

13° CONGRESSO NAZIONALE AIOM GIOVANI

# **2019 NEWS IN ONCOLOGY**

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La sorveglianza post-marketing dei farmaci:
Il ruolo dei Big Data nella valutazione e
nel monitoraggio dei farmaci in Europa

Regulating the internet giants

The Economist 2017

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

The data economy demands a new approach to antitrust rules





#### Convergence: Artificial Intelligence, Big Data, and Prediction in Cancer Collection



The AACR Journal editors proudly present this collection of articles related to the 30th Anniversary: AACR Special Conference Convergence Artificial Intelligence, Big Data, and Prediction in Cancer meeting.







Big data versus the big C

The torrents of data flowing out of cancer research and treatment are yielding fresh insight into the disease

# **VOLUME**

Huge amount of data



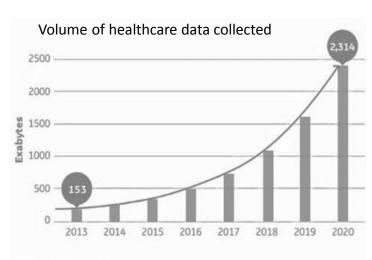
# Big Data in Healthcare

**90%** Of the world's data has been created in the past 2 years

**24 months** Frequency at which electronic healthcare data doubles

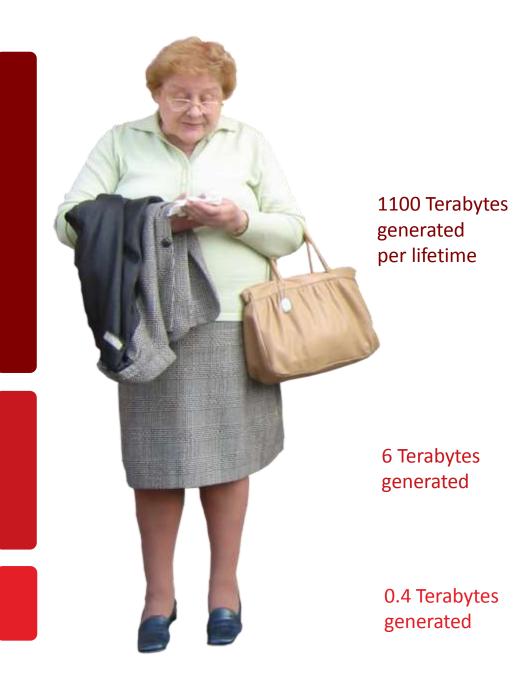
60% EXOGENOUS FACTORS

**75%+** Percentage of patients expected to use digital health services in the future



30% GENOMIC FACTORS

10% CLINICAL FACTORS



# Big Data in oncology: which sources?



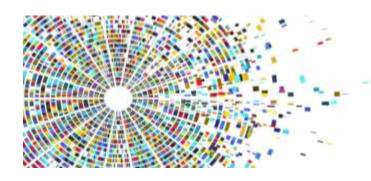
# Big Data in oncology: which applications?



