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

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IDEAL conference, NYC

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Outreach to Industry Regarding IDEAL: "Industry" is NOT homogeneous

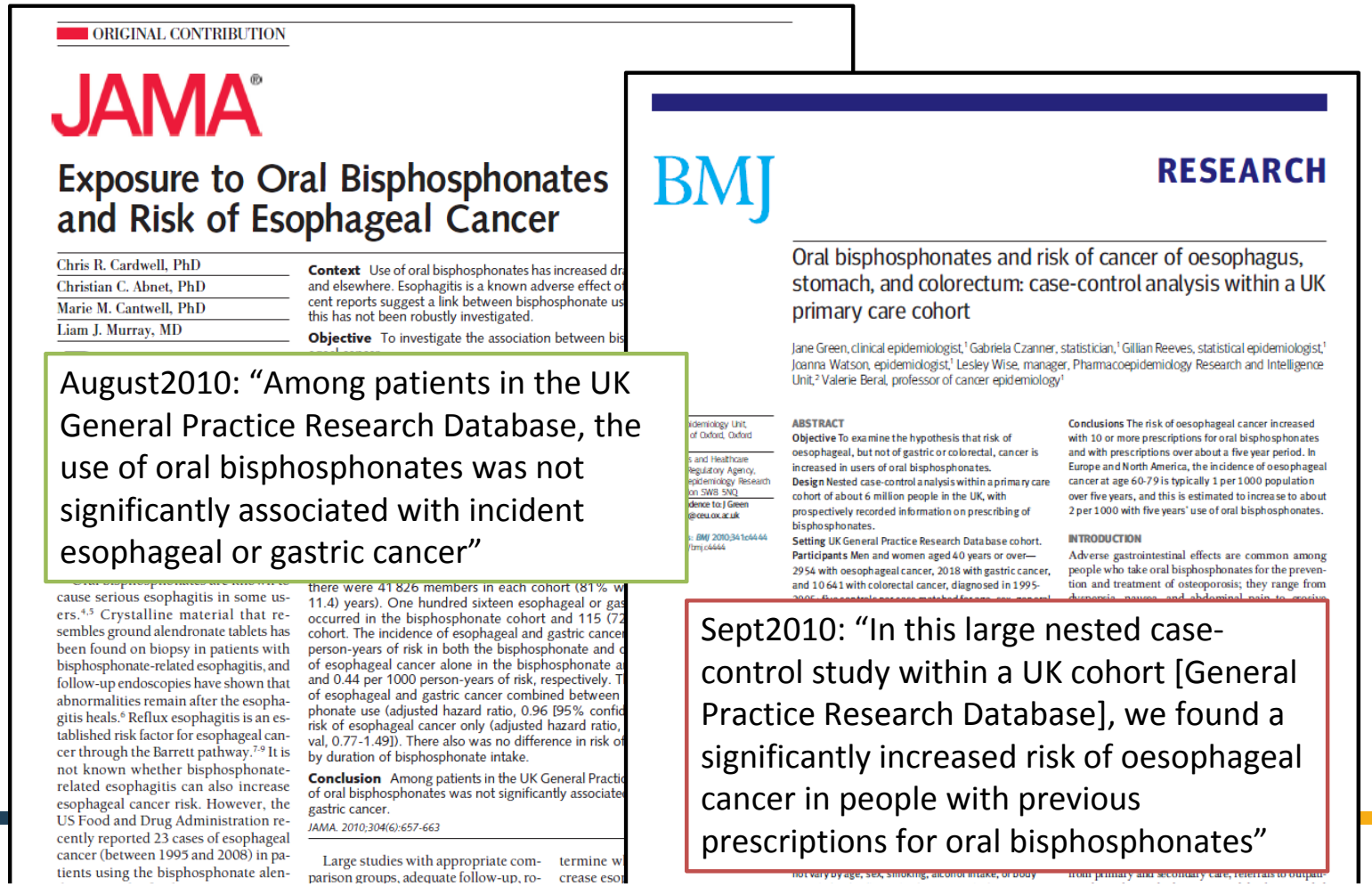
- Industry is not homogenous
  - Clinical operations
  - Medical Affairs
  - Epidemiology
  - Safety (several aspects)
  - Commercial (multiple aspects)
- Each function has its own external stakeholders
  - FDA
  - Payers
  - Surgeons
  - Hospitals
- POINT: NOT ONE SINGLE AUDIENCE

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?



