

# Multi-player Influence on Research Results

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**Duke** Clinical Research Institute

FROM THOUGHT LEADERSHIP  
TO CLINICAL PRACTICE

# Disclosures

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## Research

- American Regent
- Amgen
- Bayer
- Boehringer Ingelheim
- Merck
- NIH: NIA, NCATS, NCCIH, NHLBI
- Novartis
- PCORI
- Verily

## Consulting

- AstraZeneca
- Biofourmis
- Boston Scientific
- Bristol Myers Squibb
- Cytokinetics
- Eidos Therapeutics
- Intercept
- Novartis
- Novo Nordisk

## Editorial

- AMA: JAMA Cardiology



# Working with others to find answers

## Biopharma



## Medical and Digital Devices



## Government Agencies and Institutes



## Medical Associations and Societies; Patient Advocacy Groups



## Other Collaborators



## Who influences research results?

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- A. Sponsors
- B. Funders
- C. Investigators
- D. Technologies
- E. All of the above



## Which funders may influence research results *the most* ?

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- A. Private life science industry
- B. Public life science industry
- C. Government agencies
- D. Contract research organizations
- E. Data aggregators
- F. Research technology companies
- G. Social networks
- H. Any of the above



# Case #1

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- Its 2011 & a large clinical trial is completed
  - First of its kind
  - Largest ever
  - Published in NEJM
  - Sponsor interest is low or completely cool to continue funding any additional analyses
- Young faculty member is the coordinating center PI
  - *Friendly* advice from a colleague
    - “You should hold on to everything. That trial will make your career...”
- **Funding:** Multiple **future** mechanisms

**Is there any potential risk for sponsor influence?**



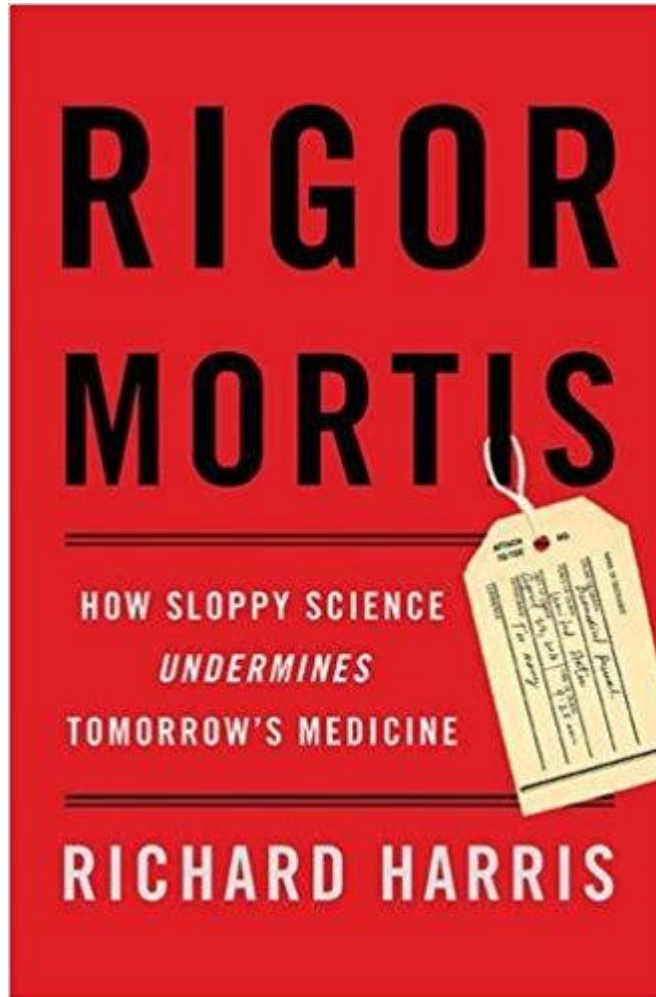
## Sponsor influences?

