, as was discussed earlier. Sowan and Stember (2000) examined outcomes through 14 months of age. In their fully adjusted model, each 5-pound increment in total weight gain was associated with an odds ratio of 0.8 for obesity defined as BMI > 84th percentile within the study population (*n* = 630). Inferences from this study are

uncertain for a number of reasons. Li et al. (2007) empirically derived three weight-gain trajectories through childhood. Gestational weight gain was a predictor of the "early-onset" trajectory (which was defined as "children with an early-onset of overweight that persisted throughout childhood") total weight gain of at least 45 pounds (versus 25-35 pounds) was associated with an increased risk of 1.7 for being in the early-onset rather than the normal trajectory class in an analysis adjusted for maternal BMI and other factors.

Since the publication of the AHRQ review (Viswanathan et al., 2008), Wrotniak et al. (2008) studied approximately 10,000 seven-year-old term-born offspring of participants in the 1950s-1960s Collaborative Perinatal Project (see Table 6-3). Not surprisingly, mean maternal BMI (21.9 kg/m^2), total weight gain (9.5 kg), and birth weight (3.23 kg), and the proportions of women with excessive gain (11 percent) and children with obesity (defined as BMI > 95th percentile—5.7 percent) were lower than in current cohorts. Both total weight gain and excessive weight gain were associated with child obesity. For example, compared with adequate gain, excessive gain was associated with an adjusted odds ratio of 1.48 (95% CI: 1.06, 2.06) for BMI ≥ 95th versus < 95th percentile). The association appeared stronger for women who entered pregnancy underweight (BMI < 19.8 kg/m^2) than for heavier mothers.

In another recent study, Moreira et al. (2007) found that total weight gain was directly associated with childhood overweight defined by the International Obesity Task Force standards (Cole et al., 2000) (see Table 6-3). Compared with weight gains < 9 kg, gains ≥ 16 kg were associated with an adjusted odds ratio for overweight of 1.27 (95% CI: 1.01–1.61).

Among nearly 12,000 participants in the Growing Up Today Study, Oken et al. (2008) found a strong, nearly linear association between total GWG and obesity (BMI >95th versus < 85th percentile) at 9-14 years of age after adjusting for maternal BMI and other covariates (see Figure 6-3 and Table 6-3). Overall, each 5-lb increment in GWG was associated with an odds ratio of 1.09 (95% CI: 1.06-1.13) for obesity. Expressing GWG in terms of recommended weight gain ranges (IOM, 1990), the authors found that, compared to adequate weight gain, the odds ratio for excessive gain was 1.42 (95% CI: 1.19-1.70). Inadequate gain was not clearly associated with lower risk of obesity. The authors did not find that maternal BMI modified associations of GWG with adolescent obesity, although—if anything—the association was weaker among underweight mothers, in contrast to the findings of Wrotniak et al. (2008).

TABLE 6-3 Published Studies ($N > 1,000$) Relating Total GWG to Child Obesity

	Moreira et al., 2007	Oken et al., 2007	Oken et al., 2008	Wrotniak et al., 2008
Age at Outcome (y)	6-12	3	9-14	7
N	4,845	1,044	11,994	10,226
Birth Years	1990-1997	1999-2002	1982-1987	1959-1966
GWG Exposure	<9 kg 9-13.5 13.6-15.9 16+	per 5 kg; A/E v. I	per 5 lb; I/E v A	per 1 kg; I/E v A
Child BMI Outcome	OR for overweight (IOTF)	OR for ≥ 95th v. < 50th	OR for ≥ 95th v. < 85th	OR for ≥ 95th v. < 95th
Outcome Prevalence	~19.5%	9.0%	6.5%	5.7%
Overall results	1.0 (ref) 1.12 (0.91-1.37) 1.20 (0.90-1.60) 1.27 (1.01-1.67)	1.66 (1.31-2.12) [1.44 (1.17- 1.79) for BMI 95th v. < 85th][a]	1.09 (1.06-1.13)	1.03 (1.02, 1.05)
		A 3.77 (1.38-10.3) E 4.35 (1.69, 11.2)	I 0.91 (0.74-1.13) E 1.42 (1.19-1.70)	I 0.88 (0.68, 1.14) E 1.48 (1.06, 2.06)
Approximate OR per 5 kg (11 lb)	1.14 (ninth root of 1.27 raised to the fifth power)[b]	1.44	1.21 (1.09 raised to the power 2.2)	1.16 (1.03 raised to the fifth power)
Maternal BMI Category			WHO Categories	IOM Categories
Underweight	NA	NA	0.94 (0.71-1.23)	1.09 (1.01, 1.16)
Normal weight	NA	NA	1.09 (1.04-1.14)	1.02 (1.14, 2.23)
Overweight	NA	NA	1.11 (1.04-1.19)	1.02 (1.14, 2.23)
Obese	NA	NA	1.04 (0.95-1.15)	1.02 (1.14, 2.23)

[a] Not in published paper but subsequently calculated by authors (personal communication, E. Oken, Harvard Medical School and Harvard Pilgrim Health Care, Boston, Ma., December 2008)

[b] Assumes OR of 1.27 is for 9-kg difference between top and bottom categories

NOTES:

A = adequate GWG per 1990 IOM recommendations; E = excessive; I = inadequate

BMI = body mass index

OR = odds ratio; values in parentheses are 95% confidence intervals

NA = data not available

WHO BMI categories = < 18.5, 18.5-24.9, 25-29.9, 30+ kg/m^2

IOM BMI categories = < 19.8, 19.8-26.0, 26.0-29.0, > 29.0 kg/m^2

IOTF = International Obesity Task Force (Cole, 2000)

SOURCES: Moreira et al., 2007; Oken et al., 2007; Oken et al., 2008; Wrotniak et al., 2008.
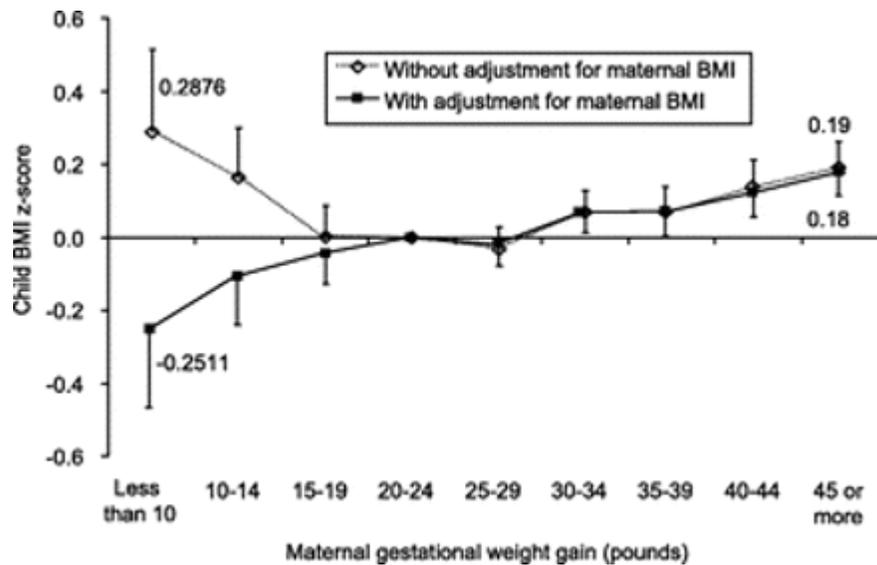
FIGURE 6-3 Associations of maternal gestational weight gain with child BMI *z* score at age 9-14 years, with and without adjustment for maternal prepregnancy BMI. All estimates are adjusted for maternal age, race/ethnicity, marital status, household income, paternal education, child sex, gestation length, age, and Tanner stage at outcome assessment. SOURCE: Oken et al., 2008. Maternal gestational weight gain and offspring weight in adolescence. *Obstetrics and Gynecology* 112(5): 999-1006. Reprinted with permission.

Other studies have not demonstrated associations between GWG and adiposity-related measures in the offspring. Some of these were suggestive but small (Gale et al., 2007), while others were sufficiently large but did not focus on GWG as a main study exposure or adequately control for confounding factors (Fisch et al., 1975; Maffeis, 1994; Whitaker, 2004).

Overall, evidence to date is suggestive but not conclusive that GWG outside the ranges recommended by IOM (1990) is associated with higher BMI in the offspring. Evidence for effect modification by maternal BMI is scant. No data are available to address the timing of weight gain during pregnancy. Most of the studies rely on child's BMI as the only outcome, but direct measures of adiposity and cardio-metabolic status would strengthen evidence. Only one study to date has reported on blood pressure as an outcome (Oken et al., 2007), although a recent report suggests that higher amounts of weight gain are associated with increase in left ventricular mass from birth to six months (Geelhoed et al., 2008).

The National Children's Study will offer an opportunity to address many of these limitations. Now in early recruitment, this is a cohort study of parents and children from the prenatal (or, in a subset, preconceptional) period through 20 years of age. The sample, to include 100,000 children, is meant to be representative of the US population. This sample will be large enough to assess effect modification by race/ethnicity and other characteristics as well as maternal BMI, and to address timing of weight gain during pregnancy. Child outcomes will include direct measures of adiposity and cardio-metabolic risk factors from birth onwards in addition to length/height and weight. Statistical modeling will allow adjustment for many potential confounding variables.

Nevertheless, as discussed in the chapter opening, even strong observational studies that have valid exposure and outcome measures, large sample sizes, and appropriate control for confounding cannot fully address the question of causality. Randomized controlled trials that are designed to modify GWG and include follow-up of the children would provide the most compelling evidence for or against intensive clinical or public health efforts to curb excessive weight gain.

Other Outcomes

Neurodevelopment

The effect of alterations in fuel metabolism during pregnancy resulting from intended or unintended weight loss, fasting, or poorly controlled diabetes include ketonemia and/or ketonuria, and consequences from those conditions for the neurocognitive development of the infant (see Chapter 3). The committee reviewed the evidence for long-term neurodevelopmental consequences of ketonemia/ketonuria in pregnancy (See Appendix G). As a result of the association between lower GWG and SGA (see discussion above) one indirect way to evaluate the impact of GWG on neurodevelopment is by assessing associations of term and preterm SGA with neurodevelopmental outcomes.

Long term neurodevelopment in term SGA Only observational prospective studies and review articles were identified that evaluate long-term neurodevelopmental outcomes in term SGA infants. With the exception of one study conducted in China, all were conducted in industrialized nations including the U.S. (Goldenberg et al., 1996; Nelson et al., 1997). Of 18 studies identified, six examined neurodevelopmental outcomes during infancy/childhood (Watt and Strongman, 1985; Nelson et al., 1997; Sommerfelt et al., 2000; Hollo et al., 2002; Geva et al., 2006; Wiles et al., 2006), nine during adolescence (Westwood et al., 1983; Paz et al. 1995; Pryor et al., 1995; Goldenberg et al., 1996; Strauss, 2000; Paz et al., 2001; O'Keefe et al., 2003; Indredavik et al., 2004; Peng et al., 2005; Kulseng et al., 2006) and two during adulthood (Viggedal et al., 2004; Wiles et al., 2005).

A study from a Finnish cohort found that SGA children performed worse at school than gestational age-matched controls at 10 years of age (Hollo et al., 2002). Another cohort of children in Norway found a slightly lower mean intelligence quotient (IQ) at five years of age associated with SGA. However, in this study parental factors were more strongly related with IQ than SGA (Sommerfelt et al., 2000).

In studies of development related to SGA results have been mixed. Nelson et al. (1997) found that SGA was not associated with the Bayley Mental Development Index (MDI) and Fagan Test of Infant Intelligence score at one year of age. In contrast, they found that SGA was associated with a lower Bayley Psychomotor Development Index (PDI) among black males but not among females or white male and female infants. Watt and Strongman (1985) documented that SGA was inversely associated with MDI developmental scores at 4 months, whereas Goldenberg et al. (1996) found an inverse relationship between SGA and IQ at 5.5 years of age. Wiles et al. (2006) did not find a relationship between low birth weight and behavioral problems at 6.8 years of age.

An effect size analysis was conducted based on cognitive measures. Of the 18 studies reviewed, 12 reported cognitive scores by SGA status. Of these, two reported lower Bayley scores (Watt and Strongman, 1985; Nelson et al., 1997) and 10 reported lower IQ measures

(Westwood et al., 1983; Paz et al. 1995; Pryor et al., 1995; Goldenberg et al., 1996; Sommerfelt et al., 2000; Paz et al., 2001; Hollo et al., 2002; Viggedal et al., 2004; Peng et al., 2005; Kulseng et al., 2006) associated with term-SGA status, although these differences were not always statistically significant. Among infants, the Bayley score difference associated with SGA ranged from 4-7 points (Watt and Strongman, 1985; Nelson et al., 1997). Among children (Goldenberg et al., 1996; Sommerfelt et al., 2000; Hollo et al., 2002), IQ differentials were 4-5 points. Among adolescents (Westwood et al., 1983; Paz et al. 1995; Pryor et al., 1995; Paz et al., 2001; Peng et al., 2005; Kulseng et al., 2006) the corresponding range was 2-12 points.

The upper range limit was derived from a study conducted in China that did not control for socioeconomic and other potential confounding factors (Peng et al., 2005). The only study among adults that reported IQ documented a relatively large 19-point IQ differential (based on scores' median instead of average) associated with term-SGA infants. However, it also failed to account for confounding factors (Viggedal et al., 2004). Overall, studies consistently reported small cognitive differentials associated with being born at term and SGA. The meaning of these small differentials is unclear as in all studies average scores among individuals born SGA fell within the normal IQ range.

Although there was a large body of evidence, associations between SGA and longer term neurodevelopmental outcomes among term newborns were inconsistent, especially among adolescents. Among studies that supported this association, major methodological shortcomings (which included substantial attrition rates, lack of standard definitions of SGA across studies, not properly accounting for key confounders [such as socioeconomic status and parental cognitive functioning as well as asphyxia at birth], and lack of testing for effect modification by environmental factors) limit their interpretation. The committee's evaluation of the evidence concurs with previous reviews (Grantham-McGregor, 1995; Goldenberg et al., 1998) that SGA is associated with minimal neurologic dysfunction (e.g., poor school performance) and is not associated with major handicaps, such as cerebral palsy, unless accompanied by asphyxia at birth and that, as a whole, the studies were not designed to identify the influence of SGA, independent of socioeconomic factors, on lower IQs associated with SGA.

Long-term neurodevelopment in preterm SGA In preterm SGA infants, the majority of longitudinal studies reviewed focused on extremely premature (Feldman and Eidelman, 2006; Kono et al., 2007; Paavonen et al., 2007; Leonard et al., 2008) or very low birth weight (VLBW) (Litt et al., 1995; Hack et al., 1998; Brandt et al., 2003; Kilbride et al., 2004; Litt et al., 2005; Feldman and Eidelman, 2006; Hille et al., 2007; Paavonen et al., 2007; Strang-Karlsson et al., 2008a, 2008b) infants. Among 14 studies in children, 11 found that SGA was associated with cognitive and/or neurodevelopment impairments, although this relationship may be modified by degree of postnatal catch-up growth and maternal-child interactions (Casey et al., 2006; Feldman and Eidelman, 2006). In general, the effect size was proportional to the severity of prematurity (Calame et al., 1983; Feldman and Eidelman, 2006; Kono et al., 2007). The two studies conducted among adolescents found an association of VLBW with IQ (Hille et al., 2007) and breathing-related seep disorders (Paavonen et al., 2007). Among adults, VLBW was associated with emotional instability (Strang-Karlsson et al., 2008b) and SGA with lower head circumference among individuals who did not fully catch-up in their head circumference growth during their first 12 months of life.

An effect size analysis was conducted based on cognitive measures. Of 19 studies reviewed, 13 reported cognitive scores by SGA status; and of these one reported a lower Bayley score (Feldman and Eidelman, 2006), and 12 reported lower IQ measures (Escalona, 1982; Calame et

al., 1983; Silva et al., 1984; Holwerda-Kuipers, 1987; Litt et al., 1995; McCarton et al., 1996; Hutton et al., 1997; Kilbride et al., 2004; Litt et al., 2005; Casey et al., 2006; Hille et al., 2007; Kono et al., 2007) associated with preterm SGA status, although these differences were not always statistically significant. Among 2-year old children, one study found an 8-point difference in the Bayley Mental Development Index score (Feldman and Eidelman, 2006). In contrast, a study conducted among 3.5-year-old children found no differences in IQ scores associated with preterm SGA (Escalona, 1982). Among the rest of studies with children (Calame et al., 1983; Silva et al., 1984; Holwerda-Kuipers, 1987; Litt et al., 1995; McCarton et al., 1996; Hutton et al., 1997; Kilbride et al., 2004; Litt et al., 2005; Casey et al., 2006; Kono et al., 2007), IQ differentials were 2-11 points. The only study among adults that reported IQ, documented a 2-point differential associated with VLBW. Overall, the cognitive differentials appear to be relatively stronger among individuals born SGA preterm (mean ± std. dev: 6.5 ± 3.8 IQ points, *n* = 11 studies) than among those born SGA term (5.3 ± 3.0, *n* = 9 studies IQ points). However, as with term SGA, the meaning of these still relatively small differentials is unclear because in the vast majority of studies, the average scores for individuals born preterm SGA fell within the normal IQ range.

The overwhelming majority of studies reviewed support an association between preterm SGA and lower neurodevelopment in the longer term. Consistent with the studies on term SGA, many of the studies on preterm SGA did not properly control for key perinatal (e.g., asphyxia), socio-economic, parental, and home environment confounders (e.g., maternal-child interactions). In addition, although some studies included term births as reference groups (Calame et al., 1983; Silva et al., 1984; Holwerda-Kuipers, 1987; Litt et al., 1995; Hack et al., 1998; Brandt et al., 2003; Kilbride et al., 2004; Litt et al., 2005; Paavonen et al., 2007; Leonard et al., 2008; Strang-Karlsson et al., 2008a, 2008b), others used preterm subgroups as comparison groups (McCarton et al., 1996; Hutton et al., 1997; Casey et al., 2006; Kono et al., 2007). Thus, the effect size or the proportion of the variance in neurodevelopmental outcomes that can be attributed to being born premature per se or to the combination of prematurity and SGA still needs to be determined taking into account these study design limitations.

In summary, as was the case with infant mortality, one must link GWG to being born preterm or small- or large-for-gestational age and, from there, to neurodevelopmental outcomes. This sequence is biologically plausible and it is possible that it is causal, but the evidence to establish causality is not available.

Apgar score Apgar score (see Glossary in Appendix A) assessments are usually conducted one and five minutes after birth and scores can range from 0 to 10. They are not adequate predictors of longer term morbidity and mortality although very low scores (0-3) associated with low birth weight do predict neonatal mortality. Apgar scores in term infants, even at five minutes do not correlate well with neurological outcomes (ACOG, 2006). The AHRQ review (Viswanthan et al., 2008) identified five studies in which the influence of GWG on newborn's Apgar score was examined (Stevens-Simon and McAnarney, 1992; Nixon et al., 1998; Cedergren et al., 2006, Stotland et al., 2006, Wataba et al., 2006). These studies provide only modest evidence that excessive GWG is associated with low Apgar score, and one study suggested that low GWG in nulliparous women also predicts low Apgar score.

Childhood cognition No published studies directly examine the link between GWG and neurocognitive development in infants and children. As discussed in Chapter 3, however, weight loss or failure to gain during pregnancy due to dietary caloric insufficiency may possibly induce maternal hormonal and metabolic responses that may have subsequent consequences for the

intellectual development of the child. Because of the obligatory weight gain in maternal tissues (uterus, breast, blood) and the fetal-placental unit, a weight gain less than ~7.5-8.5 kg would likely result in mobilization of maternal adipose tissue and possibly lean body mass.

No studies have addressed the gestational metabolic milieu or offspring outcomes of the pregnant woman who experiences weight loss. Studies do exist, however, on the associations of ketonemia or ketonuria, which can occur among pregnant women subjected to short-term fasting (see Chapter 3), on cognition in offspring. Some, but not all, of these studies have found an association between biomarkers of maternal metabolic fuel alterations and child intellectual development (Stehbens et al., 1977; Rizzo et al. 1991; Silverman et al. 1991). In contrast, Persson et al., (1984) and Naeye and Chez (1981) did not find any association of maternal acetonuria, weight loss or low GWG with psychomotor development and IQ in children (see Chapter 3). In summary, although no studies specifically address the impact of very low GWG or weight loss on child intellectual development, some evidence suggests that biomarkers of short-term negative energy balance during pregnancy may be related to the child's intellectual development. These associations may be limited to women with diabetes during pregnancy.

Allergy/Asthma

Preterm birth is a risk factor for childhood asthma, often as a result of suboptimal lung function and resulting neonatal respiratory morbidity (Dombkowski et al., 2008). Inasmuch as GWG has, in turn, been associated with risk of preterm birth, the committee considered the plausibility that GWG may also be a risk factor for childhood asthma. In a case-control study of 262 African-American 4-9-year-old children receiving care at a hospital-based clinic, Oliveti et al. (1996) used maternal self-report and child medical records to examine pre- and perinatal risk factors for asthma, defined by physician diagnosis in addition to wheezing or coughing that required asthma medication. Among children with asthma, 24.6 percent were born preterm compared to 13.7 percent of controls. Multivariate logistic regression analyses showed that odds of prevalent asthma were 3.42 (95% CI: 1.72-6.79) times higher among women who gained less (versus more) than 20 total pounds during pregnancy. However, the authors neither adjusted for prepregnancy BMI nor examined the BMI-GWG interaction.

Gestational weight gain may be associated with an increased risk for asthma in offspring through alteration of the developing fetal immune system. Willwerth et al. (2006) found that both inadequate and excessive GWG were associated with increased cord blood mononuclear cell proliferative responses to stimulation (OR = 2.3 and 2.6, respectively), compared to controls with adequate GWG. In this study, however, maternal smoking (OR = 18) was the major determinant of the response.

Cancer

Whether associations exist between GWG, birth weight, and risk for childhood cancers is not clear, however, there are a few studies that have examined the possibility.

Childhood leukemia There may be an indirect relationship between GWG and childhood leukemia because of the established relationship between higher GWG and macrosomia (see discussion above). A recent meta-analysis (Hjalgrim et al., 2003) estimated that the odds for acute lymphoblastic childhood leukemia (ALL) were higher (OR = 1.26 [95% CI: 1.17-1.37]) for infants with birth weight over 4,000 g compared to those under 4,000 g. Although not statistically significant, results were of similar magnitude for acute myelogenous leukemia

(AML). McLaughlin et al. (2006) examined the association between pregnancy outcomes and leukemia diagnosed before 10 years of age registered in the state of New York. Information on prepregnancy weight (BMI not generally available) and GWG was obtained from birth certificates. Multivariate regression analyses, adjusted for prepregnancy weight, showed that total GWG greater than 14 kg conferred an increased risk for ALL (OR = .31 [95% CI: 1.07, 1.60]). No interaction of GWG with maternal weight was found and there was no association of GWG with AML. The authors speculated that higher GWG could result in higher fetal exposure to insulin-like growth factor I (IGF-I) which in turn may increase the risk of childhood ALL.

