11TH ANNUAL MEETING OF ISMPP

OPTIMIZING SCIENTIFIC VALUE:
SMART AND SYSTEMATIC APPROACHES TO MEDICAL PUBLICATIONS

April 27–29, 2015
Hyatt Regency Crystal City
Arlington, VA, USA

ISMPP International Society for Medical Publication Professionals™

Panel

- **Mariam Bibi, PhD**

Director of Real World Evidence, Complete True Life

- **Alexander Liede, MSc, PhD**

Director, Centre for Observational Research, Amgen, Inc

- **Robert LoCasale, PhD**

Director of Quality, Design & Analytics in Medical Evidence and Observational Research, AstraZeneca

11TH ANNUAL MEETING OF ISMPP

Embracing Real-World Evidence

International Society for Medical Publication Professionals™

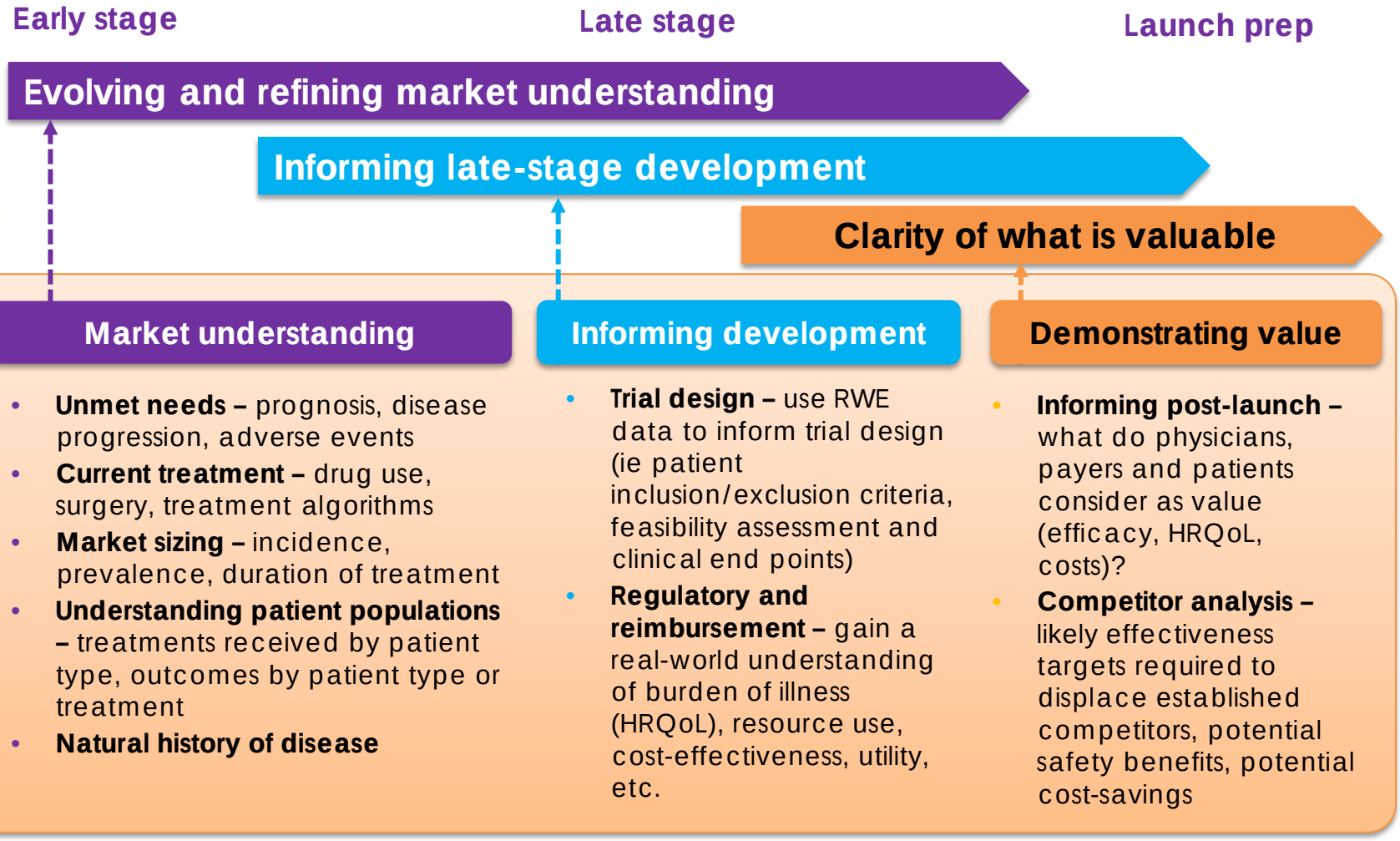
A rose by any other name would smell as sweet…

- Real-world data, real-world evidence (RWE)
- Big data
- Observational research
- Non-interventional research

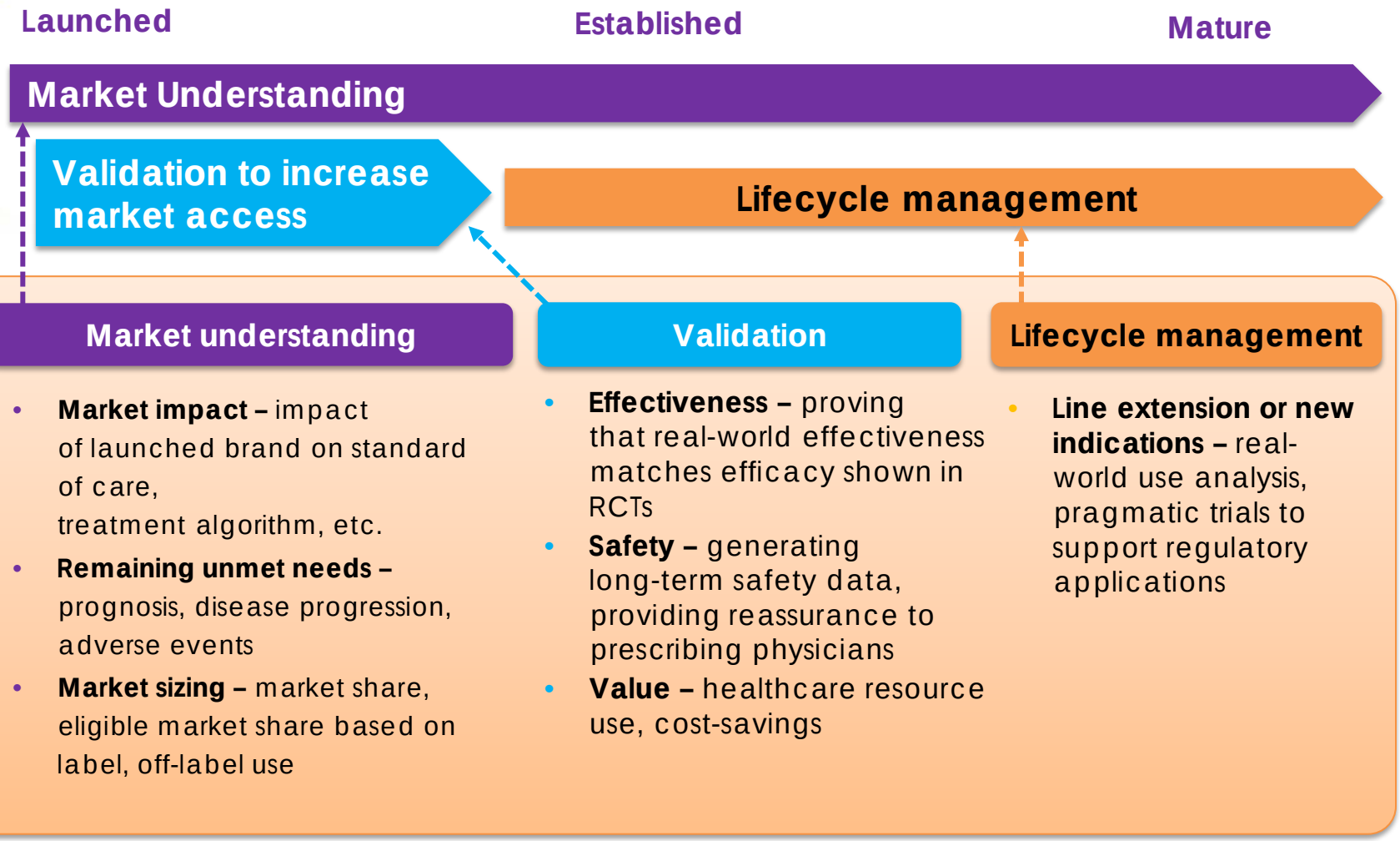
"… any data not collected in conventional randomised controlled trials. It includes data from existing secondary sources (e.g. databases of national health services) and the collection of new data, both retrospectively and prospectively."
RAND Europe 2014

RWD is the cornerstone of epidemiology

How can real-world studies add to generating evidence and value strategy pre-launch?



How can real-world studies add to generating evidence and value strategy post-launch?



