HMA / EMA Joint Big Data Task force initiative

Presentation of the Report and next steps

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The landscape is changing rapidly – the challenges numerous

- Traditionally we have relied on RCTs Randomised double-blind placebo controlled studies for evidence – this is the best way to eliminate bias and get the best source of information on **effect**/safety of a single intervention/ therapy
- The Goal: **Effectiveness** in the intended target populations is something else, however.
- When can we start trusting Big Data based evidence without reverting to 100% empirical thinking?
- How can we ensure adequate evidence for regulatory decision making

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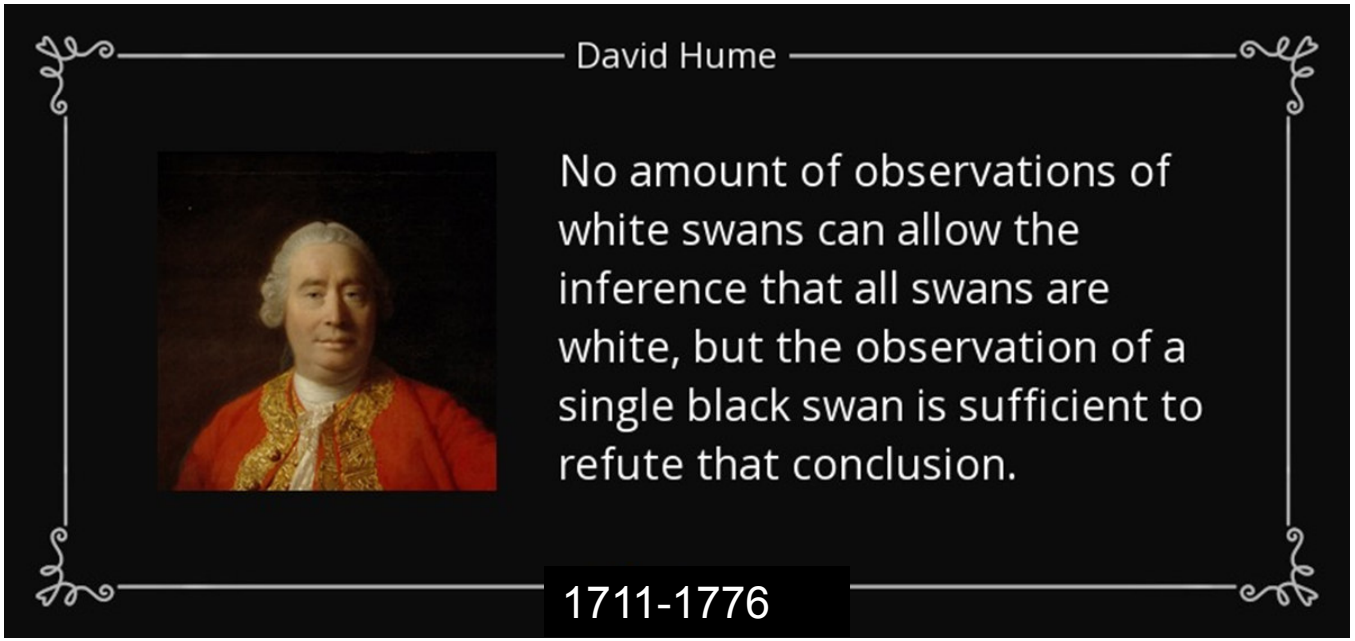
Empirical theory is not the final answer – Bias is (still) important!

When is an observation the truth?
When are a LOT of observations the truth?
How can Real World Evidence help us predict future observations?



