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Thirty-Six-Month Outcomes of a Generalist Paraprofessional Perinatal Home Visiting Intervention in South Africa on Maternal Health and Child Health and Development

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Abstract Almost all pregnant women (98 %) in 24 Cape Town neighborhoods were randomized by neighborhood to (1) the standard care (SC) condition ($n = 12$ neighborhoods; $n = 594$ pregnant women) or (2) the Philani Intervention Program (PIP) in which home visits by Community Health Workers (CHW) were conducted ($n = 12$ neighborhoods; $n = 644$ pregnant women). At 36 months post-birth (84.6 % follow-up), PIP mothers were significantly less depressed compared to the SC mothers. Children in PIP were significantly less likely to be stunted (24.3 vs 18.1 %, $p = 0.013$), to have better vocabularies, and were less likely to be hospitalized than children in the SC condition. These data suggest home visits may need to continue for several years post-birth. Sustainable, scalable perinatal intervention models are needed in LMIC.

Keywords Maternal depression · Perinatal home visiting · Community health workers

Introduction

Investment in children's early years is critical for improving lifelong well-being (Victora et al. 2008). Delivering interventions in the first 1000 days and in the early years have been shown to be cost effective (Heckman 2006), to reduce health inequities (Marmot et al. 2008), and there is an increasing evidence base for how early childhood investments can substantially improve adult health (Campbell and Scott 2011). However, poverty and both infectious and non-communicable diseases in low and middle-income countries (LMIC) are implicated in poor child outcomes. Traditionally, global health programs have focused on disease targeted "magic bullet" solutions to complex health problems, with a proliferation of a silo mentality (Panter-Brick et al. 2014). Increasingly however, many programs in LMIC are focusing on multiple behaviors and risk and protective factors. In most LMIC, it is community health workers (CHW) who are the

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primary work-force that will have to deliver these generalist interventions. While a rigorous evidence base exists for the efficacy of single disease targeted CHW interventions, there is a dearth of evidence detailing whether CHWs can be trained to deliver broader interventions focusing on multiple domains and risk factors with the same positive outcomes.

Perinatal nurse home visiting is the most efficacious EBI to date (Olds et al. 2014). When mounted in LMIC, paraprofessionals deliver home visits, typically to address only one risk, and efficacy has been repeatedly demonstrated in randomized controlled trials (RCTs) (Peacock et al. 2013). Most of these trials have been in the USA (Michalopoulos et al. 2015). However, when scaling these programs, efficacy typically disappears (Peacock et al. 2013). There have been at least four studies in LMIC in the most recent reviews that meet rigorous scientific standards and demonstrate efficacy (Peacock et al. 2013). Perinatal home visitors in Pakistan (Rahman et al. 2009) intervened in maternal depression and had benefits not only on maternal depression but also in breastfeeding. Home visiting in Jamaica over 1 year (Grantham-McGregor et al. 1991) and in Bangladesh (Nahar et al. 2012) and Chile (Aracena et al. 2009) provided nutritional supplements and early stimulation—improving children's outcomes. Our project, the Philani Intervention Model (PIM) (Rotheram-Borus et al. 2011) was one of the successful programs in LMIC (Peacock et al. 2013).

Philani Intervention

In the Philani+ intervention, paraprofessional CHW were trained to address multiple health challenges during home visits. The CHW aimed to reduce mother's risk of acquiring HIV; follow protocols to Prevent Maternal to Child Transmission (PMTCT); improve maternal and child health including TB and illness detection; reduce maternal alcohol use; improve infant and child nutrition; and foster children's growth and development. A cluster RCT was mounted in the townships of Cape Town, South Africa, in 2009–2010 (Rotheram-Borus et al. 2011). Local township women were trained to be CHW and to apply cognitive-behavioral skills to support mothers to manage daily activities and improve their children's outcomes. Atypically, the Philani effectiveness trial had both high internal (85 % follow-up) and external validity (98 % recruitment), and a longitudinal follow-up lasting 36 months post-birth. This cohort included all Mothers Living with HIV (MLH) in a neighborhood, unlike the perinatal HIV cohorts of MLH and their children which are clinic-based samples. Also different from the perinatal HIV cohorts, which had substantial loss-to-follow-up (from 19 to 89 % at 1 year (Kalembo and Zgambo 2012), there were very high follow-up rates over 36 months. The CHW did not replicate a manual with fidelity, as typically advocated by prevention researchers (Flay et al. 2005). CHW were selected on the basis of having their own children that were thriving (positive peer deviants), good communication skills as well as having good problem solving skills. CHW were trained for 1 month using role plays and watching videotapes of common challenging situations that CHW might face during home visits. This study offers a different option for diffusing EBI: CHW were trained on (1) foundational skills common across many EBI; (2) application of key health information about HIV, alcohol use, malnutrition, and general maternal and child health; and (3) coping with their own life challenges.

Previous Results

Earlier analyses of outcomes for households in the home visiting condition compared to households in a control condition demonstrated multiple benefits of the intervention up to the age of 18 months for mothers and their children (le Roux et al. 2013; Rotheram-Borus et al. 2014) including fewer post-birth complications and hospitalizations for children; longer and exclusive breastfeeding; 50 % higher cumulative rate of adherence to PMTCT tasks; higher rates of condom use; and less stunting. The intervention also had fewer low birth weight (LBW) infants than the control condition.

Given the likelihood that mothers and children living in adversity will be subjected to ongoing and sustained adversity and risk, as well as the fact that there is an increasing evidence base about how initial benefits of early interventions may not be sustained over time (Maselko et al. 2015), this paper examines maternal and child outcomes at 36 months.

Methods

Ethics Statement

The Institutional Review Boards of University of California Los Angeles (UCLA), Stellenbosch University, and Emory University approved the study, whose methods have previously been published (Rotheram-Borus et al. 2011). Written, voluntary, informed consent was received from all study mothers. Three independent teams conducted the assessment (Stellenbosch), intervention (Philani Project), and randomization and data analyses (UCLA). This cluster randomized control trial is registered with ClinicalTrials.gov (NCT00996528; https://clinicaltrials.gov/ct2/show/NCT00972699).

Participants

Neighborhood clusters ($N = 24$) of 450–600 households were identified and matched based on the housing type, presence of

electricity, water, sanitation, size and density, alcohol bars, child care resources, distance to clinics, and length of residence. Buffer neighborhoods prevented cross-neighborhood contamination. UCLA randomized neighborhoods in six blocked sets of four neighborhoods each, for 12 PIP neighborhoods ($n = 644$) and 12 SC neighborhoods ($n = 594$).

