Leiden University Medical Center

Persuasiveness of Real-World Evidence

A multi-faceted approach

Pivotal Evidence Project

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PUTTING REAL WORLD EVIDENCE INTO PRACTICE

Conflicts of interest

- PhD candidate at dept. of Clinical Epidemiology
  Leiden University Medical Center (LUMC)
- Pivotal Evidence Project
  Sponsored by GetReal Institute

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Project team

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Prof.dr. L Hooft
Prof.dr. A de Boer
Dr. H Gardarsdottir

Introduction

- Shift medicine development: more complex therapies often intended for smaller populations (rare diseases, high unmet need, mutation-specific)
- RCTs may sometimes not be ethical or feasible, or are based on very small sample sizes
  → more uncertainty at regulatory (and HTA) review

- RWE may fill certain evidence gaps
- Increasing opportunities with big data

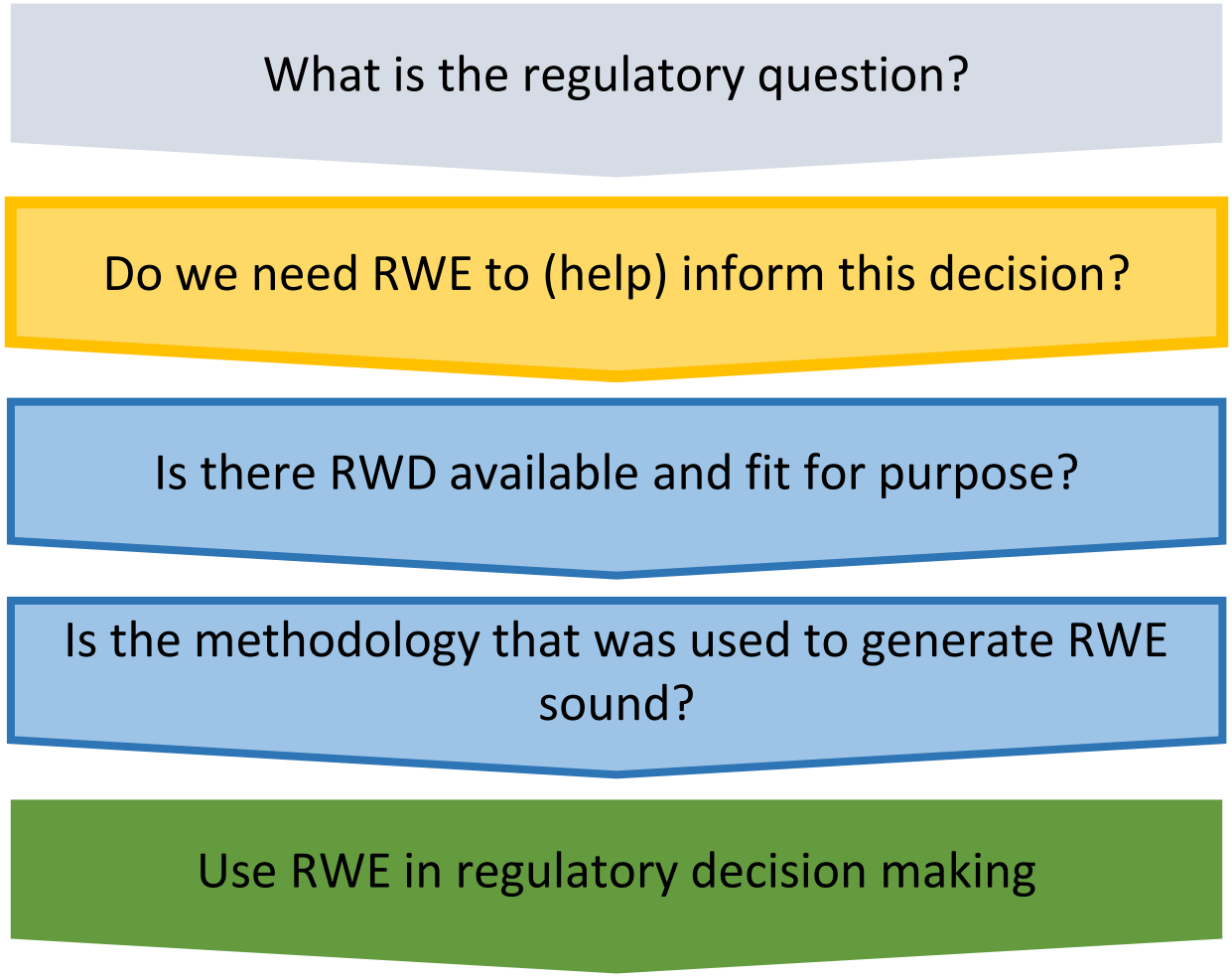
- Expectancy of increased need of RWE to support regulatory decision-making

