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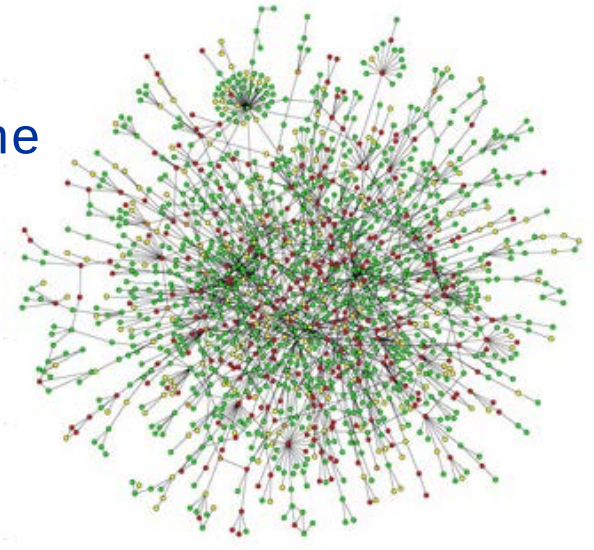
SCIENCE MEDICINES HEALTH

Reflections on the Findings and Conclusions of the European Medicines Agency (EMA) Workshop on "Big Data" and Healthcare



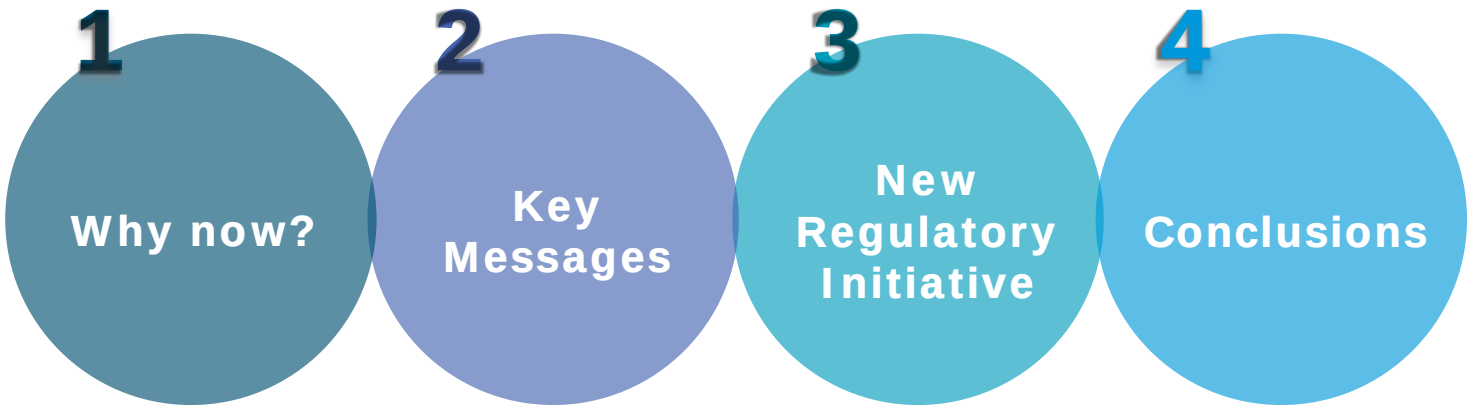
ADEPT 4 Workshop

Dr Alison Cave,
Principal Scientific Administrator,
Pharmacovigilance and Epidemiology Department

Disclaimer

The views expressed in this presentation are my personal views and may not be understood or quoted as being made on behalf of or reflecting the position of the European Medicines Agency or one of its committees or working parties.

Objectives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Why now?
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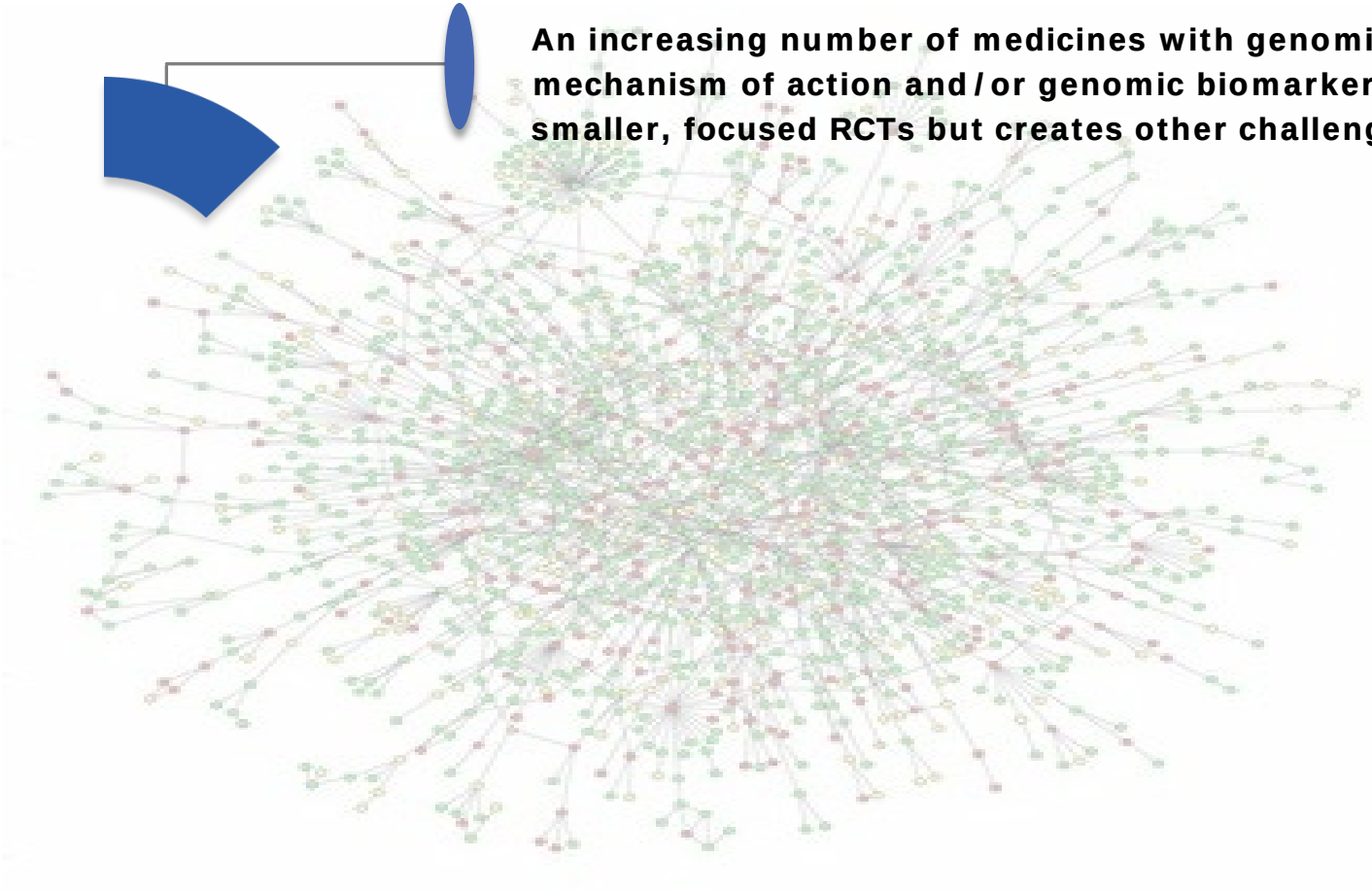
Key Messages
3
New Regulatory Initiative
4
Conclusions

Objectives

1

Why Now?

Why Now?



An increasing number of medicines with genomic mechanism of action and/or genomic biomarkers enabling smaller, focused RCTs but creates other challenges.

Genomic Based Mechanism of Action

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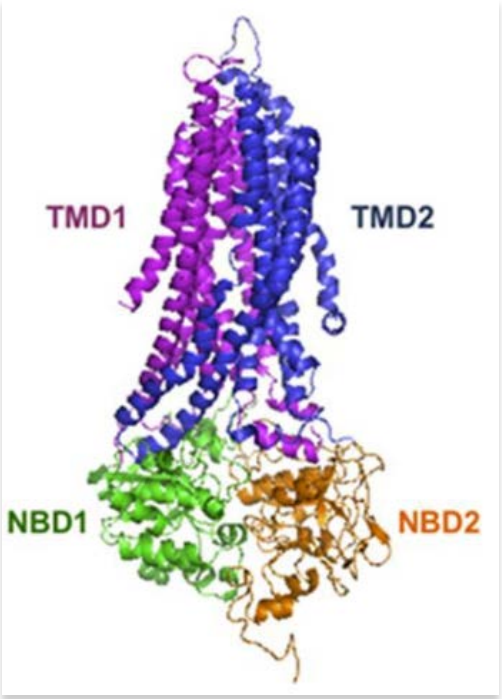
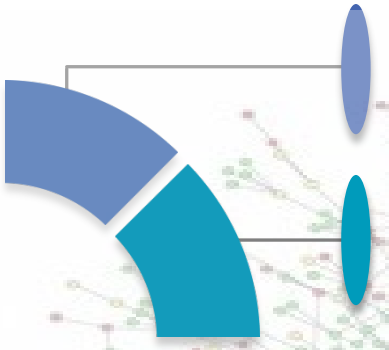
- Cystic fibrosis is caused by one of nearly 2000 mutations.
- CF drug, ivacaftor which targets *G551D* mutation in the *CFTR* gene (4% of CF population).
- Delivers increases in FEV_1 ~10%.

Indication gradually expanded to covers further mutations



The future

Challenge of determining the level of evidence required to extend indications when further mutations are identified.



An increasing number of medicines with genomic **mechanism** and / or genomic biomarkers enabling smaller, focused RCTs but increasing uncertainties

Innovative medicines and personalised prescribing creates regulatory challenges.

Genetics Driving Patient Selection

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The Opinion Pages | OP-ED CONTRIBUTOR

Angelina Jolie Pitt: Diary of a Surgery

By ANGELINA JOLIE PITT MARCH 24, 2015

Michela Buttignol

LOS ANGELES — TWO years ago I wrote about my choice to have a preventive double mastectomy. A simple blood test had revealed that I carried a mutation in the BRCA1 gene. It gave me an estimated 87 percent risk of breast cancer and a 50 percent risk of ovarian cancer. I lost my mother, grandmother and aunt to cancer.

I wanted other women at risk to know about the options. I promised to follow up with any information that could be useful, including about my next preventive surgery, the removal of my ovaries and fallopian tubes.

I had been planning this for some time. It is a less complex surgery than the mastectomy, but its effects are more severe. It puts a woman into forced menopause. So I was readying myself physically and emotionally,

Review

Genetics of dementia

Clement T Loy, Peter R Schofield, Anne M Turner, John B J Kwok

Lancet 2014; 383: 828–40
Published Online August 6, 2013
http://dx.doi.org/10.1016/S0140-6736(13)60630-3

School of Public Health, University of Sydney, Sydney, NSW, Australia (C T Loy FRACP); Neuroscience Research Australia, Randwick, NSW, Australia (C T Loy,

25% of all people aged 55 years and older have a family history of dementia. For most, the family history is due to genetically complex disease, where many genetic variations of small effect interact to increase risk of dementia. The lifetime risk of dementia for these families is about 20%, compared with 10% in the general population. A small proportion of families have an autosomal dominant family history of early-onset dementia, which is often due to mendelian disease, caused by a mutation in one of the dementia genes. Each family member has a 50% chance of inheriting the mutation, which confers a lifetime dementia risk of over 95%. In this Review, we focus on the evidence for, and the approach to, genetic testing in Alzheimer's disease (*APP*, *PSEN1*, and *PSEN2* genes), frontotemporal dementia (*MAPT*, *GRN*, *C9ORF72*, and other genes), and other familial dementias. We conclude by discussing the practical aspects of genetic counselling.