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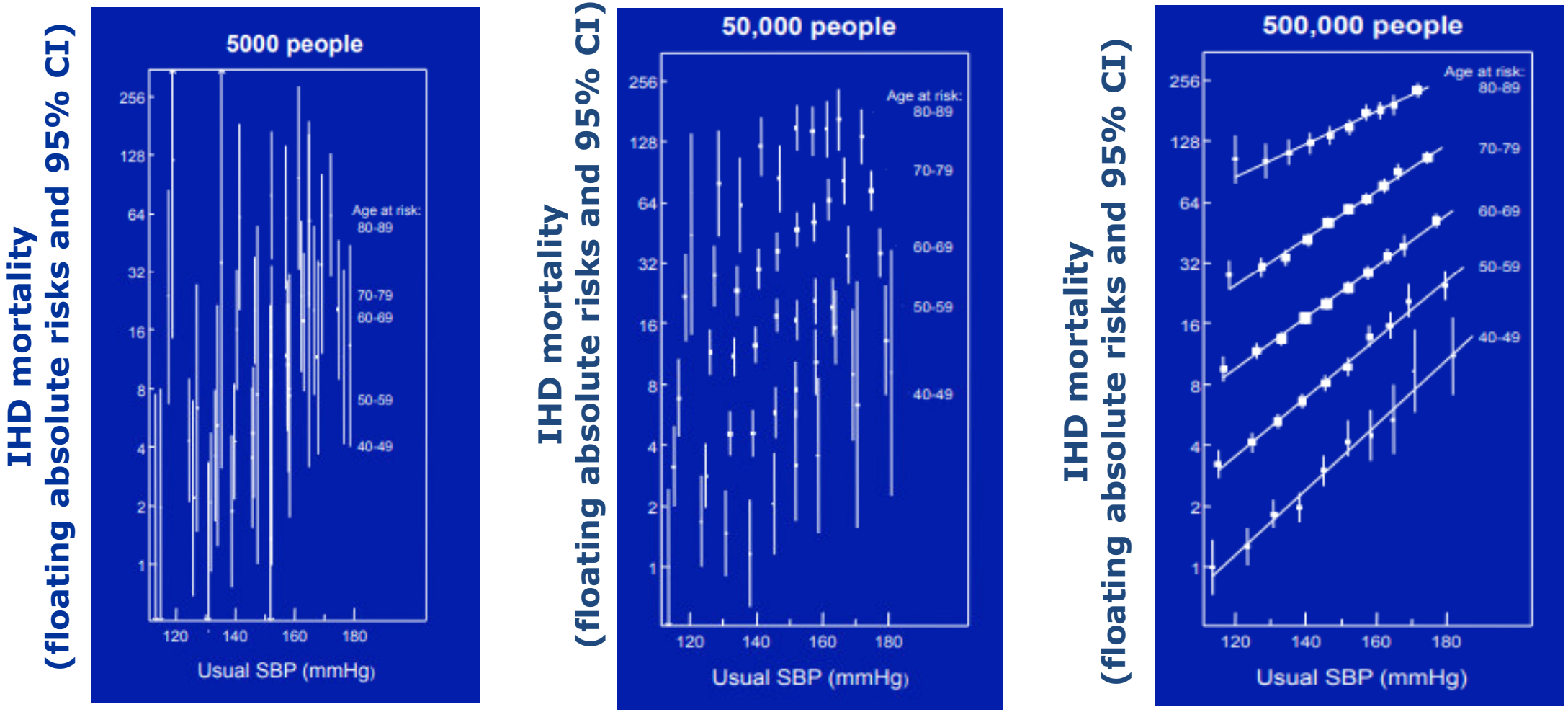
How can large volumes of data support decision making?

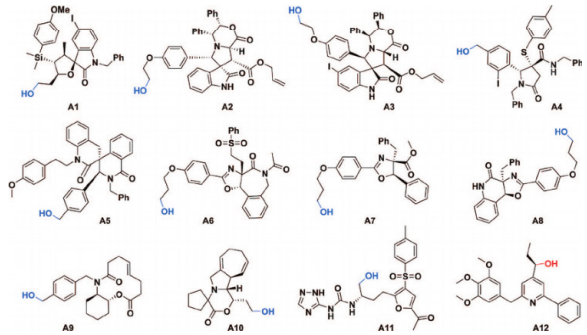
Ischaemic Heart Disease versus SBP for 5K vs 50K vs 500K people in the Prospective Studies Collaboration (PSC, Oxford, UK, courtesy Rory Collins)



NCB1

From

- Small molecules /MAbs
- Treatment of disease



To

- Advanced therapy
- Early intervention
- Biosystem modification

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NCB1 forebyggende behandling

Nikolai Constantin Brun; 28.02.2019

From

- *One size fits all*

To

- Precisionmedicine

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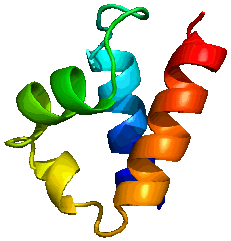
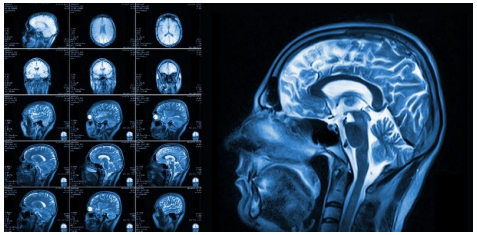
Precisionmedicine

