

## THE “RESEARCH TRIPLE AIM”: ETHICS AS A POLICY DRIVER FOR FUNDING MEDICAL RESEARCH

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### ABSTRACT

Just as the allocation of limited healthcare resources is an ethics issue, we can say the same of the finite dollars spent by the federal government on biomedical research. Misappropriated and wasted money delays improving the lives of those afflicted with disease. From this, we conclude quickly that research dollars should be distributed and used in ways that meet ethical tests including that of distributive justice. Policy levers, a common and effective means of pushing national activities in a desired direction, could be targeted to achieve a more ethical approach to how we allocate research funding in the US.

One approach to answering the ethics question is to take the healthcare Triple Aim as a framework. The Triple Aim has been a successful scaffolding for discussing ways to improve healthcare delivery. Translating the original aims, this paper examines three critical research aims: 1) Researching to improve population health; 2) Improving the experience of research subjects; and 3) Lowering the total cost of research per unit of disease burden improved. For each aim, we discuss key stakeholders, relevant ethical principles, and specific policy recommendations.

### KEYWORDS

Ethics; Ethics, Research; Research; Financing, Government; National Institutes of Health (U.S.); Policy; Triple Aim

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## Why is medical research impact an ethics question?

Daniels and Sabin (2002) established that the existence of limits in healthcare resources creates an ethical question. Biomedical research, as a subset of healthcare, also faces constraints including cost, availability of subjects, sufficiency of researchers, regulatory and logistical constraints. The US federal government spends approximately \$37 billion per year to fund medical research, yet only 20% of grant submissions will receive funding (NIH Grants & Funding, 2016; NIH Funding Facts, 2016). Of the funded grants, only ~30% will produce new knowledge that is made available publically (National Public Radio, 2016; Kitterman, Cheng, Dilts, & Orwoll, 2011; Chan, Lai, Groessi, etc., 2013). In addition to cost, there are not enough research subjects enrolled in studies to complete the research (Kitterman, et al., 2011; Damen, van Agt, de Boo & Huysmans, 2015), and there are too few physicians-scientists participating in research (Milewicz, Lorenz, Dermody, & Brass, 2015). Finally, there are enormous regulatory and logistical barriers, growing over the past decade (Martinez, Tsalatsanis, Yalcin, et al., 2016). As with all constrained systems, we make decisions every day about priorities, although these decisions may be unwitting, ill-conceived, and ill-perceived (Dresser, 2009). How do we as a society – or how should we – make decisions? On what ethical principles should we decide which biomedical research projects to fund? Conversely, how do we justify denying research funding of the 80% of projects passed over?<sup>1</sup> Following Daniels and Sabin’s (2002) “regulative condition”, what policy changes can we make that might address the ethics issues related to limits in the system of medical research?

This paper lays out the conceptual framework of the “**Research Triple Aim**” as an ethical test for policy-making about how we fund and conduct biomedical research (Berwick, Nolan, & Whittington, 2008).

## 1) Research to improve population health

### *Stakeholders:*

Patients with disease burden; taxpayers.

### *Ethical Principles:*

The US has the worst population health outcomes in the OECD countries despite contributing to 44% of the global medical research budget annually (Squires & Anderson, 2015). The teleological principle of utilitarianism – maximizing utility – might lead us to prioritize research that produces the greatest outcome for the most people (Folland, Goodman, & Stano, 2013). NIH has taken this approach to some extent, funding projects to improve public health based on proportional disease burden, a function of prevalence and morbidity (NIH Funding information on disease burden, 2016). There are other research priorities that we might decide to fund despite lower disease burden to address stakeholders not covered by the utility framework. The NIH also funds research on conditions where, in addition to disease burden, society has a responsibility to impacted stakeholders, including fetal alcohol syndrome, diethylstilbestrol exposure, or Agent Orange and Dioxin exposure (\$1M, \$33M, and \$9M in FY2015 respectively; NIH Funding estimates for various research, 2016). The decision to fund such research could be viewed from both a Rawlsian “maximin” perspective (helping those who are worst off) or based on the principle of compensatory justice (Berwick, Nolan, & Whittington, 2008).

