

Maintaining Trustworthiness In NIH Public-Private Partnerships

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The Greenwall Foundation

October 9, 2018

Conflicts of interest

- **2016 CDC Workgroup on Ethical Considerations for Public-Private Partnerships**

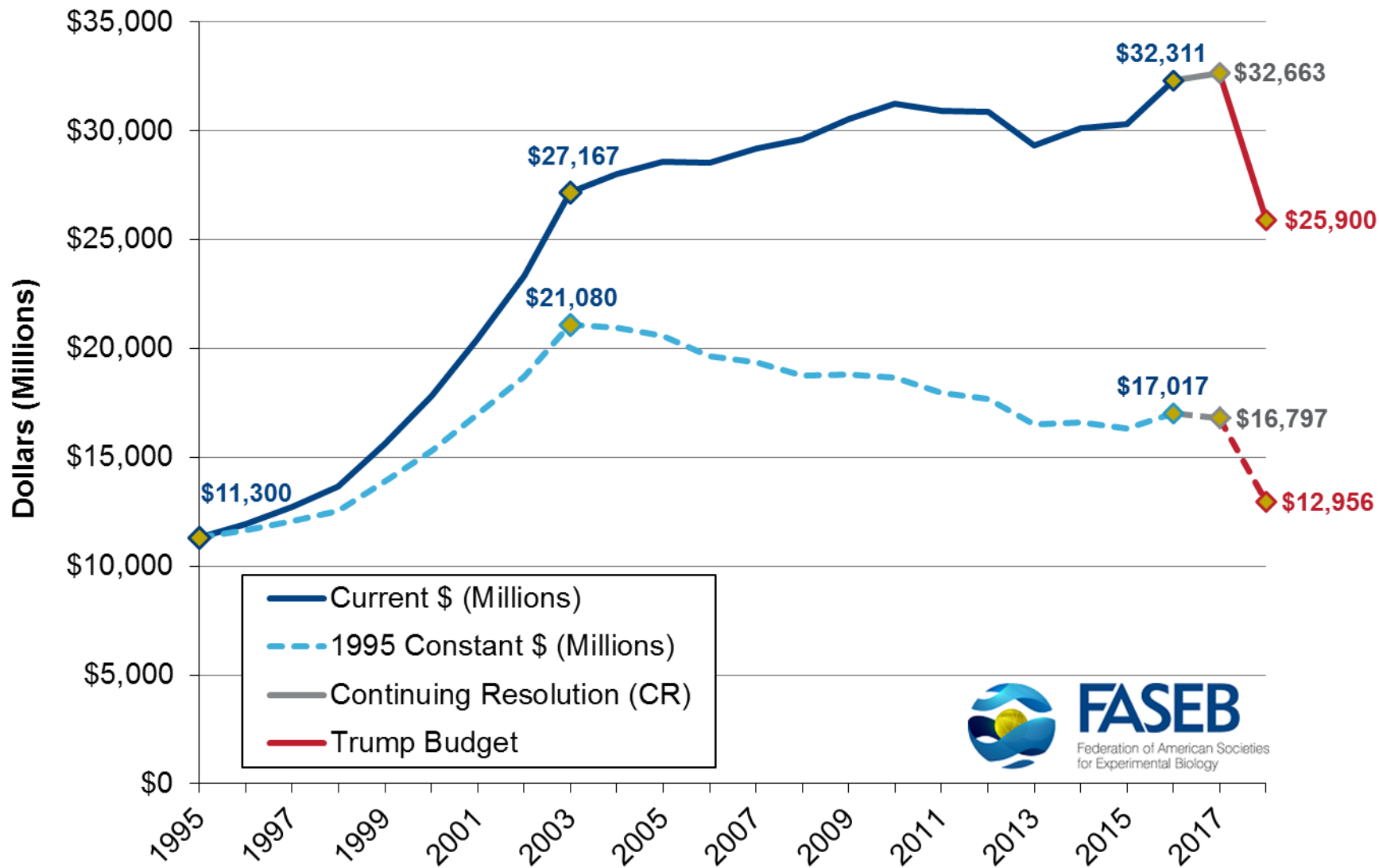
Overview of talk

- **NIH public-private partnerships (PPPs)**
 - Opioid use disorder
 - Moderate alcohol consumption
- **What's at stake for NIH?**
- **Recommendations to address conflicts of interest in PPPs**

