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

Michelle Jenks

Providing Consultancy &
Research in Health Economics

University of York

INVESTORS IN PEOPLE

YHEC
York Health Economics Consortium

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

University of York

INVESTORS IN PEOPLE

YHEC
York Health Economics Consortium

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

Size of company

Profitability period

Device modifications

Learning curve

Organisational change

Randomisation and blinding

- 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

UNIVERSITY of York

INVESTORS IN PEOPLE

YHEC
York Health Economics Consortium

Profitability period

Size of company

Profitability period

Device modifications

Learning curve

Organisational change

Randomisation and blinding

- 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

UNIVERSITY of York

INVESTORS IN PEOPLE

YHEC
York Health Economics Consortium

Device modifications

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

- 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

UNIVERSITY of York INVESTORS IN PEOPLE

YHEC York Health Economics Consortium

Learning curve

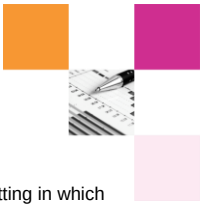
- Size of company
- Profitability period
- Device modifications
- **Learning curve**
- Organisational change
- Randomisation and blinding

- 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

UNIVERSITY of York INVESTORS IN PEOPLE

YHEC York Health Economics Consortium

Organisational change



Size of company

Profitability period

Device modifications

Learning curve

Organisational change

Randomisation and blinding

- 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 use
  - 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

UNIVERSITY of York INVESTORS IN PEOPLE

YHEC York Health Economics Consortium

Randomisation and blinding

Size of company

Profitability period

Device modifications

Learning curve

Organisational change

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

UNIVERSITY of York INVESTORS IN PEOPLE

YHEC York Health Economics Consortium

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

- Chapman AM, Taylor CA, Girling AJ. Are the UK systems of innovation and evaluation of medical devices compatible? The role of NICE's medical technologies evaluation programme (MTEP). Appl Health Econ Health Policy. 2014;12(4):347–57.
- Craig et al. A Review of the Economic Tools for Assessing New Medical Devices. Applied Health Economics and Health Policy. 2015. 13 (1): 15-27
- Drummond M, Griffin A, Tarricone R. Economic evaluation for devices and drugs—same or different? Value Health. 2009;12:402–4.
- European Commision. Clinical Evaluation: A Guide For Manufacturers and Notified Bodies Under Directives 93/42/EEC and 90/385/EEC. 2016.
- Kirisits A, Redekop WK. The economic evaluation of medical devices: challenges ahead. Appl Health Econ Health Policy. 2013;11:15–26.
- Medicines and Healthcare products Regulatory Agency. Medical devices: EU regulations for MDR and IVDR. 2018. Available from: https://www.gov.uk/guidance/medical-devices-eu-regulations-for-mdr-and-ivdr
- Walker R, Huxley L, Juttner M, et al. (2017) A pilot randomized controlled trial using prophylactic dressings to minimize sacral pressure injuries in high-risk hospitalized patients. Clinical Nursing Research 26(4),pp. 484-503.

UNIVERSITY of York INVESTORS IN PEOPLE

YHEC
York Health Economics Consortium

Thank you

michelle.jenks@york.ac.uk

Telephone: +44 1904 324870

Website: www.yhec.co.uk

http://tinyurl.com/yhec-facebook

http://twitter.com/YHEC1

http://tinyurl.com/YHEC-LinkedIn

MINERVA http://www.minerva-network.com/

Providing Consultancy &
Research in Health Economics

UNIVERSITY of York INVESTORS IN PEOPLE

YHEC
York Health Economics Consortium