Get Real

Real-Life Data in Drug Development

Real World Evidence and Pragmatic trials: GetReal

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The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no [115546], resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution.
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Disclosure

- I have nothing to disclose

- This work has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no [115546], resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007/2013) and EFPIA companies' in kind contribution. For further information please refer to http://www.imi-getreal.eu/.

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Introduction

- Often clinical evidence insufficient to guide physicians/policy makers on optimal treatment at approval
- Real-World Evidence (RWE) on relative effectiveness needed!
- Traditional phase III RCTs and observational studies have limitations in providing this
- GetReal aims to show how RWE can be adopted in medicine development, especially 'peri-launch' after evidence of efficacy/safety

Calvert et al. J Clin Epidemiol 2011, Hemkens LG, BMJ 2016;

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Get Real

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Real-Life Data in Drug Development

Overall goal GetReal:

To better understand and show how real-world data, analytical techniques and study design can be used to improve the relevance of knowledge generated during development

Software and methodology

Identifying the efficacy effectiveness gap and signalling solutions

Innovative approaches to study design and analytics

Analytical software

Toolboxes and framework

RWE Navigator to guide strategy, design, and interpretation by all stakeholders

PragMagic to guide study implementation

Education and training

Education of stakeholders and end users in the use and implications of RWE is key to ensure the legacy of GetReal

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GetReal WP3: Pragmatic Trials

- Combine RW nature of observational studies with scientific rigour of randomized trials
  - Features other that randomization are a matter of choice rather than principle
- May lead to different/unanticipated operational challenges
- Aim: Raise awareness for consequences of design choices and possible solutions
  - Maximize pragmatic design, ensure feasibility, generalisability and validity

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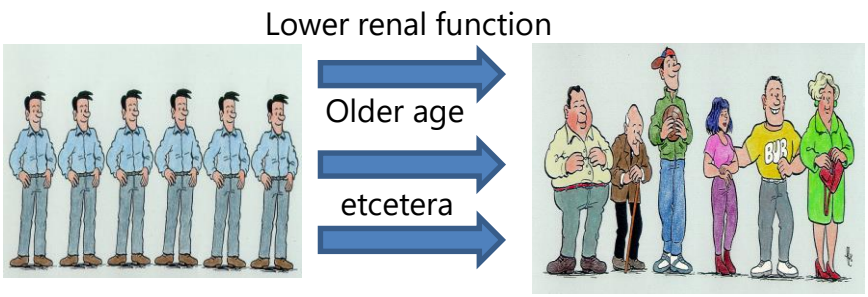
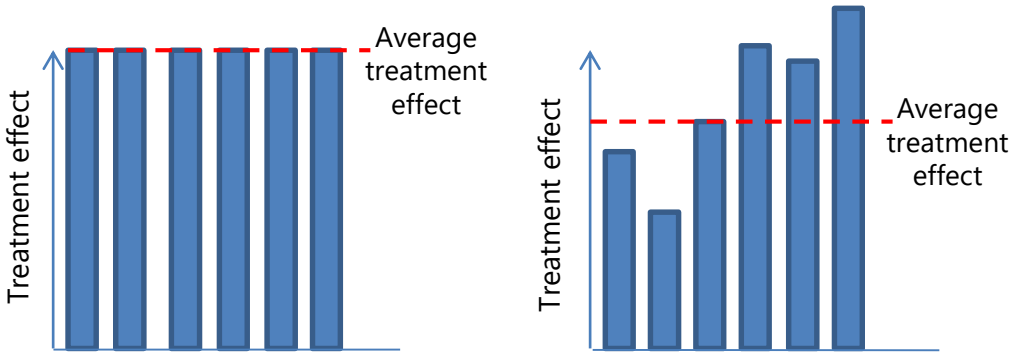
Generalizability of study results to patient population of interest