Embracing Real-World Evidence

European perspective

ISMPP International Society for Medical Publication Professionals™

RWE gains momentum: 2008

- “I think we give too much attention to the results of randomised controlled trials.” He called for observational studies, including historical controlled trials and case-control studies, to be used more widely

- Professor Rawlins explained that RCTs are good at looking at effectiveness among the particular group of people being studied but that the results do not necessarily apply “in the real world”

- Professor Rawlins pointed out that, throughout its existence, NICE has given weight to other methods, like observational studies, as well as RCTs. “I think this approach should be used more widely,” he said, adding that it could lead to drugs being available on the market earlier

RWE complements RCTs

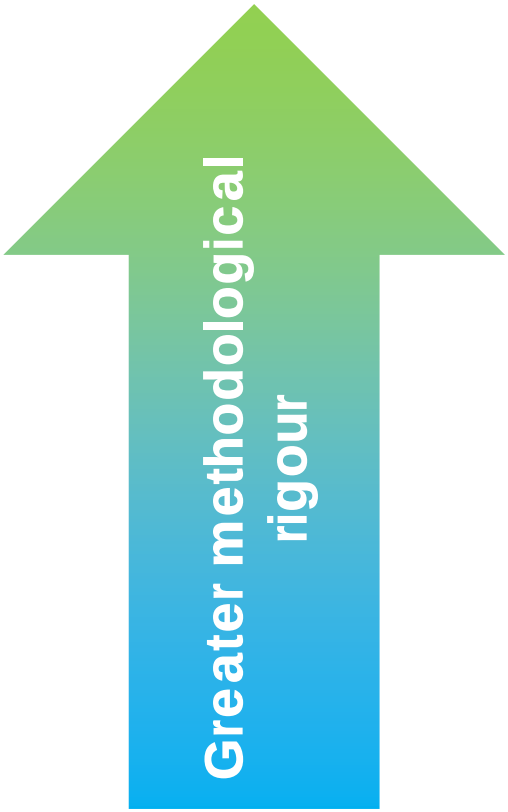
- Effectiveness:
  - Real-world effectiveness in routine clinical practice (HCP and patient behaviour)
  - Adherence, guideline implementation, comorbidities, prescribing behaviour
- Risk/benefit profile
  - Long-term clinical benefits and adverse events
- Comparative evidence
  - Comparison against standard of care (varies by geographic location and patient type)
- Additional end points
  - QoL, patient perceptions, direct/indirect costs

A number of factors have aligned to make real-world data an integral component of evidence generation

1. Healthcare systems are having to derive increased value from medicines in targeted patient populations to maximise healthcare resources while providing optimal patient outcomes
2. Innovative high-cost technologies
3. Stakeholders' appetite for data beyond efficacy and safety
4. Advances in technology have allowed easier, faster access to multiple data sources

Perceived hierarchy of evidence

- Pragmatic trials
- Administrative/claims data
- Electronic medical records
- Disease registries – active
- Disease registries – passive
- Observational studies (prospective, retrospective)
- Patient-reported outcomes
- Questionnaires/health surveys



RWE Europe 2015:
A collaborative approach

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

efpia
European Federation of Pharmaceutical Industries and Associations

abpi
Bringing medicines to life

NICE National Institute for Health and Care Excellence

Get Real

Working collaboratively to develop robust methodologies for real-world studies

Key takeaways

- RWD is applicable to multiple stakeholders (payers/providers, HTA bodies, regulators, HCPs and patients) – translate data to evidence
- Develop a value driven evidence base, incorporating multiple data sources (RCTs and RWE) – 'tapestry of evidence'
- Iterative evidence generation – communicated to relevant stakeholders

LEVERAGING ELECTRONIC MEDICAL RECORD DATA FOR APPROVAL, COMMERCIAL AND DEVELOPMENT PURPOSES

Alexander Liede, PhD
Center for Observational Research
Amgen Inc.

April 29, 2015

ISMPP International Society for Medical Publication Professionals™

The Center for Observational Research formed in 2010

Clinical Development

Contribution to excellence in clinical program design and implementation

Pharmacovigilance

PV in support of global safety commitments

Forecasting

Profiling diseases for market potential

Reimbursement

Contribution to ongoing assessment of benefits and risks (value)

We maintain, curate & analyze RWD datasets that provide longitudinal patient-level data

OPTUMInsight™

CPRD
MORE DIMENSIONS TO DATA

Fresenius Medical Care

TRUVEN
HEALTH ANALYTICS
Formerly the Healthcare Business of Thomson Reuters
TRUSTED. PROVEN.

FLATIRON

DaVita.

GEISINGER

cegedim
Strategic Data

PYGARGUS
Real World Outcomes Research
Pygargus is now part of IMS Health

DOPPS

aro

ims | INTELLIGENCE. APPLIED.

United States Renal Data System

We aim to develop an integrated, efficient and progressive RWD system to support a multitude of efforts

- Ready-access to descriptive epidemiology in target diseases and treatments
- Treatment patterns
- Planning for post-marketing commitments
- Comparative effectiveness research
- RCT design
  - background rates
  - inclusion/exclusion
  - geographic footprint
- Regulatory filings
- Drug safety research
- Quality of care research

Data

Information

Evidence/Insights

Knowledge

EpicGraphic.com

Big Data Defined

An all-encompassing term for any collection of data sets so large and complex that it becomes difficult to process using on-hand data management tools or traditional data processing applications.

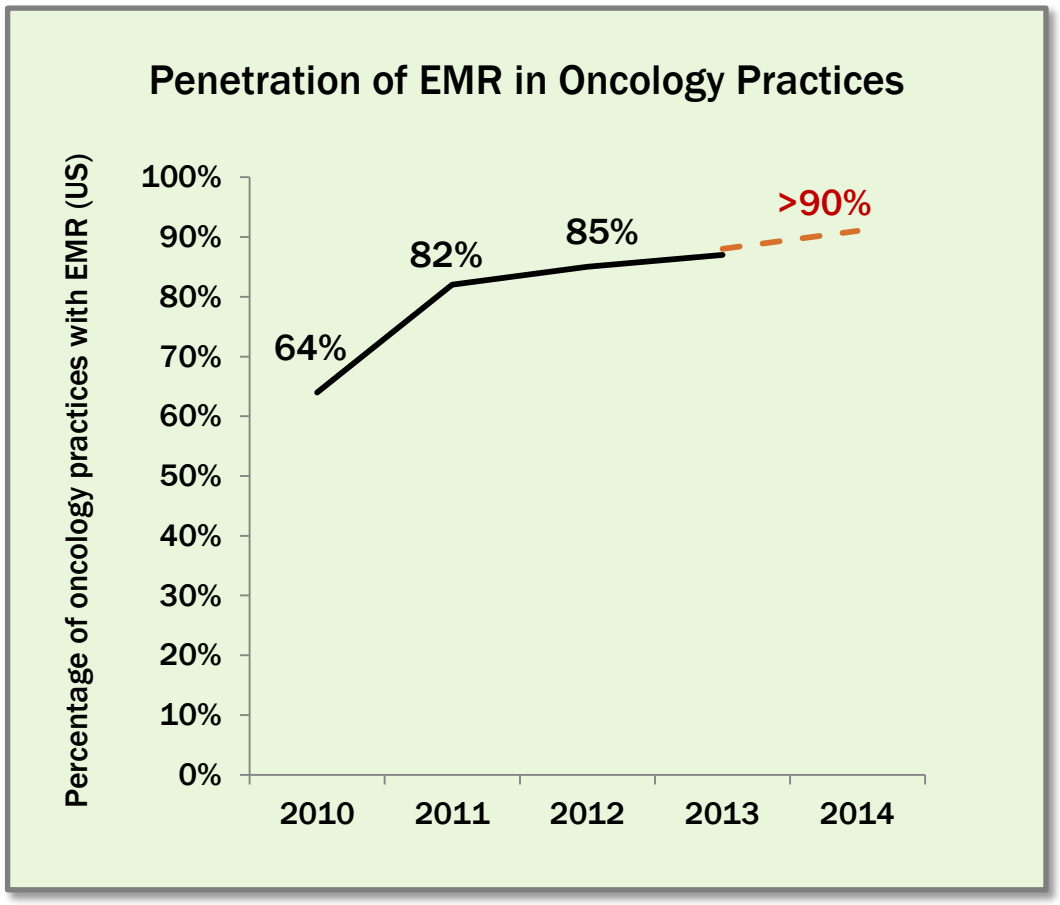
From Wikipedia, accessed 8/22/14

FULFILLING THE PROMISE OF RWD: CASE STUDIES IN ONCOLOGY

Motivating Ideas

- Most data about treatment and outcomes of cancer patients resides in EMR & claims databases
- Advances in technology will soon enable us to harvest information contained in EMRs that, until now, has been largely inaccessible
- The resulting granularity of information per patient, rather than the large number of patients accessible, is the key to valid real-world research