From Real World Data to Real World Evidence

Post-marketing drug surveillance





Genomic databases

**Artificial Intelligence and Predictive Analytics** 



# Big Data in oncology: which applications?



#### From Real World Data to Real World Evidence

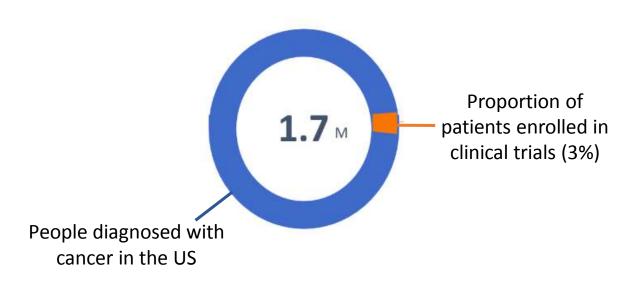
# Post-marketing drug surveillance



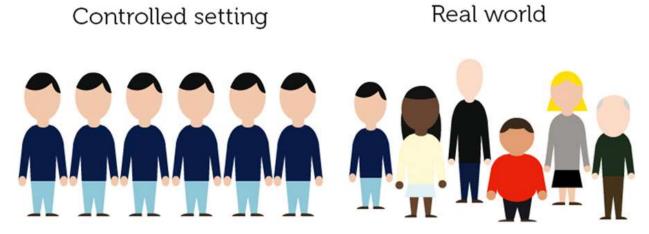


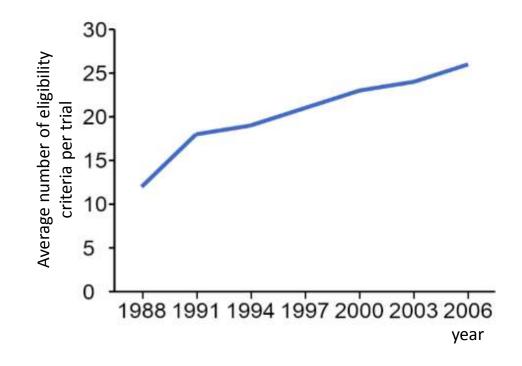


#### From "Randomized Controlled Trials" to "Real World Data"



Patients enrolled in clinical trials are highly selected. The 'real-world' patient is unlikely to be fully represented.





#### From "Randomized Controlled Trials" to "Real World Data"

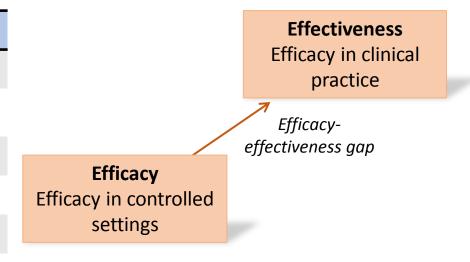
Term and source	Definition
RWD (ISPOR [7])	Data used for decision making that are not collected in conventional RCTs.
RWD (ABPI [8])	For the purposes of this guidance, "RWD" will refer to data obtained by any non-interventional methodology that describe what is happening in normal clinical practice.
RWD (RAND [9])	"RWD" is an umbrella term for different types of health care data that are not collected in conventional RCTs. RWD in the health care sector come from various sources and include patient data, data from clinicians, hospital data, data from payers, and social data.
RWD (IMI-GetReal	An umbrella term for data regarding the effects of health interventions (e.g., benefit, risk, and resource use) that are not collected in the context of conventional RCTs. Instead, RWD are collected both prospectively and retrospectively from observations of routine clinical practice. Data collected include, but are not limited to, clinical and economic outcomes, patient-reported outcomes, and health-related quality of life. RWD can be obtained from many source including patient registries, electronic medical records, and observational studies.

**RWD** definition

- Heterogeneous nature
- Multiple sources
- Uncontrolled collection, both retrospective and prospective

Makady et al. Value in health 2017

	RCTs	RWD
Туре	Interventional/experimental	Non interventional/Observational
Outcomes	Efficacy and safety	Effectiveness and economic assessment
Population	Narrow and selected	Wide and unselected
Randomization and blinding	Yes	No
Cost	High	Low
Relevance	Internal validity	Clinical practice



# From "Real World Data" to "Real World Evidence": the case of Alectinib

#### Media Release

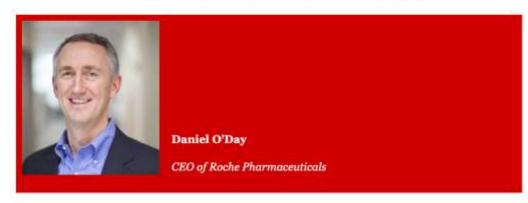
Basel, 21 February 2017

Roche receives EU approval of Alecensa (alectinib) for people with previously treated ALK-positive non-small cell lung cancer

 Alecensa provides an efficacious, systemic treatment option for people with ALK-positive NSCLC, which is also active in patients with brain metastases, who have been previously treated with crizotinib

#### Conversation with the Cancer Letter

# Roche CEO O'Day: Our investment in Flatiron will accelerate their mission



Roche's purchase of Flatiron Health will accelerate the development of real-world data suitable for supporting regulatory decisions, said Daniel O'Day, CEO of Roche Pharmaceuticals.

Alectinib received a conditional approval from FDA for the treatment of ALK+ NSCLC. US approval was based on data from two single-arm Phase II trials (NCT01801111 and NCT01871805).

National Health Technology Assessment (NHTA) authorities in EU requested additional evidence of the effectiveness of alectinib relative to the SoC (ceritinib) in order to provide a coverage decision.

