EFSPI

European Federation of Statisticians in the Pharmaceutical Industry

Promoting Professional Standards in Europe

Data sources to help inform drug development – what you give is also what you get

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Introduction: Who are we?

- Rebecca – Global Lead Patient Level Data Sharing, Roche UK; Chair of PSI External Affairs Committee; EFSPI Data Transparency Working Group
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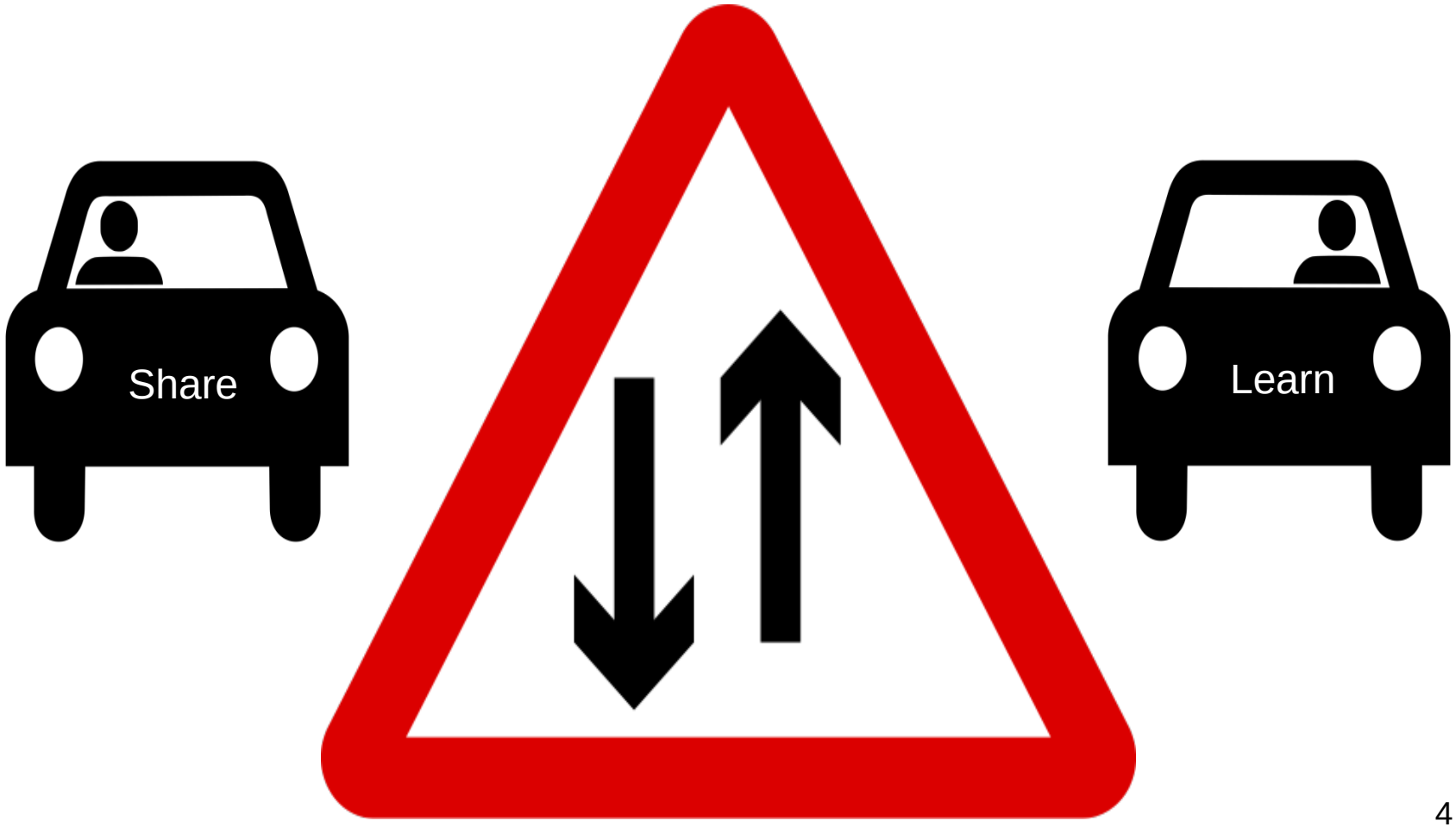
- Disclaimer
  The views and opinions expressed in this presentation are those of the individual presenter and should not be attributed to any organisation with which the presenter is employed or affiliated.

Objectives of this session

Increase your

- **knowledge** of sources of clinical trial information outside of medical literature and registries and how to access them
- **awareness** of the sorts of insights that access to documents and/or datasets may afford
- **appreciation** that the clinical trials we work on have a life and scientific value beyond the protocol and regulatory filing …..

Data sharing is a 2-way street ….



