DNA RESEARCH FINDINGS AND PARTICIPANTS:

WHETHER TO SHARE

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ABSTRACT

During the first quarter-century of this millennium, biomedical research perspective shifted to multifaceted systems biology on the molecular level—to simultaneous analysis of thousands of molecules and the way they influence each other. In 2018, the National Institutes of Health (NIH) launched the All of Us Research Program ("All of Us") to build a biobank (the organized collection of individuals' DNA and accompanying information) of 1,000,000+ participants representative of diversity in the U.S. population with expansive information collection. To incentivize participation, All of Us offered to share DNA research information with participants, began sharing ancestry and trait results with participants in December 2020, and began sharing actionable health-related genetic results with them in December 2022. But then, on October 16, 2024, the program announced that it would cease return of research results ("RoRs") beginning the following month.

This Commentary addresses All of Us' decision to engage in RoRs with program participants and focuses on its experience doing so with health-related personal genome information between 2022 and 2024. Resulting complications and controversies are discussed in the context of an expansive, intense, and ongoing global RoRs debate that impacts research community norms, research participants, and responsible, evidentiary science-based PGM.

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INTRODUCTION

On May 6, 2018, the U.S. National Institutes of Health ("NIH") launched an ambitious enrollment initiative for its All of Us Research Program ("All of Us").[1] The All of Us mission is to build a biobank—the organized collection of DNA sequences and associated information—of 1,000,000+ participants representative of diversity in the U.S. population, and to encompass voluminous participant information:

> The goal is to find one million people in the United States, from all walks of life and all racial and ethnic groups, who are willing to have their genomes sequenced, and to provide their medical records and regular blood samples.
>
> They may choose to wear devices that continuously monitor physical activity, perhaps even devices not yet developed that will track heart rate and blood pressure. They will fill out surveys about what they eat and how much.
>
> If all goes well, experts say, the result will be a trove of health information like nothing the world has seen.[2]

All of Us incentivized (rewarded) participation with an offer to share biomarker information—to engage in return of research results ("RoRs")—over time.[3] On its official site, the program declared:[4]

> One of the goals of All of Us is to return information back to you if you want it. If you want to learn about your DNA and you give us a blood or saliva sample, we can give your DNA results to you. We would share the results—which are not a medical diagnosis—with you through your All of Us account. We will only show you the results you want to see.
>
> We plan to check your DNA for a variety of information. This information may include:
>
> - Your genetic ancestry (where your family might have lived hundreds of years ago)
> - Your genetic traits, such as why you might love or hate cilantro
> - Whether you may have a higher risk for certain health conditions
> - How your body might react to certain medications
>
> All of Us developed protocols for doing so responsibly, began sharing ancestry and trait results with its research participants in December 2020, and began RoRs for *actionable* health-related genetic information in December 2022.[5] The All of Us recruitment methodology proved

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[1] News Release, Nat'l Inst. of Health, NIH Announces National Enrollment Date for All of Us Research Program to Advance Precision Medicine (May 1, 2018), https://www.nih.gov/news-events/news-releases/nih-announces-national-enrollment-date-all-us-research-program-advance-precision-medicine [https://perma.cc/H6HX-PP9C]; *see also About*, NAT'L INST. OF HEALTH: ALL OF US RESEARCH PROGRAM (Oct. 16, 2025), https://allofus.nih.gov/article/about [https://perma.cc/2ZSK-TL4X] (providing background on the All of Us program).

[2] Gina Kolata, *The Struggle to Build a Massive 'Biobank' of Patient Data*, N.Y. TIMES (Mar. 20, 2018), www.nytimes.com/2018/03/19/health/nih-biobank-genes.html [https://perma.cc/TZ3A-F6RW].

[3] *See id.* (paraphrasing Dr. Francis Collins, then Director of NIH, the article explains, "For participants, there will be a reward…. The program will give them genetic information and health data, and tell them how they compare to others in the population.").

[4] *Genomics and Your DNA Results, What Can You Learn About Yourself?*, NAT'L INST. OF HEALTH: ALL OF US RESEARCH PROGRAM (last visited Oct. 25, 2024) (removed from site in Nov. 2024) (on file with author). For All of Us' current statement about sharing DNA results with participants, *see infra* note 11 and accompanying text.

[5] *See* News Release, Nat'l Inst. of Health, NIH's All of Us Research Program Returns Genetic Health-Related Results to Participants (Dec. 13, 2022) (byline: "Landmark precision medicine effort returns value to research participants by sharing tailored, actionable health-related reports"), https://www.nih.gov/news-events/news-releases/nih-s-all-us-research-program-returns-genetic-health-related-results-

bountiful—800,000+ official participants by November 2024.[6] Moreover, another 575,000+ individuals had completed the first step of the program by registering and responding to the initial survey questions.[7]

Nevertheless, on October 16, 2024, All of Us announced that it was disengaging from RoRs.[8] The program emailed participants that, effective November 22, 2024, genetic ancestry and trait DNA results would be deleted from their accounts and they would lose access to notes from genetic counseling sessions.[9] Participants would not be able to schedule appointments with genetic counselors after that date, they would have access to health-related results as PDFs on another system only if they logged on to view them before November 22, 2024, and these PDFs too would be deleted at the end of 2025.[10] All of Us modified its statement about sharing DNA research results with participants to simply express an intention to do so in the future in some manner: "Between 2020 and 2024, All of Us returned research DNA results to eligible participants. While we are no longer offering research DNA results, we are exploring other opportunities to return different types of results to participants."[11] Subsequently, All of Us modified the statement again to a decisive "All of Us is no longer returning research DNA results."[12]

The following discussion begins by addressing social, cultural, and commercial influences on NIH's decision to have All of Us engage in RoRs.[13] Next, the discussion profiles All of Us' experience engaging in RoRs for actionable health-related genetic information between 2022 and 2024, and the resulting complications and controversies that caused the program to suspend RoRs.[14] The discussion explains how All of Us engaged in *wholly predictable* RoRs error and caused controversy with the global consequences of shifting research community sentiment in favor of health-related RoRs to the detriment of research participant trust (All of US undermined its stated objective of building participant trust with RoRs), ongoing clinical care, health care systems, and the transition to responsible, evidentiary science-based personal genome medicine (PGM).[15]

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participants [https://perma.cc/4WQ7-KVEG]. For discussion of All of Us's protocol development for sharing, *see infra* notes 49–51 and accompanying text.

[6] NAT'L INST. HEALTH: ALL OF US RSCH. HUB, *Data Snapshots* (real time compilation; last visited Jan. 26, 2026), https://www.researchallofus.org/data-tools/datasnapshots/#:~:text=Note%3A%20There%20are%20many%20stages,All%20of%20Us%20Research%20Program [https://perma.cc/8X4G-PZ4X].

[7] *Id.*

[8] *See generally* Forest Ray, *All of Us Program to Delete Genetic Ancestry, Trait, Health Info From Participant Accounts*, GENOMEWEB (Oct. 16, 2024), https://www.genomeweb.com/research-funding/all-us-program-delete-genetic-ancestry-trait-health-info-participant-accounts [https://perma.cc/C6QF-KVS5].

[9] *Id.*

[10] *Id.*

[11] ALL OF US RSCH. PROGRAM, *DNA and Research* (last visited Jan. 27, 2025, subsequently modified, and on file with author); *see also* Forest Ray, *supra* note 8.

[12] ALL OF US RSCH. PROGRAM, *DNA and Research* (last visited Jan. 26, 2026), https://www.joinallofus.org/DNA-and-Research [https://perma.cc/7PK8-7EB4].

[13] *See infra* notes 16–44 and accompanying text ("Social, Cultural, and Commercial Influences on NIH's Decision to Share").

[14] *See infra* notes 45–71 and accompanying text ("All of Us RoRs: Trial, Controversy—and Error").

[15] *See infra* notes 72–102 and accompanying text ("*Predictable* Error: Guidance All of Us Chose Not to Follow"); notes 103–120 ("Global Consequences of NIH's Predictable RoRs Error"). *See also infra* notes 119–120 (addressing the All of Us participant trust hypocrisy). *See generally* MICHAEL J. MALINOWSKI, PERSONAL GENOME MEDICINE: THE LEGAL AND REGULATORY TRANSFORMATION OF U.S. MEDICINE (2023).

I. SOCIAL, CULTURAL, AND COMMERCIAL INFLUENCES ON NIH'S DECISION TO SHARE

When interviewed by the New York Times in December 2018 about the recruitment launch for All of Us, Dr. Francis Collins, then Director of NIH, declared, "For participants, there will be a *reward* . . . . The program will give them genetic information and health data, and tell them how they compare to others in the population."[16] In December 2022, in conjunction with publicly announcing that All of Us had begun returning health-related DNA results to more than 155,000 participants, NIH declared a program milestone: "delivering on its promise to share information and return value to participants."[17] NIH also self-acknowledged that, "'By returning health-related DNA information to participants, we are *changing the research paradigm*, turning it into a two-way street . . . . This type of partnership with our participants is crucial for building trust . . . .'"[18]

The All of Us's decision to share DNA research results with its participants was influenced by the daunting challenge of expeditiously recruiting an expansive, diverse target cohort of participants willing to share extensive personal health information, potentially including information collected through real-time monitoring.[19] All of Us sought to draw participants from a population of U.S. consumers heavily marketed for years about options to readily purchase genetic ancestry and health risk information from a DTC personal genome testing sector.[20] These companies made personal genome information easily accessible, allowing consumers to obtain detailed genetic insights and contribute to genomics research using a simple at-home kit.[21] Potential All of Us participants also had ample opportunity to access *clinical* genetic testing through their medical providers, potentially with health insurer coverage, given an abundance of laboratory-developed tests (LDTs) on the U.S. market.[22] The increased availability of personal genome testing reflects the advancement of next-generation DNA sequencing technologies (NGS), aided by a lax U.S. LDT regulatory environment and Supreme Court decisions in 2012 and 2013

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[16] Kolata, *supra* note 2 (emphasis added).