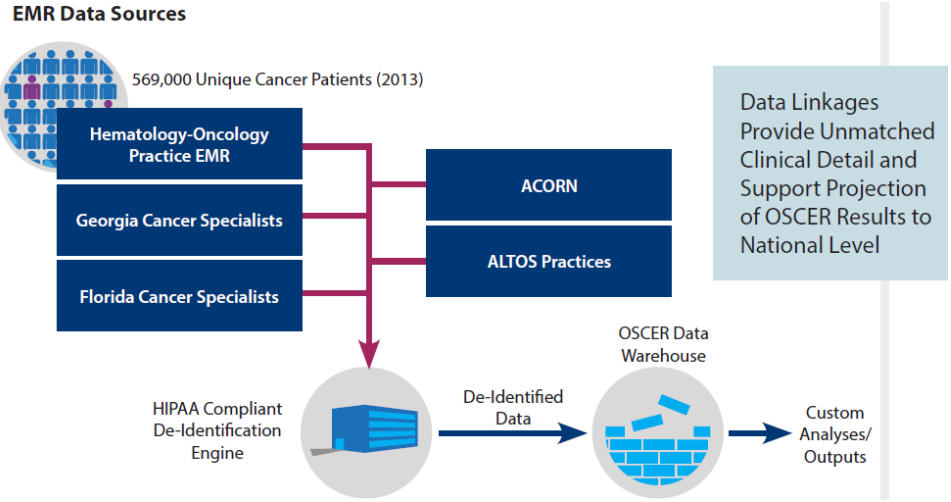
In the US, oncology clinics use EMR to track patient care

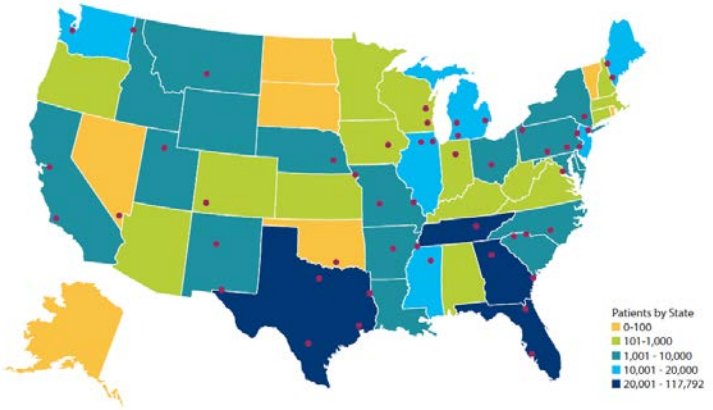


Source: National Practice Benchmark for Oncology (2011-2013 publications)

OSCER (Oncology Services Comprehensive Electronic Records)

- OSCER is a customized source of RWD in oncology
  - Amgen recognized the value of EMR early on (tracing back to 2004)
- From OSCER, teams have conducted impactful observational research and published meaningful insights on cancer care





JNCCN "Amgen, in collaboration with IMS Health, has created a robust EMR data platform for business analytics, safety, clinical development, effectiveness, outcomes, and epidemiologic research."

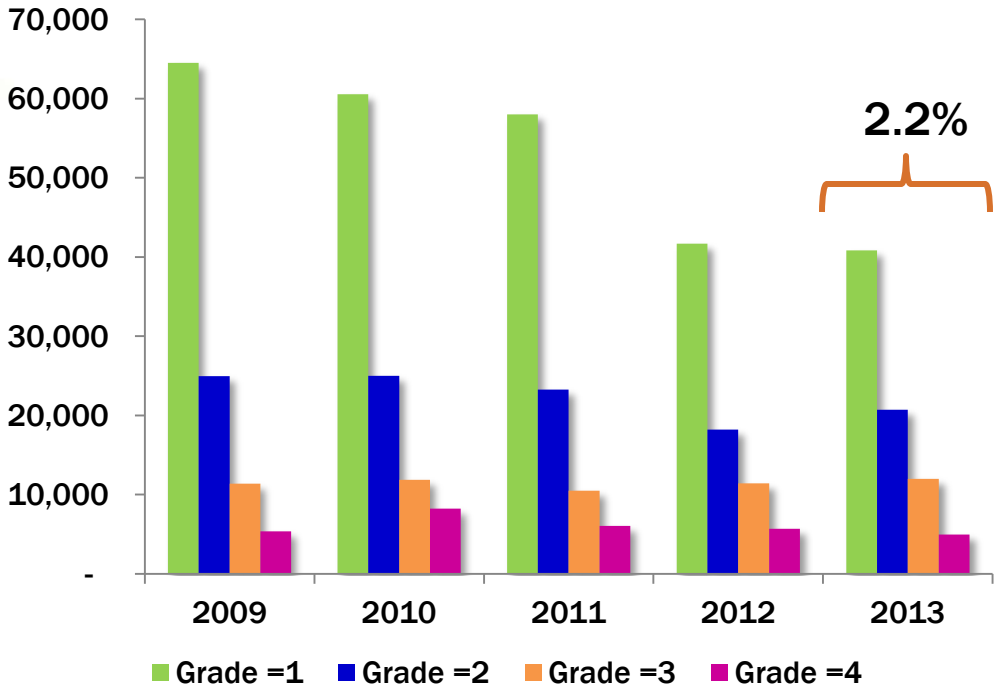
JNCCN 2013;11:S-1-S-12

Achieving Orphan Drug Designation using EMR data (Sep 2013)

2013 ASBMR, 2013/15 ECC posters; manuscript phase

Prevalence of Hypercalcemia of Malignancy

patients in OSCER 2009–2013
w/ serum calcium & albumin (n=224,817)



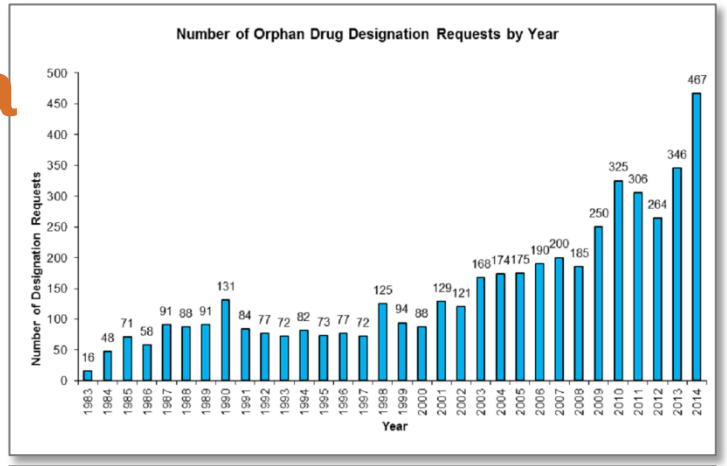
Bottom line:

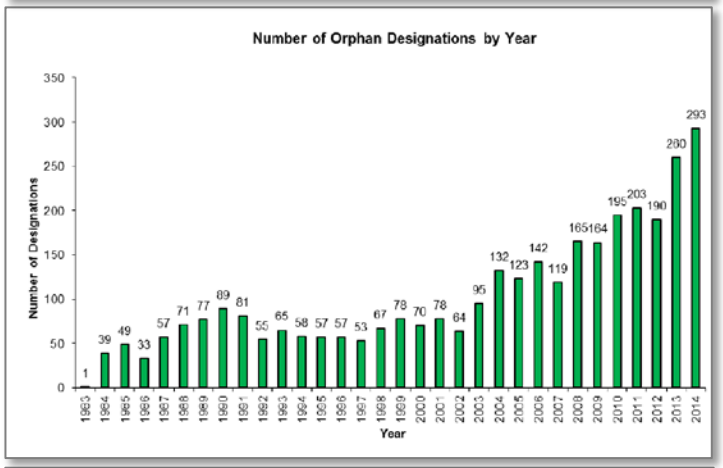
- <100,000 cancer patients in a given year experience grade ≥1 HCM
- Highest among multiple myeloma (8.4%), and lung cancer (3.8%); consistent with literature (range <1% to 30% depending on tumor type)*
- Survival worse among HCM vs. non-HCM patients

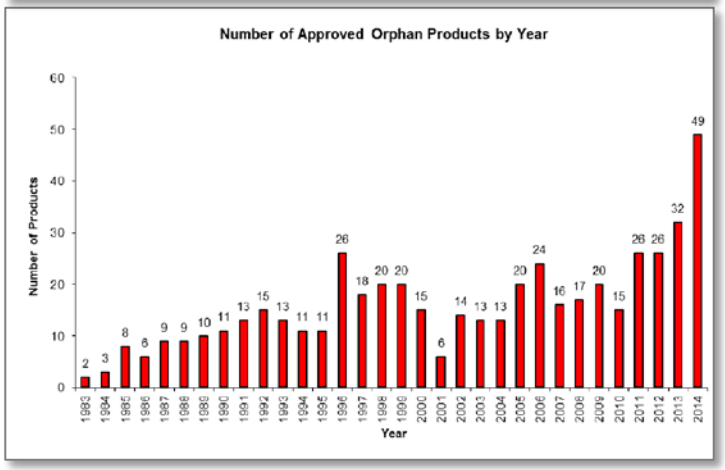
*Most common in multiple myeloma, breast cancer, lung cancer;
Basso U et al. Malignant Hypercalcemia. Curr Med Chem 2011;18:3462-7

