Data quality and data verification in registries: results of a stakeholders' survey

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Disclaimer and Disclosure Statement

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 Dutch Medicines Evaluation Board.

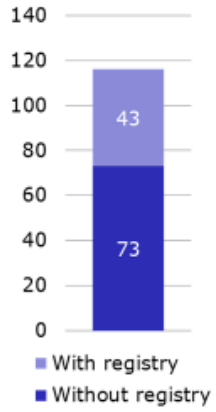
- ✓ I have no real or apparent relevant financial relationships to disclose
- ✓ I am employed by a regulatory agency, and have nothing to disclose

Background

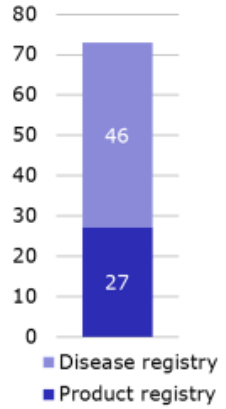
Registries supporting new drug applications

1 Jan 2007 to 31 Dec 2010

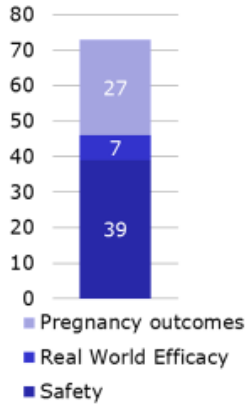
New Drugs



Type of Registry



Primary Aim



Key facts

43 new drugs with 1 to 6 registries

9 imposed registries

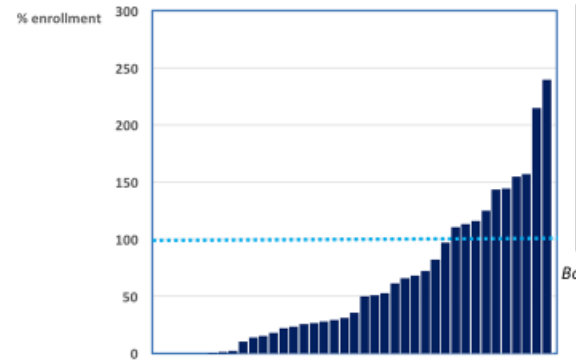
15 Orphan drugs

13 Conditional Approval / Exceptional Circumstances

-> level of innovation and orphan status predict approval with registries

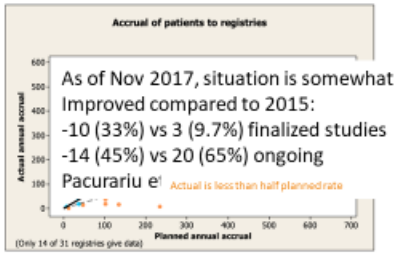
C. Jonker et al. Pharmacoepidemiol Drug Saf. 2017;1–7

Enrolment



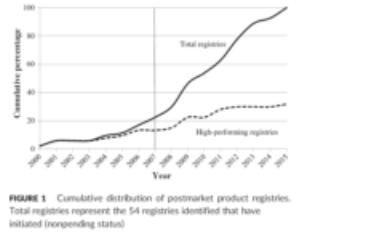
Enrolment in 41 of 73 registries (registry studies) with predefined sample sizes (a median of) 5 years after approval

Jonker C et al. Clin Ther. 2018 40(5):768-773



As of Nov 2017, situation is somewhat Improved compared to 2015:
-10 (33%) vs 3 (9.7%) finalized studies
-14 (45%) vs 20 (65%) ongoing
Pacurariu e