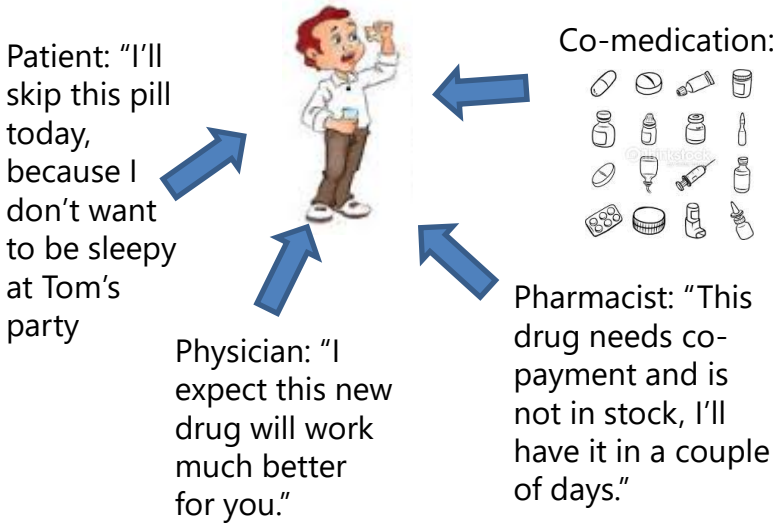
possible modifiers of drug response

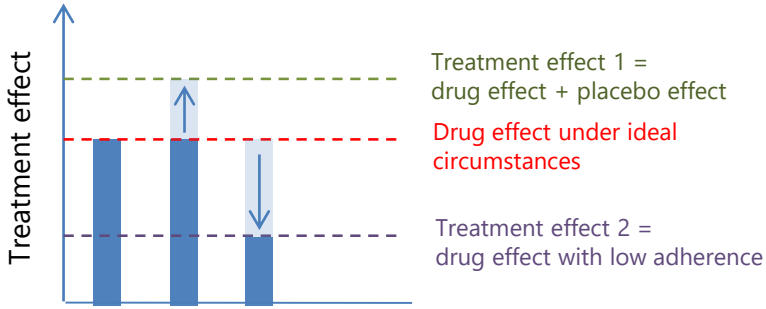




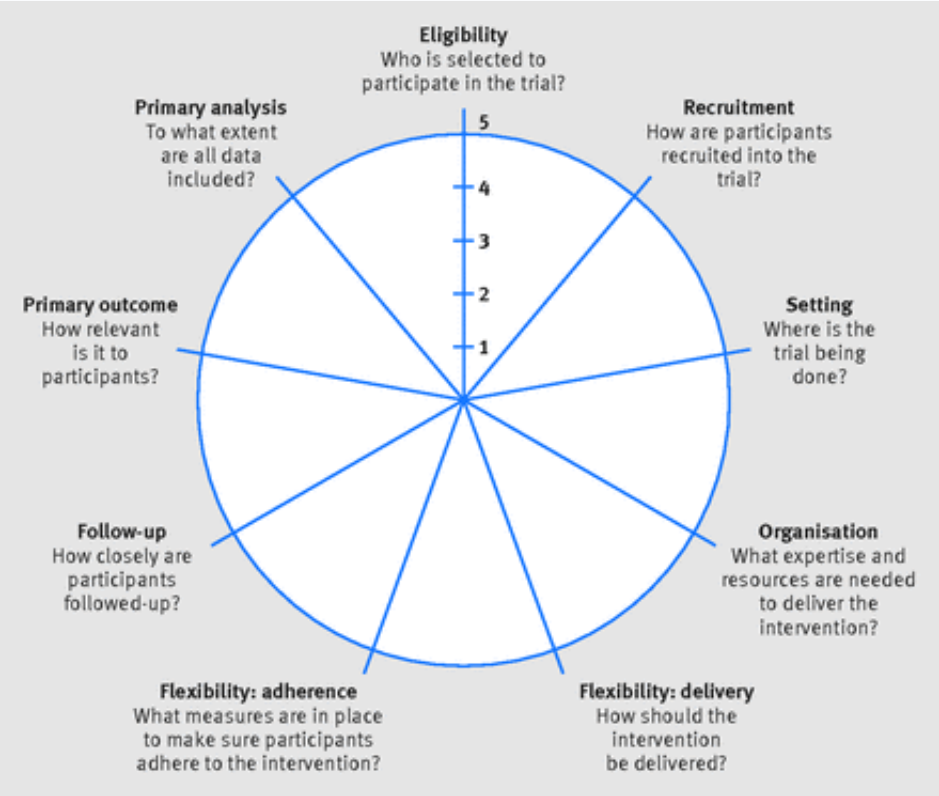
Drug vs treatment strategy

extraneous factors





A Research continuum: PRECIS-2



- Designing trials fit for purpose
- Focus on trial applicability of a trial (not internal validity)
- To be used by trial design team
- Makes judgements explicit
- Little guidance on impact/ challenges of pragmatic trial conduct

*PRagmatic-Explanatory Continuum Indicator Summary 2 (PRECIS-2) wheel. *(Loudon K et al. BMJ* 2015;350:h2147)

Impact of design choices & Operational challenges

- *Generalizability:* change from usual practice in population & setting, comparator, allocation & implementation treatment, type & frequency measurement/collection systems used

- *Risk of Bias:* Preferences/expectations/skeptism and open label? Observer bias? Selective loss-to-follow-up? Information bias? (i.e. measure 'on indication', 'recall bias')

- *Precision:* measurement in usual care expected to be inconsistent/variable/missing?

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Impact of design choices & Operational challenges

- *Relevance of results for patients/physicians/HTA/regulatory*: specific preference for comparators and outcomes and focus on (assuring) data quality vs generalisability

- *Ethical:* IC requirements, equipoise & suboptimal care, dual role conflict physician-researchers