Cancer is increasingly a set of Orphan Diseases

- Last year, FDA's Orphan Drug Program shattered records: 293 (2014) vs. 88 (2000)
- With personalized medicines, genetically-defined populations and biomarker-driven efficacy/safety data…
  - fewer patients for clinical trials, resulting in single-arm trials
  - how to produce appropriate comparator arm?
- FDA encourages inclusion of RWD
  - historical comparator data contributed to recent drug approval (Dec 2014)
  - FDA hosting ***Accelerating Anticancer Agent Development and Validation (AAADV) Workshop***, May 6-8, Bethesda MD featuring four case studies:
    - http://www.acceleratingworkshop.org/2015-program/







Source: FDA Orphan Drug Designations and Approvals database
http://www.fdalawblog.net/fda_law_blog_hyman_phelps/orphan-drugs/

Supporting forecasting with EMR data linked to claims to estimate and project prevalence of breast cancer

- OncoTypeDx testing is routine (ER, PR, HER2)… so, why are results found in only 30-40% of structured EMR?
- Linkage of EMR data allowed for stratified weighting, imputation of missing data and projections
- Approx. 800,000 women with early-stage (stage I-III) breast cancer were under treatment or surveillance in 2012

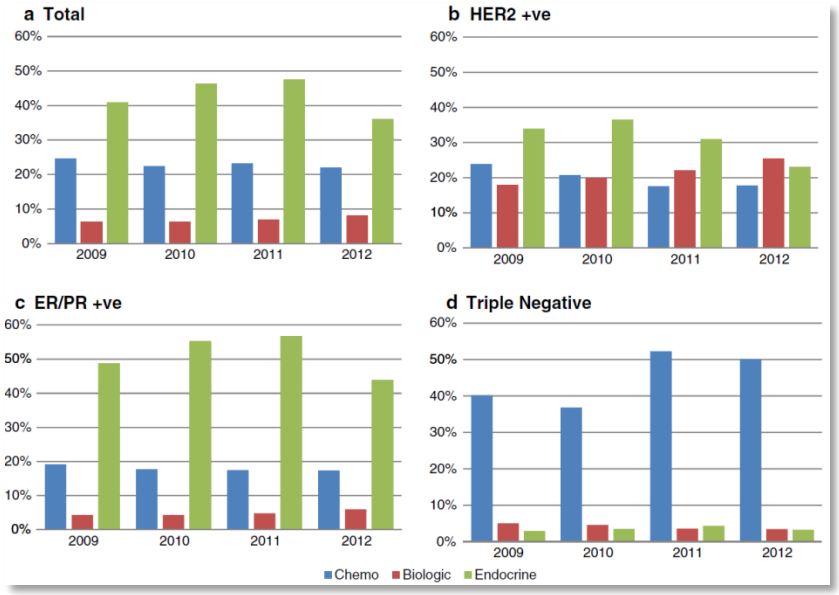
Breast Cancer Res Treat (2014) 146:637–646
DOI 10.1007/s10549-014-3052-1

EPIDEMIOLOGY

Prevalence of women with early-stage breast cancer receiving active management using electronic health records from oncology clinics in the United States

Rohini K. Hernandez · David Quach · Sally W. Wade · Melissa Pirolli · Jane Quigley · Steven A. Narod · Alexander Liede

Received: 26 June 2014 / Accepted: 27 June 2014 / Published online: 23 July 2014



Scandinavia: An Epidemiologist's Dream

Science 31 March 2000:
Vol. 287 no. 5462 pp. 2398-2399
DOI: 10.1126/science.287.5462.2398

NEWS FOCUS

EPIDEMIOLOGY

When an Entire Country Is a Cohort

Lone Frank*

Lone Frank writes from Copenhagen, Denmark.

Denmark has gathered more data on its citizens than any other country.

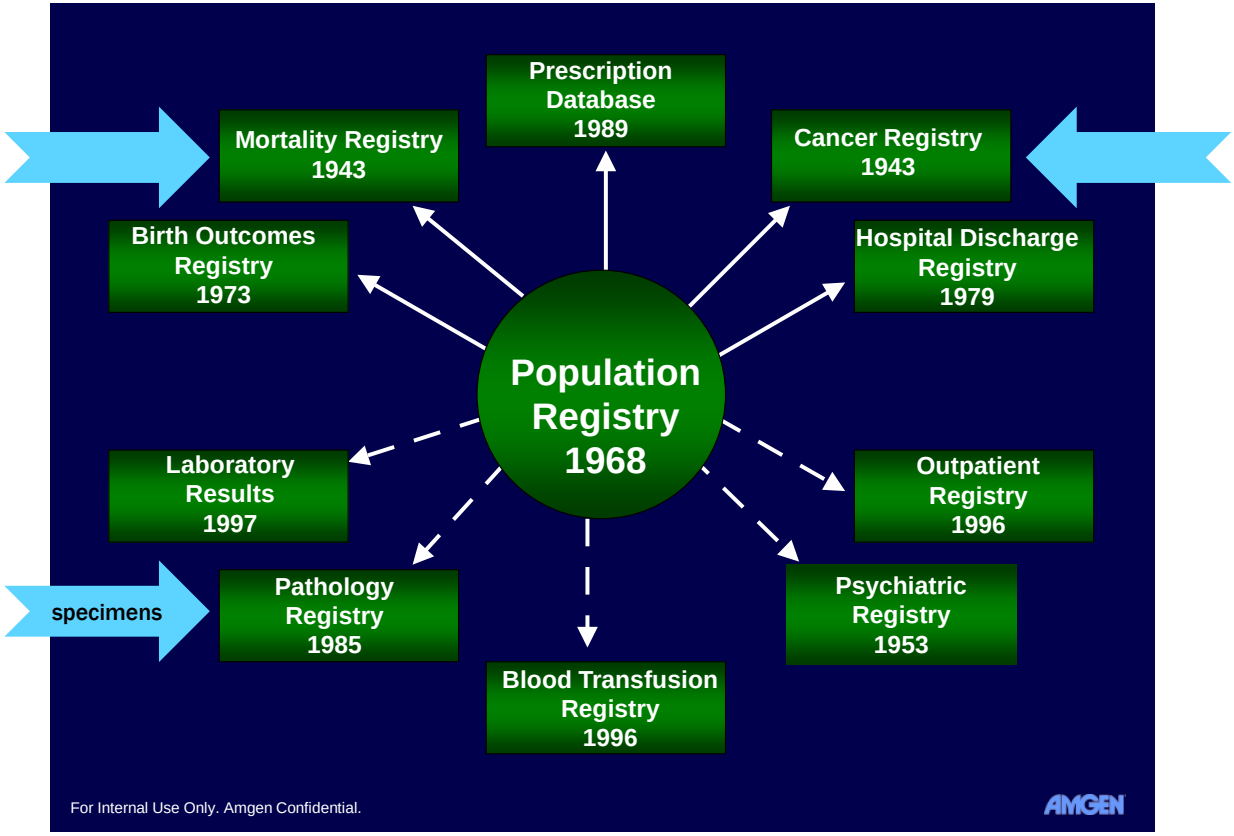
Science 11 July 2003:
Vol. 301 no. 5630 p. 163
DOI: 10.1126/science.301.5630.163

NEWS FOCUS

EPIDEMIOLOGY

The Epidemiologist's Dream: Denma

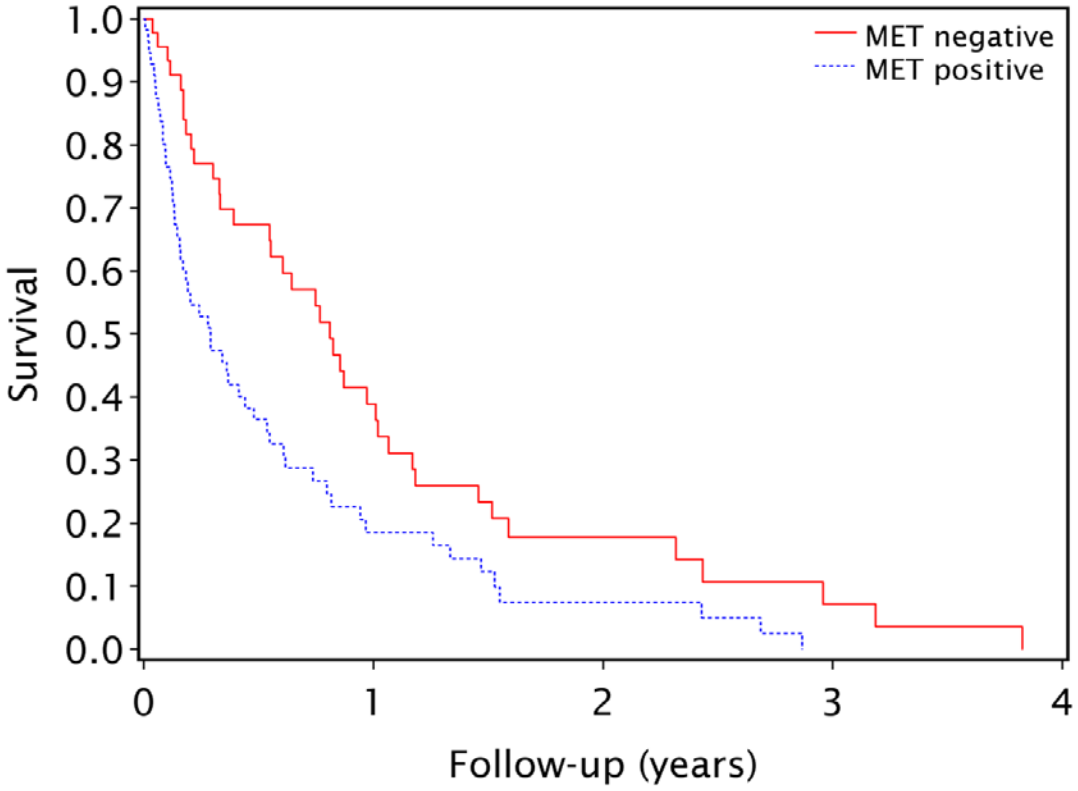
Lone Frank*



For example, linking cancer patient data to biomarker analyses, and mortality outcomes