[17] *See* News Release, Nat'l Inst. of Health *supra* note 5.

[18] *Id.* (emphasis added).

[19] *See supra* notes 1–4 and accompanying text.

[20] By 2018, DTC personal genome testing companies had been selling access to ancestry information for over a decade, a commercial sector had emerged, and some DTC personal genome testing services cost under $100 during aggressively marketed holiday sales and consumer plus-one sales (a complementary companion service with each purchase). *See* MALINOWSKI, *supra* note 15, at 7, 167–72, 200–01 (n.182); *How Much Does Direct-to-Consumer Genetic Testing Cost, and is it Covered by Health Insurance?,* MEDLINEPLUS (June 21, 2022), https://medlineplus.gov/genetics/understanding/dtcgenetictesting/dtccost/ [https://perma.cc/ESW3-DHSV]. *See also* Carmel Shachar et al., *Introduction, in* CONSUMER GENETIC TECHNOLOGIES 1 (J. Glenn Cohen, Nita A. Farahany, Henry T. Greely, & Carmel Schachar eds., 2021), *citing* GRAND VIEW RESEARCH, PREDICTIVE GENETIC TESTING AND CONSUMER GENETICS MARKET SIZE, SHARE & TRENDS ANALYSIS REPORT BY TESTING (POPULATION SCREENING, SUSCEPTIBILITY), BY APPLICATION, BY SETTING TYPE, AND SEGMENT FORECASTS, 2019–2025 (2019) (projecting the global genetic testing and consumer wellness genomic market, valued at $2.24 billion in 2015, to double by 2025). Although DTC personal genome testing without a health care provider referral typically is paid for out-of-pocket and not covered by health insurers, "the tests may be eligible for reimbursement through flexible spending accounts (FSA) or health spending accounts (HSA) if the testing included health information." MEDLINE PLUS*, supra*.

[21] MALINOWSKI, *supra* note 15, at 319–23.

[22] The Pew Charitable Trusts issued a report in 2021 that assessed the U.S.'s buyer beware market for in vitro diagnostic LDTs (IVDs), which documented expansive availability and clinical uptake. *See generally* THE PEW CHARITABLE TRUSTS, THE ROLE OF LAB-DEVELOPED TESTS IN THE IN VITRO DIAGNOSTICS MARKET 4–7, 23 (Oct. 2021) (assessing the U.S. market availability and regulation of laboratory-performed IVDs run with blood and other bodily samples, including noninvasive prenatal tests/NIPTs), www.pewtrusts.org/-/media/assets/2021/10/understanding-the-role-of-lab-developed-tests-in-vitro-diagnostics.pdf [https://perma.cc/F5XR-LE5A].

that cleared a patent thicket around genetic testing.[23]

In recent years, millions of U.S. consumers purchased at-home DTC personal genome testing kits to engage in DNA self-discovery and as "it" gifts.[24] Consumer purchase options also included health risk testing.[25] U.S. public receptiveness to and demand for genetic health testing surged in 2013 when actress, filmmaker, human rights activist, and popular culture icon Angelina Jolie announced that she had undergone a preventative double mastectomy based on Myriad BRCA test results and family history, shared her personal story in an opinion-editorial published in *The New York Times*, and triggered "a cultural and medical earthquake"[26] that was coined "the Angelina effect."[27]

The U.S. FDA seemed to respond to this effect on April 6, 2017, when the agency approved an application submitted by 23andMe to market a portfolio of direct-to-consumer, genetic-health risk (DTCGHR) testing services for ten diseases, including Alzheimer's Disease and Parkinson's Disease, even though the company's genetic tests did not meet evidentiary-science clinical standards and medical professional involvement was wholly consumer optional.[28] In addition, the FDA established a regulatory express lane to market by recognizing a DTCGHR testing category.[29] Once sponsors satisfy requirements for the category, the FDA exempts new DTCGHR testing from regulatory review altogether, including its premarket notification (PMN) requirement, and clears

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[23] A proliferation of LDTs and other genetic testing in the U.S. was enabled by Supreme Court decisions that substantially undermined the patentability of genetic testing. In 2012, a unanimous Supreme Court held that claims directed to adjusting prescription drug (Rx) dosage based on the measurement of properties naturally produced by patients are not patentable subject matter. *See generally* Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 182 L. Ed. 2d 321 (2012). The following year, a unanimous Court invalidated Myriad's patents on human genes (BRCA1 and BRCA2 alleles), holding that patent protection does not extend to the isolation of natural forms of DNA. *See generally* Assoc. for Mol. Path. v. Myriad Genetics, Inc., 133 S. Ct. 2107, 569 US 12 (2013). Congress attempted but failed to enact legislation responsive to the proliferation of largely unregulated LDTs during its 2023-24 session. *See* Verifying Accurate Leading-edge IVCT Development Act (VALID Act), S. 2209, H.R. 4128, 118th Congress (2023–2024). The VALID Act failed even with strong support from Advanced Medical Technology Association (AdvaMed), the world's largest medical device association. *See Medical Device Industry Facts,* ADVAMED (last visited July 21, 2024), https://www.advamed.org/medical-device-industry-facts/ [https://perma.cc/2QM4-HKWD].

[24] *See* Maren Estrada, *DNA Tests are the Hottest Christmas Gifts of the Season, and There's Still Time to Get One on Sale*, BOY GENIUS REP. (Dec. 22, 2018, at 08:15 ET), https://bgr.com/2018/12/22/dna-test-deals-last-minute-christmas-sale/ [https://perma.cc/J6BC-X8G8] ("As was the case during last year's big holiday shopping season, DNA tests are among the hottest gifts of Christmas 2018."). For discussion of the evolution of U.S. DTC genetic testing services from those offered by Oncormed, Inc. in 1996 to 23andMe's personal genome health services, *see* MALINOWSKI, *supra* note 15, at 158–201.

[25] *See infra* notes 28–30 and accompanying text (FDA approval of DTCGHR testing).

[26] Jeffrey Kluger, *The Angelina Effect*, TIME (May 15, 2013), http://healthland.time.com/2013/05/15/the-angelina-effect-times-new-cover-image-revealed/ [https://perma.cc/C3CH-VEMY].

[27] *Id.*; *see* Angelina Jolie, *My Medical Choice*, N.Y. TIMES (May 14, 2013), www.nytimes.com/2013/05/14/opinion/my-medical-choice.html?module=inline [https://perma.cc/Q2PS-XXXE]. Subsequently, in a 2015 opinion-editorial also published by *The New York Times*, Ms. Jolie shared that she also underwent surgery to remove her ovaries and fallopian tubes, as well as a small, benign tumor, and more about her BRCA testing and decision-making experience. *See also* Angelina Jolie Pitt, *Diary of a Surgery*, N.Y. TIMES (Mar. 24, 2015), www.nytimes.com/2015/03/24/opinion/angelina-jolie-pitt-diary-of-a-surgery.html [https://perma.cc/K6JF-49XE].

[28] U.S. FOOD & DRUG ADMIN., DEN160026, EVALUATION OF AUTOMATIC CLASS III DESIGNATION FOR THE 23ANDME PERSONAL GENOME SERVICE (PGS) GENETIC HEALTH RISK TEST FOR HEREDITARY THROMBOPHILIA, ALPHA-1 ANTITRYSPIN DEFICIENCY, ALZHEIMER'S DISEASE, PARKINSON'S DISEASE, GAUCHER DISEASE TYPE 1, FACTOR XI DEFICIENCY, CELIAC DISEASE, G6PD DEFICIENCY, HEREDITARY HEMOCHROMATOSIS AND EARLY-ONSET PRIMARY DYSTONIA: DECISION SUMMARY (2017). *See also* MALINOWSKI, *supra* note 15, at 171.