Recruiters

Township women conducted house-to-house visits every other month from May 2009 to September 2010 to identify all pregnant women and refer to the study; only 2 % refused participation. Assessments were conducted at a research office in the township, with transport provided. Table 1 shows that at recruitment the women were nearly equivalent across conditions on almost all measures (le Roux et al. 2013; Rotheram-Borus et al. 2014).

Figure 1 summarizes participant flow through the study. One thousand two hundred thirty-eight women were assessed at baseline. Follow-up assessments were conducted at 2 weeks post-birth (92 %; mean = 1.9 weeks; SD = 2.1 weeks), 6 months (87 %; mean = 6.2 months, SD = 0.7), 18 months (91 %; mean = 19.1 months; SD = 3.0), and 36 months (85 %; mean = 37.3 months; SD = 2.2 months). All assessments were completed by 80 % of mothers; 1.6 % ($n = 20$) completed no follow-up reassessments.

Assessments Township women were recruited, trained, and certified as interviewers, entering responses on mobile phones (Nokia E61i and 2630) programmed by Mobenzi

Table 1 Characteristics of the sample grouped by the intervention ($N = 644$) and standard care ($N = 594$) conditions

	Intervention ($N = 644$)		Standard care ($N = 594$)		Total ($N = 1238$)	
	n	%	*n*	%	*n*	%
Demographic characteristics						
Mean age (SD)	26.5	5.5	26.3	5.6	26.4	5.5
Mean highest education level (SD)	10.3	1.8	10.3	1.8	10.3	1.8
Currently employed	129	20.0	104	17.5	233	18.8
Married or lives with partner	377	58.5	324	54.6	701	56.6
Monthly household income >2000 Rand	280	45.6	279	48.1	559	46.8
Formal housing	197	30.6	191	32.2	388	31.3
Water on site	333	51.7	327	55.1	660	53.3
Flush toilet	340	52.8	343	57.7	683	55.2
Electricity	569	88.4	543	91.4	1112	89.8
Mother hungry past week	312	48.4	301	50.7	613	49.5
Children hungry past week	175	27.2	185	31.1	360	29.1
Alcohol						
Use during pregnancy	56	8.7	49	9.8	105	9.2
AUDIT-C >2 at pregnancy	113	17.6	101	20.2	214	18.7
AUDIT-C >2, after pregnancy discovery	41	6.4	24	4.8	65	5.7
Maternal health and mental health						
Mean weeks pregnant at assessment (SD)	26	7.9	25.8	8.4	25.9	8.1
Non-primipara	422	65.5	394	66.3	816	65.9
Previous LBW infants	61	14.5	69	17.5	130	15.9
EPDS, mean score (SD)	11.2	6.9	10.4	7.1	10.8	7.0
EPDS >13	238	37.0	195	32.8	433	35.0
HIV and reproductive health behavior						
Recent Sexual partner[a]	580	90.1	522	87.9	1102	89.0
Ever tested for HIV	590	91.6	550	92.6	1140	92.1
Received HIV test results	584	99.0	547	99.5	1131	99.2
Knowledge of partner HIV status						
Partner HIV+	46	7.9	50	9.6	96	8.7
Partner HIV−	325	56.0	296	56.7	621	56.4
Partner serostatus unknown	209	36.0	176	33.7	385	34.9
Request partner HIV test	391	82.5	355	83.1	746	82.8
Mothers living with HIV (MLH)	149	25.5	146	26.7	295	26.1
Mean number of people disclosed to (SD)	3.8	4.5	5	7.2	4.4	6.0
Recent sexual partner[a]	127	85.2	125	85.6	252	85.4
Disclosed HIV status to partner	99	73.9	105	82.7	204	78.2
Knowledge of partner HIV status						
Partner HIV+	42	33.1	50	40.0	92	36.5
Partner HIV−	13	10.2	17	13.6	30	11.9
Partner serostatus unknown	72	56.7	58	46.4	130	51.6

[a] "Recent" always refers to the last 3 months

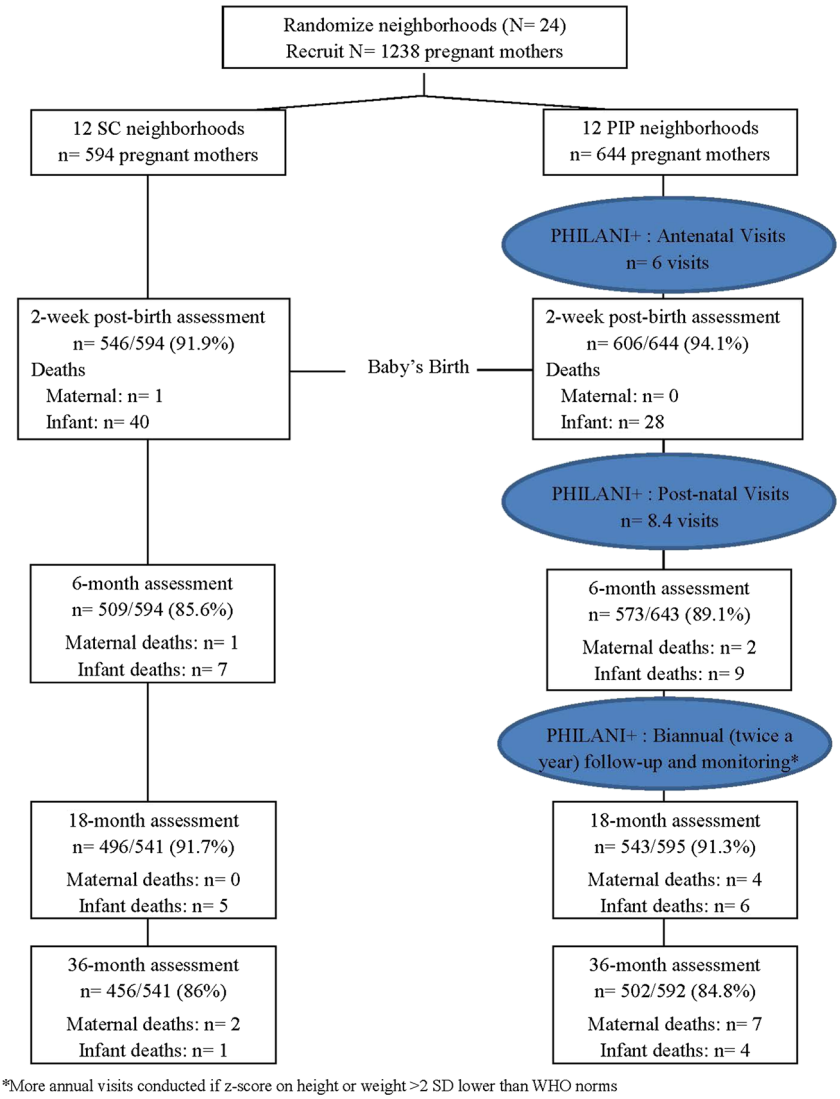

Fig. 1 Movement of participants through the RCT at assessment points comparing mothers in a control condition and a home visiting intervention

(http://www.mobenzi.com/researcher/). Supervisors monitored and gave feedback on the data quality weekly. Data collection ended in May 2014.