After deciding what projects to fund, how do we know that we are producing the greatest outcome for the most people? Ethicists and economists have struggled with this question, and there is no simple answer. After defining the population of interest, researchers can attempt to quantify the utility with quality adjusted life years (QALYs) from a proposed intervention, though QALY introduce their own ethical dilemmas (Follan, Goodman, & Stano, 2013; Cubbon, 1991). Such measures are sometimes

<sup>1</sup> The NIH and similar funding bodies have well-developed methods for blinded peer-review of grant submission, and this

commentary will not delve into the mechanisms or ethical considerations of the grant review process.

calculated by researchers, but this is the exception (National Research Council, 2010).

QALY is part of the basis by payers to make decisions about plan coverage, and thus treatment priorities by extension, although ethical considerations of injustice exist (La Puma, 1992; Callahan, 1991). This practice does not extend to setting research priorities. Even more rare is the concept of using estimated improved QALY to decide which type of medical research should be prioritized. If there were two research studies, both needing \$10 million over 5 years, and one study was far more likely to result in a treatment that increased QALY, would we treat the two research projects equally in NIH study section?

In many cases, research priorities are set using a consensus method. While this may address some of the ethical principles of legitimacy and transparency, the process may not include the right stakeholders at the table (test of fairness) and the priorities may not be followed (test of accountability; McGregor, Henderson, & Kaldor, 2014).

#### *Recommendation:*

*Every federally funded research projects should, when applicable, report QALY associated with the results along with a brief discussion of the application and limitations of interpreting QALYs in the context of the study.*

## 2) Improving the experience of research subjects

#### *Stakeholders:*

Research participants

#### *Ethical Principles:*

Many important ethical considerations are already in place to insure ethical treatment in human subjects research, and the US is now considering updates to the Common Rule (45 CFR 46) in order to stay current with technical and social changes (DHHS, 2016; Federal Registry for Policy, 2016).

One of the basic ethical principles underpinning the Common Rule is Kant’s Categorical Imperative (Golden Rule Principle), rephrased in this context as, “If I were a research subject, how would I want to be treated?” The 2010 publication of the Henrietta Lacks story (a failure of the Categorical Imperative) brought national attention to research ethics and consent, and it showed the power of the press in helping steer conversations of ethics, referred to at times as the “test of making something public” or the “front page test” (Skloot, 2011; Western City, 2012).

The research constraint on the low numbers of subjects recruited to clinical trials suggests there is another gap in the research experience. While low accrual is often a failure to find and contact subjects, it is also clearly a failure of the biomedical research community to engage with the community on its terms. For too long, researchers have taken the position that we conduct experiments on people not with partners in the community. The very term “subject” defines a passive, dependent, or even coerced role – in direct opposition to the ethical principle of autonomy (Varelius, 2006). To address the lack of community involvement in defining the research agenda, the federal government in 2010 funded an independent research organization, the Patient Centered Outcomes Research Institute (PCORI). PCORI has patients on its board of directors, its grant review committees, and it requires that each funded grant have clear involvement from patients in every step of the research (Patient Centered Outcomes Research Institute, 2016).

There has also been rapid growth recently of self-organizing, online, patient affinity groups based on a shared disease. Many of these groups are eager to participate in research, even posting their medical records and outcomes online for researchers to use freely. For example, patientslikeme.org now has 400,000 members, 31 million data points, and it has led to more than 70 published research studies (patientslikeme, 2016). “Let’s Get Healthy”, a national and international program led by Oregon Health and Science University, has had success in the same domain of educating the public on medical

research and getting people to participate (Oregon Clinical & Translational Research Institute, 2016). The public wants to help; the medical research community needs to be more creative in meeting patients at the table as partners not subjects.

Finally, biomedical researchers have a duty to report the findings of the study to patient participants, although this only happens in 23% of clinical studies (Kost, Lee, Yessis, et al., 2013).