Genomics



Proteomics



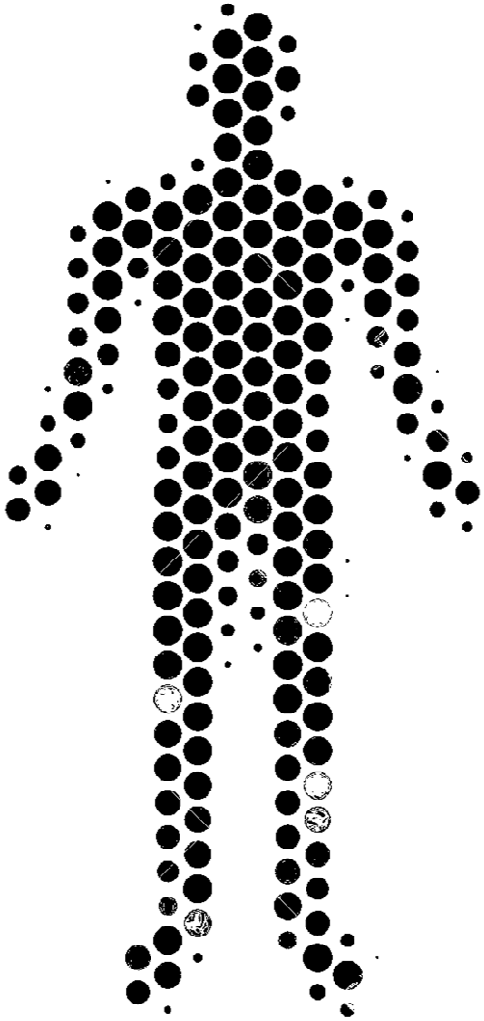
Imaging

Behavioromics

Clinical data

Wearables

SoMe data

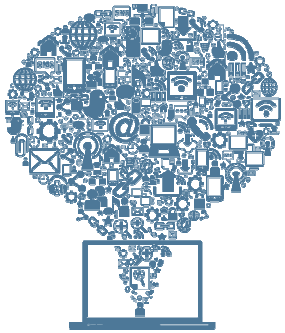


EN

Present regulatory paradigm

Structured data

Less structured data



Clinical Trials

Benefit/risk

HTA

Pharmacovigilance

Drug development
RCTs ~ 10 years

Approval

Post approval Surveillance

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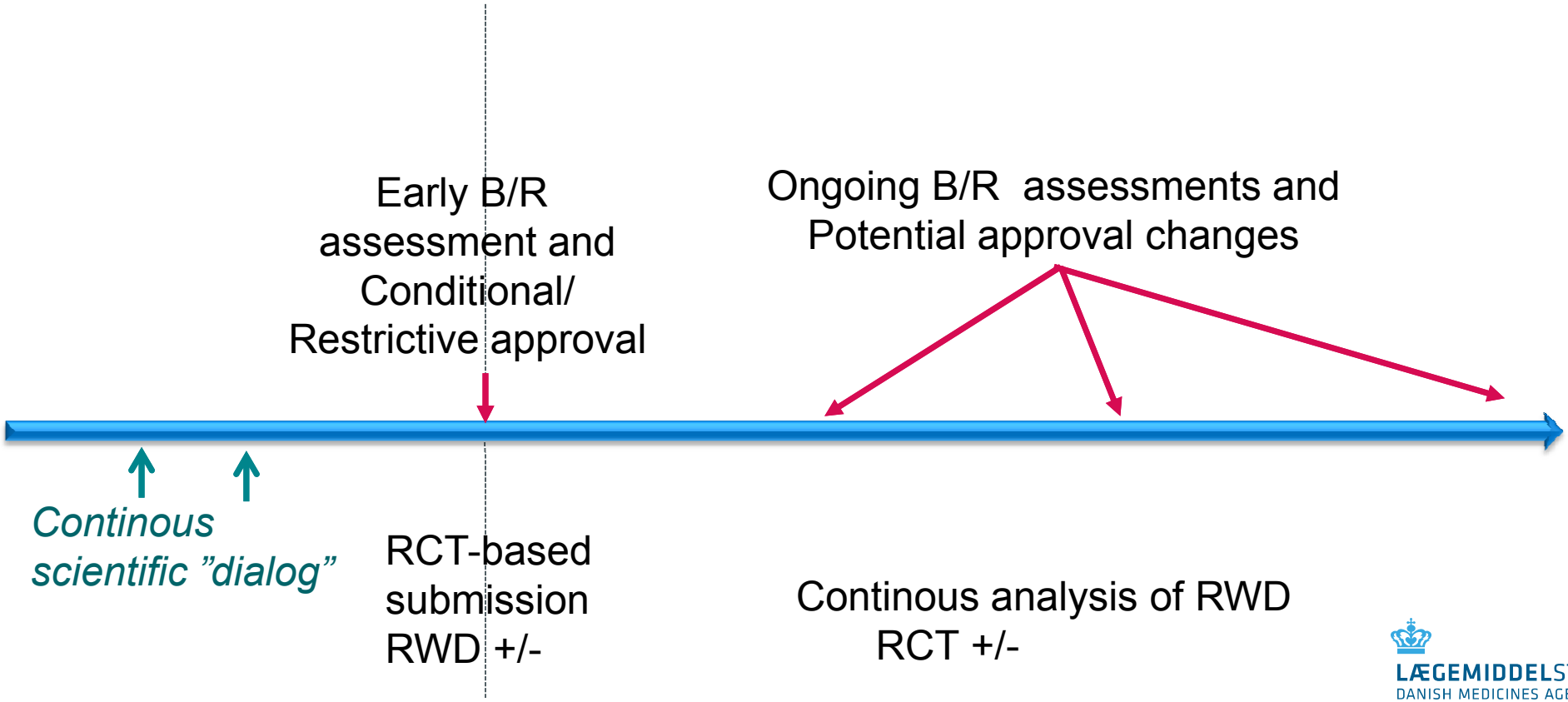
Future regulatory paradigm?



