Evaluating Medical Devices: How Do Randomised Clinical Trial Data and Real-world Data Fit Together? An Industry Perspective

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Overview

- Nature of medical devices and device companies compared with pharmaceuticals
- Barriers to undertaking double-blind RCTs and how RWE fits with this
- Potential opportunities associated with changes in regulation
A couple of caveats

- This presentation aims to outline the perspective of industry, but is mindful of:
  - The arguments around opportunity cost and devices/pharmaceuticals being funded from the same pot of money (thus requiring similar scrutiny), but note wider considerations (e.g. incentives for innovation)
  - Some of the issues outlines in this presentation will also apply to some pharmaceuticals and pharmaceutical companies (annotated with *)

Nature of devices

- Size of company
- Profitability period
- Device modifications
- Learning curve
- Organisational change
- Randomisation and blinding
Size of company

- Device companies are typically SMEs*
  - Companies have a limited portfolio and products serve small markets
  - Companies may be dependent on venture capital until product launch (Kirisits et al, 2013)

- Barriers to undertaking RCTs
  - Limited research and development budgets (especially for adequately powered studies)*
  - Limited expertise in clinical study design to inform future reimbursement and HTA decisions

- How RWE may fit
  - The cost of research (with sufficient sample sizes) may be less prohibitive
  - Potentially richer data (i.e. long term effects) may better inform future reimbursement and HTA submissions

Profitability period

- Devices have a short profitability duration
  - Imitators can quickly enter the market
  - Exacerbated by burden of demonstration on performance falling on first device in class

- Barriers to undertaking RCTs
  - Short period of profitability may preclude investors from funding RCTs (particularly of sufficient size or follow-up duration)

- How RWE may fit
  - May allow data to be collected on a larger sample size with longer follow-up time without the potentially prohibitive costs of RCTs
  - Broader inclusion criteria may result in larger sample sizes in a shorter period of time
Device modifications

- Devices undergo regular incremental change
  - Device lifetime = around 18 months versus pharmaceutical lifetime of 57 years (Chapman et al., 2014)

- Barriers to undertaking RCTs
  - Data becomes quickly outdated and another RCT is required
  - Trial data may be confounded by the use of different versions of the device during the trial

- How RWE may fit
  - Data may be collected continually and iterations of device used as a variable in statistical analyses to assess if differences in outcomes occur between device iterations

Learning curve

- Learning curve*
  - Performance of operator controlled devices may improve with use as the user gains more experience

- Barriers to undertaking RCTs
  - RCTs are often undertaken by "expert" users, hence data lack external validity (Craig et al, 2015)*

- How RWE may fit
  - Collecting data on all procedures would allow for evidence to be gathered by users before they become expert
Organisational change

- Setting impact on performance
  - The performance of the device may depend on the setting in which it is used or the person using it
  - Organisational changes (e.g., physical alterations to settings) may be required to achieve maximum performance (Craig et al., 2015)

- Barriers to undertaking RCTs
  - Performance may vary depending on the setting in which the device is used
  - RCTs may not reflect the way in which the device will be used in clinical practice

- How RWE may fit
  - Observational evidence may better reflect how the device will be used in practice and provide data that are more externally valid

Randomisation and blinding

- Patients may not want to risk being randomised*
  - For example, being randomised to an invasive surgical procedure rather than a minimally invasive one (Drummond et al., 2009)

- Patients and clinicians cannot be blinded to the device being used
  - Unethical to insert sham or placebo devices
  - Attempts to blind assessors may be unsuccessful if tell-tale signs are left by the device (Walker et al., 2017)

- Barriers to undertaking RCTs
  - Patients opting out of RCTs may reduce the generalisability of the data
  - Non-blinded RCTs may be subject to bias (particularly for behavioural outcomes)

- How RWE may fit
  - RWE can include all patients (i.e., reduce self-selection)
  - Bias relating to blinding will still exist
What does this mean for RCT and RWE?

- These issues lead to the following arguments:
  - RCTs may be the wrong vehicle for the evaluation of medical devices
  - RWE or observational data could replace RCTs in the evaluation of medical devices

Changes in regulation

- Conformity assessment states that:
  “Benefits must outweigh risks and achieve the claimed performance - this must be proven with supporting clinical evidence and investigation” (MHRA, 2018)

- Whereby:
  - Clinical investigation = systematic investigation of humans to assess safety or performance
  - Clinical evaluation = The above investigation plus analyses of data and assessment of whether evidence is sufficient (European Commission, 2016)

- Conformity assessment doesn’t appear prescriptive around the type of evidence that is required:
  - Therefore, there may be opportunities for industry to make use of observational data
References


Thank you

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