Breast cancer Almost two decades ago, Trichopoulos (1990) hypothesized that breast cancer originates from alterations in the prenatal endocrine milieu, in particular higher estrogen levels. Although longitudinal studies are unavailable, observational studies showing direct associations between birth weight and breast cancer provide some support for an association (Michels et al., 1996; Vatten et al., 2002; Ahlgren et al., 2007). Therefore, it is of interest to examine determinants of hormone levels in the maternal-placental-fetal unit. Lagiou et al. (2006) examined the association between GWG and maternal sex hormones at 16 and 27 weeks of gestation. After adjusting for prepregnancy BMI and other covariates no associations were found between GWG and maternal estradiol, estriol or prolactin levels. However, among women with high GWG, there was an association between lower levels of maternal progesterone and of sex hormone binding globulin (-0.7 percent [95% CI -1.5, 0.0] at 16 weeks and -1.2 percent [95% CI -2.0, -0.4] at 27 weeks, respectively, for every 1 kg increment in GWG.

In addition, one study directly addressed the association of GWG with incident breast cancer. Analyzing data from the Finnish Cancer Registry, Kinnunen et al. (2004) found that mothers in the upper tertile of GWG (> 15 kg) had a 1.62-fold higher breast cancer risk than mothers who gained within the recommended range (11–15 kg), after adjusting for parity, mother's age at menarche, at first birth, and at index pregnancy, and prepregnancy BMI. Together these findings provide some support for the hypothesis that excessive weight gain in pregnancy could lead to elevated breast cancer risk in the offspring.

Attention Deficit Hyperactivity Disorder It is possible that maternal body fat reserves and GWG can influence fetal central nervous pathways that ultimately result in behavioral disorders such as attention deficit hyperactivity disorder (ADHD) because the human brain rapidly develops during gestation and the early postnatal period. Only one study (Rodriguez et al., 2008) was identified that examined associations of early pregnancy BMI and GWG with ADHD. Within three cohorts of 7-12-year-old Scandinavian children, teachers rated the children's inattention and hyperactivity symptoms with standard questionnaires. About 8.5 percent of children were classified as having ADHD symptoms. A large majority of women (86.4 percent) had a normal prepregnancy BMI and adequate GWG (mean gestational age = 39.6 ± 1.6 weeks; and mean birth weight = 3.6 ± 0.5 kg). Multivariate linear regression analyses showed that among women with a high prepregnancy BMI, GWG (weekly gain in 100-g increments) was associated with increased odds of child ADHD (OR = 1.24, 95% CI 1.07-1.44). Among lean women, those who experienced weight loss during pregnancy also had higher odds for child ADHD than their counterparts who did not lose weight during gestation (OR: 1.52, 95% CI: 1.07-2.15). The mechanisms for these effects are unknown, although the authors speculated on the possibility of neurotoxin transfer from maternal adipose tissue to the developing fetal brain.

CONCLUDING REMARKS

Assessing the impact of GWG on child outcomes requires both a short- and long-term outlook. Strong observational evidence links GWG directly with fetal growth, so that higher weight gain predicts LGA and lower weight gain predicts SGA, both themselves markers of neonatal morbidity. The literature on preterm birth is more ambiguous because of a less-extensive body of epidemiologic evidence, a nonlinear relationship between GWG and preterm birth, and uncertainty about biologic mechanisms. Even the proper measurement of GWG to take into account the shortened time period of pregnancy is subject to some uncertainty. The U-shaped association of GWG with preterm birth is harder to interpret than the monotonic dose-response gradient with birth weight for gestational age, post-partum weight retention, and childhood obesity. It may reflect distinct causal processes on the low and the high end of GWG.

Among the most important long-term child outcomes are obesity and its sequelae, chiefly cardio-metabolic consequences and neurodevelopmental disorders. Observational evidence is growing that GWG predicts childhood adiposity after adjusting for key factors including prepregnancy BMI, although some older studies do not show this association. The evidence for neurodevelopmental outcomes is dependent on inferences from intermediate endpoints of fetal size and duration of gestation.

Randomized trials are especially important because to date there is no appropriate animal experimental model for GWG, thus reducing one of the criteria—biological plausibility—that epidemiologists often use to support causal inference. Nevertheless, as reviewed in this chapter, pathways involving insulin resistance and fetal hyperglycemia may underlie associations of GWG with subsequent obesity in the offspring. At the other end of the spectrum, reduced GWG is associated with lower fetal growth and preterm birth, themselves associated with later central obesity, insulin resistance, and metabolic syndrome. Very little current evidence, however, suggests that inadequate or low GWG predicts obesity-related outcomes in children.

FINDINGS AND RECOMMENDATIONS

Findings

1. Causal inferences relating GWG to childhood outcomes are tenuous as a result of the paucity of experimental studies.
2. Epidemiologic support for an association between gestational weight gain and stillbirth is weak; there are few methodologically sound studies.
3. Many epidemiologic studies are consistent in showing a linear, direct relationship between GWG and birth weight for gestational age. Thus, lower GWG predicts SGA, and higher GWG predicts LGA. Despite a limited number of randomized controlled trials, biological plausibility from animal models is strong. Relative risks appear higher among women with lower prepregnancy BMI.
4. The evidence for a relationship between GWG and preterm birth, or continuous gestational age is weaker than evidence for fetal growth, and biological plausibility is weak. Most studies show associations between lower GWG and preterm birth among underweight, and to a lesser extent, normal weight women. Higher GWG among all BMI categories may also be associated with preterm birth. Evidence is insufficient on associations with spontaneous versus induced preterm birth.

5. A small number of studies show that GWG is directly associated with fat mass in the newborn period. Insufficient evidence is available on associations between GWG and adiposity in infancy.
6. A small number of relatively large and recent epidemiologic studies show that higher GWG is associated with childhood obesity as measured by BMI. Although biological plausibility is strong, evidence is insufficient to address effect modification by maternal BMI. Only one study has examined blood pressure as an outcome (finding associations in the same direction as BMI) and none has evaluated fat mass or other cardiometabolic consequences of adiposity.
7. Lower GWG may be associated with risk of childhood asthma, chiefly through complications of preterm birth although evidence is limited.
8. Higher GWG may be associated with ALL, breast cancer, and ADHD. Data are limited.
9. Concern exists that metabolic consequences of weight loss during pregnancy may be associated with poorer childhood neurodevelopmental outcomes. Data are limited but raise the possibility that ketonemia among diabetic women could lead to suboptimal neurologic development.

Recommendation for Research

Research Recommendation 6-1: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct observational and experimental studies to assess the impact of variation in GWG on a range of child outcomes, including duration of gestation, weight and body composition at birth, and neurodevelopment, obesity and related outcomes, and asthma later in childhood.

Areas for Additional Investigation

The committee identified the following areas for further investigation to support its research recommendations. The research community should conduct studies on:

- Child outcomes related to GWG to provide support for causal inference. Randomized trials and a combination of observational epidemiology and animal models may be a more attainable benchmark to enhance certainty regarding causal links between GWG and infant outcomes;
- Statistical models that follow sound theoretical frameworks and clearly distinguish among confounding, mediating, and moderating (effect modifying) variables. Statistical models based on path analysis such as structural equation modeling may be able to improve interpretation of complex data; and
- Preventing excessive weight gain with all of the attributes listed above for observational studies. Even relatively small studies that can evaluate intermediate endpoints, if not the clinically important outcomes, would make a significant contribution.

Furthermore, future research on GWG and child outcomes should:

- Not assume linear relationships between GWG and offspring obesity, but should look for U- or J-shaped associations as well;

- Determine whether the pattern of maternal weight gain matters for short- or long-term child outcomes, e.g., whether weight gain earlier in pregnancy is more harmful than later gain; and
- Determine whether critical or sensitive periods of adiposity accretion exist in pregnant women, and if so when weight gain is an adequate measure to capture those periods.

REFERENCES

ACOG (American College of Obstetricians and Gynecologists). 2006. ACOG Committee Opinion. Number 333, May 2006 (replaces No. 174, July 1996): The Apgar score. *Obstetrics and Gynecology* 107(5): 1209-1212.

Aerts L. and F. A. Van Assche. 2003. Intra-uterine transmission of disease. *Placenta* 24(10): 905-911.

Ahlgren M., J. Wohlfahrt, L. W. Olsen, T. I. Sorensen and M. Melbye. 2007. Birth weight and risk of cancer. *Cancer* 110(2): 412-419.

Allen L. H. 2001. Biological mechanisms that might underlie iron's effects on fetal growth and preterm birth. *Journal of Nutrition* 131(2S-2): 581S-589S.

Anderson J. L., D. K. Waller, M. A. Canfield, G. M. Shaw, M. L. Watkins and M. M. Werler. 2005. Maternal obesity, gestational diabetes, and central nervous system birth defects. *Epidemiology* 16(1): 87-92.

Baird J., D. Fisher, P. Lucas, J. Kleijnen, H. Roberts and C. Law. 2005. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *British Medical Journal* 331(7522): 929.

Barker D. J., J. G. Eriksson, T. Forsen and C. Osmond. 2002. Fetal origins of adult disease: strength of effects and biological basis. *International Journal of Epidemiology* 31(6): 1235-1239.

Barker D. J., C. Osmond, T. J. Forsen, E. Kajantie and J. G. Eriksson. 2005. Trajectories of growth among children who have coronary events as adults. *New England Journal of Medicine* 353(17): 1802-1809.

Ben-Shlomo Y. and D. Kuh. 2002. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *International Journal of Epidemiology* 31(2): 285-293.

Benyshek D. C., C. S. Johnston and J. F. Martin. 2006. Glucose metabolism is altered in the adequately-nourished grand-offspring (F3 generation) of rats malnourished during gestation and perinatal life. *Diabetologia* 49(5): 1117-1119.

Bhargava S. K., H. S. Sachdev, C. H. Fall, C. Osmond, R. Lakshmy, D. J. Barker, S. K. Biswas, S. Ramji, D. Prabhakaran and K. S. Reddy. 2004. Relation of serial changes in childhood body-mass index to impaired glucose tolerance in young adulthood. *New England Journal of Medicine* 350(9): 865-875.

Bloomfield F. H., M. H. Oliver, P. Hawkins, M. Campbell, D. J. Phillips, P. D. Gluckman, J. R. Challis and J. E. Harding. 2003. A periconceptional nutritional origin for noninfectious preterm birth. *Science* 300(5619): 606.

Bloomfield F. H., M. H. Oliver, P. Hawkins, A. C. Holloway, M. Campbell, P. D. Gluckman, J. E. Harding and J. R. Challis. 2004. Periconceptional undernutrition in sheep accelerates maturation of the fetal hypothalamic-pituitary-adrenal axis in late gestation. *Endocrinology* 145(9): 4278-4285.

Bodnar L. M., R. B. Ness, G. F. Harger and J. M. Roberts. 2005. Inflammation and triglycerides partially mediate the effect of prepregnancy body mass index on the risk of preeclampsia. *American Journal of Epidemiology* 162(12): 1198-1206.

Brandt I., E. J. Sticker and M. J. Lentze. 2003. Catch-up growth of head circumference of very low birth weight, small for gestational age preterm infants and mental development to adulthood. *Journal of Pediatrics* 142(5): 463-468.

Calame A., S. Ducret, L. Jaunin and B. Plancherel. 1983. High risk appropriate for gestational age (AGA) and small for gestational age (SGA) preterm infants. Neurological handicap and developmental abnormalities at five years of age. *Helvetica Paediatrica Acta* 38(1): 39-50.

Carmichael S. L., G. M. Shaw, D. M. Schaffer, C. Laurent and S. Selvin. 2003. Dieting behaviors and risk of neural tube defects. *American Journal of Epidemiology* 158(12): 1127-1131.

Casanueva E., C. Ripoll, C. Meza-Camacho, B. Coutino, J. Ramirez-Peredo and A. Parra. 2005. Possible interplay between vitamin C deficiency and prolactin in pregnant women with premature rupture

of membranes: facts and hypothesis. *Medical Hypotheses* 64(2): 241-247.

Casey P. H., L. Whiteside-Mansell, K. Barrett, R. H. Bradley and R. Gargus. 2006. Impact of prenatal and/or postnatal growth problems in low birth weight preterm infants on school-age outcomes: an 8-year longitudinal evaluation. *Pediatrics* 118(3): 1078-1086.

Catalano P. M., J. P. Kirwan, S. Haugel-de Mouzon and J. King. 2003. Gestational diabetes and insulin resistance: role in short- and long-term implications for mother and fetus. *Journal of Nutrition* 133(5 Suppl 2): 1674S-1683S.

Catalano P. M. and H. M. Ehrenberg. 2006. The short- and long-term implications of maternal obesity on the mother and her offspring. *British Journal of Obstetrics and Gynaecology* 113(10): 1126-1133.

Catalano P. M., M. Hoegh, J. Minium, L. Huston-Presley, S. Bernard, S. Kalhan and S. Hauguel-De Mouzon. 2006. Adiponectin in human pregnancy: implications for regulation of glucose and lipid metabolism. *Diabetologia* 49(7): 1677-1685.

Cedergren M. 2006. Effects of gestational weight gain and body mass index on obstetric outcome in Sweden. *International Journal of Gynaecology and Obstetrics* 93(3): 269-274.

Chen A., S. A. Feresu, C. Fernandez and W. J. Rogan. 2009. Maternal obesity and the risk of infant death in the United States. *Epidemiology* 20(1): 74-81.

Churchill J. A., H. W. Berendes and J. Nemore. 1969. Neuropsychological deficits in children of diabetic mothers. A report from the Collaborative Sdy of Cerebral Palsy. *American Journal of Obstetrics and Gynecology* 105(2): 257-268.

Cole T. J., M. C. Bellizzi, K. M. Flegal and W. H. Dietz. 2000. Establishing a standard definition for child overweight and obesity worldwide: international survey. *British Medical Journal* 320(7244): 1240-1243.

Crowther C. A., J. E. Hiller, J. R. Moss, A. J. McPhee, W. S. Jeffries and J. S. Robinson. 2005. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *New England Journal of Medicine* 352(24): 2477-2486.

Diaz J. and E. M. Taylor. 1998. Abnormally high nourishment during sensitive periods results in body weight changes across generations. *Obesity Research* 6(5): 368-374.

Dietz P. M., W. M. Callaghan, M. E. Cogswell, B. Morrow, C. Ferre and L. A. Schieve. 2006. Combined effects of prepregnancy body mass index and weight gain during pregnancy on the risk of preterm delivery. *Epidemiology* 17(2): 170-177.

Dombkowski K. J., S. W. Leung and J. G. Gurney. 2008. Prematurity as a predictor of childhood asthma among low-income children. *Annals of Epidemiology* 18(4): 290-297.

Dorner G., A. Plagemann, J. Ruckert, F. Gotz, W. Rohde, F. Stahl, U. Kurschner, J. Gottschalk, A. Mohnike and E. Steindel. 1988. Teratogenetic maternofoetal transmission and prevention of diabetes susceptibility. *Experimental and Clinical Endocrinology* 91(3): 247-258.

Elmes M. J., D. S. Gardner and S. C. Langley-Evans. 2007. Fetal exposure to a maternal low-protein diet is associated with altered left ventricular pressure response to ischaemia-reperfusion injury. *British Journal of Nutrition* 98(1): 93-100.

Escalona S. K. 1982. Babies at double hazard: early development of infants at biologic and social risk. *Pediatrics* 70(5): 670-676.

Feldman R. and A. I. Eidelman. 2006. Neonatal state organization, neuromaturation, mother-infant interaction, and cognitive development in small-for-gestational-age premature infants. *Pediatrics* 118(3): e869-878.

Fisch R. O., M. K. Bilek and R. Ulstrom. 1975. Obesity and leanness at birth and their relationship to body habitus in later childhood. *Pediatrics* 56(4): 521-528.

Freinkel N., D. L. Cockroft, N. J. Lewis, L. Gorman, S. Akazawa, L. S. Phillips and G. E. Shambaugh, 3rd. 1986. The 1986 McCollum award lecture. Fuel-mediated teratogenesis during early organogenesis: the effects of increased concentrations of glucose, ketones, or somatomedin inhibitor during rat embryo culture. *American Journal of Clinical Nutrition* 44(6): 986-995.

Gale C. R., M. K. Javaid, S. M. Robinson, C. M. Law, K. M. Godfrey and C. Cooper. 2007. Maternal size in pregnancy and body composition in children. *Journal of Clinical Endocrinology and*

Metabolism 92(10): 3904-3911.

Geelhoed J. J., V. A. N. O.-G. L, B. O. Verburg, E. A. Steegers, A. Hofman, W. Helbing, J. C. Witteman and V. W. Jaddoe. 2008. Maternal anthropometrics in pregnancy are associated with left ventricular mass in infancy. The generation R study. *Pediatric Research* 63(1): 62-66.

Geva R., R. Eshel, Y. Leitner, A. F. Valevski and S. Harel. 2006. Neuropsychological outcome of children with intrauterine growth restriction: a 9-year prospective study. *Pediatrics* 118(1): 91-100.

Gillman M. W. 2005. Developmental origins of health and disease. *New England Journal of Medicine* 353(17): 1848-1850.

Gillman M. W. 2008. The first months of life: a critical period for development of obesity. *American Journal of Clinical Nutrition* 87(6): 1587-1589.

Gluckman P. D. and M. A. Hanson. 2006. Changing times: the evolution of puberty. *Molecular and Cellular Endocrinology* 254-255: 26-31.

Gluckman P. D. and M. A. Hanson. 2006. Evolution, development and timing of puberty. *Trends Endocrinol Metab* 17(1): 7-12.

Goldenberg R. L., M. B. DuBard, S. P. Cliver, K. G. Nelson, K. Blankson, S. L. Ramey and A. Herman. 1996. Pregnancy outcome and intelligence at age five years. *American Journal of Obstetrics and Gynecology* 175(6): 1511-1515.

Goldenberg R. L., H. J. Hoffman and S. P. Cliver. 1998. Neurodevelopmental outcome of small-for-gestational-age infants. *European Journal of Clinical Nutrition* 52 Suppl 1: S54-58.

Grantham-McGregor S. 1995. A review of studies of the effect of severe malnutrition on mental development. *Journal of Nutrition* 125(8 Suppl): 2233S-2238S.

Greaves M. 2003. Pre-natal origins of childhood leukemia. *Reviews in Clinical and Experimental Hematology* 7(3): 233-245.

Hack M. 1998. Effects of intrauterine growth retardation on mental performance and behavior, outcomes during adolescence and adulthood. *European Journal of Clinical Nutrition* 52 Suppl 1: S65-70; discussion S70-61.

Hanson M. A. and P. D. Gluckman. 2008. Developmental origins of health and disease: new insights. *Basic & Clinical Pharmacology & Toxicology* 102(2): 90-93.

Hille E. T., N. Weisglas-Kuperus, J. B. van Goudoever, G. W. Jacobusse, M. H. Ens-Dokkum, L. de Groot, J. M. Wit, W. B. Geven, J. H. Kok, M. J. de Kleine, L. A. Kollee, A. L. Mulder, H. L. van Straaten, L. S. de Vries, M. M. van Weissenbruch and S. P. Verloove-Vanhorick. 2007. Functional outcomes and participation in young adulthood for very preterm and very low birth weight infants: the Dutch Project on Preterm and Small for Gestational Age Infants at 19 years of age. *Pediatrics* 120(3): e587-595.

Hillier T. A., K. L. Pedula, M. M. Schmidt, J. A. Mullen, M. A. Charles and D. J. Pettitt. 2007. Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia. *Diabetes Care* 30(9): 2287-2292.

Hjalgrim L. L., T. Westergaard, K. Rostgaard, K. Schmiegelow, M. Melbye, H. Hjalgrim and E. A. Engels. 2003. Birth weight as a risk factor for childhood leukemia: a meta-analysis of 18 epidemiologic studies. *American Journal of Epidemiology* 158(8): 724-735.

Hofman P. L., F. Regan, W. E. Jackson, C. Jefferies, D. B. Knight, E. M. Robinson and W. S. Cutfield. 2004. Premature birth and later insulin resistance. *New England Journal of Medicine* 351(21): 2179-2186.

Hollo O., P. Rautava, T. Korhonen, H. Helenius, P. Kero and M. Sillanpaa. 2002. Academic achievement of small-for-gestational-age children at age 10 years. *Archives of Pediatrics and Adolescent Medicine* 156(2): 179-187.

Holwerda-Kuipers J. 1987. The cognitive development of low-birthweight children. *Journal of Child Psychology and Psychiatry and Allied Disciplines* 28(2): 321-328.

Hovi P., S. Andersson, J. G. Eriksson, A. L. Jarvenpaa, S. Strang-Karlsson, O. Makitie and E. Kajantie. 2007. Glucose regulation in young adults with very low birth weight. *New England Journal of*

Medicine 356(20): 2053-2063.

Hutton J. L., P. O. Pharoah, R. W. Cooke and R. C. Stevenson. 1997. Differential effects of preterm birth and small gestational age on cognitive and motor development. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 76(2): F75-81.

Hwang H. S., J. Y. Kwon, M. A. Kim, Y. W. Park and Y. H. Kim. 2007. Maternal serum highly sensitive C-reactive protein in normal pregnancy and pre-eclampsia. *International Journal of Gynaecology and Obstetrics* 98(2): 105-109.

Indredavik M. S., T. Vik, S. Heyerdahl, S. Kulseng, P. Fayers and A. M. Brubakk. 2004. Psychiatric symptoms and disorders in adolescents with low birth weight. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 89(5): F445-450.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

IOM. 2007. *Preterm Birth: Causes, Consequences, and Prevention*. Washington, DC: The National Acadmies Press.

Jaquiery A. L., M. H. Oliver, F. H. Bloomfield, K. L. Connor, J. R. Challis and J. E. Harding. 2006. Fetal exposure to excess glucocorticoid is unlikely to explain the effects of periconceptional undernutrition in sheep. *Journal of Physiology* 572(Pt 1): 109-118.

Kiel D. W., E. A. Dodson, R. Artal, T. K. Boehmer and T. L. Leet. 2007. Gestational weight gain and pregnancy outcomes in obese women: how much is enough? *Obstetrics and Gynecology* 110(4): 752-758.

Kilbride H. W., K. Thorstad and D. K. Daily. 2004. Preschool outcome of less than 801-gram preterm infants compared with full-term siblings. *Pediatrics* 113(4): 742-747.

