The Dawn of Diverse Drug Clinical Trials:

How the NIH Inclusion Policy Ensured the Rights of Women and Minorities While Establishing New Responsibilities for the Research Community

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Process Paper

Inspiration for this project came from a lunch discussion during my internship at the University of Michigan last summer, where a female postdoctoral researcher shared the challenges women face in advancing to principal investigator roles. She explained that family responsibilities and a lack of compensation for them contributed to this gender disparity. It was mind-opening to learn about the inequalities women face in research, and that discussion stayed with me throughout the summer. Although I had long been aware of the gender gap in STEM, I had never fully considered its impact. When I came across the NIH Inclusion Policy during my topic selection process, I was shocked to learn that up until the 90s, women and minorities were frequently excluded from clinical trials for commonly used drugs. However, the most recent NIH Inclusion Policy finally ended this inequality by mandating the participation of women and minorities in clinical research.

Initially, I planned to focus my paper solely on the aspect of the NIH Inclusion Policy related to women, mentioning minorities only briefly due to a paucity of sources and limited space. However, my perspective shifted when my school welcomed an alumni speaker, Dr. Cho, a research doctor who conducted studies at Rockefeller University and later became the Chief Medical Officer of the largest non-profit organization for multiple myeloma. During my preliminary research on him, I discovered his paper on increasing minority participation in multiple myeloma clinical trials. This prompted me to find time to chat with him, yielding insights into the importance of minority representation. Dr. Cho also highlighted concerns about Trump's new executive order that could undermine the progress made by the NIH inclusion policy.

I relied heavily on two of my secondary sources: *The Disfranchisement of Fertile Women in Clinical Trials* and *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*. The historical stories and stakeholder perspectives provided by these secondary sources complemented the statistical evidence from my journal articles, enabling me to craft a well-rounded and comprehensive paper. By reading about events leading up to the NIH Inclusion Policy and its groundbreaking mandates, I gained a deeper understanding of the arguments put forth by women's rights activists to advocate for change.

My topic of rights and responsibilities associated with the NIH Inclusion Policy is significant because of its positive impact in promoting health equity. It ended researchers' irresponsible practice of excluding women and minorities to save money, making sure that clinical trial results apply to everyone who uses the drug. Thus, the shift in the research paradigm brought about by the NIH Inclusion Policy introduced a profound responsibility for the research community to uphold the rights of women and minorities to participate in clinical trials, ensuring that medical research serves the needs of all populations.

Introduction

Imagine taking a medication without knowing if it's truly safe or effective for you—this was the reality for millions of women in the late 20th century, including the 11% who used aspirin to prevent heart attacks and strokes[1]. Aspirin had been widely used in the U.S. since the late 19th century, but its cardiovascular benefits were only rigorously tested in the mid-20th century through clinical trials. In 1989, The New England Journal of Medicine published the first U.S. randomized aspirin trial for primary cardiovascular disease, finding that the drug taken every other day significantly reduced the risk of a first heart attack in those older than fifty years old but also increased stroke risk.[2] Notably, the study enrolled 22,071 men and no women[3], with the authors acknowledging "the possibility that aspirin in low doses may have a different pharmacologic effect in women."[4] At the time, researchers almost exclusively tested drugs on males because they assumed that the data was readily applicable to females.[5] This paucity of knowledge led to "uncertainty as to whether there will be similar beneficial effects on women."[6] As a result, before aspirin was tested on women in 2005, those taking it for primary prevention lacked critical information on its risks and benefits.[7]

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[1] Russell V. Luepker et al., "Population Trends in Aspirin Use for Cardiovascular Disease Prevention 1980–2009: The Minnesota Heart Survey," *Journal of the American Heart Association* 4, no. 12 (2015):accessed December 6, 2024,
[2] Steering Committee of the Physicians' Health Study Research Group, "Final Report on the Aspirin Component of the Ongoing Physicians' Health Study," *New England Journal of Medicine* 321, no. 3 (1989): 132, accessed November 10, 2024,
[3] Steering Committee of the Physicians' Health Study Research Group, "Final Report," 133.
[4] Steering Committee, 134.
[5] L. Elizabeth Bowles, "The Disfranchisement of Fertile Women in Clinical Trials: The Legal Ramifications of and Solutions for Rectifying the Knowledge Gap," Vanderbilt Law Review, last modified May 1992, accessed January 2, 2025, https://scholarship.law.vanderbilt.edu/cgi/viewcontent.cgi?article=2378&context=vlr.
[6] Bowles, "The Disfranchisement," Vanderbilt Law Review.
[7] Luepker et al., "Population Trends".

In response to underrepresentation, the National Institutes of Health (NIH) created an official Inclusion Policy in 1994 to address gender and racial discrepancies in medical research. This policy marked a significant departure from the pervasive use of white male subjects in clinical trials by not only granting women and minorities the right to participate but also requiring it. By issuing this mandate, the NIH created new responsibilities for principal investigators and the research community to ensure diversity in clinical research, thus setting a global precedent.

The Age of Exclusion

The historical exclusion of women from clinical trials in the 20th century was driven by concerns over fetal safety, especially following the thalidomide tragedy[8]. The birth defects caused by thalidomide in the 1960s heightened public alert over protecting fetuses from medical risks,[9] leading to the creation of policies like the FDA Policy of 1977, which aimed to protect women of childbearing potential by barring their participation in early-phase clinical trials.[10]

FDA policymakers in the late 70s sought to prevent harm to fetuses by restricting women's participation in clinical trials[11]. However, scholars and advocates later criticized this

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[8] Daniel Federman, Ruth Faden, and Anna C. Mastroianni, *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies* (Washington, D.C.: National Academies Press, 1994), 1:40, ProQuest Ebook Central.

