Industry exposure to IDEAL: education and outreach (and related ideas)

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Outreach to Industry Regarding IDEAL: “Industry” is NOT homogeneous

• Industry is not homogenous
  • Clinical operations
  • Medical Affairs
  • Epidemiology
  • Safety (several aspects)
  • Commercial (multiple aspects)

• Each function has its own external stakeholders
  • FDA
  • Payers
  • Surgeons
  • Hospitals

• POINT: NOT ONE SINGLE AUDIENCE
Challenges to IDEAL-D Adoption

• We live in a highly regulated environment
  • As noted in IDEAL-D, any framework needs to be compatible with existing regulations OR needs to be embraced by regulators (and legislators)

• We need to show value to payers and providers
  • Better outcomes (efficacy or safety or, preferably, both)

• Question: How does IDEAL-D help us?
  • Answer: The framework helps us think more clearly and systematically about the broader needs for rigorous scientific EVIDENCE

• Some companies already have evidence generation “road maps”

• So – let’s continue the discussion with this in mind
What does “industry” need to learn?
What is the quality of the current evidence from observational analyses?

August 2010: “Among patients in the UK General Practice Research Database, the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer”

Sept 2010: “In this large nested case-control study within a UK cohort [General Practice Research Database], we found a significantly increased risk of oesophageal cancer in people with previous prescriptions for oral bisphosphonates”
What is the quality of the current evidence from observational analyses?

April 2012: “Patients taking oral fluoroquinolones were at a higher risk of developing a retinal detachment”

Dec 2013: “Oral fluoroquinolone use was not associated with increased risk of retinal detachment”
What did we just learn (and what else do we need to know to move forward)?

• Results from non-interventional studies can vary due to:
  • Data source
  • Choice of design
  • Choice of design “parameters” within a type of design, e.g., broad vs. narrow definition of exposure

• Things are very different for pharmaceuticals than for devices
  • Identification of specific products (easy for drugs, hard for devices without UDI)
  • Exposure “window” (easier for devices, hard for pharmaceuticals)
  • Operator effects not (or at least less) relevant to pharmaceuticals
  • Ability to follow over time (connecting in-hospital to outpatient data) (but duration of follow-up in a given database is also a problem for pharmaceuticals)
Where IDEAL can help
Proposal: Follow open science in observational research

Patient-level Data + Statistical programming = Evidence repository

Open Science tenets:
- Transparency
- Reproducibility
- Replicability - same data + different analysis = similar evidence?
  different data + same analysis = similar evidence?
- Reliability - evidence can be interpreted honestly with known operating characteristics
- Efficiency - access to evidence can be minutes instead of months
Best practices for population-level effect estimation

**Evidence Generation**
- Write and share protocol
- Open source study code
- Use validated software
- Replicate across databases

**Evidence Evaluation**
- Produce standard diagnostics
- Include negative controls
- Create positive controls
- Calibrate confidence interval and p-value

**Evidence Dissemination**
- Don’t provide only the effect estimate
- Also share protocol, study code, diagnostics and evaluation
- Produce evidence at scale
RWE Research Process
to Ensure Quality, Rigor, and Transparency (of methods AND results)

*Time to complete shown is approximate minimum required.
Details of Analytical Process

Supporting Tools and Templates

- Standard Vocabulary Documents
- Search Strategy Template
- Standardized Code Library
- Output Automation
- Data Specification File
- Publication Policy
- DRRA Complaint Forwarding Form
- Phased CER

Protocol Driven Research Check List Initiated

Loop 1

Protocol

Data Specification File

Attrition Flow

Creation of Data Analytic File

Frequency Check

Loop 2

 QC & Approval Required*

 QC check : Clinical PI QC check & Stats program

 Automated Table Shell

 Descriptives & Bivariate

 Multivariable Analysis

 Report/Abstract

Manuscript

Approval Required**

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Guidance Tools

Core Fill in Templates

Protocol Appendices

- Supporting Tools and Templates

- Protocol Driven Research Check List Initiated

- Loop 1

- Protocol

- Data Specification File

- Attrition Flow

- Creation of Data Analytic File

- Frequency Check

- Loop 2

- Automated Table Shell

- Descriptives & Bivariate

- Multivariable Analysis

- Report/Abstract

- Manuscript

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Potential fora
(or forums, if you don’t like the correct Latin pluralization)

• MDIC
• Surgical conferences (e.g., American College of Surgeons, or ACS journal club)
• Society of Thoracic Surgeons
• NSQIP (national surgery quality initiative program)
• American Society of Plastic Surgeons / Plastic Surgery Foundation (National Breast Implant Registry)
• Non-clinical:
  • International Society for Pharmaco economics and Outcomes Research (ISPOR): Device Special Interest Group (SIG)
  • International Society for Pharmaco epidemiology (ISPE): also has a Device SIG
  • RAPS (regulatory affairs professional society)
Conclusions

• IDEAL-D makes a useful framework for considering the needs for evidence
• There are different stakeholders within industry, and each of those stakeholders has different external stakeholders, so the nature of the education on IDEAL-D (or other) may need to be adapted to each audience
• Fundamental principles of rigorous science need to be emphasized, especially the need for protocols and transparency regarding methods and results
• There are many venues in which IDEAL-D can be disseminated (you know these better than I do)