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Heads of Medicines Agencies

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SCIENCE MEDICINES HEALTH

Two important organisations – one goal

What is Big Data ?

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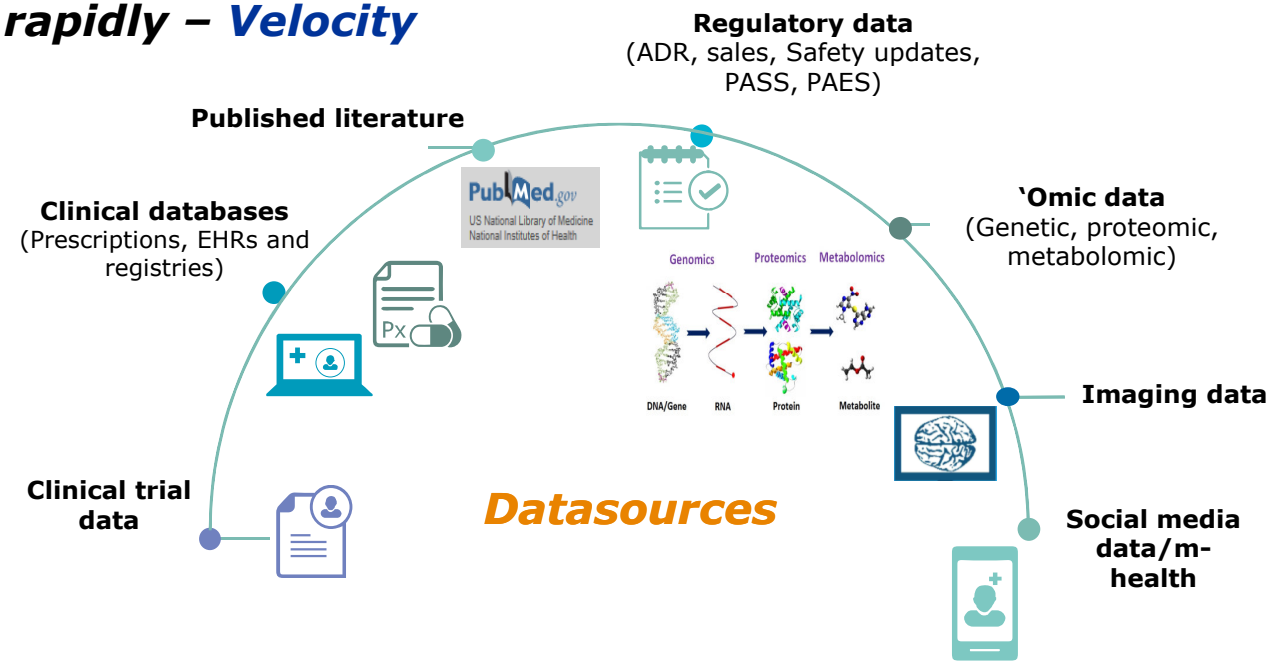
- ***Extremely large – Volume***
- ***Complex and multi-dimensional – Variable***
- ***Unstructured and heterogeneous – Variety***
- ***Accumulating rapidly – Velocity***



Vast scope of Big data .....*we need to prioritise – Value*

What do we need?.....*reliable evidence to support regulatory decusions – Value*

Current Regulatory Landscape

- Non clinical models fail to mirror human disease
- Unknown generalisability of RCTs
- Limited size of clinical database at approval
- Transparency of data
- B/R evaluated one and rarely in special/ high risk populations

- Multiple challenges in the use of RWD
- Increasing reporting of ADRs
- Monitoring the impact of risk minimisation measures
- Long term validation of digital/ surrogate endpoints
- Patient access to new medicines

Pre-authorisation | Authorisation | Post authorisation

Future Regulatory Challenges

- More complex trial designs
- Growth in biomarker use
- Increasing numbers of products unable to align with traditional drug development pathway
- Personalised medicine
- AI algorithms, more unregulated players e.g. Google
- Greater use of modelling and simulation approaches