RWD can be used to validate case reports or smaller (biomarker) studies

MET +ve gastric cancer associated with appreciably shorter survival (n=101)

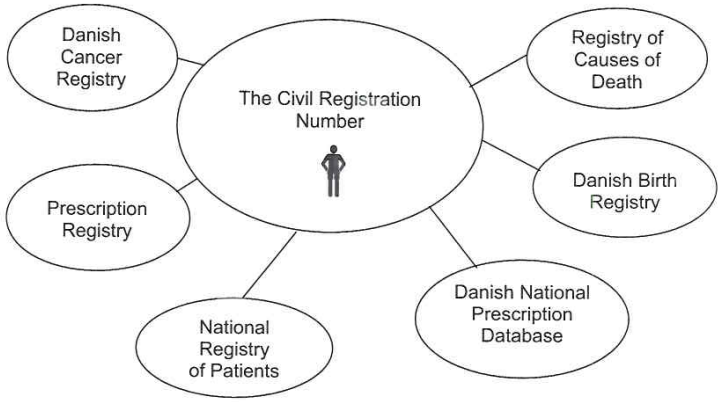


Source: Erichsen et al. Tumor MET expression in patients with gastric cancer in Denmark. ASCO GI 2013

Data quality remains a concern

Two Solutions:

1. Link and Merge Data
   - Link to claims data
   - Link beyond oncology clinic
   - Big Data
   - Build Scandinavia



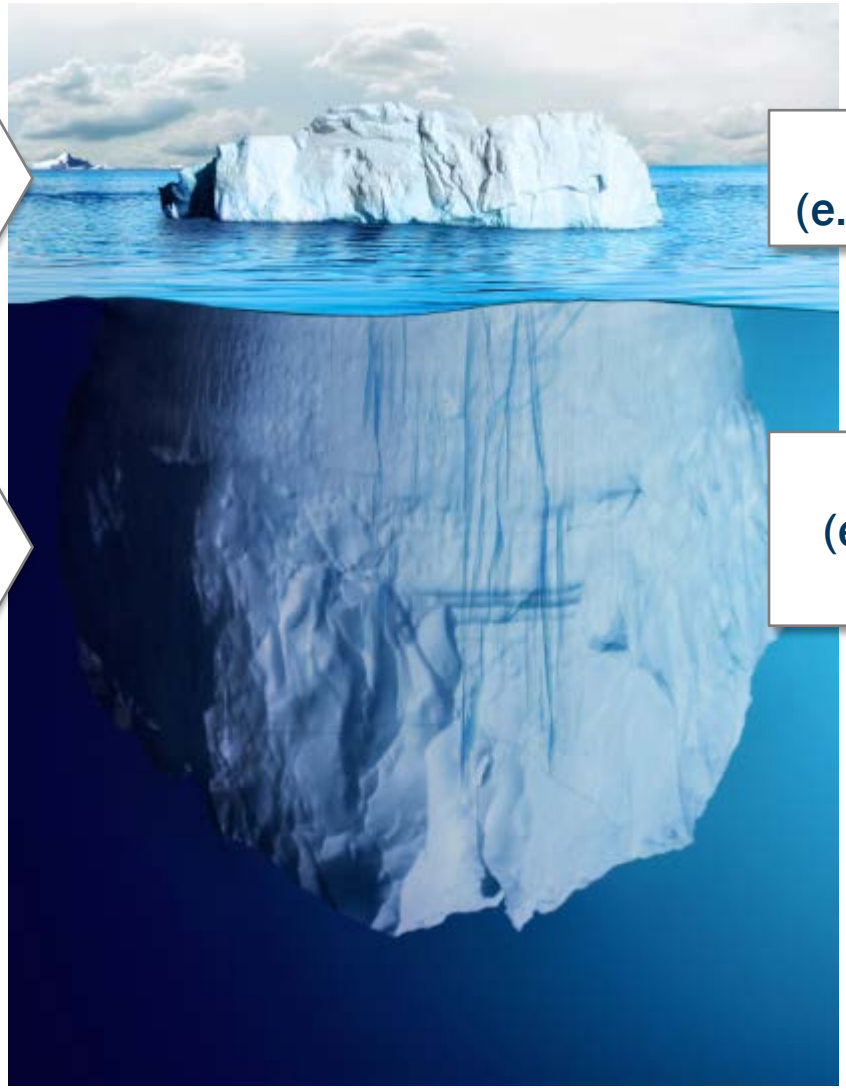
2. Improve Data Capture and Completeness
   - Clinics to capture more data
     - Stakeholders (call to action)
     - Patient reported data
   - Leverage technological developments for EMRs

NEXT GENERATION EMR

Much of the EMR data remains untapped

EMR research to date

There's more to EMR



Structured data
(e.g., demographics, stage, diagnosis)

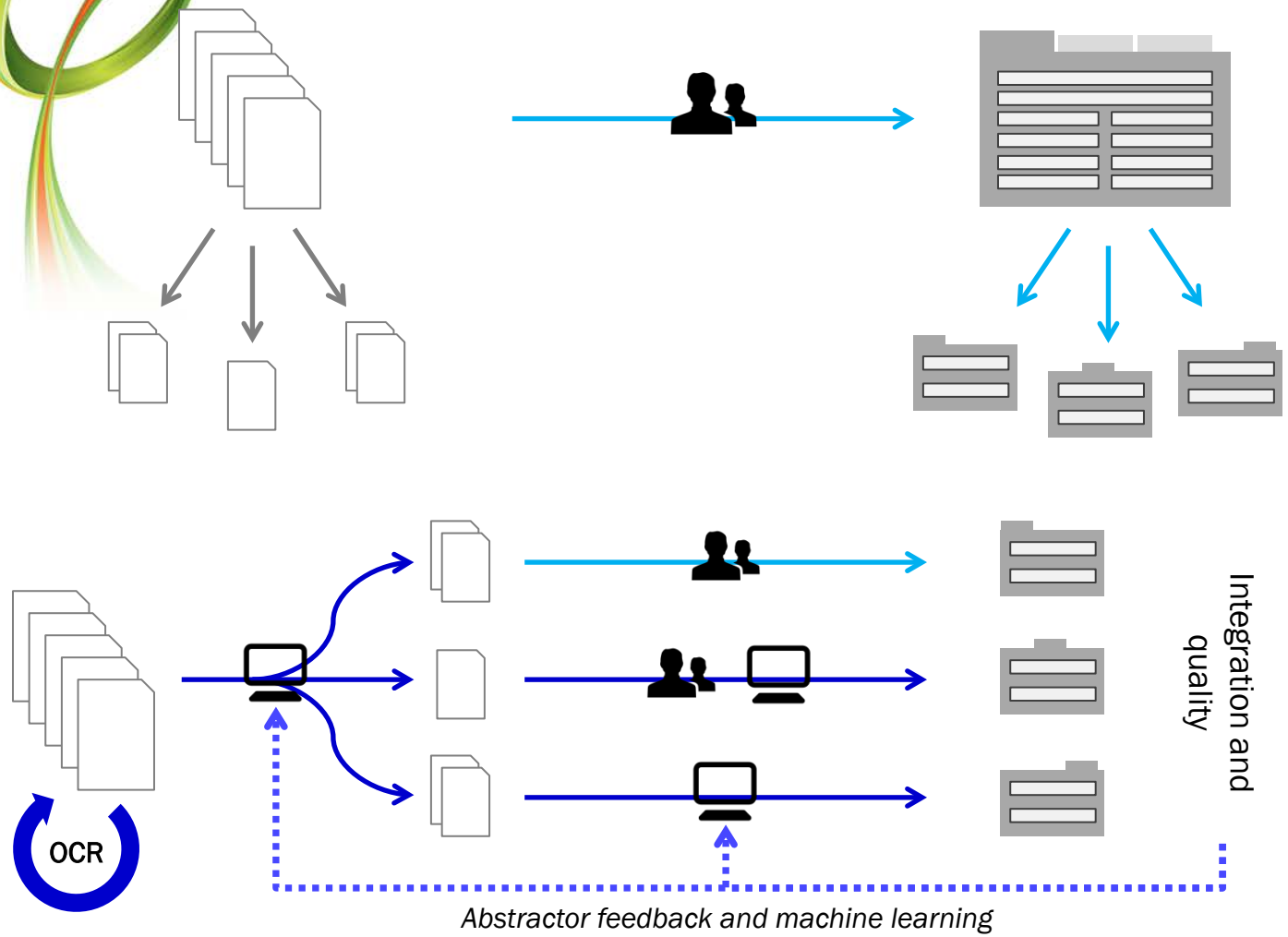
Unstructured data
(e.g., pathology, stage, biomarkers, physician notes)