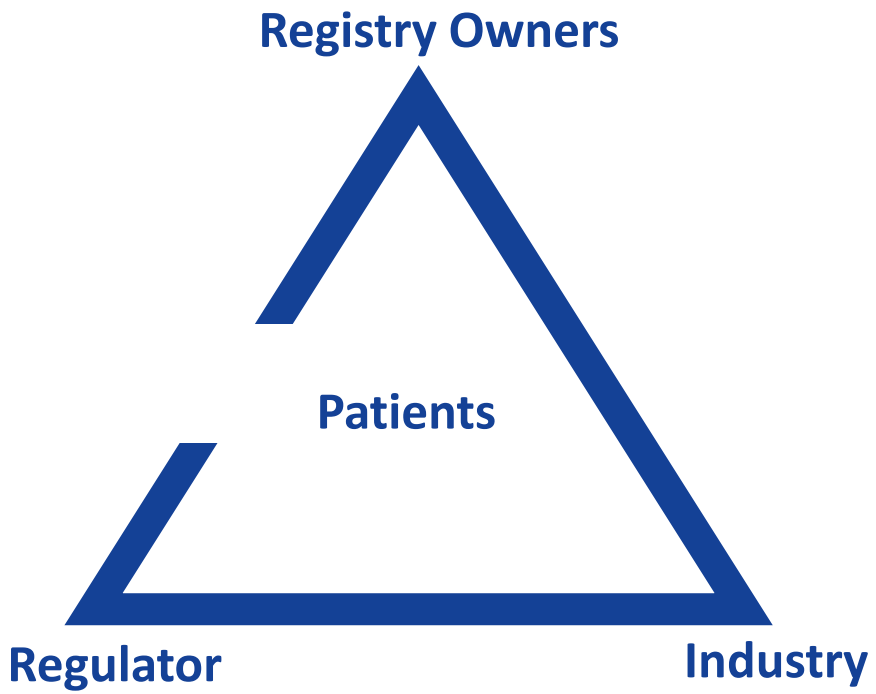
Bouvy J et al. Pharmacoepidemiol Drug Saf. 2017;1–8



Zhao Y et al. Pharmacoepidemiol Drug Saf. 2018;1–8

The EMA's Patient Registry Initiative

- Launched September 2015
- ***Aims to facilitate use of patient (disease) registries by introducing and supporting a systematic approach to their contribution to the benefit-risk evaluation of medicines***
- To promote dialogue between regulators, companies and registry holders to understand barriers and opportunities of using disease registries.
- ***Draft Guideline on registry-based studies***



https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-registry-based-studies_en.pdf

Aim

1. To quantify the opinion of stakeholders about key elements of registries as source data for studies that support regulatory decision-making in the field of rare diseases.

2. To assess whether the importance attached to these key elements differed between industry stakeholders versus others.

Web-based survey

47 questions included

- Participant characteristics (2 questions)
- General (2 questions)
- Common data elements (24 questions)
- Data quality (10 questions)
- Governance (4 questions)
- Registry-based studies (5 questions)