ORIGINAL CONTRIBUTION

JAMA®

Exposure to Oral Bisphosphonates and Risk of Esophageal Cancer

Chris R. Cardwell, PhD
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Marie M. Cantwell, PhD
Liam J. Murray, MD

Context Use of oral bisphosphonates has increased dr
and elsewhere. Esophagitis is a known adverse effect o
cent reports suggest a link between bisphosphonate us
this has not been robustly investigated.

Objective To investigate the association between bis

cause serious esophagitis in some users.[4,5] Crystalline material that resembles ground alendronate tablets has been found on biopsy in patients with bisphosphonate-related esophagitis, and follow-up endoscopies have shown that abnormalities remain after the esophagitis heals.[6] Reflux esophagitis is an established risk factor for esophageal cancer through the Barrett pathway.[7-9] It is not known whether bisphosphonate-related esophagitis can also increase esophageal cancer risk. However, the US Food and Drug Administration recently reported 23 cases of esophageal cancer (between 1995 and 2008) in patients using the bisphosphonate alen-

there were 41 826 members in each cohort (81% w
11.4) years). One hundred sixteen esophageal or gas
occurred in the bisphosphonate cohort and 115 (72
cohort. The incidence of esophageal and gastric cancer
person-years of risk in both the bisphosphonate and c
of esophageal cancer alone in the bisphosphonate a
and 0.44 per 1000 person-years of risk, respectively. T
of esophageal and gastric cancer combined between
phonate use (adjusted hazard ratio, 0.96 [95% confid
risk of esophageal cancer only (adjusted hazard ratio,
val, 0.77-1.49]). There also was no difference in risk of
by duration of bisphosphonate intake.

Conclusion Among patients in the UK General Practi
of oral bisphosphonates was not significantly associate
gastric cancer.

JAMA. 2010;304(6):657-663

Large studies with appropriate comparison groups, adequate follow-up, ro- termine w crease eso

August2010: "Among patients in the UK General Practice Research Database, the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer"

BMJ

RESEARCH

Oral bisphosphonates and risk of cancer of oesophagus, stomach, and colorectum: case-control analysis within a UK primary care cohort

Jane Green, clinical epidemiologist,[1] Gabriela Czanner, statistician,[1] Gillian Reeves, statistical epidemiologist,[1] Joanna Watson, epidemiologist,[1] Lesley Wise, manager, Pharmacoepidemiology Research and Intelligence Unit,[2] Valerie Beral, professor of cancer epidemiology[1]

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: *BMJ* 2010;341:c4444
7/bmj.c4444

ABSTRACT

Objective To examine the hypothesis that risk of oesophageal, but not of gastric or colorectal, cancer is increased in users of oral bisphosphonates.

Design Nested case-control analysis within a primary care cohort of about 6 million people in the UK, with prospectively recorded information on prescribing of bisphosphonates.

Setting UK General Practice Research Database cohort.

Participants Men and women aged 40 years or over—2954 with oesophageal cancer, 2018 with gastric cancer, and 10 641 with colorectal cancer, diagnosed in 1995-

Conclusions The risk of oesophageal cancer increased with 10 or more prescriptions for oral bisphosphonates and with prescriptions over about a five year period. In Europe and North America, the incidence of oesophageal cancer at age 60-79 is typically 1 per 1000 population over five years, and this is estimated to increase to about 2 per 1000 with five years' use of oral bisphosphonates.

