Options for using RWE earlier in drug development

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Objective

- At the time of initial Market Authorisation, Regulators and HTA bodies / payers and prescribers have to make decisions with some uncertainty as to population and individual benefits
- The overall value achieved in everyday clinical practice (RW) can only be predicted at launch and confirmed after launch (RWE)
- But predictions can be better informed by using pragmatic trials and RWD analytics earlier...
- …post launch RWE can be transformed through technology and investment in improved infrastructure…
- ...and smart sequencing of evidence generation and assessment could accelerate access to new medicines

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Get Real

Real-Life Data in Drug Development

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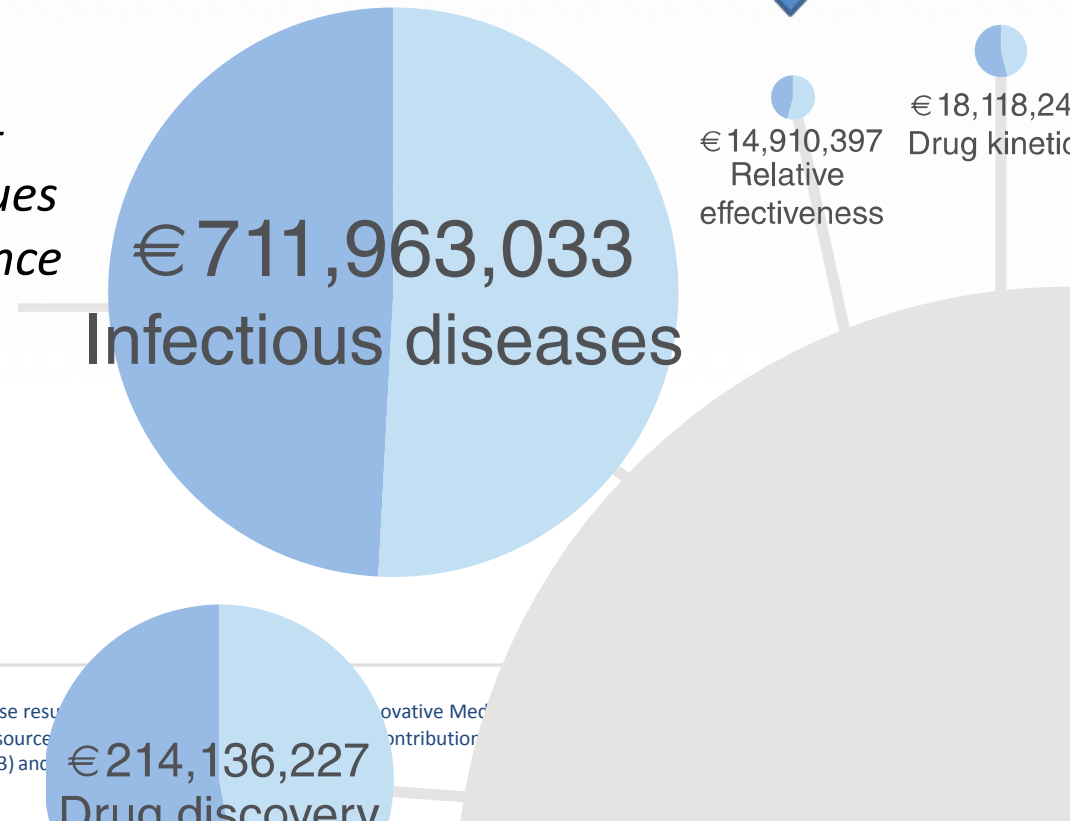
Get Real

Three-year project

" … to better understand how real-world data and analytical techniques can be used to improve the relevance of knowledge generated during development, e.g., through innovation in clinical trial design"



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Using RWD earlier

Real-Life Data in Drug Development

Before phase3	During phase3	After Launch
Potential Value	Predict Value of new Medicine	Confirm Value
Background RWE on disease, treatments, care pathways, unmet need etc	Analytical Approach to drivers of real world effectiveness Comparative Trials; Pragmatic Trials, giving information on effectiveness Evidence Synthesis to combine all sources of information: RCT + PCT + OBS	Post Launch RWE on: use of new medicine, relative effectiveness, longer term outcomes

How much can be done pre-launch?