Measures

Maternal Outcomes Demographic characteristics were reported at baseline. At each assessment, current housing and household status was checked.

Alcohol Use The frequency of drinking alcohol was assessed at each assessment (0–9 scale ranging from 0 = never to 9 = every day), including the amount of alcohol on days using (0–5 scale ranging from 0 = none to 5 = 10 or more drinks). The Derived Alcohol Use Disorder Identification Test (Derived AUDIT-C) (Dawson et al. 2005) is a three-item scale, with each rated 0–4 on intensity, which documents the severity of alcohol dependence when the score is greater than 3 (Saunders et al. 1993) and has been used extensively among Cape Town residents.

Depressive Symptoms These were reported at each assessment using the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al. 1987), with a cutoff of >13 to indicate depressed mood (Lawrie et al. 1998). The Hopkins Depression Measure (Derogatis et al. 1974) was administered at the 36-month assessment, which is a 21-item measure with good internal reliability and construct validity (Deane et al. 1992).

Health Assessed by self-reports of diabetes, high blood pressure, and tuberculosis on a single question. HIV status and new pregnancies/childbirths were reported at each assessment.

HIV Prevention All mothers reported their number of recent sexual partners (i.e., last 3 months) and the numbers of

episodes of using condoms on each of the last 10 sexual encounters. Partner serostatus and disclosures of serostatus by MLH were reported, as well as re-engagement in HIV care following childbirth and receipt of ARV.

Family Support This was monitored by receipt of the government child grant, a child receiving day care at a crèche, employment, and moving residences.

Child Measures

Peabody Picture Vocabulary Test (PPVT) The PPVT (Dunn 1965) was administered at 36 months, using a form adapted for South Africa (Pakendorf and Alant 1996).

Each child had a Road to Health card issued by the government on which each clinic visit and hospitalization was recorded. Growth was measured at each assessment; interviewers measured children's weight, height, and head circumference, after being trained and certified. Infant anthropometric data were then converted to *z* scores based on the World Health Organization's (WHO) age-adjusted norms (http://www.who.int/childgrowth/standards/en/). A *z* score below −2 was considered a serious health deficit (de Onis and Blossner 2003), as being stunted (> −2 for HAZ) or malnourished (> −2 for weight-for-age *z* scores (WAZ)). About 1 % ($n = 9$) of children had height-for-age *z* scores (HAZ) >3 or < −3; 6.1 % ($n = 54$) of children had WAZ >3 or < −3; similarly, 7.0 % ($n = 62$) had weight-for-length *z* scores (WFLZ) >3 or < −3; and 5.8 % ($n = 51$) had head-circumference *z* scores (HCZ) >3 or < −3. Growth scores >3 or < −3 values may represent measurement errors and, therefore, these scores were omitted from the final analyses.

SC and Intervention Conditions

SC Condition Standard clinic care in Cape Town is accessible within 5 km of each study neighborhood. Each antenatal clinic provides comprehensive PMTCT services, including HIV testing. Stand-alone HIV clinics provide access to ARVs for persons with CD4 <350.

Intervention Condition In addition to access to clinic services similar to the SC condition, home visits were conducted. The Philani Nutrition Programme has operated for 29 years in Cape Town, conducting home visits. Township women, who typically have never worked outside the home and who have less than a high school education, were trained as CHW for 1 month in cognitive-behavioral change strategies. CHWs were women selected for having good social and problem solving skills and raising healthy children using their own coping skills, and were trained to provide and apply health information about general maternal and child health, HIV, alcohol use, and nutrition. Videotaped models of common situations that CHWs might face were provided. CHWs were certified and supervised biweekly with random observations of home visits. Eight health messages were delivered on HIV/TB prevention, strategies for PMTCT, the consequences of alcohol use/abuse, the importance of breastfeeding, and how to avoid malnutrition. CHW were to deliver these messages in at least four antenatal visits and four post-natal visits within the first 2 months of life. On average, CHWs made six antenatal visits (SD = 3.8), five postnatal visits between birth and 2 months post-birth (SD = 1.9), and until 6 months post-birth about 1.4 visits/month (range, 0.1–6.4 visits/month). Sessions lasted on average 31 min each. Visits were biannual after 6 months, primarily to check for growth and/or abuse.

Data Analysis We examined the distribution of all variables by the intervention and SC condition. For continuous or discrete variables assessed at multiple time points, we analyzed the data using a longitudinal model with random intercepts for mother or child. We included fixed effects for the neighborhoods and estimated intervention effects as the average of the intervention neighborhood effects minus the SC neighborhood effects. For continuous child variables collected only a single time, we omit the child random effect, but otherwise use the same analysis with random neighborhood effects. Missing data are assumed missing at random; we used all observations that were possible to use, up to the point where mothers or children died or were lost to follow-up. Mothers and children could return to the study even if they missed an assessment. HIV-positive children were omitted from child analyses ($n = 23$ total). All analyses were adjusted for mothers' HIV status. Given their lack of comparability to singleton births, twin and triplet births were excluded from the analyses of child growth scores ($n = 25$). All longitudinal and regression analyses were conducted in SAS Proc Mixed and Proc Glimmix (version 9.4; SAS Institute Inc., Cary, North Carolina). We used Fisher exact tests to compare mortality across conditions. All analyses were based on intent-to-treat models.

Results

Initial Sample Table 1 summarizes the characteristics of the mothers in the intervention and the SC conditions during pregnancy, which have been presented previously (le Roux et al. 2013; Rotheram-Borus et al. 2014). There are very few differences across conditions. Mothers were typically in their mid-20s, without a high school education or job, living in a shack, and about half had experienced food insecurity. Only 9.2 % drank alcohol after recognizing they were pregnant and 25 % prior to pregnancy. Most women had recent sexual partners. Almost every woman had been tested for HIV during

pregnancy and 26.1 % ($n = 295$) were MLH. Table 2 is a correlation matrix of the outcome variables at the baseline assessment.