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- Are there **current** influences?
- \$0 current funding
- Are there **future** influences?
- \$XX future funding



# Benefits vs. Risks



“American taxpayers spend \$30 billion annually funding biomedical research, but **over half of these studies can't be replicated** due to poor experimental design, improper methods, and sloppy statistics. Bad science doesn't just hold back medical progress, it can sign the equivalent of a death sentence for terminal patients.”

2011 [Bayer](#): Found 14/67 (21%) replicated the original results with in-house experiments.

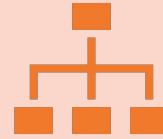
2012 [Amgen](#): Found 6/53 (11%) pre-clinical cancer studies had replications that could confirm conclusions from the original studies

# What may cause the research reproducibility crisis?

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Fierce competition (due to lower funding levels)



Structural problems and hierarchies



Higher future stakes



Complexity of science and data providence



## Case #2

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Junior investigator develops a concept to improve functional capacity for patients with cardio-pulmonary disease

**Potential medical product:** Novel intervention targeting the mechanism of interest

**Experimental plan:** 3 series of early phase studies:

- Small, short duration intense physiological
- Small, short duration cardiopulmonary exercise
- 60 participant, longer duration activity test

**Funding:** Academic center

**Future plans** – K or equivalent □ R01

Industry/Intellectual property pending



## Sponsor influences?

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- Are there **current** influences?
- Yes, current funding
- Are there **future** influences?
- Yes, potential intellectual property and medical product



## Case #3

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Novel trial being designed with new direct to participant methods that will harvest automatically electronic health records

**Research technology:** Promising platform that could solve the world's trial problems by allowing patients anywhere to enroll and get their data seamlessly

**Trial plan:**

- **Pilot phase:** Enroll 100 to evaluate feasibility
- **Full phase:** Enroll 10000 for a fully decentralized trial

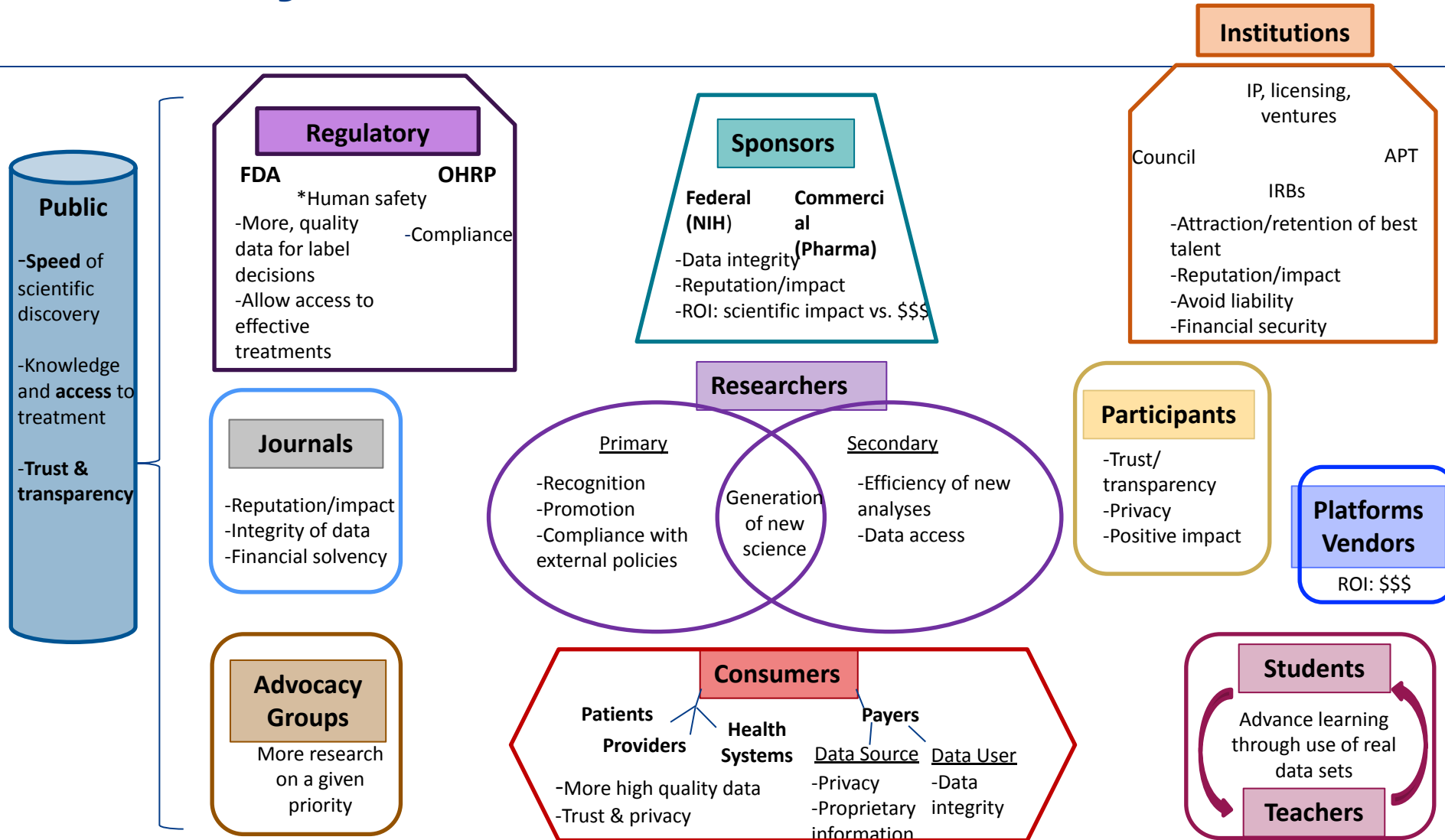
**Funding:** Non-profit organization; Research technology company in-kind support/highly discounted