- *Operational challenges* Possibility/willingness of sites/patients to participate, burden & workload, technical issues, variation in care, identification modifiers & (future) use of treatment

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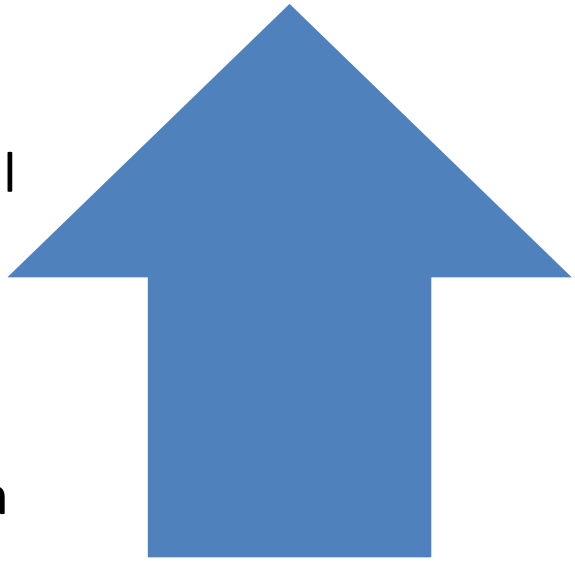
Minimize bias/variability: Use preference design? Blinding outcome assessment? Use ‘objective outcomes’/ training/standardizing?, Select research naïve sites?, Use realistic/flexible treatment strategies?

Maximize Generalizability/Feasibility: Randomization at cluster level?, select real life sites/settings?, use realistic/flexible treatment strategies?, outcomes as in practice?, Integrate data collection with care systems?, Minimize ‘Hawthorne effect’? Discuss design in early phase with all stakeholders?



Summary & Conclusion

- Trials can be on the continuum between explanatory and pragmatic trials
- Specific design choices can have impact on feasibility, generalizability, precision and validity
- Various stakeholders should be involved in design process to realize most pragmatic approach to answer research question
- GetReal will offer tools to guide this process
- When carefully executed, pragmatic trials have the potential to deliver valid RWE earlier in development

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Questions

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