Maternal Outcomes By 36 months after birth, 1.4 % of mothers ($n = 17$) had died; more often, MLH died compared to mothers without HIV ($p < 0.0001$, OR = 7.9, 95 % CI = (2.4, 33). Significantly more intervention MLH died than SC MLH ($n = 11$ intervention MLH; $n = 2$ SC MLH, $p = 0.02$, OR = 0.19, 95 %CI = [0.02, 0.88]). From 6 to 36 months postbirth, 47 additional mothers (5.4 %) reported an HIV diagnosis, with similar numbers across conditions. Almost all MLH (94.1 %; 318/338) had received antenatal care and PMTCT, as previously reported (Rotheram-Borus et al. 2014). Migration from Cape Town to the Eastern Cape occurred among 2.6 % of participating mothers (27/1052) by the time of the child's birth. At the 6-month assessment, 8.6 % of children were living in the Eastern Cape (87/1006), 29.9 % of these without their mother (26/87). At 18 months, 13.3 % (128/960) of children were in the Eastern Cape, 39.1 % (50/128) without their mother. At 36 months, 24.0 % were in the Eastern Cape (211/878), 62.1 % (131/211) without their mother.

Table 3 compares mothers in the intervention and SC conditions on multiple measures at 36 months (see Web Appendix for summaries of outcomes at each time point and reliability between time points). Mothers in the intervention condition reported significantly less depression on both the EPDS (mean difference, 0.8; $p = 0.009$) and the Hopkins Depression Measure (mean difference, 3.3; $p = 0.011$). There were no significant differences in alcohol use at 36 months or in the frequency of having problematic alcohol use on the AUDIT. Mothers' health was similar across conditions; 18.7 % had given birth again. There were no significant differences in partner-related behaviors, including the likelihood of having a current partner, living with a partner, partner violence, or the number of sexual partners. Similar to earlier reports, most women have a sexual partner, but only about half of the partners live in the household. Mothers were equally likely to receive the child grant (80.5 %), to leave their child in a crèche (59.7 %; day care), and to be employed (44.1 %) across conditions. MLH were equally like to re-engage with HIV care and to receive ARV over time across conditions.

Child Outcomes By 36 months, 8.2 % ($n = 101$) of the children had died; however, children of MLH were no more likely to die than children of mothers without HIV ($p = 0.3$, OR = 0.76, 95 %CI = [0.45, 1.23]). Only 6.2 % ($n = 23$; 10 intervention, 13 SC) of children were seropositive, similar across conditions. Table 4 summarizes the child outcomes. Intervention children had significantly higher scores on the Peabody Picture Vocabulary Test ($p = 0.039$) and were also significantly less likely to have been hospitalized compared to children in the SC condition ($p = 0.026$).

Children were similar across conditions at 36 months on weight, height, and head circumference for age z scores. Intervention children were significantly less likely to be stunted compared to children in the SC condition (24.3 vs 18.1 %. $p < 0.013$, as shown on Fig. 2 and Table 4), but rates of malnutrition were similar across conditions (1.6 %). Overall, 27.3 % have a height, weight, or head circumference for age z score < −2. Figure 2 shows the proportion of stunted children over time from birth to 36 months for the intervention and SC conditions. Post-birth, children across conditions had significantly lower height-for-age z scores at each assessment point, compared to height-for-age z scores at birth: 6 months (est. 0.16, SE = 0.05, df = 2270, $t = 3.32$ $p < 0.0001$); 18 months (est.−0.25, SE = 0.05, df = 2270, $t = -5.2$, $p < 0.0001$); and 36 months (est.−0.87, SE = 0.05, df = 2270, $t = -17.97$, $p < 0.0001$).

Discussion

At 36 months postpartum, intervention mothers were significantly less depressed and intervention children had better vocabularies and were less likely to be hospitalized and

Table 2 Correlation matrix among the outcome variables at the baseline assessment. Overall baseline Pearson correlation

	EPDS	AUDIT	Alcohol	Disease	Partner	Violence	#Partners	Condom
AUDIT score	0.08**	1						
Recent alcohol use	0.08**	0.34***	1					
TB, high BP, or diabetes	0.06*	0.03	−0.01	1				
Current partner	−0.13***	−0.10**	−0.10**	−0.02	1			
Any violence with partner	0.15***	0.17***	0.22***	0.00	0.00	1		
Number of partners	−0.04	−0.05	−0.09**	−0.04	0.53***	0.04	1	
Consistent condom use	−0.04	−0.04	0.02	0.02	0.06	−0.03	0.03	1
Full/part-time/or self-employed	−0.06*	0.02	−0.06*	−0.02	0.05	−0.12***	0.00	0.02

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

Table 3 Maternal outcomes at 36 months grouped by the intervention ($N = 502$) and control ($N = 456$) conditions

	Intervention ($N = 502$)		Standard care($N = 456$)		Total ($N = 958$)	
	n	%	*n*	%	*n*	%
Maternal depression						
Mean EPDS score (SD)	6.1	7.34	6.9	7.9	6.5	7.6**
Mean Hopkins score (SD)	34.2	14.9	36.2	17.4	35.1	16.1**
Alcohol use						
Recent use[a]	84	16.8	85	18.7	169	17.7
AUDIT >2	61	12.2	69	15.2	130	13.6
Maternal health						
TB, high BP, or diabetes	49	9.8	49	10.7	98	10.2
New pregnancies	95	19.0	84	18.5	179	18.7
Develop new HIV case by 36 months	25	5.5	22	5.3	47	5.4
Acquired during pregnancy	12	1.9	10	1.7	22	1.8
Acquired by 6 months	2	0.3	5	0.8	7	0.6
Acquired by 18 months	1	0.2	3	0.5	4	0.3
Acquired by 36 months	10	1.6	4	0.7	14	1.1
HIV prevention						
Maternal partner						
Current partner	442	88.2	394	86.4	836	87.4
Lives with mother	266	53.1	229	50.3	495	51.8
Any violence with intimate partner	72	14.4	70	15.4	142	14.9
Number of recent sexual partners[a]						
0	70	14.0	73	16.0	143	15.0
1	419	83.6	371	81.5	790	82.6
>1	12	2.4	11	2.4	23	2.4
Consistent condom use (10/10)	200	46.4	159	41.7	359	44.2
Linked to care	81	59.1	84	66.1	165	62.5
ARV use by MLH	73	53.3	67	52.8	140	53.0
Family support						
Child grant	401	80.0	369	80.9	770	80.5
Child in Crèche[b]	299	61.1	257	58.1	556	59.7
Full/part-time/or self-employed	220	43.9	202	44.3	422	44.1
Household moves	146	29.1	128	28.1	274	28.6

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

[a] "Recent" always refers to the last 3 months

[b] Measured at 3 year assessment only

stunted compared to those in the control condition. Importantly, we have shown that these benefits accrue, even though home visiting was only about twice a year after the child was 6 months old. While mothers continued to experience poverty, had partners who were typically unemployed, abused alcohol, and became violent at times, their children's developmental capacities evolved. Given these stressors, it may be seen as surprising that any intervention benefits remained at 36 months.