INTRODUCTION

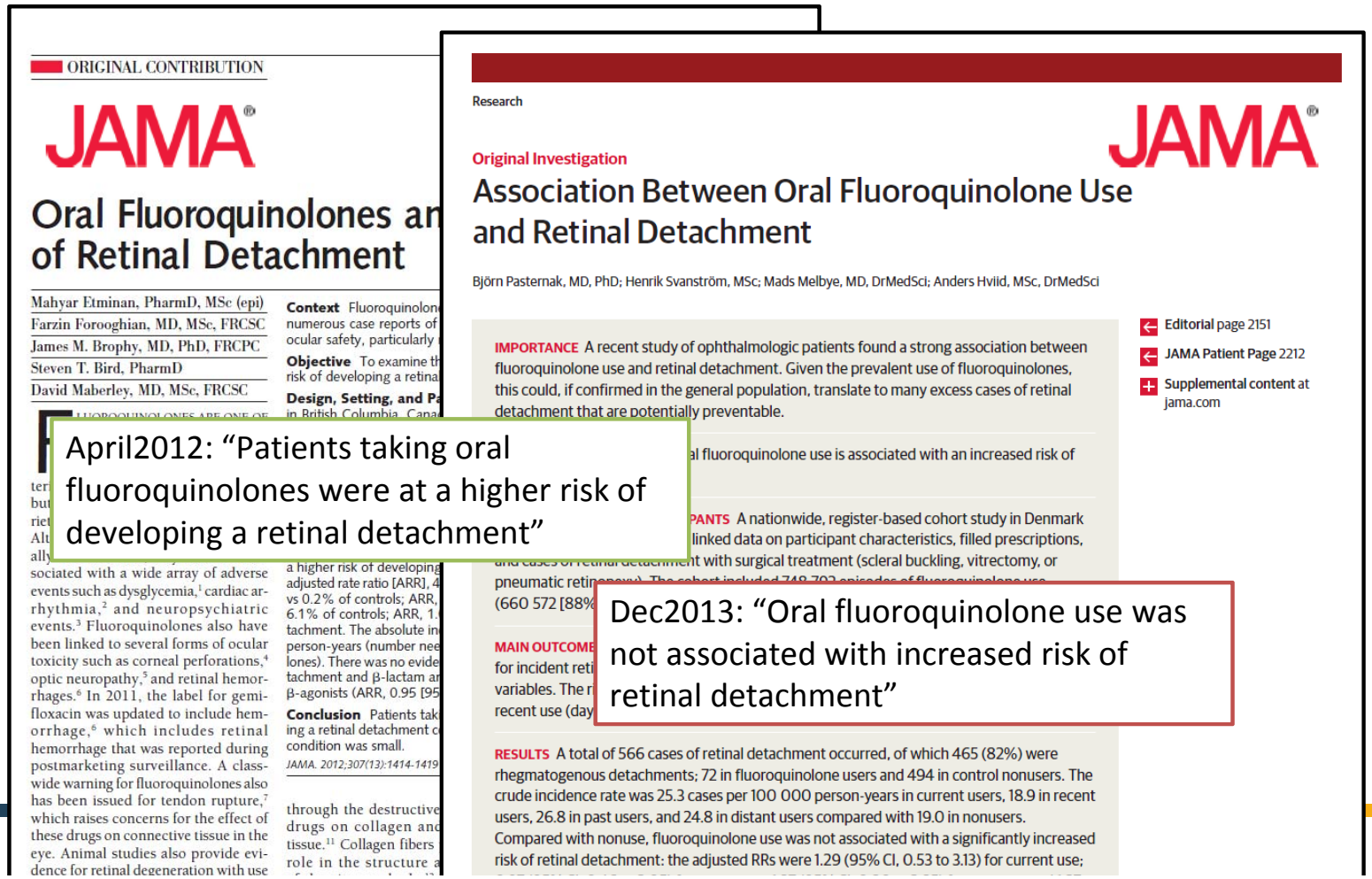
Adverse gastrointestinal effects are common among people who take oral bisphosphonates for the prevention and treatment of osteoporosis; they range from

not vary by age, sex, smoking, alcohol intake, or body

from primary and secondary care, referrals to outpati-

Sept2010: "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?