King J. C. 2006. Maternal obesity, metabolism, and pregnancy outcomes. *Annual Review of Nutrition* 26: 271-291.

Kinnunen T. I., R. Luoto, M. Gissler, E. Hemminki and L. Hilakivi-Clarke. 2004. Pregnancy weight gain and breast cancer risk. *BMC Women's Health* 4(1): 7.

Kono Y., J. Mishina, T. Takamura, H. Hara, I. Sakuma, S. Kusuda and H. Nishida. 2007. Impact of being small-for-gestational age on survival and long-term outcome of extremely premature infants born at 23-27 weeks' gestation. *Journal of Perinatal Medicine* 35(5): 447-454.

Kramer M. S. and R. Kakuma. 2003. Energy and protein intake in pregnancy. *Cochrane Database Syst Rev*(4): CD000032.

Kuh D. and Y. Ben-Shlomo. 2004. *A life course approach to chronic disease epidemiology: tracing the origins of ill-health from early to adult life*. London: Oxford University Press.

Kulseng S., A. Jennekens-Schinkel, P. Naess, P. Romundstad, M. Indredavik, T. Vik and A. M. Brubakk. 2006. Very-low-birthweight and term small-for-gestational-age adolescents: attention revisited. *Acta Paediatrica* 95(2): 224-230.

Kumarasamy V., M. D. Mitchell, F. H. Bloomfield, M. H. Oliver, M. E. Campbell, J. R. Challis and J. E. Harding. 2005. Effects of periconceptional undernutrition on the initiation of parturition in sheep. *American Journal of Physiology Regulatory Integrative and Comparative Physiology* 288(1): R67-72.

Kwong W. Y., A. E. Wild, P. Roberts, A. C. Willis and T. P. Fleming. 2000. Maternal undernutrition during the preimplantation period of rat development causes blastocyst abnormalities and programming of postnatal hypertension. *Development* 127(19): 4195-4202.

Lagiou P., A. Lagiou, E. Samoli, C. C. Hsieh, H. O. Adami and D. Trichopoulos. 2006. Diet during pregnancy and levels of maternal pregnancy hormones in relation to the risk of breast cancer in the offspring. *European Journal of Cancer Prevention* 15(1): 20-26.

Leonard H., N. Nassar, J. Bourke, E. Blair, S. Mulroy, N. de Klerk and C. Bower. 2008. Relation between intrauterine growth and subsequent intellectual disability in a ten-year population cohort of children in Western Australia. *American Journal of Epidemiology* 167(1): 103-111.

Li C., M. I. Goran, H. Kaur, N. Nollen and J. S. Ahluwalia. 2007. Developmental trajectories of overweight during childhood: role of early life factors. *Obesity (Silver Spring)* 15(3): 760-771.

Litt R., A. Joseph and R. Gale. 1995. Six year neurodevelopmental follow-up of very low birthweight children. *Israel Journal of Medical Sciences* 31(5): 303-308.

Litt J., H. G. Taylor, N. Klein and M. Hack. 2005. Learning disabilities in children with very low birthweight: prevalence, neuropsychological correlates, and educational interventions. *Journal of Learning Disabilities* 38(2): 130-141.

Lof M., L. Hilakivi-Clarke, S. Sandin and E. Weiderpass. 2008. Effects of pre-pregnancy physical activity and maternal BMI on gestational weight gain and birth weight. *Acta Obstetricia et Gynecologica Scandinavica* 87(5): 524-530.

Luo Z. C., W. D. Fraser, P. Julien, C. L. Deal, F. Audibert, G. N. Smith, X. Xiong and M. Walker. 2006. Tracing the origins of "fetal origins" of adult diseases: programming by oxidative stress? *Medical Hypotheses* 66(1): 38-44.

Maffeis C., R. Micciolo, A. Must, M. Zaffanello and L. Pinelli. 1994. Parental and perinatal factors associated with childhood obesity in north-east Italy. *International Journal of Obesity and Related Metabolic Disorders* 18(5): 301-305.

McCarton C. M., I. F. Wallace, M. Divon and H. G. Vaughan, Jr. 1996. Cognitive and neurologic development of the premature, small for gestational age infant through age 6: comparison by birth weight and gestational age. *Pediatrics* 98(6 Pt 1): 1167-1178.

McLaughlin C. C., M. S. Baptiste, M. J. Schymura, P. C. Nasca and M. S. Zdeb. 2006. Birth weight, maternal weight and childhood leukaemia. *British Journal of Cancer* 94(11): 1738-1744.

McMillen I. C. and J. S. Robinson. 2005. Developmental origins of the metabolic syndrome: prediction, plasticity, and programming. *Physiological Reviews* 85(2): 571-633.

McMullen S. and S. C. Langley-Evans. 2005. Maternal low-protein diet in rat pregnancy programs blood pressure through sex-specific mechanisms. *American Journal of Physiology Regulatory Integrative and Comparative Physiology* 288(1): R85-90.

Michels K. B., D. Trichopoulos, J. M. Robins, B. A. Rosner, J. E. Manson, D. J. Hunter, G. A. Colditz, S. E. Hankinson, F. E. Speizer and W. C. Willett. 1996. Birthweight as a risk factor for breast cancer. *Lancet* 348(9041): 1542-1546.

Millis R. M. and G. U. Offiah. 2007. Dietary protein deficiency in pregnant mice and offspring. *Life Sciences* 80(13): 1184-1188.

Monteiro P. O. and C. G. Victora. 2005. Rapid growth in infancy and childhood and obesity in later life-- a systematic review. *Obesity Reviews* 6(2): 143-154.

Moreira P., C. Padez, I. Mourao-Carvalhal and V. Rosado. 2007. Maternal weight gain during pregnancy and overweight in Portuguese children. *Int J Obes (Lond)* 31(4): 608-614.

Naeye R. L. 1979. Weight gain and the outcome of pregnancy. *American Journal of Obstetrics and Gynecology* 135(1): 3-9.

Naeye R. L. and R. A. Chez. 1981. Effects of maternal acetonuria and low pregnancy weight gain on children's psychomotor development. *American Journal of Obstetrics and Gynecology* 139(2): 189-193.

NCHS (National Center for Health Statistics). 1986. *Maternal weight gain and the outcome of pregnancy, United States, 1980. Vital Health and Statistics. Series 21, No. 44. DHHS Pub. No. (PHS) 86-1922. Public Health Service*. Washington, DC: Government Printing Office.

Nelson K. G., R. L. Goldenberg, H. J. Hoffman and S. P. Cliver. 1997. Growth and development during the first year in a cohort of low income term-born American children. *Acta Obstetricia et Gynecologica Scandinavica. Supplement* 165: 87-92.

Nixon S. A., M. D. Avery and K. Savik. 1998. Outcomes of macrosomic infants in a nurse-midwifery service. *Journal of Nurse-Midwifery* 43(4): 280-286.

Nohr E. A., B. H. Bech, M. Vaeth, K. M. Rasmussen, T. B. Henriksen and J. Olsen. 2007. Obesity, gestational weight gain and preterm birth: a study within the Danish National Birth Cohort. *Paediatric and Perinatal Epidemiology* 21(1): 5-14.

Nohr E. A., M. Vaeth, J. L. Baker, T. Sorensen, J. Olsen and K. M. Rasmussen. 2008. Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of

pregnancy. *American Journal of Clinical Nutrition* 87(6): 1750-1759.

O'Keeffe M. J., M. O'Callaghan, G. M. Williams, J. M. Najman and W. Bor. 2003. Learning, cognitive, and attentional problems in adolescents born small for gestational age. *Pediatrics* 112(2): 301-307.

Oken E., E. M. Taveras, K. P. Kleinman, J. W. Rich-Edwards and M. W. Gillman. 2007. Gestational weight gain and child adiposity at age 3 years. *American Journal of Obstetrics and Gynecology* 196(4): 322 e321-328.

Oken E., S. L. Rifas-Shiman, A. E. Field, A. L. Frazier and M. W. Gillman. 2008. Maternal gestational weight gain and offspring weight in adolescence. *Obstetrics and Gynecology* 112(5): 999-1006.

Oladapo O. T., D. A. Adekanle and B. O. Durojaiye. 2007. Maternal risk factors associated with fetal death during antenatal care in low-resource tertiary hospitals. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 47(5): 383-388.

Oliveti J. F., C. M. Kercsmar and S. Redline. 1996. Pre- and perinatal risk factors for asthma in inner city African-American children. *American Journal of Epidemiology* 143(6): 570-577.

Ong K. K., M. L. Ahmed, P. M. Emmett, M. A. Preece and D. B. Dunger. 2000. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. *British Medical Journal* 320(7240): 967-971.

Ong K. K. and R. J. Loos. 2006. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. *Acta Paediatrica* 95(8): 904-908.

Otani L., N. Shirasaka, H. Yoshizumi and T. Murakami. 2004. The effects of maternal mild protein restriction on stroke incidence and blood pressure in stroke-prone spontaneously hypertensive rats (SHRSP). *Bioscience Biotechnology and Biochemistry* 68(3): 488-494.

Paavonen E. J., S. Strang-Karlsson, K. Raikkonen, K. Heinonen, A. K. Pesonen, P. Hovi, S. Andersson, A. L. Jarvenpaa, J. G. Eriksson and E. Kajantie. 2007. Very low birth weight increases risk for sleep-disordered breathing in young adulthood: the Helsinki Study of Very Low Birth Weight Adults. *Pediatrics* 120(4): 778-784.

Paz I., R. Gale, A. Laor, Y. L. Danon, D. K. Stevenson and D. S. Seidman. 1995. The cognitive outcome of full-term small for gestational age infants at late adolescence. *Obstetrics and Gynecology* 85(3): 452-456.

Paz I., A. Laor, R. Gale, S. Harlap, D. K. Stevenson and D. S. Seidman. 2001. Term infants with fetal growth restriction are not at increased risk for low intelligence scores at age 17 years. *Journal of Pediatrics* 138(1): 87-91.

Peng Y., B. Huang, F. Biro, L. Feng, Z. Guo and G. Slap. 2005. Outcome of low birthweight in China: a 16-year longitudinal study. *Acta Paediatrica* 94(7): 843-849.

Persson B. and J. Gentz. 1984. Follow-up of children of insulin-dependent and gestational diabetic mothers. Neuropsychological outcome. *Acta Paediatrica Scandinavica* 73(3): 349-358.

Pirc L. K., J. A. Owens, C. A. Crowther, K. Willson, M. J. De Blasio and J. S. Robinson. 2007. Mild gestational diabetes in pregnancy and the adipoinsular axis in babies born to mothers in the ACHOIS randomised controlled trial. *BMC Pediatrics* 7: 18.

Plagemann A., T. Harder, R. Lindner, K. Melchior, A. Rake, F. Rittel, W. Rohde and G. Dorner. 1998. Alterations of hypothalamic catecholamines in the newborn offspring of gestational diabetic mother rats. *Brain Research. Developmental Brain Research* 109(2): 201-209.

Pryor J., P. A. Silva and M. Brooke. 1995. Growth, development and behaviour in adolescents born small-for-gestational-age. *Journal of Paediatrics and Child Health* 31(5): 403-407.

Reece E. A., C. Homko and A. Wiznitzer. 1994. Metabolic changes in diabetic and nondiabetic subjects during pregnancy. *Obstetrical and Gynecological Survey* 49(1): 64-71.

Rizzo T., B. E. Metzger, W. J. Burns and K. Burns. 1991. Correlations between antepartum maternal metabolism and child intelligence. *New England Journal of Medicine* 325(13): 911-916.

Rodriguez A., J. Miettunen, T. B. Henriksen, J. Olsen, C. Obel, A. Taanila, H. Ebeling, K. M. Linnet, I. Moilanen and M. R. Jarvelin. 2008. Maternal adiposity prior to pregnancy is associated with ADHD symptoms in offspring: evidence from three prospective pregnancy cohorts. *International*

Journal of Obesity (London) 32(3): 550-557.

Rudra C. B., I. O. Frederick and M. A. Williams. 2008. Pre-pregnancy body mass index and weight gain during pregnancy in relation to preterm delivery subtypes. *Acta Obstetricia et Gynecologica Scandinavica* 87(5): 510-517.

Rydhstrom H. and B. Walles. 1996. Lack of correlation between maternal body weight or weight gain and stillbirth in twin pregnancy. *Gynecologic and Obstetric Investigation* 42(1): 8-12.

Salihu H. M., A. P. Alio, R. E. Wilson, P. P. Sharma, R. S. Kirby and G. R. Alexander. 2008. Obesity and extreme obesity: new insights into the black-white disparity in neonatal mortality. *Obstetrics and Gynecology* 111(6): 1410-1416.

Samuelsson A. M., P. A. Matthews, M. Argenton, M. R. Christie, J. M. McConnell, E. H. Jansen, A. H. Piersma, S. E. Ozanne, D. F. Twinn, C. Remacle, A. Rowlerson, L. Poston and P. D. Taylor. 2008. Diet-induced obesity in female mice leads to offspring hyperphagia, adiposity, hypertension, and insulin resistance: a novel murine model of developmental programming. *Hypertension* 51(2): 383-392.

Schieve L. A., M. E. Cogswell and K. S. Scanlon. 1999. Maternal weight gain and preterm delivery: differential effects by body mass index. *Epidemiology* 10(2): 141-147.

Segal P., J. K. Hamilton, M. Sermer, P. W. Connelly, A. J. Hanley, B. Zinman and R. Retnakaran. 2008. Maternal obesity and familial history of diabetes have opposing effects on infant birth weight in women with mild glucose intolerance in pregnancy. *Journal of Maternal-Fetal & Neonatal Medicine* 21(1): 73-79.

Sewell M. F., L. Huston-Presley, D. M. Super and P. Catalano. 2006. Increased neonatal fat mass, not lean body mass, is associated with maternal obesity. *American Journal of Obstetrics and Gynecology* 195(4): 1100-1103.

Shaw G. M., K. Todoroff, S. L. Carmichael, D. M. Schaffer and S. Selvin. 2001. Lowered weight gain during pregnancy and risk of neural tube defects among offspring. *International Journal of Epidemiology* 30(1): 60-65.

Siega-Riz A. M., L. S. Adair and C. J. Hobel. 1996. Maternal underweight status and inadequate rate of weight gain during the third trimester of pregnancy increases the risk of preterm delivery. *Journal of Nutrition* 126(1): 146-153.

Silva P. A., R. McGee and S. Williams. 1984. A longitudinal study of the intelligence and behavior of preterm and small for gestational age children. *Journal of Developmental and Behavioral Pediatrics* 5(1): 1-5.

Silverman B. L., T. Rizzo, O. C. Green, N. H. Cho, R. J. Winter, E. S. Ogata, G. E. Richards and B. E. Metzger. 1991. Long-term prospective evaluation of offspring of diabetic mothers. *Diabetes* 40 Suppl 2: 121-125.

Simmons R. A. 2007. Developmental origins of diabetes: the role of epigenetic mechanisms. *Current Opinion in Endocrinology, Diabetes, and Obesity* 14(1): 13-16.

Sinclair K. D., R. G. Lea, W. D. Rees and L. E. Young. 2007. The developmental origins of health and disease: current theories and epigenetic mechanisms. *Society of Reproduction and Fertility Supplement* 64: 425-443.

Sommerfelt K., H. W. Andersson, K. Sonnander, G. Ahlsten, B. Ellertsen, T. Markestad, G. Jacobsen, H. J. Hoffman and L. Bakketeig. 2000. Cognitive development of term small for gestational age children at five years of age. *Archives of Disease in Childhood* 83(1): 25-30.

Sowan N. A. and M. L. Stember. 2000. Parental risk factors for infant obesity. *MCN; American Journal of Maternal Child Nursing* 25(5): 234-240; quiz 241.

Spector L. G., S. M. Davies, L. L. Robison, J. M. Hilden, M. Roesler and J. A. Ross. 2007. Birth characteristics, maternal reproductive history, and the risk of infant leukemia: a report from the Children's Oncology Group. *Cancer Epidemiology, Biomarkers and Prevention* 16(1): 128-134.

Spinillo A., E. Capuzzo, G. Piazzi, A. Ferrari, V. Morales and M. Di Mario. 1998. Risk for spontaneous preterm delivery by combined body mass index and gestational weight gain patterns. *Acta Obstetricia et Gynecologica Scandinavica* 77(1): 32-36.

Stehbens J. A., G. L. Baker and M. Kitchell. 1977. Outcome at ages 1, 3, and 5 years of children born to diabetic women. *American Journal of Obstetrics and Gynecology* 127(4): 408-413.

Stephansson O., P. W. Dickman, A. Johansson and S. Cnattingius. 2001. Maternal weight, pregnancy weight gain, and the risk of antepartum stillbirth. *American Journal of Obstetrics and Gynecology* 184(3): 463-469.

Stevens-Simon C. and E. R. McAnarney. 1992. Adolescent pregnancy. Gestational weight gain and maternal and infant outcomes. *American Journal of Diseases of Children* 146(11): 1359-1364.

Stotland N. E., A. B. Caughey, M. Lahiff and B. Abrams. 2006. Weight gain and spontaneous preterm birth: the role of race or ethnicity and previous preterm birth. *Obstetrics and Gynecology* 108(6): 1448-1455.

Stotland N. E., Y. W. Cheng, L. M. Hopkins and A. B. Caughey. 2006. Gestational weight gain and adverse neonatal outcome among term infants. *Obstetrics and Gynecology* 108(3 Pt 1): 635-643.

Strang-Karlsson S., K. Raikkonen, E. Kajantie, S. Andersson, P. Hovi, K. Heinonen, A. K. Pesonen, A. L. Jarvenpaa, J. G. Eriksson and E. J. Paavonen. 2008a. Sleep quality in young adults with very low birth weight--the Helsinki study of very low birth weight adults. *Journal of Pediatric Psychology* 33(4): 387-395.

Strang-Karlsson S., K. Raikkonen, A. K. Pesonen, E. Kajantie, E. J. Paavonen, J. Lahti, P. Hovi, K. Heinonen, A. L. Jarvenpaa, J. G. Eriksson and S. Andersson. 2008b. Very low birth weight and behavioral symptoms of attention deficit hyperactivity disorder in young adulthood: the Helsinki study of very-low-birth-weight adults. *American Journal of Psychiatry* 165(10): 1345-1353.

Strauss R. S. 2000. Adult functional outcome of those born small for gestational age: twenty-six-year follow-up of the 1970 British Birth Cohort. *Journal of the American Medical Association* 283(5): 625-632.

Sullivan M. C., K. Hawes, S. B. Winchester and R. J. Miller. 2008. Developmental origins theory from prematurity to adult disease. *Journal of Obstetric, Gynecologic, and Neonatal Nursing* 37(2): 158-164.

Susser M. 1991. Maternal weight gain, infant birth weight, and diet: causal sequences. *American Journal of Clinical Nutrition* 53(6): 1384-1396.

Taveras E. M., S. L. Rifas-Shiman, M. B. Belfort, K. P. Kleinman, E. Oken and M. W. Gillman. 2009. Weight status in the first 6 months of life and obesity at 3 years of age. *Pediatrics* 123(4): 1177-1183.

Tavris D. R. and J. A. Read. 1982. Effect of maternal weight gain on fetal, infant, and childhood death and on cognitive development. *Obstetrics and Gynecology* 60(6): 689-694.

Trichopoulos D. 1990. Hypothesis: does breast cancer originate in utero? *Lancet* 335(8695): 939-940.

Udal J. N., G. G. Harrison, Y. Vaucher, P. D. Walson and G. Morrow, 3rd. 1978. Interaction of maternal and neonatal obesity. *Pediatrics* 62(1): 17-21.

Van Assche F. A., L. Aerts and W. Gepts. 1979. Morphological changes in the endocrine pancreas in pregnant rats with experimental diabetes. *Journal of Endocrinology* 80(2): 175-179.

Vatten L. J., B. O. Maehle, T. I. Lund Nilsen, S. Tretli, C. C. Hsieh, D. Trichopoulos and S. O. Stuver. 2002. Birth weight as a predictor of breast cancer: a case-control study in Norway. *British Journal of Cancer* 86(1): 89-91.

Viggedal G., E. Lundalv, G. Carlsson and I. Kjellmer. 2004. Neuropsychological follow-up into young adulthood of term infants born small for gestational age. *Medical Science Monitor* 10(1): CR8-16.

Villamor E., P. Sparen and S. Cnattingius. 2008. Risk of oral clefts in relation to prepregnancy weight change and interpregnancy interval. *American Journal of Epidemiology* 167(11): 1305-1311.

Viswanathan M., A. M. Siega-Riz, M.-K. Moos, A. Deierlein, S. Mumford, J. Knaack, P. Thieda, L. J. Lux and K. N. Lohr. 2008. *Outcomes of Maternal Weight Gain, Evidence Report/Technology Assessment No. 168. (Prepared by RTI International-University of North Carolina Evidence-based Practice Center under contract No. 290-02-0016.) AHRQ Publication No. 08-E-09.* Rockville, MD: Agency for Healthcare Research and Quality.

Wataba K., T. Mizutani, K. Wasada, M. Morine, T. Sugiyama and N. Suehara. 2006. Impact of

prepregnant body mass index and maternal weight gain on the risk of pregnancy complications in Japanese women. *Acta Obstetricia et Gynecologica Scandinavica* 85(3): 269-276.

Watkins M. L., S. A. Rasmussen, M. A. Honein, L. D. Botto and C. A. Moore. 2003. Maternal obesity and risk for birth defects. *Pediatrics* 111(5 Part 2): 1152-1158.

Watt J. and K. T. Strongman. 1985. Mother-infant interactions at 2 and 3 months in preterm, small-for-gestational-age, and full-term infants; their relationship with cognitive development at 4 months. *Early Human Development* 11(3-4): 231-246.

Westwood M., M. S. Kramer, D. Munz, J. M. Lovett and G. V. Watters. 1983. Growth and development of full-term nonasphyxiated small-for-gestational-age newborns: follow-up through adolescence. *Pediatrics* 71(3): 376-382.

Whitaker R. C. 2004. Predicting preschooler obesity at birth: the role of maternal obesity in early pregnancy. *Pediatrics* 114(1): e29-36.

Wiles N. J., T. J. Peters, D. A. Leon and G. Lewis. 2005. Birth weight and psychological distress at age 45-51 years: results from the Aberdeen Children of the 1950s cohort study. *British Journal of Psychiatry* 187: 21-28.

Wiles N. J., T. J. Peters, J. Heron, D. Gunnell, A. Emond and G. Lewis. 2006. Fetal growth and childhood behavioral problems: results from the ALSPAC cohort. *American Journal of Epidemiology* 163(9): 829-837.

Williams D. 2003. Pregnancy: a stress test for life. *Current Opinion in Obstetrics and Gynecology* 15(6): 465-471.