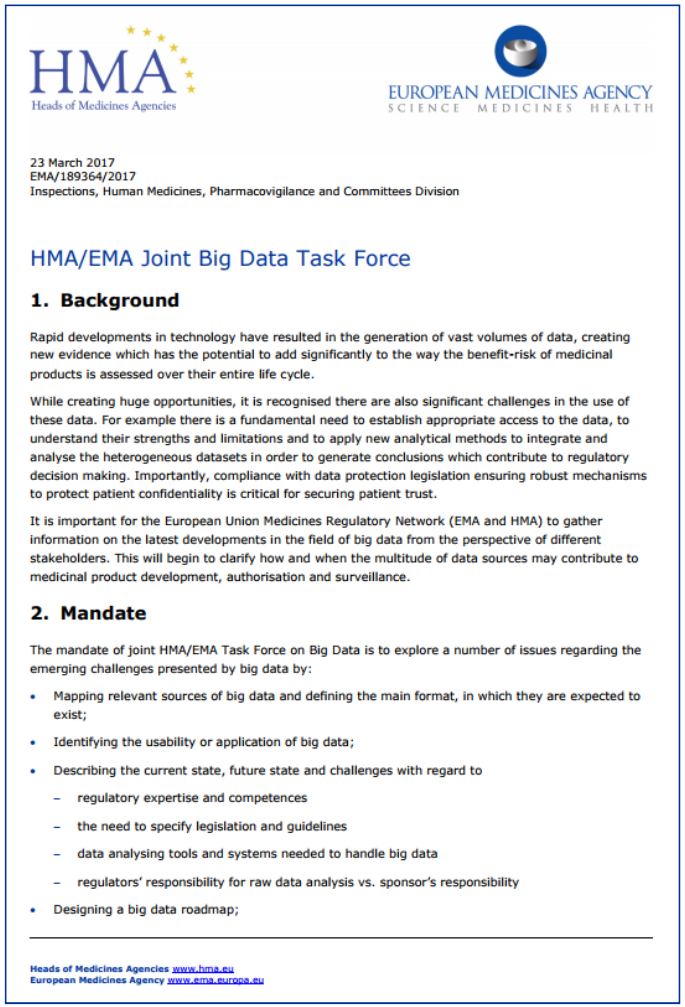
- Greater use of RWD across the product life cycle
- Increased incorporation of composite endpoints/ PROMS
- Greater development of preventative medicines
- More combination therapies
- Personalisation of dose and risk profiles
- Incorporation of patient preferences into decisions

Pre-authorisation

Authorisation

Post authorisation

HMA-EMA Joint Big Data Taskforce



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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;

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European Medicines Agency www.ema.europa.eu

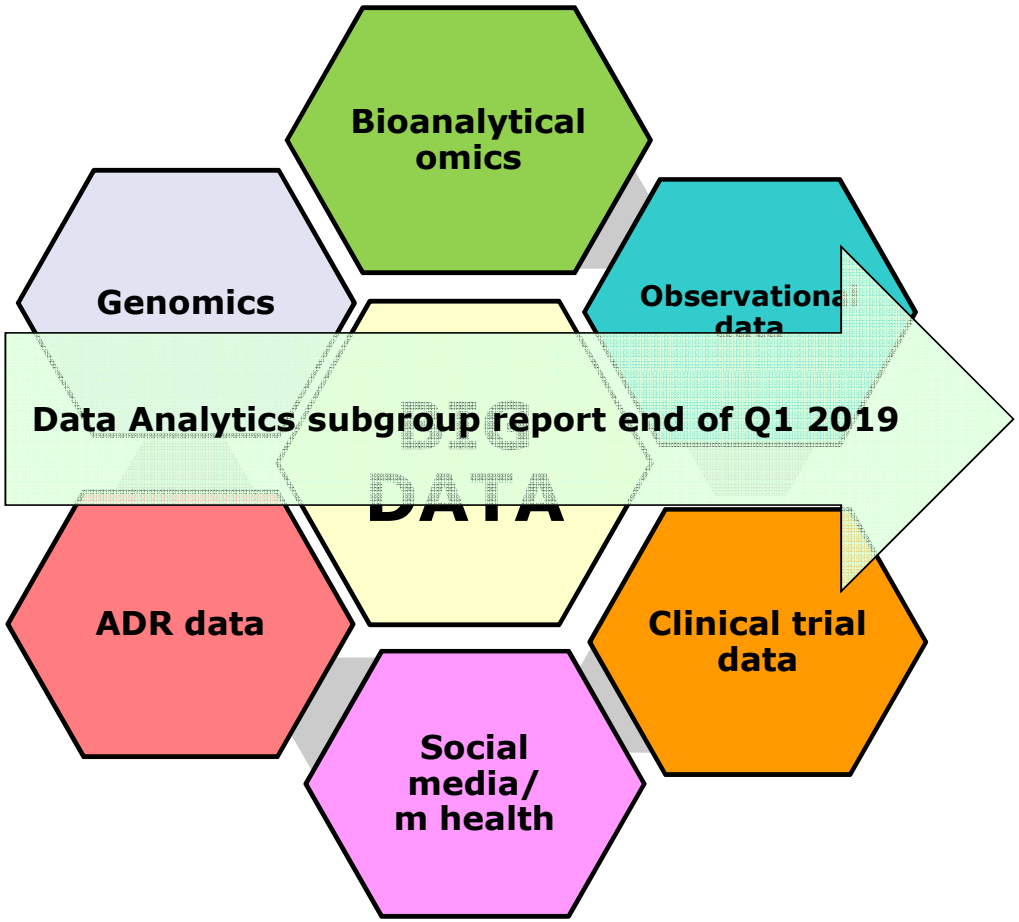
1. The Task Force should ***characterise*** relevant sources of big data and define the main format, in which they can be expected to exist in