[29] 21 C.F.R., § 866.5950(b) (2020) provides, in part:

> The genetic health risk assessment system device, when it has previously received a first-time FDA marketing authorization (e.g., 510(k) clearance) for the genetic health risk assessment system (a "one-time FDA reviewed genetic health risk assessment system"), is exempt from the premarket notification procedures in part 807, subpart E, of this chapter subject to the limitations in 866.9. The device must comply with the following special controls ….

them for market use.[30]

During the decade before All of Us launched its recruitment initiative in 2018, Ancestry, 23andMe, and other DTC personal genome testing companies began amassing biobanks with their consumers' DNA and associated information.[31] They made them fodder for revenue-generating licenses and research and development ("R&D") engagements by obtaining consumer consent for unspecified secondary research uses by unspecified users.[32] In 2017, the U.S. Department of Health and Human Services (HHS) condoned such broad consent in the final revisions to the Common Rule to protected human subjects—the first major update since the rule was officially recognized in 1991, and realized after more than two decades of exhaustive dialogue, debate, and deliberation during expansive, evolving, and escalating U.S. genomics R&D in real time.[33] Broad consent is consent for the storage and secondary research with identifiable (encrypted, but with a code to identify) biospecimens and accompanying private information.[34] "The final rule allows for the optional use of broad consent for storage and secondary research use of identifiable private information or identifiable biospecimens in lieu of obtaining study-specific informed consent."[35]

NIH's 2018 decision to share DNA research results with All of Us participants was consistent with the FDA's 2017 decision to allow commercial entities to do the same for a fee—market approval of DTCGHR testing not meeting evidentiary science-based clinical standards and with medical provider involvement wholly consumer optional.[36] Socially and culturally, the U.S. public wanted access to personal genome information (PGI)—as demonstrated by consumer demand for DTC personal genome testing services leading up to and after these decisions.[37] The

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[30] *See* MALINOWSKI, *supra* note 15, at 171, 329, 368, 378.

[31] *See id.* at 323–30.

[32] *See id*. *See also* Stuart Leavenworth, *Ancestry Wants Your Spit, Your DNA and Your Trust. Should You Give Them All Three?,* MCCLATCHY NEWSPAPERS (May 29, 2018), www.mcclatchydc.com/news/nation-world/article210692689.html#cardLink=row1_card1 [https://perma.cc/9R9P-ZS4E]; Terry Gross, *A Science Writer Explores the 'Perversions and Potential' of Genetic Tests*, NPR FRESH AIR (June 11, 2018, at 14:43 ET), www.npr.org/sections/health-shots/2018/06/11/618870881/a- science-writer-explores-the-perversions-and-potential-of-genetic-tests [https://perma.cc/W5LY-DER3].

[33] *See generally* U.S. DEP'T HEALTH & HUM. SERVS., *Revised Common Rule*, www.hhs.gov/ohrp/regulations-and-policy/regulations/finalized-revisions-common-rule/index.html [https://perma.cc/8YGA-EGM7]; *Common Rule Overview*, COUNCIL ON GOV. REL. (Feb. 1, 2017), www.cogr.edu/sites/default/files/Summary%20of%20Changes%20to%20the%20Common%20Rule_COGR.pdf [https://perma.cc/X32L-SPZ8]. *See also* Jerry Menikoff, Julie Kaneshiro & Ivor Pritchard, *The Common Rule, Updated*, 376 N. ENG. J. MED. 613, 613–14 (2017). Notably, debate about Common Rule reform surged and the entire field of gene therapy stalled in 1999 when research participant Jesse Gelsinger died during a clinical trial run by the University of Pennsylvania, which triggered national and international media coverage of conflicts of interest and other controversies. *See* WALTER ISAACSON, THE CODE BREAKER: JENNIFER DOUDNA AND THE RACE TO UNDERSTAND OUR GENETIC CODE 279 (2021); *see generally* Robin Fretwell Wilson, *The Death of Jesse Gelsinger: New Evidence of the Influence of Money and Prestige in Human Research*, 36 AM. J. L. & MED. 295, 295–96 (2010).

[34] *See Revised Common Rule Q&As, Broad Consent in the Revised Common Rule*, Office for Hum. Rsch. Protections (Feb. 25, 2019), https://www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/revised-common-rule-q-and-a/index.html [https://perma.cc/C7R9-DYVL].

[35] COUNCIL ON GOV. REL., *supra* note 33.

[36] *See supra* notes 28–30 and accompanying text (FDA approval of DTCGHR testing).

[37] North America, with a 60.46% revenue share in 2023, dominates the DTC personal genome testing global market; the global market was valued at $1.9 billion USD in 2023, and with a projected 24.4% compound annual growth rate for 2024–2030. GRAND VIEW RSCH., MARKET ANALYSIS REPORT: DIRECT-TO-CONSUMER GENETIC TESTING MARKET (2024–2030): SIZE, SHARE & TRENDS ANALYSIS REPORT BY TEST TYPE (NUTRIGENOMICS, CARRIER), BY TECHNOLOGY (WHOLE GENOME SEQUENCING), BY DISTRIBUTION CHANNEL, BY REGION, AND SEGMENT FORECASTS (2023). The DTC personal genome testing sector includes (identified in the report as "Key Direct-to-Consumer Genetic Testing Companies") 23andMe, Family Tree DNA, Ancestry, Genesis HealthCare, EasyDNA, Veritas, Myriad Genetics Inc., Full Genomes Corporation, Inc., Living DNA Ltd., and Color Health, Inc. *Id.* Interestingly, 23andMe, the seminal DTCGHR

FDA directly acknowledged as much when it made its DTCGHR market approval decision. In related communication with patients and physicians, the FDA stated, "Consumers are increasingly embracing direct-to-consumer genetic testing to better understand their ancestry or individual risk for developing diseases."[38] NIH's decision to share was also consistent with the 2017 revisions to the Common Rule (implemented on January 21, 2019), responsive to the research community's need and insatiable demand for access to DNA samples and accompanying information in an "omics" century with remarkable NGS capabilities that shifted the forefront of biomedical research to the molecular level.[39]

The All of Us decision to share also was pragmatic given the research project's mission and the scope of its participant recruitment challenge in competition with other public and private biobanking recruitment initiatives, and the broadening availability of clinical personal genome testing alternatives through medical providers with health care insurance reimbursement.[40] NIH decided that the program would share DNA research results with participants consistent with the All of Us mission "to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us"[41] and to raise participation appeal to the 1,000,000+ diverse U.S. residents it was competing to recruit.

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personal genome testing company, overextended to become a full bench-to-market biopharmaceutical company and a clinical care delivery company, did not develop a business plan to generate ongoing DTCGHR consumer demand commensurate with ongoing data compilation, and went bankrupt. *See supra* notes 28–30 and accompanying text; *see generally Wojcicki, TTAM Research Institute's $305M Offer Wins Bidding for 23andMe in Second Auction,* GENOMEWEB (June 13, 2025), https://www.genomeweb.com/business-news/wojcicki-ttam-research-institutes-305m-offer-wins-bidding-23andme-second-auction [https://perma.cc/W4YW-8QCD]; Ainsley Harris, *23andMe CEO Anne Wojcicki Wants to Take the Struggling Company Private—Then Comes the Real Work*, FAST CO. MAG. (Aug. 1, 2024), https://www.fastcompany.com/91150769/what-went-wrong-at-23andme [https://perma.cc/JJ7W-7TGQ]. The company's assets were auctioned and purchased by TTAM Research Institute—a not-for-profit medical research organization headed by Anne Wojcicki, 23andMe's cofounder and former CEO—for $305 million in June 2025. *Wojcicki, TTAM Research Institute's $305M Offer Wins Bidding for 23andMe in Second Auction,* GENOMEWEB (June 13, 2025), https://www.genomeweb.com/business-news/wojcicki-ttam-research-institutes-305m-offer-wins-bidding-23andme-second-auction [https://perma.cc/W4YW-8QCD].

[38] News Release, U.S. Food & Drug Admin., Jeffrey Shuren, M.D., J.D., Director of the FDA's Center for Devices and Radiological Health and Janet Woodcock, M.D., Director of the FDA's Center for Drug Evaluation and Research on Agency's Warning to Consumers About Genetic Tests that Claim to Predict Patients' Responses to Specific Medications (Nov. 1, 2018) (on file with PR Newswire), https://www.prnewswire.com/news-releases/jeffrey-shuren-md-jd-director-of-the-fdas-center-for-devices-and-radiological-health-and-janet-woodcock-md-director-of-the-fdas-center-for-drug-evaluation-and-research-on-agencys-warning-to-consumers-about-genetic-te-300742281.html [https://perma.cc/M64H-9SVT].

[39] *See supra notes* 33–35 and accompanying text (revision of the Common Rule). *See generally* Michael J. Malinowski, *Regulation to Reinforce the Evidentiary-Science Base of U.S. Medicine in the Age of "Omics"*, 28 SMU SCI. & TECH. L. REV. 485, 485-578 (2025). For comprehensive, timely discussion of omics, visit NHGRI, https://www.genome.gov/search?terms=Omics [https://perma.cc/C2RM-LUDB] (last visited Mar. 22, 2026), and especially, visit *Multi-Omics for Health and Disease*, NAT'L HUM. GENOME RSCH. INST., https://www.genome.gov/research-funding/Funded-Programs-Projects/Multi-Omics-for-Health-and-Disease [https://perma.cc/PZ5R-NA5Z] (last visited Mar. 22, 2026). Recognized omics fields, which are plentiful and propagating, include genomics (the study of genes in the context of the interactive community of whole genomes—an organism's complete set of genes and DNA instructions), proteomics (the study of proteins, which impact gene expression and cellular differentiation in the context of the complete set of proteins that is or can be expressed—a proteome—in a genome, cell, tissue, or organism at a given time under defined conditions), epigenomics (the study of environmental influences that modify the genome to change observable traits without changing the DNA sequence), transcriptomics (the study of a complete set of all the ribonucleic acid/RNA molecules—called transcripts—expressed in a cell, tissue, or organism), metabolomics (comprehensive measurement of all metabolites and low-molecular-weight molecules in a biological specimen), and lipidomics (the study of reaction pathways involved in lipid—an organic compound insoluble in water, such as fats and hormones—metabolism within biological systems). *See generally* Timothy D. Veenstra, *Omics in Systems Biology: Current Progress and Future Outlook*, PROTEOMICS, Feb. 2021, at 1, 1; Sagar Aryal, *Genomics vs. Proteomics: 10 Major Differences*, MICROBE NOTES (Aug. 3, 2023, https://microbenotes.com/difference-between-genomics-and-proteomics/ [https://perma.cc/25TG-KLDY].