Participants

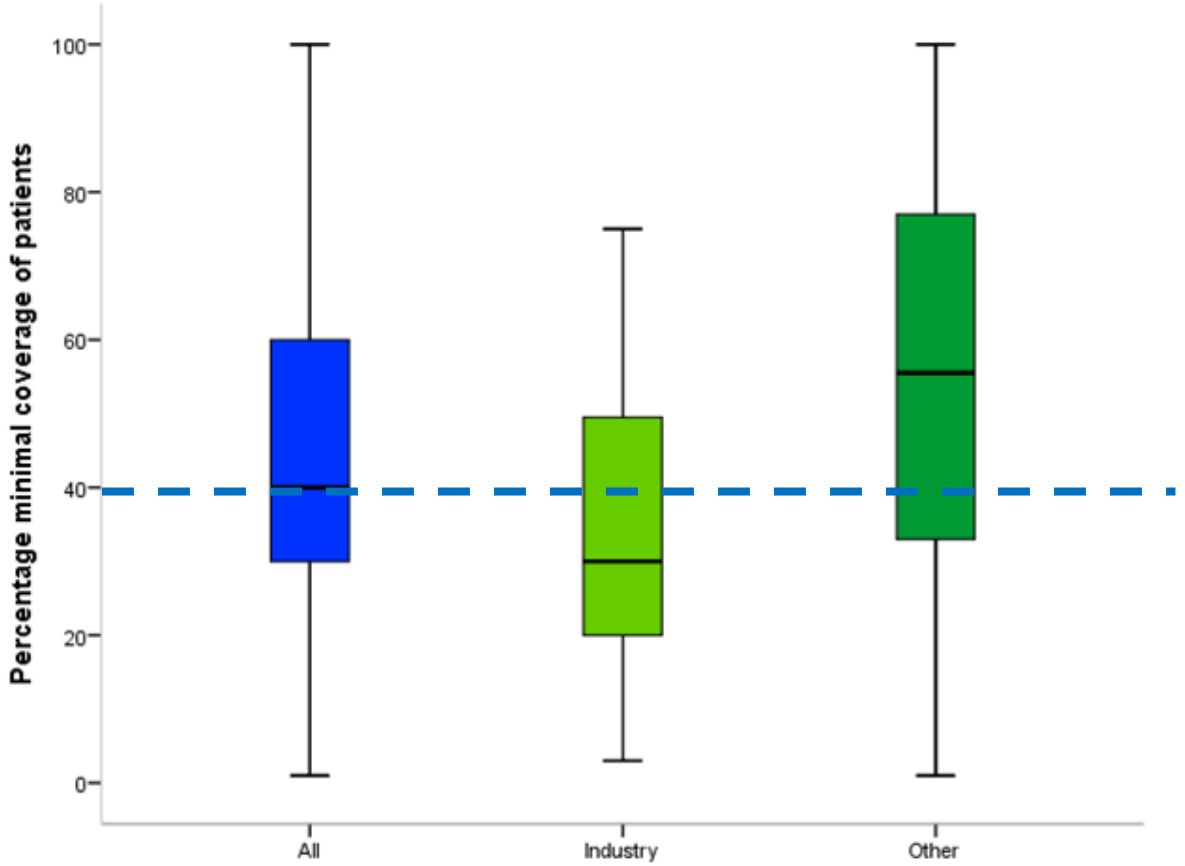
- Pharmaceutical companies
- Regulatory Authorities
- Registry owners
- Patients
- HTA assessors

Results

- ✓ In total 73 respondents completed more than 80% of the survey

- ✓ The respondents were divided in 2 groups:
  - 42 people working in industry
  - 31 other stakeholders