Even structured EMR data poses challenges in research

2220	Blood Serum Albumin	g/dL
QD25001600	ALBUMIN/GLOBULIN RATIO QD	(calc)
QD25001400	ALBUMIN QD	g/dL
QD50058600	ALBUMIN	%
QD50055700	ALBUMIN	g/dL
CL3215104	Albumin % (EPR)	%
LC001081	ALBUMIN, SERUM (001081)	g/dL
LC003718	Albumin, U	%
LC001488	Albumin	g/dL
LC133751	Albumin, U	%
CL3215162	Albumin%, Urine	%
CL3215160	Albumin, Urine	mg/24hr
3234	ALBUMIN SS	g/dL
LC133686	Albumin, U	%
QD50060710	MICROALBUMIN	mg/dL
QD50061100	MICROALBUMIN/CREATININE RATIO, RANDOM URINE	mcg/mg creat
QD85991610	ALBUMIN	relative %
50058600	ALBUMIN UPEP RAND	%
CL3210074	ALBUMIN LEVEL	g/dL
QD86008211	ALBUMIN/GLOBULIN RATIO	(calc)
LC149520	Albumin	g/dL
QD45069600	PREALBUMIN	mg/dL
QD900415245	ALBUMIN, SERUM	mg/dl
QD900429745	ALBUMIN	g/dL
CL3215124	Albumin Electrophoresis	g/dL
LC016931	Prealbumin	mg/dL
QD50060800	MICROALBUMIN, 24 HOUR UR	mg/24 h
QD50060900	MICROALBUMIN, 24 HOUR UR	mcg/min
QD85994821	ALBUMIN,SERUM	g/dL
CL3213320	PREALBUMIN	mg/dL
QD85995225	PROTEIN ELECTROPHORESIS ALBUMIN	g/dL

Albumin [Mass/volume] in Serum or Plasma	**g/dL**

Technology-Enabled EMR Abstraction



"Traditional"

Chart abstraction

- Expensive
- Inaccurate

Technology-enabled abstraction

Modular Approach

- Use a machine wherever appropriate
- Human review to ensure quality
- Extremely efficient
- Always improving

Improving Data Depth and Completeness

Demographics	Structured Only	With Unstructured
Date of birth	100%	100%
Gender	100%	100%
ECOG at bone met dx	0%	⇧ 65%
Pain at bone met dx	< 5%	⇧ 75%
Menopause status	< 5%	⇧ 71%
Smoking status	< 5%	⇧ 88%

Diagnosis	Structured Only	With Unstructured
ER/PR	35%	⇧ 98%
HER2	36%	⇧ 85%
Histology	36%	⇧ 79%
Primary resection	-	99%

Labs[1]	Structured Only	With Unstructured
Lab name	100%	100%
Result / units	100%	100%

Medications[1]	Structured Only	With Unstructured
Drug name	100%	100%
Dose, Admin date	100%	100%

Bone metastases	Structured Only	With Unstructured
Date of bone diagnosis[2]	*inaccurate*	100%
Extent of bone mets	-	83%
Weight-bearing vs. non	-	90%

Visceral metastases	Structured Only	With Unstructured
Location of visceral mets	20-25%	⇧ 99%
Date of diagnosis	*inaccurate*	⇧ 99%

SREs	Structured Only	With Unstructured
Date of SRE	*varies*	⇧ 99%
Type of SRE	*varies*	⇧ 100%

Improving EMR data quality in OSCER

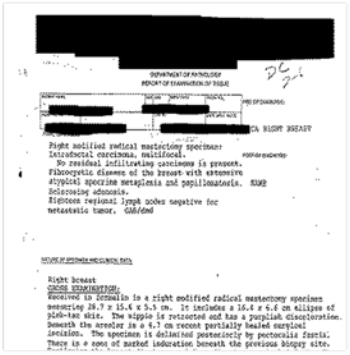
Structured data harmonization

2220	Blood Serum /Albumin	g/dL
QD25001600	ALBUMIN/GLOBULIN RATIO QD	(calc)
QD25001400	ALBUMIN QD	g/dL
QD50058600	ALBUMIN	%
QD900415245	ALBUMIN, SERUM	mg/dl

1751-7	Albumin [Mass/volume] in Serum or Plasma	g/dL

Mapping of all structured EMR fields to a common vocabulary standard

Unstructured data processing



Leverage unstructured data processing to drive accuracy and completeness of metrics

PUBLICATION AND ETHICAL CONSIDERATIONS

Are we developing a caste system in clinical epidemiology research?

"Under the new Policy, ASCO ***will not accept*** an abstract or paper describing ***company-funded original research*** if the first, last, or corresponding author has been the Company's employee, investor, or paid speaker during the previous 2 years."

ASCO 2013. Policy for Relationships with Companies: Background and Rationale. J Clin Oncol Published Ahead of Print on April 22, 2013 as 10.1200/JCO.2013.49.4997

ISPE responds and ASCO reconsiders its Policy

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2014; **23**: 1–2
Published online 21 November 2013 in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3546

ISPE COMMENTARY

International Society for Pharmacoepidemiology (ISPE) statement on American Society of Clinical Oncology's new policy for relationships with companies

John Acquavella[1], Til Sturmer[2] and Jesper Hallas[3]*

[1] *Amgen, Global Epidemiology, Thousand Oaks, California, United States*
[2] *Deparment of Epidemiology, University of North Carolina at Chapel Hill, School of Public Health, Chapel Hill, North Carolina, United States*
[3] *Research Unit of Clinical Pharmacology, University of Southern Denmark, Odense, Denmark*

"ASCO leadership has carefully considered the concerns expressed by the biomedical community regarding the author restrictions in the 2013 COI policy and has decided to ***suspend enforcement*** of these restrictions for a period of ***at least 3 years***."

ASCO 2014. The Changing Landscape of Conflict of Interest Supports Further Study of ASCO Authorship Restrictions for Research Studies J Clin Oncol: Published Ahead of Print on February 10, 2014 as 10.1200/JCO.2014.55.4006

Scientific work should be judged on merit, not on presumed conflict of interest

"The ***objectivity*** of the [scientific] process depends on each contribution receiving its due regard, whatever the motivations for bringing it. It depends on ***judging a work on its merits, rather than on the inferred state of mind of the author***."

From Ken J. Rothman. JAMA 1993; 269:2782-2784, p 2783.

Big Data: Mobile technology, social media, and the future of medicine

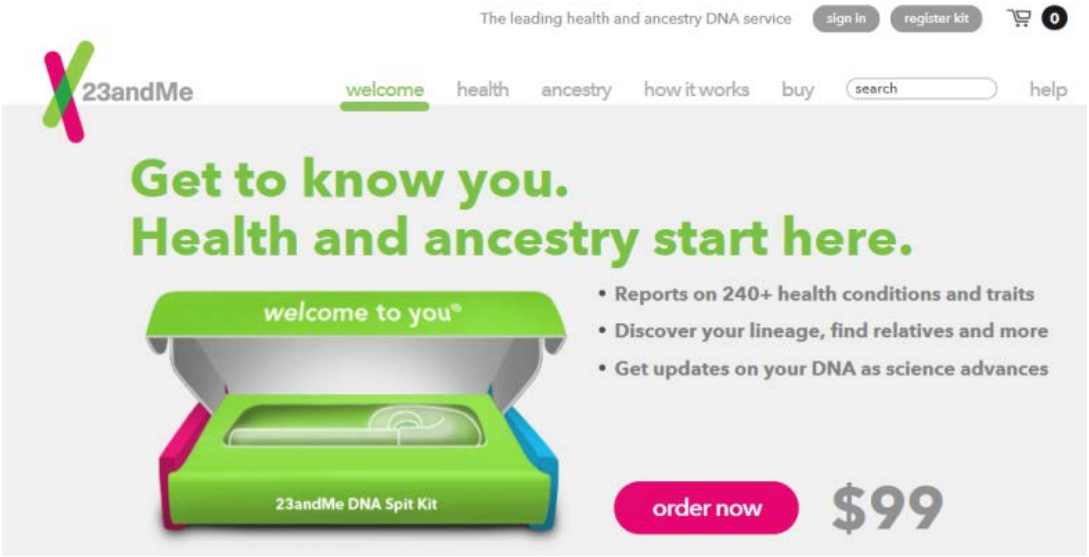
- Big Data refers to very large super-sets of data that include RWD and data from other sources
  - social media (Twitter, Facebook)
  - consumer data (purchasing habits)
  - health technologies (Fitbit)
  - non-health behaviors
- Big Data is also a conceptualization in which all of these sources of information may be integrated and used for healthcare decision-making
- Technological advances are being made to help FDA monitor social media to identify safety signals/adverse events
- The FDA currently uses mobile apps
- MedWatcher.org and app allow individuals to report adverse events

Value of Big Data stems from linkage to other data sources

- Is the consent process clear?
- Who owns these meta-data?
- What about security and privacy?

