Racial Myths and Regulatory Responsibility

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Abstract: Calls to abolish race as a proxy for biology or genetics in clinical care have reached a fever pitch in the latter half of 2020, including articles in the *New England Journal of Medicine*, and urgent letters from prominent Senators.

Introduction

In her 2020 book *Caste*, Isabel Wilkerson opens Chapter Two with a vivid image of an old house, as a metaphor for America's deeply embedded structural racism. She asks the reader to imagine everything that breaks down in an old house: cracks in the foundation, mold in the basement, welts in the plaster walls, uneven pillars. Then, to the person who moves into or inherits this old house, she writes, even though we did not cause the breakdown, "any further deterioration is, in fact, on our hands."[1] She goes on to say:

> America is an old house. [...] Unaddressed, the ruptures and diagonal cracks will not fix themselves. The toxins will not go away but rather, will spread, leach, and mutate, as they already have. When people live in an old house, they come to adjust to the idiosyncrasies and outright dangers skulking in an old structure. They put buckets under a wet ceiling, prop up groaning floors, learn to step over that rotting wood tread in the staircase. The awkward becomes acceptable, the unacceptable becomes merely inconvenient. Live with it long enough, and the unthinkable becomes normal. Exposed over the generations, we learn to believe that the incomprehensible is the way life is supposed to be.[2]

The slippage between and conflation of genetics and race is a leaky ceiling. Rather than fixing it, we are letting a bucket catch the drip. Much like the old house, our common and continued use of the social and political category of race as a proxy for biology and genetics, a conflation which is logically and scientifically

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inconsistent — has become normal. Although some researchers clearly understand race to be a social construct, a still sizable number of modern-day researchers continue to step over the rotting wood tread of pseudoscience and eugenics, ignoring its history while perpetuating its fundamental myths. Modern day institutional review boards (IRBs) have lived with and perpetuated the unthinkable for so long — the unscientific practice of substituting one variable for another, when the two are unrelated — that it appears thoroughly normal.

In 2000, Craig Venter, after the completion of the Human Genome Project, asserted that race has no biological or genetic basis.[3] At the time, the statement was met with uncertainty.[4] But now, 20 years later, the idea that race is a social construct is repeated often. Articles in the most prestigious medical journals, such as the *New England Journal of Medicine*, reiterate the point, and call for an abolishment of race as a proxy for biology or genetics in clinical algorithms.[5] And, in September of 2020, four prominent US Senators, including Elizabeth Warren, wrote to the *Agency for Healthcare Research and Quality*, urging them to examine whether race categorizations are "an appropriate means of distinguishing human populations."[6]

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However, while there is renewed attention to the ways race is being used in clinical care — and a fervor around dissecting the evidence upon which each algorithm is based — a cursory search in ClinicalTrials.gov reveals that the very same flawed science that led to the use of race in clinical care is still being conducted today. (I say "cursory" because a full review of current research that conflates biology and race is outside the scope of this article. However, I sit on the IRB of my institution and can say firsthand that governmental and pharmaceutical funders continue to launch research that makes the same conflation, I simply cannot quantify the volume here.) If one types "African American" into the "conditions" field on the website, dozens of studies currently recruiting across the country appear, that make the same scientifically flawed assumption upon which our current predicament is based — conflating race with biology and/or with genetics.[7] For example, one study, called Genomics, Environmental Factors and Social Determinants of Cardiovascular Disease in African-Americans Study (GENE-FORECAST), funded by the National Institutes of Health (NHGRI), hypothesizes that "race-ancestry differences in the burden of cardiovascular disease (CVD) reflects the influence of a unique interplay *between the distinct genomic variation characteristic* of African-Americans (AA) and the exposome of social determinants and environmental factors that influence the pathogenesis of CVD in AA" [emphasis mine].[8] And yet, just like the studies that came before it, it conflates several variables and uses inaccurate proxies, for example, by claiming to investigate ancestral genetic difference, but recruiting "self-identified African Americans" — two completely different constructs; and claims that African Americans have a distinct genomic makeup. (One might argue that the investigators are attempting to parse the group "African American" into distinct ancestral groups, however, this effort will lead to further conflation of race and ancestry, since only "self-identified" African Americans are being recruited. In our popular conception, African American refers to Black race, however, non-Black people may share common African ancestry and therefore share the genomic mutations investigated by this study but will be missed because of the recruitment strategy). This is merely one study on the list of

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currently active clinical trials that make this mistake, but it is one of many.