[40] *See supra* notes 1–2 (scope of the All of Us recruitment initiative), 22–25 (competition with other biobanks and personal genome testing sector), 39 (broadening availability of clinical genetic testing) and accompanying text.

[41] *About*, ALL OF US RSCH. PROGRAM (Oct. 16, 2025), https://allofus.nih.gov/article/about#Mission [https://perma.cc/5CZ7-JPEZ].

The results of a study published in 2022 by forty-seven co-authors concluded that returning DNA research results motivates participation in the U.S., and distinguishably so amidst the populations of the twenty-two countries surveyed.[42] Among U.S. participants in the survey, 30.5 percent reported that they would be wholly influenced and another 22.8 percent reported that they would be partially influenced by the RoRs.[43] The study results correlate with All of Us' impressive recruitment success in competition with other participant recruitment initiatives, as recognized by the study's authors: "Studies in the United States, notably All of Us, have been at the forefront of making results available to participants, reflecting a commendable responsiveness of the research community to the expressed patient and public wishes to drive a shift in approach to RoRs over the last 2 decades."[44]

II. ALL OF US RORS: TRIAL, CONTROVERSY—AND ERROR

With support from the Centers for Medicare and Medicaid Services (CMS), FDA, and NIH, the National Academies of Sciences, Engineering, and Medicine (NASEM) compiled and published *Returning Individual Research Results to Participants: Guidance for a New Research Paradigm* in 2018—the same year NIH launched its All of Us participant recruitment initiative.[45] As relayed by Jeffrey R. Botkin, who chaired the NASEM committee that generated the report:

> A participant might ask, "If the findings are good enough to publish, why can't my results be shared with me?" This conflict in values is central to this report. In struggling with the complex and competing considerations, *we have attempted to achieve a new balance, one that leans toward communication of results while seeking to enhance the quality of results emerging from research laboratories.* Our push toward more disclosure, we believe, is part and parcel of *the larger cultural transition toward more engagement, collaboration, and transparency between investigators and research participants*.
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> * * *
>
> We are recommending a transition away from firm rules, such as those embodied in current interpretations of the Clinical Laboratory Improvement Amendments [(CLIA)] and the Health Insurance Portability and Accountability Act [(HIPAA)] regulations, that stipulate when results must or cannot be disclosed toward a process-based approach. In many circumstances, and on a study-by-study basis, *we recommend a peer-review process to assess the risks and benefits of results disclosure with careful attention to laboratory quality*. Establishing supporting processes will require motivation, resources, and time.[46]

The NASEM report provided a comprehensive framework and recommendations for ethically and effectively returning results in large-scale research studies. In alignment with the All

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[42] *See generally* Richard Milne et al., *Return of Genomic Results Does Not Motivate Intent to Participate in Research for All: Perspectives Across 22 Countries*, 24 GEN. IN MED. 1120 (2022). This survey of public perspectives on genomic data sharing was based on responses from 36,268 individuals across 22 low, middle, and high-income countries, gathered in 15 languages. Survey participants were asked whether the return of research results would motivate their decision to donate DNA or health data. *See id.* at 1120.

[43] *Id.* at 1122, 1125 tbl.3.

[44] *Id.* at 1124.

[45] COMMITTEE ON THE RETURN OF INDIVIDUAL-SPECIFIC RESEARCH RESULTS GENERATED IN RESEARCH LABORATORIES, RETURNING INDIVIDUAL RESEARCH RESULTS TO PARTICIPANTS: GUIDANCE FOR A NEW RESEARCH PARADIGM (Jeffrey R. Bodkin, Michelle Mancher, Emily R. Busta & Autumn S. Downey eds., 2018).

[46] *Id.* at ix–x (emphasis added).

of Us approach to participant engagement and data sharing, the report:

- presented a structured approach to decide when and how to return individual research results with consideration of fundamental, established clinical genetics criteria, including clinical validity (reliable test and testing accuracy), clinical utility (potential benefits to participants), and the feasibility of returning DNA research results;
- emphasized the importance of ensuring participants fully understand the implications of their results;
- acknowledged and addressed regulatory complexities for a wide range of data types, notably under diagnostic clinical laboratory regulations (CLIA) and national medical privacy regulations (HIPAA); and
- advocated for increased transparency in research through RoRs.[47]

All of Us worked to implement the NASEM report from its participant recruitment launch in May 2018 to returning DNA research results for ancestry and traits beginning in December 2020, and to returning actionable health-related research results beginning in December 2022.[48] "Changing the research paradigm, turning it into a two-way street" [49] required developing protocols, policies, and procedures for sharing DNA research results, which proved to be more challenging, multilayered, resource-consuming, expensive, and time-consuming than All of Us estimated at the outset. As summarized by Anastasia Wise, Director of Scientific Return to Participants for the All of Us Research Program:

> Returning health-related genetic results to participants was a significant undertaking. It included working with the program's institutional review board [(IRB)] on protocols for returning results, seeking guidance from community partners to ensure information is shared in a way that's easy to understand and returned with an eye toward diversity and inclusivity, and obtaining an investigational device exemption (IDE) from the US Food and Drug Administration. All of Us received the long-awaited IDE from the FDA in 2020; at the time, All of Us officials had estimated the program would start returning health-related genetic results in late 2021.[50]

Logistically,

> The program's Data and Research Center, Participant Technology Systems Center, and Genetic Counseling Resource worked closely with the program and other partners to develop the process for returning health-related genetic results. The program's Biobank and Genome Centers collaborated to generate the genomic data that informs the personalized results.[51]

Notably, in August 2019, NIH awarded $4.6 million in initial funding to Color Health, Inc., a California-based company, to serve as the genetic counseling resource for All of Us and to provide the digital infrastructure for returning results.[52]

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[47] *See generally id.* at 22, 28, 175, 213.
[48] *See supra* note 5 and accompanying text.
[49] News Release, Nat'l Inst. of Health*, supra* note 5.
[50] Jessica Kim Cohen, *NIH All of Us Program Returns First Health-Related Genetic Results to Participants*, GENOMEWEB (Dec. 13, 2022), www.genomeweb.com/sequencing/nih-all-us-program-returns-first-health-related-genetic-results-participants#.YJjs6XbMK3A [https://perma.cc/MH6C-FH79].
[51] News Release, Nat'l Inst. of Health, *supra* note 5.
[52] *See generally* News Release, Nat'l Inst. of Health, NIH Funds Genetic Counseling Resource Ahead of Million-Person Sequencing Effort (Aug. 21, 2019), https://www.nih.gov/news-events/news-releases/nih-funds-genetic-counseling-resource-ahead-million-person-

Even with NASEM's guidance and a commendable All of Us planning and implementation effort, returning DNA research results proved direly problematic. Although the exploration of RoRs by NASEM and others prior to All of Us engaging in it was substantial, the program's RoRs raised foreseeable issues its architects claimed were "less thoroughly investigated in vulnerable individuals and populations."[53] Specifically, "issues and challenges associated with the return of individual research results (such as genomic, proteomic, or other biomarker data) to potentially vulnerable individuals and populations, including those who may be vulnerable for cognitive, communicative, institutional, social, deferential, medical, economic, or social reasons."[54] However, months before All of Us began RoRs for actionable health-related genetic results (December 2022), the *American Journal of Pathology* published an article (September 2022) that cited and discussed on-point, well-established (some dating back more than a decade), evidence-based, peer-reviewed studies that recognized, for example:

> Many individuals who identify as Native American may belong to groups that are not formally recognized by the US government. However, Respect for Persons requires researchers to be sensitive to concerns of groups that lack such recognition. In addition, nearly 30% of individuals identified as American Indian or Alaska Native are impoverished. Both poverty and geographic isolation limit access of these individuals to resources that inform interpretation of [individual research results (IRRs)], thus limiting their ability to benefit from IRRs. This imposes responsibility for researchers to ensure that a decision to return results does not disadvantage members of indigenous participants by comparison with others.[55]

NASEM's report and guidance understandably elevated All of Us' confidence about engaging in RoRs over time. Nevertheless, NIH launched the program *to biobank diversity in the U.S. population* with RoRs well aware that it was stepping onto the forefront of a volatile, decades-long debate over whether, what, and how "incidental" DNA research results (also commonly referred to as "secondary findings") should be shared with research participants.[56] The debate and RoRs endeavors prior to All of Us had generated much thoughtful, careful consideration of implications for individuals and groups they self-identify with—including access, equity, and inclusion disparities in the U.S.'s largely privatized and fragmented health care system.[57]

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sequencing-effort [https://perma.cc/JP33-H3LN].