[9] Carol S. Weisman and Sandra D. Cassard, "Health Consequences of Exclusion or Underrepresentation of Women in Clinical Studies (I)," in *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*, ed. Daniel Federman, Ruth Faden, and Anna C. Mastroianni (Washington, D.C.: National Academies Press, 1994), 1:40, ProQuest Ebook Central.

[10] U.S. Department of Health, Education, and Welfare., "Guidance for Industry," Center for Drug Evaluation and Research, Food and Drug Administration, last modified February 1977, accessed December 2, 2024, https://www.fda.gov/media/71495/download.

[11] Ruth B. Merkatz, "Inclusion of Women in Clinical Trials: A Historical Overview of Scientific Ethical and Legal Issues," *Journal of Obstetric, Gynecologic and Neonatal Nursing*, accessed January 11, 2025, https://www.jognn.org/article/S0884-2175(15)33526-7/fulltext.

approach, arguing that it was overprotective and ultimately harmed the people it aimed to protect[12]. Similarly, minorities have historically faced underrepresentation in clinical trials due to limited access to healthcare facilities and services.[13] For example, African Americans and Hispanics represent 12% of Americans but only 5% of clinical trial participants.[14] This disparity is evident in the Framingham Heart Study, an NIH-funded initiative launched in 1948 to define cardiovascular disease risk factors.[15] Despite its groundbreaking contributions, its participants are "predominantly White individuals of Western European descent."[16] During my conversation with Dr. Hearn Jay Cho, a former postdoc at Rockefeller University and now an associate professor of medicine at the Icahn School of Medicine, he expressed deep frustration over the low minority representation in multiple myeloma clinical trials while criticizing Trump's recent executive order against DEI initiatives[17]. Dr. Cho stressed that inclusion is not merely a political issue but also a biological one, citing diseases like multiple myeloma and sickle cell anemia that predominantly impact individuals of African descent[18]. Given that drugs can have varying effects based on race and gender,[19] "access to clinical trials can mean the difference between life and death, and equal access to healthcare and quality of treatment will benefit all."[20]

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[12] Federman, Faden, and Mastroianni, *Women and Health*, 1:2.
[13] Alice McCarthy, "Embracing Diversity: The Imperative for Inclusive Clinical Trials," Trends in Medicine, last modified June 30, 2023, accessed November 9, 2024, https://postgraduateeducation.hms.harvard.edu/trends-medicine/embracing-diversity-imperative-inclusive-clinical-trials.
[14] Meghan Coakley et al., "Dialogues on Diversifying Clinical Trials: Successful Strategies for Engaging Women and Minorities in Clinical Trials," *Journal of Women's Health* 21, no. 7 (2012): https://doi.org/10.1089/jwh.2012.3733.
[15] Connie W. Tsao and Ramachandran S. Vasan, "Cohort Profile: The Framingham Heart Study (FHS): Overview of Milestones in Cardiovascular Epidemiology," International Journal of Epidemiology 44, no. 6 (2015): https://doi.org/10.1093/ije/dyv337.
[16] Tsao and Vasan, "Cohort Profile".
[17] Hearn Jay Cho, interview by the author, Hudson, OH, January 31, 2025.
[18] Cho.
[19] McCarthy, "Embracing Diversity," Trends in Medicine.
[20] Coakley et al., "Dialogues on Diversifying,"

In response to this issue of underrepresentation, government agencies took steps to encourage pharmaceutical companies and researchers to include women in clinical trials.[21] Yet, their first attempts were met with limited success. For example, the NIH introduced the original inclusion policy in 1986, urging "funding applicants to include women in clinical research."[22] However, the Government Accountability Office (GAO) found in 1990 that "the application booklet used by most NIH grant applicants [...] contain[ed] no reference to the policy."[23] Since "a revised version of the form and its instructions [would] not appear until April 1991, over 4 years after the policy was first articulated,"[24] it was unclear if the policy had even somewhat succeeded in reaching its goal.[25] Growing public awareness about the NIH policy's inadequate implementation mechanisms "stimulat[ed] legislative efforts to correct the [disparities]."[26]

By the early 90s, many in the medical community believed that addressing "inequitable research practices"[27] would require leadership and action from women themselves.[28] For example, women's health advocates, including Cynthia Pearson, the former executive director of the National Women's Health Network[29], played a crucial role in drawing attention to what they saw as "the relative absence of women and racial and ethnic groups from the research agenda."[30]

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[21] Bowles, "The Disfranchisement," Vanderbilt Law Review.
[22] Federman, Faden, and Mastroianni, *Women and Health*, 1:43.
[23] Mark Nadel, "National Institutes of Health: Problems in Implementing Policy on Women in Study Populations," United States General Accounting Office, last modified June 18, 1900, accessed November 12, 2024, https://www.gao.gov/assets/t-hrd-90-38.pdf.
[24] Nadel, "National Institutes," United States General Accounting Office.
[25] Bowles, "The Disfranchisement," Vanderbilt Law Review.
[26] Federman, Faden, and Mastroianni, *Women and Health*, 1:2.
[27] Federman, 37.
[28] Bowles, "The Disfranchisement," Vanderbilt Law Review.
[29] Cindy Pearson, interview by Judy Waxman, Veteran Feminists of America, last modified March 2023, accessed January 14, 2025, https://veteranfeministsofamerica.org/interview-with-cindy-pearson/.
[30] Federman, Faden, and Mastroianni, *Women and Health*, 1:37.