Question for audience

- **Is it harder now to get RO1's funded?**
 - Yes
 - No
 - Uncertain or it depends

NIH Appropriations in Current and Constant Dollars



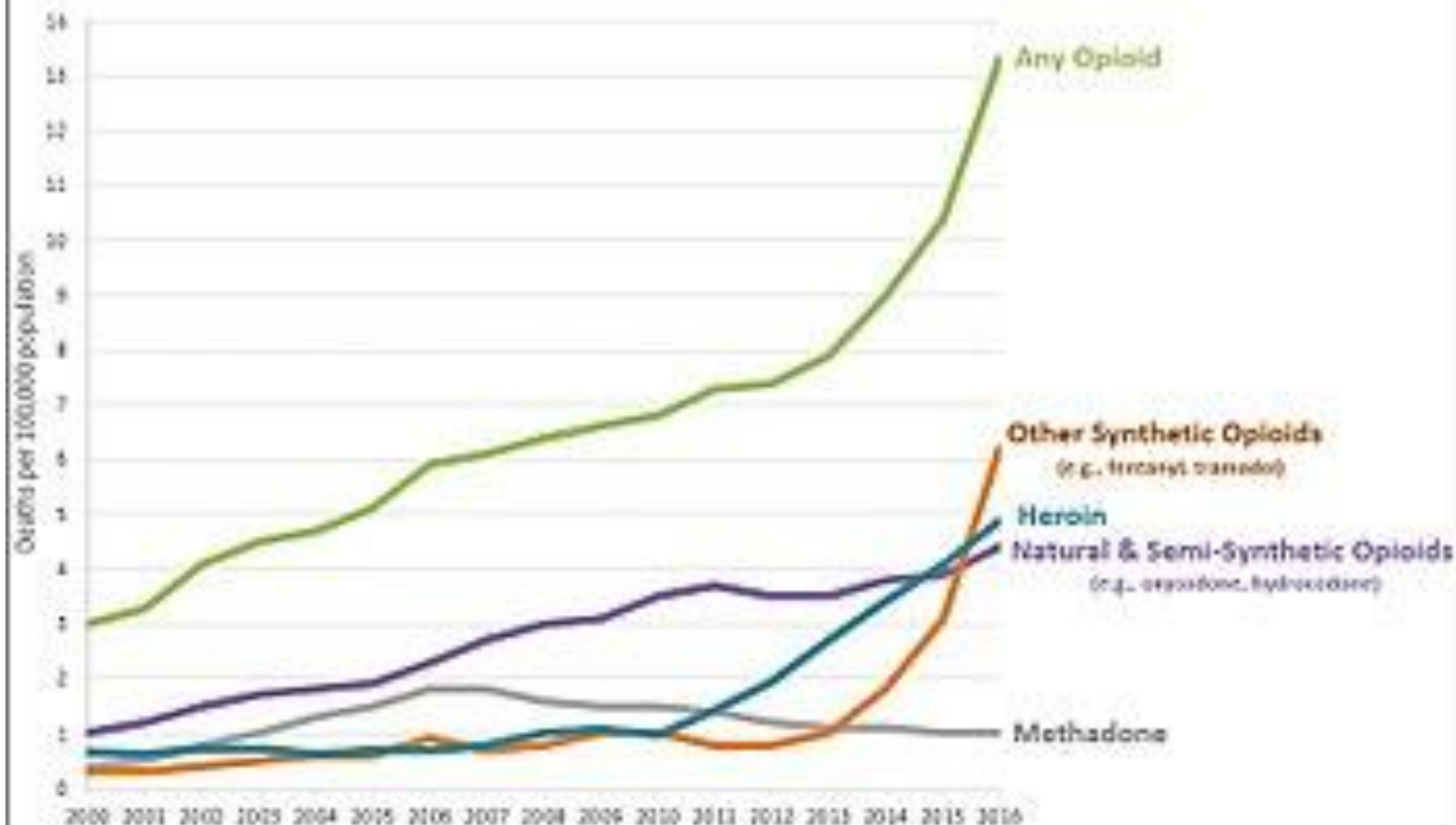
Rationale for public-private partnerships (PPPs)