This article will tackle race-based research. In section I, I will examine race as a social and biological construct, tracing the roots of race-based medicine, and describing what "race" can and cannot be used as a proxy for in well-designed scientific research. In section II, I will explore avenues for IRB review, based on the existing regulatory framework, and propose a conceptual model for IRB review of race-based research. And in section III, I will examine other avenues for ending scientifically flawed race-based research and make recommendations for policymakers.

I. Race Is Politics, Not Genetics

There is, perhaps, no more vivid political and legal construct to illustrate that race is a political category than the "one-drop rule" of the early 20th century. In the 1600s, slavery was the law of the land in the United States, and political and economic forces continued to incentivize it. Slaves built and sustained an economy, and moral arguments for abolishing the practice were countered with assertions that people kidnapped from Africa were fundamentally biologically inferior, or at least different, from white Europeans.[9] Slavery worked best for those in power when it was impossible for anyone with dark skin to escape it. More slaves meant more unpaid labor which meant more economic opportunity for whites. Centuries later, after the abolishment of slavery and during the Jim Crow era, it remained politically advantageous for white people to limit entry into their race and limit the voting power and other civil rights of Black people. Beginning in Tennessee in 1910 and spreading to other southern states, the one-drop rule asserted that any person with just "one drop" of Black blood was to be considered Black, replicating the same political reality that existed in the 1600s which made it such that even if slaves were raped by their masters and bore children, and if those children were raped and bore children, despite the diluting of "Black blood," a single drop was enough to keep those children and grandchildren in bondage.[10]

It should be quite obvious to us now that a person with 3 white grandparents and one Black grandparent would have had more European ancestry than African, and yet the political and social rules prevailed and categorized those people as Black. Yet, as clear as it is to us now that this was a case of deliberate conflation of biology and politics, the fundamental assumption upon which the one-drop rule was based is threaded through science and clinical medicine still today. When Barack Obama walks into a doctor's office, he is treated in clinical algorithms as Black. When we measure his lung function, we adjust it because we assume his body is different from a white body.[11] When we estimate his kidney function, we use a different equation, because we assume his muscles and the proteins they produce are different from someone with white skin.[12] And we know very well that his mother was white.

Dorothy Roberts has detailed painstakingly in *Fatal Invention* why and how a political and social category, race, has been so thoroughly conflated with biology.[13] Genomic scientists who are invested in reifying the political racial categories seek out genetic difference between races, but Roberts points out, "Genomic scientists have not discovered race in our genomes. They are taking already accepted racial categories and telling us a new way, based on computer-generated genetic differences, to verify them scientifically."[14] Roberts describes a study conducted by Rosenberg and colleagues that purported to show that the races are genetically distinct, but when she peels apart the layers, we discover that the researchers made a choice to instruct the computer-programmed algorithm to group statically significantly different clusters of genetic mutations into 2-6 groups. When instructed instead to create 20 distinct groups, the computer program showed, in fact, that our clusters of human genetic variation do not fall along racial lines, but instead roundly refute the theory that racial groups are biologically distinct from one another.[15]

Studies that continue to rely on the fundamentally flawed assumption that race is a good indicator of biological difference suffer from confirmation bias, among others design flaws, and those results get added to the data that feeds into our clinical algorithms and tells health care providers to treat races as though they are biologically distinct. A recent *Lancet* article described, and depicted through a flowchart, exactly how research in which race is "inferred to have biological significance" leads to the reinforcement of biological concepts of race, clinical practices tailored to race, and ultimately exacerbation of racial health disparities.[16] Perhaps the most well-known case of race-based research translating into the clinic is the case of BiDil.