[53] Christi L. Kolarcik, Marianna J. Bledsoe & Timothy J. O'Leary, *Returning Individual Research Results to Vulnerable Individuals*, 192 AM. J. OF PATHOLOGY 1218, 1218 (2022). For a thoughtful discussion of whether medically underserved individuals would receive any benefit from participating in All of Us when they have little prospect of any clinical benefit, see generally Mark A. Rothstein, *Do Medically Underserved Individuals Benefit from Participating in All of Us?*, 24(3) AM. J. BIOETHICS 94, 94–96 (2024).

[54] Kolarcik, Bledsoe, O'Leary, *Returning*, *supra* note 53, at 1218.

[55] *Id.* at 1225 (internal citation omitted). Although the authors proposed that *more* research is needed to address the impact of RoRs on potentially vulnerable individuals and populations, they based their argument on supportive, on-point, published research dating back more than a decade. *See id.*

[56] *See generally* Danya F. Vears et al., *Return of Individual Research Results from Genomic Research: A Systematic Review of Stakeholder Perspectives*, PLOS ONE, Nov. 8, 2021, at 1, 3.

[57] *See generally* Kolarcik, Bledsoe & O'Leary, *supra* note 53; Meredith Wadman, *Controversy Flares Over Informing Research Subjects About 'Incidental' Genetic Findings,* 373 SCIENCE 610 (2021). *See also* Keolu Fox, *The Illusion of Inclusion — The "All of Us" Research Program and Indigenous Peoples' DNA*, 383 NEW ENG. J. MED. 411 (2020). For discussion of distinguishing complex features of the U.S. health care system in comparison with the health care systems of other developed-economy countries, *see generally* EZEKIEL J. EMANUEL, WHICH COUNTRY HAS THE WORLD'S BEST HEALTH CARE? 19 (2020). *See also* MALINOWSKI, *supra* note 15, at 251–56, 386–87. Most fundamental and troubling, disparate access to health care, even to meet basic health care needs, distinguishes the U.S. health care system and it has for some time. In a 2024 report based on comparative analysis of the healthcare systems in ten industrialized-economy countries, the Commonwealth Fund concluded: "The U.S. continues to be in a class by itself in the underperformance of its health care sector. While

Notably, the American College of Medical Genetics and Genomics (ACMG) had tested the environment for receptiveness to RoRs in 2013 when it published a list of fifty-seven genes (genes for pathogenic mutations that could indicate the presence of any of twenty-four disorders for which early intervention is likely to reduce or prevent serious morbidity and/or early mortality) it recommended should be tested in all patients undergoing any genetic screening in a clinical setting.[58] When the recommendation stirred a pushback hurricane, including advocacy for recognition of a "right not to know (RNTK)" with much support, ACMG adopted the position that patients should be allowed to opt out of receiving such findings during the informed consent process prior to the primary genetic testing.[59] ACMG provided further guidance in 2015, which included:

> Because of the increased complexity of analysis and interpretation of clinical genetic testing described in this report, the ACMG strongly recommends that clinical molecular genetic testing should be performed in a CLIA-approved laboratory [, meaning a laboratory certified to perform *clinical diagnostic testing*,] with results interpreted by a board-certified clinical molecular geneticist or molecular genetic pathologist or equivalent.[60]

A cohort of NIH researchers inflamed the RNTK debate in July 2021, some sixteen months before All of US began health-related RoRs (December 2022), when they published online the results of a study to survey research participants who had actively decided whether to accept or refuse such information.[61] According to the authors, nearly half of the initial refusers changed their minds when presented with new information, Black participants initially rejected receipt of secondary findings at twice the rate of White participants, and Black participants were less likely to change their minds after being reapproached.[62] Based on their overall study findings, the authors recommended departing from voluntary, informed consent—"the central tenet of researcher obligations to people who participate in research."[63] Rather than research participants expressly, voluntarily opting to receive secondary research findings once fully informed with sufficient assurance of comprehension and understanding, the authors recommended an *opt-out system* in which researchers notify participants that they *will receive secondary findings* and only withhold them when participants actively refuse.[64] As stated by the authors,

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the other nine countries differ in the details of their systems and in their performance on domains, unlike the U.S., they all have found a way to meet their residents' most basic health care needs, including universal coverage." DAVID BLUMENTHAL ET AL., COMMONWEALTH FUND, MIRROR, MIRROR 2024: A PORTRAIT OF THE FAILING U.S. HEALTHCARE SYSTEM 3 (2024) (comparing the health systems of Australia, Canada, France, Germany, the Netherlands, New Zealand, Sweden, Switzerland, the United Kingdom, and the United States).

[58] *See generally* Robert C. Green et al., *ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing*, 15 GENETICS IN MED. 565, 566 (2013).

[59] *See generally* American College of Medical Genetics and Genomics*, Incidental Findings in Clinical Genomics: A Clarification,* 15 GENETICS IN MED. 664, 664 (2013). *See also* Will Schupmann et al., *Exploring the Motivations of Research Participants Who Chose Not to Learn Medically Actionable Secondary Genetic Findings About Themselves*, 23 GENETICS IN MED. 2281, 2281 (2021).

[60] Sue Richards et al., *Standards and Guidelines for the Interpretation of Sequence Variants: A Joint Consensus Recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology*, 17 GENETICS IN MED. 405, 405 (2015).

[61] *See generally* Schupmann et al., *supra note* 59, at 2282; Wadman, *supra* note 57, at 610.

[62] *See* Schupmann et al., *supra* note 59, at 2282–84.

[63] MALINOWSKI, *supra* note 15, at 323. *See* Schupmann et al., *supra* note 59, at 2286.. For explanatory discussion in the context of DTC personal genome testing with supportive authority, *see* MALINOWSKI, *supra* note 15, at 324–30.

[64] *See* Schupmann et al., *supra* note 59, at 2286.

> We argue that our data support a default practice of attempting to return [secondary findings (SFs)] without soliciting the preferences of research participants, while also providing a clearly defined (though implicit) opt-out mechanism for people that independently raise concerns about the [right not to know (RNTK) genetic information about oneself].[65]

After this participant survey to study motivations was closed (January 2020) but before the results were published (July 2021), All of US opened a survey to *its participants* (November 2020 to March 2021) for a study intended "[t]o understand participant preferences for receiving specific types of research information, whether information preferences vary across sociodemographic groups, and the types of health providers participants could access to understand returned information."[66] The published results revealed that:

> Although genetic information was most valuable to participants, preferences about specific information types varied across sociodemographic groups. Researchers should not assume that participant preferences for receiving research results are uniform within diverse study populations. *Future work is needed* to ensure that all research participants receive results they find valuable and understandable, and to identify other information of value that research participants want to receive in addition to genetic health information.[67]

On February 19, 2024, while the authors of the All of Us participant perspectives study were assessing and preparing their findings and conclusions for publication, All of Us published comprehensive genomic sequencing results from 245,388 clinical-grade genome sequences in *Nature*.[68] This triggered another wave of stinging backlash by again ignoring something well established in the science literature:

> The publication faced public criticism almost instantaneously. At the heart of the matter is how the study presented the diversity of race and ethnicity in their dataset. It gets a little technical, but it focuses on the fact that the researchers used a type of graph called uniform manifold approximation and projection. UMAP reduces the complexity of a given dataset to something that can be plotted in a classic 2D graph. So UMAP is almost designed to find and exaggerate differences, creating new patterns that might not exist in the original data. *In other words, the graph reinforces the misconception that races and ethnicity follow neatly distinct genetic components*.
>
> This misconception is often misused and exaggerated by people looking to validate racist or xenophobic views on the basis of "science." Now, the discussion about UMAP has become much louder than the findings of the study, which discovered over 3,000 previously unknown mutations concerning 117 diseases.
>
> There are sound scientific arguments both against and for using UMAP in this study, but the decision points to a much broader issue at hand: an inability of scientists to grasp the societal impacts of their research — often to the detriment of the people they attempt to help. [69]

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[65] *Id.*

[66] Jennifer Richmond, et al., *All of Us Participant Perspectives on the Return of Value in Research*, 26(8) GENET. IN MED. 101163, 101164 (2024).

[67] *Id*. at 101171–72 (emphasis added).

[68] *See* The All of Us Research Program Genomics Investigators, *Genomic Data in the All of Us Research Program,* 627 NATURE 340, 340–346 (2024).