Maternal depression, especially among mothers of young children, often sets lifelong negative developmental trajectories for their children (Tomlinson et al. 2006). Earlier evaluations of this intervention did not find that mothers were less depressed (le Roux et al. 2013; Rotheram-Borus et al. 2014). Yet, it was found at 6 and 18 months that depressed mothers were better caretakers, in being significantly more likely to breastfeed, to breastfeed longer, and to have children with better early growth and higher scores on the Bayley Scales of Infant Development at 18 months (Tomlinson et al. 2015). Even so, mothers had not benefited earlier by being less depressed themselves at 6 or 18 months. The CHWs consistently stressed the importance of maternal caretaking and breastfeeding, but had not been trained to treat maternal depression. Even though there were both direct and indirect intervention effects on maternal depression,

Table 4 Child outcomes at 36 months grouped by the intervention ($N = 492$) and standard care ($N = 447$) conditions

	Intervention ($N = 492$)		Standard care ($N = 447$)		Total ($N = 939$)	
	n	%	*n*	%	*n*	%
Age in months	35.6	2.2	36.5	2.2	36.6	2.2
Child language (SD)						
PPVT score	20.0	7.9	19.2	8.2	19.6	8.1*
Health						
Child admitted to hospital (*N*/%)	122	24.8	141	31.6	263	28.1*
Zero	369	75.2	305	68.4	674	71.9
One	92	18.7	95	21.3	187	20.0
Two	13	2.6	26	5.8	39	4.2
Three	8	1.6	9	2.0	17	1.8
Four	5	1.0	6	1.3	11	1.2
Five +	4	0.8	5	1.1	9	0.9
Growth measures						
Height for age *z* score	−1.2	1.0	−1.0	1.0	−1.1	1.0
Weight for age *z* score	0.1	1.0	0.1	1.0	0.1	1.0
Weight for height by age *z* score	1.0	1.0	1.1	1.0	1.0	1.0
Head circ. for age *z* score	0.9	1.0	0.9	0.9	0.9	1.0
Height/age < −2SD score	75	18.1	95	24.3	170	21.1*
Weight/age < −2SD score	8	1.8	6	1.5	14	1.6

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

the next iteration of the Philani intervention should also target maternal depression.

Children in LMIC are often at a substantial disadvantage by the time that school starts (Engle and Black 2008). Children in the intervention neighborhoods continue to have some advantages over children in the control neighborhoods. Their language development was significantly better than their peers, which should substantially help prepare children for school. There is a substantial literature detailing the impact of combined nutrition and stimulation interventions on improved child language (Aboud and Akhter 2011; Super et al. 1990; Waber et al. 1981). Our vocabulary finding is notable, as cognitive stimulation is not a specific focus of the Philani intervention. What the Philani intervention does focus on is increasing rates of early breastfeeding, illness detection, and early engagement of mothers and infants. We would suggest that the focus of the Philani intervention on the mother-child dyad may have facilitated a process where

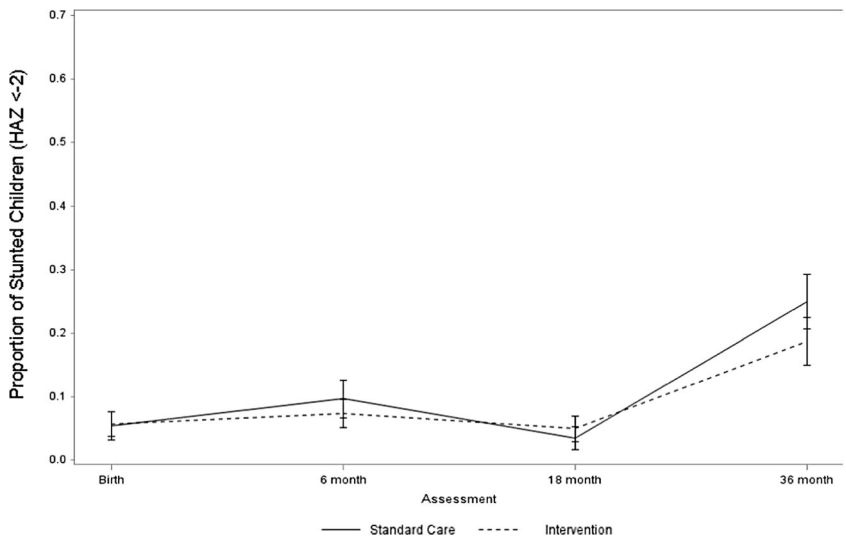

Fig. 2 Proportion of children with height-for-age < −2 (stunting) +/−2 SE at assessment for intervention and control groups

caregivers were able to more sensitively follow infant cues and engage infants in reciprocal exchange (Vally et al. 2015). The precursors to language are extremely complex, but there is evidence of how these early social interaction play a role in language development (Bruner 1985).

Physical health status also appears better, as there were fewer hospitalizations and fewer stunted children. These benefits are key given stunting influences lifelong health and well-being (Victora et al. 2008). The pattern of results for mothers and children across intervention conditions demonstrates the consequences of HIV. More than 5 % of mothers report HIV from 6 to 36 months post-birth; it may be that women knew they were infected earlier and only later disclosed their serostatus to the research team. We could validate maternal HIV status on the government-issued Road-to-Health card, but we did not independently assess HIV status or access clinic records. One third of the newly identified MLH were identified when tested for HIV during a subsequent pregnancy. Messages regarding condom use may have influenced about half of the mothers—an insufficient number to stop a generalized epidemic. Only 1.4 % of mothers died overall, and these were more likely to be MLH and more likely to be in the intervention condition (11 vs 2 MLH deaths). Even though we had 85 % follow-up, if two more mothers in the SC condition had died, there would be no significant difference between the conditions in maternal deaths. Such small numbers lead us to interpret this finding conservatively. A substantial minority of children are missing key supportive services. Even 36 months post-birth, 20 % of households are not receiving a child grant (100 % are eligible). Two of five children get no preschool or crèche experiences, and about one in five has a younger sibling, competing for maternal caretaking. It is also distressing to see the rise in stunting at 36 months and the consistently lower *z* scores in height for age over time.