New mindset needed

- Opportunities
  - New data sources that we can use in development planning and trial design
    - CSR level detail versus publication level detail
    - Operational aspects when embarking in a new disease area
- Challenges
  - All the “data” generated during a study has the potential to become publicly available
  - No longer limited to sharing with regulators

Data sharing evolution continues ….

2013 2014 2015 2016 2017 2018

AllTrials Campaign launched Jan 2013

efpia efpia/PhRMA principles published July 2013

EMA Policy 70 effective Jan 2015

Report Jan 2015 INSTITUTE OF MEDICINE

CT.gov update effective Jan 2017 ClinicalTrials.gov

ICMJE Proposal for provision of PLD with journal articles ICMJE

What the regulators are doing

- EudraCT study and results registry
- EMA Transparency Policy – redacted CSRs etc to 3rd parties (companies include redacted copies of documents as part of MA application)
- Future phase will address patient level data

- CT.gov Sept 2016 update: expand criteria for posting, include all 2º endpoints, protocol and SAP.
  Scope for NIH funded research expanded.
- Work with consortia to address disease wide issues – e.g. earlier endpoints to predict SVR in Hepatitis
- Targeted opportunities to advance medical science

Health Canada March 2017 White Paper, similar to Policy 70 approach

efpia/PhRMA Commitments Implemented from Jan 2014

1. Enhancing data sharing with **researchers**
2. Enhancing **public** access to clinical study information
3. Sharing results with **patients** who participate in clinical trials
4. Certifying procedures for sharing clinical trial information
5. Re-affirming commitments to publish clinical trial results

“Data” can have many meanings

Increasing level of detail

Regulatory Reviewer Assessment Reports 

Registry posting (protocol and summary results) 

Journal article 

Regulatory summary document (multiple studies) 

Clinical Study Report (single study / datacut) 

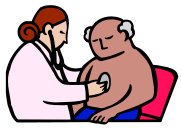
Aggregated data

Statistical Analysis Plan 

Trial correspondence – ICF, ethics committee communications 

Supporting info

Patient Level Data files for a trial 

Individual’s patient record 

Individual Patient Data (IPD)

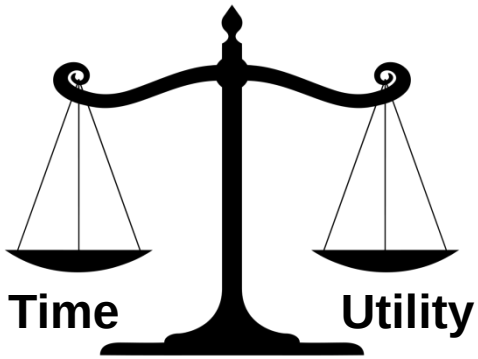
Aggregate Data or PLD?

Aggregate / Study Level Data

- Many CSRs, protocols and SAPs available online
- Generally open access when available
- Results available on CT.gov
- Considerably more detail than publications

Patient Level Data

- EU and US approved products/indications only
- Research proposal required
- Time to access data from submission 6 months or more
- Commitment to publish your findings
- Complexity of different data models



How could CSR access help me?

Meta-analyses using summary statistics

Access to 2° and exploratory results

Better understand details of analysis methodologies and assumptions used

Designing more efficient trials

Access to unpublished studies

Access to negative studies

Trial design

Sample size estimation

Case Study: Using CSRs

EMA provide redacted CSRs on request

Rare subgroup of disease population to be studied. 4 registrational studies identified using the same control arm.

6 weeks from request to receipt

Confirmed sample size assumptions for sub-group
Additionally:

- Insights from protocol amendments
- Detailed efficacy endpoint definitions
- Analysis population definitions

CSR Resources

- CT.gov - summary results
- EU portal– proactive sharing and on request
- Company policies (e.g GSK and Novo Nordisk)
- CSRs available “on request” from some companies
- Equivalent full report may not be produced for academic studies

How could access to PLD help me?

Secondary research questions:

- Exploring effects across trials (IPD meta-analyses)
- New indications
- Refine/relevant endpoints
- Sample sizing (diff endpoint or population)
- Prognostic factors
- Investigating patients most likely to ….
- HTA analyses

Independent replication

Time to understand data and utlilise it to its full potential inc. failed studies/drugs

Connecting researchers / new collaborations?

Increase research community understanding of pharma data

- Size and complexity of datasets
- Good statistical and programming practice

PLD Resources

- Clinicalstudydatarequest.com [CSDR.com]
  - 13 Pharma companies, 3374 studies listed, enquiry route available for unlisted trials
- Institution specific sites
  - Pharma companies outwith CSDR.com have request processes in line with efpia/PhRMA Commitment. Easy to access from corporate website, e.g. Pfizer, Amgen, AZ, Janssen (YODA)
  - Academic Institutions may have a process, but likely to be harder to find and access. Processes being put in place, e.g. UK Clinical Trial Units
- Disease Specific Resources
  - E.g. Project DataSphere, 90 oncology studies, control arm data

How do we need to adapt?