**Future plans:** Research technology company scaling up over next year with series of funding rounds...public offering

## Is there any potential risk for research tech company influence?



# Research Ecosystem: Influencers and Stakeholders



# Addressing Professionalism and Ethics Throughout the System

| CONFERENCE REPORT                                                                                                                                    |                                                                 |                                                                                        |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| 2020 American Heart Association and American College of Cardiology Consensus Conference on Professionalism and Ethics: A Consensus Conference Report |                                                                 |                                                                                        |                                                                                     |
| Executive Committee                                                                                                                                  | Ivor J. Benjamin, MD, FAHA, FACC, Conference Co-Chair, AHA      | William J. Oetgen, MD, MBA, MACC, Executive Committee Author, Task Force 2 Author, ACC |                                                                                     |
|                                                                                                                                                      | C. Michael Valentine, MD, MACC, FAHA, Conference Co-Chair, ACC  | Katherine A. Sheehan, PhD, Executive Committee Author, AHA                             |                                                                                     |
| Task Force 1                                                                                                                                         | Ralph G. Brindis, MD, MPH, MACC, FAHA, Task Force Co-Chair, ACC | Glenn N. Levine, MD, FACC, FAHA, Author                                                |                                                                                     |
|                                                                                                                                                      | William H. Roach, Jr, MS, JD, Task Force Co-Chair, AHA          | Rita F. Redberg, MS, MD, FACC, FAHA, Author                                            |                                                                                     |
|                                                                                                                                                      | Robert A. Harrington, MD, FAHA, MACC, Author                    | Bernadette M. Broccolo, JD, Discussant                                                 |                                                                                     |
|                                                                                                                                                      |                                                                 | Adrian F. Hernandez, MD, MHS, FAHA, Discussant                                         |                                                                                     |

Benjamin IJ, 2020 American Heart Association and American College of Cardiology Consensus Conference on Professionalism and Ethics: A Consensus Conference Report. J Am Coll Cardiol. 2021

