MAKING PRAGMATIC TRIALS WORK

identification of operational challenges &
development of a decision support tool for pragmatic trial design

WP3
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The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no [115303], 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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Pragmatic trials as a solution for RWE need

Randomization = prognostic comparability between patient groups

Explanatory trial

Pragmatic trial

Observational study

Real World Evidence = How does treatment strategy A compare to treatment strategy B (often usual care) in daily clinical practice?

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What are pragmatic trials?

<table>
<thead>
<tr>
<th>explanatory</th>
<th>continuum</th>
<th>pragmatic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Can treatment work?</strong></td>
<td><strong>WHAT?</strong></td>
<td>Generalisable to real world population</td>
</tr>
<tr>
<td>➔ <strong>EFFICACY</strong></td>
<td><strong>WHY?</strong></td>
<td>In relation to real world alternatives</td>
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<tr>
<td>Hypothesis testing: Assess cause – effect of drug</td>
<td><strong>HOW?</strong></td>
<td>Important to decision/policy makers &amp; patients</td>
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<td>Minimize variation: Rigid protocol, ideal circumstances</td>
<td><strong>WHO?</strong></td>
<td></td>
</tr>
<tr>
<td>- Selective inclusion of participants &amp; sites</td>
<td><strong>METHOD?</strong></td>
<td></td>
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<tr>
<td>- Compare drugs or against placebo</td>
<td>- Compare usual treatment</td>
<td></td>
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<tr>
<td>- Outcomes research relevant</td>
<td>- Outcomes research relevant</td>
<td></td>
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<tr>
<td>- Data collection &amp; monitoring &gt; usual practice</td>
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Effectiveness of Fluticasone Furoate–Vilanterol for COPD in Clinical Practice

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Pragmatic trial example

Salford Lung Study (GSK)

Design choices
- Pre-launch
- Treatment strategy with once-daily inhaler
- Broad patient inclusion in GP practices
- Usual care comparator
- Clinically relevant outcome COPD exacerbation

Operational challenges
- Timely safety reporting
- Real world drug supply
- Informed consent
- GCP training
- Linkage of EHR

BUT! Generalisability beyond Salford?

Nawar 2013; New 2014
Pragmatic trials

😊  opportunity to generate RWE in early stage of drug development

😊  limited experience & unanticipated operational challenges

- Identify operational challenges
- Analyse impact on generalizability, validity, precision, stakeholder & ethical acceptability, resource use
- Identify and propose solutions
- Overview paper series
- Develop decision support tool for pragmatic trial design PragMagic

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PRAGMAGIC
a decision support tool for pragmatic trial design
Forces at work

Retropro & eLung
Van Staa 2014

59% of sites expressed interest in trial participation

4% of sites actually recruited patients

Generalizability ↓ & feasibility ↓

participating GPs differed from those not participating

eLung trial did not recruit sufficient N of patients
The goal of PragMagic

- Facilitate the design & planning of pragmatic trials
- Insights: consequences of design & operational challenges
- Visualize complex interplay systematically: decision support tool
- Maximize generalizability of trial findings
- Ensure validity & operational feasibility

What PragMagic is NOT

- NOT a decision-making tool;
- NOT a checklist to assure (regulatory/ethical) compliance;
- NOT a quality check/verdict on study design.

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Watch this space: WWW.PRAGMAGIC.EU
first version of tool available early 2017

Run through a “touch-and-feel” version of PragMagic 12:00h-13:15h this afternoon!

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