To meet this requirement, Roche collaborated with Flatiron Health to conduct a retrospective analysis of EHRs of patients treated with ceritinib. The real-world external control arm was compared to the phase II single-arm and submitted to NHTA authorities, satisfying coverage requirements

98P

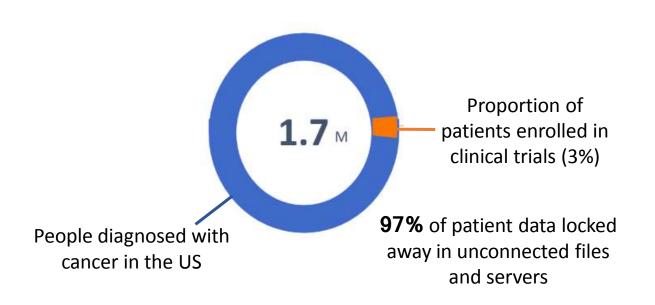
Retrospective indirect comparison of alectinib phase II data vs ceritinib real-world data in ALK+ NSCLC after progression on crizotinib •

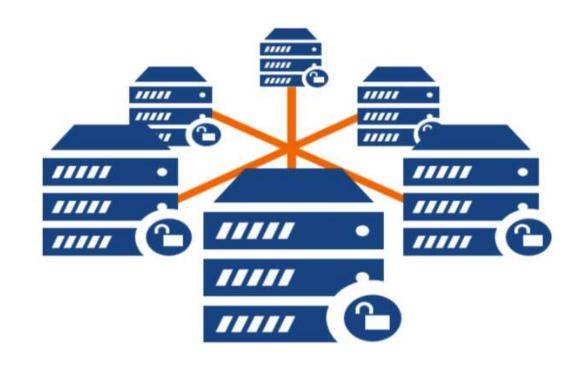
J. Davies, M. Martinec, R. Martina, P. Delmar, M. Coudert, W. Bordogna, S. Golding, G. Crane

Annals of Oncology, Volume 28, Issue suppl\_2, April 2017, mdx091.018, https://doi.org/10.1093/annonc/mdx091.018

Published: 03 April 2017

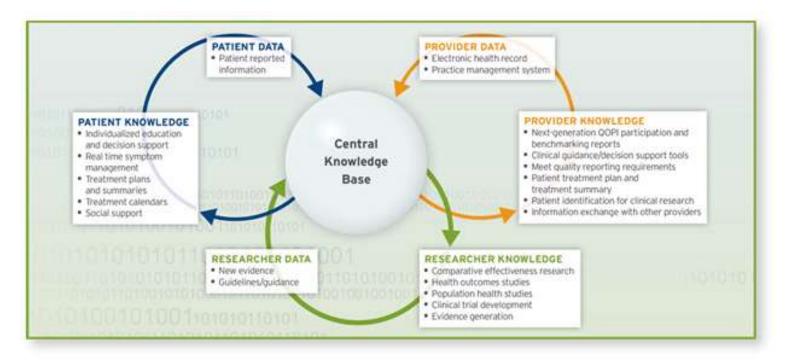
# From "Real World Data" to Big-Data Platforms

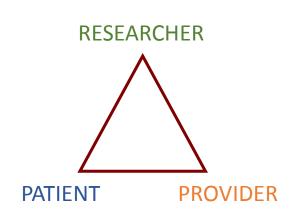




#### WHAT IF...

We could bring all the electronic data that is collected from the every day care of every cancer patient into one rapid learning network?





#### **Objectives**:

- Generate new knowledge and insights from RWD
  - better, faster, and cheaper
  - Increased *effectiveness*
  - From observation to causation
- Promote better quality of care and more cost-effective care
- Design of hypothesis-driven clinical trials
- Learning from the data with the goal of improving clinical guidelines

- Monitor drug safety
- Clinical decision support
- Clinical trial matching
- Improved risk stratification
- Patient-reported outcomes

# And many others...



To improve lives by learning from the experience of every cancer patient.



# An up-to-date intelligence source for the European oncology community

CODE aims to connect information on anticancer medicine use for all cancers, all patients, across all treatment centres in Europe who wish to join

# syapse

Powering precision medicine with insights from a global oncology network



Big Data for Better Outcomes

# **IBM Watson for Oncology**



Watson for Oncology helps physicians quickly identify key information in a patient's medical record, surface relevant evidence and explore treatment options.