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**

Deliverables



Gap Analysis

Survey of NCAs and pharmaceutical industry

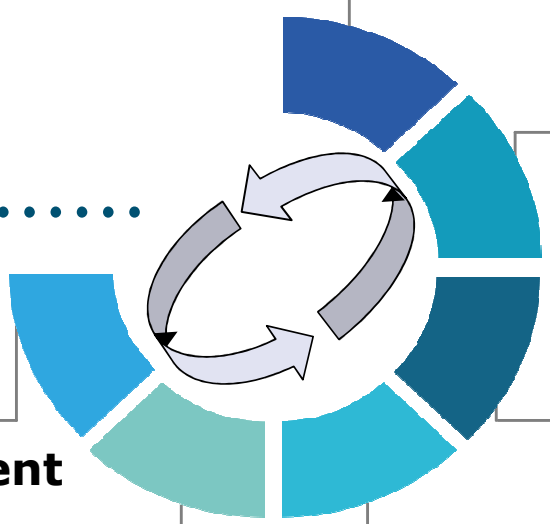
Subgroup Reports

Characterisation of the data landscape and detailed table of prioritised recommendations

Summary report

Set of core recommendations (Technical annexes not for publication)

Core recommendations
components underpinning acceptability



- Data Standardisation
- Data Quality
- Data Sharing and Access
- Data Linkage
- Data Analytics
- Skills and knowledge
- Communication & Engagement

Horizontal cross cutting recommendations – next steps to target priority areas

Data Standardisation

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

- **Minimise the number of standards**; strongly support the use of available global data standards or the development of new standards in fields where none are available to ensure early alignment
- Where data cannot be standardised at inception, establish the regulatory requirements to **confirm the validity of mapped data**
- Promote use of **global open source standards**
- Standards should be **platform independent and appropriately validated.**

Data Quality

Characterisation of data quality across multiple data sources is essential to understand the reliability of the derived evidence

- **Characterise and document** data quality in a sustainable EU inventory.
- Establish minimum **sets of data quality standards**. Where possible, quality attributes e.g. compliance to GCP requirements should be integrated to facilitate selection of appropriate data sets for analysis.
- Implement **data quality framework/attributes** for big data sets.
- Establish a **clear framework for the validation** of innovative bioanalytical methods e.g. 'omics.

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

- Strongly recommend the establishment of **distributed data networks**
- Establish disease-specific **minimum data elements** to enable harmonisation of data
- Require the submission of **data management plans**
- Promote **mandatory sharing of the analysis** arising from data sharing activities
- Promote the sharing of **qualified models**
- Support the development of policy initiatives to drive a **data sharing culture**
- Develop guidance for **robust data governance** and **data anonymisation**

Data Linkage and Integration

Promote mechanisms to enable data linkage to deliver novel insights

Facilitate harmonisation of similar datasets

- Encourage **sharing of raw data, associated meta-data and processed data** to enable meaningful data linkage whilst complying with the obligations in data processing set forth in the GDPR.
- Data linkage and timely data access will require **proactive mapping** and validation.
- Support mechanisms to **maintain up to date mappings** across terminologies.
- Promote the inclusion of **medicinal treatments** and **clinical outcome data** relevant to regulatory questions in public databases.

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**

- **Move the analysis to the data**
- Make publicly available **data analysis plans** for studies submitted for regulatory approval.
- Support, define and validate **innovative outcome measures** which leverage additional information from high-frequency or high-dimensional data.
- Strongly support **novel analytics approaches to interrogate unstructured data**
- Promote the increased utilisation of **scientific advice and the EMA Qualification Advice** process to enable regulators to influence more mature approaches.
- Form an **advisory group** to explore:
  - the applicability of novel analytics methodologies for regulatory decisions;
  - suitable data standards, IT architecture and tools for evidence generation.