But for other diseases the genetic risk is less predictive e.g. Alzheimer's, Parkinson's

How do you identify patients to be treated prophylactically and how do you assess the benefit-risk profile?

An increasing number of medicines with genomic mechanism and/or genomic biomarkers enabling smaller, focused RCTs but increasing uncertainty.

Innovative medicines and personalised prescribing creates regulatory challenges.

Rare diseases may be associated with more limited information at authorisation

Strimvelis - Corrective gene therapy for children with SCID-ADH (Severe Combined Immunodeficiency due to adenosine deaminase deficiency). Occurrence: 0.22-0.68 per 100,000 population

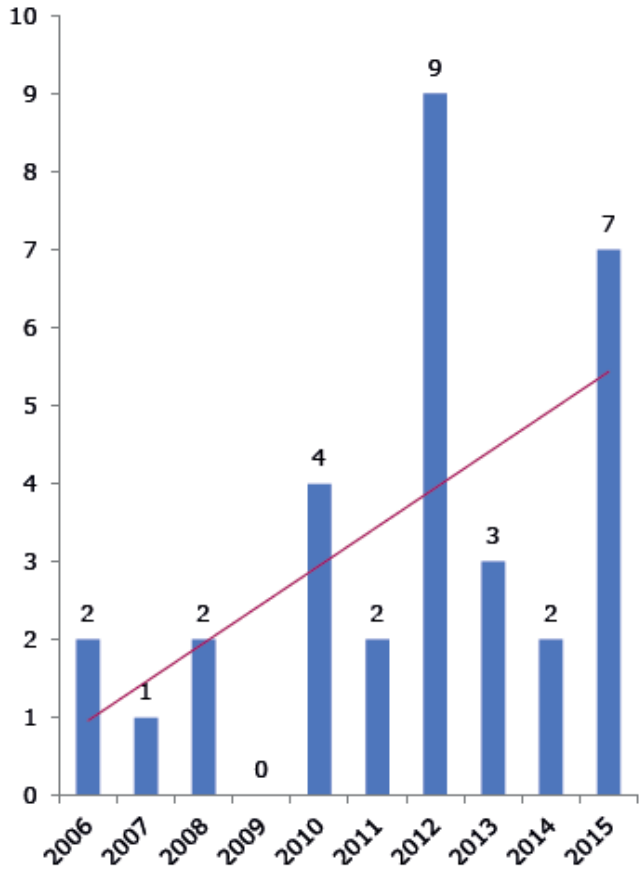
- 12-patient pivotal study; Open label
- Primary outcome: 3-year survival
- Secondary outcome: severe infections

- 3-year survival: 12/12
- 9/12 successful response
- 12/18 auto-immune AEs

Uncertainties

- Long term durability of benefit (comparison with stem cell transplant)
- Late failure – need for further treatment eg stem cell transplant
- Late toxicity
- Long-term immunogenicity

Conditional MA



Number of applications requesting conditional marketing authorisation at submission, by year of submission

107 post-authorisation obligations

(of these, 57 obligations were fulfilled before June 2016)

Categories of specific obligations imposed to companies

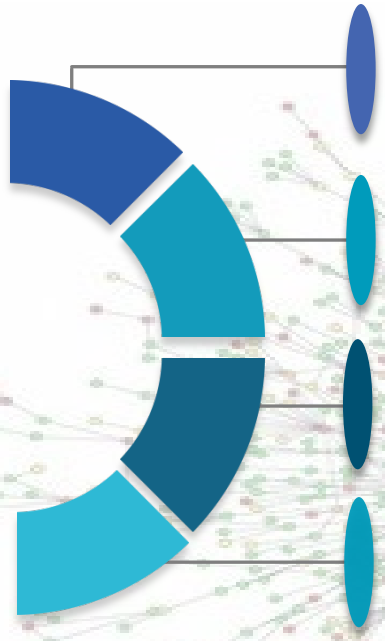
78	Final results from clinical studies or pool of studies
9	Interim results of a clinical trial
8	Additional analysis
3	Quality data
9	Other measures

How timely was the submission of specific obligation results?

33	Due date +/- 1 month
15	Early (1-6 months)
4	Early (6-12 months)
1	>1 year early
2	Late (1-6 months)
2	Late (6-12 months)

>90% of completed specific obligations did not have major changes to their scope

≈70% of specific obligations were completed within specified timelines



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Unknown generalisability of RCT results to normal clinical practice: Need for new approaches to gather complementary evidence

Unknown generalisability of RCTs

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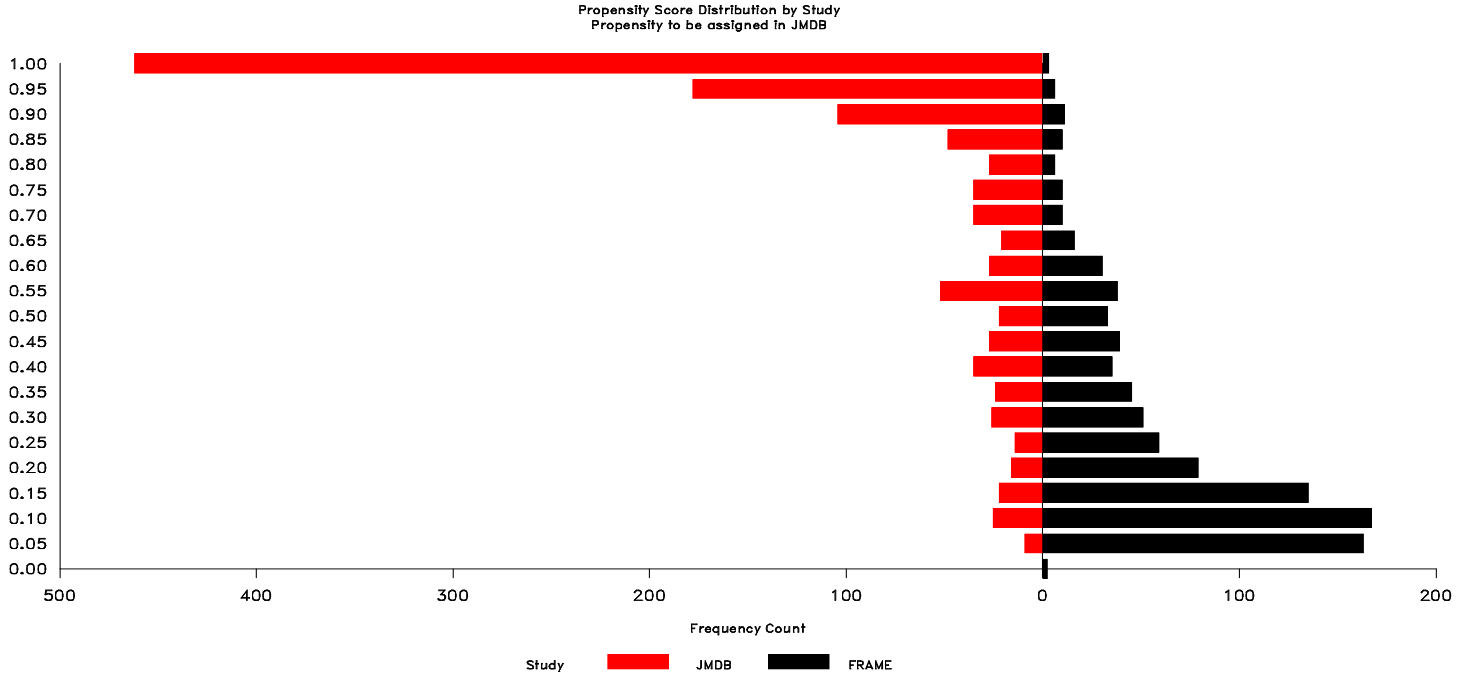
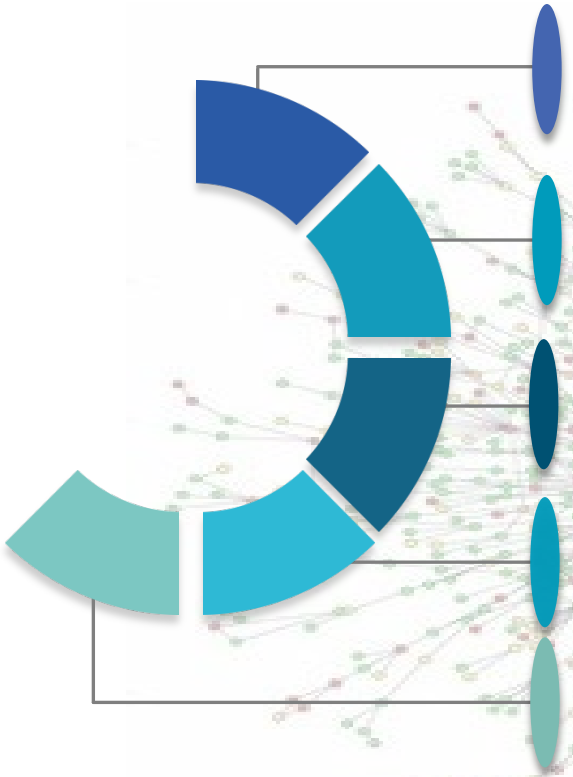
Happich *et al* (ISPOR 19th Annual European Congress, GETREAL) developed a propensity score model that predicts participation in either a RCT (JMDB) or the real world (FRAME), given a set of common total baseline characteristics.

Resulting propensity scores were used to assess the overlap between the two cohorts.





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Innovative medicines and personalised prescribing creates regulatory challenges.

Rare diseases to may be associated with more limited information at authorisation

Unknown generalisability of RCT results to normal clinical practice: need for new approaches to gather complementary evidence

Additional data sources are needed to better monitor risk / benefit in high risk groups often excluded from clinical trials

Meeting needs? Pharmacoepidemiological paediatric safety studies

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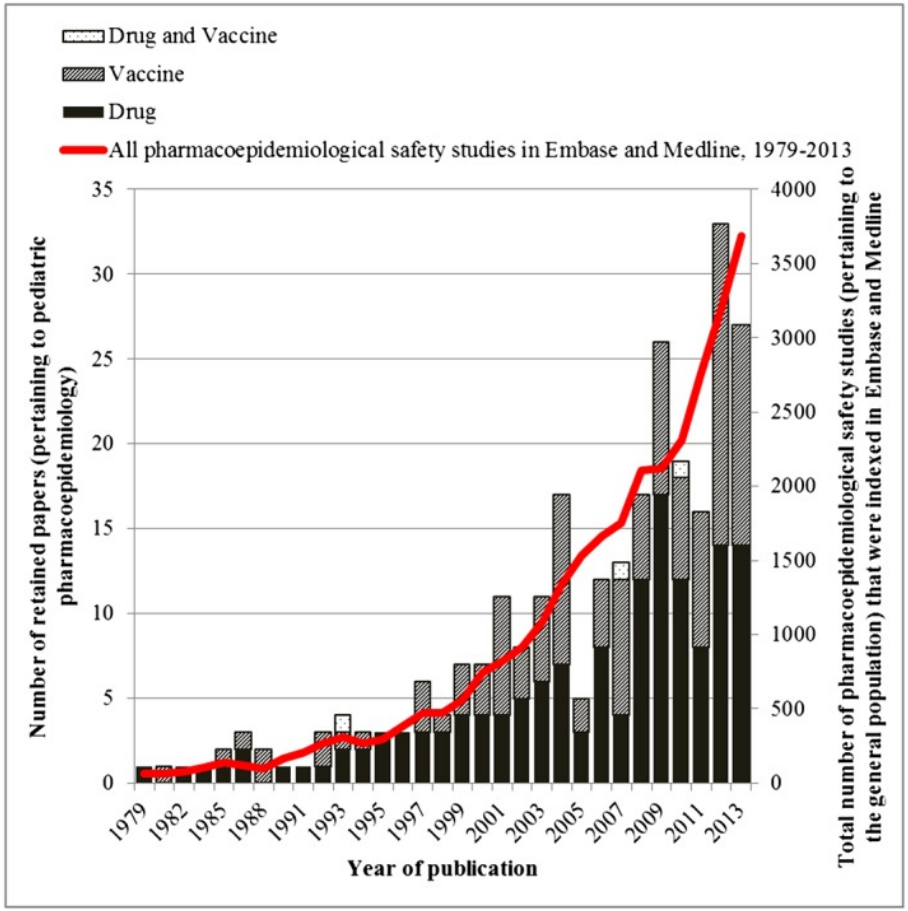