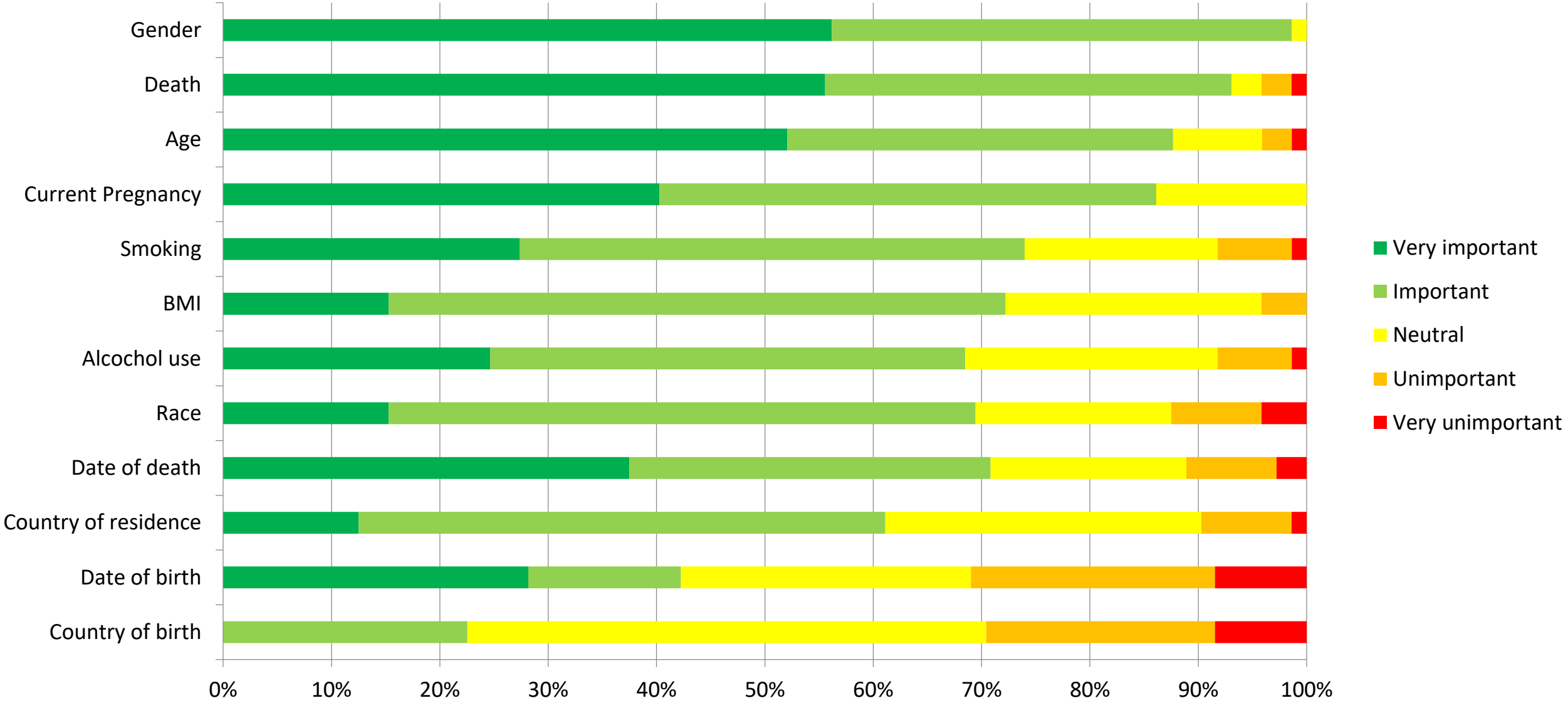
Coverage



Coverage (~40%);
p<0.01

Other stakeholders felt that the percentage of *minimal coverage of patients* should be higher dan people working in industry.

Common data elements: demographic data



Common data elements: medication

Details important to collect for medicinal products:

• Dosage	96%
• Substance name	90%
• Reason for stop/switch to other product registered	89%
• Start- and stop-date	84%
• Duration of the treatment	67%
• ATC classification	45%

Common data elements: pregnancy

Details important if a woman becomes pregnant:

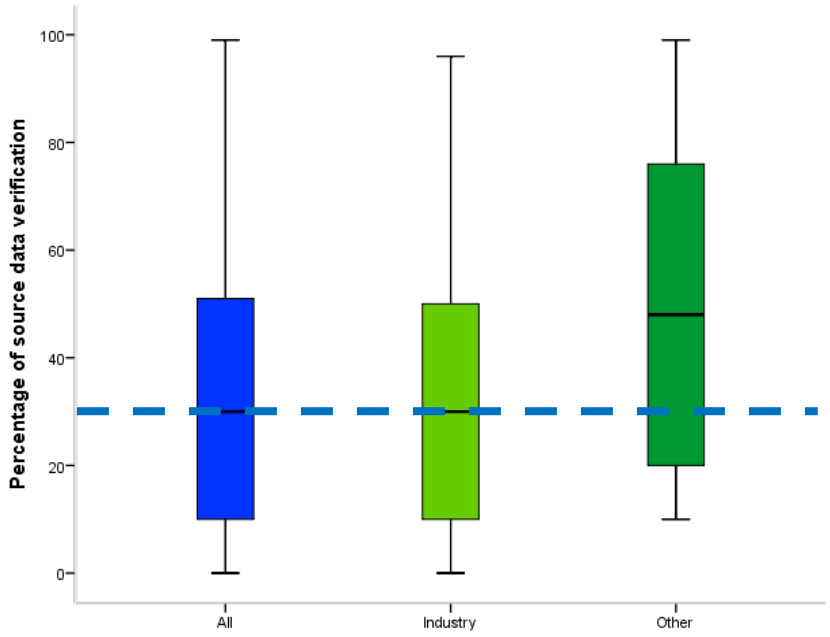
• Exposure during pregnancy*	90% (100% vs 76%; p<0.01)
• Outcome of pregnancy	90%
• Trimester during pregnancy	84%
• Follow-up teratogenic events	84%
• Follow-up child	80%
• Follow-up mother	75%
• Birth weight	63%