[69] Thiago Arzua, *First Opinion, Lessons for Scientists from the All of Us Research Program Backlash*, STAT NEWS (Mar. 15, 2024) https://www.statnews.com/2024/03/15/all-of-us-genomic-sequencing-results-umap-science-history-sociology/.[https://perma.cc/D9F5-

On October 16, 2024, All of Us notified participants that it was suspending RoRs.[70] Although $184 million had been cut from the program's FY24 budget (a 34% decrease from its FY23 budget), according to Anastasia Wise, Director of Scientific Return to Participants, "[T]he decision [to stop RoRs] was not motivated by the budget reduction . . . 'It is aimed at improving the way we return DNA results to participants' . . . ."[71]

III. *PREDICTABLE* ERROR: GUIDANCE ALL OF US CHOSE NOT TO FOLLOW

Whether, what, and how genetic information derived from personal genome testing should be shared has been debated with fervor across disciplines since the 1990s—formatively so as work progressed on the Human Genome Project (HGP).[72] Over the last quarter-century, DNA sequencing technologies have evolved remarkably and have become familiar to the public.[73] Nevertheless, the core standards for responsible, evidentiary science-based clinical diagnostic practice—notably clinical validity, clinical utility, positive predictive value (PPV), and negative predictive value (NPV)—have remained fundamentally constant.[74]

The remarkable progress of NGS, including astonishingly affordable whole genome sequencing capabilities in this "omics" century, have elevated the our understanding of human genetics to breathtaking heights in a brief period of time, but has not simplified them.[75] Environmental influences on human health remain dizzyingly complex, and common diseases remain as genetically complicated.[76] Though we can now generate enormous amounts of personal genome information cost-effectively, the clinical challenges of delivering that information to individuals clearly, ethically, and effectively remain unsolved—as All of Us demonstrated through its RoRs debacle.[77]

52YA]. *See generally* Max Kozlov, *News, 'All of Us' Genetics Chart Stirs Unease over Controversial Depiction of Race*, NATURE (Feb. 23, 2024) (byline: "Debate over figure connecting genes, race and ethnicity reignites concerns among geneticists about how to represent human diversity"), https://www.nature.com/articles/d41586-024-00568-w [https://perma.cc/K8H2-E282].

[70] *See supra* note 8 and accompanying text.

[71] *See* Ray, *supra* note 8; According to NIH, the FY24 budget decrease "necessitated funding cuts for All of Us at NIH and our partner organizations, decreasing our enrollment capabilities, slowing new data collection, and delaying our ability to build a robust pediatric cohort." *All of Us Research Program Overview, How is All of Us Funded?,* NIH (last reviewed Nov. 22, 2024), https://allofus.nih.gov/about/program-overview [https://perma.cc/U68U-2KX3]. All of Us funding is dependent on Cures Act funding, which was decreased by $199 million in FY25 and resulted in a 71% decrease in All of Us funding from FY23—prior to commencement of the Trump Administration, its establishment of the Department of Government Efficiency (DOGE), and DOGE's substantial federal government budget cuts and firings. *See generally* Suzanne Blake, *List of What DOGE Aims to Cut From U.S. Government So Far*, NEWSWEEK (Feb. 6, 2025) https://www.newsweek.com/doge-elon-musk-cuts-list-donald-trump-meaning-2027436 [https://perma.cc/CHT3-L729].

[72] *See infra* notes 84–88 and accompanying text (discussing SACGT's report and recommendations published in 2000).

[73] *See supra* notes 24–27 and accompanying text (popularity of ancestry testing at the outset of this millennium and the Angelina effect). *See generally* Vears, et al., *Stakeholder Perspectives*, *supra* note 56, at 2/71.

[74] *See generally* SACGT, ENHANCING THE OVERSIGHT OF GENETIC TESTS: RECOMMENDATIONS OF THE SACGT (July 2000) (addressing the clinical complexities of human genetics and identifying and applying established clinical standards for diagnostic testing), https://osp.od.nih.gov/ sagct_document_archi/enhancing-the-oversight-of-genetic-tests-recommendations-of-the-sacgt.

[75] Soon after a draft map of the human genome sequence was completed in 2003, the research community realized that 20,000 or fewer active genes account for human health diversity, which jolted research community perspective about the extent to which genes multitask and, with NGS, evolved genomics into an omics portfolio of recognized scientific disciplines. *See* MALINOWSKI, *supra* note 15, at 2-3, 95; *supra* note 33 (discussing omics).

[76] *See generally* Arzua, *supra* note 69*; see* MALINOWSKI, *supra* note 15, at 303–17 (discussing the clinical complexities of genetic testing).

[77] *See supra* notes 53–71 and accompanying text.

Responsiveness to current popular sentiment in support of individual access to personal genome information is evident in the FDA's decision to grant market approval to DTCGHR testing (2017),[78] NASEM's report on and guidance for RoRs (2018),[79] All of Us' engagement in RoRs,[80] and the global biomedical research community's present receptiveness to RoRs.[81] Popular opinion was very different in the 1990s. In 1996, U.S. federal and state government initiatives, legislative and regulatory, encompassing a deluge of stakeholder input with multidisciplinary perspectives, were triggered when three small biotech companies introduced DTC BRCA1 ("breast cancer 1 alleles") and BRCA2 ("breast cancer 2 alleles") predictive genetic testing to the U.S. market to identify heightened susceptibility to breast and ovarian cancers.[82] These companies' DTC personal genome tests were culled from limited general population data, and the companies had not submitted them to the FDA for review and approval. They declared that they did not have to.[83]

By 1999, forty-four states had enacted responsive genetics legislation.[84] Representative of what transpired in dozens of states, I served (1995-97) on a Special Committee on Genetic Information Policy—a legislative task force assembled by the Commonwealth of Massachusetts. We were inundated with input from diverse public and private stakeholders for two years and hosted forums for public commentary that drew at-capacity attendance and overwhelming requests to testify. Nationally, the Ethical, Legal, and Social Implications Program (ELSI) of HGP established a Joint Committee (between NIH and the Department of Energy, both sponsors of HGP) to assess U.S. regulation of genetic testing, the Clinton Administration established a Task Force on Genetic Testing, and the efforts of these working groups culminated in HHS establishing a Secretary's Advisory Committee on Genetic Testing (SACGT) charged "to assess, in consultation with the public, the adequacy of current oversight of genetic tests and, if warranted, to recommend options for additional oversight."[85]

SACGT undertook its own exhaustive investigation involving solicitation of multidisciplinary input from a broad portfolio of experts and public and private stakeholders, gathered substantial commentary, engaged in multiple phases of deliberation with transparency, and issued a report with thoughtful, well-substantiated recommendations based upon long-established clinical standards—positive predictive value (PPV), negative predictive value (NPV), clinical validity, and clinical utility—applied to the complexities of genetic testing in human

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[78] *See supra* notes 28–30, 36–38 and accompanying text.
[79] *See supra* notes 45–47 and accompanying text.
[80] *See supra* notes 3–4, 16–27 and accompanying text.
[81] *See generally* Vears, et al., *Stakeholder Perspectives*, *supra* note 56.
[82] *See* Michael J. Malinowski, Robin J.R. Blatt, *Commercialization of Genetic Testing Services: The FDA, Market Forces, and Biological Tarot Cards*, 71 TUL. L. REV. 1211, 1214–15 (1997); Staff, *OncorMed BRCA1 Testing Service Commercialization Enters Second Phase Through New IRB Protocol*, 39 BLUE SHEET 6, 6–7 (1996). *See also* MALINOWSKI, *supra* note 15, at 160-66 ("Era of FDA Restraint").
[83] *See* Malinowski, Blatt, *supra* note 82, at 1214–15; *New IRB Protocol*, *supra* note 80, at 6–7. *See generally* William F. Mulholland, II, Ami S. Jaeger, *Genetic Privacy and Discrimination: A Survey of State Legislation*, 39 JURIMETRICS J. 317-318 (1999). *See* Michael J. Malinowski, *Separating Predictive Genetic Testing from Snake Oil: Regulation, Liabilities, and Lost Opportunities*, 41 JURIMETRICS J. 21 (2001) (symposium).
[84] *See generally* Mulholland, Jaeger, *State Legislation, supra* note 83, at 318. *See also* Malinowski, *Snake Oil*, *supra* note 83, at 21.
[85] SACGT, ENHANCING THE OVERSIGHT, *supra* note 74, at 1. *See* MALINOWSKI, *supra* note 15, at 299–364 (chapter 6, which addresses the complexities of PGM decision making).

health.[86] SACGT addressed the clinical challenges of delivering genetic test results to individuals in a manner that achieves meaningful comprehension with sufficient understanding (communication) and contains identified risks of harm, recognized associated risks to biological family members and groups individuals self-identify with, and pragmatically identified work needed to be done in real time to introduce reliable regulatory oversight of medical genetic testing available on the US market.[87] SACGT's report and recommendations were released in July 2000, the U.S. presidency transitioned from the Clinton Administration to the George W. Bush Administration after a heavily contested election, and SACGT's recommendations were not meaningfully implemented; rather, they were essentially delegated to regulatory purgatory.[88]

Long-established evidentiary-science *clinical* standards and the insightful, bountiful work done by SACGT and others applying those standards with multidisciplinary *clinical* experience in the context of genetic testing, much documented in the published literature, made the RoRs complexities, complications, and controversies experienced by All of Us predictable.[89] The Global Alliance for Genomics and Health ("GA4GH"), formed in 2013, addressed a bountiful portfolio of these complexities, complications, and controversies with much deliberation, generated templates to streamline gaining consent for clinical genomics and large-scale initiatives, and completed its Regulatory and Ethics Work Stream (REWS) Consent Toolkit on August 11, 2022.[90]

The GA4GH Policy on Clinically Actionable Genomic Research Results, finalized in 2023 after approximately a two-year approval process preceded by a longer drafting process—both contentious (innumerable hours of debate and revision) and encompassing deliberation of an abundance of comments from GA4GH members and the public—emphasizes that local clinical standards should govern the process (be deferred to) when returning genomic findings to research participants.[91] The policy identifies minimal international standards that all research projects that sequence individuals' DNA should follow, with consensus on six points that new research programs should consider when establishing their RoRs policies:

> 1. Prepare a clear, concise protocol for returning results at the start of their project, which will require advanced planning and accountability.
>
> 2. Establish funding and personnel resources prior to the start of the project to ensure dependability and reliability.
>
> 3. Develop [RoRs] policies with local clinical standards in mind.