Eichler HG, Pignatti F, Schwarzer-Daum B, Hidalgo-Simon A, Eichler I, Arlett P, Humphreys A, Vamvakas S, Brun N, Rasi G. Randomized Controlled Trials Versus Real World Evidence: Neither Magic Nor Myth. Clin Pharmacol Ther. 2021 May;109(5):1212-1218. doi: 10.1002/cpt.2083. Epub 2020 Nov 12. PMID: 33063841; PMCID: PMC8246742.

Introduction

- Regulatory and HTA agencies are looking how to better incorporate RWE in decision making

- **Gap: <u>when</u> is RWE needed to help inform regulatory decision making?**


What is the regulatory question?
Do we need RWE to (help) inform this decision?
Is there RWD available and fit for purpose?
Is the methodology that was used to generate RWE sound?
Use RWE in regulatory decision making

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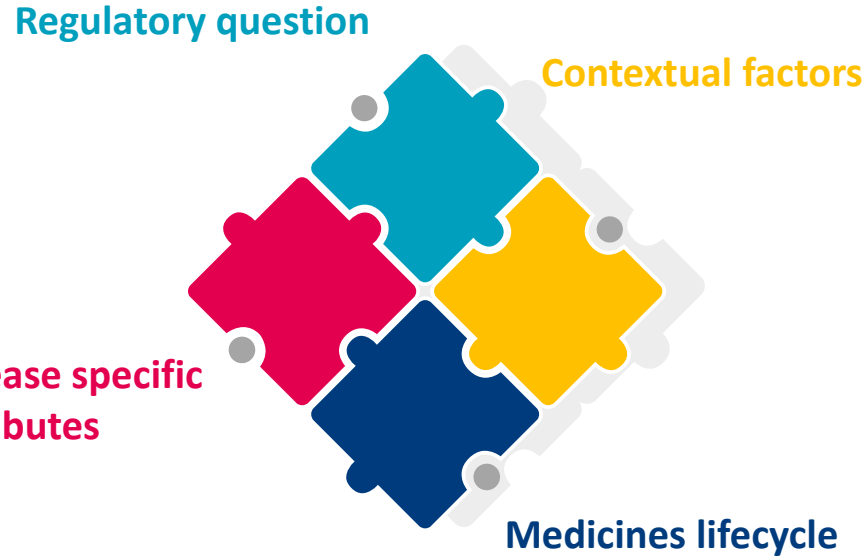
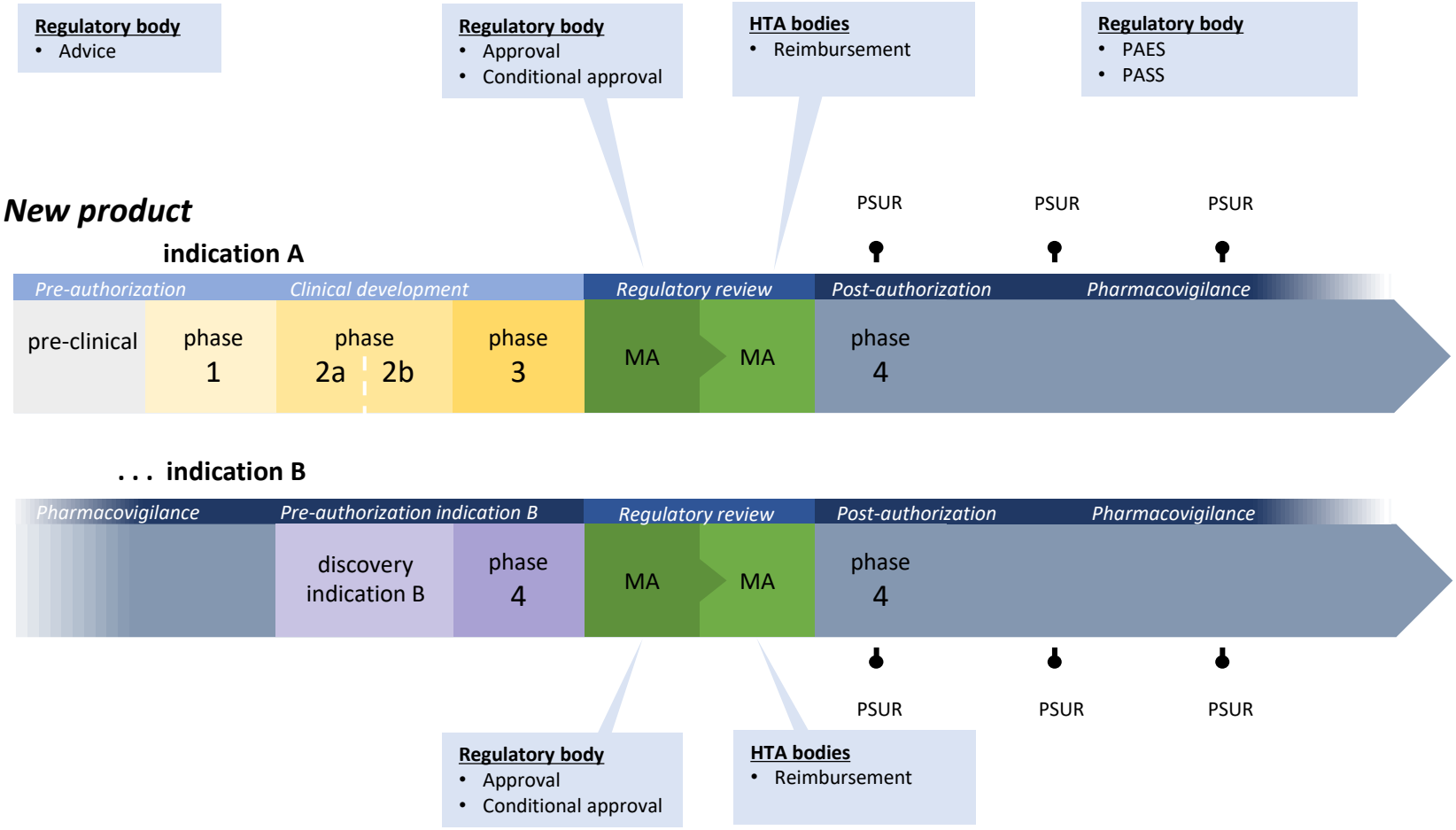
- When do we want to see RWE, as a regulator?
- Which factors make RWE necessary to (help) inform regulatory decision making?



Aim:

- **To identify factors that make RWE necessary or desirable to inform regulatory decision making**