Willwerth B. M., B. Schaub, K. G. Tantisira, D. R. Gold, L. J. Palmer, A. A. Litonjua, D. L. Perkins, C. Schroeter, F. K. Gibbons, M. W. Gillman, S. T. Weiss and P. W. Finn. 2006. Prenatal, perinatal, and heritable influences on cord blood immune responses. *Annals of Allergy, Asthma, and Immunology* 96(3): 445-453.

Wolff S., J. Legarth, K. Vangsgaard, S. Toubro and A. Astrup. 2008. A randomized trial of the effects of dietary counseling on gestational weight gain and glucose metabolism in obese pregnant women. *International Journal of Obesity (London)* 32(3): 495-501.

Wrotniak B. H., J. Shults, S. Butts and N. Stettler. 2008. Gestational weight gain and risk of overweight in the offspring at age 7 y in a multicenter, multiethnic cohort study. *American Journal of Clinical Nutrition* 87(6): 1818-1824.

7

Determining Optimal Weight Gain

INTRODUCTION

In this chapter, the approach used by the committee for arriving at its recommendations for revision of the current guidelines for weight gain during pregnancy is discussed. First, a brief discussion of the principles used by the committee to develop a strategy for making its recommendations is presented. The strategy is then described in some detail, along with the results of applying this approach. Finally, the committee's recommendations are detailed and discussed.

As was the case for the report, *Nutrition During Pregnancy* (IOM, 1990), the committee used a conceptual framework to organize the evidence for a causal relationship between gestational weight gain (GWG) and both short- and long-term outcomes. The frequency and severity of these outcomes were considered. In particular, although a possible trade-off between maternal and child health was recognized in the Institute of Medicine report (IOM, 1990) as being a consequence of changing the weight gain guidelines, evaluation of that trade-off was not possible with the data then available. The committee made evaluating this trade-off a central element of its process to develop new guidelines, while recognizing that although the available data have increased, they are still less than fully adequate for this purpose. In making its recommendations, the committee sought to recognize unintended consequences and to develop guidelines that are both feasible and potentially achievable. It is important to note that these guidelines are intended for use among women in the United States. They may be applicable to women in other developed countries, however, they are not intended for use in areas of the world where women are substantially shorter or thinner than American women or where adequate obstetric services are unavailable.

STRATEGIC APPROACH FOR DEVELOPING RECOMMENDATIONS

The committee identified a set of consequences for the short- or long-term health of the mother and the child that are potentially causally related to GWG. These consequences included those evaluated in a systematic review of outcomes of maternal weight gain prepared for the Agency for Healthcare Research and Quality (AHRQ) (Viswanathan et al., 2008) as well as others based on data from the literature outside the time window considered in that report. To develop estimates of both the risk of these outcomes and their frequency in the population, the committee used data available in the published literature and also commissioned additional analyses (see below).

The committee considered several of potential outcomes associated with GWG and compared their incidence, long-term sequelae, and baseline risk (additional information about these outcomes appears in Appendix G). Postpartum weight retention, cesarean delivery, gestational diabetes mellitus (GDM), and pregnancy-induced hypertension or preeclampsia emerged from this process as being the most important maternal health outcomes. The committee

removed preeclampsia from consideration because of the lack of sufficient evidence that GWG was a cause of preeclampsia and not just a reflection of the disease process in this condition. The committee also removed GDM from consideration because of the lack of sufficient evidence that GWG was a cause of this condition. Postpartum weight retention and, in particular, unscheduled primary cesarean delivery were retained for further consideration.

Measures of size at birth (e.g. small-for-gestational age [SGA] and large-for-gestational age [LGA]), preterm birth and childhood obesity emerged from this process as being the most important infant health outcomes. The committee recognized that both SGA and LGA, when defined as < 10th percentile and > 90th percentile of weight-for-gestational age, respectively, represent a mix of individuals who are appropriately or inappropriately small or large. In addition, the committee recognized that being SGA was likely to be associated with deleterious outcomes for the infant but not the mother, while being LGA was likely to be associated with consequences for both the infant and the mother (e.g., cesarean delivery). The committee addressed this mix of outcomes in the approach used to develop its recommendations (see below).

Previous Approaches for Developing Weight Gain Recommendations

Many approaches have been and are currently being used for making recommendations for how much weight women should gain during pregnancy. At one extreme is the advice from the National Center for Clinical Excellence in the United Kingdom that women should not be weighed at all during pregnancy "as it may produce unnecessary anxiety with no added benefit" with the exception being "pregnant women in whom nutrition is of concern" (National Collaborating Centre for Women's and Children's Health, 2008). In the United States, the 1970 report *Maternal Nutrition and the Course of Pregnancy* (NRC, 1970) recommended a single target, and average gain of 10.9 kg (24 pounds), with a range of 9.1-11.3 kg (20-25 pounds). This target was based on the amount of weight that healthy women gain when meeting the physiologic needs of pregnancy (e.g., the products of conception, expansion of plasma volume, red cell mass and maternal fat stores).

Still another approach has been used in Chile. Since 1987, maternal weight gain recommendations for the Chilean population have been based on a single target, but instead of an absolute amount of weight, a proportion (120 percent) of the woman's "standard weight" for her height is used (Rosso, 1985; Mardones and Rosso, 2005). This results in a recommendation for a higher gain in underweight women and a lower gain in heavier women, with an upper limit of 7 kg for women with prepregnant weights over 120 percent of the standard (Figure 7-1). The objective of this recommendation is to increase birth weight among underweight women, and it is considered successful in having done so (Mardones and Rosso, 2005). The IOM (1990) report also recommended higher gains for underweight women and lower gains (but at least 6.8 kg) for heavier women. The desired outcome was expressed as specific target ranges for each of 3 prepregnant body mass index (BMI) groups. The rationale for this approach was to achieve the birth weight (3-4 kg) associated with "a favorable pregnancy outcome" in all prepregnant BMI groups while avoiding the birth of infants with weight > 4 kg because of "the possible risks to the mother and infant of complicated labor and delivery" (IOM, 1990).

BASELINE
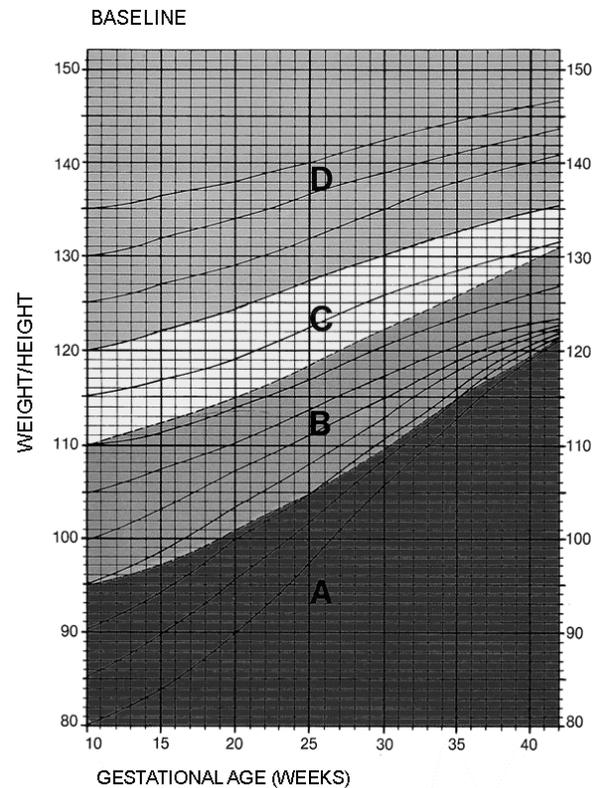
FIGURE 7-1 Graphic showing weight increase for pregnant women
NOTE: A = underweight; B = normal weight; C = overweight; D = obese
SOURCE: A weight gain chart for pregnant women designed in Chile, Mardones F. and P. Rosso. Copyright © 2005, Maternal and Child Nutrition. Reproduced with permission of Blackwell Publishing Ltd.

In constructing their recommendations, both the Chilean investigators (Mardones and Rosso, 2005) and the IOM (1990) committee explicitly recognized the trade-off between raising the birth weight of infants born to underweight women and increasing the risk of high birth weight in some infants as well as obesity and other undesirable outcomes in their mothers. In fact, the IOM (1990) committee recommended that a formal decision analysis be undertaken "in which probabilities and utilities (values) are assigned to each potential outcome" so as to assist in balancing the risks and benefits of any recommendation.

Since the publication of the IOM (1990) report, several groups of investigators have offered their own approaches for determining the optimal GWG. All of the studies of this type identified by the committee are discussed below. It is noteworthy that, with one exception (Nohr et al., 2008), maternal and infant outcomes beyond the immediate neonatal period were not included in these investigations. In each of these investigations, the researchers studied GWG as a categorical, not a continuous, variable, and each group defined the categories differently. Bracero and Byrne (1998) used data from 20,971 pregnant women and their singleton infants who were delivered at a single hospital in New York City (1987-1993). They identified the GWG at which the proportion of women who had infants with any one of 11 adverse perinatal outcomes was minimal. This list included outcomes not generally associated with GWG. Adverse maternal outcomes were not considered. In general, they found that this point was at a higher GWG than recommended in the IOM (1990) report. Therefore, they recommended gains of 16.3-18.1 kg

(36-40 pounds), 14.1-18.2 kg (31-40 pounds) and 11.8-13.6 kg (26-30 pounds) for underweight, normal weight and overweight or obese women categorized by the cutoff points in the IOM (1990) report, respectively.

Cedergren (2007) conducted a population-based cohort study (1994-2004) that included the data from 298,648 Swedish women obtained from the Swedish Medical Birth Registry. She calculated the risk of a variety of pregnancy outcomes by maternal prepregnant BMI category. She did this "to estimate weight gain limits that were associated with a significantly decreased risk of the most clinically dangerous situations for the mother and the infant." It is important to note that her selection of adverse outcomes "was not based primarily on possible correlations with weight gain or maternal BMI" (Cedergren, 2007). In addition to SGA and LGA, her analysis included six maternal and seven fetal outcomes that were unweighted for either their frequency or severity. Preeclampsia was included, but not GDM. With this approach, Cedergren (2007) found that the optimal GWG was lower than that recommended in the IOM (1990) report in all categories, especially for overweight or obese women.

In three studies that used population-based cohorts from Missouri, DeVader et al. (2007) studied 94,696 normal weight women (1999-2001), Langford et al. (2008) studied 34,143 overweight women (1990-2004), and Kiel et al. (2007) studied 120,251 obese women (1990-2001) who delivered full-term, singleton infants. These three groups of investigators calculated the risk of pregnancy outcomes that are routinely collected on all birth certificates according to reported GWG. DeVader et al. (2007) and Langford et al. (2008) assessed the risk of these outcomes according to whether the women had gained < 11.4 kg (25 pounds), 11.4-15.9 kg (25-35 pounds) or > 15.9 kg (> 35 pounds). Both groups found that the primary hazard of gaining less than the IOM (1990) report recommendation was delivering an SGA or low birth weight (< 2500 g) infant (Langford et al., 2008 only); gaining in excess of the recommendation was associated with an increased risk of several adverse outcomes, including preeclampsia, cesarean delivery and delivery of an LGA or macrosomic infant (Langford et al., 2008 only). After balancing these risks, DeVader and her colleagues (2007) concluded that the "ideal" gestational weight gain for their population of normal weight women was 11.4-15.5 kg (25-34 pounds). Langford and her colleagues (2008) found that overweight women "should gain within the current recommendations (15-25 lbs)" and that "there may be additional benefit of gaining below the recommendations, specifically in the 6-14 lbs range."

The number of obese women in their sample was large enough so that Kiel et al. (2007) were able to distinguish among obesity classes I, II, and III. They found that the risk of delivering an SGA infant continued to decrease with increasing degrees of maternal obesity and was minimal among women who gained < 6.8 kg (15 pounds) during pregnancy. In addition, although the pattern of increasing risk of preeclampsia, cesarean delivery and LGA birth with increasing GWG was the same across the obesity classes, Kiel et al. (2007) found that the point at which the risk of these outcomes considered as a group was minimal differed for each obesity class. This minimal risk corresponded to GWG of 4.5-15.5 kg (10-25 pounds), and 0-4.1 kg (0-9 pounds) for obesity class I and obesity classes II and III, respectively. In all of these studies of women from Missouri, the authors chose to consider outcomes that have been related to GWG (although the validity of using preeclampsia is open to question, see Chapter 5). As was the case for Cedergren's analysis (2007), these investigators did not consider the frequency or severity of these events and the outcomes of pregnancy were restricted to those at delivery.

In the most recent of the research reports in which authors have tried to identify optimal GWG, Nohr and colleagues (2008) used data from the Danish National Birth Cohort (1996-

2002). This study included 60,892 women with term pregnancies. Data on weight before pregnancy, weight gain during pregnancy and postpartum weight were obtained during telephone interviews of the mother and outcome data were obtained from birth and hospital discharge registries. Nohr et al. (2008) calculated the risks of a variety of maternal and neonatal outcomes associated with prepregnant BMI and GWG and their interaction. For those with a strong independent association with GWG and little possibility of reverse causality (unscheduled primary cesarean delivery, SGA, LGA, and postpartum weight retention ≥ 5 kg), they calculated the absolute risk of these outcomes for women in each of the four major categories of prepregnant BMI. Although the trade-off between reducing the risk of SGA and increasing the risk of cesarean delivery was evident in these data as it was in those from Sweden (Cedergren, 2007) and Missouri (Devader et al., 2007; Kiel et al., 2007; Langford et al., 2008), what is unique in this presentation is the inclusion of postpartum weight retention. Nohr et al. (2008) showed a dramatic increase in postpartum weight retention ≥ 5 kg with increasing GWG in all categories of prepregnant BMI. Nohr and her colleagues (2008) calculated the proportion of women who had changed from one BMI category to another at six months postpartum according to their GWG. In this analysis, only 0.4 percent of underweight women had become overweight at the highest GWG (≥ 20 kg) studied. Thus, they concluded that high GWG was "probably not disadvantageous for either underweight women or their infants" (Nohr et al., 2008). For normal weight, overweight and obese women, however, the tradeoff between SGA and these other outcomes particularly postpartum weight retention, occurred at lower GWG values: 16-19 kg, 10-15 kg and <10 kg, respectively (Nohr et al., 2008). As was the case for the other studies, Nohr et al. did not weight their outcomes by their frequency or severity; however, it is clear that the authors sought the point of minimum risk of SGA and postpartum weight retention ≥ 5 kg in their decision making.

Although the analytic approaches used by these research groups have many similarities, their conclusions about optimal weight gain varied widely (Table 7-1). This was particularly striking for underweight and normal weight women, but was also present for overweight women. The differences in conclusions may have resulted from the different mix of outcomes that were considered. The report of Nohr and coworkers (2008) was the only one to exclude preeclampsia and include postpartum weight retention. Cedergren (2007) included a number of outcomes of pregnancy that lack a clear association with GWG. None of these reports included the development of obesity during childhood as an outcome or provided information about the consequences of variation in GWG among women in the racial and ethnic subgroups common in the American population or among women who are young or short—groups that were explicitly considered in the IOM (1990) report. As noted above, none of these analyses was weighted (at least explicitly) by the severity or frequency of the adverse outcomes considered and the categories of GWG were constructed separately by each group of investigators.

TABLE 7-1 Summary of Research Published since the IOM (1990) Report in which Recommendations for Optimal Weight Gain During Pregnancy are Developed

Maternal Prepregnant BMI (kg/m²)	1990 IOM Guidelines (kg)	Proposed Optimal Weight Gain During Pregnancy (kg)					
		Bracero and Byrne, 1998	Cedergren, 2007	DeVader et al., 2007	Kiel et al., 2007	Langford et al., 2008	Nohr et al., 2008
IOM BMI Categories							
Underweight (< 19.8)	12.5-18	16.4-18.2	—	—	—	—	—
Normal weight (19.8-26.0)	11.5-16	14.1-18.2	—	11.4-15.5	—	—	—
Overweight (26.0-29.0)	7-11.5	11.8-13.6	—	—	—	6.8-10.9 (or 2.7-6.4)	—
Obese (> 29)	≥ 6	11.8-13.6	—	—	—	—	—
WHO BMI Categories							
Underweight (< 18.5)	—	—	4-10*	—	—	—	> 20
Normal weight (18.5-24.9)	—	—	2-10*	—	—	—	16-19
Overweight (25-29.9)	—	—	< 9	—	—	—	10-15
Obese (≥ 30)	—	—	< 6	—	—	—	< 10
Obese Class I (30-34.9)	—	—	—	—	4.5-11.4	—	
Obese Class II (35-39.9)	—	—	—	—	0-4.1	—	—
Obese Class III (≥ 40)	—	—	—	—	loss of 0-4.1	—	—

*BMI cutoff of 20 kg/m².

APPROACH USED BY THE COMMITTEE IN DEVELOPING ITS RECOMMENDATIONS

To address these conflicts and gaps within the available literature, the committee commissioned several additional analyses that informed its decision making (Table 7-2) (see Appendix G). Dr. Ellen Nohr provided two sets of analyses from the Danish National Birth Cohort. She expanded her published analyses (Nohr et al., 2008) to provide information on an additional lower and an additional higher category of GWG and replicated her published analyses for obese class I women separately from obese class II and III women. She conducted analogous new analyses of several important subgroups of the population of pregnant women, namely primiparous, short, and young women as well as smokers (information contributed to the committee in consultation with Nohr [see Appendix G, Part I]). Dr. Amy Herring analyzed the 1988 National Maternal and Infant Health Survey (NMIHS) to explore the association between GWG and outcomes important to the committee separately for white and black women. She also linked it to its 1991 follow-up to examine the association between GWG and postpartum weight retention in this sample. She was unable to examine the long-term weight status of infants born LGA because access to the data could not be obtained in a timely manner (information contributed to the committee in consultation with Herring [see Appendix G, Part II]). Dr. Cheryl Stein analyzed adverse outcomes associated with GWG stratified by racial/ethnic group in the subsample of births during 1995-2003 in New York City for which prepregnant BMI was available (information contributed to the committee in consultation with Stein [see Appendix G, Part III]). In addition, the committee commissioned a quantitative analysis of risk trade-offs between maternal and child health outcomes associated with GWG by Dr. James Hammitt (information contributed to the committee in consultation with Hammitt [see Appendix G, Part IV]).

The committee relied on both standard criteria for evaluating the quality of research studies (such as those provided by the American Academy of Pediatrics, 2004) as well as its expert judgment when evaluating the evidence. It used evidence from the published scientific literature as well as the analyses it commissioned. In the development of its recommendations, the committee evaluated the overall quality of the evidence as well as the balance between benefits and risks. The committee relied on the highest level of evidence (randomized controlled trials, and experimental studies in women and animal models). However, few such experimental studies were available in the literature relevant to the committee's task. In addition, the committee used data from the general population in those instances in which data on minority populations were unavailable.

TABLE 7-2 Research Commissioned by the Committee: Characteristics of the Datasets Used

Characteristic	Consultant		
	Nohr	**Herring**	**Stein**
Population Studied	• Danish National Birth Cohort • National sample • 1996-2002 • $n = 60,892$ • Singleton term births	• National Maternal and Infant Health Survey (NMIHS) • Nationally representative sample • 1988 linked to 1991 follow-up	• New York City births • 1995-2003 • Subset of 34,307 births (those with maternal height among 913,320 singleton births)
Subgroups Available	• Primiparous versus multiparous • < 20 years old versus older • Smokers versus non-smokers • Short versus non-short stature • Obesity classes II and III • GWG < 5 kg and = 25 kg	• White versus black	• White versus black
Outcomes Included	• SGA/LGA • Emergency cesarean delivery • PPWR (≥ 5 kg at 6 months)	• Primary cesarean delivery ($n = 5,433$) • Preterm birth ($n = 7,728$) • SGA and LGA ($n= 7,748$) • PPWR, 6-12 months ($n = 1,089$) • Breastfeeding initiation and duration • Infant mortality	• Spontaneous preterm birth • Primary cesarean delivery • SGA/LGA

NOTE: GWG = gestational weight gain; SGA = small-for-gestational age; LGA = large-for-gestational age; PPWR = postpartum weight retention.

CONSTRUCTION OF GUIDELINES FOR GESTATIONAL WEIGHT GAIN

Prepregnant BMI Category

After the publication of the IOM (1990) report, the World Health Organization (WHO) held a consultation that developed a categorization of BMI values for adults based on different cutoff

points (WHO, 1995). The WHO cutoff points were subsequently endorsed by the National Institutes of Health (NHLBI, 1998). These categories have been widely adopted in the United States and internationally and, if used in formulating recommendations for GWG, would provide opportunities for a consistent message to women and health care providers about weight status for all groups of adults, including women of childbearing age. For these reasons, the committee adopted the WHO BMI categories for its recommendations.

Evidence from the scientific literature is remarkably clear that prepregnant BMI is an independent predictor of many adverse outcomes of pregnancy (see Chapter 5). These data provide ample justification for the choice made in the IOM (1990) report to construct weight gain guidelines according to prepregnant BMI. That approach has been retained in the current document.

Special Populations

Women of Short Stature

The IOM (1990) report guidelines recommended that women of short stature (< 157 cm) should gain at the lower end of the range for their prepregnant BMI. The committee was unable to identify evidence sufficient to continue to support a modification of GWG guidelines for women of short stature (Vishwanathan et al., 2008). The limited data available to the committee indicated that women of short stature had an increased risk of emergency cesarean delivery but that this risk was not modified by GWG; they did not have an increased risk of having an SGA or LGA infant or of excessive postpartum weight retention compared to taller women (Appendix G). No information was available with which to evaluate whether a modification of guidelines might be necessary for very short (<150 cm) women.

Adolescents

Evidence to continue to support a modification of the GWG guidelines for adolescents (females < 20 years old) was also insufficient (Vishwanathan et al., 2008) (see Chapter 4). For adolescents < 18 years old, the WHO BMI cutoff points for overweight and obesity often do not correspond to the 85th and 95th percentiles, respectively, of the Centers for Disease Control (CDC) pediatric growth charts that used to assess growth in these girls [Available: http://www.cdc.gov/nchs/data/nhanes/growthcharts/set2/chart%2016.pdf (accessed December 3, 2008)]. The younger the girl, the more likely it is that she will reach the 85th or 95th percentile of the growth charts at a lower BMI value than the corresponding WHO cutoff points. Thus, if the adult cutoff points are used to determine the prepregnant BMI category of younger adolescents, some of them will be categorized as being in a lighter group. As a result, the GWG recommendation would be higher than would be the case if the pediatric growth charts were used to categorize them. The committee determined that this was a tolerable risk for two reasons. First, research has shown that young teens often need to gain more than adult women to have an infant of the same size (Scholl, 2008). Second, it would be difficult to implement a recommendation in obstetric practices to use pediatric growth charts to categorize the prepregnant BMI of these girls.