In response, policymakers introduced the National Institutes of Health's 1994 Inclusion Policy, addressing these long-standing imbalances.

A New Landscape

The appointment of Dr. Bernadine Healy, "the first woman director of NIH,"[31] in 1991 not only showed the increasing female leadership in medical research but also signaled the start of the expansion of women's rights in clinical research. Dr. Healy stated that "medical researchers should undertake broad exploration and dismiss useless forms of discrimination,"[32] launching the $625 million Women's Health Initiative (WHI) to address the effects of various preventive measures on cancer and cardiovascular disease in postmenopausal women[33]. This initiative sheds light on understudied areas of women's health, such as the side effects of hormone replacement therapy, a common treatment for menopause.[34] The premise underlying the movement is that findings from men's health research cannot always generalize to women and that research involving women from one ethnic group may not necessarily apply to those from another.[35] Dr. Healy's efforts helped to establish the NIH inclusion policy, fundamentally shifting the landscape of clinical research and women's rights in medical research.

In 1993, fueled by increasing pressure from women's health advocates and a growing body of evidence highlighting gender disparities in research, President Clinton signed the NIH

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[31] Federman, 45.
[32] Bowles, "The Disfranchisement," Vanderbilt Law Review.
[33] Federman, Faden, and Mastroianni, *Women and Health*, 1:45.
[34] Maryann Teale Snell, "Healthy Woman: Bernadine Healy '65," Vassar, last modified 2004, accessed January 12, 2025, https://www.vassar.edu/vq/issues/2004/03/features/healthy-woman.html#:~:text=Healy%20has%20played%20a%20key,diseases%20affecting%20women%20over%2050.
[35] Barbara J. Culliton, "NIH Push for Women's Health," Nature 353, no. 6343 (1991): 383, accessed March 22, 2025, https://doi.org/10.1038/353383a0.

Revitalization Act into law[36]. This act led to an update to the original 1986 NIH Inclusion Policy. While the previous policy merely encouraged the inclusion of women in clinical trials, the updated 1994 Inclusion Policy mandated that if the condition studied affected both sexes, NIH-funded clinical trials must include both men and women.[37] Additionally, the policy required the inclusion of minorities, compelling researchers to provide scientific justifications for any exclusions, regardless of cost.[38] Finally, the policy officially established the Office of Research on Women's Health (ORWH) to oversee implementation, ensure compliance, and advocate for women's health research.[39] These changes "mean that a wider inclusion of women in clinical trials and more detailed gender analyses will become the norm."[40] Researchers agreed that the updated policy helped improve representation, with 69% of the laboratory professors in 2002 reporting success in increasing gender diversity and 55% noting progress in racial diversity. [41]

By mandating the inclusion of women in clinical trials, the NIH Inclusion Policy granted them the right to equitable representation in research and the right to be informed of gender-specific side effects through more generalizable research[42]. The policy also created new responsibilities for the NIH, requiring it to include women and minority groups in all human

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[36] Federman, Faden, and Mastroianni, *Women and Health*, 1:44-45.
[37] National Institute of Health, "Dr. Bernadine Healy," Changing the Face of Medicine, National Institute of Health, last modified June 3, 2015, accessed December 2, 2024, https://cfmedicine.nlm.nih.gov/physicians/biography_145.html.
[38] National Institute of Health, "NIH Guidelines on the Inclusion of Women and Minorities as Subject in Clinical Research," Grants and Funding, National Institute of Health, last modified March 18, 1994, accessed October 23, 2024, https://grants.nih.gov/grants/guide/notice-files/not94-100.html.
[39] United States. Congress., *NIH Revitalization Act: Hearing before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, House of Representatives* (Washington DC: US GPO, 1993), 33, PDF.
[40] Merkatz, "Inclusion of Women,"
[41] Giselle M. Corbie-Smith, Raegan W. Durant, and Diane Marie M St. George, "Investigators' Assessment of NIH Mandated Inclusion of Women and Minorities in Research," *Contemporary Clinical Trials* 27, no. 6 (2006): https://doi.org/10.1016/j.cct.2006.05.012.
[42] Aaron L. Schwartz et al., "Why Diverse Clinical Trial Participation Matters," *New England Journal of Medicine* 388, no. 14 (2023): https://doi.org/10.1056/nejmp2215609.

subject research[43]. In addition, the ORWH proposed that clinical trial reviewers evaluate research plans to compare experimental findings between males and females[44]. As a result, researchers now bear the responsibility of studying how sex and gender affect outcomes, motivating them to "embrace research that focuses on women's health and sex differences."[45] However, as the clinical trial researcher I interviewed acknowledged, "There was a lot of harm done to marginalized people, and that memory has stuck around."[46] She stressed that improving the generalizability of clinical trials requires "gaining the trust of patients,[47]" which can only be achieved over time as researchers take responsibility for "offering promising therapies for anyone.[48]"

Despite the NIH Inclusion Policy's positive influence on providing women new rights in health research, some scientists raised concerns. Marcia Angell, the first female editor-in-chief of the New England Journal of Medicine, wrote an editorial in the journal's pages in 1993, expressing her view that "the proposed amendment […] would create worse problems than it would solve."[49] She stated that "to provide a valid analysis of results in subjects of both sexes and all minorities would require unreasonably large trials of new interventions,"[50] which also come with enormous price tags. For this reason, many investigators fear that the "politically