- **NIH funding decreasing in real dollars**
 - Cannot fund meritorious RO1s
- **Leverage public funds**
- **Promote scientific collaboration**
 - Industry has datasets, abandoned compounds, know-how to develop drugs

Previous NIH PPPs

- **Biomarkers consortium**
- **Accelerating Medicines**
- **Observational Medical Outcomes**
- **Grand Challenges in Global Health**
- **Training for early career scientists**

Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2016



SHANNON GAFFORD



NIH initiative on opioid use disorder: Goals

- **New non-addictive pain medications**
- **Treatments for opioid use disorder**

NIH initiative on opioid use disorder: Planning 2017

- **Set scientific agenda through meetings with academic researchers, government agencies, industry, public**
- **Over 30 drug companies interested**

NIH initiative on opioid use disorder: Aims

- **Repurpose existing and abandoned medications**
- **Identify biomarkers and surrogate endpoints**
- **Establish clinical trials network**

Harris County sues drug makers, doctors over opioid epidemic

By Keri Blakinger

10-13 minutes



Concerns about opioid PPP

- **Drug manufacturers sued by state and local governments**
 - Including industry partners
 - Concerns about PPP
- **NIH appointed working group Feb 2018**

NIH working group recommendations April 3, 2018

- **Only public funds for this PPP**
- **No funding or governance role for companies involved in litigation**
- **Private funding should**
 - Place no restrictions except opioid research
 - Be received before RFPs announced

NIH working group recommendations

- **NIH retain sole authority for**
 - Peer review
 - Selection of specific projects
 - Monitoring and oversight

NIH working group recommendations

- **Governance structure**
 - Exclude companies involved in litigation
 - Include diverse stakeholders
 - Augment vetting process
- **Increased transparency**
 - Governance structure and decisions
 - Agenda and research plan

NIH working group recommendations

- **Recommendations accepted by
Director**

Helping End Addiction Long Term (HEAL)

- **\$100 million, new public funds**
 - No leveraging with private funds



Moderate Alcohol and Cardiovascular Health Trial (MACH)

- **RCT of one drink daily or abstinence**
 - Endpoints cardiovascular outcomes or death
 - 7800 high-risk participants
 - Followed for 6 years
 - \$100 million cost entirely from alcohol manufacturers
 - Enrollment began February 2018

Suggested alternative name

- **Cardiovascular Health Effects of Ethanol Research Study**

Suggested alternative name

- **Cardiovascular Health Effects of Ethanol Research Study**
- **CHEERS**

COI allegations about MACH

- **Investigative journalists March 2018**
 - NIH officials and PI met potential industry funders
 - Presented study design
- **By law only Foundation for NIH may suggest or solicit gift**
- **NIH Director ordered investigation**

Before working group report

- Enrollment suspended
- One alcohol manufacturer withdrew support

NIH review of MACH trial

- **Improper contact between NIAAA staff, extramural investigators, industry**
 - Apparently to persuade industry to support
 - Hid key facts from other NIAAA staff
 - “Calls into question impartiality of process and casts doubt that scientific knowledge gained ... would be ... believable”

NIH review of MACH trial

- **Sustained interactions between eventual PI and NIAAA leadership before FOA**
 - Provided competitive advantage
 - “Effectively steered funding to this investigator”

NIH review of MACH trial

- **Bias towards showing benefit of moderate alcohol consumption**
 - Insufficient patients and follow up to assess cancer endpoints
 - Composite cardiac endpoint not include heart failure
 - Study could miss showing harm

NIH review of MACH trial

- **Recommend termination of trial**
- **Consider how**
 - Avoid providing (or appearing to provide) advantage to investigator
 - Prevent NIH staff from solicit co-funding
 - Identify potential industry influence or irregularities in funding opportunity design

NIH actions on MACH trial June 2018

- Report accepted
- Trial terminated



Bldgs.
38, 38A, 41, 45



Building 16

Southern University of Science and Technology

What's at stake for NIH?

