Why explore Real-World Evidence (RWE)?

- RCTs: a golden standard?
- The efficacy-effectiveness gap (Eichler et al.)
- Expansion of mandates:
  - Systematic evaluation of all aspects of an intervention
  - Questions go beyond treatment X vs. Y (or placebo)
  - Societal perspective of analyses
  - Different evidence is also needed
RWE use in HTA Practice: 5 European HTA Agencies

Relative Effectiveness Assessments (REAs)  Cost-effectiveness Assessments (CEAs)

RWE use in HTA Practice: Appraisal of RWE
RWE in Practice: Conditional Financing

T=0: Assessment
- Therapeutic value & 1e CE/BIA
- Uncertainties identified
- Outcomes research proposal discussed

Outcomes Research
- Dutch clinical practice
- Eg: registries

T=4: Re-assessment
- Conclusions
- Advice to MoH on reimbursement

Stakeholder Perspectives (n=30)

Did it work?  Now what?

[Pie chart showing responses to the question 'Did CF achieve its aims?' with options 'Yes', 'No', 'Partially (early access)', and other]

[Pie chart showing future perspectives with options 'replace CF with new policy', 'adopt evidence generation', and other]
Practicalities of RWE use in CER

What was IMI-GetReal?
Public-Private partnership
RWE use throughout drug lifecycle
3-year project

Aim:
Categorize practical issues encountered in accessing and using RWE in CER

Methods:
Qualitative analysis of case study reports
Consensus-seeking amongst co-leads

Practicalities of RWE use in CER

1. Accessing Individual Patient Data (IPD):
   - RCTs: access to 41/43 (95%) studies
   - RWE repositories: access to 7/20 (35%) repositories

2. Alternatives to IPD from RWE: Aggregate Data
   - Advantages: more accessible
   - Disadvantages: limited data on covariates
   - Remote querying of IPD to report AD

3. Methodological challenges in using IPD from RWE:
   - Making datasets research-ready
   - Differences in definitions of outcome measures (RCT vs. RWE)
Implications for decision making?

Accessibility to RWE Remains Low

Little opportunity to demonstrate value of RWE in CER through sophisticated analyses

Persistence of low trust in RWE use amongst decision-makers

Moving Forwards on Data Governance

Collaborative efforts needed to develop alternative mechanisms:
1) Joint Action & Patient-Goals
2) Public registry contracts
3) FDA Sentinel

Which path to choose? Joint Decision

Where to next? ZIN’s Vision

Basic Health Insurance Package

Quality Institute

Appropriate Care Program

Societal Fees Management

HTA
RWE for New HTA Methodology

Indication - metastatic melanoma (post-)effectiveness of immunotherapies

Proactive Electronic Record task: Preliminary discussions on scope etc.

Patient registries to assess effectiveness

International Initiatives & Future Directions

• **EUnetHTA WP5B**: Core datasets for HTA registries
• **EMA Adaptive Pathways**: Iterative evidence development & assessment
• **EMA-EUnetHTA Joint Work Plan**: increased HTA/reg. collaboration on RWE
• **IMI-GetReal I & II**: RWE use for clinical effectiveness of (Alzheimer’s) drugs

• **REPEAT Initiative**: Reliability and reproducibility of results from RWE studies
• **NEWDIGS**: Drug development paradigms (incl. AP)
• **ISPOR/ISPE Special Task Force**: Good procedural & reporting practices for RWE studies
• **INAHTA RWE Task Force**: Global HTA standpoints on RWE
Thank you for your attention.

Questions?

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