These data suggest it may be useful to maintain frequent CHW visits past the first 6 months of life. A considerable evidence base has emerged demonstrating the enduring impact of adversity during pregnancy and the first 2 years, resulting in an increased focus of global health policy and intervention on the "first 1000 days" (Black and Aboud 2011; Gertler et al. 2014). Coupled with this, Heckman (1995) has demonstrated the cost effectiveness of early investments in children's well-being compared to later interventions at school or job training programs post-school. We would argue however that the benefits to child development and adult health that accrue across the life-course may require more than simply efficacious interventions in the first 1000 days, and that if early benefits are to be sustained and built upon, that services such as preschool, primary school, and health care need to be widely available to children and families in the years following interventions in the first 1000 days. This has been demonstrated in a recent follow-up of a trial for perinatal depression by Maselko et al. (2015) that showed how the cognitive, socio-emotional, and physical developmental outcomes of children at age 7 years whose mother had prenatal depression did not differ between those who received the intervention and those who did not. In communities without later supports and services, it may be important to sustain visits over the 36–60 months post-birth period, which would cover the phases of children' language development, goal setting, and key processes central to cognitive and socio-emotional development. Children would likely also benefit indirectly by the improved health of their mothers, if visits were extended.

The Philani Programme was implemented with strategies outlined in each of the two most recent literature reviews: CHW selection criteria were based on social competency; CHWs were paid a stipend, and monitoring and supervision was consistent over time and utilized mobile phones. Mentor Mothers received ongoing training with a random visit from their supervisor once every 2 weeks and went to a half day of in-service training monthly. Mentor Mothers were trained on a within-session protocol and a between-session approach to implementing a behavior change program. However, we have no real-time measures of the content covered or the skills addressed in each session. We only can ensure that the Mentor Mothers actually delivered a visit (based on the Global Positioning Information collected).

Mentor Mothers were always cautioned to not provide only information. Features of the Philani that make it successful include a focus on establishing strong relationships; setting goals and helping the mothers acquire the skills to problem solve daily events, especially related to HIV, alcohol, and malnutrition; enduring that the Mentor Mother did not take-on solving the mother's daily challenges, but to keep responsibility with the mothers for creating healthy routines for their children; and explicitly addressing the barriers to reducing alcohol use, seeking HIV treatment, and providing adequate nutrition.

We can only speculate, however, on the competitive advantages of the CHWs employed by the Philani Programme that may have led to these sustained benefits at 36 months. Five features distinguish these CHW: (1) they are selected based on being *positive peer deviants* (Bolles et al. 2002); (2) CHW are trained to address multiple health challenges, not only one; (3) there are clear expectations for performance (e.g., a defined caseload of 40 families) and accountability structures for both interpersonal supervision and monitoring by paper documentation of visits or mobile phones; (4) CHWs are encouraged to leverage their relationship to motivate mothers to care well for their infants; and (5) the CHW are paid a stipend and

only employed half time (as this is the first job for almost all the CHW).

These features appear to the researchers to offer a competitive advantage, but must be empirically evaluated to confirm if they are, in fact, advantageous. The opportunity exists currently as Philani Intervention Model is being diffused to rural South Africa, Ethiopia, and Swaziland.

A universal goal for developing interventions in LMIC is sustainability. Africa has particular challenges with broad implementation of effective interventions due to the poorly trained and poorly monitored health personnel. Philani has been operating since the early 1990s. CHW salaries and experience are in line with South African government guidelines and would therefore be sustainable. As the South African government begins to implement a model that targets multiple domains, we have demonstrated a strategy to implement and to evaluate such an intervention. In addition to sustainability, home visits offer a viable strategy to circumvent challenges associated with obtaining healthcare from clinics such as appointment scheduling, long waiting lines, and expensive transport. A CHW approach grounded in cognitive-behavioral skills, with local-tailored content addressing local health risks, strong supervision, and accountability be a strategy that is scalable globally. The results of this RCT will be applicable to the existing 1.2 million CHW globally (Singh and Sachs 2013) to the 50 % of Africa that is similarly deeply rural, and responds to the recent Accra Call for Action for global funding at the national level for CHW (One Million Community Health Worker's Campaign 2015).

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Compliance with Ethical Standards

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Conflict of Interest The authors disclose that they have no conflict of interest.

Ethical Approval The Institutional Review Boards of University of California Los Angeles (UCLA), Stellenbosch University, and Emory University approved the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

Appendix

Table 5 Web Appendix: summary statistics for outcomes and reliability between time points

Variable	Summary statistics			Reliability over time
	Assessment month	Statistic	Value	
EPDS	0	*N*	1209	0.63
	0	Mean	10.72	
	0	SD	6.95	
	3	*N*	1030	
	3	Mean	7.89	
	3	SD	7.62	
	6	*N*	1032	
	6	Mean	7.47	
	6	SD	7.80	
	18	*N*	1004	
	18	Mean	6.80	
	18	SD	7.30	
	36	*N*	929	
	36	Mean	6.53	
	36	SD	7.64	
Any alcohol use	0	*N*	1115	0.69
	0	*n*	272	
	0	%	24 %	
	3	*N*	1030	
	3	*n*	3	
	3	%	0 %	
	6	*N*	979	
	6	*n*	101	
	6	%	10 %	
	18	*N*	1004	
	18	*n*	122	
	18	%	12 %	
	36	*N*	928	
	36	*n*	163	
	36	%	18 %	
Current partner	0	*N*	1113	0.57
	0	*n*	1037	
	0	%	93 %	
	6	*N*	979	
	6	*n*	838	
	6	%	86 %	
	18	*N*	1004	
	18	*n*	874	
	18	%	87 %	
	36	*N*	929	
	36	*n*	809	
	36	%	87 %	
Audit score	0	*N*	1115	0.73
	0	Mean	1.42	
	0	SD	2.94	
	3	*N*	1029	
	3	Mean	0.44	
	3	SD	1.71	
	6	*N*	979	
	6	Mean	0.57	
	6	SD	1.88	
	18	*N*	1004	
	18	Mean	0.71	
	18	SD	2.09	
	36	*N*	928	
	36	Mean	0.98	
	36	SD	2.37	
TB, high BP, or diabetes	0	*N*	1209	0.64
	0	*n*	142	
	0	%	12 %	
	3	*N*	1030	