The history of the studies leading up to the race-based patenting of BiDil are detailed thoroughly elsewhere.[17] For the purposes of this article, we can summarize it as such: an investigator, Jay Cohn, invested in an idea for a vasodilator as a first-line treatment for heart failure, and sought and secured a patent for his new branded drug, BiDil, in 1989. However, other developments in the field, including the discovery of ACE inhibitors, caused BiDil to lose its financial potential. Cohn, who had done the initial BiDil trials on veterans, returned to his old data to see if he could

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find a way to parse it such that he could save his drug's future. Despite the veterans' trials not being designed for this purpose, and the total number of people identifying as Black in his data being quite small, he was able to find a small statistical significance suggesting that BiDil might be "particularly" effective in Black patients — in a post-hoc subgroup analysis. Because the initial trials were not designed to make claims about race, he was not able to say with any confidence that it was the patients' "Blackness" per se that led the drug to be more effective — it could have been any number of other clinical or environmental factors that were not investigated. Nonetheless, he submitted for a new patent in 2000 — the first race-specific patent for BiDil in African American patients.[18]

Cohn approached the FDA to ask if he could start marketing the drug, but FDA said they needed to be convinced with new data. So he designed a new trial, the AA-HeFT, or African American Heart Failure Trial. This trial only recruited self-identified African American patients, meaning Cohn did not attempt to actually prospectively compare BiDil's effectiveness in Black people versus white people. Instead, he aimed to show that, in his "AA-only" trial, when BiDil was added to standard therapy, it worked better than standard therapy alone. When FDA reviewed the data from the new trial, it was clear that the panel noticed that there was no data to support BiDil as a race-specific drug.[19] Jonathan Kahn, a participant in the approval meeting, said, "Most drugs on the market today were approved by the FDA based on trials conducted almost exclusively in white patients, but they're not designated as white drugs, and rightly so."[20] But nonetheless, FDA approved BiDil for use in Black patients, despite insufficient data for a claim about race. There was no evidence offered, biomedical or otherwise, to explain why the drug should work better in one race versus another. The assumption was that it must be due to a genetic difference, as opposed to a statistical fluke or social variable.[21]

As Roberts notes, "The familiar defense that, despite being a 'crude marker,' and 'blunt tool,' and 'imprecise proxy,' a 'makeshift solution,' or an 'imperfect placeholder,' race is the best that science can do at the moment is not a justification. The reason the BiDil investigators did not have a better marker is that they did not look for one. They stopped at race."[22] These imprecise proxies get threaded throughout clinical care, and they continue to be used even despite more recent evidence that other proxies or direct measures might yield better clinical results.

New research in the area of kidney function assessment has helped us understand that race corrections are not only flawed, but actually might exacerbate health disparities. For decades, nephrologists have used estimated glomerular filtration rates (eGFR) to determine kidney function, using an equation that is adjusted based on the patient's race. This race adjustment came about as a result of an accumulation of data from different sources, some suggesting that Black people might excrete creatinine differently than other people, and others, based in old notions dating back from slavery, suggesting that Black people had higher muscle mass than white people.[23] Despite some factions of the scientific community objecting to this continued use of race as a proxy for some other, known or unknown, variable that might result in differential serum creatinine, the practice has continued and is widely used in hospitals today. Only recently is the pushback generating some results. Advocates have called for the abolishment of race as a factor in the eGFR equation, and a handful of hospitals across the country have eliminated the practice.[24] In 2020, a paper was published in the *Journal of General Internal Medicine* that showed that the practice is actually harmful to patients. African Americans suffer disproportionately from kidney disease, and also have some of the lowest transplant rates. The authors showed that, if the race adjustment were removed, 1 in 3 Black patients would be reclassified as having a more severe stage of kidney disease, allowing for better, more appropriate care, and more timely referral to transplant.[25] In January of 2021, another article, this time published in *JAMA*, drew a similar conclusion: "inclusion of the race coefficient in the estimation of GFR was associated with greater bias in GFR estimation and with delayed achievement of clinical threshold for kidney transplant referral and eligibility" for Black patients.[26] In other words, the continued use of race as a biological category is actually exacerbating racial health disparities.