Pharmacoepidemiological safety studies in children: a systematic review

Osemeke U. Osokogu[1]*, Julijana Dukanovic[1], Carmen Ferrajolo[1], Caitlin Dodd[1], Alexandra C. Pacurariu[1], Wichor M. Bramer[2], Geert 'tJong[3], Daniel Weibel[1], Miriam C. J. M. Sturkenboom[1] and Florentia Kaguelidou[1,4]

2006 Regulation (EC) 1901/2006
on medicinal products for paediatric use

Main provisions applied from July 2008 & January 2009
PDCO established

2009-2013: <1% of P'epi safety studies conducted in paediatric populations

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 2016; **25**: 861–870
Published online 3 June 2016 in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.4041

Geriatric Population – Underrepresentation in clinical trials

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CLINICAL INVESTIGATION

Exclusion of Elderly People from Randomized Clinical Trials of Drugs for Ischemic Heart Disease

Florence T. Bourgeois, MD, MPH,†‡ Liat Orenstein, MSc,‡ Sarita Ballakur,§ Kenneth D. Mandl, MD, MPH,*†‡ and John P. A. Ioannidis, MD, DSc¶***

OBJECTIVES: To measure exclusion of elderly adults from randomized trials studying drug interventions for ischemic heart disease (IHD) and describe the characteristics of these trials.

DESIGN: Cross-sectional analysis.

SETTING: Interventional clinical trials studying a drug intervention for IHD that started in 2006 and after were identified in ClinicalTrials.gov. Data were extracted on study features, including age-based inclusion criteria. Data on participants and their age distribution were collected from trial publications, investigator inquiry, and result data in ClinicalTrials.gov.

PARTICIPANTS: Individuals aged 65 and older.

MEASUREMENTS: Proportion of trials excluding individuals based on age, mean age of trial participants, and proportion of enrolled participants aged 65 and older and 75 and older.

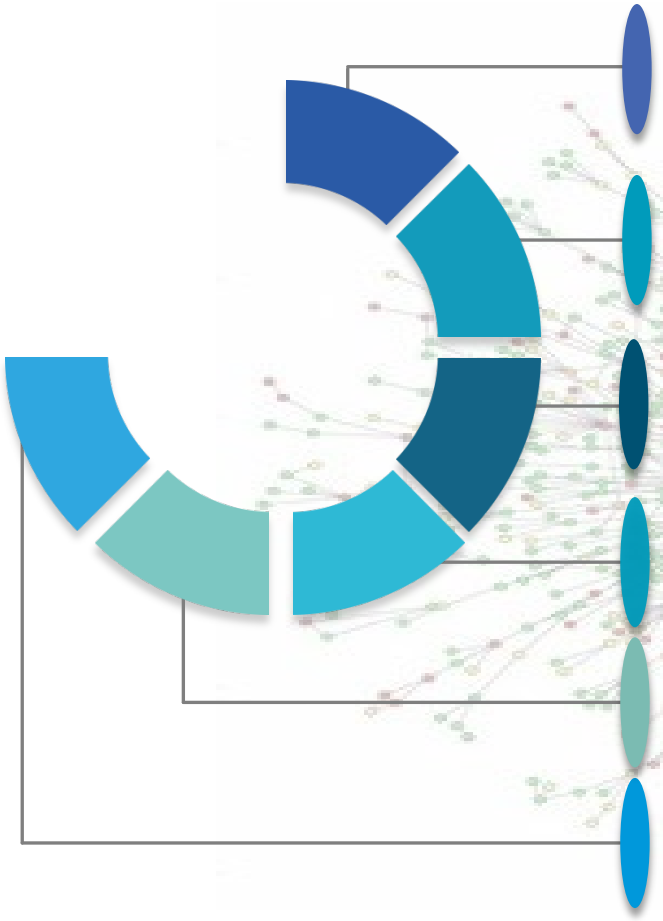
RESULTS: Of 839 identified trials, 446 (53%) explicitly excluded elderly adults. The most-frequent upper age limits were 80 (n = 164) and 75 (n = 114), with a median upper age limit of 80 (interquartile range 75–80). Trials with upper age limit exclusions tended to be smaller (median number of participants 100 vs 201, $P < .001$) and were more likely to be funded primarily by nonindustry sources (78.3% vs 70.0%, $P = .006$). The overall mean age of trial participants was 62.7 (mean maximum age 74). The estimated proportion of participants aged 65 and

CONCLUSION: Despite the high burden of IHD in elderly adults, the majority of drug trials do not enroll participants reflective of age-related prevalence of the disease. **J Am Geriatr Soc 2017.**

Key words: ischemic heart disease; evidence-based medicine; research methodology

Individuals age 65 and older account for 14% of the U.S. population, but bear a large and disproportionate amount of the healthcare burden.[1,2] More than 60% of individuals with cancer, for example, and nearly 65% of those hospitalized with heart disease are age 65 and older.[3,4] Overall, this age group consumes more than one-third of total U.S. personal healthcare expenses every year and 30% of all prescription drug costs,[2] but there is strong evidence that elderly adults are persistently excluded from or underrepresented in clinical trials for a range of conditions, including osteoarthritis, diabetes mellitus, and various types of cancer.[5–7] As many as half of all clinical trials have explicit upper age limitations, and others limit participation of older adults based on indirect exclusion criteria

Of 839 identified trials, 446 (53%) explicitly excluded elderly adults.



An increasing number of medicines with genomic mechanism and/or genomic biomarkers enabling smaller, focused RCTs but increases uncertainty.

New innovative medicines and personalised prescribing creates regulatory challenges.

Welcome activity in the rare disease area to meet unmet medical needs is associated with more limited information at authorisation

The high internal validity of clinical trials at the expense of external validity demands new approaches to gather complementary evidence

Additional data sources are needed to appropriately monitor risk/benefit in high risk groups often excluded from clinical trials

Increasing interest in combination therapies to treat complex diseases creates regulatory challenges

Ceftazidime-avibactam: a novel cephalosporin/β-lactamase inhibitor

Clinical Pharmacist | 10 MAY 2017 | By Sharanie V. Sims CA, Elizabeth A. Neuner, Robert A. Bonomo

Sulphonylurea compared to DPP-4 inhibitors in combination with metformin carries increased risk of severe hypoglycemia, cardiovascular events, and all-cause mortality

Jan W. Eriksson, Johan Bodegard, David Nathanson, Marcus Thuresson, Thomas Nyström, Anna Norhammar

RHEUMATOID ARTHRITIS

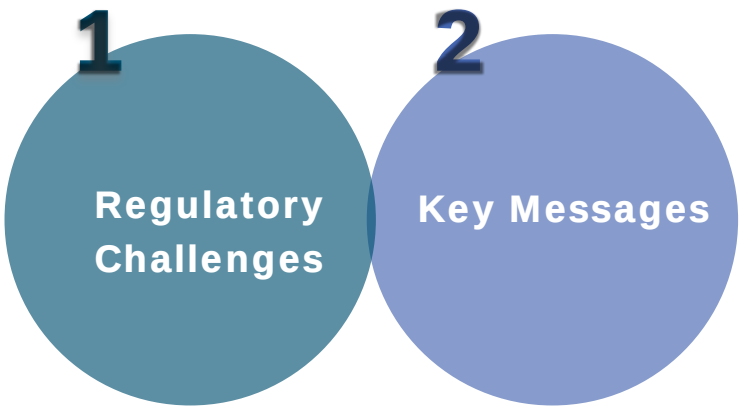
Comparing durability of combination therapies

According to observations from a follow-up study of the RACAT trial looking at patients with rheumatoid arthritis who have suboptimal responses to methotrexate, triple therapy with methotrexate, sulfasalazine and hydroxychloroquine is more durable than combined methotrexate–etanercept therapy. Of the 289 patients followed up, 78% remained on triple therapy at 1 year compared with 63% who remained on methotrexate– etanercept therapy; significantly more patients changed from methotrexate–etanercept therapy to triple therapy than vice versa ($P = 0.005$).

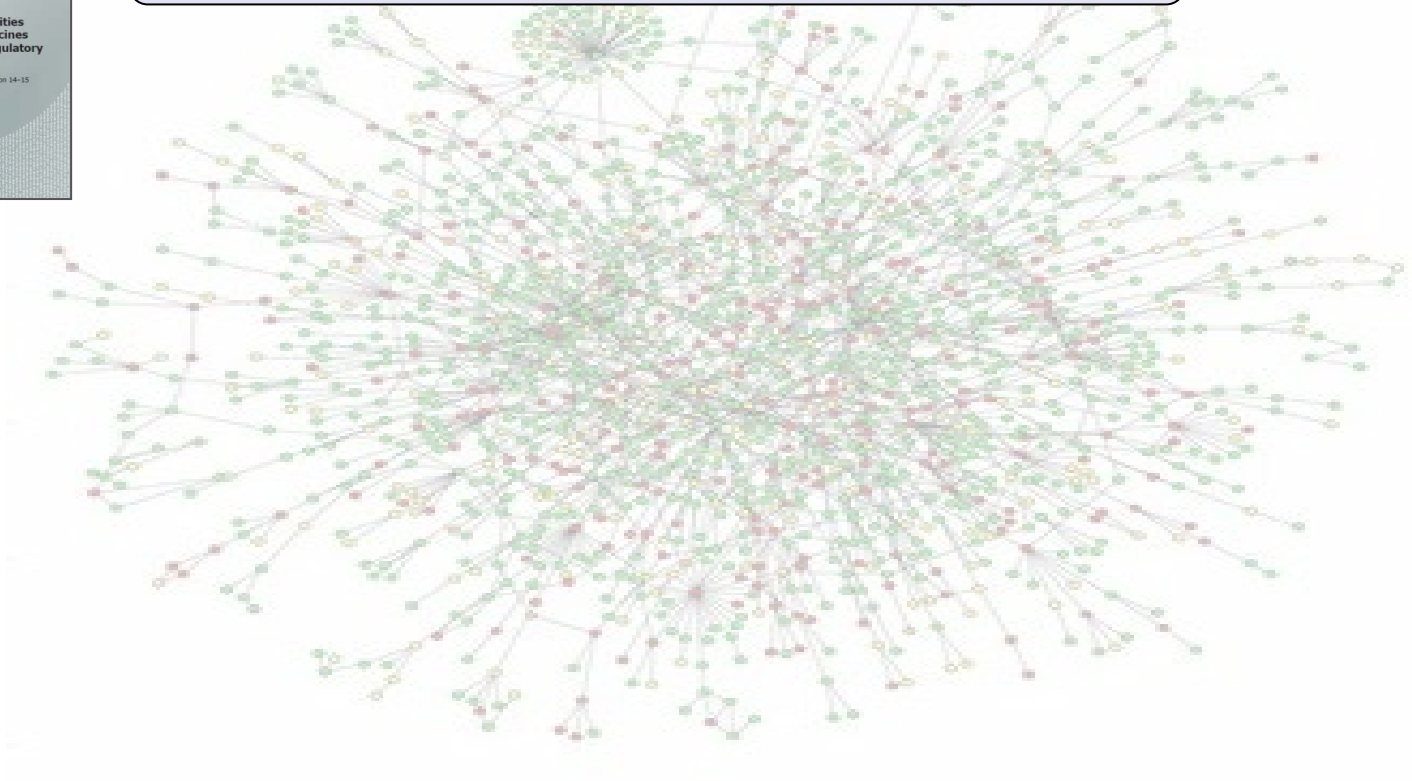
ORIGINAL ARTICLE Peper, S. M. *et al.* Rheumatoid arthritis treatment after methotrexate: triple therapy is more durable than etanercept. *Arthritis Care Res. (Hoboken)* http://dx.doi.org/10.1002/acr.23255 (2017)

- **Define the Big Data landscape from a regulatory perspective**
- **Clarify the opportunities and the challenges**
- **Identify what is needed for Big Data to be exploited to support medicines development and regulatory decision making**

Objectives



Defining the Big Data Landscape



Big Data – how will we meet it?