Women with Multiple Fetuses

The evidence base for women carrying multiple fetuses remains, as it was in 1990, limited. In that report (IOM, 1990), women carrying twins were encouraged to gain 16-20.5 kg (35-45 pounds) without respect to their prepregnancy BMI category. However, recent data suggest that the weight gain of women with twins who have good outcomes varies with prepregnancy BMI (see Chapter 3) as is clearly the case for women with singleton fetuses. Unfortunately, the committee was unable to conduct the same kind of analysis for women with twins as it did for women with singletons because the necessary data are unavailable. Therefore, the committee offers provisional guidelines, which are based specifically on the work of Luke and Hediger (Appendix C) and are corroborated by the work of others (Chapter 4). Unfortunately, these data sources do not provide sufficient information to develop provisional guidelines for underweight women. The provisional guidelines are: normal weight women should gain 17-25 kg (37-54 pounds), overweight women, 14-23 kg (31-50 pounds) and obese women, 11-19 kg (25-42 pounds) at term. These provisional guidelines reflect the interquartile (25th – 75th percentiles) range among women who delivered their twins, who weighted ≥ 2,500 g on average, at 37-42 weeks of gestation.

Racial/Ethnic Group

The descriptive observational data cited in Chapter 4 suggested that inadequate GWG was more common in some racial/ethnic groups. However, only Dr. Stein's analysis of data from New York City in 1995-2003 and Dr. Herring's analysis of the nationally representative data from the NMIHS in 1988-1991 provided insight into whether a woman's racial or ethnic group modified the relationship between GWG and the various outcomes of interest. The predominant finding from these analyses was that racial/ethnic group did not modify the association between GWG and these outcomes. As a result the committee concluded that, although confirmatory research is needed, its recommendations should be generally applicable to the various racial or ethnic groups that make up the U.S. population.

Obesity Classes II and III

Although a record-high number of American women of childbearing age have BMI values in obesity classes II and III, the evidence identified and reviewed by the committee was insufficient to develop more specific recommendations for GWG among these women.

Parity

It has long been known that primiparous women have smaller infants than multiparous women (as reviewed in Chapter 4) and they also gain more weight. The analyses by Nohr (information contributed to the committee in consultation with Nohr [see Appendix G, Part I]). show that primiparous women must gain more weight during pregnancy than multiparous women to have equally low risk of having an SGA birth, but primiparous women are similar to multiparous women in their likelihood of retaining ≥ 5 kg at 6 months postpartum in every category of prepregnant BMI. This means that the tradeoff between lowering the risk having an SGA infant and increasing the risk of retaining an excessive amount of weight postpartum occurs at a different GWG value for primiparous and multiparous women. This is a novel finding that warrants additional study.

Smokers

It has also long been known that smokers have smaller infants than non-smokers. Analyses prepared by Nohr (information contributed to the committee in consultation with Nohr [see Appendix G]) show that smokers who gain more weight, as expected, have larger infants, but they also retain more weight postpartum. For example, among normal weight multiparous women, smokers would have to gain at least 16-19 kg instead of 5-9 kg to have a 10 percent risk of having an SGA infant. If they were to gain in this higher range, their risk of retaining ≥ 5 kg at 6 months postpartum would becomes over 20 percent instead of being about 5 percent. Thus, the weight gain trade-off to prevent an SGA birth is particularly unfavorable for smokers, which is perhaps because (as reviewed in Chapter 4) at least some of the effect of smoking on birth weight is independent of GWG. As a result, additional GWG may fail to increase birth weight but, nonetheless, still increase postpartum weight retention. This unfavorable trade-off is best resolved by smoking cessation.

DEVELOPMENT OF RECOMMENDED WEIGHT-GAIN RANGES

Guidelines for Gestational Weight Gain

As was the case for the current guidelines for GWG, the committee chose to formulate the new guidelines with a range for each category of prepregnant BMI. This range reflects the imprecision of the estimates on which these recommendations are based, the reality that good outcomes are achieved with a range of weight gains and the many additional factors that may need to be considered when making a recommendation for an individual woman.

To develop these ranges (Table 7-3), the committee proceeded as follows. Based on the available published literature (Appendix E and F) as well as the reports of its consultants (Appendix G), the committee ascertained the GWG value or range of GWG values associated with lowest prevalence of the outcomes of greatest interest (namely, cesarean delivery, postpartum weight retention, preterm birth, small- or large-for gestational age birth and childhood obesity). When weighting the trade-off among these outcomes, the committee considered, within each category of prepregnant BMI (a) the incidence or prevalence of each of these outcomes, (b) whether the outcomes were permanent (e.g. neurocognitive deficits) or potentially modifiable (e.g. postpartum weight retention) and (c) the quality of the available data. The committee compared the resulting ranges with those developed in the quantitative risk analysis conducted by its consultant, Dr. Hammitt. Finally, the committee considered how its recommendations might be accepted and used by clinicians and women.The committee intends these guidelines be used in concert with good clinical judgment as well as a discussion between the woman and her prenatal care provider about diet and exercise. If a woman's GWG is not within the proposed guidelines, prenatal care providers should consider other relevant clinical evidence as well as both the adequacy and consistency of fetal growth and any available information on the nature of excess (e.g. fat or edema) or inadequate GWG before suggesting that the woman modify her pattern of weight gain. The safety of intentional weight loss during pregnancy among obese women has not been determined. Thus, priority should be given to addressing weight loss issues preconceptionally or between pregnancies, not during pregnancy.

In constructing these guidelines, the committee recognized that they fall within the category of personalized medicine. Use of these guidelines will require standardized assessment procedures to inform clinical judgment as well as support of ancillary services (e.g. counseling

on nutrition and physical activity) or other interventions that might be deemed necessary to achieve them. Thus, the committee recognizes that full implementation of these guidelines may entail additional medical expenses. The committee did not attempt to estimate the magnitude of these potential additional medical expenses.

TABLE 7-3 New Recommendations for Total and Rate of Weight Gain during Pregnancy, by Prepregnancy BMI

	Total Weight Gain		Rates of Weight Gain* 2nd and 3rd Trimester	
Prepregnancy BMI	**Range in kg**	**Range in lbs**	**Mean (range) in kg/week**	**Mean (range) in lbs/week**
Underweight (< 18.5 kg/m^2)	12.5–18	28–40	0.51 (0.44–0.58)	1 (1–1.3)
Normal weight (18.5–24.9 kg/m^2)	11.5–16	25–35	0.42 (0.35–0.50)	1 (0.8–1)
Overweight (25.0–29.9 kg/m^2)	7–11.5	15–25	0.28 (0.23–0.33)	0.6 (0.5–0.7)
Obese (≥ 30.0 kg/m^2)	5–9	11–20	0.22 (0.17–0.27)	0.5 (0.4–0.6)

*Calculations assume a 0.5–2 kg (1.1– 4.4 lbs) weight gain in the first trimester (based on Siega et al., 1994; Abrams et al., 1995; Carmichael et al., 1997)

Rate of Weight Gain

Pregnant women typically gain ~1-2 kg in the first trimester. According to the new recommended GWG values, normal weight women should gain ~0.4 kg per week in the second and third trimesters of pregnancy. Underweight women should gain slightly more (~0.5 kg per week) and overweight women slightly less (~0.3 kg per week) than this amount (Table 7-3). Obese women should gain about ~0.2 kg per week (Table 7-3). These guidelines were constructed based on the assumption that GWG is linear during the second and third trimesters of pregnancy.

The IOM (1990) report made a series of recommendations about how to implement its guidelines in the context of caring for an individual patient. As they remain appropriate, the committee endorses the key elements of these recommendations. These key elements are:

1. Before conception, use consistent and reliable procedures to measure and record the woman's weight and height without shoes in the medical record.
2. Determine the woman's prepregnancy BMI.
3. Measure the woman's height without shoes and weight in light clothing at the first prenatal visit carefully by procedures that have been rigorously standardized at the site of prenatal care and use consistent, reliable procedures to measure weight at each subsequent visit.
4. Estimate the woman's gestational age from the onset of her last menstruation or from an early ultrasound examination.
5. At the initial comprehensive prenatal examination, set a weight gain goal together with the pregnant woman that is based on her prepregnant BMI and other relevant considerations, and explain to her why weight gain is important.
6. Monitor the woman's prenatal course to identify any abnormal pattern of gain that may indicate a need to intervene, displaying the results graphically for the woman (see Chapter 8, Figures 8-1 through 8-4). When abnormal gain appears to be real, rather than a result of an error in measurement or recording, try to determine the cause and then develop and implement corrective actions jointly with the woman.

DISCUSSION OF THE NEW GUIDELINES

These new guidelines differ from those issued in 1990 in two important ways. First, they are based on a different set of cutoff points for prepregnant BMI. Compared to the new cutoff points used in the 1990 guidelines, using the WHO guidelines reduces the proportion of the population in the underweight and obese groups, as these groups are based on more extreme BMI values, and raises the proportion of the population in the normal weight and overweight groups, as these groups are based on wider ranges of BMI values.

Second, these new guidelines include a specific, relatively narrow range of recommend gain for obese women. This recommendation reflects the data available to the committee, the preponderance of which cover women in obesity class I (BMI 30.0-34.9 kg/m^2) rather than obesity classes II and III. As noted in Chapter 2, in the last two decades more American women of childbearing age have prepregnant BMI values in obesity classes II and III. Unfortunately, only two studies provide data on women in these obesity classes (Kiel et al. 2007; information contributed to the committee in consultation with Nohr [see Appendix G]) and few of the women

studied gained < 5 kg. It is possible, based on the data collected in these investigations, that weight gains < 5 kg may be associated with a more favorable trade-off among outcomes than higher gains. However, the committee's review showed insufficient evidence to recommend gains this low and thus it was concerned about the potential for doing harm that is associated with fetal growth restriction and ketonemia (see Chapters 3 and 6). Ketonemia can occur with the accelerated starvation that is characteristic of pregnancy and may be more frequent with low weight gains. The committee recognized that women in obesity classes II and III may, without intervention, gain little during pregnancy and manage their pattern of dietary intake so as to avoid ketonemia and other problems. However, there is no evidence to determine whether a guideline for very low weight gain during pregnancy among women in obesity classes II and III would be managed well enough by these women and their care providers to avoid ketonemia.

Although there is ample justification for continuing to structure the new guidelines according to maternal prepregnancy BMI, this approach is not without limitations. Maternal height, for example, has long been known to be a determinant of birth weight among women with a narrower range of prepregnancy weight (40-80 kg) than commonly observed today (Tanner and Thomson, 1970). In addition, height appears to be a stronger predictor of GWG than prepregnancy BMI (Straube et al., 2008). However, the research necessary to show that height or another attribute might be a superior alternative to prepregnancy BMI for constructing guidelines for subgroups of pregnant women has not been conducted.

The committee based its guidelines, in part, on the presumption that the extensive, consistent observational data that link GWG to fetal growth, as measured by SGA and LGA, as well as those that link GWG to postpartum weight retention are causal. The committee recognizes, however, that the simple model in which increased caloric intake increases maternal weight and maternal weight, in turn, increases fetal weight, is likely to be more complex—and may even be incorrect. The limited results from randomized trials among undernourished women provide indications of this pathway in some cases (Susser, 1991). The results from more recent but very small randomized trials designed to control excess weight gain (see Chapter 8) provide suggestive support for this pathway. Although there are possible non-causal explanations linking GWG to fetal growth, including diet composition, affecting both GWG and fetal growth independently, or shared genetic determinants of GWG and fetal growth, none of these alternatives has been proven valid. Therefore, the committee determined that it would be prudent to consider the evidence linking inadequate GWG, especially in underweight and normal weight women, with increased risk of SGA; and the evidence linking excessive GWG, especially in overweight and obese women, with increased risk of LGA and its consequences in developing these guidelines.

As additional experimental data are generated to confirm or refute a causal interpretation of the evidence linking GWG and fetal growth, this reasoning may need to be revised. In contrast, the likelihood that the link from increased caloric intake to increased GWG and, in turn, from increased GWG to increased postpartum weight retention is causal seems more certain. However, postpartum weight retention reflects not only GWG, but also maternal actions postpartum, including but not limited to changes in dietary intake and physical activity associated with new motherhood as well as breastfeeding behavior (Baker et al., 2008).

It is noteworthy that these guidelines are structured as the ranges associated with good outcomes for both mother and infant. For example, women who are more concerned with postpartum weight retention than with the birth of a small baby, can choose to gain at the lower instead of the higher end of the range for their prepregnancy BMI category.

As American women of childbearing age have become heavier, the trade-off between maternal and child health created by variation in GWG has become more difficult to reconcile than it was when prevention of SGA births was paramount and there was relatively low risk of excessive weight retention postpartum and childhood obesity with additional GWG. The effort made by the committee to project the short- and long-term consequences of GWG for both mothers and their children so as to reconcile the trade-offs between them is a unique feature of the process used to develop these new guidelines. For this purpose, the committee used data from the NMIHS (information contributed to the committee in consultation with Herring [see Appendix G, Part II]) to provide estimates for the probability infant mortality and data from the Danish National Birth Cohort (Nohr et al., 2008) to provide estimates for the probability of postpartum weight retention related to GWG within each category of prepregnant BMI. Dr. Hammitt linked the data on postpartum weight retention to estimates of morbidity and mortality associated with additional maternal weight. Similarly, data from the Growing Up Today Study (Oken et al., 2008) and supporting studies (see Chapter 6) were used to provide estimates of the risk of childhood obesity at ages 9-14 years related to additional GWG. The committee chose these three outcomes because they are quantitatively important and their consequences could be estimated with available data. Dr. Hammitt used the literature currently available to calculate quality adjustments for each outcome, which resulted in quality-adjusted life-years (QALY) for comparison across outcomes (information contributed to the committee in consultation with Hammitt [see Appendix G, Part IV]).

In broad terms, the results of this quantitative risk analysis by Dr. Hammitt provided support for the GWG guidelines that the committee developed from published and commissioned research. Although it was possible to develop this quantitative analysis of risk trade-offs, the data needed to support a more complete and persuasive analysis were unavailable. In particular, information is needed on associations between GWG and longer-term maternal outcomes, such as postpartum weight retention and later reproductive function and health as well as child health outcomes, such as fetal growth restriction, child neurocognitive outcomes and obesity. Such data would include not only the frequencies of outcomes but also the utilities associated with each to calculate appropriate quality adjustments.

Overall, these guidelines are remarkably similar to those included in the IOM (1990) report. The research that has appeared since their publication as well as the committee's commissioned analyses support the robustness of the prior recommendations. It remains true that, within a given prepregnancy BMI category, healthy women can deliver healthy infants at a relatively wide range of weight gain values. Unfortunately, an already large and increasing proportion of the population is gaining outside of the prior recommendations (see Chapter 2) and this is also likely to be case with these new guidelines. As a result, it is time to focus attention on helping women to adhere to these guidelines. If research on adherence is conducted with experimental designs of adequate statistical power, such studies could finally provide causal evidence of gaining within these new guidelines results in superior outcomes of pregnancy for both mother and infant.

FINDINGS AND RECOMMENDATIONS FROM THE COMMITTEE'S ANALYSES

Findings

The committee found that:

1. The WHO cutoff points have been widely adopted for categorizing BMI among non-pregnant adults and should be used for categorizing prepregnancy BMI as well; the committee also found that these categories are also acceptable to use for categorizing the prepregnancy BMI of adolescents.
2. Evidence from the scientific literature is remarkably clear that prepregnant BMI is an independent predictor of many adverse outcomes of pregnancy. As a result, women should enter pregnancy with a BMI in the normal weight category.
3. Although a record-high number of American women of childbearing age have BMI values in obesity classes II and III, available evidence is insufficient to develop more specific recommendations for GWG among these women.
4. There are only limited data available to link GWG to health outcomes of mothers and children that occur after the neonatal period.
5. There is insufficient evidence to continue to support a modification of GWG guidelines for African-American women, women of short stature or adolescents younger than 16 years of age.
6. There is insufficient data with which to establish how much more weight women carrying multiple fetuses should gain beyond that recommended for women carrying singleton fetuses.
7. The committee reaffirms the clinical recommendations in IOM (1990) for implementation of these guidelines.
8. There is insufficient evidence to reject the possibility that racial/ethnic group modifies the association between GWG and important maternal and child health outcomes.

Recommendation for Action

Action Recommendation 7-1: The committee recommends that federal agencies, private voluntary organizations, and medical and public health organizations adopt these new guidelines for GWG and publicize them to their members and also to women of childbearing age.

Recommendation for Research

Research Recommendation 7-1: To permit the development of improved recommendations for GWG in the future, the committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to (a) conduct studies to assess utilities (values) associated with short- and long-term health outcomes associated with GWG for both mother and child and (b) include these values in studies that employ decision analytic frameworks to estimate optimal GWG according to category of maternal prepregnancy BMI and other subgroups.

Additional Recommendation for Research

Additional Research Recommendation 7-1: The committee recommends that the National Institutes of Health and other relevant agencies should provide support to researchers to conduct studies among women carrying multiple fetuses that link GWG to relevant health outcomes among both mothers and their infants.

REFERENCES

Abrams B., S. Carmichael and S. Selvin. 1995. Factors associated with the pattern of maternal weight gain during pregnancy. *Obstetrics and Gynecology* 86(2): 170-176.

American Academy of Pediatrics. 2004. Classifying recommendations for clinical practice guidelines. *Pediatrics* 114(3): 874-877.

Baker J. L., M. Gamborg, B. L. Heitmann, L. Lissner, T. I. Sorensen and K. M. Rasmussen. 2008. Breastfeeding reduces postpartum weight retention. *American Journal of Clinical Nutrition* 88(6): 1543-1551.

Bracero L. A. and D. W. Byrne. 1998. Optimal maternal weight gain during singleton pregnancy. *Gynecologic and Obstetric Investigation* 46(1): 9-16.

Carmichael S., B. Abrams and S. Selvin. 1997. The pattern of maternal weight gain in women with good pregnancy outcomes. *American Journal of Public Health* 87(12): 1984-1988.

Cedergren M. I. 2007. Optimal gestational weight gain for body mass index categories. *Obstetrics and Gynecology* 110(4): 759-764.

DeVader S. R., H. L. Neeley, T. D. Myles and T. L. Leet. 2007. Evaluation of gestational weight gain guidelines for women with normal prepregnancy body mass index. *Obstetrics and Gynecology* 110(4): 745-751.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

Kiel D. W., E. A. Dodson, R. Artal, T. K. Boehmer and T. L. Leet. 2007. Gestational weight gain and pregnancy outcomes in obese women: how much is enough? *Obstetrics and Gynecology* 110(4): 752-758.

Langford A., C. Joshu, J. J. Chang, T. Myles and T. Leet. 2008. Does Gestational Weight Gain Affect the Risk of Adverse Maternal and Infant Outcomes in Overweight Women? *Maternal and Child Health Journal*.

Mardones F. and P. Rosso. 2005. A weight gain chart for pregnant women designed in Chile. *Maternal and Child Nutrition* 1(2): 77-90.

National Collaborating Centre for Women's and Children's Health. 2008. *Antenatal care: Routine care for the healthy pregnancy woman*. London: Royal College of Obstetricians and Gynaecologists.

NHLBI (National Heart, Lung, and Blood Institute). 1998. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. (National Institutes of Health Publication 98-4083). Washington, DC: National Institutes of Health.

Nohr E. A., M. Vaeth, J. L. Baker, T. Sorensen, J. Olsen and K. M. Rasmussen. 2008. Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy. *American Journal of Clinical Nutrition* 87(6): 1750-1759.

NRC (National Research Council). 1970. *Maternal Nutrition and the Course of Pregnancy*. Washington, DC: National Academy Press.

Oken E., S. L. Rifas-Shiman, A. E. Field, A. L. Frazier and M. W. Gillman. 2008. Maternal gestational weight gain and offspring weight in adolescence. *Obstetrics and Gynecology* 112(5): 999-1006.

Rosso P. 1985. A new chart to monitor weight gain during pregnancy. *American Journal of Clinical Nutrition* 41(3): 644-652.

Scholl T. O. 2008. *Biological Determinants of Gestational Weight Gain*. Presentation at the Workshop on Implications of Weight Gain for Pregnancy Outcomes: Issues and Evidence, March 10, 2008, Washington, DC.

Siega-Riz A. M., L. S. Adair and C. J. Hobel. 1994. Institute of Medicine maternal weight gain recommendations and pregnancy outcome in a predominantly Hispanic population. *Obstetrics and Gynecology* 84(4): 565-573.

Straube S., M. Voigt, V. Briese and K. T. Schneider. 2008. Weight gain in pregnancy according to maternal height and weight. *Journal of Perinatal Medicine* 36(5): 405-412.

Susser M. 1991. Maternal weight gain, infant birth weight, and diet: causal sequences. *American Journal*

of Clinical Nutrition 53(6): 1384-1396.

Tanner J. M. and A. M. Thomson. 1970. Standards for birthweight as gestation periods from 32 to 42 weeks, allowing for maternal height and weight. *Archives of Disease in Childhood* 45(242): 566-569.

Viswanathan M., A. M. Siega-Riz, M.-K. Moos, A. Deierlein, S. Mumford, J. Knaack, P. Thieda, L. J. Lux and K. N. Lohr. 2008. *Outcomes of Maternal Weight Gain, Evidence Report/Technology Assessment No. 168. (Prepared by RTI International-University of North Carolina Evidence-based Practice Center under contract No. 290-02-0016.) AHRQ Publication No. 08-E-09.* Rockville, MD: Agency for Healthcare Research and Quality.

WHO (World Health Organization). 1995. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organization Technical Report Series* 854: 1-452.

Website:
http://www.cdc.gov/nchs/data/nhanes/growthcharts/set2/chart%2016.pdf

8

Approaches to Achieving Recommended Gestational Weight Gain

To understand the challenges that may arise in implementing the proposed guidelines on gestational weight gain (GWG) presented in Chapter 7, the committee reviewed the present environment for childbearing (see Chapter 2 for details). The committee also reviewed the interventions that had been conducted to improve GWG in response to the Institute of Medicine (IOM, 1990) guidelines and considered the guidance that these interventions might provide for implementation of these revised guidelines. Although proposing a complete implementation and evaluation plan is beyond the scope of the committee's work, this chapter provides a framework from which such a plan can be developed.

Current Context for Childbearing and Gestational Weight Gain

Women who are having children today are substantially heavier than at any time in the past (see Chapter 2). Over half of their pregnancies are unwanted or mistimed (IOM, 1995). These facts highlight the difficulties that women face in achieving one of our primary recommendations, namely that they should conceive at a weight within the normal range of BMI values. It is beyond the committee's scope of work to consider how to achieve this objective. Nonetheless, it is important for women to do so and for the government as well as private voluntary organizations to assist them.