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[86] *See generally* SACGT, ENHANCING THE OVERSIGHT, *supra* note 74.

[87] *See generally id*.

[88] President George W. Bush took office on January 20, 2001, after defeating Vice President Al Gore in a nationally debated and legally contested election (Gore had won the popular vote), which ended with a controversial Supreme Court ruling that settled a recount dispute over "hanging chads" (partially punched holes in paper ballots) in Florida. *See generally Bush v. Gore*, 531 US 98 (2000).

[89] *See supra* notes 84–87.

[90] *See* GA4GH, News Release, New Templates Streamline Gaining Consent for Clinical Genomics and Large-scale Initiatives — Completing the GA4GH Consent Toolkit (Aug. 11, 2022), https://www.ga4gh.org/news_item/new-templates-streamline-gaining-consent-for-clinical-genomics-and-large-scale-initiatives-completing-the-ga4gh-consent-toolkit/.

[91] *See generally* GA4GH, *Policy on Clinically Actionable Genomic Research Results* (2023), https://www.ga4gh.org/product/policy-on-clinically-actionable-genomic-research-results/; GA4GH, News Release, An international framework for returning clinically actionable genomic results to research participants (Feb. 11, 2022), https://www.ga4gh.org/news_item/an-international-framework-for-returning-clinically-actionable-genomic-results-to-research-participants/.

> 4. Establish unity between researchers and participants by engaging the community in the development of a return of results policy (the authors recommend study designers look to the GA4GH Engagement Framework for guidance).
>
> 5. Make their tools, protocols, and resources accessible to other study designers in order to reduce barriers to responsibly returning research results to participants.
>
> 6. Call on funders to support the responsible return of genomic results, as these entities have a unique opportunity to effect change across the community.[92]

All of Us, though an Organisational Member of GA4GH, meaning a signatory to its vision and mission, apparently chose to ignore much of this pragmatic guidance and the caution it embodies when it began to return actionable health-related research results in December 2022.[93]

The All of Us architects responsible for its RoRs decision making were also more influenced by current popular culture opinion favoring RoRs and much responsive research community sentiment than dissuaded by analogous program experiences.[94] For example, deCODE genetics, a Reykjavík, Iceland-based biopharma company founded in 1996 to engage in population genetics, proposed reaching into its biobank (more than two-thirds of the adult population of Iceland was participating in the company's research efforts as of 2019) to identify carriers of the BRCA2 gene in some 60,000 Icelanders whose DNA had been fully sequenced.[95] Before and in sync with All of Us' participant recruitment initiative (launched in 2018), Icelandic regulators repeatedly refused to let the company de-encrypt the participant data to identify and notify them.[96] The regulators determined that, although these individuals contributed their DNA and, in many instances, medical records to advance biomedical science and enable medical breakthroughs, they did not explicitly consent to be notified of personal health risks identified by researchers, and the regulators concluded that neither the government nor private industry may notify people of these risks.[97] When interviewed in 2018 about this deCode experience, Stephanie Devaney, a geneticist and deputy director of All of Us, assured that "NIH is taking several steps to avoid the kind of dilemma Iceland is facing."[98]

Even more on point with All of Us, the UK Biobank, which contains de-identified genetic, lifestyle and health information and biological samples from half a million UK participants,[99]

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[92] *See generally* GA4GH, *News, international framework*, *supra* note 91. REWS developed this policy to bridge the gap between research and clinical care, while supporting the human right to benefit from scientific advancement. *See id*. The policy emphasizes that actionable results—those with immediate medical utility—should be returned, but the specific, actionable thresholds and procedures should be guided by local regulations and standards, ensuring, for example, proper validation of findings before return. *See id.*

[93] *See* GA4GH, *Our Community, Organisational Members* (visited Jan. 28, 2026), https://www.ga4gh.org/our-community/organisational-members/#/ [https://perma.cc/W5JM-92DH]; *See supra* note 48 and accompanying text.

[94] *See supra* notes 3–4, 16–27 and accompanying text (All of Us' leadership determination to share liberally); *See generally* Vears, et al., *Stakeholder Perspectives*, *supra* note 56; *See also supra* notes 78-80 and accompanying text (overall U.S. government responsiveness to public demand for access to personal genome information, including All of Us responsiveness in the context of its ambitious participant recruitment agenda).

[95] *See* deCODE Genetics (visited Nov. 6, 2024), https://www.decode.com/ [https://perma.cc/CY5V-236B]; *See* Stuart Leavenworth, *This Nation Faces a DNA Dilemma: Whether to Notify People Carrying Cancer Genes*, MCCLATCHY NEWSPAPERS (Jun. 14, 2018), https://www.mcclatchydc.com/news/nation-world/article213014904.html [https://perma.cc/CJ8M-7JX8].

[96] *See* Leavenworth, *supra* note 92.

[97] *Id.*

[98] *Id.*

[99] UK Biobank, *Who We Are*, https://www.ukbiobank.ac.uk/ [https://perma.cc/M5LX-PVDB] (last visited Nov. 5, 2024).

contemplated returning research results to participants and decided not to after an experiment:

> It involved participants getting whole body scans for the program. For some subjects, a radiologist systematically assessed the scans to see if anything seemed abnormal. If it did, the patient and the patient's doctor were informed.
>
> As it turned out, 20 percent of the participants had abnormalities. They often went on to have other tests, some of which were invasive and involved major surgery, like removal of a lobe of the lung.
>
> Yet in the end, only one in eight with abnormal scans actually had a medical problem, and even then there was nothing they could do about it most of the time, said Dr. Rory Collins, chief executive of the U.K. project.[100]

All of Us and the UK Biobank share a primary objective: build a large-scale biomedical database that provides information as a research resource. Neither is commercially selling anything to research participants.[101] All of Us and UK Biobank researchers are not their program participants' delivery-of-care clinicians and, as stated by Dr. Rory Collins, chief executive of the UK Biobank, "Feedback can cause more harm than good."[102]

IV. GLOBAL CONSEQUENCES OF NIH'S PREDICTABLE RORS ERROR

The global omics research community—government entities, public and private institutions, and their legions of researchers—is competing to access and amass the biobank fodder needed to utilize increasing NGS capabilities in a collective marathon to translate the human genome sequence into medical meaning.[103] "Although next generation sequencing technologies (NGS) were implemented in the research setting well over a decade ago, debate continues about whether and to what extent results from genomic research should be returned to participants."[104] The current state and scope of omics research has made the implications of RoRs sharing much more tangible and the debate more expansive, decibels louder, and more public.[105]

According to an impressive 2021 systematic review of the empirical literature (primarily North American and Canada) exploring the perspectives of stakeholders in primary genomic research on returning individual research results (IRR), the "whether to share" debate has shifted.[106] The study authors concluded that "it is time to move away from questions about whether individual research results should be returned and to focus on which types of IRR to return in each

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[100] Kolata, *The Struggle to Build, supra* note 2.

[101] *See Overview of All of Us Research Program Policies for Researchers*, NAT'L INST. OF HEALTH (last visited Mar. 22, 2026), https://support.researchallofus.org/hc/en-us/articles/4415498292244-Overview-of-All-of-Us-Research-Program-Policies-for-Researchers https://web.archive.org/web/20251017053419/https://support.researchallofus.org/hc/en-us/articles/4415498292244-Overview-of-All-of-Us-Research-Program-Policies-for-Researchers]; *Access to UK Biobank Data*, UK BIOBANK (last visited Mar. 22, 2026), https://www.ukbiobank.ac.uk/about-us/how-we-work/access-to-uk-biobank-data/[https://perma.cc/9KKH-82X4].

[102] Kolata, *The Struggle to Build, supra* note 2.

[103] *See supra* notes 31–35, 39 and accompanying text (biobanking and NIH's Common Rule update to provide research community needed access to DNA samples and accompanying information).

[104] Vears, et al., *supra* note 56, at 1. For discussion of the advancement of genome sequencing during this timeframe, see MALINOWSKI, *supra* note 15, at 1–26 ("Prologue: Revolution, Transition, and Transformation").

[105] *See generally* Vears, et al., *supra* note 56.

[106] *Id.* at 1, 2, 24.

context and how to return them in an ethically appropriate and supportive manner."[107] NASEM advised the same in its 2018 RoRs report with guidance when it advocated for increased transparency in research through RoRs.[108] All of US's decision to engage in RoRs attests to this shift and, given NIH's esteemed legacy and profound influence over the global research community, added much momentum.