There are tangible harms that result from our continued use of race correction in spirometry, the measurement of lung function, as well. As Braun describes in her book *Breathing Race Into Medicine*, the obsessive focus on finding a genetic reason why Black Americans might have lower lung function than white Americans distracts us from the more likely root causes and directs resources away from studying and working to solve them.[27] For example, she notes that lung function, over time, "has increased among Black Africans and decreased among African Americans," and there is clear evidence that the American disparity is due to environmental racism, historical trauma, and other social and environmental factors.[28] One reason among many for why the attempt to connect racial differences in health outcomes to genetics is improper science is that there is no evidence that genetic muta-

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tions are shared within people of the same race, or different across races. Race is far too imprecise a category to capture meaningful biological difference. For example, Black Americans in the United States in 2020 have an incredibly rich and complex genetic and ancestral makeup. And the genetic diversity in Africa is the greatest of any continent in the world.[29] The attempt to infer a meaningful biological distinction from a social and political one is misguided. Even in studies that attempt to make claims not about race, but instead about "ancestry," often do not ask their participants detailed questions about their families' migration patterns (though most of us would not know the answers anyway) — they simply ask participants to self-identify.

Braun puts it well in her book when she says, "Although useful in studying the effects of discrimination, self-report [of race or ancestry] is a sociopolitical act that does not represent a stable racial or ethnic 'essence.' However we try to fix them, racial and ethnic identities are fluid, changing continuously over time and place."[30] And also notes that reference values for racial groups are often based on U.S. Census categories, which have changed every decade since the Census started in 1790.[31]

What entity is the appropriate gatekeeper for dismantling the conflation and insisting on better, more well-designed research? One logical answer is that the IRB should stand in the way of these flawed studies. The next section will explore the avenues that IRBs might have to break the cycle, and propose a conceptual framework for reviewing race-based research.

II. IRB Review of Race-Based Research

The two types of protocols that are relevant to this discussion are: ones that use race as a study variable, and ones that recruit from only one racial group. An IRB has two potential mechanisms for scrutinizing and potentially rejecting or requesting modifications for protocols like these. The first involves risk, and the second involves study design.

Race-based research is risky because it perpetuates myths about race and biology, infects clinical care with biased assumptions, and causes harm down the line — either direct harm (as in the eGFR example where the race adjustment results in improper care) or indirect harm (as in the spirometry example where a hunt for genetic difference detracts from true root cause) — is risky and damaging. It is challenging to parse the scientific design issues from the risk issues. But suppose for a moment that we could separate them — that even properly designed research could still cause harm in these ways. Are IRBs permitted to consider this *type* of harm in their risk/benefit calculation? A straight reading of the federal regulation governing human subjects research might suggest that they are not. The regulation states: "The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility."[32] The "possible long-range effects of applying knowledge" that race-based research generates are: exacerbating racial health disparities and perpetuating racial myths based in slavery. These are both clearly risks of race-based research, perhaps of the kind that HHS explicitly singled out as not within the IRB's purview.

A qualitative study of IRB members, conducted in 2013, revealed a patchwork of IRB responses to this dictum (I am calling that sentence in the regulation dictum here, as it has been referred to elsewhere, primarily because it is not clear whether it is merely a suggestion or an outright prohibition). Overall, the author concluded that many IRB members are aware of the caution against taking long-range effects into account, but almost all of them do it anyway, to varying degrees.[33] To my knowledge, there has not been a case of an institution being chastised by the Office for Human Research Protections (OHRP) for inappropriately taking long-range effects into account. On the contrary, one of the issues upon which the lawsuit concerning the Arizona State University Havasupai research was based was that the IRB *failed* to consider the potential stigma and group harms that might result from the knowledge generated from the research, *not* as a consequence of the process of participation, but rather as a direct impact of the knowledge generated being revealed or applied in the world.[34] (The case concerned researchers at Arizona State University who obtained consent to collect genetic material from the Native American tribe the Havasupai, but subsequently published conclusions about the tribe that were stigmatizing and disruptive to them — the *content* of the knowledge generated was a primary focus of concern in the controversy).[35]

But we must end our thought experiment now and return to the reality, which is that flaws in scientific method cannot be separated out from these risks. The regulatory provision assumes that the knowledge is true, or, for that matter, that research always generates Truth. And it asks IRBs not to evaluate the risks of that Truth being applied to the world at hand. What was HHS contemplating when it wrote this dictum? The National Commission for the Protection of Human Subjects (the precursor to the regulations) debated this topic.[36] Some believed that, since IRBs were asked to consider potential long-range *benefits*