Data Standardisation

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

Data Quality

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Data Linkage and Integration

Promote mechanisms to enable data linkage to deliver novel insights

Facilitate harmonisation of similar datasets

Medical devices regulation (MDR) / In vitro Diagnostics Regulation

Ensure effective implementation of the new regulations for devices and in-vitro diagnostics (IVDs) associated with the use of medicinal products

Monitor its impact in delivering safe and effective devices and IVDs

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.

Regulatory acceptability

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

Skills and knowledge

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

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

Task Force Conclusions

- Big data offers the possibility to derive novel insights to support decision making but also brings unknowns around data quality and hence the robustness of the evidence generated
- A regulatory strategy is required now to determine how and when in the product life cycle the utilisation of such data can bring value
- There is an **urgent need** to ensure the regulatory network has sufficient expertise to interpret and critically assess big data
- The current reports sets out in some detail '**the what**' but '**the how**' and '**the when**' will need further work and in the view of the Task Force requires a extension of the current mandate for up to 12 months with an interim assessment as 6 months. This will allow the data analytics group to complete their work and develop the scope for future work.

Next steps :
'The How'

Next steps

We need to move from well documented issues and theoretical solutions to practical, feasible and concrete actions.

Each subgroup will consider the recommendations relevant to their group and prioritise down to 3-5 key recommendations.

Prioritisations will be based on strategic importance, stakeholders priority, regulatory impact, potential public heath impact and feasibility.

Recommendations should be finalised by Q1 of 2020.

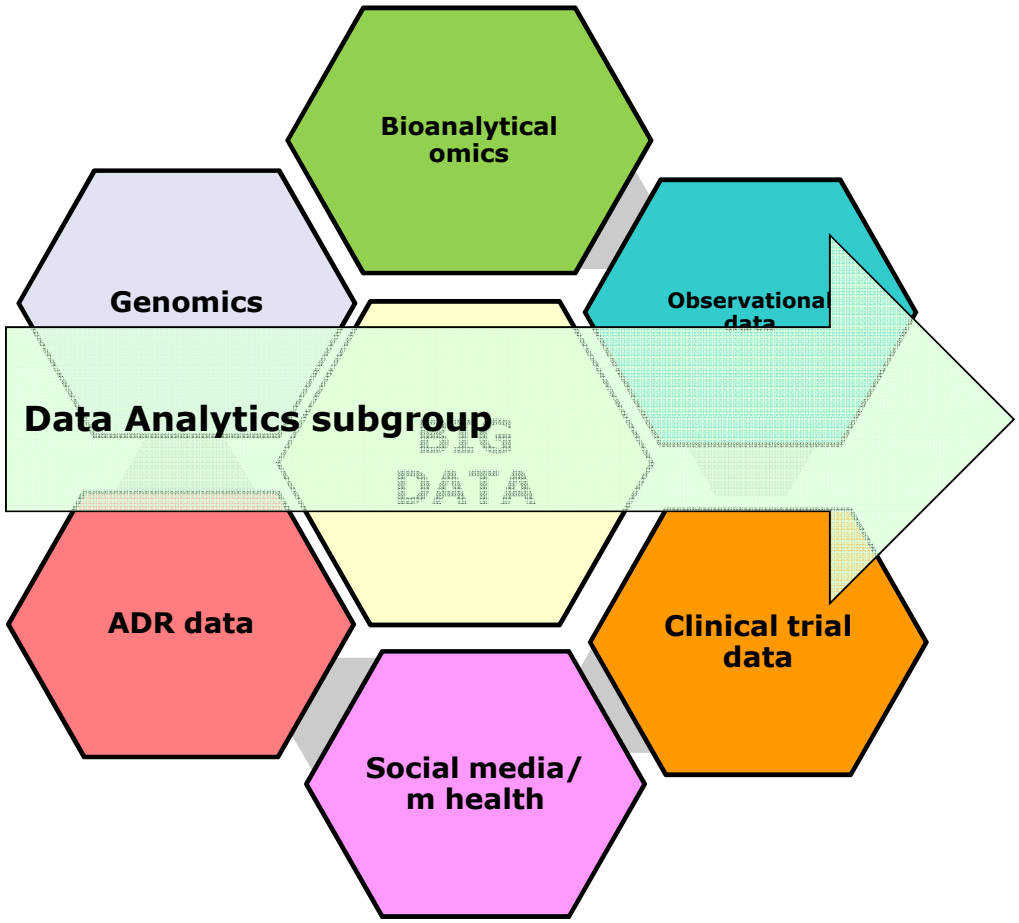
In order to deliver on the vision, building collaborations between stakeholders will be key.