Global research community sentiment about RoRs may have shifted in alignment with current popular culture opinion about individual access to personal genome information, but "Great things are not accomplished by those who yield to trends and fads and popular opinion."[109] The dizzying progress of NGS and omics has propelled evidentiary science understanding on the molecular level into a universe beyond most learned person predictions in the 1990s, but the progress of omics has not simplified human genetics or the complexity and diversity in individual human psychology, deliberation, and decision making. The complexities of clinical genetics, of communicating genetic research results with individual research participants in a manner that truly achieves meaningful communication, comprehension and understanding, and of delivering research results responsibly and ethically—as recognized by SACGT in its 2000 report and recommendations—remain dauntingly constant.[110] Moreover,

> The rapid evolution of genomic knowledge has made reanalysis and reinterpretation of clinical genetic testing results an ethical imperative to ensure optimal patient care. However, significant discrepancies persist between policies, laboratory practices, and stakeholder perspectives regarding the responsibility for initiating and communicating reclassified variants.[111]

Consider that today's certified genetic counselors (CGCs) are grappling with the extent to which they, in established provider-patient clinical relationships with definitive duty of clinical care, should share unsolicited findings (UFs)—the discovery of pathogenic variants that cause disease but are not related to why the patient underwent testing in the first place.[112] According to researchers who conducted an interview-based study of genetic counselors published in the *Journal of Genetic Counseling* in 2022, an expert panel should be established to help support clinical geneticists determine which UFs are medically actionable.[113]

CGCs and physicians, especially primary care and family medicine physicians whose expansive scope of practice encompasses the entire human genome, also are increasingly receiving

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[107] Vears, et al., *Stakeholder Perspectives*, *supra* note 56, at 7.

[108] *See supra* notes 45–47 and accompanying text.

[109] Charles Kuralt, Commencement Speech, Skidmore College (May 1996) (essayist, journalist, and originator of TV news segment feature "On the Road" awarded doctor of humane letters), https://news.google.com/newspapers?nid=1298&dat=19960527&id=yf8yAAAAIBAJ&sjid=yQcGAAAAIBAJ&pg=3106,5606314 [https://perma.cc/6JLM-YPPZ].

[110] *See generally* SACGT, *supra* note 74.

[111] Zac Sentell &Ma'n Zawati, *Ethical, Legal, and Policy Dimensions and Contentions for Reanalysis and Reinterpretation of Clinical Genetic Testing Results*, 16 FRONT. IN GEN., Oct. 2025, at 1https://www.frontiersin.org/journals/genetics/articles/10.3389/fgene.2025.1685854/full [https://perma.cc/B5FK-GJD2].

[112] *See generally* Editorial Staff, *Analysis of How Geneticists Discuss Unsolicited Findings With Patients*, GENOMEWEB (Nov. 14, 2022), https://www.genomeweb.com/scan/analysis-how-geneticists-discuss-unsolicited-findings-patients.

[113] *See* Vyne van der Schoot, Carlijn Damste, Helger G. Yntema et al., *Clinical Geneticists' Views on and Experiences with Unsolicited Findings in Next-Generation Sequencing: "A Great Technology Creating New Dilemmas", 32* J. GENETIC COUNSELING 387 (2023) (abstract).

genomic test results *wholly independent from what they order for their patients*, termed "unsolicited genomic results (UGRs)."[114] UGRs encompass research participant RoRs and bundles of results from DTC personal genome tests that do not meet evidentiary-science clinical standards, purchased by and delivered directly from their patients.[115] As relayed in a *Perspectives* contribution published on the National Society of Genetic Counselors (NSGC) internet site in 2021, "Direct-to-consumer genetic testing (DTC-GT) seems to be a blemish on our practice that just won't go away. Despite attempts to pop, squeeze, and extract the blemish, it is here to stay."[116] For the genetic counseling profession, UGRs have become a *global health care systems* problem:

> Direct-to-consumer genetic testing for disease ranges from well-validated diagnostic and predictive tests to "research" results conferring increased risks. While being targeted at public curious about their health, they are also marketed for use in reproductive decision-making or management of disease. By virtue of being "direct-to-consumer" much of this testing bypasses traditional healthcare systems. We argue that direct-to-consumer genetic testing companies should make genetic counseling available, pre as well as post-test. While we do not advocate that mandatory genetic counseling should gate-keep access to direct-to-consumer genetic testing, if the testing process has the potential to cause psychological distress, then companies have a responsibility to provide support and should not rely on traditional healthcare systems to pick up the pieces.[117]

The authors of a study to ascertain physician perspectives on receiving UGRs, published 2019 in *Genetics in Medicine,* concluded, "The prospect of receiving UGRs for otherwise healthy patients raises important concerns for physicians. Their responses informed development of an in-depth survey for physicians following return of UGRs. Strategic workflow integration of UGRs will likely be necessary to empower physicians to serve their patients effectively."[118]

Omics researchers should only share health-related research results when research participants have given informed consent, when the results are actionable (for health conditions preventative, treatable, and/or contribute meaningfully to treatment decision making) or definitive (notably, Mendelian traits), only to the extent participants have specified, and only to duly learned and licensed clinician(s) designated by them in the consent process—not directly with research participants. When the transaction cost of achieving such "cafeteria-style consent in research"[119] *with reliability* is too great, as it will be generally in basic research (as demonstrated by All of Us), researchers should recognize that using RoRs is not a viable option. In this era of remarkable omics progress, researchers should take care to stay in their non-clinician lane, cognizant of the clinical

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[114] *See generally* MALINOWSKI, *supra* note 15; Douglas B. Pet, Ingrid A. Holm, Janet L. Williams et al., *Physicians' Perspectives on Receiving Unsolicited Genomic Results*, 21(2) GENETICS IN MEDICINE 311, 311–18 (2019); Anna Middleton, Alvaro Mendes, Caroline M. Benjamin & Heidi Carmen Howard, *Direct-to-Consumer Genetic Testing: Where and How Does Genetic Counseling Fit*?, 14 PERSONALIZED MEDICINE 249 (2017) (abstract), https://pubmed.ncbi.nlm.nih.gov/29767582/ [https://perma.cc/B6UP-EFRR].

[115] *See generally* MALINOWSKI, *supra* note 15; Pet, et al., *Physicians' Perspectives, supra* note 114; Middleton, et al, *Genetic Counseling Fit*?, *supra* note 114.

[116] Sara Spencer, *Perspectives: Providing Counseling to Patients Using Direct-to-Consumer Testing* (Apr. 29, 2021) (page nos. unavailable), https://perspectives.nsgc.org/Article/ TitleLink/Providing-Counseling-to-Patients-Using-Direct-to-Consumer-Testing [https://perma.cc/LDC3-8CZZ].

[117] Middleton, et al., *Genetic Counseling Fit?, supra* note 114, at 249.

[118] Pet, et al., *Physicians' Perspectives, supra* note 114, at 311. *See generally id*.

[119] Bartha Maria Knoppers, email communication with author (Apr. 17, 2025) (on file with author).

complexities of human genetics, and aware that "'[f]eedback can cause more harm than good.'"[120]

CONCLUSION

The dizzying progress of omics research through astonishing NGS capacity is transitioning clinical care to PGM with breathtaking potential to improve individual health care and human health.[121] Especially given the accelerating pace of progress and expanding scale of the ongoing, competitive global omics research and development (R&D) enterprise, established ethical and evidentiary science-based standards in biomedical research and clinical care must be firmly adhered to during the journey to realize the human health potential of responsible, evidentiary-science based PGM.[122]

The All of Us RoRs endeavor must be recognized and embraced as a learning event well beyond the program's administrators. Rather than "changing the research paradigm, turning it into a two-way street[,]"[123] and building trust with research participants through RoRs, All of Us demonstrated what was exhaustively deliberated, defined, and recognized a quarter-century before: The clinical challenges and complexities of delivering genetic test results to individuals in a responsible manner that achieves meaningful communication with understanding and contains risks of harm.[124]

The All of Us pretext for RoRs was to build trust with research participants, but instead the program *lost* trust as reflected by the resulting controversies, its own published studies, and ultimately, its decision to stop RoRs altogether.[125] Hopefully, both NIH and All of Us have reminded the global research and medical communities of the importance of adhering to established ethical and evidence-based scientific standards in biomedical research and clinical care, the clinical complexities of human genetics, and that "[f]eedback can cause more harm than good."[126]

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[120] Kolata, *The Struggle to Build, supra* note 2 (quoting Dr. Rory Collins, chief executive of the UK Biobank). For a timely assessment of the current landscape of ethical, legal, and practical challenges for laboratories, clinicians, and patients, *see* Sentell & Zawati, supra note 107 ("We highlight the tension between the duty of care and resource constraints, finding that while the ethical importance of reinterpretation is acknowledged, the lack of standardized guidelines and legal clarity fuels uncertainty and discordant stakeholder views"). For insightful discussion of the role physicians play in clinical research and the ethical and other professional obligations of research physicians to participants, see generally Mark A. Rothstein, *Research Participant Bill of Rights: Clarifying the Role of Research Physicians*, 47(5) ETHICS & HUMAN RES. 29, 29–36 (2025).

[121] *See generally* Lori Knowles, Westerly Luth & Tania Bubela, *Paving the Road to Personalized Medicine: Recommendations on Regulatory, Intellectual Property and Reimbursement Challenges*, 4(3) J. L. & BIOSCIENCES 453 (2017).

[122] *See generally* MALINOWSKI, *supra* note 15.

[123] NIH, *Health-Related Results, supra* note 5.

[124] *See supra* notes 84–88 and accompanying text (discussing national debate and deliberation that culminated in SACGT's report and recommendations); *see* SACGT, ENHANCING THE OVERSIGHT, *supra* note 74.

[125] *See supra* notes 18, 55–71 and accompanying text.

[126] Kolata, *supra* note 2 (page no's unavailable online) (quoting Dr. Rory Collins, chief executive of the UK Biobank).