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of research, symmetry would suggest that they should also be able to take into account long-range harms. However, ultimately the Commission and the regulators rejected this argument on two accounts — the speculative nature of those long-range harms, and the potentially political nature of judgments about the normative value of those outcomes.[37] IRBs are not in a position to evaluate policy or social consequences. They are to take each protocol individually, evaluate the *process* risks to participants — the direct risks individuals are exposed to by participating in the research, such as side effects, psychological distress, or legal exposure — and use that to determine whether the research is ethical.

However, risk does not stand alone. IRBs are tasked with evaluating the risks *in relationship to* the benefits. And here, they must take into account what the investigators hope to achieve with the research. In the case of BiDil for example, the stated purpose of the AA-HeFT trial was to produce a drug that would work to treat heart failure in Black patients. Embedded within the stated benefit is the notion that a drug might work better in one population than in another because of some inherent biological difference between the two populations. Embedded within the stated benefit, in other words, is the notion that Black bodies are different than white bodies, and that we must develop drugs and clinical protocols tailored specifically to them. And with the investigators making no effort to determine *why* a drug might work better in one population than other, the default assumption is that it is an as-yet-unknown biological mechanism. An IRB need not weave hypothetical tales of the long-range effects of a potential discovery on humanity, it need only read the investigators' own words. The investigators state the potential benefit of the AA-HeFT trial as a drug developed specially for Black patients, but the IRB need not take this benefit at face value. It is free to view this in light of context and existing knowledge, in light of history and of current calls to abolish race in clinical care because it is risky, and it can, at its discretion, determine that in fact the stated benefit is just a risk in disguise.

For example, if an investigator approached an IRB with a protocol to study thinner helmets for football players and stated the potential benefit of the research as "discovering a more effective way for football players to tackle one another and cause more damage, resulting in more exciting game play," the IRB is free to construe this stated benefit as, instead, a risk, and it need not speculate as to the potential long-range consequences — the investigators have clearly stated them. The same is true here. While investigators might construe race-based "precision medicine" as a benefit of their research, IRBs can take the stated *purpose* of the research at face value but need not blindly accept the investigators' normative claims about the moral valence of that purpose.

Let's use another example. Some scholars fear that without the long-range effects provision, IRBs would become arms of social policy, and that they would be free to stop science in its tracks if they believed that it might lead to social policies they are against. For example, some worry about IRBs (as an arm of academic institutions) stopping Charles Murray-esque research that seeks to discover differences in IQ between races,[38] or worry about them stopping genetic research that seeks to discover a "gay gene." This research, they say, might reveal a Truth that is uncomfortable or that could be used to further certain groups' preferred social policy, but IRBs are not empowered to consider these potential impacts. However, we can imagine an investigator explicitly stating the purpose of their research as "discovering a gay gene in order to empower expecting pregnant people to abort fetuses that possess it so that we can rid the world of homosexuality." In a case such as this, wouldn't an IRB not just be permitted, but in fact obligated, to take the investigator's stated purpose at face value? And, must they view this stated purpose through the same normative lens as the investigator, or can they construe this instead as a risk, using the same ethical judgment they are empowered to use throughout their role as IRB members, and reject this protocol?

We may not need to reach the question of whether IRBs can construe these stated benefits as long-range risks. There is extensive ethics literature, including one of the most widely-cited clinical research ethics articles, arguing that scientific validity is a part of sound ethical analysis.[39] The argument is that an IRB is charged with balancing the risks of research against potential benefit, but benefit cannot accrue if the study is poorly designed. However, how to operationalize this scientific validity review is much more complicated. As Beier and Gelinas point out, first, IRB members are not always equipped with the methodological expertise to evaluate the validity of a protocol.[40] Tools would need to be developed to help guide an IRB in making a validity determination. Second, presumably investigators and funders are invested in the scientific validity of their research, such that they would not propose it if they did not believe in it. This puts IRBs in a difficult position of either taking the protocol and supporting materials at face value or bringing in experts or scholarship that contradicts the proposed methods. Whether or not an IRB has grounds to reject a protocol based on scientific validity depends entirely on how well the IRB members are equipped to comment