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Big data

Data sets that are so large or complex that traditional data processing applications are inadequate (Wikipedia)

In the context of Medicines Regulation it could mean data in large amounts or of a complex nature reaching regulatory authorities in the margins of the more traditional analysed and structured data

Data lying underneath the regulatory submissions, for which it would be crucial to understand their presence and the robustness by which they were generated in order to make a competent evaluation of the submission as a whole

The data landscape: which data?

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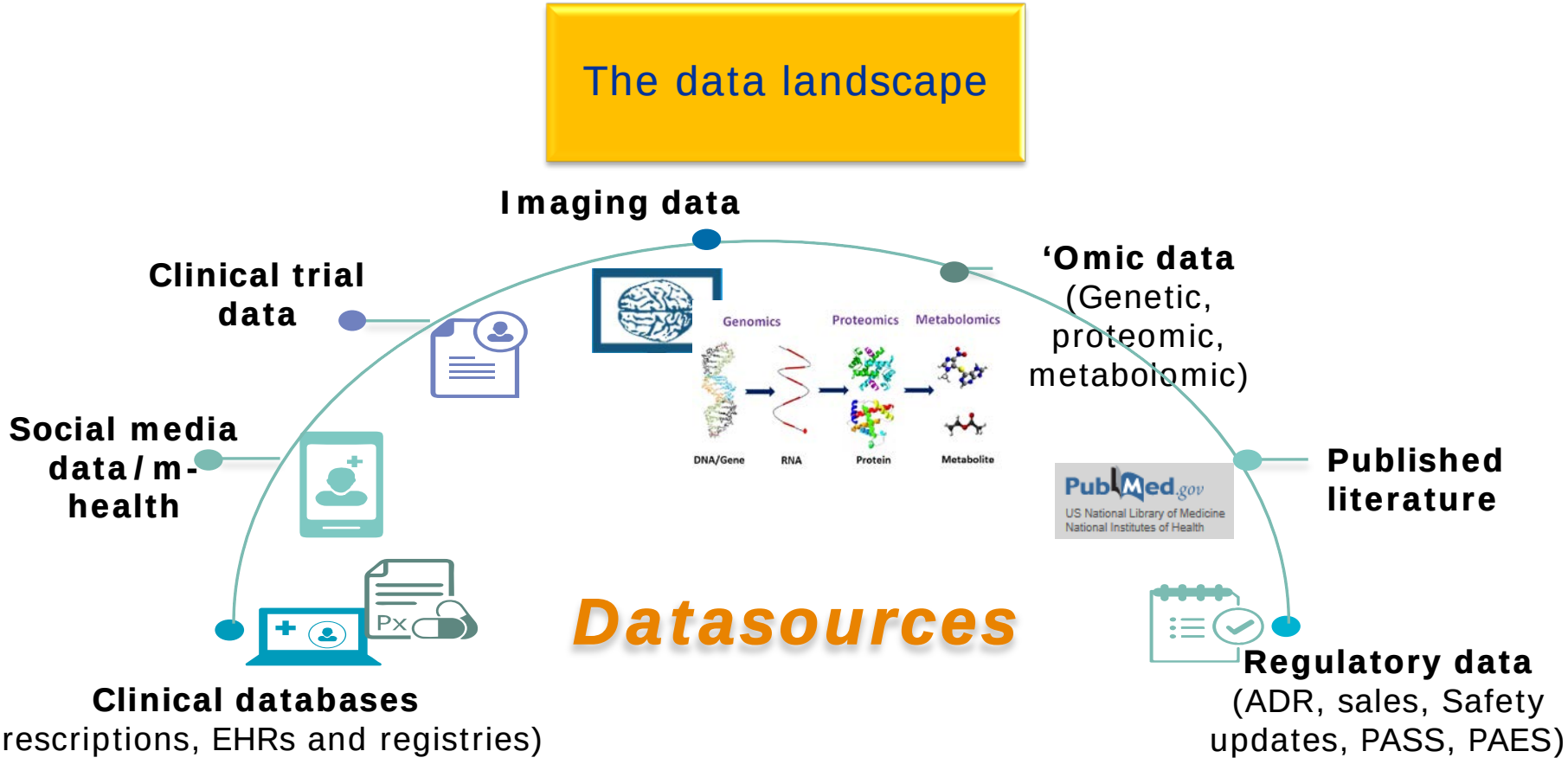

Challenges

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90%

Of the world's data has been created in the past 2 years.

24 months

Frequency at which electronic healthcare data doubles

75%+

Percentage of patients expected to use digital health services in the future

Data per individual

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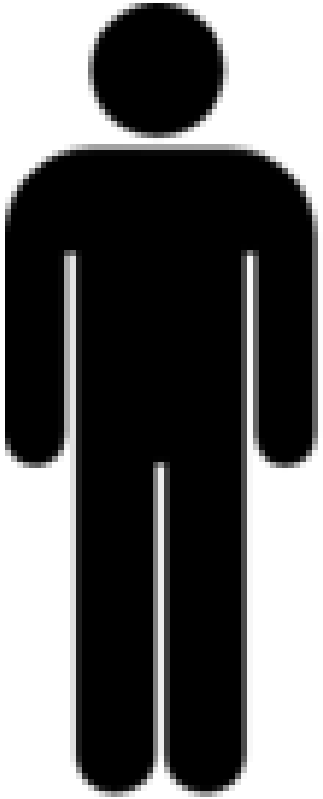
70%
Social and
Environment
And
Behavioral

20%
Genomics
Factors

10%
Clinical Factors



1100 Terabytes
Generated
Per lifetime

6 Terabytes
Per lifetime

0.4 Terabytes
Per lifetime

Defining the Big Data Landscape

Data Accessibility and Integration

Distributed Data Networks

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Sentinel Initiative

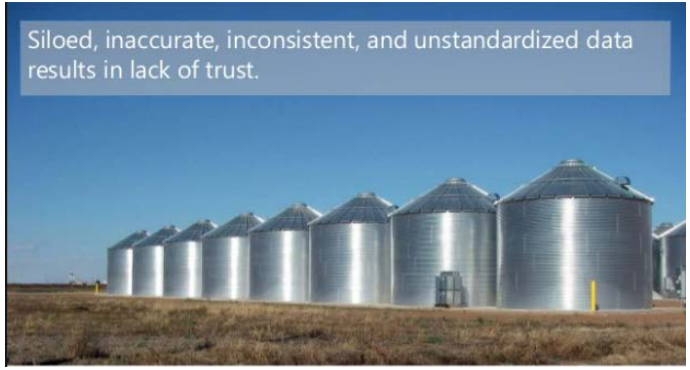
Sentinel is a network of distributed data approach which allows the FDA to rapidly and securely access information via a CDM from large amounts of electronic healthcare data, such as EHRs, insurance claims data and registries. Pilot project delivers access to 99 million patient lives, 2,9 billion drug prescriptions and 38 million acute hospital stays

CNODES
CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

The CNODES network delivers access to the health and prescription records of over 40 million people and a widely distributed network of academic and data analytics experts to rapidly evaluate the risk:benefit profiles of medicines

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

OHDSI is a multi-stakeholder, interdisciplinary collaborative to bring out the value of health data through large-scale analytics. All the solutions are open-source. Currently the community has converted >50 databases covering >660 milliion patients



Data is siloed at individual centres, hard to access, analyse and use.

Productivity tools (especially IT) built for individual local usage focusing on local data analytics solutions

Bringing the data together is very hard. It needs to be "standardised", structured and stored together to deliver insight

We need centralised IT solutions to store data safely and securely and enable machine learning solutions

Data needs to be **FAIR**: Findable, Accessible, Interoperable and Reusable

Regulating the internet giants

The world's most valuable resource is no longer oil, but data

The data economy demands a new approach to antitrust rules

The Economist
May 6th 2017

Defining the Big Data Landscape

Data Accessibility and Integration

Clinical Utility

Data Collection should be targeted

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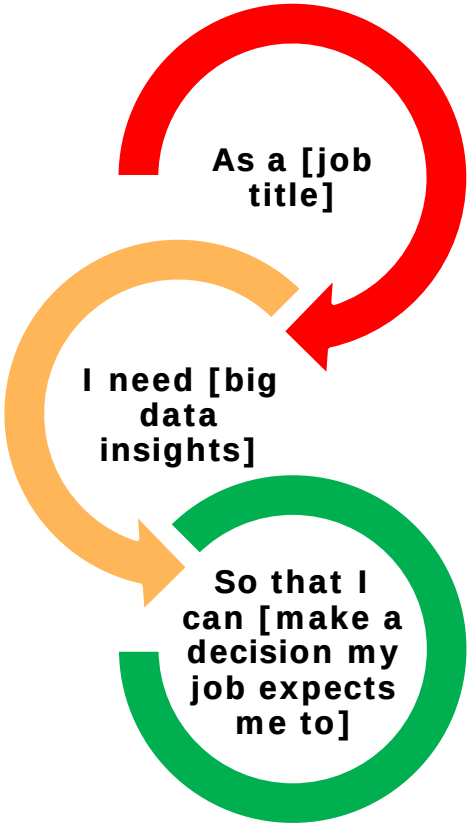
Clinical utility starts by asking the right question

Data should be collected to respond to questions that will translate to benefit



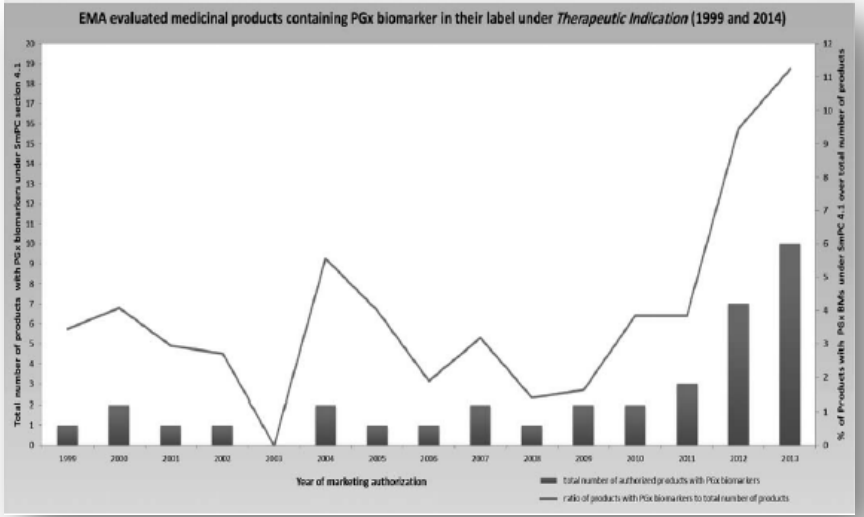
The Pharmacogenomics Journal (2015) 15, 201–210

PERSPECTIVE

Pharmacogenomic information in drug labels: European Medicines Agency perspective

F Ehmann[1], L Caneva [1], K Prasad[2,3], M Paulmichl[2,4], M Maliepaard[2,5,6], A Llerena[2,7], M Ingelman-Sundberg[8] and M Papaluca-Amati[1]

- 15% of EMA evaluated medicines containing PGx information
  - Therapeutic indication (3.5%)
  - Posology and method of administration(4.4%)
  - Contraindications (6.4%)



Original Investigation

Clinical Evidence Supporting Pharmacogenomic Biomarker Testing Provided in US Food and Drug Administration Drug Labels

JAMA Intern Med. 2014;174(12):1938-1944.