Regulatory body
• Advice
Regulatory body
• Approval
• Conditional approval
HTA bodies
• Reimbursement
Regulatory body
• PAES
• PASS
New product
indication A
PSUR
PSUR
PSUR
Pre-authorization
Clinical development
Regulatory review
Post-authorization
Pharmacovigilance
pre-clinical
phase 1
phase 2a
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phase 3
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Regulatory body
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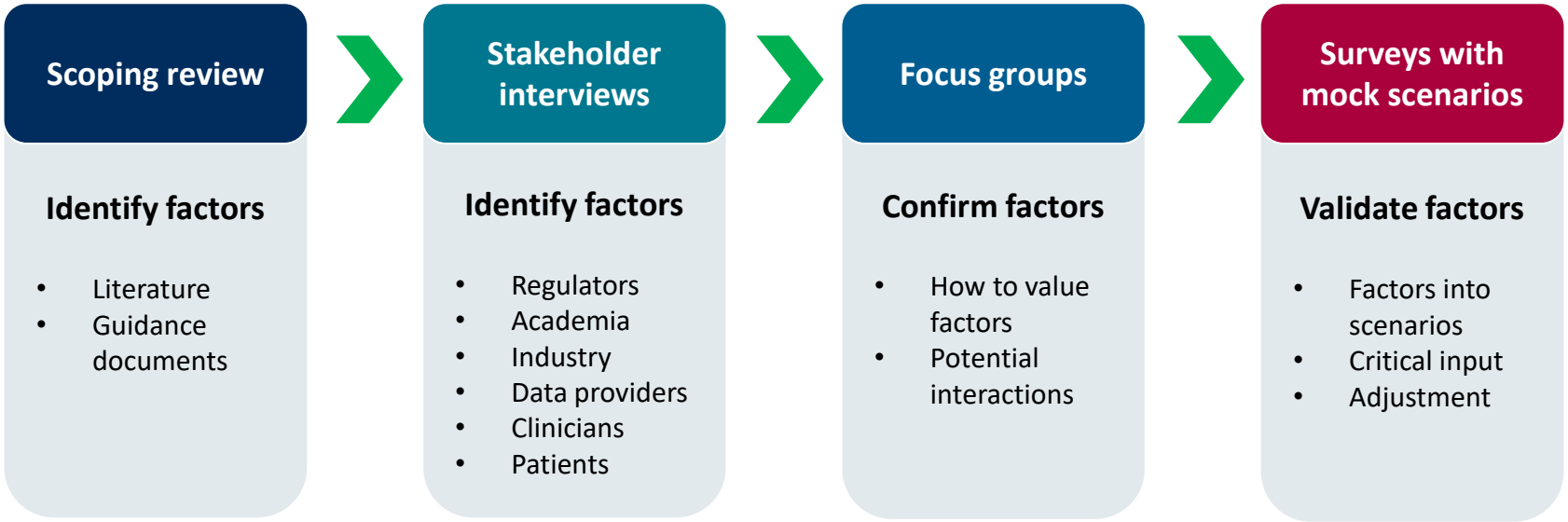
Project approach



output

- Publications
- Educational material
- Foundation for a potential framework: when could RWE help inform regulatory decision making

Scoping review methods

Which factors make RWE necessary or desirable to (help) inform regulatory decision making?

Inclusion criteria

- RWE in regulatory (and/or HTA) decision making
- Peer-reviewed articles of any study design (incl. reviews, opinion papers)
- Corporate, policy, guidance documents
- English, Dutch

Exclusion criteria

- Conference abstracts, presentations
- Perspectives outside NA & EU
- RWE studies without regulatory component
- Exclusively animal research

Literature search

Databases:
PubMed, Embase, Emcare, Web of Science, Cochrane Library

Keywords:
real world evidence; real world data; regulatory science *

Results

Search: 646 articles
Title & abstract screening: 158 articles
Full-text screening: 91 articles

Grey literature search

Websites:
EMA, FDA, Health Canada, MHRA
EUnetHTA, NICE, ZIN, CADTH, ICER
Duke-Margolis, GetReal, ImpactHTA
ISPOR, ISPE, HTAi, INAHTA

Keywords:
real world evidence; real world data

Results

Search: 67 articles
Full-text screening: 30 articles

* Full search details (ie, string) not presented here

Preliminary results - sneak peek

- List of factors identified from literature

Overview themes:

1. Generalizability
2. Ethical considerations
3. Feasibility
4. Contextualisation of investigational arm
5. Real-world aspects of care
6. Epidemiology of disease
7. HTA
8. Other

Examples

- Representativeness of population
- Representativeness of study setting
- Surrogate endpoints

Acknowledgements

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GetReal Institute

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All steering group members

And special thanks to all interview candidates who have agreed to participate in our project!

Also interested in contributing?
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