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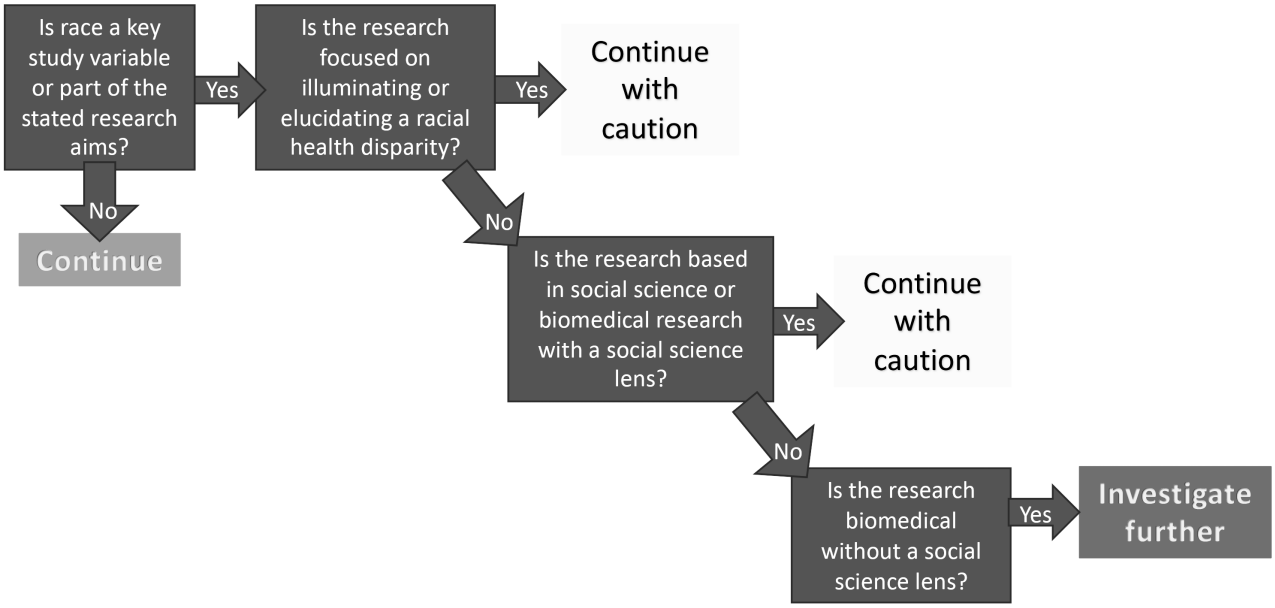
Figure 1
IRB decision flowchart for race-based research



on the methodological merit. For example: have they studied the flaws in race-based science? Does their institution have a policy regarding how to review protocols that involve race? Whether they are equipped can depend on their personal knowledge, as well as on their institutions' available resources and training. And, as to whether race can be used as a proxy for genetics, there remains controversy and difference of opinion even in the scientific community, putting IRB members that know better in a difficult position. Thus, if an IRB is going to reject a protocol based on scientific merit, it needs a firm conceptual model for reviewing such protocols, and a clear process for making its decision.

Figure 1 is an IRB decision flowchart for evaluating race-based research. In combination with IRB member education, this decision tree can help IRBs work with investigators to avoid the flawed assumptions of race-based research, and disambiguate research that does involve race, but does not make problematic conflations.

The first step is to ask whether the research uses race as a key study variable or a part of the stated research aims. IRB members should be sure to also check for words that investigators sometimes use as synonyms as a part of the ongoing issue of conflation: ancestry, ethnicity, geographic origin, and others. If none of these words appear as key study variables or part of the study aims, they can return to their usual review. If they do, the next question is whether the study aims to illuminate or elucidate racial health disparities. This is generally epidemiologic or social science research, that aims to show a disparity (for example: are Black people dying of COVID-19 more frequently than non-Black people?) or that aims to understand the reasons behind the disparity (for example: given that Black people are dying at a higher rate from COVID-19, what are the root causes of the disparity?) This research is valuable and should continue unabated — we must encourage first generation (do disparities exist) research, as well as second (why) and third (what can we do about it). However, the decision tree suggests IRBs should proceed with caution. Careful reading of the protocols will reveal whether investigators are aiming to uncover innate, immutable, biological reasons for the disparity, or whether they understand that root causes are much more likely to be sociobiological.