Bo Wang, PharmD; William J. Canestaro, MSc; Niteesh K. Choudhry, MD, PhD

- 119 drug-biomarker combinations
- 43 (36.1%) had convincing clinical validity evidence
- 18 (15.1%) evidence of clinical utility
- 61 labels (51.3%) – clinical decisions based on results of biomarker test: 36 (30%) contained convincing clinical utility data

"It may be premature to include biomarker testing recommendations in drug labels when convincing data that link testing to patient outcomes do not exist."

Sir Munir Pirmohammed, Nov 2016

Defining the Big Data Landscape

Data Accessibility and Integration

Clinical Utility

Differentiating causality from co-incidence

Conflicting results creates Uncertainties

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ORIGINAL CONTRIBUTION

Exposure to Oral Bisphosphonates and Risk of Esophageal Cancer

Chris R. Cardwell, PhD
Christian C. Abnet, PhD
Marie M. Cantwell, PhD
Liam J. Murray, MD

BISPHOSPHONATES INHIBIT OSTEOclast-mediated bone resorption and are mainly used to prevent or treat osteoporosis, especially in postmenopausal women. Bisphosphonate use has increased dramatically in recent years in the United States and other Western populations,[1,2] and bisphosphonates are now commonly prescribed in elderly women; eg, in 2005, approximately 10% of UK women older than 70 years received a bisphosphonate prescription.[3]

Oral bisphosphonates are known to cause serious esophagitis in some users.[4,5] Crystalline material that resembles ground alendronate tablets has been found on biopsy in patients with bisphosphonate-related esophagitis, and follow-up endoscopies have shown that abnormalities remain after the esophagitis heals.[6] Reflux esophagitis is an established risk factor for esophageal cancer through the Barrett pathway.[7-9] It is not known whether bisphosphonate-related esophagitis can also increase esophageal cancer risk. However, the US Food and Drug Administration recently reported 23 cases of esophageal cancer (between 1995 and 2008) in patients using the bisphosphonate alendronate and a further 31 cases in pa-

Results Mean follow-up time was 4.5 and 4.4 years in the bisphosphonate and control cohorts, respectively. Excluding patients with less than 6 months' follow-up, there were 41 826 members in each cohort (81% women; mean age, 70.0 (SD, 11.4) years). One hundred sixteen esophageal or gastric cancers (79 esophageal) occurred in the bisphosphonate cohort and 115 (72 esophageal) in the control cohort. The incidence of esophageal and gastric cancer combined was 0.7 per 1000 person-years of risk in both the bisphosphonate and control cohorts; the incidence of esophageal cancer alone in the bisphosphonate and control cohorts was 0.48 and 0.44 per 1000 person-years of risk, respectively. There was no difference in risk of esophageal and gastric cancer combined between the cohorts for any bisphosphonate use (adjusted hazard ratio, 0.96 [95% confidence interval, 0.74-1.25]) or risk of esophageal cancer only (adjusted hazard ratio, 1.07 [95% confidence interval, 0.77-1.49]). There also was no difference in risk of esophageal or gastric cancer by duration of bisphosphonate intake.

Conclusion Among patients in the UK General Practice Research Database, the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer.

JAMA. 2010;304(6):657-663 www.jama.com

Large studies with appropriate comparison groups, adequate follow-up, robust characterization of bisphospho- termine whether bisphosphonates increase esophageal cancer risk. We undertook such a study within the UK

August 2010: "the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer"

Sept2010: we found a significantly increased risk of oesophageal cancer in people with previous prescriptions for oral bisphosphonates"

BMJ

RESEARCH

Oral bisphosphonates and risk of cancer of oesophagus, stomach, and colorectum: case-control analysis within a UK primary care cohort

Jane Green, clinical epidemiologist,[1] Gabriela Czanner, statistician,[1] Gillian Reeves, statistical epidemiologist,[1] Joanna Watson, epidemiologist,[1] Lesley Wise, manager, Pharmacoepidemiology Research and Intelligence Unit,[2] Valerie Beral, professor of cancer epidemiology[1]

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Correspondence to: J Green
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Cite this as: BMJ 2010;340:b4444
doi:10.1136/bmj.c4444

ABSTRACT

Objective To examine the hypothesis that risk of oesophageal, but not of gastric or colorectal, cancer is increased in users of oral bisphosphonates.

Design Nested case-control analysis within a primary care cohort of about 6 million people in the UK, with prospectively recorded information on prescribing of bisphosphonates.

Setting UK General Practice Research Database cohort.

Participants Men and women aged 40 years or over— [illegible] with oesophageal cancer, 18 [illegible] with gastric cancer, and 10 641 with colorectal cancer, diagnosed in 1995-2008. Three controls per case matched for age, sex, general practice, and duration of [illegible].

Main outcome measures Relative risks for incident [illegible] cancer, adjusted for [illegible] smoking, alcohol, and body mass index.

Results [illegible] oesophageal cancer was increased in people with one or more previous prescriptions for oral bisphosphonates compared with those with no such prescriptions (relative risk 1.30, 95% confidence interval 1.02 to1.66; P=0.02). Risk of oesophageal cancer was significantly higher for 10 or more prescriptions (1.93, 1.37 to 2.70) than for one to nine prescriptions (0.93, 0.66 to 1.31) (P for heterogeneity=0.002), and for use for over 3 years (on average, about 5 years: relative risk v no prescription, 2.24, 1.47 to 3.43). Risk of oesophageal cancer did not differ significantly by bisphosphonate type, and risk in those with 10 or more bisphosphonate prescriptions did not vary by age, sex, smoking, alcohol intake, or body mass index; by diagnosis of osteoporosis, fracture, or upper gastrointestinal disease; or by prescription of acid suppressants, non-steroidal anti-inflammatory drugs, or corticosteroids. Cancers of the stomach and colorectum were not associated with prescription of bisphosphonate: relative risks for one or more versus no prescriptions were 0.87 (0.64 to 1.19) and 0.87 (0.77 to 1.00). The specificity

Conclusions The risk of oesophageal cancer increased with 10 or more prescriptions for oral bisphosphonates and with prescriptions over about a five year period. In Europe and North America, the incidence of oesophageal cancer at age 60-79 is typically 1 per 1000 population over five years, and this is estimated to increase to about 2 per 1000 with five years' use of oral bisphosphonates.

INTRODUCTION

Adverse gastrointestinal effects are common among people who take oral bisphosphonates for the prevention and treatment of osteoporosis; they range from dyspepsia, nausea, and abdominal pain to erosive oesophagitis and oesophageal ulcers.[1] Recent case reports have suggested a possible increase in the risk of oesophageal cancer with use of such bisphosphonate preparations.[2] We report here on the relation between prospectively recorded prescribing information for oral bisphosphonates and the subsequent incidence of cancers of the oesophagus, stomach, and colorectum, using data from the UK General Practice Research Database cohort.

METHODS

The General Practice Research Database is a computerised database containing anonymised patient records for about 6 million people in the United Kingdom registered with a National Health Service primary care physician (general practitioner).[3] Every prescription issued by the general practitioner, all consultations with the general practitioner, test results and diagnoses from primary and secondary care, referrals to outpatient clinics, hospital admissions, and deaths are coded by the general practitioner and entered into the database, as are basic demographic data and certain lifestyle data. General Practice Research Database prescription data have been shown to be virtually complete, and the data on incidence of cancer (based on hospital records) are around 95% valid and

Sources of Variability in Multiple Database Studies

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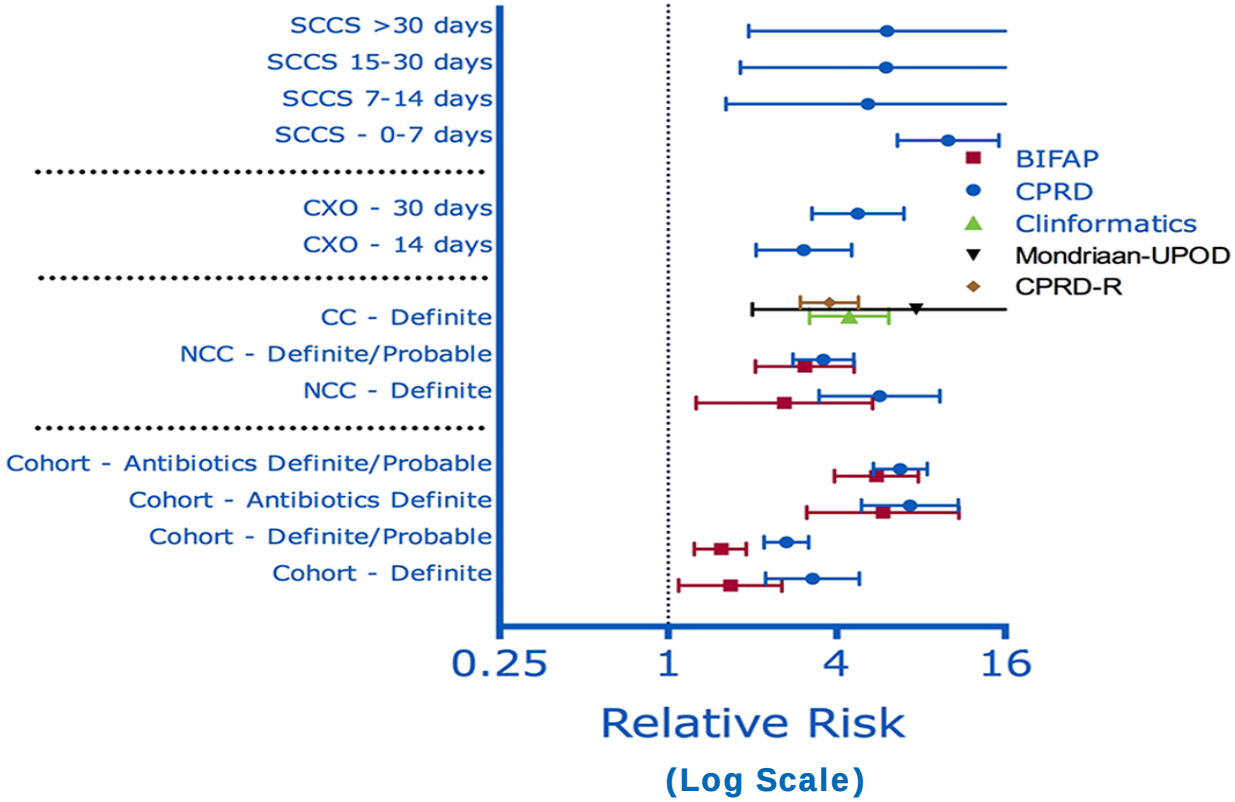

PROTECT

Antibiotics and the risk of acute liver injury

Joint development of Common protocol

Independent conduct in different databases

Pharmacoepidemiology and Drug Safety
2016;156-165. DOI: 10.1002/pds.3968

SCCS: self-controlled case series, CXO: case cross-over, CC: case–control, NCC: nested case–control