Ethical debate will follow Big Data

Are the proper standards in place?



F.D.A. Orders Genetic Testing Firm to Stop Selling DNA Analysis Service

Peter DaSilva for The New York Times

The personal genome testing company 23andMe is backed by Google and run by Anne Wojcicki, wife of the Google co-founder Sergey Brin.

By ANDREW POLLACK
Published: November 25, 2013

In a crackdown on genetic testing that is offered directly to consumers, the Food and Drug Administration has demanded that 23andMe immediately cease selling and marketing its DNA testing service until it receives clearance from the agency.

In a scathing warning letter that the agency posted on its website on Monday, it said that 23andMe had failed to provide adequate evidence that its product, Personal Genome Service, provided accurate results.

"F.D.A. is concerned about the public health consequences of inaccurate results from the P.G.S. device," the agency said in its letter.

FACEBOOK
TWITTER
GOOGLE+
SAVE
EMAIL
SHARE
PRINT
REPRINTS

FDA vs. 23andMe… a business plan develops

November 2013

- FDA Warning Letter about the accuracy and standards of test results from the Personal Genome Service
  - Of greatest concern was testing for mutations related to high risk of breast cancer, stating that a false positive could lead to an unnecessary preventive mastectomy
- Class-action lawsuit

September 2014

- Informed consent and privacy controversy (Close Relatives check box)… ***"One step forward, 23 Steps back"***
- Creation of Chief Privacy Officer

December 2014

- Expansion to UK sparks privacy concerns… *"Will my data be sold to Google?"*

January 2015

- 23andMe strike $60M with Genentech to analyze DNA from 3000 Parkinson's patients

Concluding Thoughts

- Real world data are underutilized
- Computer technology will vastly increase the richness and accuracy of data per patient
- Given sufficiently rich/accurate data, methods for the analysis of non-randomized RWD have advanced markedly to enable valid effect estimates in many instances
- FDA is increasingly interested in observational data
- Clinical journals and reviewers are sometimes less comfortable with observational research
- Ethical debate will follow

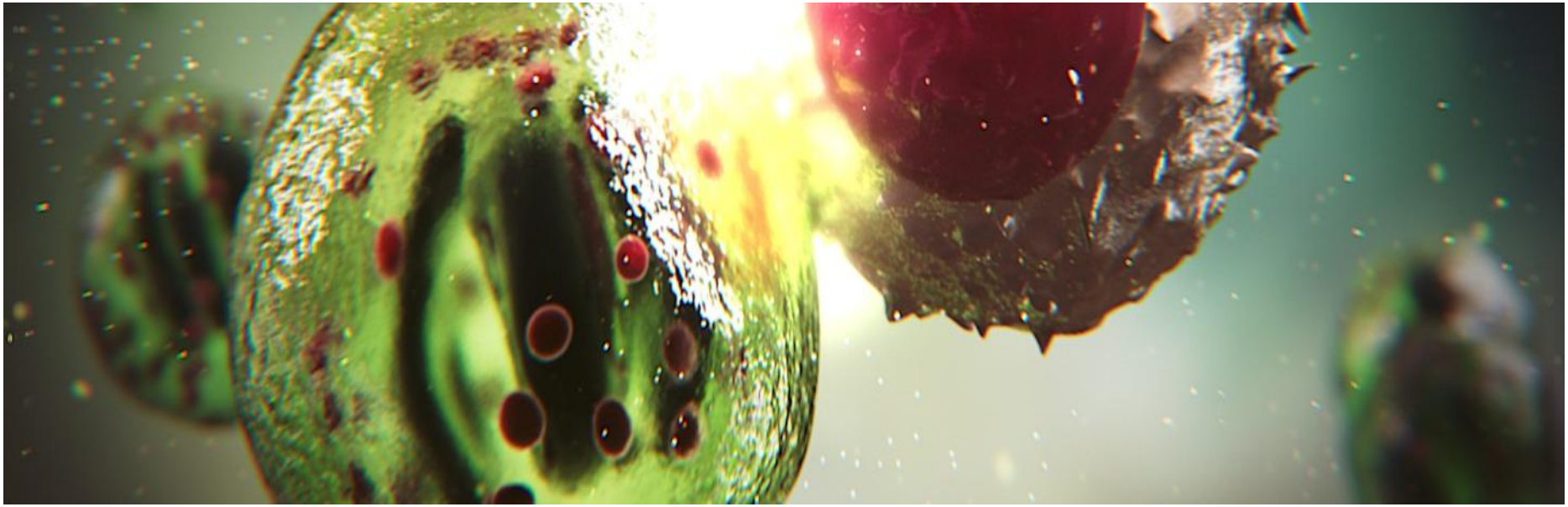
AstraZeneca Real World Evidence Vision

Robert LoCasale

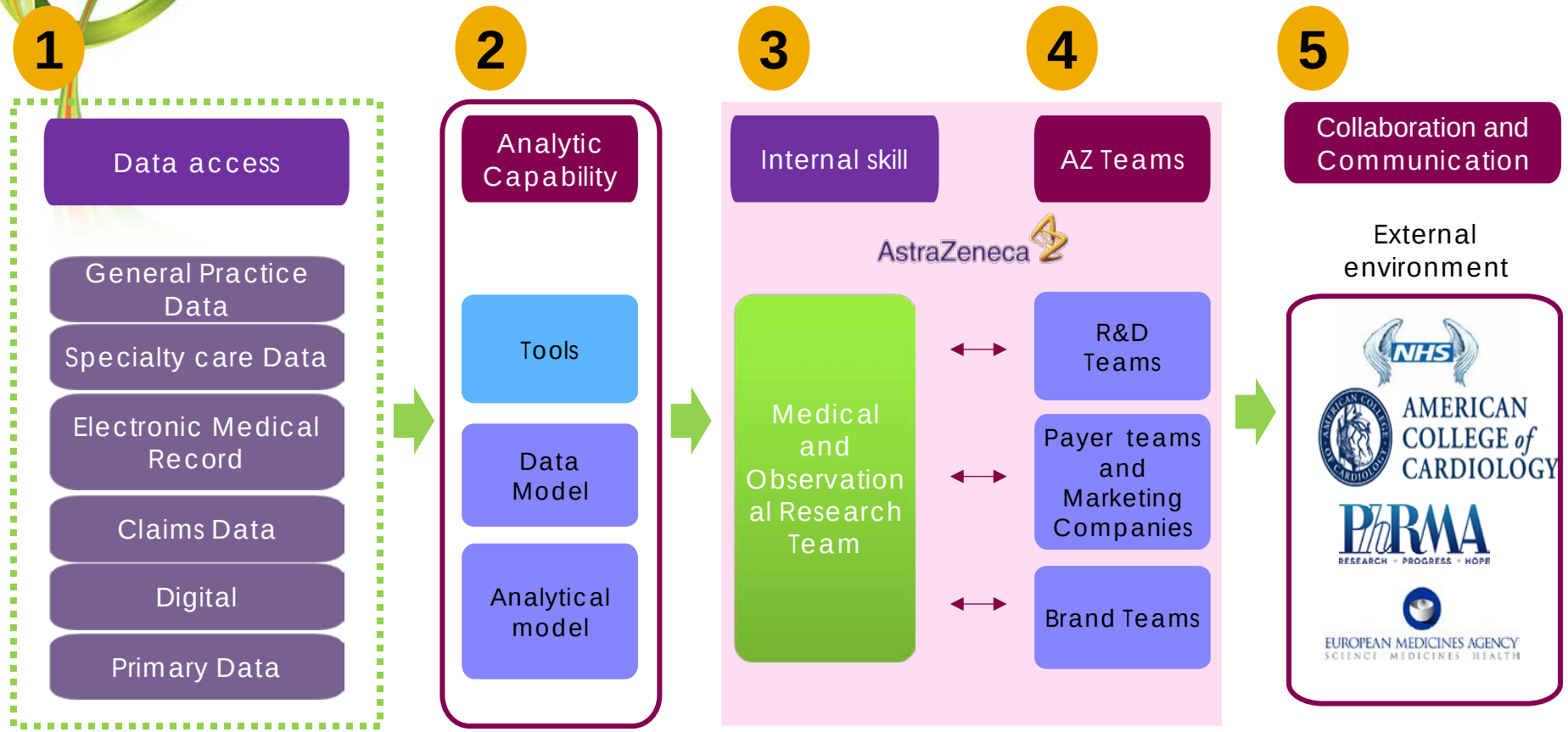
Group Director of Quality, Design & Analytics
Global Medical Affairs | Medical Evidence & Observational Research

International Society for Medical Publication Professionals
Hyatt Regency Crystal City
Arlington, VA, USA

April 27-29 2015



Five priorities of the AstraZeneca Real World Evidence vision to drive innovation and scientific leadership



A single skill center delivering Real World Evidence for all the company

3

Medical Evidence & Observational Research Team

- Epidemiologists
- RWE Specialists
- Study Delivery Specialists
- Methods & Data Analysts