The same factors that have caused women of childbearing age to be heavier than in the past challenge them to meet the previous (IOM, 1990) as well and these new guidelines for GWG. Some of the trends that are of concern include an increase in consumption of foods with low nutrient density. This has special implications for pregnancy and lactation, which require modest increases in energy but greater increases in vitamin and mineral intake. In addition, national data (see Chapter 2) indicates that a high proportion of women of childbearing age fail to meet current guidelines for physical activity. Improvement in these statistics could contribute toward helping women enter pregnancy at a healthy weight as well as to meet the proposed guidelines for GWG.

These new guidelines should also be considered in the context of data on women's reported GWG. Compared to data assembled from the studies reviewed by the committee, in which information was available for relatively large samples of women, the mean gains of underweight women are within the new guidelines (Table 8-1). This is less often the case for normal weight women, where the mean gain in some samples is at or above the upper limit of the new guidelines. This indicates that a substantial proportion of normal weight women would exceed desired GWG ranges according to the new guidelines. The mean GWG values for overweight and obese women exceed the upper end of the new guidelines by several kilograms.

TABLE 8-1 Gestational Weight Gain (kg) by Prepregnant BMI Categories among Large Studies Compared to New Guidelines

Prepregnant BMI Category	New GWG Guidelines	Study				
		Sweden, National (1994-2002)[a]	Danish National Birth Cohort (1996-2002)[b]	Pregnancy Risk Assessment Monitoring System (2002-03)[c]	New York City Vital Statistics Birth Data (1995 to 2003)[d]	Pregnancy, Infection, and Nutrition Cohort Study (2001-2005)[e]
Underweight (< 18.5 kg/m^2)	12.5 - 18.0	13.5 ± 0.03 (SEM) ($n = 72,361$)	15.3 ± 5.1 (SD) ($n = 2,648$)	14.8 ± 0.27 (SEM) ($n = 1,628$)	15.1 ± 5.01 (SD) ($n = 1,632$)	15.4 ± 4.4 (SD) ($n = 176$)
Normal weight (18.5-24.9 kg/m^2)	11.5 - 16.0	13.8 ± 0.01 (SEM) ($n = 368,063$)	15.8 ± 5.2 (SD) ($n = 41,569$)	15.0 ± 0.10 (SEM) ($n = 11,513$)	15.1 ± 5.25 (SD) ($n = 19,892$)	16.6 ± 5.3 (SD) ($n = 652$)
Overweight (25.0-29.9 kg/m^2)	7.0 - 11.5	13.2 ± 0.02 (SEM) ($n = 153,769$)	14.7 ± 6.4 (SD) ($n = 11,861$)	13.9 ± 0.16 (SEM) ($n = 5,027$)	14.1 ± 6.07 (SD) ($n = 7,893$)	15.5 ± 6.2 (SD) ($n = 126$)
Obese (≥ 30 kg/m^2)	5.0 – 9.0	---	10.5 ± 8.3 (SD) ($n = 4,814$)	11.2 ± 0.20 (SEM) ($n = 4,588$)	11.9 ± 6.84 (SD) ($n = 4,890$)	12.0 ± 7.1 (SD) ($n = 277$)
Obese, class I (30-35 kg/m^2)	Not specified	11.1 ± 0.05 (SEM) ($n = 43,128$)	11.4 ± 7.5 (SD) ($n = 3,541$)	---	12.7 ± 6.53 (SD) ($n = 3,077$)	---
Obese, class II (35-40 kg/m^2)	Not specified	8.7 ± 0.11 (SEM) ($n = 14,713$)	7.7 ± 9.4 (SD) ($n = 1,273$)	---	11.1 ± 7.17 (SD) ($n = 1,166$)	---
Obese, class III (≥ 40 kg/m^2)	Not specified	---	---	---	9.5 ± 7.00 (SD) ($n = 647$)	---

[a]Cedergren, 2006 (BMI categories: Underweight = < 20 kg/m^2; Normal weight = 20-24.9 kg/m^2; Obese, Class II = ≥ 35 kg/m^2)

[b]Information contributed to the committee in consultation with Nohr [see Appendix G, Part I]); Obese Class II and III are combined.

[c]P. Dietz, CDC, personal communication January 2009 (states included: AL, AK, FL, ME, NY [excludes NYC], WA, OK, SC, WV)

[d]Information contributed to the committee in consultation with Stein [see Appendix G, Part III]).

[e]Deierlein et al., 2008 (BMI categories: Underweight = < 19.8 kg/m^2; Normal weight = 19.8-26.0 kg/m^2; Overweight = 26.0-29.0 kg/m^2; Obese = > 29.0 kg/m^2)

If this analysis is restricted to the most recent (2002-2003) multi-state data from PRAMS, the same conclusions are evident (Figure 8-1). These data provide a strong reason to assume that interventions will be needed to assist women, particularly those who are overweight or obese at the time of conception, in meeting the new GWG guidelines. Although the committee recognizes that developing graphical representations to assist caregivers and their clients in conveying the importance of appropriate weight gain during pregnancy is important, the type of expertise represented on the committee as well as the commitment of time and resources limited the extent to which it could develop such material into a format that could be readily disseminated.

These data provide a strong reason to assume that interventions will be needed to assist women, particularly those who are overweight or obese at the time of conception, in meeting the new GWG guidelines. The review of interventions that were conducted based on *Nutrition During Pregnancy* (IOM, 1990) (see below) provide a preview of the challenges that will be faced in implementing the new guidelines in this report.

Data from observational studies have been consistent in showing an association between gaining within the IOM (1990) guidelines and having a lower risk of adverse outcomes (Carmichael et al., 1997; Abrams et al., 2000; Langford et al., 2008; Olson, 2008), This does not mean, however, that women who gain outside the guidelines will have a bad outcome (Parker and Abrams, 1992). This is because many factors other than GWG are related to the short- and long-term outcomes of pregnancy. Nonetheless, monitoring GWG is useful for identifying women who might benefit from intervention (Parker and Abrams, 1992), and some interventions have been beneficial (see below).
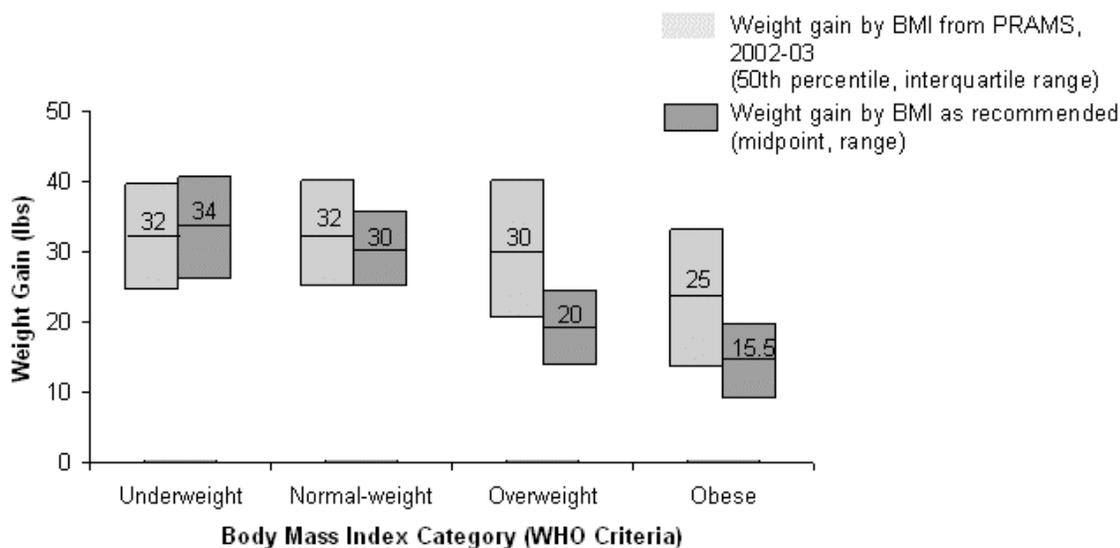

FIGURE 8-1 Comparison of weight gain by BMI category between data reported in the Pregnancy Risk Assessment Monitoring System (PRAMS), 2002-2003, and weight gain as recommended in the new guidelines.

REVIEW OF INTERVENTION STRATEGIES

The report *Nutrition During Pregnancy* (IOM, 1990) made specific suggestions to improve the utility and success of its guidelines. These included providing guidance on measurement of GWG as well as on counseling of pregnant women. In particular, it was recommended that women and their care providers "set a weight gain goal together" early in pregnancy and that women's progress toward that goal should be monitored regularly. Two additional publications from the Committee on Nutritional Status During Pregnancy and Lactation also provided guidance on how to achieve the weight gain guidelines. *Nutrition Services in Perinatal Care* (IOM, 1992b) called for integrating "basic, patient-centered, individualized nutrition care" into the medical care of every woman beginning before conception and continuing until the end of the breastfeeding period. *Nutrition During Pregnancy and Lactation: An Implementation Guide* (IOM, 1992a) called for a dietary assessment of pregnant women early in gestation with a referral to a dietitian if needed. Such services are not uniformly available today and may not be covered by medical insurance plans. As noted in Chapter 7, the committee endorses these recommendations as they have only become more important as childbearing women have become heavier. The American College of Obstetricians and Gynecologists (ACOG) recently made similar recommendations for nutrition counseling specifically for obese women (ACOG, 2005).

Only limited information is available to determine what advice women have been given about GWG since the publication of the IOM (1990) guidelines. In the two studies that have been conducted (see Chapter 4), both Cogswell et al. (1999) and Stotland et al. (2005) reported that a high proportion of women were either given no advice on how much weight to gain during pregnancy or were advised to gain outside of the recommended range for their prepregnant BMI value. These investigators called for greater effort to educate health care providers about the IOM (1990) guidelines. This issue has also been considered from the physician's perspective. Power et al. (2006) reported that the majority of the 900 obstetrician-gynecologists who responded to a mailed questionnaire used BMI to screen for obesity and counseled their patients about weight control, diet and physical activity. Taken together, these studies suggest that there is a discrepancy between what physicians say they are doing and what women say they are receiving. As a result, there is room for improvement in the process of advising women about GWG.

Status of Interventions to Meet the IOM (1990) Guidelines

The IOM (1990) report called for testing the recommended ranges of GWG against outcomes as well as the effectiveness of specific interventions that are used to improve weight gain. To date, only a limited number of investigators have developed interventions to help women gain within the guidelines (reviewed in Olson, 2008). Few studies are available to provide guidance on helping women gain more weight during pregnancy. In their review, Kramer and Kakuma (2003) found that advice to increase energy and protein intake was successful in achieving those goals but not in increasing GWG. Balanced energy and protein intake were associated with very small (21 g/week) increases in GWG. In contrast, high-protein supplements were not associated with an increase in GWG.

Kramer and Kakuma (2003) also reviewed studies of energy/protein restriction in overweight women or those with high GWG. They found that this approach was associated with reduced weekly weight gain. The most recent studies have been focused on various ways to help women

to limit their weight gain during pregnancy. None of the four trials that have been conducted in North American populations was completely successful in helping women to limit GWG and adhere to the IOM (1990) guidelines. Gray-Donald et al. (2000) used a pre-post design and included 107 women in the control and 112 women in the intervention groups. This study of Cree women from Quebec showed that the subjects were obese before conception and at high risk of developing gestational diabetes mellitus. They were "offered regular, individual diet counseling, physical activity sessions and other activities related to nutrition." The intervention had only a "minor impact" on the subjects' diets and no effect on GWG, plasma glucose concentration, birth weight, the rate of cesarean delivery or postpartum weight. Olson and her coworkers (2004) also used a pre-post design in their study of normal- and overweight white women from rural community in New York. The intervention included monitoring of weight gain by health care providers and patient education by mail. Overall, there was no difference between the control (*n* = 381) and intervention (*n* = 179) groups in GWG or postpartum weight retention at one year. Among the low-income women in the sample, however, those in the intervention group gained less than those in the control group. Polley et al. (2002) randomized 120 normal or overweight women recruited from a hospital clinic that served low-income women to a stepped-care behavioral intervention or usual care. This intervention was successful in reducing the proportion of normal weight but not overweight women who exceeded the IOM (1990) guidelines for GWG. It did not, however, affect weight retention measured at eight weeks postpartum.

In the most recent report, Asbee et al. (2009) randomized women to receive either an organized, consistent program of intensive dietary and lifestyle counseling or routine prenatal care. Among the 100 women who completed the trial, those randomized to the intervention group gained less weight during pregnancy (29 pounds) than those randomized to routine care (36 pounds), but they were not more successful in adhering to the recommended guidelines.

In contrast, women in two of the three studies that have been conducted in Scandinavian populations were successful in reducing GWG. The exception was the pilot study in Finland by Kinnunen et al. (2007), in which primiparous pregnant women were recruited from six public health clinics. Most of these women had a normal prepregnant body mass index (BMI). The 49 women in the intervention group received five individual counseling sessions on diet and leisure-time physical activity; the 56 controls received usual care. Although the intervention improved various aspects of the subjects' diets, it did not prevent excessive GWG. In Sweden, Claesson et al. (2008) offered 160 pregnant women additional visits with a midwife that were designed to motivate them to change their behavior and obtain information relevant to their needs. Those who attended the program were also invited to an aqua aerobic class once or twice a week that was specially designed for obese women. The 208 obese pregnant women in the control group received usual care. Compared to the control group, women in the intervention group gained 2.6 kg less weight during pregnancy and 2.8 kg less between early pregnancy and the postnatal check-up. There were no differences between the groups in type of delivery or infant weight at birth. In Denmark, Wolff et al. (2008) randomized 50 obese pregnant women to receive 10 one-hour dietary consultations that were designed to help them restrict their GWG to 6-7 kilograms or usual care. The women in the intervention group were successful in limiting both their energy intake and their gestational weight gain compared to those in the control group.

The studies in Sweden (Claesson et al., 2008) and Denmark (Wolff et al., 2008) demonstrate that it is possible to motivate obese pregnant women to limit their weight gain during pregnancy to 6-7 kilograms. Achieving this goal required a substantial investment in individual dietary or

motivational counseling and, in Sweden, also the provision of specially designed aqua aerobics classes. However, some measure of individualized attention was provided in all of the studies—but not all of them were successful. Only normal weight and/or overweight women were enrolled in three of the studies (Polley et al., 2002; Olson et al., 2004; Kinnunen et al., 2007). None of these studies was uniformly successful. Only obese women were enrolled in the other three studies (Gray et al., 2000; Claesson et al., 2008; Wolff et al., 2008); two of these were successful.

The individualized attention that characterized the successful interventions would be expensive to duplicate on a wide scale. However, the significant improvement in serum insulin concentrations seen in the study of obese Danish women by Wolff and her coworkers (2008) might provide adequate justification for this expenditure. It is noteworthy that none of these trials had sufficient statistical power to establish that those whose weight gain stayed within the IOM guidelines or reached the investigators' target had better obstetric outcomes than those who did not. In contrast, there is evidence that these interventions helped some of the subjects reduce postpartum weight retention (Olson, 2004; Kinnunen et al., 2007; Claesson et al., 2008).

For the first time, these new guidelines provide a specific weight-gain range for obese women. This specificity should assist researchers in developing targeted interventions to determine how best to help women to gain within this range as well as to evaluate whether those who do gain appropriately have better short- and long-term outcomes for themselves and their infants than those who do not.

IMPLEMENTATION STRATEGIES

The committee worked from the perspective that the reproductive cycle begins before conception and continues through the first year postpartum. Opportunities to influence maternal weight status are available through the entire cycle. Although it is beyond the scope of this report to consider the evidence associated with timing, duration or strength of specific strategies or interventions, the committee offers a basic framework for possible approaches to the implementation guidelines, with a particular focus on consumer education and strategies to assist practitioners and public health programs. A basic goal of this framework is to help women improve the quality of their dietary intake and increase their physical activity to be able to meet these new guidelines. These behavioral changes will need to be supported by both individualized care and community-level actions to alter the physical and social environments that influence dietary behaviors. A comprehensive review of the evidence associated with such actions, and guidelines for their use, will require future analyses, as was done in the report *Nutrition During Pregnancy and Lactation: An Implementation Guide* (IOM, 1992).

Conceiving at a Normal BMI Value

To meet the recommendations of this report fully, two different challenges must be met. First, a higher proportion of American women should conceive at a weight within the range of normal BMI values. Meeting this first challenge requires preconceptional counseling and, for many women some weight loss. Such counseling may need to include additional contraceptive services (ACOG, 2005) to assist women in planning the timing of their pregnancies. Such counseling also may need to include services directed toward helping women to improve the quality of their diets (Gardiner et al., 2008) and increase their physical activity. This is because only a small proportion of women who are planning a pregnancy—and even fewer of those who

are not planning a pregnancy but become pregnant nonetheless—comply with recommendations for optimal nutrition and lifestyle (Inskip et al., 2009).

Preconception counseling is an integral part of the recommendations from the Centers for Disease Control and Prevention (CDC) (Johnson et al., 2006) that are designed to enable women to enter pregnancy in optimal health, avoid adverse health outcomes associated with childbearing and reduce disparities in adverse pregnancy outcomes. Practical guidelines for preconceptional care are provided in *Nutrition During Pregnancy and Lactation: An Implementation Guide* (IOM, 1992a). It is noteworthy that few intervention studies have evaluated ways to improve the nutritional choices of women of childbearing age (McFadden and King, 2008), so this is an area in which further investigation is necessary. There is, however, evidence that preconceptional counseling improves women's knowledge about pregnancy-related risk factors as well as their behaviors to mitigate risks (Elsinga et al., 2008). In addition, there is also evidence that pre- and interconceptional counseling will improve attitudes and behavior about nutrition and physical activity in response to a behavioral intervention (Hillemeier et al., 2008). Women with the highest BMI values may even require bariatric surgery to achieve a better weight before conception. Recent systematic reviews suggest women who undergo such surgery have better pregnancy outcomes than women who remain obese (reviewed in Maggard et al., 2008; Guelinckx et al., 2009).

Gaining Weight During Pregnancy Within the New Guidelines

Second, a higher proportion of American women should limit their weight gain during pregnancy to the range specified in these guidelines for their prepregnant BMI. Meeting this second challenge requires a different set of services**.** The first step in assisting women to gain within these guidelines is letting them know that they exist, which will require educating their healthcare providers as well as the women themselves. Government agencies, those who provide healthcare to pregnant women or those who are planning pregnancies as well as private voluntary organizations could provide this education as well as medical societies that have adopted these guidelines as their standard of care.

Women who know about the guidelines and have developed a weight gain goal with their care provider may need additional assistance to achieve their goal. Individualized attention is called for in the IOM (1990) guidelines and was an element in all of the recent interventions that have been successful in helping women to gain within their target range. As noted above, however, not every intervention with individualized attention was successful, so additional services clearly are needed. The IOM report, *Nutrition Services in Perinatal Care* (1992b) calls for "basic, patient-centered individualized nutritional care" to be integrated into the primary care of every woman, beginning before conception and continuing throughout the period of breastfeeding. Guidelines on providing such care are provided in *Nutrition During Pregnancy and Lactation: An Implementation Guide* (IOM, 1992a). The increase in prevalence of obesity that has occurred since 1990 suggests that this recommendation has only become more important.

In offering women individualized attention, a number of kinds of services could be considered. As noted in Chapter 7, health care providers should chart women's weight gain and share the results with them so that they become aware of their progress toward their weight-gain goal. To assist healthcare providers in doing this, the committee has prepared charts (see Figures 8-2 through 8-5) that could be used as a basis for this discussion with the pregnant woman and could also be included in her medical record. These charts reflect the fact that some weight gain

usually occurs in the first trimester and that weight gain is close to linear in the second and third trimesters (see Chapter 7 for the rates used in preparing these charts). The range around the target line in the second and third trimesters reflects the final width of the target range. In presenting these graphics, the committee emphasizes that graphical formats should be carefully and empirically tested before adoption to insure that the final product effectively communicates the intended messages to women about GWG.