Sources of Variability in Multiple Database Studies

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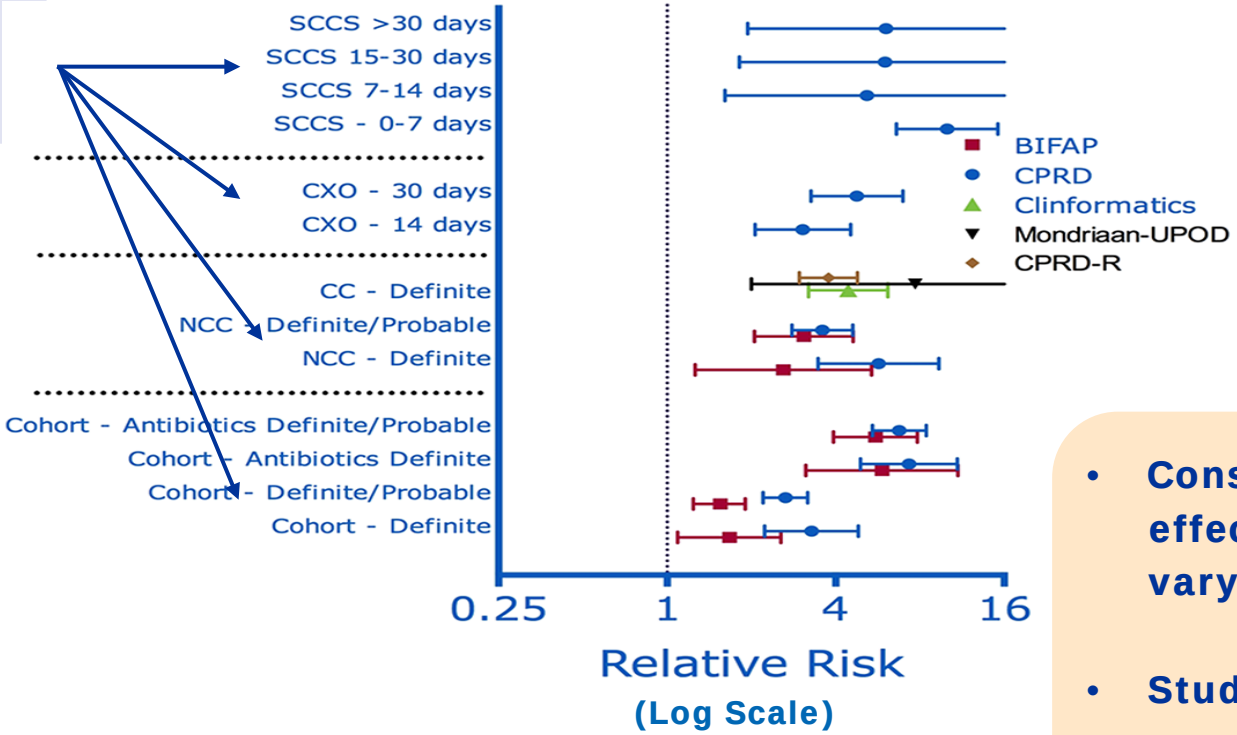
Study design



- **Consistent direction of effect estimate but of varying magnitude**
- **Study design should be a conscious decision**

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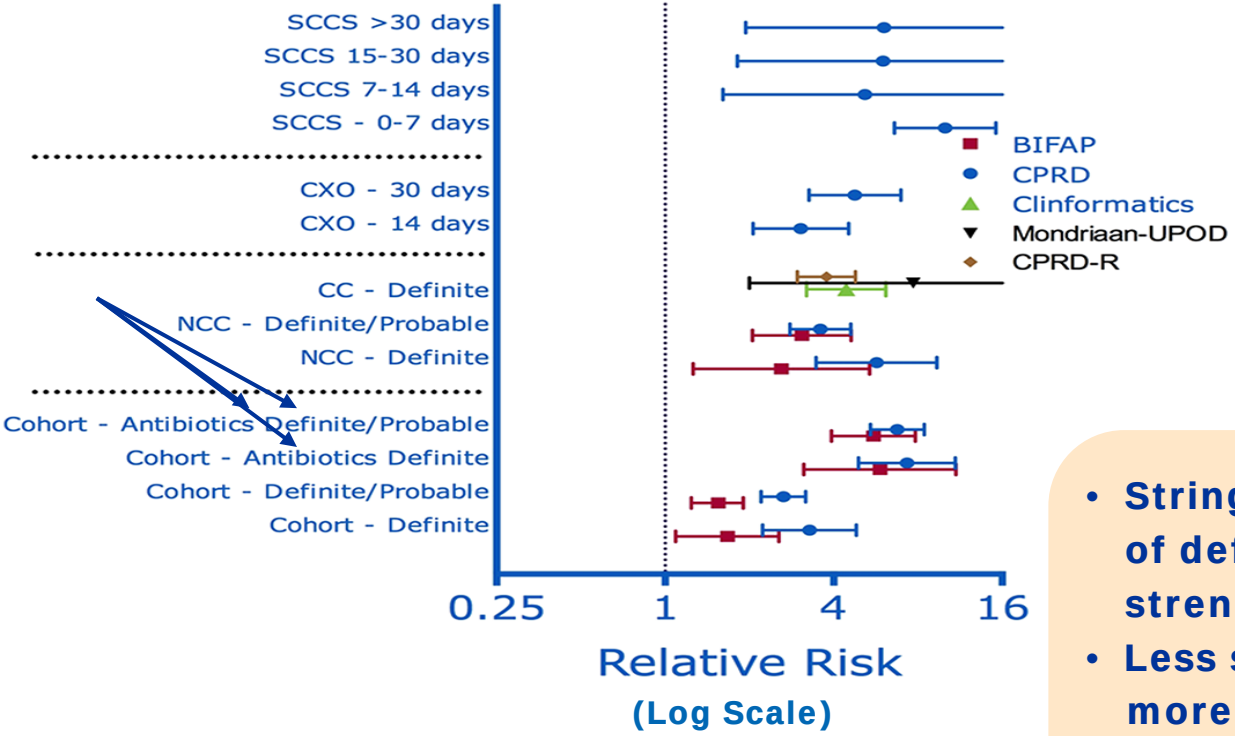
Study design

Outcon



- **Stringency and accuracy of definition increased strength of association**
- **Less stringency led to more false positives**
- **Outcome needs to be carefully defined.**

Sources of Variability in Multiple Database Studies

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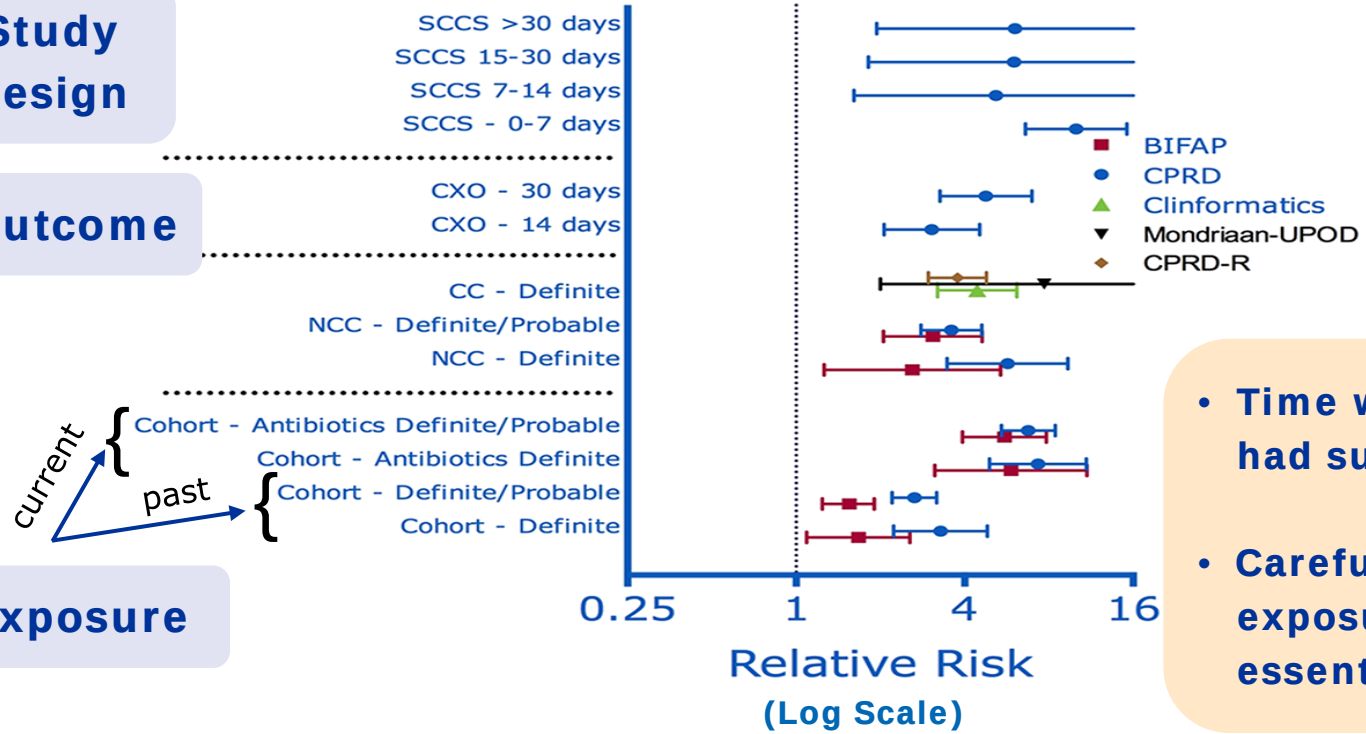
Study design

Outcome

Exposure



- **Time window of exposure had substantial impact**
- **Careful definition of exposure window is essential**

Sources of Variability in Multiple Database Studies

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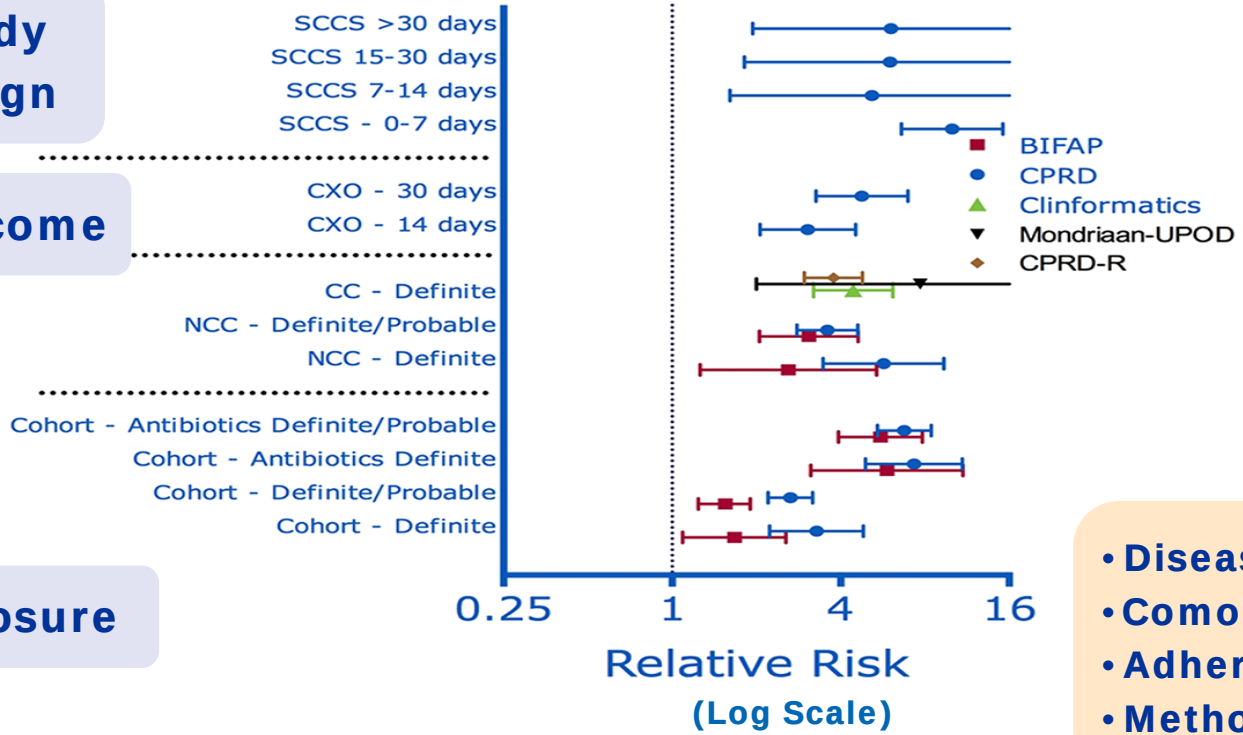
Study design