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[43] Merkatz, "Inclusion of Women,"
[44] Carolyn M. Mazure and Daniel P. Jones, "Twenty Years and Still Counting: Including Women as Participants and Studying Sex and Gender in Biomedical Research," *BMC Women's Health* 15, no. 1 (2015): accessed November 9, 2024, https://doi.org/10.1186/s12905-015-0251-9.
[45] Mazure and Jones, "Twenty Years"
[46] Franson, interview by the author.
[47] Franson.
[48] Franson.
[49] Steven Epstein, *Inclusion: the Politics of Difference in Medical Research* (Chicago, IL: University of Chicago Press, 2007), 105, ProQuest Ebook Central.
[50] Epstein, Inclusion: the Politics, 105.

correct clinical studies" required by the NIH Inclusion Policy will only reduce the quality of such research.[51]

Altering the Research Paradigm

With "62% of the 387 drugs approved from 2010-2019"[52] receiving funding from the NIH, the institution's influence on medical research is undeniable. In the fiscal year 2023, NIH clinical research funding reached approximately 18.9 billion U.S. dollars,[53] further highlighting its crucial role in shaping rights and responsibilities in the field. The 1994 NIH inclusion policy was pivotal in addressing gender disparities in clinical research and significantly improved racial diversity in clinical trials. A study published in the journal *Contemporary Clinical Trials* discovered that the representation of women in phase 1 clinical trials improved dramatically from 22% before the policy to 43.8% between 2016 and 2019.[54] The policy also placed a strong emphasis on researchers' responsibility to include minority participants, leading to a "4-fold increase in [minority] inclusion (an increment from 2.78% to 11.10%)" in NIH-funded studies from 1993 to 2018. By contrast, non-NIH-funded clinical trials saw only a "2.2-fold [increase]

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[51] Epstein, 105.
[52] Helen Floersh, "Industry, Not NIH, Fronts Most of the Cash for Clinical Trials: Report," Fierce Biotech, last modified July 14, 2023, accessed November 14, 2024, https://www.fiercebiotech.com/research/report-industry-not-nih-fronts-most-cash-clinical-trials#:~:text=Ledley's%20team%20found%20that%20the%20NIH%20funding,an%20average%20of%20$33.8%20million%20per%20drug.
[53] Matej Mikulic, "Total Clinical Research Funding by National Institutes for Health 2013-2025," Statista, last modified May 17, 2024, accessed January 14, 2025, https://www.statista.com/statistics/716602/total-clinical-research-funding-by-the-national-institutes-for-health/
[54] Alexandra Z. Sosinsky et al., "Enrollment of Female Participants in United States Drug and Device Phase 1–3 Clinical Trials between 2016 and 2019," *Contemporary Clinical Trials* 115 (April 2022): 5, accessed November 9, 2024, https://doi.org/10.1016/j.cct.2022.106718.

(from 1.23% to 2.78%)"[55] during the same period. These figures and disparities underscore the policy's effectiveness in promoting diversity in clinical research.

The mandated inclusion also led to research that shed light on how drugs affect women and men differently in the short term. A prime example is an NIH-funded 2005 research article that replicated the 1989 study on aspirin use and heart disease[56]. Under the requirements of the 1994 NIH Inclusion Policy, researchers acknowledged that "the current recommendations for the use of aspirin in primary prevention in women [were] based on limited direct data from women"[57] and, in response, they replicated the clinical trial with 39,876 female participants. The study results revealed that a regular intake of aspirin reduced the risk of total stroke without reducing the risk of major cardiovascular events.[58] This contrasted with earlier trials on men, which suggested increased stroke risk and reduced heart attack risk. Ultimately, this disparity "demonstrat[ed] the importance of studying women as well as men in major cardiovascular clinical trials."[59]

The policy played a significant role in promoting racial diversity in clinical trials. For instance, during the follow-up to the Framingham Heart Study in 1994, researchers recognized the importance of establishing a new group of participants that reflected the growing diversity of the population.[60] To address this, they established a new cohort that consisted of 507 men and women of African-American, Hispanic, Asian, Indian, Pacific Islander, and Native American

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[55] Manuel A. Ma et al., "Minority Representation in Clinical Trials in the United States," *Mayo Clinic Proceedings*, accessed December 4, 2024, https://www.mayoclinicproceedings.org/article/S0025-6196(20)31259-3/fulltext.
[56] Bowles, "The Disfranchisement," Vanderbilt Law Review.
[57] Paul M. Ridker et al., "A Randomized Trial of Low-Dose Aspirin in the Primary Prevention of Cardiovascular Disease in Women," *New England Journal of Medicine* 352, no. 13 (2005): accessed November 10, 2024, https://doi.org/10.1056/nejmoa050613.
[58] Ridker et al., "A Randomized,"
[59] Ridker et al.
[60] Framingham Heart Study, "Participant Cohorts," Framingham Heart Study, accessed March 22, 2025, https://www.framinghamheartstudy.org/participants/participant-cohorts/.

origins.[61] This shift revealed the increased emphasis on racially inclusive clinical trials the NIH inclusion policy brought about.

Overall, the Framingham Heart Study, along with the aspirin trials and countless others, highlighted the NIH Inclusion Policy's impact in helping researchers understand gender and racial differences in drug effects. The benefits of this knowledge are significant, "not only improving women's health care but also the health of the nation."[62] While the NIH Inclusion Policy profoundly impacted American medical research, its influence extended beyond the U.S., shaping policies in Canada, the European Union, and beyond.