These charts are meant to be used as part of the assessment of the progress of pregnancy and a woman's weight gain, looking beyond the gain from one visit to the next and toward the overall pattern of weight gain. This is because the pattern of GWG, like that of total GWG, is highly variable even among women with good outcomes of pregnancy (Carmichael et al., 1997). Carmichael et al. (1997) have recommended that women should be evaluated for modifiable factors (e.g. lack of money to buy food, stress, infection, medical problems, etc.) that might be causing them to have excessively high or low gains before any corrective action is recommended; the committee endorses this approach.
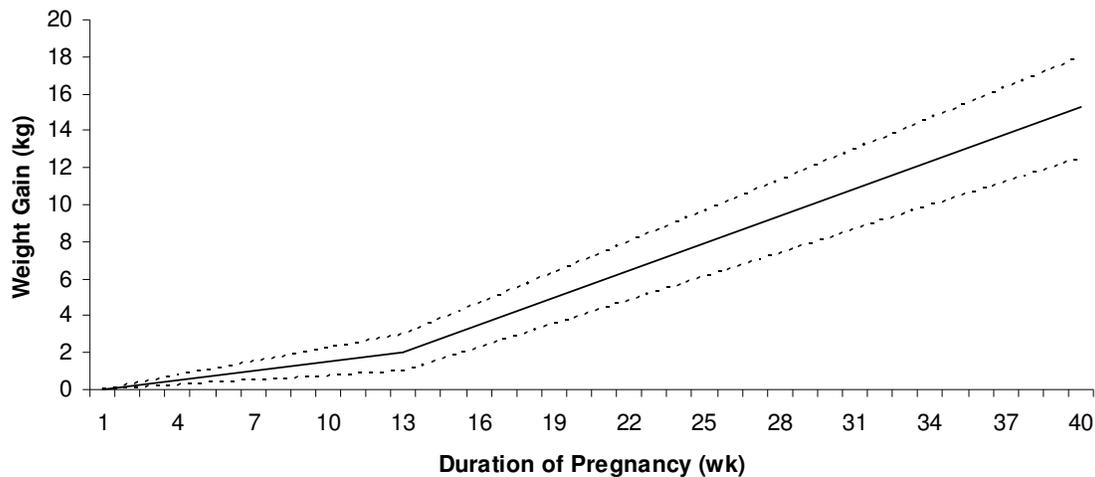
FIGURE 8-2 Recommended weight gain by week of pregnancy for underweight (BMI: < 18.5 kg/m^2) women (dashed lines represent range of weight gain).
NOTE: First trimester gains were determined using three sources (Siega-Riz et al., 1994; Abrams et al., 1995; Carmichael et al., 1997).
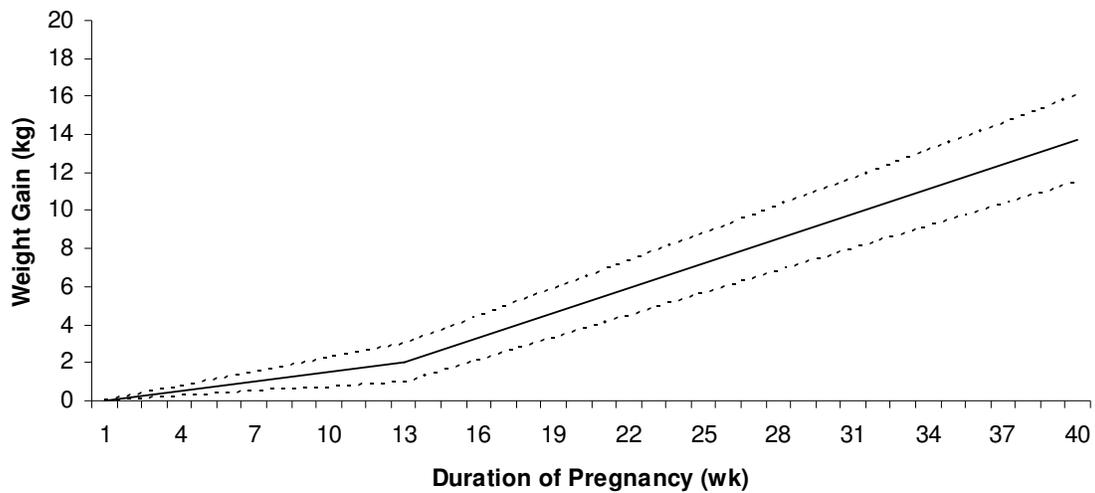
FIGURE 8-3 Recommended weight gain by week of pregnancy for normal weight (BMI: 18.5 - 24.9 kg/m^2) women (dashed lines represent range of weight gain).
NOTE: First trimester gains were determined using three sources (Siega-Riz et al., 1994; Abrams et al., 1995; Carmichael et al., 1997).
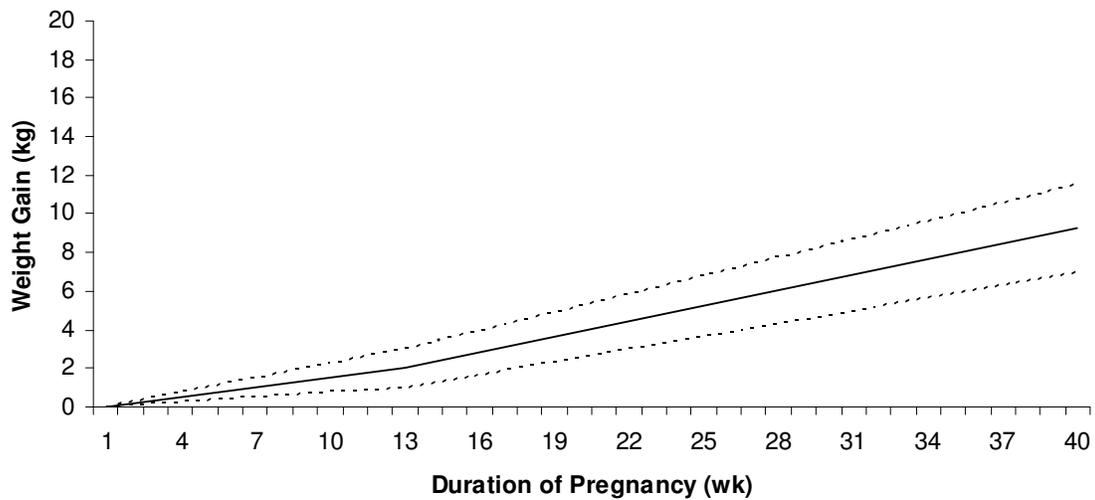
FIGURE 8-4 Recommended weight gain by week of pregnancy for overweight (BMI: 25.0-29.9 kg/m^2) women (dashed lines represent range of weight gain).
NOTE: First trimester gains were determined using three sources (Siega-Riz et al., 1994; Abrams et al., 1995; Carmichael et al., 1997).
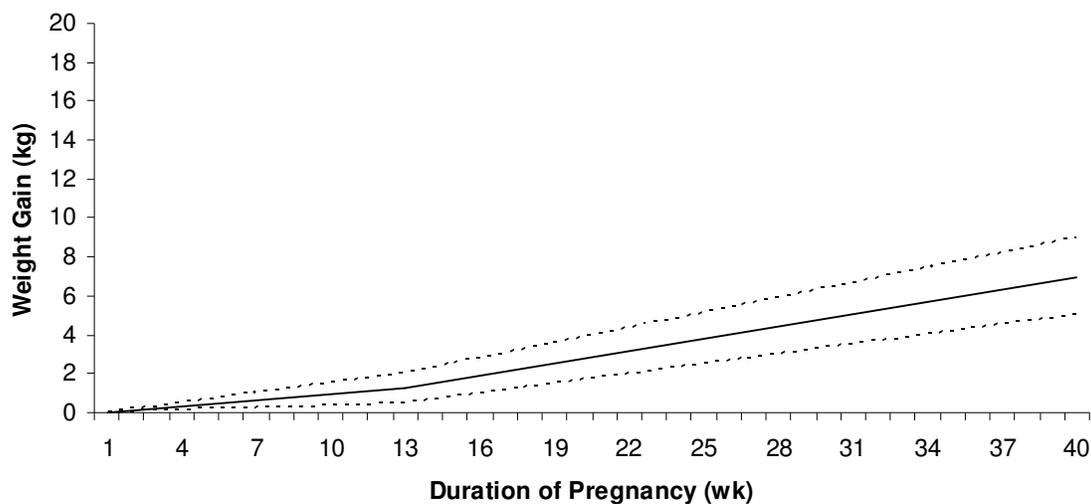
FIGURE 8-5 Recommended weight gain by week of pregnancy for obese (BMI: ≥ 30 kg/m^2) women (dashed lines represent range of weight gain).
NOTE: First trimester gains were determined using three sources (Siega-Riz et al., 1994; Abrams et al., 1995; Carmichael et al., 1997).

In addition, women should be provided with advice about both diet and physical activity (ACOG, 2002). This may require referral to a dietitian as well as other appropriately qualified individuals, such as those who specialize in helping women to increase their physical activity. These services may need to continue into the postpartum period to give women the maximum support to return to their prepregnant weight within the first year and, thus, to have a better chance of returning to a normal BMI value at the time of a subsequent conception.

Individualized nutrition services for pregnant women can be provided by a dietitian, as recommended in *Nutrition Services in Perinatal Care* (IOM, 1992b). Individualized dietary advice is also available for pregnant women on the internet [see, for example, MyPyramid.gov (http://mypyramid.gov/mypyramidmoms/index.html. Accessed February 18, 2009)].

Individualized assessment of physical activity patterns and recommendations for improvement can be provided by a woman's health care provider or by trained practitioners in many health clubs and community-based exercise facilities. General advice on increasing physical activity is available on the internet [see, for example, MyPyramid.gov (http://mypyramid.gov/pyramid/physical_activity_tips.html. Accessed February 18, 2009)] as is advice specifically designed for pregnant women (http://www.acog.org/publications/patient_education/bp045.cfm. Accessed February 18, 2009). According to ACOG (2002), in the absence of either medical or obstetric complications, 30 minutes or more of moderate exercise a day on most, if not all, days of the week is recommended for pregnant women. Participation in a wide range of recreational activities appears to be safe for pregnant women, including pregnant women with diabetes (Kitzmiller et al., 2008). The recent report of the Physical Activity Guidelines Advisory Committee (DHHS, 2008) also offered support for physical activity during pregnancy. Based on the limited number of studies available, this group concluded that "unless there are medical reasons to the contrary, a pregnant woman can begin or continue a regular physical activity program throughout gestation, adjusting the frequency, intensity and time as her condition warrants." This committee added that "in the

absence of data, it is reasonable for women during pregnancy and the postpartum period to follow the moderate-intensity recommendations set for adults unless specific medical concerns warrant a reduction in activity." However, it is recognized that adequately powered randomized, controlled intervention studies on the potential benefits and risks of regular physical activity at various doses in pregnant women are urgently needed.

Individualized attention is likely to be necessary but not sufficient to enable most women to gain within the new guidelines. For example, pregnant or postpartum women will have difficulty following advice to increase their physical activity by walking unless there is a safe place to walk in their community. Similarly, pregnant or postpartum women will have difficulty following advice to improve the quality of their diets unless healthy foods are available at local markets at prices they can afford. Only limited information is available on the link between community factors and GWG, but it suggests characteristics of neighborhoods influence women's ability to gain weight appropriately during pregnancy (Laraia et al., 2007). The behavior changes that will be required for the majority of pregnant women to gain within the guidelines are difficult and complex. As noted in the report *Promoting Health: Intervention Strategies from Social and Behavioral Sciences* (IOM, 2000), "It is unreasonable to expect that people will change their behavior easily when so many forces in the social, cultural, and physical environment conspire against such change." As a result, these factors must also be addressed if women are to succeed in gaining within these guidelines. For example, hospital-based obstetric programs could link to community facilities with exercise programs for pregnant or postpartum women. The family, and especially the partner, can have a strong influence on maternal behaviors during pregnancy. Yet, at present, their influence on GWG is understudied and underutilized. Further research on these kinds of multilevel, ecological determinants of GWG (see Chapter 4) is needed to guide the development of comprehensive and effective implementation strategies to achieve these guidelines.

Special attention should be given to low-income and minority women, who are at risk of being overweight or obese at the time of conception, consuming diets of lower nutritional value, and of performing less recreational physical activity. The low health literacy levels that characterize this group also represent a major barrier for understanding and acting upon health recommendations (IOM, 2004). The use of culturally appropriate channels and approaches to convey this information at both the individual and population level is essential (Huff and Kline, 1999; Glanz et al., 2002). Approaches considered should range from social marketing (Siegel and Lotenberg, 2007) to improving the cultural skills of the health care providers (Haughton and George, 2008), who will convey the GWG recommendation at an individual level. The community has a particularly important role to play in fostering appropriate GWG in low-income women.

CONCLUDING REMARKS

Although the guidelines developed as part of this committee process are not dramatically different from those published previously (IOM, 1990), fully implementing them would represent a radical change in the care women of childbearing age. In particular, the committee recognizes that full implementation of these guidelines would mean:

- Offering preconceptional services, such as counseling on diet and physical activity as well as access to contraception, to all overweight or obese women to help them reach a

healthy weight before conceiving. This may reduce their obstetric risk and normalize infant birth weight as well as improve their long-term health.

- Offering services, such as counseling on diet and physical activity, to all pregnant women to help them achieve the guidelines on GWG contained in this report. This may also reduce their obstetric risk, reduce postpartum weight retention, improve their long-term health, normalize infant birth weight and offer an additional tool to help reduce childhood obesity.
- Offering services, such as counseling on diet and physical activity, to all postpartum women. This may help them to eliminate postpartum weight retention and, thus, to be able to conceive again at a healthy weight as well as improve their long-term health.

The increase in overweight and obesity among American women of childbearing age and failure of most pregnant women to gain within the IOM (1990) guidelines alone justify this radical change in care as women clearly require assistance to achieve the recommendations in this report in the current environment. However, the reduction in future health problems among both women and their children that could possibly be achieved by meeting the guidelines in this report provide additional justification for the committee's recommendations.

These new guidelines are based on observational data, which consistently show that women who gained within the IOM (1990) guidelines experienced better outcomes of pregnancy than those who did not (see Chapters 5 and 6). Nonetheless, these new guidelines require validation from experimental studies. To be useful, however, such validation through intervention studies must have adequate statistical power not only to determine if a given intervention helps women to gain within the recommended range but also to determine if doing so improves their outcomes. In the future, it will be important to reexamine the trade-offs between women and their children in pregnancy outcomes related to prepregnancy BMI as well as GWG, and also to be able to estimate the cost-effectiveness of interventions designed to help women meet these recommendations.

FINDING AND RECOMMENDATIONS

Finding

The committee found that:

1. Existing research is inadequate to establish the characteristics of interventions that work reliably to assist women in meeting the 1990 guidelines for GWG or to avoid postpartum weight retention.

Recommendations for Action

Action Recommendation 8-1: The committee recommends that appropriate federal, state and local agencies as well as health care providers inform women of the importance of conceiving at a normal BMI and that all those who provide health care or related services to women of childbearing age include preconceptional counseling in their care.

Action Recommendation 8-2: To assist women to gain within the guidelines, the committee recommends that those who provide prenatal care to women should offer them counseling,

such as guidance on dietary intake and physical activity, that is tailored to their life circumstances.

Recommendation for Research

Research Recommendation 8-1: The committee recommends that the Department of Health and Human Services provide funding for research to aid providers and communities in assisting women to meet these guidelines, especially low-income and minority women. The committee also recommends that the Department of Health and Human Services provide funding for research to examine the cost-effectiveness (in terms of maternal and offspring outcomes) of interventions designed to assist women in meeting these guidelines.

REFERENCES

Abrams B., S. Carmichael and S. Selvin. 1995. Factors associated with the pattern of maternal weight gain during pregnancy. *Obstetrics and Gynecology* 86(2): 170-176.

ACOG (American College of Obstetricians and Gynecologists). 2002. ACOG committee opinion. Exercise during pregnancy and the postpartum period. Number 267, January 2002. American College of Obstetricians and Gynecologists. *International Journal of Gynaecology and Obstetrics* 77(1): 79-81.

ACOG. 2005. Committee Opinion number 315, September 2005. Obesity in pregnancy. *Obstetrics and Gynecology* 106(3): 671-675.

Asbee S. M., T. R. Jenkins, J. R. Butler, J. White, M. Elliot and A. Rutledge. 2009. Preventing excessive weight gain during pregnancy through dietary and lifestyle counseling: a randomized controlled trial. *Obstetrics and Gynecology* 113(2 Pt 1): 305-312.

Carmichael S., B. Abrams and S. Selvin. 1997. The pattern of maternal weight gain in women with good pregnancy outcomes. *American Journal of Public Health* 87(12): 1984-1988.

Cedergren M. 2006. Effects of gestational weight gain and body mass index on obstetric outcome in Sweden. *International Journal of Gynaecology and Obstetrics* 93(3): 269-274.

Claesson I. M., G. Sydsjo, J. Brynhildsen, M. Cedergren, A. Jeppsson, F. Nystrom, A. Sydsjo and A. Josefsson. 2008. Weight gain restriction for obese pregnant women: a case-control intervention study. *British Journal of Obstetrics and Gynaecology* 115(1): 44-50.

Cogswell M. E., K. S. Scanlon, S. B. Fein and L. A. Schieve. 1999. Medically advised, mother's personal target, and actual weight gain during pregnancy. *Obstetrics and Gynecology* 94(4): 616-622.

Deierlein A. L., A. M. Siega-Riz and A. Herring. 2008. Dietary energy density but not glycemic load is associated with gestational weight gain. *American Journal of Clinical Nutrition* 88(3): 693-699.

DHHS (U.S. Department of Health and Human Services). 2008. *Physical Activity Guidelines Advisory Committee Report*. Washington, DC.

Elsinga J., L. C. de Jong-Potjer, K. M. van der Pal-de Bruin, S. le Cessie, W. J. Assendelft and S. E. Buitendijk. 2008. The effect of preconception counselling on lifestyle and other behaviour before and during pregnancy. *Womens Health Issues* 18(6 Suppl): S117-125.

Gardiner P. M., L. Nelson, C. S. Shellhaas, A. L. Dunlop, R. Long, S. Andrist and B. W. Jack. 2008. The clinical content of preconception care: nutrition and dietary supplements. *American Journal of Obstetrics and Gynecology* 199(6, Supplement 2): S345-S356.

Glanz K., Rimer B.K. and L. F.M., Eds. (2002). *Health Behavior and Health Education: Theory, Research, and Practice, 3rd Ed*. San Francisco, CA, Jossey-Bass.

Gray-Donald K., E. Robinson, A. Collier, K. David, L. Renaud and S. Rodrigues. 2000. Intervening to reduce weight gain in pregnancy and gestational diabetes mellitus in Cree communities: an evaluation. *Canadian Medical Association Journal* 163(10): 1247-1251.

Guelinckx I., R. Devlieger and G. Vansant. 2009. Reproductive outcome after bariatric surgery: a critical review. *Human Reproduction Update*.

Haughton B. and A. George. 2008. The Public Health Nutrition workforce and its future challenges: the US experience. *Public Health Nutrion* 11(8): 782-791.

Hillemeier M. M., D. S. Downs, M. E. Feinberg, C. S. Weisman, C. H. Chuang, R. Parrott, D. Velott, L. A. Francis, S. A. Baker, A. M. Dyer and V. M. Chinchilli. 2008. Improving women's preconceptional health: findings from a randomized trial of the Strong Healthy Women intervention in the Central Pennsylvania women's health study. *Womens Health Issues* 18(6 Suppl): S87-96.

Huff R. M. and M. V. Kline, Eds. (1999). *Promoting Health in Multicultural Populations: A Handbook for Practitioners* Thousand Oaks, CA, Sage.

Inskip H. M., S. R. Crozier, K. M. Godfrey, S. E. Borland, C. Cooper and S. M. Robinson. 2009. Women's compliance with nutrition and lifestyle recommendations before pregnancy: general population cohort study. *British Medical Journal* 338: b481.

IOM (Institute of Medicine). 1990. *Nutrition During Pregnancy*. Washington, DC: National Academy Press.

IOM. 1992a. *Nutrition During Pregnancy and Lactation: An Implementation Guide*. Washington, DC: National Academy Press.

IOM. 1992b. *Nutrition Services in Perinatal Care: Second Edition*. Washington, DC: National Academy Press.

IOM. 1995. *The Best Intentions: Unintended Pregnancy and the Well-Being of Children and Families*. Washington, DC: National Academy Press.

IOM. 2000. *Promoting Health: Intervention Strategies from Social and Behavioral Sciences*. Washington, DC: National Academy Press.

IOM. 2004. *Health Literacy: A Prescription to End Confusion*. Washington, DC: The National Academies Press.

Johnson K., S. F. Posner, J. Biermann, J. F. Cordero, H. K. Atrash, C. S. Parker, S. Boulet and M. G. Curtis. 2006. Recommendations to improve preconception health and health care--United States. A report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. *MMWR Recommendations and Reports* 55(RR-6): 1-23.

Kinnunen T. I., M. Pasanen, M. Aittasalo, M. Fogelholm, L. Hilakivi-Clarke, E. Weiderpass and R. Luoto. 2007. Preventing excessive weight gain during pregnancy - a controlled trial in primary health care. *European Journal of Clinical Nutrition* 61(7): 884-891.

Kitzmiller J. L., J. M. Block, F. M. Brown, P. M. Catalano, D. L. Conway, D. R. Coustan, E. P. Gunderson, W. H. Herman, L. D. Hoffman, M. Inturrisi, L. B. Jovanovic, S. I. Kjos, R. H. Knopp, M. N. Montoro, E. S. Ogata, P. Paramsothy, D. M. Reader, B. M. Rosenn, A. M. Thomas and M. S. Kirkman. 2008. Managing preexisting diabetes for pregnancy: summary of evidence and consensus recommendations for care. *Diabetes Care* 31(5): 1060-1079.

Kramer M. S. and R. Kakuma. 2003. Energy and protein intake in pregnancy. *Cochrane Database Syst Rev*(4): CD000032.

Langford A., C. Joshu, J. J. Chang, T. Myles and T. Leet. 2008. Does Gestational Weight Gain Affect the Risk of Adverse Maternal and Infant Outcomes in Overweight Women? *Maternal and Child Health Journal*.

Laraia B., L. Messer, K. Evenson and J. S. Kaufman. 2007. Neighborhood factors associated with physical activity and adequacy of weight gain during pregnancy. *Journal of Urban Health* 84(6): 793-806.

Maggard M. A., I. Yermilov, Z. Li, M. Maglione, S. Newberry, M. Suttorp, L. Hilton, H. P. Santry, J. M. Morton, E. H. Livingston and P. G. Shekelle. 2008. Pregnancy and fertility following bariatric surgery: a systematic review. *Journal of the American Medical Association* 300(19): 2286-2296.

McFadden A. and S. King. 2008. *The effectiveness of public health interventions to promote nutrition of pre-conceptional women*. York, UK: NICE Maternal and Child Nutrition Programme.

Nohr E. A., M. Vaeth, J. L. Baker, T. Sorensen, J. Olsen and K. M. Rasmussen. 2008. Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy. *American Journal of Clinical Nutrition* 87(6): 1750-1759.

Olson C. M., M. S. Strawderman and R. G. Reed. 2004. Efficacy of an intervention to prevent excessive gestational weight gain. *American Journal of Obstetrics and Gynecology* 191(2): 530-536.

Olson C. M. 2008. Achieving a healthy weight gain during pregnancy. *Annual Review of Nutrition* 28: 411-423.

Parker J. D. and B. Abrams. 1992. Prenatal weight gain advice: an examination of the recent prenatal weight gain recommendations of the Institute of Medicine. *Obstetrics and Gynecology* 79(5 (Pt 1)): 664-669.

Polley B. A., R. R. Wing and C. J. Sims. 2002. Randomized controlled trial to prevent excessive weight gain in pregnant women. *International Journal of Obesity and Related Metabolic Disorders* 26(11): 1494-1502.

Power M. L., M. E. Cogswell and J. Schulkin. 2006. Obesity prevention and treatment practices of U.S.

obstetrician-gynecologists. *Obstetrics and Gynecology* 108(4): 961-968.

Siega-Riz A. M., L. S. Adair and C. J. Hobel. 1994. Institute of Medicine maternal weight gain recommendations and pregnancy outcome in a predominantly Hispanic population. *Obstetrics and Gynecology* 84(4): 565-573.

Siegel M. and L. D. Lotenberg. 2007. *Marketing public health: Strategies to promote social change, 2nd ed*. Sudbury, MA: Jones & Bartlett.

Stotland N. E., J. S. Haas, P. Brawarsky, R. A. Jackson, E. Fuentes-Afflick and G. J. Escobar. 2005. Body mass index, provider advice, and target gestational weight gain. *Obstetrics and Gynecology* 105(3): 633-638.

Wolff S., J. Legarth, K. Vangsgaard, S. Toubro and A. Astrup. 2008. A randomized trial of the effects of dietary counseling on gestational weight gain and glucose metabolism in obese pregnant women. *International Journal of Obesity (London)* 32(3): 495-501.