Outcome

Exposure



Study population

- **Disease stratification**
- **Comorbidities / medications**
- **Adherence**
- **Methodology for matching**

Sources of Variability in Multiple Database Studies

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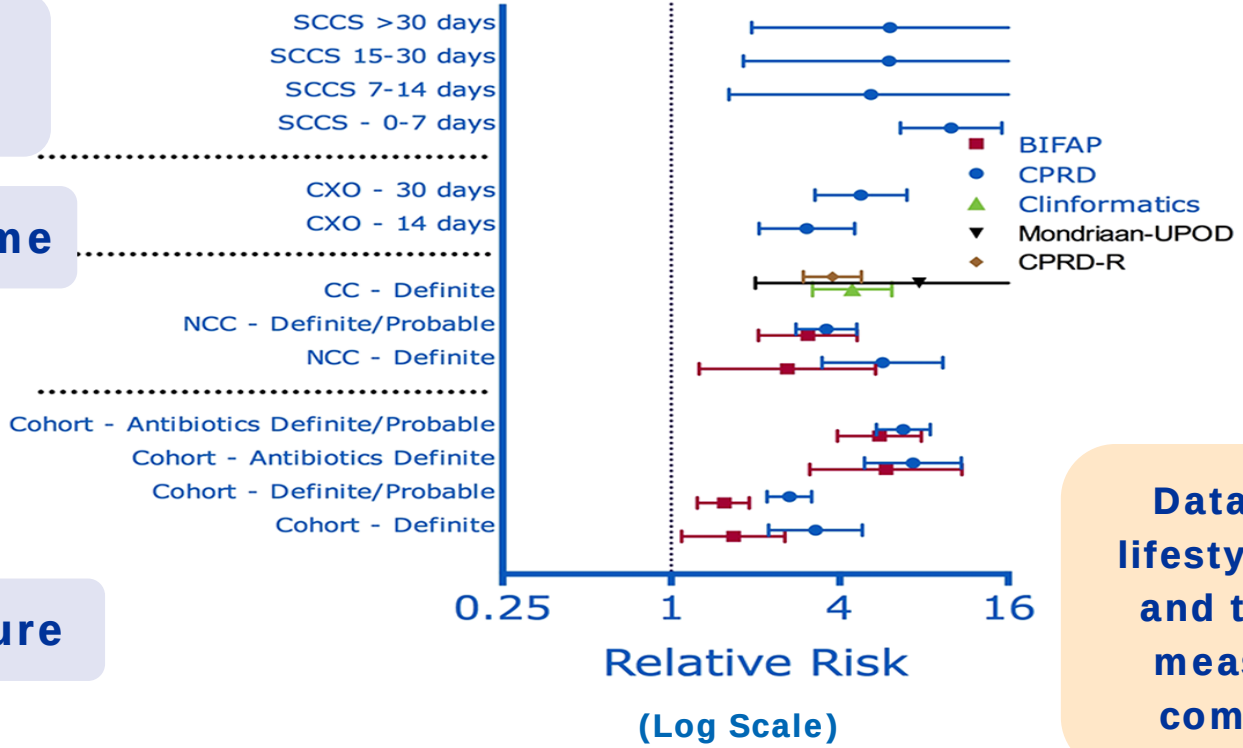
Study design

Outcome

Exposure



Study population

Confounding adjustment

Databases vary in the lifestyle factors recorded and the quality of their measurement making comparisons difficult

Sources of Variability in Multiple Database Studies

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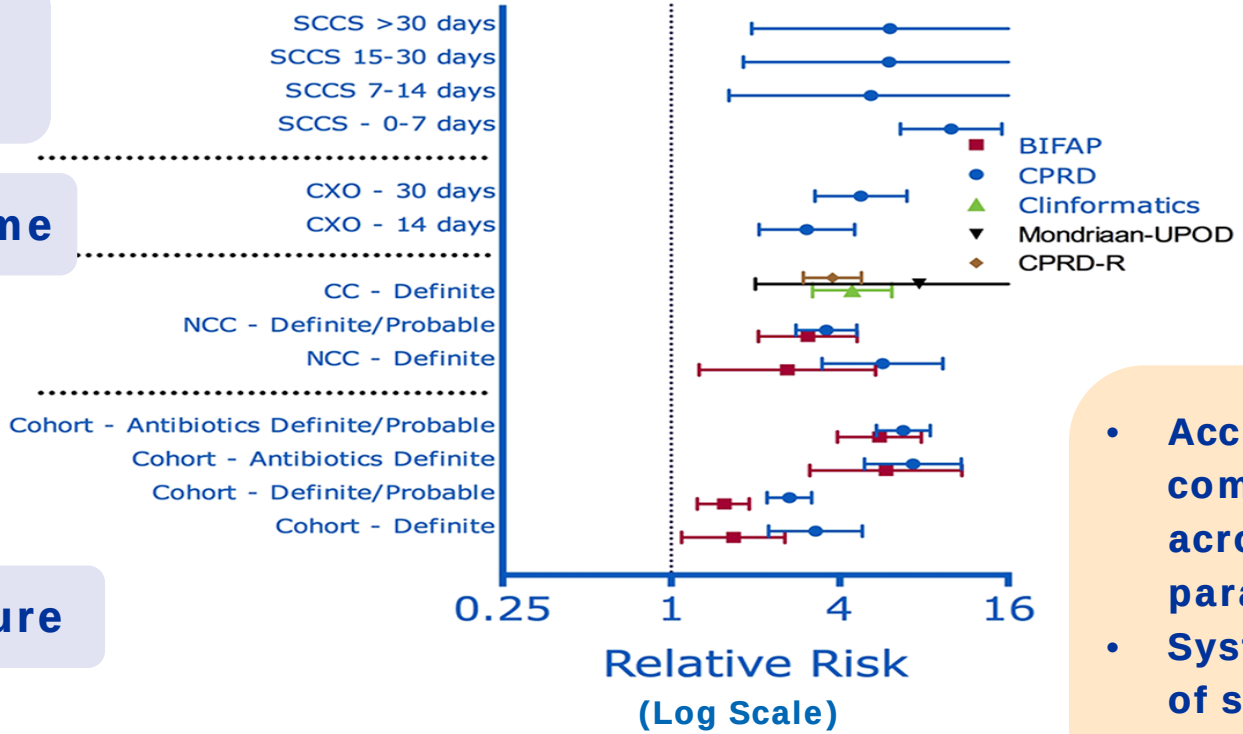
Study design

Outcome

Exposure



Study population

Confounding adjustment

Database

- **Accuracy and completeness data across different parameters is variable**
- **Systematic evaluation of strengths and limitations is essential**

Regulatory Challenges

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Structured data (RCT) generated in accordance with strict guidelines and known provenance

High certainty

Unstructured, unvalidated data of unknown provenance

more uncertainty

Looking to the Future

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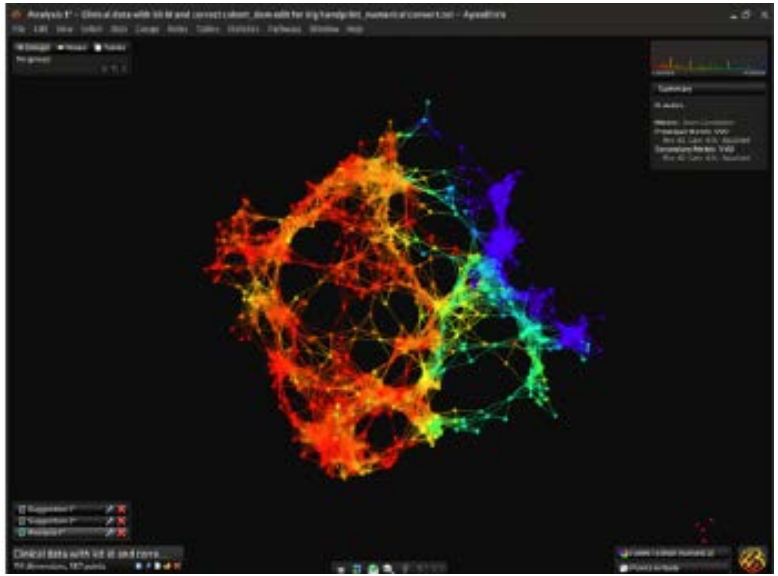
Visualization of the topology of complex data from the U-BIOPRED consortium of adult severe asthma cohorts



Cohorts are generated following the integration of multiple biomarkers

- How are the individual components validated?
- How reproducible are the cohorts?
- How is data weighted within the algorithms to define the cohorts?
- How do you identify the stability of the cohorts over time?
- Are the cohorts translatable to a defined patient population?

Aim: how do we generate certainty for regulatory decision making?

Deriving Causal Associations

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The Lancet Commissions

Dementia prevention, intervention, and care

Prof Gill Livingston, MD, Andrew Sommerlad, MSc, Vasiliki Orgeta, PhD, Sergi G Costafreda, PhD, Jonathan Huntley, PhD, Prof David Ames, MD, Prof Clive Ballard, MD, Prof Sube Banerjee, MD, Prof Alistair Burns, MD, Prof Jiska Cohen-Mansfield, PhD, Claudia Cooper, PhD, Prof Nick Fox, MD, Laura N Gitlin, PhD, Prof Robert Howard, MD, Prof Helen C Kales, MD, Prof Eric B Larson, MD, Prof Karen Ritchie, PhD, Prof Kenneth Rockwood, MD, Elizabeth L Sampson, MD, Quincy Samus, PhD, Prof Lon S Schneider, MD, Prof Geir Selbæk, PhD, Prof Linda Teri, PhD, Naaheed Mukadam, MSc

Published: 19 July 2017

DOI: http://dx.doi.org/10.1016/S0140-6736(17)31363-6 | CrossMark

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Health

Nine lifestyle changes can reduce dementia risk, study says

By Fergus Walsh
Medical correspondent

20 July 2017 | Health | 82 Share

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8 minutes ago

Defining the Big Data Landscape

Data Accessibility and Integration

Clinical Utility

Differentiating causality from co-incidence

Solutions

Changes in the Traditional Regulatory Paradigm

EUROPEAN MEDICINES AGENCY

- Structured data (RCT) generated in accordance with strict guidelines and known provenance
- High certainty