Table 5 (continued)

Variable	Summary statistics			Reliability over time
	Assessment month	Statistic	Value	
	3	*n*	79	
	3	%	8 %	
	6	*N*	979	
	6	*n*	97	
	6	%	10 %	
	18	*N*	1004	
	18	*n*	102	
	18	%	10 %	
	36	*N*	928	
	36	*n*	95	
	36	%	10 %	
Any violence with intimate partner	0	*N*	1209	0.66
	0	*n*	448	
	0	%	37 %	
	6	*N*	979	
	6	*n*	225	
	6	%	23 %	
	18	*N*	993	
	18	*n*	148	
	18	%	15 %	
	36	*N*	927	
	36	*n*	139	
	36	%	15 %	
Consistent condom use	0	*N*	883	0.67
	0	*n*	133	
	0	%	15 %	
	6	*N*	724	
	6	*n*	289	
	6	%	40 %	
	18	*N*	820	
	18	*n*	357	
	18	%	44 %	
	36	*N*	787	
	36	*n*	343	
	36	%	44 %	
Full time, part-time, or self-employed	0	*N*	1209	0.63
	0	*n*	180	
	0	%	15 %	
	6	*N*	979	
	6	*n*	212	
	6	%	22 %	
	18	*N*	1004	
	18	*n*	259	
	18	%	26 %	
	36	*N*	929	
	36	*n*	410	
	36	%	44 %	
Number of partners	0	*N*	1209	0.51
	0	Mean	0.89	
	0	SD	0.32	
	6	*N*	979	
	6	Mean	0.75	
	6	SD	0.44	
	18	*N*	1004	
	18	Mean	0.83	
	18	SD	0.40	
	36	*N*	928	
	36	Mean	0.87	
	36	SD	0.40	

References

Aboud, F. E., & Akhter, S. (2011). A cluster-randomized evaluation of a responsive stimulation and feeding intervention in Bangladesh. *Pediatrics, 127*, e1191–e1197. doi:10.1542/peds.2010-2160.

Aracena, M., Krause, M., Pérez, C., Méndez, M. J., Salvatierra, L., Soto, M., & Altimir, C. (2009). A cost-effectiveness evaluation of a home visit program for adolescent mothers. *Journal of Health Psychology, 14*, 878. doi:10.1177/1359105309340988.

Black, M. M., & Aboud, F. E. (2011). Response feeding is embedded in a theoretical framework of responsive parenting. *Journal of Nutrition, 141*, 490–494.

Bolles, K., Speraw, C., Berggren, G., & Lafontant, J. G. (2002). Ti Foyer (hearth) community-based nutrition activities informed by the positive deviance approach in Leogane, Haiti: A programmatic description. *Food & Nutrition Bulletin, 23*, 9.

Bruner, J. (1985). Child's talk: Learning to use language. *Child Language Teaching and Therapy, 1*, 111–114.

Campbell, C., & Scott, K. (2011). Retreat from Alma Ata? The WHO's report on Task Shifting to community health workers for AIDS care in poor countries. *Global Public Health, 6*, 125.

Cox, J. L., Holden, J. M., & Sagovsky, R. (1987). Detection of postnatal depression—Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry, 150*, 782–786.

Dawson, D. A., Grant, B. F., & Stinson, F. S. (2005). The AUDIT-C: Screening for alcohol use disorders and risk drinking in the presence of other psychiatric disorders. *Comprehensive Psychiatry, 46*, 405–416.

de Onis, M., & Blossner, M. (2003). The World Health Organization Global Database on Child Growth and Malnutrition: Methodology and applications. *International Journal of Epidemiology, 32*, 518–526.

Deane, F. P., Leathem, J., & Spicer, J. (1992). Clinical norms, reliability and validity for the Hopkins Symptom Checklist-21. *Australian Journal of Psychology, 44*, 21–25. doi:10.1080/00049539208260158.

Derogatis, L. R., Lipman, R. S., Rickels, K., Uhlenhuth, E. H., & Covi, L. (1974). The Hopkins Symptom Checklist (HSCL): A self-report symptom inventory. *Behavioral Science, 19*, 1–15.

Dunn, L. M. (1965). *Peabody Picture Vocabulary Test*. Circle Pines: American Guidance Service.

Engle, P. L., & Black, M. M. (2008). The effect of poverty on child development and educational outcomes. *Annals of the New York Academy of Sciences, 1136*, 243–256. doi:10.1196/annals.1425.023.

Flay, B. R., Biglan, A., Boruch, R. F., Castro, F. G., Gottfredson, D., Kellam, S., . . . Ji, P. (2005). Standards of evidence: Criteria for efficacy, effectiveness and dissemination. *Prevention Science, 6*, 151–175. Retrieved from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=16365954.

Gertler, P., Heckman, J., Pinto, R., Zanolini, A., Vermeersch, C., Walker, S., . . . Grantham-McGregor, S. (2014). Labor market returns to an early childhood stimulation intervention in Jamaica. *Science, 344*, 998–1001. doi:10.1126/science.1251178.

Grantham-McGregor, S. M., Powell, C. A., Walker, S. P., & Himes, J. H. (1991). Nutritional supplementation, psychosocial stimulation, and mental development of stunted children: The Jamaican Study. *The Lancet, 338*, 1. doi:10.1016/0140-6736(91)90001-6.

Heckman, J. J. (1995). Lessons from the Bell Curve. *Journal of Political Economy, 103*, 1091–1120. doi:10.1086/262014.

Heckman, J. J. (2006). Skill formation and the economics of investing in disadvantaged children. *Science, 312*, 1900–1902. doi:10.1126/science.1128898.

Kalembo, F. W., & Zgambo, M. (2012). Loss to followup: A major challenge to successful implementation of prevention of mother-to-child

transmission of HIV-1 programs in Sub-Saharan Africa. *ISRN AIDS, 2012*, 598817. doi:10.5402/2012/589817.