# **ESME Research Program**

EPIDEMIOLOGICAL STRATEGY and MEDICAL ECONOMICS

Academic Real-world Data Platform



# Big Data in oncology: which applications?



From Real World Data to Real World Evidence

# Post-marketing drug surveillance



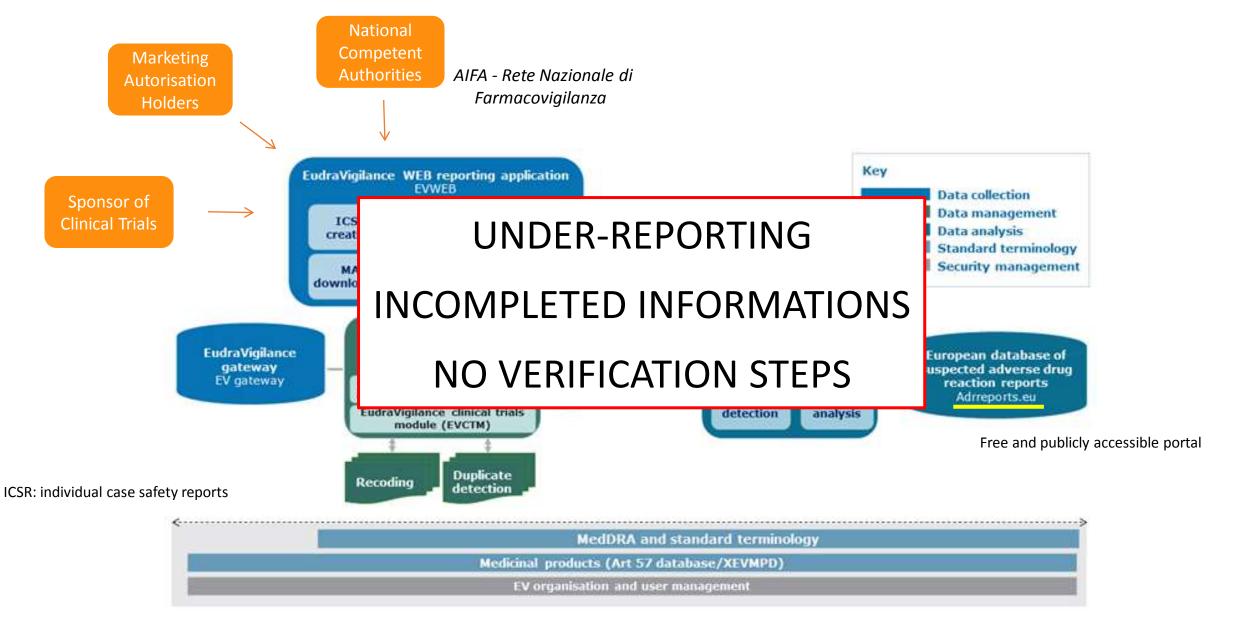




Artificial Intelligence and Predictive Analytics

# Post-marketing drug surveillance by EMA: EudraVigilance









14 National Competent Authorities (NCAs) EMA representatives

HMA-EMA Joint Big Data Taskforce

#### **Objective:**

USE OF BIG DATA FOR MEDICINE REGULATION

- map relevant **sources** of big data and define the main **format**, in which they can be expected to exist and through a regulatory lens describe the current landscape, the future state and challenges;
- identify areas of usability and applicability of emerging data sources;
- perform a gap analysis to determine the current state of expertise across the European regulatory network, future needs and challenges;
- generate a list of **recommendations** and a Big Data Roadmap.