- **Statistical Support**
- **IT/IS Support**
- **Health Informatics Support**
- **Publication Support**

Case Example: Opioid-Induced Constipation

The Landscape for Opioid Use and OIC

- Chronic pain is a persistent and debilitating condition that affects almost one-third of the adult population in the US and nearly 20% of adult Europeans.
- IOM estimates annual direct and indirect economic and social costs exceeding $600 billion
- Diagnosing opioid-induced constipation since it yields multiple definitions and has no clear consensus
- Prevalence estimates vary from 15% to 90%
- No consensus on how to effectively manage OIC
  - However, recommendations for subsequent lines of treatment vary and often highlight options that indirectly address symptoms of OIC
- Patients often cycle through options and may even go off their opioid when their pain subsides

Purpose and Impact of RWE for OIC

Need for OIC Burden of Illness (BOI) Data

- Payers do not recognize OIC burden and reluctant to reimburse without evidence to show need for new treatment options
- Support FDA Advisory Committee and Trial Generalizability needs

– BOI Study was designed to address Payer Needs and fill an evidence gap

- **Disease Education** – data used in pre-launch materials to establish the Clinical, QoL burden of OIC to highlight need for new treatment options
- **Payer Value Dossiers** – data used in payer dossiers submissions to establish Burden and Unmet Need
- **Economic Models** – data was used from the study to build Cost Effectiveness Models for informing the Economic Impact of OIC

– Need for Background Cardiovascular Event Rates in OIC

- Database studies were designed to address Risk Management Plan and an Advisory Committee activities

OIC BOI Study: Study Design Summary and Objectives

- Prospective 6-month longitudinal study was conducted in the US, Canada, UK, and Germany to understand the burden of OIC in chronic opioid users
- Cohort study design that includes web-based longitudinal patient and physician questionnaires collected at baseline and follow-up plus site-based retrospective chart data abstraction
- Exposed to daily opioid therapy for ≥ 4 weeks for the treatment of chronic non-cancer or cancer pain and who have OIC
- Primary Objective: To estimate the proportion of laxative inadequate response (LIR)
- Secondary Objectives:
  1. To describe patient-reported impact of OIC on health-related quality of life, productivity, and pain management
  2. To describe patient-reported treatment satisfaction with laxative use
  3. To describe physician-reported awareness of OIC, symptoms, and understanding of patient-reported impact of OIC

OIC BOI Study: Constipation-related GI Symptoms, Pain Management and Laxative Inadequate Response

- At Baseline, participants reported having 3.7 BMs on average per week, however, 83% reported wanting to have at least 1 BM a day or more
- Many of the constipation symptoms were highly prevalent (97%), frequent in occurrence (>86%), and highly bothersome (>61%)
- ~49% reported constipation moderately or completely interfered with the ability of their opioid medication to control pain
- Proportion of laxative inadequate response (1xLIR) was 93%

OIC BOI: Physician-Patient Concordance

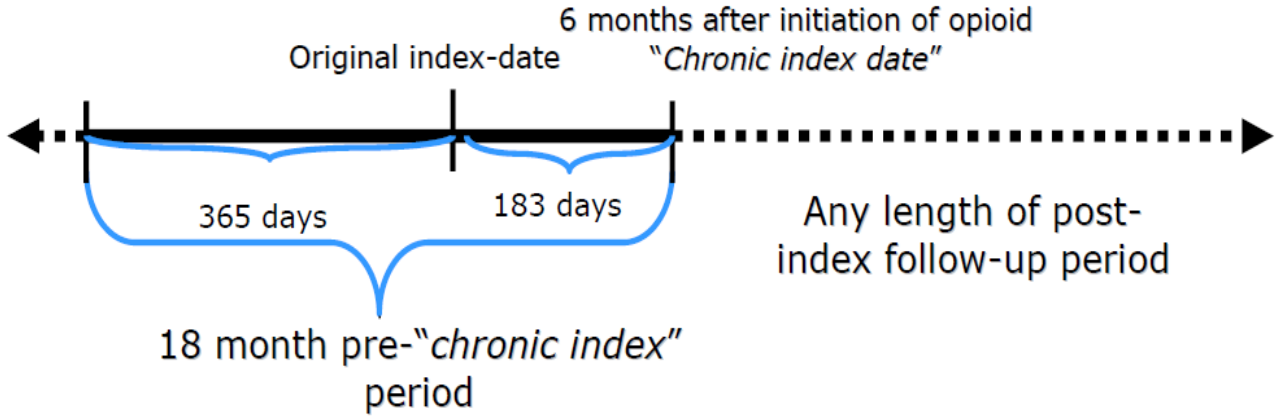
- 17% of patients' HCPs were unaware of how few weekly BMs their patients were having
- In contrast, HCPs were aware of patients' pain severity (both patient- and HCP-reported mean ratings were 6.3)
- OIC interference with pain management was reported by patients as ≥ moderate (49%), while HCPs most commonly perceived these patients' pain as "mostly managed" (46%)
- HCPs reported not knowing laxative treatment status of 25% of their patients at baseline
- Discordance between patient and HCP reports of satisfaction or benefit with constipation treatment was observed:
  - Of patients that were "very dissatisfied" with treatment (23%), this dissatisfaction was only perceived in 3% of HCPs
  - The percentage of patients who reported "no benefit" of treatment (34%) was higher than that of HCPs who reported treatment was inadequate in their patients (10%)

OIC BOI Study: Messages for Dissemination

- Significant unmet need for effective treatment of OIC remains
  - Patients with chronic pain and OIC frequently report moderate to severe GI symptoms
  - Prevalence of symptoms suggests patients may be undertreating OIC and/or that currently utilized therapies may be lacking in efficacy and tolerability
  - Pain management is affected by OIC
- Despite reported discussions on OIC symptoms and pain severity between physicians and patients, many physicians were unaware of their patients':
  - OIC symptom severity, level of interference with pain management, level of laxative use and limited benefit
  - However, identical average pain ratings between physician and patients were reported indicating clear communication about level of pain experienced
- Poor communication between HCPs and patients about OIC may contribute to a lack of awareness of the impact of OIC.
- Development of a consensus definition of OIC and clear treatment guidelines should help establish best practices in the identification and treatment of OIC
- Clinical education and coordination of care by additional HCPs, including nursing staff, may add to the critical need to appreciate and proactively address the burden of disease.

Database Studies: Study Design Summary and Objectives

- Retrospective observational cohort study using real life healthcare data extracted from administrative claims databases in the US and electronic medical record databases in the UK and Germany
- Between 2006-2011, for each country, identify new (or incident) chronic (≥6 month) and continuous opioid users for non-cancer pain



- Objectives:
  1. To assess new occurrences of MI, stroke, all-cause death, TIA, unstable angina, CHF, serious ventricular arrhythmia and cardiac arrest, stable angina/coronary artery disease/other ischemic heart disease, fractures, bowel perforation, and malignancy
  2. To describe the demographics and clinical characteristics of the opioid users
  3. To describe healthcare resource use and costs during the pre and post-index periods

Database Studies: Conclusion from Results

- Relationship between the use of opioid analgesics and the risk of cardiovascular (CV) events is not well understood.
- In all 3 countries, CV disease, back pain, and depression were prevalent preexisting comorbidities, with a majority of patients newly initiating chronic therapy on various weak opioids.
- Rates of MI in the US, UK and, Germany were 10.7 (95% CI 9.1–12.5), 6.7 (95% CI 5.6–8.0), and 2.7 (95% CI 1.9–3.7), respectively, whereas those for stroke were 9.3 (95% CI 7.8–10.9), 5.4 (95% CI 4.4–6.6), and 5.3 (95% CI 4.1–6.7), respectively.
- Event rates were higher in patients with preexisting CV disease compared with those without established CV disease.
- Examination of preexisting comorbidities and geographic differences (i.e., population heterogeneity) is important when evaluating CV risk associated with the use of opioids or therapies utilized by chronic opioid users.

Pubs Leads Support and Key Takeaways for RWE

- Publication leads are critical in assisting the RWE scientists in getting the evidence out to the right audience in time and at the right time
  - As with pivotal RCTs, RWE publication plans should be a core activity in pharmaceutical development
- Key Takeaways:
  - Real world evidence is not a temporary nor new phenomena but born out of the discipline of epidemiology
  - Application across the product lifecycle and relevant to patients, providers, payers and regulators
  - Companies are investing heavily to build RWE capability
  - Generalizability:
    - RWE can complement trials by providing information on post-market utilization, safety and effectiveness
    - Population level information (e.g. disease burden) may no longer generalize as medicine becomes more personalized so we need to the capability (data, analyses, skillset) to look at these specific populations to improve development

Confidentiality Notice

THANK YOU

11TH ANNUAL MEETING OF ISMPP

OPTIMIZING SCIENTIFIC VALUE:
SMART AND SYSTEMATIC APPROACHES TO MEDICAL PUBLICATIONS

April 27–29, 2015
Hyatt Regency Crystal City
Arlington, VA, USA

ISMPP International Society for Medical Publication Professionals™