Vision

*Our vision is a **strengthened regulatory system that can efficiently integrate data analysis into its assessment processes** to improve decision making. This will be supported by knowledge of data sources, their quality and their relevance for the European population, continual optimisation of data quality and analytical approaches and promotion of a secure and ethical data sharing culture. Training and external collaborations will be key in order to build expertise.*

***Knowing when and how to have confidence in novel technologies and the evidence generated from big data will benefit public health** by accelerating medicines development, improving treatment outcomes and facilitating earlier patient access to new treatments.*

Next steps


Bioanalytical omics
Genomics
Observational data
Data Analytics subgroup
BIG DATA
ADR data
Clinical trial data
Social media/ m health

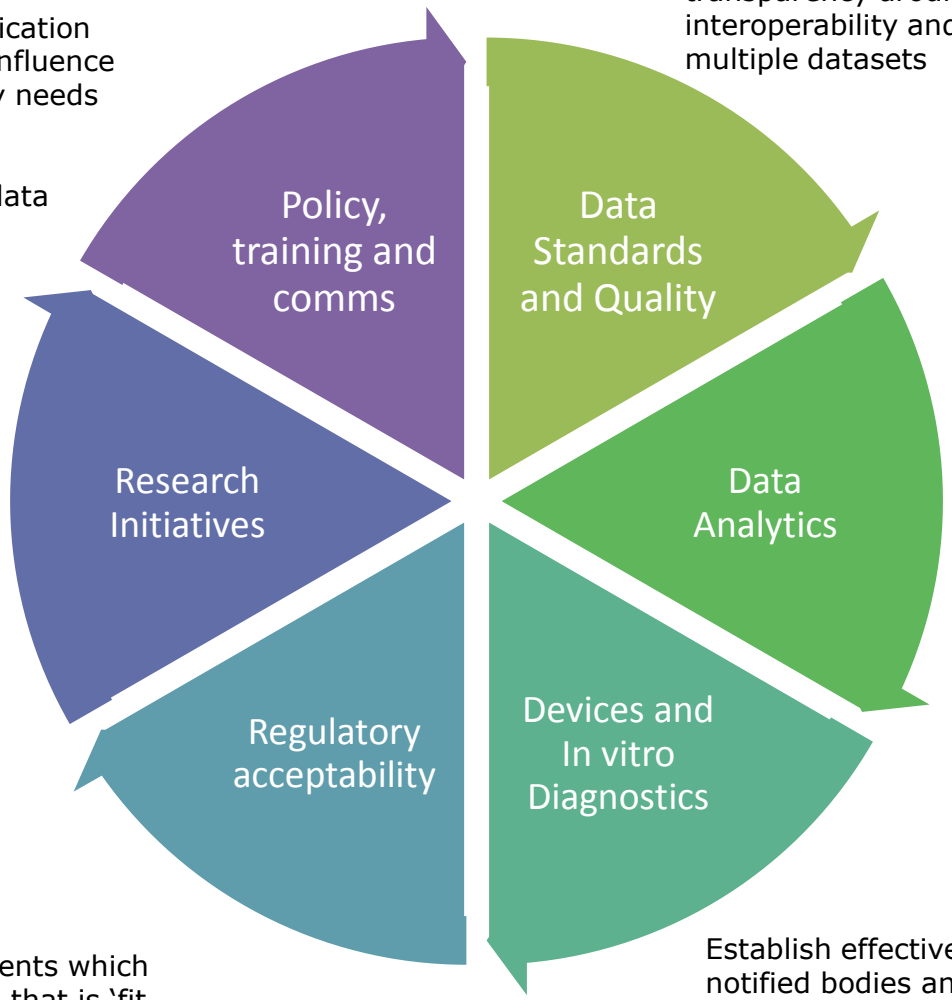

Policy, training, comms
Data standards and quality
Research Initiatives
Data analytics
Regulatory acceptability
Devices and in vitro diagnostics

Support and maintain relevant skills in the regulatory network

Promote bidirectional communication with external stakeholders to influence strategy and ensure regulatory needs are highlighted

Identify potential barriers for data sharing and analyses

Promote the use of global, harmonised and comprehensive standards to provide transparency around quality, enhance interoperability and facilitate linkage across multiple datasets



To strengthen and foster research to create an environment that supports the development of innovative approaches

To optimise the use of healthcare related data to support regulatory decisions

Support the development and validation of novel analytical approaches

To define the elements which results in evidence that is 'fit for purpose'.

Establish effective co-ordination between notified bodies and NCAs to deliver safe and effective devices and in vitro diagnostics

Thank you for your attention

Any questions? NCBR@DKMA.DK

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Any questions?

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