A Global Legacy

The NIH inclusion policy's success in improving health equity prompted follow-up acts in the United States, such as the 2022 DEPICT Act. This act strengthened the previous mandates established by the NIH inclusion policy by requiring the submission of a "diversity action plan for how the sponsor will meet such [enrollment] targets, including demographic-specific outreach and enrollment strategies, study-site selection, clinical trial inclusion and exclusion practices, and any diversity training for trial personnel."[63] Furthermore, the act reflects ongoing efforts to improve women's right to representation in clinical research by building from the foundation of the NIH inclusion policy.

In addition to sparking change in the U.S., the creation of the NIH Inclusion policy had a worldwide impact. For example, in 2013, the Canadian government issued policies that recommended the inclusion of women in early-stage clinical trials to identify potential

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[61] Framingham Heart Study, "Participant Cohorts," Framingham Heart Study.
[62] Bowles, "The Disfranchisement," Vanderbilt Law Review.
[63] US government, "H.R.6584 - DEPICT Act," Congress.gov, last modified February 3, 2022, accessed November 9, 2024, https://www.congress.gov/bill/117th-congress/house-bill/6584/text.

sex-related differences.[64] The European Union soon followed suit in 2014, recommending that subjects included in a clinical trial represent the same gender and age groups that will use the investigated drug.[65] However, the new policies only encouraged but did not require inclusion, meaning researchers often overlooked or failed to prioritize women's right to representation in medical research. While the recommendations serve as a step forward, they did not bring about the same level of impact as seen with the NIH Inclusion Policy.

Areas for Improvement

Despite official policies that mandated the inclusion of women and minorities in clinical research trials in the U.S. and around the world, "there was no serious mention of the need for inclusion of women in the community of researchers or in the decision-making groups that set research agendas."[66] Statistics also highlight this imbalance; as of 2023, only 39.6% of the principal investigators, those in charge of a research project, are women.[67] Increasing the number of female primary researchers is important because although women lead less than one-fifth of clinical trials, they often enroll more female participants, helping generate results applicable to a

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[64] "Guidance Document: Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences," Government of Canada, last modified May 29, 2013, accessed October 29, 2024, https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/considerations-inclusion-women-clinical-trials-analysis-data-sex-differences.html#a13.

[65] "Regulation (EU) No 536/2014 of the European Parliament and of the Counsil of 16 April 2014," *Official Journal of the European Union* 158, no. 1 (2014): 3, accessed October 29, 2024, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536.

[66] Abby Lippman, *The Inclusion of Women in Clinical Trials: Are We Asking the Right Questions?*, 8, March 2006, accessed October 23, 2024, https://whp-apsf.ca/pdf/clinicalTrialsEN.pdf.

[67] Jennifer R. Southall, "Disparities Persist in Clinical Trial Leadership across Specialties," Hemonc Today, last modified October 30, 2023, accessed December 4, 2024, https://www.healio.com/news/hematology-oncology/20231030/disparities-persist-in-clinical-trial-leadership-across-specialties.

wider range of people.[68] Similarly, “research has shown that minority patients seek physicians of their own race, so bringing these doctors into trials is [also] critical.”[69] Since “physicians are the gateway to the patient,”[70] increasing diversity in clinical leadership directly supports the NIH inclusion policy by improving the representation of women and minorities in clinical research.

Conclusion

A diverse population of clinical trial participants is essential to ensuring that a tested drug will be safe and effective for everyone. Decades ago, millions of women, like those who took aspirin to prevent heart attacks, were left in the dark because the 1977 FDA policy had excluded them from clinical trials. Thanks to the NIH Inclusion Policy, women finally gained the right to equitable representation in research and to be informed of sex-specific side effects. The policy’s impact on improving gender and racial diversity is evident in numerous NIH-funded studies, including the 2005 aspirin study, which revealed the drug’s differing effects on men and women, and the Framingham Heart Study, which included more diverse cohorts after its establishment. This shift also created new responsibilities for principal investigators and the research community, including training researchers to look for gender and racial differences and addressing barriers to participation by building trust. On a broader scale, the success of the NIH Inclusion Policy spread internationally, inspiring similar laws in Canada and the EU while paving the way for a more equitable and representative future in medicine.

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[68] Bridget Balch, "Why We Know so Little about Women's Health," AAMC News, last modified March 26, 2024, accessed December 4, 2024, https://www.aamc.org/news/why-we-know-so-little-about-women-s-health.
[69] Coakley et al., "Dialogues on Diversifying,"
[70] Coakley et al.

Bibliography

Primary Sources

Cho, Hearn Jay. Interview by the author. Hudson, OH. January 31, 2025.
Dr. Cho came to the WRA campus as a guest speaker after winning a science award. During my preliminary research, I found his paper about the inclusion of minorities in multiple myeloma clinical trials, which fits perfectly with my topic. Thus, I had a conversation with him, which led to insights on the importance of minority inclusion and Trump's executive order that might end the NIH inclusion policy.

Corbie-Smith, Giselle M., Raegan W. Durant, and Diane Marie M St. George. "Investigators' Assessment of NIH Mandated Inclusion of Women and Minorities in Research." *Contemporary Clinical Trials* 27, no. 6 (2006): 571-79. https://doi.org/10.1016/j.cct.2006.05.012.
This survey shows the opinion of researchers ten years after the enactment of the NIH inclusion policy. The majority expressed that the policy helped improve the representation of women and minorities, revealing the success of the policy.