Lawrie, T. A., Hofmeyr, G. J., de Jager, M., & Berk, M. (1998). Validation of the Edinburgh Postnatal Depression Scale on a cohort of South African women. *The South African Medical Journal, 88*, 1340–1344.

le Roux, I. M., Tomlinson, M., Harwood, J. M., O'Connor, M., Worthman, C. M., Mbewu, N., & Rotheram-Borus, M. J. (2013). Outcomes of home visits for pregnant mothers and their infants: A cluster randomised controlled trial. *Aids, 27*, 1461. doi:10.1097/QAD.0b013e3283601b53.

Marmot, M., Friel, S., Bell, R., Houweling, T. A., Taylor, S., & Health, C. o. S. D. o. (2008). Closing the gap in a generation: Health equity through action on the social determinants of health. *Lancet, 372*, 1661–1669. doi:10.1016/S0140-6736(08)61690-6.

Maselko, J., Sikander, S., Bhalotra, S., Bangash, O., Ganga, N., Mukherjee, S., . . . Rahman, A. (2015). Effect of an early perinatal depression intervention on long-term child development outcomes: Follow-up of the Thinking Healthy Programme randomised controlled trial. *Lancet Psychiatry, 2*, 609–617. doi:10.1016/S2215-0366(15)00109-1.

Michalopoulos, C., Lee, H., Duggan, A., Lundquist, E., Tso, A., Crowne, S. S., . . . Knox, V. (2015). The mother and infant home visiting program evaluation: Early findings on the maternal, infant, and early childhood home visiting program. *ACF Web Report.* Retrieved from http://www.acf.hhs.gov/sites/default/files/opre/mihope_report_to_congress_final_1.pdf.

Nahar, B., Hossain, M. I., Hamadani, J. D., Ahmed, T., Grantham-McGregor, S., & Persson, L. A. (2012). Effects of psychosocial stimulation on improving home environment and child-rearing practices: Results from a community-based trial among severely malnourished children in Bangladesh. *BMC Public Health, 12*, 622. doi:10.1186/1471-2458-12-622.

Olds, D. L., Kitzman, H., Knudtson, M. D., Anson, E., Smith, J. A., & Cole, R. (2014). Effect of home visiting by nurses on maternal and child mortality: Results of a 2-decade follow-up of a randomized clinical trial. *JAMA Pediatrics, 168*, 800. doi:10.1001/jamapediatrics.2014.472.

One Million Community Health Worker's Campaign. (2015). Financing community health worker systems at scale in sub-Saharan Africa: Workshop report. Retrieved from http://1millionhealthworkers.org/files/2015/09/1mCHW_SSC_Workshop_Report_External_2015-09-10_Final.compressed-1.pdf.

Pakendorf, C., & Alant, E. (1996). Culturally valid assessment tools: Northern Sotho translation of the Peabody Picture Vocabulary Test-Revised. *The South African Journal of Communication Disorders, 44*, 3–12.

Panter-Brick, C., Eggerman, M., & Tomlinson, M. (2014). How might global health master deadly sins and strive for greater virtues? *Global Health Action, 7*, 23411. doi:10.3402/gha.v7.23411.

Peacock, S., Konrad, S., Watson, E., Nickel, D., & Muhajarine, N. (2013). Effectiveness of home visiting programs on child outcomes: A systematic review. *BMC Public Health, 13*, 17. doi:10.1186/1471-2458-13-17.

Rahman, A., Iqbal, Z., Roberts, C., & Husain, N. (2009). Cluster randomized trial of a parent-based intervention to support early development of children in a low-income country. *Child: Care, Health and Development, 35*, 56. doi:10.1111/j.1365-2214.2008.00897.x.

Rotheram-Borus, M. J., le Roux, I. M., Tomlinson, M., Mbewu, N., Comulada, W. S., le Roux, K., & Swendeman, D. (2011). Philani Plus (+): A Mentor Mother community health worker home visiting program to improve maternal and infants' outcomes. *Prevention Science, 12*, 372. doi:10.1007/s11121-011-0238-1.

Rotheram-Borus, M. J., Richter, L. M., van Heerden, A., van Rooyen, H., Tomlinson, M., Harwood, J. M., . . . Stein, A. (2014). A cluster randomized controlled trial evaluating the efficacy of peer mentors to support South African women living with HIV and their infants. *PLoS One, 9*, e84867. doi:10.1371/journal.pone.0084867.

Saunders, J. B., Aasland, O. G., Babor, T. F., de la Fuente, J. R., & Grant, M. (1993). Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption. *Addiction, 88*, 791. doi:10.1111/j.1360-0443.1993.tb02093.x.

Singh, P., & Sachs, J. D. (2013). 1 million community health workers in sub-Saharan Africa by 2015. *Lancet, 382*, 363–365. doi:10.1016/S0140-6736(12)62002-9.

Super, C. M., Herrera, M. G., & Mora, J. O. (1990). Long-term effects of food supplementation and psychosocial intervention on the physical growth of Colombian infants at risk of malnutrition. *Child Development, 61*, 29–49. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/2307045.

Tomlinson, M., Cooper, P. J., Stein, A., Swartz, L., & Molteno, C. (2006). Post-partum depression and infant growth in a South African peri-urban settlement. *Child: Care, Health and Development, 32*, 81–86. doi:10.1111/j.1365-2214.2006.00598.x.

Tomlinson, M., Rotheram-Borus, M. J., Harwood, J., le Roux, I. M., O'Connor, M., & Worthman, C. (2015). Community health workers can improve child growth of antenatally-depressed, South African mothers: A cluster randomized controlled trial. *BMC Psychiatry, 15*, Artn 225. doi:10.1186/S12888-015-0606-7.

Vally, Z., Murray, L., Tomlinson, M., & Cooper, P. J. (2015). The impact of dialogic book-sharing training on infant language and attention: A randomized controlled trial in a deprived South African community. *Journal of Child Psychology and Psychiatry, 56*, 865–873. doi:10.1111/jcpp.12352.

Victora, C. G., Adair, L., Fall, C., Hallal, P. C., Martorell, R., Richter, L., . . . Child Undernutrition Study, G. (2008). Maternal and child undernutrition: Consequences for adult health and human capital. *Lancet, 371*, 340–357. doi:10.1016/S0140-6736(07)61692-4.

Waber, D. P., Vuori-Christiansen, L., Ortiz, N., Clement, J. R., Christiansen, N. E., Mora, J. O., . . . Herrera, M. G. (1981). Nutritional supplementation, maternal education, and cognitive development of infants at risk of malnutrition. *The American Journal of Clinical Nutrition, 34*, 807–813. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7223696.