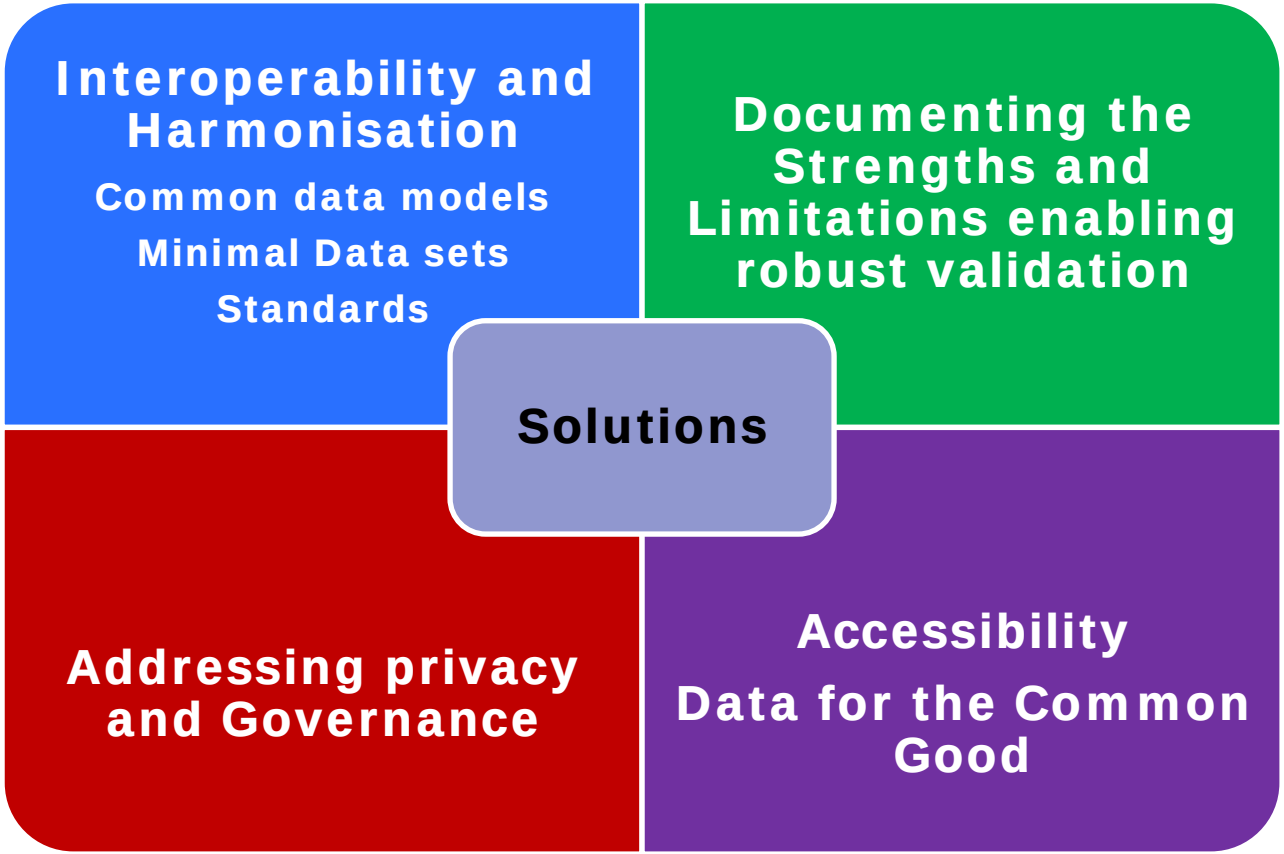
Currently

Challenge

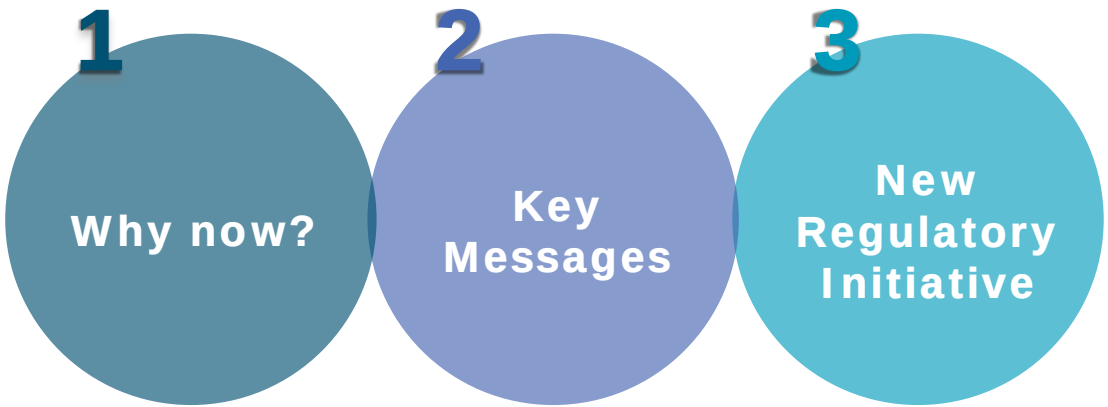
- Unstructured, unvalidated data of unknown provenance
- Turning data into knowledge
- More uncertainty

Need to develop a deep understanding of the data, to define the strengths and limitations so that the evidence arising from its analysis can be appropriately challenged

Solution


Interoperability and Harmonisation
Common data models
Minimal Data sets
Standards
Documenting the Strengths and Limitations enabling robust validation
Solutions
Addressing privacy and Governance
Accessibility
Data for the Common Good

Objectives



HMA Heads of Medicines Agencies

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SCIENCE MEDICINES HEALTH

Mandate HMA / EMA Joint Task Force Big Data

Priority: Reinforce the scientific and regulatory capacity and capability of the network, Innovation and access to new medicines, Optimisation of the regulatory operations

Chair: Thomas Senderovitz, DK

Co Chair: Alison Cave, EMA

Members: DE, DK, ES, FI, HU, IE, NL, NO, RO, UK

Regulatory science initiatives - EMA planned activity and projects

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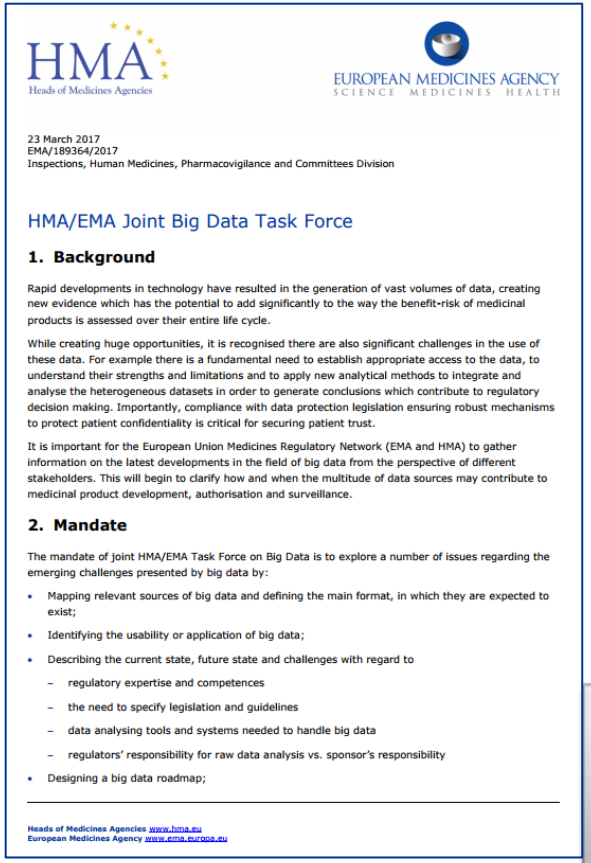


HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 March 2017
EMA/189364/2017
Inspections, Human Medicines, Pharmacovigilance and Committees Division

HMA/EMA Joint Big Data Task Force

1. Background

Rapid developments in technology have resulted in the generation of vast volumes of data, creating new evidence which has the potential to add significantly to the way the benefit-risk of medicinal products is assessed over their entire life cycle.

While creating huge opportunities, it is recognised there are also significant challenges in the use of these data. For example there is a fundamental need to establish appropriate access to the data, to understand their strengths and limitations and to apply new analytical methods to integrate and analyse the heterogeneous datasets in order to generate conclusions which contribute to regulatory decision making. Importantly, compliance with data protection legislation ensuring robust mechanisms to protect patient confidentiality is critical for securing patient trust.

It is important for the European Union Medicines Regulatory Network (EMA and HMA) to gather information on the latest developments in the field of big data from the perspective of different stakeholders. This will begin to clarify how and when the multitude of data sources may contribute to medicinal product development, authorisation and surveillance.

2. Mandate

The mandate of joint HMA/EMA Task Force on Big Data is to explore a number of issues regarding the emerging challenges presented by big data by:

- Mapping relevant sources of big data and defining the main format, in which they are expected to exist;
- Identifying the usability or application of big data;
- Describing the current state, future state and challenges with regard to
  - regulatory expertise and competences
  - the need to specify legislation and guidelines
  - data analysing tools and systems needed to handle big data
  - regulators' responsibility for raw data analysis vs. sponsor's responsibility
- Designing a big data roadmap;

Heads of Medicines Agencies www.hma.eu
European Medicines Agency www.ema.europa.eu

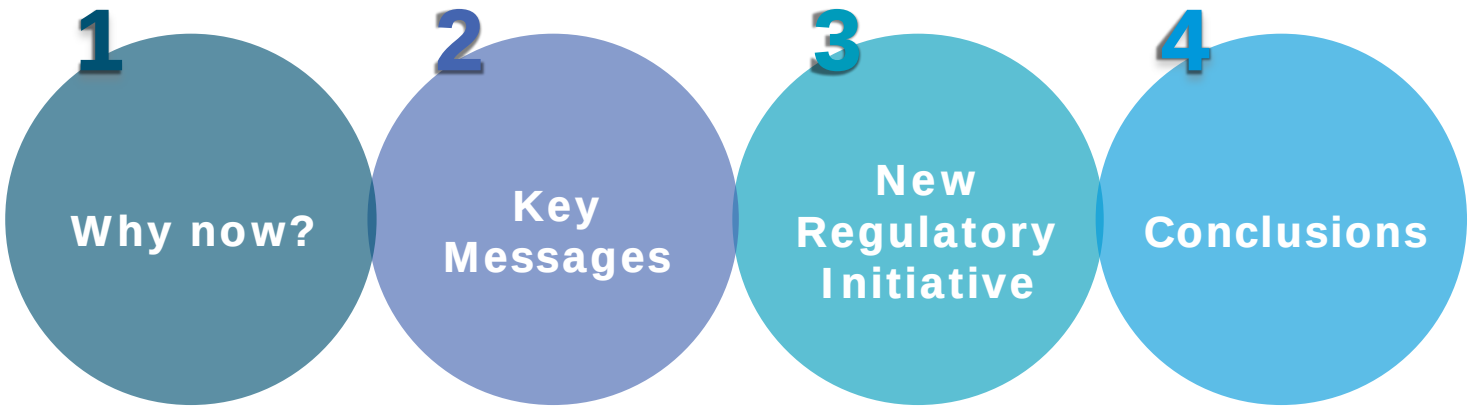
1 The Task Force should ***characterise*** relevant sources of big data and define the main format, in which they can be expected to exist in

2 Identify areas of **usability and applicability** of data

3 **Gap analysis** – describe the current status of expertise, future needs and challenges

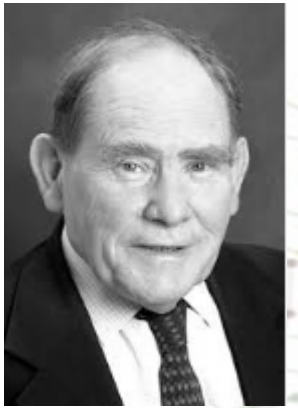
4 The Task Force will generate a **list of recommendations and Big Data Roadmap**

Objectives


1
Why now?
2
Key Messages
3
New Regulatory Initiative
4
Conclusions

Conclusions

- Vast amounts of healthcare data are continually being generated, offering huge opportunities but making it impossible to keep pace with all the information.
- Harnessing of the potential of big data by researchers and regulators is hindered by the fact that it is often unstructured, noisy and inaccessible.
- Deciding which data to collect starts by asking the right questions about the benefits sought and problems faced.
- Access to data is a significant hurdle especially for observational data. Mechanisms to integrate the data to generate meaningful knowledge is needed.
- Validation that associations are real is key for data to support regulatory decision making.



Sydney Brenner

Nobel Prize in Physiology or Medicine

“We are all drowning in a sea of data and starving for knowledge”

Nobel Lecture 2002

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Thank you

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