Not all research with race as its fulcrum involves discovering or elucidating health disparities. Which brings us to our next question — is the research based in social science, or, if it is biomedical, does it have a social science lens? For example, you could envision a study much like the one I described in the introduction, that is currently recruiting on ClinicalTrials.gov, but that has an explicit social science lens. Rather than aiming to describe the "distinct genomic variation characteristic of African-Americans," it instead aims

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to understand the distinct political and social forces that impact African Americans, to better understand the causal pathway to cardiovascular risk. Research like this would have social science cited in its protocol and might even include a social scientist as a part of its study team. Again, IRB members can proceed with this research, keeping a close eye on whether the investigators overemphasize the potential to discover genetic risk factors.

Finally, IRB members should ask whether the research is biomedical and *does not include* a social science lens, and be sure to investigate this research further, and potentially to request modifications that clear up the conflation or reject the protocol altogether. Research of this kind would include, for example, a study which starts with the premise that Black patients tend to have a different response to a certain drug, so, in order to find the right drug or dose *for Black patients*, investigators intend to study a population of self-identified Black patients, to find the drug that works best for them. This kind of research falls into two traps reminiscent of BiDil. First, it conflates self-identified race with a biological similarity that might impact drug metabolism. And second, it studies only one race, ensuring that if a good drug or dosage is determined, future researchers and clinicians will assume that it works in Black people only, or especially, because of some assumed but as yet unknown biological variable, and be unwilling to use the same mechanism on non-Black patients in the clinical setting.

For every decision in this flowchart, IRB staff and board members could be educated about the flawed studies that have come before and pay special attention to not replicating the shoddy science of the past. Readers will notice that nothing in this flowchart indicates that IRBs *must* reject certain protocols. It is intentionally only cautionary, because the world of research is vast and complex. But in each step, IRBs could be on the lookout for telltale signs that betray flawed assumptions. One need not be an expert methodologist or clinical trialist to recognize some of these flaws. For example, if a protocol claims to investigate ancestry, but recruits self-identified members of a racial group, we know that they have used a faulty proxy. If a protocol aims to discover a biomedical intervention that works better in one racial group than another, but does not include comparison groups, we know they will fail to produce evidence for their "better" claim. IRBs can be trained to spot these flaws.

III. Other Avenues for Policy Change

There are open questions with regard to an IRB's role in preventing this kind of research, and challenges to operationalizing that role. Therefore, we must consider other avenues. Research travels many places before it arrives at the desk of an IRB. It begins with investigators and their funders. All investigators who conduct race-based research should be educated in the history of the practice, and have a thorough understanding of its potential for negative impacts and worsening health disparities. It might be difficult to convince some scientists of the flaw in their logic with regard to conflating race and biology. But, it does not threaten academic freedom to help investigators situate their work within a broader social, historical, and political context. Researchers are generally altruistic and do their work in order to benefit people. Confronted with evidence that science that slips too easily between constructs like "race," "ancestry," "self-identified race," "Census-category," and does not clearly define the parameters of social variables, can lead to worsening health disparities, as in the case of the eGFR race correction, perhaps some scientists would reconsider their study designs or be compelled to con-

During the COVID-19 pandemic, we experienced not only a global recognition of health disparities, but it also coincided with a new fervor surrounding activism for Black life, including nationwide protests during the summer of 2020 following the murder of George Floyd by police in Minneapolis. What better time to dismantle our outdated notions of biological race, banish them from our clinics and our laboratories, from our medical school classrooms and our prestigious funding agencies, and replace them with our updated understanding of race as a political and social category, as an important step towards racial justice.

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sult with social scientists for help. A standard training must be developed, that each institution should have access to, just as we require human subjects researchers to take ethics training and learn about Tuskegee and Belmont, we should require that they learn the history of race-based medicine and its perils.

