Using real-world data for HTA – thoughts from industry

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On behalf of GetReal Work Packages 1 & 4

Acknowledgments

MORSE – HTA group, F. Hoffmann-La Roche Ltd, in particular Aijing Shang, Maximo Carreras, Federico Felizzi, Yovanna Castro, Monica Daigl, Nicolas Staedler, Pierre Ducournau, Marlene Gyldmark

IMI GetReal WP4, in particular Noemi Hummel, Eva-Maria Didden, Sven Trelle, Matthias Egger

IMI GetReal WP1, in particular Keith Abrams, Reynaldo Martina, David Jenkins, Sylwia Bujkiewicz
RWE – another “big data” movement in pharma

Broad interest to leverage RWE across all development stages

- Incidence / Prevalence estimates
- Define target product profile (TPP)
- Understand drug use/treatment patterns

- Background mortality
- Long-term effects
- Heterogeneous patient populations

HTA

Benchmarks & extrapolation (time and “space”)

Bridge knowledge gaps in NMA with RWD

- Bridge gaps
- Use all evidence

- Data availability
  - Most uncertainty around new compound
  - RWD on new compound will not be available at time of decision making
- How to weight RWD?
Weighting: compare discounting of historical data – how much can we learn from RCTs on a new trial?

Massive discounting needed with historical controls (exchangeable!). Expect even more discounting from (non-exchangeable) RWD?

<table>
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<th>Ref.</th>
<th>Appl.</th>
<th>Total n</th>
<th>Eff. n</th>
<th>% “use”</th>
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<td>Transplantation</td>
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<td>Gsteiger et al (2013)</td>
<td>MS</td>
<td>1936</td>
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<td>MS</td>
<td>412</td>
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<td>15%</td>
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<td>Baeten et al (2013)</td>
<td>AS</td>
<td>533</td>
<td>43</td>
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</table>

NMA with combined RCT + RWD: sensitivity analysis giving different weights $\alpha$ to RWD

Power prior model: $P(\theta | RCT, RWD) \propto L(RCT|\theta) \cdot L(RWD|\theta)^\alpha \cdot P(\theta)$

Use grid of (fixed) values $\alpha$
Extrapolation

- Benchmarks from registries
- Blending of short-term RCT with long-term RWD
- “Anchoring” predictions with registry estimate [Cf Abrams et al. WP1]

Particularly interesting in adaptive pathways context

- Extrapolation (short/mid-term)
- Monitoring
- Validation

Are these methods acceptable for decision makers?

“This new method is a black-box to me. I would not accept it.”
“I do not understand this. I could end up being so confused that I would not be willing to take any decision at all!”

[Statements from regulators at IMI GetReal WP1 workshop]

... unless you can explain the method really well.
... unless you can “fully” establish the properties of the method.
... unless the method is well accepted in the literature.

“Take NMA as an example: initially a lot of skepticism, but now a standard (in some countries)!"
Some final remarks

- RWD valuable, but not the only source to inform effectiveness
- Not forget about the local level
  - RWD: inevitably a “local reality” ...
  - Initiatives: EAMS (UK), AIFA mandated registries (IT)
- Predictions: adopt mindset including validation
- Populations: we should systematically share individual patient baseline characteristics from our trials!

References