REWEIGHTING RCT EVIDENCE TO BETTER REFLECT REAL LIFE: A CASE STUDY OF THE INNOVATION MEDICINES INITIATIVE

Hippach M1, Brabitz A1, Faries D2, Abrams KR4, Wintrei K7, Girvan A2, Jonsson P2, Johnston J2, Belder M1
1 Lilly Deutschland GmbH, Bad Homburg, Germany; 2 Eli Lilly, Sydney, Australia; 3 Eli Lilly, Indianapolis, IN, USA; 4 University of Leicester, Leicester, UK; 5 National Institute for Health and Care Excellence (NICE), Manchester, UK; 6 Eli Lilly, Ascot, UK

ABSTRACT

OBJECTIVES: Although the demonstration of improved patient and clinical outcomes within randomised controlled trials (RCTs) is a widely accepted approach to evaluate the effects of new treatments, outcomes are frequently expressed by RCTs in a way that is not directly applicable to patients. This paper explores the extent to which RCT evidence can be reweighted to better reflect real-life clinical practice. METHODS: We describe a case study that considers lung cancer, the most common cancer worldwide. We evaluate a real-world evidence study to compare the outcomes for the treatment of non-small cell lung cancer (NSCLC) (Bardouin et al, 2014), using real-world retrospective data from 5087 patients in a French administrative database. RESULTS: Our approach to reweighting evidence is conceptually similar to the matching used in propensity score weighting. Our results demonstrate a potential for reweighting evidence to better reflect real-life clinical practice, with improvements in the balance of treatment and control groups. CONCLUSIONS: This study demonstrates the potential for reweighting evidence to better reflect real-life clinical practice, with an approach that is conceptually similar to propensity score weighting.

STUDIES INCLUDED

- Bardouin et al. Jormel 2014
- GetReal (HTA provider)

WEIGHTING APPROACHES: IPS

- Two key approaches employed:
  1. Inverse propensity score method (IPS):
  2. The balancing approach method

WEIGHTING APPROACHES: IPS

- A propensity score model is fitted that predicts participation in either RWE or RCT.
- A common set of robust baseline characteristics (RWE and RCT data are pooled for the purpose).
- Resulting propensity scores are used to assess the difference/overlap between the two cohorts, and calculate weights to apply to RCT outcomes.

CASE STUDY: NSCLC

NSCLC accounts for 85% of all lung cancer
Non-small-cell lung cancer (NSCLC) subcategories
- Adenocarcinoma
- Squamous cell
- Large cell
- Others

BASELINE CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RWE</th>
<th>RCT</th>
<th>p value</th>
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<tbody>
<tr>
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<td>Smoking status</td>
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<td>Performance</td>
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LIMITATIONS

- Definitions of variables can be different between RCT and RWE studies

CONCLUSIONS

- The key objective of this case study was to assess the generalisability of RCT evidence to real-world clinical practice.

STANDARD DIFFERENCES

- As reference JMDB (RCT) results:
- Restricted
- Exploring how "real-life" clinical data can be brought in earlier in drug development
- To make the non-small cell lung cancer (NSCLC) case study on randomized clinical trial (RCT) reweighting methodology and obtain feedback from participants in referees and the approach
- Assessment of potential application in regulatory and health technology assessment (HTA) decision-making process

OBJECTIVES

- The Innovative Medicines Initiative (IMI) is Europe’s largest public-private partnership aiming to improve the drug development process by supporting a more efficient and integrative discovery and development of better and safer medicines for patients.
- With a €2 billion budget, IMI supports collaborative research projects and builds networks of industrial leaders, healthcare and health care decision makers in Europe that will boost innovation in healthcare.
- IMI supports a number of research consortia, among them GetReal about “Incorporating real-life clinical data into drug development”

RCE vs RWE

- Patient benefit and harm in experimental and clinically observed tumors (2012;131:1210–1219)
- Design minimizes bias – high internal validity
- Generalizability questionable
- Results hard to estimate
- Complexities
- Unmeasured confounders

RWE challenges

- Phase II trade-off to capture relevant effects, need to use models
- Considerable uncertainty in RWE predictions
- RWE evidence to be informed by factors (adherence etc.) not captured in Phase III, model-based estimates unreliable
- RWE biased
- Phase II/III patient population poor fit for local population
- Generalizability
- Could be used for decisions
- “Intra-individual research” is conducted
- “Only” – a lot of variance and biases

Sensitivity analysis

- Propensity score weighting
- Standardised weights
- Bootstrap
- Median OS (months)
- Hazard ratio
- Hazard ratio
- 95% LCL

Primary analysis

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Author Disclosure

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