Funders, too, and in particular the NIH which funds a tremendous amount of race-based research, should develop guidelines for investigators and should incorporate social science expertise into its study sections. If investigators and funders learn more about the harmful practice of race-based medicine before they design their trials, IRBs might be spared involvement. Nonetheless, OHRP should clarify its stance on the "long-range effects" provision and clarify, generally, through guidance documents, its stance on the practice of race-based medicine and IRBs' role in reviewing it.

Fleishman and colleagues suggested that if IRBs are uncomfortable wading into questions about long-range effects, there should instead be a national advisory body that could consult with any IRB that had questions about a protocol's potential for post-study consequences.[41] That advisory board could be unwieldy if it is tasked with considering long-range effects of all kinds, from policy to clinical care to stigma to group harm, in a variety of domains. Instead, I recommend that the next Presidential administration create a special bioethics commission dedicated to making recommendations on race-based medicine and research. This would accomplish several goals. First, it would be responsive to Senator Warren and her colleagues' letter to AHRQ asking the agency to address clinical race-based algorithms. Second, if endowed with appropriate influence or enforcement power, the commission could be tasked with making specific recommendations to relevant federal agencies, including NIH, FDA, and OHRP. To NIH, it could recommend an evidence-based framework for peer review of research proposals that use race as a variable. This review could be built into the NIH's relevant study sections and could advise principal investigators on the appropriate use of race as a political and demographic variable or a proxy for exposure to racism, and on the inappropriate use of race as a biological variable. To OHRP, it could recommend guidance that clarifies 45 CFR 46 with regard to an IRB's scope of review as it relates to scientific merit concerns with race-based research, and as it relates to the interpretation of the dictum on long-range outcomes and its relationship to inaccurate clinical algorithms. And generally, this commission could provide, once and for all, a clear stance from the federal government that race should not be conflated with genetics, that we cannot tell a person's ancestry from looking at them, or even asking them, that race-based medicine is harmful and its precursor race-based research should be halted, that anyone using social variables as fulcrums of their study design should enlist a social scientist to better understand the meaning of the variable, and that in order to reverse structural racism we must banish the notion that the social category of race is a good proxy for anything other than one's exposure to racism.

IV. Conclusion

The time has come for us to take responsibility for the old house we live in. Pseudoscientific notions of biological race began centuries ago, and so far it has been easier to ignore their flaws and continue stepping over the rotten floorboards. But now, in 2020, there is a confluence of factors that compel us to stop normalizing the practice. First, evidence has long ago accumulated that demonstrates that there is more genetic variation within racial groups than between them. Second, genetic science has reached technological capacity and economic feasibility such that it is no longer efficient to use race as a proxy for genetics, when we could simply skip the proxy and test for the relevant mutation directly. Third, medical schools are more diverse than ever in terms of their inclusion of faculty from social science disciplines. Principal investigators at medical schools should have easier access to social scientists to help review or consult on protocols that involve *social variables* such as race and can help biomedical scientists refine their understanding of them. Fourth, we are experiencing a pandemic that disproportionately kills Black Americans.[42] All relevant research thus far has made very clear that the disparity is related to social and environmental factors, including epigenetic stress from experiencing racism, and not related to biological or genetic factors.[43] COVID-19 should be the best example of our lifetimes that we must focus on expanding second and third generation health disparities research, to determine root causes of inequities and develop interventions that tackle them. Investigating potential genetic differences between Black and white people to try to find a biological explanation for the differential COVID-19 impact is a fruitless and resource-intensive distraction, that clearly misses the obvious root causes. And finally, we are in a moment of racial reckoning in this country. During the COVID-19 pandemic, we experienced not only a global recognition of health disparities, but it also coincided with a new fervor surrounding activism for Black life, including nationwide protests during the summer of 2020 following the murder of George Floyd by police in Minneapolis.[44] What better time to dismantle our out-

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dated notions of biological race, banish them from our clinics and our laboratories, from our medical school classrooms and our prestigious funding agencies, and replace them with our updated understanding of race as a political and social category, as an important step towards racial justice.

Note

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