Relevant Big Datasets → 7 subgroups

WS1: DATASET CHARACTERIZATION

WS2: USABILITY AND APPLICABILITY

Clinical trial and Imaging
Observational data
Spontaneous adverse drug reports
Social media and m-health
Genomics
Bioanalytical 'omics
Data analytics (ongoing)

WS3: STATE OF THE ART,
CHALLENGES AND EXPECTATIONS

WS4: LIST OF RECOMMENDATIONS
AND BIG DATA ROADMAP

WS: worksheet

#### **BIG DATA ROADMAP & CORE RECOMMENDATIONS**

7. Implementation of new regulations and post-marketing monitoring of devices and in-vitro diagnostics associated with the use of medicinal products

- 1. Promotion of global and harmonized standards to facilitate interoperability of data
- 6. Regulation about the acceptability of evidence derived from big data sources Regulatory acceptability agnostics Devices **Data Analytics** Data Linkage **Data Standardisation** Data Sharing and Access **Big Data**

**Data Quality** 

5. Analysis and promotion of new analytical approaches for modelling of big data sets for regulatory purpose

Engagement

and

Communication

Skills and Knowledge

- 8. Acquisition of skills required for these emerging areas
- 9. Proactive regulatory engagement with external stakeholders relevant to the Big Data Landscape, to influence strategy and ensure regulatory needs

2. Characterization and documentation of data quality, establishing minimum sets of data quality standards

3. Development of timely, efficient and sustainable frameworks for data sharing and access

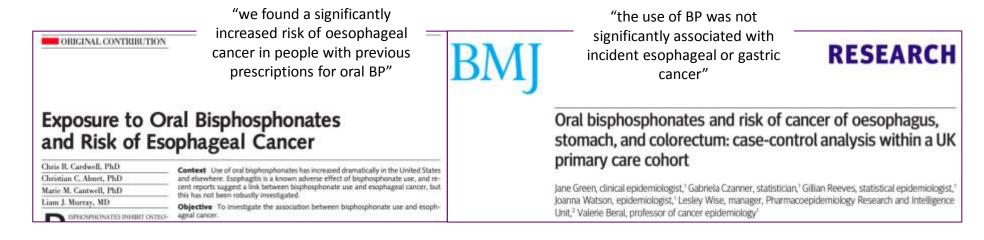
4. Promotion of mechanisms to enable data linkage to deliver novel insights Harmonisation of similar datasets

# Big Data in healthcare: which challenges?





#### SECURITY AND PRIVACY



#### **VERIDICITY AND CAUSATION DETECTION**

### **Conclusions**

- Vast amounts of healthcare data are continually being generated, offering huge opportunities to improve knowledge and increase effectiveness of therapies.
- The use of Big Data in healthcare needs to face to many technical obstacles, because of the lack of harmonised and structured data, interoperability standards, and semantical alignment between different datasets.
- Research methodology improvement and its standardisation is essential to differentiate co-incidence from real causality.
- Privacy and security must always be assured. Patients empowering, trust and direct involvement is essential to exploit Big Data as its best.
- Use of Big Data for pharmacovigilance and regulatory purpose offers the opportunity to increase reporting of ADRs, continuous and real time monitoring of drugs efficacy/toxicity (with a special attention to rare and long term toxicities), and finally increase knowledge about the real effectiveness of drugs.



Sydney Brenner (1927-2019)
Nobel Prize in Physiology or Medicine

"We are all drowning in a sea of data and starving for knowledge" Nobel Lecture 2002

# THANK YOU

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# **BACKUP SLIDES**

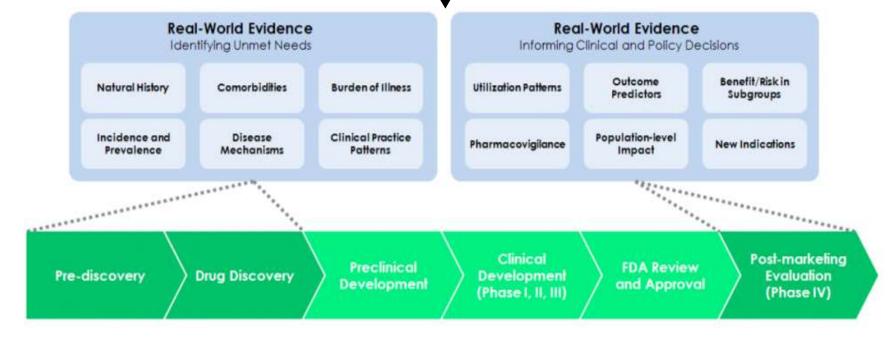
#### From "Real World Data" to "Real World Evidence"

**Real-World Data** (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.

**Real-World Evidence** (RWE) is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.

#### **Real World Data**

Curation Standardisation Anonymization Analysis



#### ASCO CancerLinQ

"First, we need to be connected"