- Documents no longer “conversations with the regulators” – now public documents
  - Protocol and SAP will be submitted to CT.gov as part of results postings for studies starting from 18 Jan 2017
  - Protocol and SAP increasingly required as supplementary information to published article (e.g. NEJM)

How do we need to adapt?

- Preparation of public facing CSRs under EMA Policy 70
  - Need for expertise in data anonymization techniques and risk quantification
  - Development of scalable solutions
  - Opportunity for “redaction/anonymization” ready document templates
  - Plain language summary (lay summary) for EMA and for trial participants

How do we need to adapt?

- Clinical trial datasets (and documents) have a life beyond the CSR and filing
- All studies and data need to be available for future re-use
- Do your processes ensure that they are
  - Findable?
  - Accessible?
  - Interoperable?
  - Re-usuable?

Closing Thoughts

Data sharing is a reality - opportunities for statisticians

- Data and insights to enhance drug development strategy
- Expertise and support in development of quantitative risk methods for data privacy
- Leaders in drug development will be those who know where the relevant data is, how to access it, aggregrate it, analyse for meaning and communicate those insights

Watch This Space …

- EMA Technical Anonymisation Group (TAG)
  - In March the European Medicines Agency (EMA) launched a call for applications to join a technical anonymisation group to assess best anonymisation practices, and any risks to privacy and re-identification of patients in the light of new technological developments. In addition, it will investigate how the anonymisation methodology used impacts the scientific utility of the published data, and establish whether secondary analysis of the data can be successfully undertaken.
- EFSPI/EFPIA data sharing workshops
  - An initial workshop in September 2016 provided an opportunity to share experiences of the early implementation of the EMA publication of clinical data. A variety of case studies were shared, a number of challenges discussed and a range of stakeholders perspectives provided.
  - The second workshop will focus on different strategies for anonymizing clinical data and methods for assessing the risk of re-identification. The aim is for sponsors to share their approaches for anonymising clinical data and share experiences. Further information and details about the second workshop will be shared in forthcoming EFSPI newsletters.

Questions & Feedback

Useful references

- IoM report : http://iom.nationalacademies.org/Reports/2015/Sharing-Clinical-Trial-Data.aspx
- Wellcome Trust report : http://www.wellcome.ac.uk/About-us/Policy/Spotlight-issues/Data-sharing/Access-to-clinical-trial-data/index.htm
- Cross-pharma data sharing request website:
  - Link to site: https://clinicalstudydatarequest.com/Default.aspx
  - Publications by Independent Review Panel: http://www.nejm.org/doi/pdf/10.1056/NEJMp1411794, http://www.nejm.org/doi/full/10.1056/NEJMp1610336
- Data Sharing Statements for Clinical Trials - A Requirement of the International Committee of Medical Journal Editors
  - http://www.nejm.org/doi/full/10.1056/NEJMe1705439
- Reviews of Trial Transparency:
  - Compare Project: http://compare-trials.org/
  - Miller et al review: http://bmjopen.bmj.com/content/5/11/e009758.full

References continued

- EFPIA/PhRMA Principles: http://transparency.efpia.eu/uploads/Modules/Documents/data-sharing-prin-final.pdf
- GSK Clinical Study Register: https://www.gsk-clinicalstudyregister.com/
- EMA
  - Clinical Data website: https://clinicaldata.ema.europa.eu/web/cdp/home
  - Access on request: http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/document_listing/document_listing_000312.jsp&mid=WC0b01ac0580999a9c
- EFSPI/PSI Data Transparency articles http://bmcmedresmethodol.biomedcentral.com/articles/supplements/volume-16-supplement-1
- OpenTrials Initiative: http://opentrials.net/2016/08/10/opentrialsfda-unlocking-the-trove-of-clinical-trial-data-in-drugsfda/
- CT.gov Sept 2016 update: https://www.nih.gov/news-events/news-releases/hhs-take-steps-provide-more-information-about-clinical-trials-public

Upcoming events

Promoting Statistical Insight

Course: Estimating sample sizes in clinical trials, 28 – 29 June 2017

Webinar: IMI PREFER — Patient preferences: why, how and when, 21 September 2017

Course: Improving Influence and Increasing Impact: Essential Skills for Industry Statisticians, 21 September 2017

One day meetings and webinars planned for late 2017, dates TBC

- Estimands
- Extrapolation
- Causal inference
- Health technology appraisals (joint with EFSPI)

www.psiweb.org/events/psi-events