#### *Recommendations:*

1) *Expand the role of the patient-researcher from PCORI into all federal funding mechanisms;* 2) *Require that all organizations receiving federal dollars have active patient representation on research leadership committees;* 3) *Require grant recipients to report results back to patient participants in a timely fashion.*

### 3) Lowering the total cost of research per unit of disease burden improved

#### *Stakeholders:*

Patients; researchers (scientists and subjects); taxpayers

#### *Ethical Principles:*

Similar to the considerations mentioned above, there is an ethical duty to do the most good for the greatest number of people. With finances limited, each dollar spent should give the greatest chance of being translated into an intervention that will lower disease burden. Unfortunately, most of the research dollars are wasted. Many academic medical centers recently failed the "front page test" when newspapers called out by name that only 36% of research results are published in a timely fashion, wasting billions of taxpayer dollars and delaying cost-effective treatments (Terry, 2016; Chen, Desai, Ross, et al., 2016). The authors of the study (Chen, et al., 2016) call this out as a failure "to fulfill the ethical obligation that investigators and sponsors have to study participants [and stakeholders], professional values, and the mission of academic medical centers."

Admittedly the measurement of costs in healthcare is difficult, but many researchers do quantify the cost-effectiveness analysis (e.g. incremental cost effectiveness ratios, or ICER; Folland, Goodman, & Stano, 2013). This is especially helpful in cases where expensive treatments with good outcomes produce greater utility than less expensive treatment options (Chan, et al., 2013).

Unfortunately, PCORI will not fund studies explicitly examining cost-effectiveness for political reasons legislated in the Affordable Care Act (ACA), even in funding designated for large, pragmatic clinical effectiveness research (CER) trials (Patient Center Outcomes Research Institute, 2016). This prohibition not only costs the US in healthcare spending, but it keeps researchers from fulfilling their ethical obligations outlined in this paper (Neumann & Weinstein, 2010).

Inefficiencies also increase the cost of conducting medical research as previously noted. Several publications have attempted to apply process improvement methodologies to quantify research efficiency, including the creation of efficiency metrics. Although NIH has made some efforts to apply such standards to funding, there are few requirements of consequence that researchers or their institutions track and report cost-effectiveness or efficiency of the research process itself (Dilts, Zell, & Orwoll, 2015; Grazier, Trochim, Dilts, & Kirk, 2013; Dembe, Lynch, Gugiu, & Jackson, 2014).

Finally, principal investigators usually rise to positions of leadership despite no formal training. Just as physicians are taking management courses in order to advance careers, investigators could be incentivized to complete training in project management, quality improvement (Lean, etc), budgeting and finance, teamwork and communication, and management and leadership. In this context, training researchers to abandon fruitless efforts would be similar to training physicians to stop ordering tests and treatments that add no value (Baron & Wolfson, 2015). Such training could be as transformative in research as it has been in healthcare delivery in reaching the Triple Aim.

### Recommendations:

1) Researchers and organizations who do not report their findings to *clinicaltrials.gov* in a timely fashion should either repay a portion of the funding as a penalty, and/or they should be limited in future access to federal funds; 2) Not only should the portion of the ACA limiting CEA from PCORI be repealed, but the federal government should require reporting a brief CEA and discussion in *clinicaltrials.gov* for all relevant studies receiving federal funding. 3) Investigators with formal management and leadership training should be given an advantage in obtaining federal funds to conduct research.

### Discussion

Numerous ethical principles and tests allow us to evaluate the current state of the medical research system in the US. From this vantage point, we can discern that there are numerous ethical gaps, from wasted money and inefficiencies, to the way we involve patients as subjects rather than partners. Fortunately, this same ethical evaluation helps us identify changes that we can make to improve our stance. Many of these recommended improvements can be made on a voluntary basis even absent legislative change, but there is also a compelling history that mandates tied to continued federal funding will have a great impact at scale. The concept of the healthcare Triple Aim provides a convenient framework for evaluating the ethical issues and for making specific recommendations that can improve research to improve population health, facilitate a better experience for patients involved in research, and lower the total costs of research per unit of disease burden ameliorated.

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