Safety outcomes

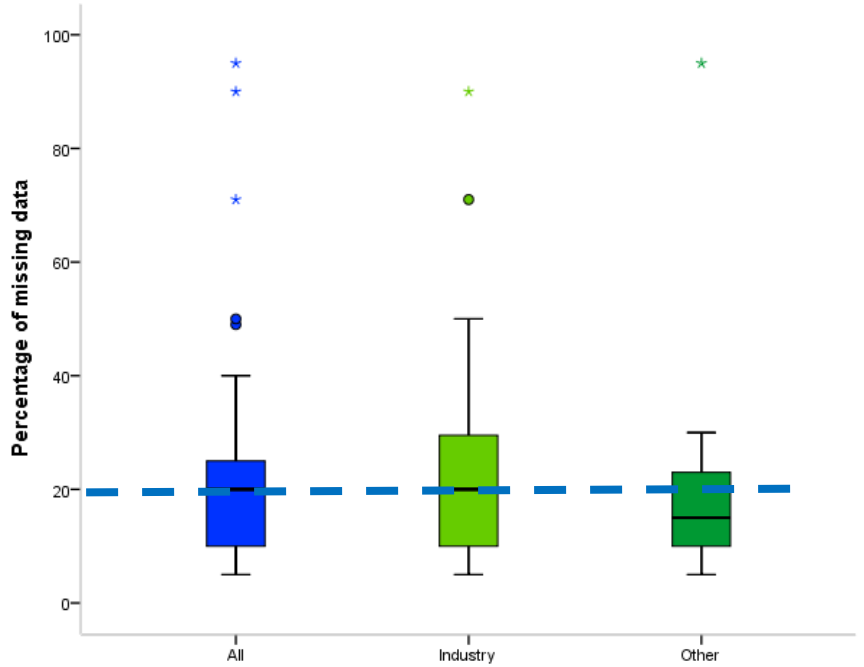
Which adverse drug events should be collected?

- Adverse events of special interest 65%
- Serious adverse events 63%
- All adverse events 43%

Data quality - source verification & missing data



Source data verification (~30%)



Missing data (~20%)

Governance aspects

To share registry data for the purpose of the regulatory decision-making process

• Regulatory authorities	95% vs 94%	p=0.69
• Academic centers	88% vs 81%	p=0.18
• Pharmaceutical companies	90% vs 45%	p<0.01

Conclusion

- Stakeholders have generally similar views on the collection of data within registries
- Our survey provides a ball-park figure for data coverage and data quality
- Stakeholders have a different opinion to share data with for regulatory decision-making
- Some of the elements are handled in the draft Guideline on registry-based studies
- In case registries are used as data source for the evaluation of safety data, one should be aware that when too little information on the adverse events is collected, registry data may not fulfil post-authorisation requirements.

Thank You

✓The participants of the survey

✓ My team: Sieta de Vries, Marijke van den Berg, Patricia McGettigan, Arno Hoes and Peter Mol