Franson, Andrea. Interview by the author. Hudson, OH. January 27, 2025.
I was connected to Dr. Franson through the professor of the lab where I interned last summer. As a mother of two and a pediatric hematology clinical trial specialist, she provided meaningful insights on the issue of a lack of information on common pregnancy drugs. She also mentioned the history of the mistreatment of minorities.

"Guidance Document: Considerations for Inclusion of Women in Clinical Trials and Analysis of Sex Differences." Government of Canada. Last modified May 29, 2013. Accessed October 29, 2024. https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/clinical-trials/considerations-inclusion-women-clinical-trials-analysis-data-sex-differences.html#a13.
This government document shows the Canadian policy that encourages the inclusion of women in clinical trials. I used this to show the global impact of the NIH inclusion policy, influencing other countries to enact similar laws.

Luepker, Russell V., Lyn M. Steffen, Sue Duval, Nicole D. Zantek, Xia Zhou, and Alan T. Hirsch. "Population Trends in Aspirin Use for Cardiovascular Disease Prevention 1980–2009: The Minnesota Heart Survey." *Journal of the American Heart Association* 4, no. 12 (2015). Accessed December 6, 2024. https://doi.org/10.1161/jaha.115.002320.
This journal article included sex-specific statistics on aspirin use from the 1980s to 2009 for primary and secondary prevention. It showed how some women used aspirin even though it had not been tested on them. I used the data to show the number of women influenced by a lack of information on aspirin's therapeutic effects.

Ma, Manuel A., Dora E. Gutiérrez, Joanna M. Frausto, and Wael K. Al-Delaimy. "Minority Representation in Clinical Trials in the United States." *Mayo Clinic Proceedings*.

Accessed December 4, 2024.
https://www.mayoclinicproceedings.org/article/S0025-6196(20)31259-3/fulltext.
I used the data from this journal article to show how NIH successfully increased the representation of minorities through its inclusion policy. This helped me understand that the problem of a lack of minorities was not overlooked.

Mazure, Carolyn M., and Daniel P. Jones. "Twenty Years and Still Counting: Including Women as Participants and Studying Sex and Gender in Biomedical Research." *BMC Women's Health* 15, no. 1 (2015). Accessed November 9, 2024. https://doi.org/10.1186/s12905-015-0251-9.
This article lists the important events in the process of including more women in research. The authors provide an analysis of the responsibility of the scientific community in educating future researchers and of NIH grant-readers to ensure compliance with the policy.

Mikulic, Matej. "Total Clinical Research Funding by National Institutes for Health 2013-2025." Statista. Last modified May 17, 2024. Accessed January 14, 2025. https://www.statista.com/statistics/716602/total-clinical-research-funding-by-the-national-institutes-for-health/.
This source provided statistics on the NIH's clinical trial funding in 2023. It helped me understand the impact of the NIH on clinical research by spending billions of dollars on funding projects.

Nadel, Mark. "National Institutes of Health: Problems in Implementing Policy on Women in Study Populations." United States General Accounting Office. Last modified June 18, 1900. Accessed November 12, 2024. https://www.gao.gov/assets/t-hrd-90-38.pdf.
This article from the GAO shows how the NIH failed to update its application booklet in compliance with its inclusion policy in 1986. I used this to show how reviewing agencies like the GAO played a role in the creation of the NIH inclusion policy by directing awareness to the issue.

National Institute of Health. "NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research." Grants and Funding. National Institute of Health. Last modified March 18, 1994. Accessed October 23, 2024. https://grants.nih.gov/grants/guide/notice-files/not94-100.html.
This is the NIH inclusion policy and is the focus of my project. It mandates the inclusion of women and minorities for a clinical trial to be funded by the NIH.

Pearson, Cindy. Interview by Judy Waxman. Veteran Feminists of America. Last modified March 2023. Accessed January 14, 2025. https://veteranfeministsofamerica.org/interview-with-cindy-pearson/.
The interview gave me a deeper perspective of Cindy Pearson, a women's health advocate. I learned about her role as the executive director of the National Women's Health Network and her motivations for fighting for women's rights. Her claim that there is an absence of women and minorities from research prompted reform from policymakers.

"Regulation (EU) No 536/2014 of the European Parliament and of the Counsil of 16 April 2014." *Official Journal of the European Union* 158, no. 1 (2014). Accessed October 29, 2024. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536.
This EU regulation recommends the inclusion of women and minorities, encouraged by the success of the NIH inclusion policy. I used this to show how the NIH inclusion policy had global impacts on improving women's health. However, the NIH inclusion policy is also better than the policy in the EU due to its requirement rather than a recommendation to include women.

Ridker, Paul M., Nancy R. Cook, I-Min Lee, David Gordon, J. Michael Gaziano, JoAnn E. Manson, Charles H. Hennekens, and Julie E. Buring. "A Randomized Trial of Low-Dose Aspirin in the Primary Prevention of Cardiovascular Disease in Women." *New England Journal of Medicine* 352, no. 13 (2005): 1293-304. Accessed November 10, 2024. https://doi.org/10.1056/nejmoa050613.
This journal article was done on all women and replicated a previous aspirin trial on all men, revealing the sex-specific effects of aspirin on preventing cardiovascular disease. In compliance with the NIH inclusion policy, the authors justified why they excluded men from the clinical trial. I used this to show how diverse trials made possible by the NIH inclusion policy provide more information on the effects of common medicines like aspirin.