**ASCO**\* Connection The professional networking site for ASCO's worldwide oncology community

Blogs

Magazine

**Tumor Boards** 

Trainee & Early Career

"We also need to make a dedicated effort to include all minorities"

Home > Blogs



2019 Presidential Address: Caring for Every Patient, **Learning From Every Patient** 

Monica M. Bertagnolli, MD @bertagnollimm Jun 02, 2019

"CancerLinQ fully connects all of us and learns from all of our patients' experiences"

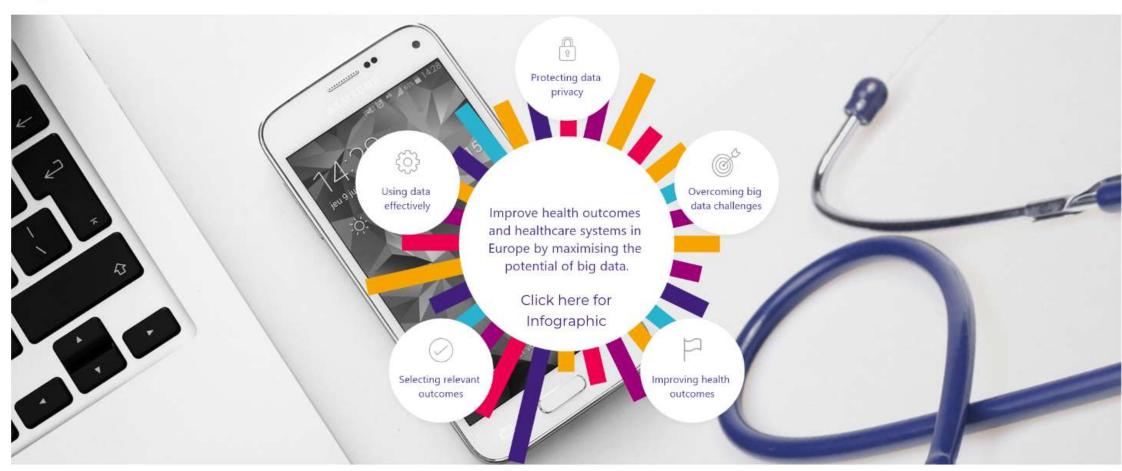
"Artificial Intelligence – machine learning – is a tool that can reveal important new insights from large datasets"

> "Finally, it's important that our connectivity flows both ways. We must invite our patients to participate"