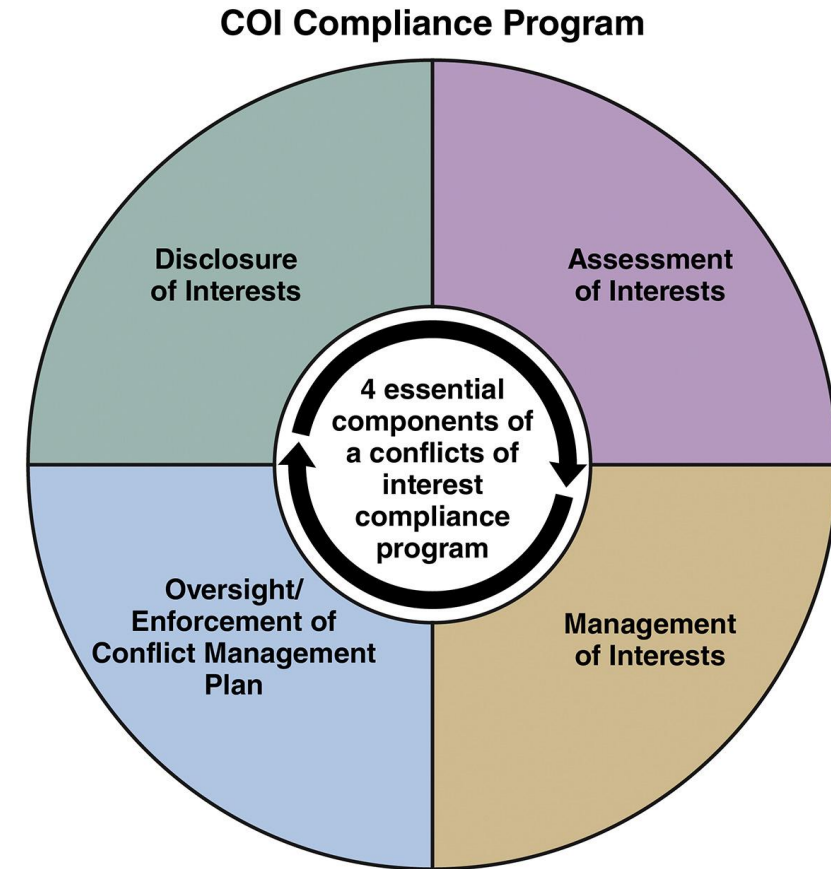


# Guiding Principles and Approach to COI

## Guiding Principles

### Process = Substance

- a. **All 4 Components are Essential**
  - Mere disclosure or reporting of interests is not enough
- b. **Mere presence of an interest is not enough to create a COI**
- c. Most COIs are manageable if the Conflict Compliance Program is effectively implemented and maintained
- d. Entire process must be conducted and overseen with complete independence



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# An example of addressing of potential implicit bias

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## 2.1.2. Recommendations Related to Associational and Intellectual Interests

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1. An associational interest should be fully disclosed and carefully assessed to determine whether the holder of the interest has a COI that would disqualify the holder from participating in an organizational activity; if participation is allowed, a plan for managing the COI should be developed, implemented, and enforced.
  2. An intellectual interest should be fully disclosed any time it is relevant to the matter under consideration and carefully assessed to determine whether the holder of the interest has a COI that would disqualify the holder from participating in an organizational activity; if participation is allowed, a plan for managing the COI should be developed, implemented, and enforced.
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# Open Science: Progress towards addressing influence...but are we there yet?

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- **Scientific organizations**
  - National Academy of Medicine
- **Regulatory agencies**
  - FDA, HHS
- **Sponsors- federal, commercial, private**
  - NIH, biopharma, Wellcome trust, PCORI
- **Journals**
  - ICMJE, BMJ, PLOS
- **Platforms**
  - Vivli, Yoda etc



# Conclusions

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- Influence on research programs and results come from many directions
  - Sponsors, funders, investigators, technologies, health care systems, academia and more....
- Most focus on funding of research due to the risk of **explicit** bias
- However, **implicit** bias may exist for future advancement/value
- Checks and balances are needed often done by regulatory agencies
- Promoting open science may help all address the risk of bias (explicit and implicit)