Sosinsky, Alexandra Z., Janet W. Rich-Edwards, Aleta Wiley, Kalifa Wright, Primavera A. Spagnolo, and Hadine Joffe. "Enrollment of Female Participants in United States Drug and Device Phase 1–3 Clinical Trials between 2016 and 2019." *Contemporary Clinical Trials* 115 (April 2022): 106718. Accessed November 9, 2024. https://doi.org/10.1016/j.cct.2022.106718.
This article shows statistics on the trend of women's representation in clinical trials. I used this to show how women's representation increased, proving the success of the NIH inclusion policy.

Steering Committee of the Physicians' Health Study Research Group. "Final Report on the Aspirin Component of the Ongoing Physicians' Health Study." *New England Journal of Medicine* 321, no. 3 (1989): 129-35. Accessed November 10, 2024. https://doi.org/10.1056/nejm198907203210301.
I used this journal article in my introduction to prove the historical underrepresentation of women in clinical trials through the example of an aspirin trial. This helped me understand the norms of clinical trials before the NIH inclusion policy

United States. Congress. *NIH Revitalization Act: Hearing before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, House of Representatives*. Washington DC: US GPO, 1993. PDF.
This hearing reflects the legislation behind passing the law that led to the policy. I used this to show other ways the NIH inclusion policy hoped to improve women's health, especially through establishing the Office of Research on Women's Health.

U.S. Department of Health, Education, and Welfare. "Guidance for Industry." Center for Drug Evaluation and Research. Food and Drug Administration. Last modified February 1977. Accessed December 2, 2024. https://www.fda.gov/media/71495/download.
This source provides the specific mandates of the FDA policy of 1977, excluding women of child-bearing potential from participating in early-phase clinical trials. I used this policy to show how previous policies regarding women in clinical research, like the FDA policy, are overprotective. This shows how the NIH inclusion policy was an important step forward to ensure that women are well-informed and also benefit from research.

US government. "H.R.6584 - DEPICT Act." Congress.gov. Last modified February 3, 2022. Accessed November 9, 2024.
https://www.congress.gov/bill/117th-congress/house-bill/6584/text.
The DEPICT Act requires researchers to provide an action plan on how they will meet diversity requirements. I used this bill to show the long-term impact of the NIH inclusion policy by prompting follow-up acts. This proves that there are ongoing efforts in the US to ensure diversity in research.

Secondary Sources

Balch, Bridget. "Why We Know so Little about Women's Health." AAMC News. Last modified March 26, 2024. Accessed December 4, 2024.
https://www.aamc.org/news/why-we-know-so-little-about-women-s-health.
This web article contains many quotes from expert researchers. I used one of the quotes about female researchers' tendency to recruit more female participants in clinical research to show how ensuring the representation of women in leadership positions can help with more gender-diverse clinical trials.

Bowles, L. Elizabeth. "The Disfranchisement of Fertile Women in Clinical Trials: The Legal Ramifications of and Solutions for Rectifying the Knowledge Gap." Vanderbilt Law Review. Last modified May 1992. Accessed January 2, 2025.
https://scholarship.law.vanderbilt.edu/cgi/viewcontent.cgi?article=2378&context=vlr.
I used this review extensively, as it contained a detailed analysis of the reason behind the historical underrepresentation of women in research and why few women lead research. The author also touches upon important events leading up to the NIH inclusion policy. In addition, I integrated quotes from Dr. Healy in my discussion of responsibilities.

Coakley, Meghan, Emmanuel Olutayo Fadiran, L. Jo Parrish, Rachel A. Griffith, Eleanor Weiss, and Christine Carter. "Dialogues on Diversifying Clinical Trials: Successful Strategies for Engaging Women and Minorities in Clinical Trials." *Journal of Women's Health* 21, no. 7 (2012): 713-16. https://doi.org/10.1089/jwh.2012.3733.
The conference touches upon the importance of including women in clinical trials and the responsibilities of sponsors. I used its data on the percentage of African Americans in America compared to in clinical trials, showing how they are underrepresented. I also learned that minorities often prefer physicians of their own race, underscoring the importance of promoting diversity in leadership roles.

Culliton, Barbara J. "NIH Push for Women's Health." *Nature* 353, no. 6343 (1991): 383. Accessed March 22, 2025. https://doi.org/10.1038/353383a0.
This article provides more details about Dr. Bernadine Healy's Women's Health Initiative. I used the premise underlying the movement to connect it to the later establishment of the NIH Inclusion Policy.

Epstein, Steven. *Inclusion: the Politics of Difference in Medical Research*. Chicago, IL: University of Chicago Press, 2007. ProQuest Ebook Central.
This book provided opposing perspectives on the NIH inclusion policy. I used quotes from editors and investigators claiming that the policy will increase the cost of conducting clinical trials, which they believe will reduce the quality of research.

Federman, Daniel, Ruth Faden, and Anna C. Mastroianni. *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*. Vol. 1. Washington, D.C.: National Academies Press, 1994. ProQuest Ebook Central.
This book gives a comprehensive overview of the factors influencing the inclusion of women in research. It was here that I first learned about the NIH's failure to enforce a prior policy, which was exposed by the GAO and led me to explore additional sources. I also referenced its argument that previous policies were overprotective of women and deprived them of valuable information about new drugs.