- NIH funding for clinical trial enhances visibility and credibility

Special Article

A Randomized Study of How Physicians Interpret Research Funding Disclosures

Aaron S. Kesselheim, M.D., J.D., M.P.H., Christopher T. Robertson, Ph.D., J.D.,
Jessica A. Myers, Ph.D., Susannah L. Rose, Ph.D., Victoria Gillet, B.A., Kathryn M.
Ross, M.B.E., Robert J. Glynn, Ph.D., Steven Joffe, M.D., and Jerry Avorn, M.D.

N Engl J Med
Volume 367(12):1119-1127
September 20, 2012



The NEW ENGLAND
JOURNAL of MEDICINE

How do MDs use disclosure?

- **MDs read abstracts for hypothetical trial**
 - 2 x 2 Random assignment
 - Funding source NIH or industry
 - Level of methodologic rigor
- **How wiling are you to**
 - Believe findings?
 - Prescribe drug?

Conclusions

- ... Industry sponsorship ... reduces their [MD's] willingness to believe and act on trial findings, independently of the trial's [methodologic] quality.
- These effects may influence the translation of clinical research into practice.



Why are NIH clinical trials respected?

- Peer review regarded as
 - Rigorous
 - Fair



CDC PPPs

- **Implementation of CDC guidelines**
 - Hepatitis C screening
 - Drug manufacturers
 - Fortifying foods with iron, zinc, folic acid
 - Flour and rice manufacturers
 - Sales of products might increase

CDC Workgroup (2016): Ethical considerations for PPPs

- **Transparency about funds, amount, partner role**
- **No undue influence**
 - No involvement beyond available to public
- **CDC must control projects**

<https://www.cdc.gov/partners/ethical-considerations.html>

CDC Workgroup: Ethical considerations for PPPs

- **Assess potential to decrease public trust or create reputational risk**
- **Heightened review if partner role in study design; data access, analysis, interpretation; publication**
- **Due diligence on private partners and upstream donors**

CDC Workgroup: Ethical considerations for PPPs

- **Apply to CDC and CDC Foundation**
 - All staff, regardless of seniority
- **Accepted by Director**

Recommendations

- **PPPs allow NIH to amplify its resources and accomplish missions**
- **Potential for undue influence and bias in all PPPs**

Protecting NIH's Integrity and Trustworthiness in Public-Private Partnerships

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**Deborah Grady, MD,
MPH**

Department of
Medicine, University

The National Institutes of Health (NIH), like other public agencies, creates public-private partnerships (PPPs) to support projects in the public interest that could not be done using only NIH resources. Although PPPs can benefit the public, recent cases illustrate how NIH PPPs may raise important concerns about conflicts of interest.

In 2017, NIH began planning a PPP to accelerate the

events) to consume either 1 standard serving of wine, or spirits per day vs no alcohol, and follow for an average of 6 years. Five large alcohol manufacturers agreed to provide most of the \$100 million of the study.⁴

In March 2018, after obtaining NIH emails and vouchers through the Freedom of Information Act, analysts reported that NIH officials and the scientist v

JAMA 2018; 320:439

Recommendations

- **Prevent need for case-by-case investigations after adverse publicity**
- **Set robust, comprehensive COI policies and procedures**

Recommendations

- **If industry partners want NIH aegis, should accept**
 - NIH peer review process
 - No undue influence
 - Same access as public
 - Provide funding based on concept paper
 - No special access to PPP proposal drafts or potential investigators

Recommendations

- **Identify caution flags**
 - Private partners stand to profit or lose
 - Perception that company harms health
 - Private funds > 50%

Take home message

- **Special role of NIH**
 - Promote scientific knowledge to improve health
- **Safeguard NIH trustworthiness and integrity**
 - Public perceptions important