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Prior to phase 2b
Develop overall evidence plan

Prior to phase 3
Detailed plan for RCTS, other studies and analyses

Prior to launch
Focus on analyses for submissions & phase IV commitments

Why should I generate real-world evidence?

- Is there a risk for an efficacy-effectiveness gap?
- Is there a compelling need to generate evidence of effectiveness, over and above RCTs for registration?

How could I understand the issue?

Identification of drivers of effectiveness: literature review, experts insight, data analyses

NMA
modelling techniques

Qualitative research, Patient insights

X

Population

Intervention

Comparator

Outcome

X

HTA CASE HISTORIES

SCIENTIFIC ADVICE

COMMERCIAL FORECAST

How could I understand the issue?

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IF YES

What should I do?

- Methodological options for an **integrated "effectiveness evidence generation plan"** (design parameters and analyses)

Prior to phase 2b
Develop overall evidence plan

Prior to phase 3
Detailed plan for RCTS, other studies and analyses

Prior to launch
Focus on analyses for submissions & phase IV commitments

How could I address the issue?

Generation of evidence on effectiveness: options

Phase 3 RCT

- Can I use **enriched RCT design**, to improve the heterogeneity in population and gain knowledge on effectiveness?

Pragmatic trial

- Shall we plan for **PCT**?
- Which aspect of PICO should be more pragmatic?
- Which are the statistical challenges

Post-launch observational study

- Is there a risk of channelling bias ?
- How to correct for this risk?

NMA
modelling techniques

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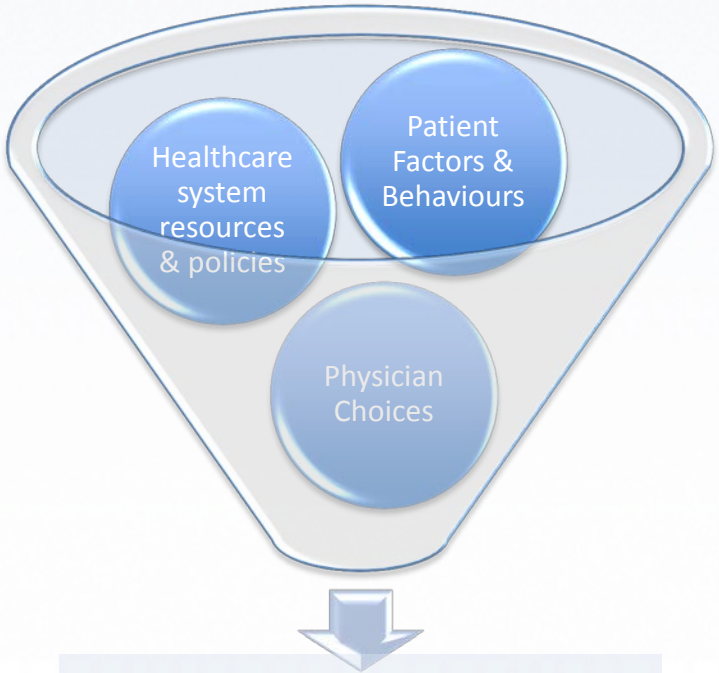
GapAnalysis and New Solutions

Systematic approach to understand and address “drivers of effectiveness”: those factors that determine how efficacy translates into real world outcomes

- Guidance on a range of methodologies useful to assess the drivers of effectiveness within a disease area
- Exploring statistical and analytical issues arising from designing trials to provide information on the impact of specific drivers of effectiveness



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Workshop Example

Stakeholder views on the role and acceptability of pragmatic trials

When should early pragmatic clinical trials be considered?

OBJECTIVE: Can we identify which effectiveness questions would be regarded by stakeholders as particularly suited to be addressed by early PCTs?

How strongly would results from pragmatic designs be accepted as evidence?

OBJECTIVE: Can we identify the factors that influence whether pragmatic trial data would be considered as "strong" or "weak" evidence by decision maker?

How can we maximise the value and acceptability of PCTs?

OBJECTIVE: How do we build on positive opportunities to utilise PCTs and address any barriers to acceptability? Generate solutions to mitigate concerns around using PCT data in decision making.

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Pragmatic trials

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Conclusions

- Introduce a systematic approach to understanding effectiveness and options for evidence at launch and post-launch
- Introduce RWE into Scientific Advice process
- Bring more pragmatic trial evidence to HTAs to build experience from both sides
- Consider options for adaptive pathways – get to post launch phase more quickly

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