ORIGINAL CONTRIBUTION

JAMA

Oral Fluoroquinolones an
of Retinal Detachment

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Farzin Forooghian, MD, MSc, FRCSC
James M. Brophy, MD, PhD, FRCPC
Steven T. Bird, PharmD
David Maberley, MD, MSc, FRCSC

April2012: "Patients taking oral fluoroquinolones were at a higher risk of developing a retinal detachment"

Research

JAMA

Original Investigation

Association Between Oral Fluoroquinolone Use and Retinal Detachment

Björn Pasternak, MD, PhD; Henrik Svanström, MSc; Mads Melbye, MD, DrMedSci; Anders Hviid, MSc, DrMedSci

Editorial page 2151
JAMA Patient Page 2212
Supplemental content at jama.com

Dec2013: "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

Data + **Analysis** = **Evidence**

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

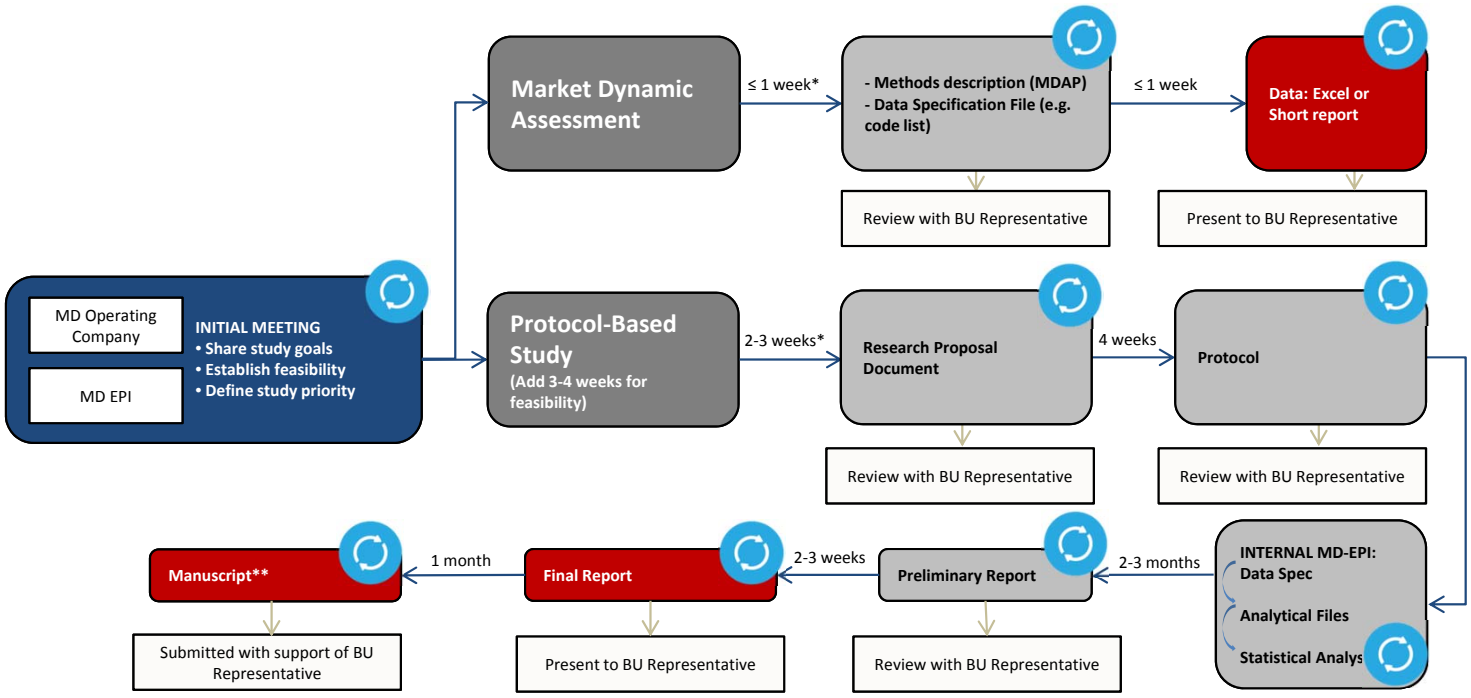
Best practices for population-level effect estimation