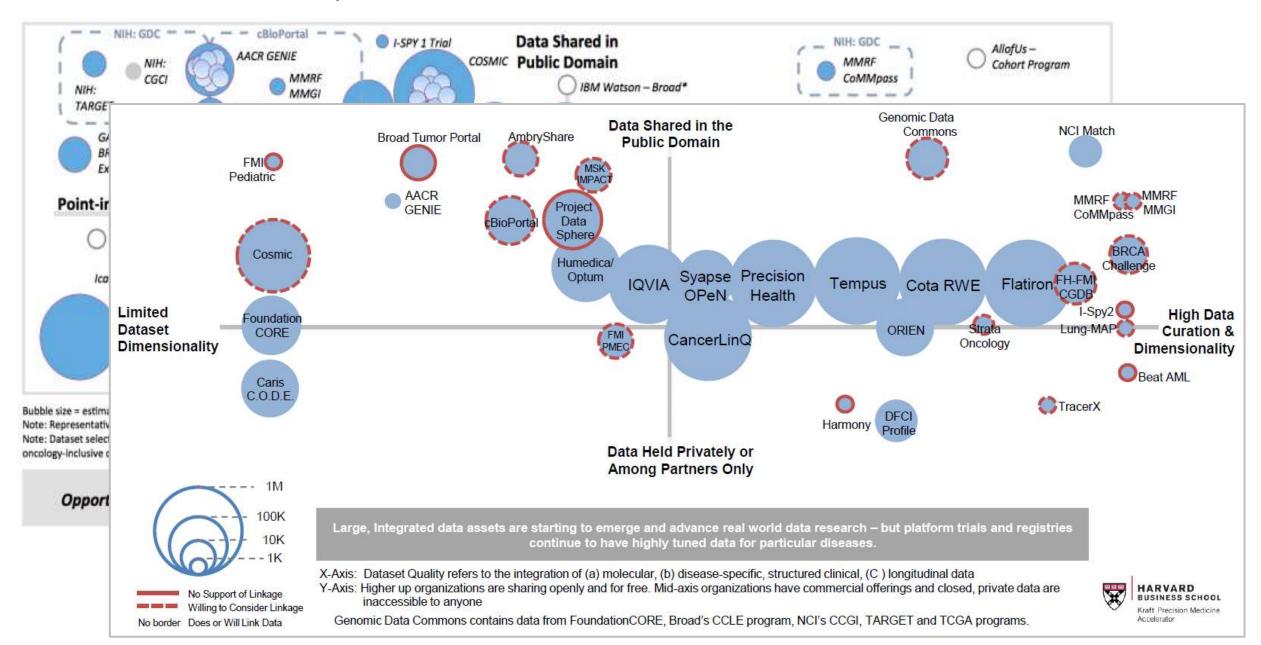
# Big Data for Better Outcomes



What is BD4BO v Why BD4BO v News & Events v Publications Contact us Login Knowledge Hub



### Real World Data landscape



# Post-marketing drug surveillance by EMA: before "Big Data"



Research and development	Marketing authorisation	Post-authorisation
EudraVigilance		
	Risk management	
System for managing and analysing information on suspected AEs to medicines studied in clinical trials in the European Economic Area (EEA)	Not all potential AEs are identified by the time an initial marketing authorisation is granted. The aim of risk management is to address uncertainties in the safety profile at different points in the lifecycle.	European Risk Management Strategy (ERMS)
		Good pharmacovigilance practice (GVP)
		Incident management plan
		Medical literature monitoring
		Medication errors
		Medicines under additional monitoring
		Periodic safety update reports
		Pharmacovigilance systems
		Post-authorisation safety studies
		Regulatory and procedural guidance
		Signal management

#### **CORE RECOMMENDATIONS**

- Data standardisation
- Promote use of global, harmonised and comprehensive standards to facilitate interoperability of data

Data quality

- Characterisation of data quality across multiple data sources is essential to understand the reliability of the derived evidence
- Data sharing and access
- The development of timely, efficient and sustainable frameworks for data sharing and access is required Further support mechanisms are needed to promote a data sharing culture
- Data linkage and integration

Promote mechanisms to enable data linkage to deliver novel insights

Facilitate harmonisation of similar datasets

Data analytics

Develop clear frameworks to enable the validation of analytical approaches to determine if they are appropriate to support regulatory decision making Promote new analytical approaches for modelling of big data sets for regulatory purpose

For more informations, see Annex III: Table of Recommendations from the Subgroups

#### **CORE RECOMMENDATIONS**

Regulatory acceptability of Big Data analyses

Regulatory guidance is required on the acceptability of evidence derived from big data sources

• Medical devices (MD) and In vitro Diagnostics (IVD) Regulation

Ensure effective implementation of the new regulations for devices and in-vitro diagnostics associated with the use of medicinal products and monitor its impact in delivering safe and effective devices and IVDs

Skills and knowledge across the regulatory network

Regulators must be equipped with the skills required for these emerging areas

External communication and engagement

Proactive regulatory engagement with external stakeholders relevant to the Big Data Landscape is needed in order to influence strategy and ensure regulatory needs are highlighted

# Post-marketing drug surveillance in EU: the PROTECT project



Coordinator: EMA

Deputy co-ordinator: GSK

34 partners, including academics, regulators, SMEs and EPFIA companies

(BIG-) DATA SOURCES: clinical trials, observational data, spontaneous reports, registries, electronic health records, databases, and patients.

**GOAL**: strengthen the monitoring of the benefit-risk of medicines in Europe.

**HOW**: developing a set of innovative tools and methods that will enhance the early detection and assessment of ADRs from different data sources, and enable the integration and presentation of data on benefits and risks.

STAKEHOLDERS: patients, prescribers, public health authorities, regulators and pharmaceutical companies.

**OUTPUT**: accurate and useful information supporting risk management and continuous benefit-risk assessment.

# Security and Privacy

Large availability of personal data



Large Computing and Storage Capabilities



Greater risk of privacy violation and security failure

More knowledge, better therapy, greater health





**PURPOSE SPECIFICATION** 

MANDATORY BREACH NOTIFICATION