Floersh, Helen. "Industry, Not NIH, Fronts Most of the Cash for Clinical Trials: Report." Fierce Biotech. Last modified July 14, 2023. Accessed November 14, 2024. https://www.fiercebiotech.com/research/report-industry-not-nih-fronts-most-cash-clinical-trials#:~:text=Ledley's%20team%20found%20that%20the%20NIH%20funding,an%20average%20of%20$33.8%20million%20per%20drug.
This article analyzes the NIH's involvement in funding clinical trials. I used statistics on the NIH's spending and role in developing new drugs to demonstrate the significant influence of its updated inclusion policy on the research community.

Framingham Heart Study. "Participant Cohorts." Framingham Heart Study. Accessed March 22, 2025. https://www.framinghamheartstudy.org/participants/participant-cohorts/.
This webpage includes data about the six groups of participants in the Framingham Heart Study. I used its description of the 1994 omni-cohort to show how the study made efforts to improve racial diversity after the establishment of the NIH Inclusion Policy.

Lippman, Abby. *The Inclusion of Women in Clinical Trials: Are We Asking the Right Questions?* March 2006. Accessed October 23, 2024. https://whp-apsf.ca/pdf/clinicalTrialsEN.pdf.
This book introduces the NIH inclusion policy and discusses other similar policies. I used parts of its intro that talks about activists and health professionals lobbying for a legislative change.

McCarthy, Alice. "Embracing Diversity: The Imperative for Inclusive Clinical Trials." Trends in Medicine. Harvard Medical School. Last modified June 30, 2023. Accessed November 9, 2024.

https://postgraduateeducation.hms.harvard.edu/trends-medicine/embracing-diversity-imperative-inclusive-clinical-trials.
This article from Harvard explains that minorities were underrepresented due to a lack of access to healthcare. I also used a quote from a medical school dean, who claims that one's genes can impact their response to drugs significantly. This reveals the importance of including minorities in drug trials to better understand how treatments affect diverse racial groups.

Merkatz, Ruth B. "Inclusion of Women in Clinical Trials: A Historical Overview of Scientific Ethical and Legal Issues." *Journal of Obstetric, Gynecologic and Neonatal Nursing* 27, no. 1 (1998): 78-84. Accessed January 11, 2025. https://doi.org/10.1111/j.1552-6909.1998.tb02594.x.
This article discusses how changes brought by the NIH inclusion policy will make diverse clinical trials the norm in the future. It also stated the responsibility of the NIH to ensure all research projects include women and minorities, which I included in the responsibility section of my essay.

National Institute of Health. "Dr. Bernadine Healy." Changing the Face of Medicine. National Institute of Health. Last modified June 3, 2015. Accessed December 2, 2024. https://cfmedicine.nlm.nih.gov/physicians/biography_145.html.
This article provides a summary of Dr. Bernadine Healy, the director of the NIH at the time of the NIH inclusion policy. I used this to introduce Dr. Healy as an important figure who brought about the NIH inclusion policy and launched the Women's Health Initiative.

Schwartz, Aaron L., Marcella Alsan, Alanna A. Morris, and Scott D. Halpern. "Why Diverse Clinical Trial Participation Matters." *New England Journal of Medicine* 388, no. 14 (2023): 1252-54. https://doi.org/10.1056/nejmp2215609.
This journal article provides examples of why clinical trial diversity matters, such as improving the generalizability of research findings and producing new biological insights. I used this to show how women gained the right to be informed of sex-specific drug effects.

Snell, Maryann Teale. "Healthy Woman: Bernadine Healy '65." Vassar. Last modified 2004. Accessed January 12, 2025. https://www.vassar.edu/vq/issues/2004/03/features/healthy-woman.html#:~:text=Healy%20has%20played%20a%20key,diseases%20affecting%20women%20over%2050.
This interview provides a first-hand account of the life of Dr. Healy, the director of NIH who brought about the NIH inclusion policy. I used the section of the interview that discusses her work after launching the Women's Health Initiative.

Southall, Jennifer R. "Disparities Persist in Clinical Trial Leadership across Specialties." Women in Oncology. Healio. Last modified October 30, 2023. Accessed December 4, 2024. https://www.healio.com/news/hematology-oncology/20231030/disparities-persist-in-clinical-trial-leadership-across-specialties.
This article summarizes the results of multiple studies on the gender makeup of research principle investigators and argues that women are underrepresented. I used the statistic of

the percentage of women leading research to suggest a possible aspect of inclusion to address in the future.

Tsao, Connie W., and Ramachandran S. Vasan. "Cohort Profile: The Framingham Heart Study (FHS): Overview of Milestones in Cardiovascular Epidemiology." *International Journal of Epidemiology* 44, no. 6 (2015): 1800-13. https://doi.org/10.1093/ije/dyv337.
This journal article summarizes the history and findings of the Framingham Heart Study. I used their summary of the purpose of the study and their comment on the predominantly white composition of the original cohort.

Weisman, Carol S., and Sandra D. Cassard. "Health Consequences of Exclusion or Underrepresentation of Women in Clinical Studies (I)." In *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*, edited by Daniel Federman, Ruth Faden, and Anna C. Mastroianni, 35-40. Vol. 1. Washington, D.C.: National Academies Press, 1994. ProQuest Ebook Central.
This book gives a good historical summary of events leading up to the NIH inclusion policy. I referenced their summary of the Thalidomide disaster in my background section to show how concerns over fetal safety led to the previous exclusion of women from clinical trials through the 1977 FDA policy.