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

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

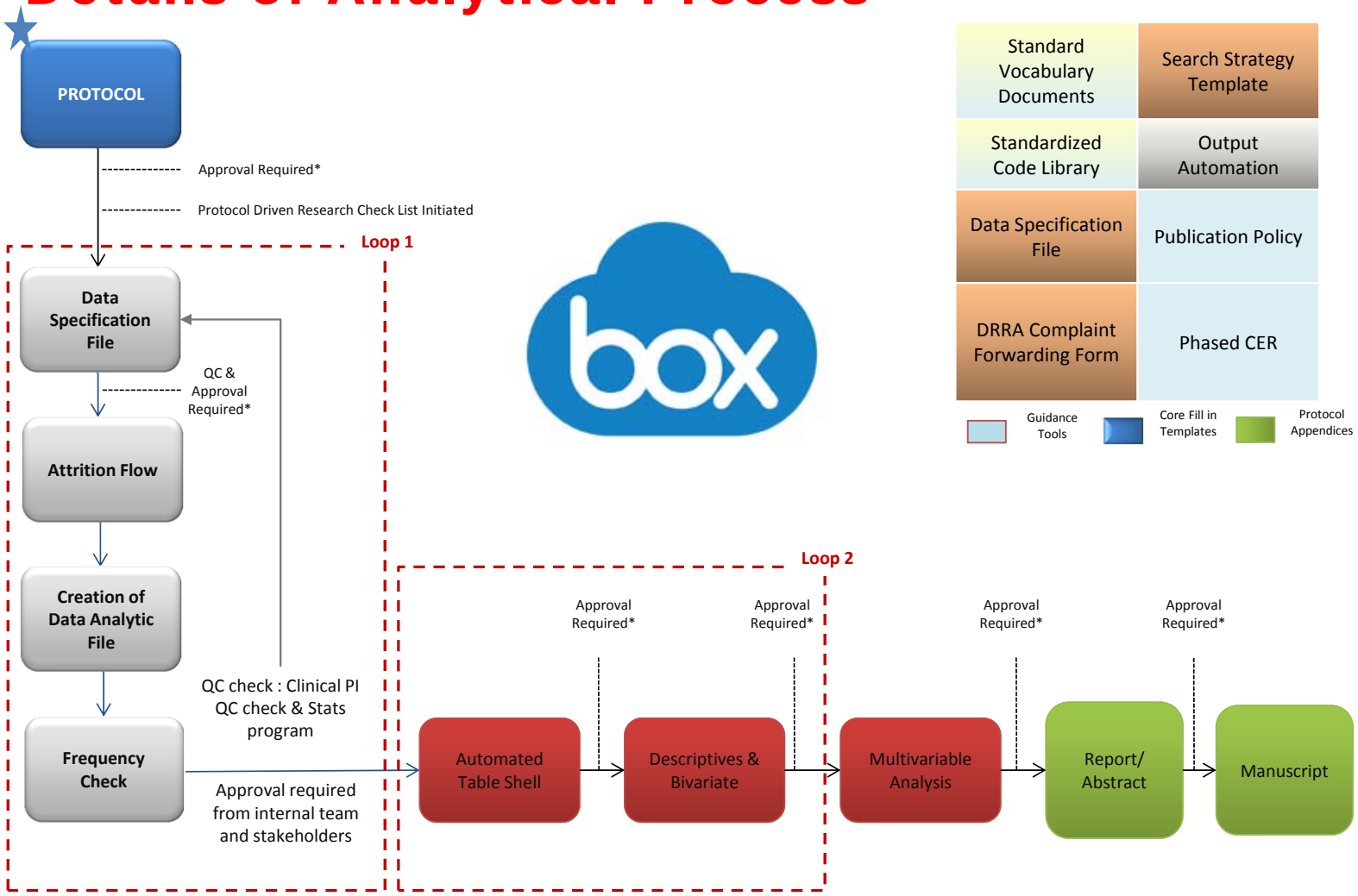
- Don't provide only the effect estimate
- Also share protocol, study code, diagnostics and evaluation
- Produce evidence at scale

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

Guidance Tools | Core Fill in Templates | Protocol Appendices

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)