Websites:

http://mypyramid.gov/mypyramidmoms/index.html

http://mypyramid.gov/pyramid/physical_activity_tips.html

http://www.acog.org/publications/patient_education/bp045.cfm

9

Open Session and Workshop Agendas

REEXAMINATION OF IOM PREGNANCY WEIGHT GUIDELINES

Institute of Medicine | National Research Council
Food and Nutrition Board
Board on Children, Youth, and Families

The National Academy of Sciences Building
2100 C Street, NW
Washington, DC

January 17, 2008

Open Session Agenda

1:00 p.m.   Welcome, Introductions, and Purpose of the Session
             Kathleen Rasmussen

1:10   Perspectives from Sponsors:

             Michele Lawler, Deputy Director, Division of State and Community Health, Maternal and Child Health Bureau, U.S. Department of Health and Human Services Health Resources and Services Administration

             Catherine Spong, Chief, Pregnancy and Perinatology Branch, National Institutes of Health, National Institute of Child Health and Human Development

             Michael Katz, Senior Vice President for Research and Global Programs, March of Dimes

             Van S. Hubbard, Director, Nutrition Research Coordination National Institutes of Health, Division of Nutrition Research Coordination

             Andrea J. Sharma, Lieutenant Commander-USPHS Commissioned Corps Senior Research Scientist Officer-Epidemiologist, Centers for Disease Control and Prevention, Division of Nutrition, Physical Activity, and Obesity

             Mary Horlick, Director, Pediatric Obesity Program, National Institutes of Health, Division of Digestive Diseases and Nutrition

             Jonelle Rowe, Senior Medical Advisor for Adolescent Women's Health, U.S. Department of Health and Human Services, Office of Women's Health

Wendy Braund, 11th Luther Terry Fellow and Senior Clinical Advisor, U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion

3:10   Break

3:20   Analysis of Data from the Pregnancy Risk Assessment Monitoring System (PRAMS)
            Patricia Dietz, Epidemiologist, Centers for Disease Control and Prevention, Division of Reproductive Health

3:40   Update on AHRQ Evidence-Based Review on Outcomes of Maternal Weight Gain
            Carmen Kelly, LCDR US Public Health Service, Agency for Healthcare Research and Quality

4:00   Committee Discussion with Sponsors

4:30   Adjourn Open Session

**DETERMINANTS OF
GESTATIONAL WEIGHT GAIN AND PREGNANCY OUTCOME**

**Arnold and Mabel Beckman Center of the National Academies
100 Academy Way
Irvine, CA**

March 10, 2008

Open Session Agenda

8:45 am   Welcome to Beckman Center and Open Session
            Kathleen Rasmussen

9:00   Presentations from Invited Speakers:

            Total Weight Gain and Pattern of Weight Gain in Pregnancy
            Marie Cedergren, Linkoping University, Sweden

            Developmental Programming Determinants of Chronic Disease
            Lucilla Poston, King's College, London

            Biological Determinants of Gestational Weight Gain
            Theresa Scholl, University of Medicine and Dentistry of New Jersey

11:00   Q&A with Committee Members

12 noon   Adjourn open session

IMPLICATIONS OF WEIGHT GAIN FOR PREGNANCY OUTCOMES:
ISSUES AND EVIDENCE

The Keck Center of the National Academies
500 Fifth Street, NW
Washington, DC

June 5, 2008

Open Session Agenda

INTRODUCTION

9:00 am   Welcome
                 Kathleen Rasmussen, Sc.D., Chair, Committee to Reexamine IOM Pregnancy Weight
                 Guidelines

SESSION 1: TRENDS IN GESTATIONAL WEIGHT GAIN

9:10   Trends in Distribution of Prepregnancy Body Mass Index
                 Andrea Sharma, Ph.D., M.P.H., Division of Nutrition, Physical Activity,
                 and Obesity, CDC, Atlanta, GA

9:30   New Analyses from the Pregnancy Risk Assessment Monitoring System
                 Patricia Dietz, Dr.P.H., M.P.H., Division of Reproductive Health, CDC, Atlanta, GA

9:50   Pregnancy's Effects on Overall and Central Obesity in Women: Influence of
                 Race/Ethnicity
                 Erica P. Gunderson, Ph.D., Kaiser Permanente, Oakland, CA

10:10   Q&**A**

10:30   BREAK

SESSION 2: DETERMINANTS OF GESTATIONAL WEIGHT GAIN

11:00   Psychosocial and Behavioral Influences on Obesity: Application to Pregnancy
                 Suzanne Phelan, Ph.D., Brown University

11:20   Biological Determinants: Developmental Origins
                 Peter Nathanielsz, M.D., Ph.D., University of Texas Health Sciences Center, San Antonio

11:40   Q&A

12:00 noon   Break for Lunch

SESSION 3: GESTATIONAL WEIGHT GAIN AND PREGNANCY OUTCOMES

1:00 pm   Gestational Weight Gain: Clinician Survey and Consequences for Mother and Child
               Emily Oken, M.D., M.P.H., Harvard University

1:20   Consequences of Gestational Weight Gain: Outcomes for the Mother and Infant
               Ellen A. Nøhr, Ph.D., Aarhus University, Denmark

1:40   Disparities in Fetal Growth and Ethnic-Specific Growth Standards
               Michael Kramer, M.D., McGill University

2:00   Q&A

2:20   Clinic and Community-Based Intervention Programs: Impact on Gestational Weight Gain
               Christine Olson, Ph.D., Cornell University

2:40   Q&A

2:50   BREAK

SESSION 4: PANEL DISCUSSION

3:15   Determinants and Consequences of Gestational Weight Gain: Clinical and Community
               Perspectives
               Moderator:
               Esa Davis, M.D., M.P.H., Case Western Reserve University, Case Western Medical
                 Center
               Panelists:
               Helen Jackson, Ph.D., R.D., L.D./N., Duval County Health Department, Jacksonville, FL
               Margie Tate, M.S., R.D., Arizona Department of Health Services, Phoenix
               Cheryl Harris, M.P.H., R.D., WIC State Agency, Washington, DC
               Deborah Bowers, M.D., Physician and Midwife Collaborative Practice, Alexandria, VA

4:15   Open Discussion

4:45   Adjourn

10

Committee Member Biographical Sketches

KATHLEEN M. RASMUSSEN, Sc.D. (*chair*), is professor of nutrition, Division of Nutritional Sciences, at Cornell University. Dr. Rasmussen is internationally known for her research on maternal and child nutrition, particularly in the areas of pregnancy and lactation. She has served as program director for Cornell's National Institutes of Health (NIH) sponsored training grant in maternal and child nutrition since 1986 and has also directed a training grant in international maternal and child nutrition. Dr. Rasmussen has taught a nationally recognized course in maternal and child nutrition for graduate students since 1980 and has co-taught a unique course on public health nutrition for undergraduate students since 1998. Continuing her interest in mentoring the future leaders in nutrition, Dr. Rasmussen serves as the principal faculty member at the Dannon Nutrition Leadership Institute, which she helped to develop in 1998. In 2006, she received the first Excellence in Nutrition Education Award to be given by the American Society for Nutrition. Dr. Rasmussen has served as secretary and then president of the American Society of Nutritional Sciences and also as president of the International Society for Research on Human Milk and Lactation. She has previously been associate dean and secretary of the University Faculty and served a 4-year term on Cornell's Board of Trustees as one of its faculty-elected members. Dr. Rasmussen was a member of the recent DBASSE-IOM (Division of Behavioral and Social Sciences and Education-Institute of Medicine) Committee on the Impact of Pregnancy Weight on Maternal and Child Health and served on the IOM Committee on Nutritional Status During Pregnancy and Lactation and its Subcommittee on Nutrition During Lactation, as well as the Committee on Scientific Evaluation of the WIC (Women, Infants, and Children) Nutrition Risk Criteria. She received her A.B. degree from Brown University in molecular biology and both her Sc.M. and Sc.D. degrees from Harvard University in nutrition.

BARBARA ABRAMS, Dr.P.H., R.D., is professor of epidemiology, maternal and child health, and public health nutrition in the School of Public Health at the University of California, Berkeley. Her expertise includes weight and weight gain in women during pregnancy, post partum, and during menopause; maternal weight, nutrition, social factors, and perinatal health outcomes; and HIV and breastfeeding. She has previously served on the IOM Committee on the Impact of Pregnancy Weight on Maternal and Child Health, the Committee on the Scientific Evaluation of WIC Nutrition Risk Criteria, the Committee on Nutritional Status During Pregnancy and Lactation, and the Subcommittee on Clinical Application Guide. She was awarded the March of Dimes Agnes Higgins Award for her contributions to the field of maternal-fetal nutrition. Dr. Abrams received her B.S. in nutrition and dietetics from Simmons College in Boston. She earned her M.P.H. in nutrition, M.S. in epidemiology, and Dr.P.H in nutrition from the University of California, Berkeley. Dr. Abrams is a member of the American Dietetic Association, the American Society for Nutrition, the Society for Epidemiologic Research, and the Society for Pediatric and Perinatal Epidemiologic Research and an affiliate member of the American College of Obstetrics and Gynecology.

LISA M. BODNAR, Ph.D., M.P.H., R.D., is assistant professor in the Department of Epidemiology at the University of Pittsburgh Graduate School of Public Health and assistant professor of obstetrics, gynecology, and reproductive sciences at the University of Pittsburgh School of Medicine. Her research interests include nutritional status and birth outcomes, nutritional psychiatry in the perinatal period, the reproductive consequences of obesity, and the use of causal modeling and longitudinal data analysis in reproductive epidemiology. Dr. Bodnar is principal investigator of two NIH grants on nutrition in pregnancy. She recently participated in the 53rd Royal College of Obstetricians and Gynaecologists Work Group on Obesity and Reproductive Health Outcomes in London. Dr. Bodnar graduated with honors from the University of North Carolina, Chapel Hill, where she also received her M.P.H. and Ph.D. in nutritional epidemiology. Dr. Bodnar is a registered dietitian, a member of the American Dietetic Association, and a licensed nutritionist. She also holds membership in the American Society for Nutrition, the Society for Epidemiologic Research, and the Society for Pediatric and Perinatal Epidemiologic Research.

CLAUDE BOUCHARD, Ph.D., is the executive director of the Pennington Biomedical Research Center and the George A. Bray Chair in Nutrition. He holds a B.Ped. (Laval), an M.Sc. (University of Oregon, Eugene) in exercise physiology, and a Ph.D. (University of Texas, Austin) in population genetics. His research deals with the genetics of adaptation to exercise and to nutritional interventions as well as the genetics of obesity and its comorbidities. He has authored and coauthored several books and more than 900 scientific papers. Dr. Bouchard is the recipient of many awards and of an honoris causa doctorate in science from the Katholieke Universiteit Leuven. He has been a foreign member of the Royal Academy of Medicine of Belgium since 1996 and was the Leon Mow Visiting Professor at the International Diabetes Institute in Melbourne in 1998. In 2001, he became a member of the Order of Canada as well as professor emeritus, Faculty of Medicine, Laval University. In 2003 he received the Alumnus of the Year Award from Laval University, and in 2004 he received the Friends of Albert J. Stunkard Award from the North American Association for the Study of Obesity. Dr. Bouchard became a knight in the Ordre National du Quebec in 2005 and also received the Earle W. Crampton Award in Nutrition from McGill University that same year. Dr. Bouchard is past president of the North American Association for the Study of Obesity and the immediate past president of the International Association for the Study of Obesity. Prior to coming to Pennington, he held the Donald B. Brown Research Chair on Obesity at Laval University where he directed the Physical Activity Sciences Laboratory for about 20 years. His research has been funded by agencies in Canada and the United States, primarily the National Institutes of Health.

NANCY BUTTE, Ph.D., M.P.H., is professor of pediatrics at the Children's Nutrition Research Center at Baylor College of Medicine. Her expertise includes energy requirements of infants, children, and women during pregnancy and lactation, as well as the environmental and genetic determinants of childhood obesity, and the contribution of food intake, total energy expenditure, basal metabolic rate (BMR), substrate utilization, physical activity, and fitness to the development of obesity in children. She holds membership in the American Society for Nutrition, the Obesity Society, and the Society of Pediatric Research. Dr. Butte has previously served on the IOM Panel on Dietary Reference Intakes for Macronutrients; the Committee on Body Composition, Nutrition, and Health of Military Women; and the Subcommittee on

Nutritional Status and Weight Gain During Pregnancy (1988-1990). Dr. Butte received her M.P.H. in public health nutrition and her Ph.D. in nutrition from the University of California, Berkeley.

PATRICK M. CATALANO, M.D., F.A.C.O.G., is professor and chair of the Department of Reproductive Biology at Case Western Reserve University at MetroHealth Medical Center. Dr. Catalano also serves on the Management Council and Executive Committee at MetroHealth Medical Center. He has published more than 130 articles in peer-reviewed journals and served on the editorial boards of the *Journal of Clinical Endocrinology* and *Metabolism and Diabetes*. He holds membership in the American College of Obstetricians and Gynecologists, the American Diabetes Association, the Perinatal Research Society, and the American Gynecological and Obstetrical Society. Dr Catalano is a member of the Maternal-Fetal Medicine Division of the American Board of Obstetrics and Gynecology. Dr. Catalano's research focus is insulin resistance and glucose metabolism in pregnancy and the role of placental cytokines in the regulation of fetal growth and adiposity. He has had research support from the National Institute of Child Health and Human Development (NICHD) for more than 20 years. Dr. Catalano received his M.D. from the University of Vermont, Burlington. He served his internship at the University of California, San Francisco, and residency and postdoctoral fellowship at the University of Vermont, Burlington. Dr. Catalano is certified by the American Board of Obstetrics and Gynecology in maternal and fetal medicine.

MATTHEW W. GILLMAN, M.D., S.M., is professor in the Department of Ambulatory Care and Prevention (DACP) at Harvard Medical School and Harvard Pilgrim Health Care. At the DACP, Dr. Gillman directs the Obesity Prevention Program, whose goal is to lessen obesity-related morbidity and mortality through epidemiologic, health services, and intervention research. Dr. Gillman conducts epidemiologic studies across the age spectrum. He has published widely and has obtained numerous federal and other grants in the areas of developmental origins of health and disease; determinants of dietary and physical activity habits; and interventions to prevent childhood overweight. He is the principal investigator of Project Viva, a prospective cohort study of pregnant women and their children whose goal is to examine pre- and perinatal determinants of offspring health. He is co-principal investigator of the Coordinating Center of the U.S. National Children's Study and a member of the Council of the International Society for Study of the Developmental Origins of Health and Adult Disease. He previously served on the National Research Council-IOM Committee on the Impact of Pregnancy Weight on Maternal and Child Health. Dr. Gillman earned his A.B. and S.M. from Harvard and his M.D. from Duke University. He served a medicine-pediatrics internship and residency at North Carolina Memorial Hospital. Dr. Gillman is a fellow of the American Academy of Pediatrics, American College of Physicians, and the American Heart Association Council on Epidemiology and Prevention.

FERNANDO A. GUERRA, M.D., M.P.H., is director of health for the San Antonio Metropolitan Health District. He is a member of the Institute of Medicine. Dr. Guerra's career reflects a long-standing interest and involvement in pediatric care, public health, and health policy. His expertise is improving access to healthcare systems for infants, women, children, and the elderly and improving access to health care for migrant children. He is also active with local, national, and international forums on a variety of health issues. Dr. Guerra has served on the

Committee on Ethical Issues in Housing-Related Health Hazard Research Involving Children; the Frontiers of Research on Children, Youth, and Families Steering Committee; the Committee on Using Performance Monitoring to Improve Community Health; and the Committee on Overcoming Barriers to Immunization. He is a former member of the Board on Children, Youth, and Families and has participated as a member of the Roundtable on Head Start Research. Dr. Guerra is recipient of the James Peavey Award from the Texas Public Health Association and the Job Lewis Smith Award from the American Academy of Pediatrics; he is a Kellogg fellow of the Harvard School of Public Health, among many other awards and honors. Dr. Guerra holds a B.A. from the University of Texas at Austin, an M.P.H. from the Harvard School of Public Health, and an M.D. from the University of Texas Medical Branch at Galveston.

PAULA A. JOHNSON, M.D., M.P.H., is executive director of the Connors Center for Women's Health at Brigham and Women's Hospital. Her expertise is in disparities in health care for women and minorities and public health efforts to address affordable and healthy foods for low-income populations. Dr. Johnson has been an active participant in the Disparities Project, an effort to eliminate racial and ethnic inequalities in health in Boston. She is also a leader in public health efforts to address the issue of affordable, healthy food for low-income residents of the city. Her efforts contributed to a major policy conference on Food in the Hub, which provided a set of recommendations regarding food and nutrition policies in Boston. She also has a clinical interest in cardiovascular disease in women, congestive heart failure, and heart transplantation. Dr. Johnson was named to serve as public health commissioner of Boston in 2007. Dr. Johnson received her M.D. and M.P.H. from Harvard Medical School. She served her internship and residency in internal medicine at Brigham and Women's Hospital. She also served a postdoctoral fellowship in cardiology at Brigham and Women's Hospital. Dr. Johnson is board certified in internal medicine and cardiovascular disease.

MICHAEL C. LU, M.D., M.P.H., M.S., is associate professor in the Department of Obstetrics and Gynecology at the University of California, Los Angeles (UCLA), School of Medicine and the Department of Community Health Sciences at UCLA School of Public Health. His research focuses on racial-ethnic disparities in birth outcomes from a life course perspective. Dr. Lu is widely recognized for his research, teaching, and clinical care. Dr. Lu received the 2003 National Maternal and Child Health Epidemiology Young Professional Award and the 2004 American Public Health Association Maternal and Child Health Young Professional Award for his research on health disparities. Dr. Lu has previously served on the IOM Committee on Understanding Premature Birth and Assuring Health Outcomes. He has also received numerous awards for his teaching, including excellence in teaching awards from the Association of Professors of Gynecology and Obstetrics. Dr. Lu also maintains an active clinical practice in obstetrics and gynecology at UCLA Medical Center and has been selected as one of the best doctors in America since 2005. Dr. Lu received a B.A. in human biology and political science from Stanford University, an M.S. in health and medical sciences, an M.P.H. in epidemiology from the University of California, Berkeley, and an M.D. from the University of California, San Francisco, School of Medicine.

ELIZABETH R. MCANARNEY, M.D., is professor and chair emerita of the Department of Pediatrics at the University of Rochester School of Medicine and Dentistry, having served as chair for 13 years. Dr. McAnarney is a member of the IOM. In addition, she has served as the

president of the Society for Adolescent Medicine, the Association of Medical School Pediatric Department Chairs, and the American Pediatric Society. Dr. McAnarney is interested in the role of nutrition and gestational weight gain as risk factors for adolescent postpartum weight retention. She also has studied the etiology of obesity and age-related differences in the composition of the weight gained by pregnant adolescents and optimal nutrition for pregnant adolescents. Dr. McAnarney served as director of the Rochester Adolescent Maternity Program (RAMP) and the university's Division of Adolescent Medicine for 22 years, prior to becoming chair. She is recipient of the 18th annual Athena Award from the Women's Council of the Rochester Business Alliance, in recognition for her career accomplishments and her role in mentoring women. Dr. McAnarney is a graduate of Vassar College and received her M.D. and an honorary D.Sc. from the State University of New York Upstate Medical Center, Syracuse, and served a postdoctoral fellowship at the University of Rochester.

RAFAEL PEREZ-ESCAMILLA, Ph.D., is professor of nutritional sciences and public health and director of the Connecticut NIH EXPORT Center for Eliminating Health Disparities among Latinos at the University of Connecticut. Dr. Pérez-Escamilla is an internationally recognized scholar in community nutrition. His research includes studies on health disparities and inequalities, maternal nutrition during pregnancy, household food insecurity measurement, nutrition and food safety education, and domestic and international community nutrition program design and evaluation. He is nutrition extension scientist for the State of Connecticut and holds a joint appointment with the Department of Community Medicine and Health Care at the University of Connecticut Health Center in Farmington. Dr. Pérez-Escamilla is leading or co-leading four nutrition capacity building and translational research programs in Connecticut, Ghana, and Brazil in the fields of nutrition-related health disparities, breastfeeding, maternal HIV, and household food security. He is a member of the 2010 Dietary Guidelines Advisory Committee. He is past chair of the Community Nutrition and Public Health Research Interest Section of the American Society for Nutrition and serves on the editorial boards of the *Journal of Human Lactation* and the *Journal of Hunger and Environmental Nutrition*. Dr. Pérez-Escamilla received a B.S. in chemical engineering from the Universidad Iberoamericana in Mexico City, Mexico. He earned an M.S. in food science and a Ph.D. in nutrition from the University of California, Davis.

DAVID SAVITZ, Ph.D., is Charles W. Bluhdorn Professor of Community and Preventive Medicine and director of the Disease Prevention and Public Health Institute at Mount Sinai School of Medicine. He was assistant professor in the Department of Preventive Medicine and Biometrics at the University of Colorado School of Medicine and moved to the University of North Carolina School of Public Health in 1985. He served as the Carey C. Boshamer Distinguished Professor and Chair of the Department of Epidemiology until the end of 2005. His teaching is focused on epidemiologic methods, and he recently authored a book entitled *Interpreting Epidemiologic Evidence*. He directed 29 doctoral dissertations at the University of North Carolina and 13 master's theses. He has served as editor at the *American Journal of Epidemiology* and as a member of the NIH Epidemiology and Disease Control-1 study section and currently is an editor at *Epidemiology*. He was president of the Society for Epidemiologic Research and the Society for Pediatric and Perinatal Epidemiologic Research and North American Regional councilor for the International Epidemiological Association. His primary research activities and interests are in reproductive, environmental, and cancer epidemiology. Dr.

Savitz received his undergraduate training in psychology at Brandeis University, a master's degree in preventive medicine at Ohio State University in 1978, and his Ph.D. in epidemiology from the University of Pittsburgh Graduate School of Public Health in 1982. He was elected to membership in the Institute of Medicine in 2007.

ANNA MARIA SIEGA-RIZ, Ph.D., is associate professor in the Department of Epidemiology with a joint appointment in the Department of Nutrition in the School of Public Health at the University of North Carolina (UNC), Chapel Hill. Dr. Siega-Riz is a fellow at the Carolina Population Center and serves as the associate chair of epidemiology and director of the Nutrition Epidemiology Core for the Clinical Nutrition Research Center in the Department of Nutrition at UNC. She is also the program leader for the Reproductive, Perinatal and Pediatric Program in the Department of Epidemiology. She has expertise in gestational weight gain, maternal nutritional status and its effects on birth outcomes, obesity development, and trends and intakes among children and Hispanic populations. Dr. Siega-Riz uses a multidisciplinary team perspective as a way to address complex problems such as prematurity, fetal programming, and racial disparities and outcomes. She received the March of Dimes Agnes Higgins Award for Maternal and Fetal Nutrition in 2007, which recognizes professional contributions and outstanding service in the area of maternal and fetal nutrition. Dr. Siega-Riz earned a B.S.P.H. in nutrition from the School of Public Health at UNC, Chapel Hill; an M.S. in food, nutrition, and food service management from UNC, Greensboro; and a Ph.D. in nutrition and epidemiology from the School of Public Health at UNC, Chapel Hill.