Inequities in Clinical Trials: Impact on Women

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You fall and scrape your knee. Naturally, you clean the cut and put on a band-aid. Because of the band-aid, you continue with your day, feeling confident that the band-aid will protect your cut. This is a remedy to a small, but real, problem.

Of course, medical issues can get far more elaborate than this and require more complicated solutions. We are made up of trillions of cells and 11 major organ systems that must interact daily (Cooke, 2023). Due to the complexity of these systems, there is no simple band-aid for many of the diseases, illnesses, or disorders that affect millions of people every day, especially the chronic ones. As a result, many people with complex medical needs enter periods of trial and error, where they experiment with different medicines until they find one that works best for them.

I was one of those individuals.

When I was nine years old, I was diagnosed with Crohn's Disease, but my complications got more severe in high school. For a few years, I kept trying different medications, dealing with unexpected side effects, and then facing defeat. This cycle felt endless. Going through this experimental trial made me wonder why my trillions of cells were failing me; why were my organs not communicating and working together like everyone else's? Eventually, I found a medicine that appeared to work. However, I only felt relief for a split second. This medicine controlled my disease but created new, unexpected side effects, requiring me to seek care from another specialist. When I asked my provider why this was the case, she did not have an answer.

The medicine for me—the one that was made to provide my relief—was not created with women in mind. Historically, women have been underrepresented in clinical trial testing in the U.S. This disparity means that women are more likely to experience adverse effects from medications and inequities in their treatment.

Clinical trials are important in healthcare because they provide a structured opportunity for researchers to innovate, learn about possible new treatments, and ensure that all medications are safe and effective before entering the market. Clinical trials are conducted in four phases. In Phase I, 20 to 80 people participate to judge the drug's safety. In Phase II, researchers recruit more participants and begin to evaluate efficacy, along with safety. In Phase III, the study expands to hundreds and thousands of participants, allowing researchers to study different populations and dosages. At this point, if researchers can prove that the drug is safe and effective in addressing a specific health concern, the FDA will approve it. Researchers will still engage in Phase IV testing to monitor the drug's use in diverse populations and uncover possible side effects from long-term use (NIA Scientists, 2023). The nature of the clinical trial process allows those involved in testing to drastically impact how researchers understand a drug and its interactions within the human body. Yet, the majority of study participants are biologically male, even though 51% of the population are biologically female (Balch, 2024). This means that we have significantly less knowledge on how drugs in the market react in a biologically female body, compared to a male one.

This pattern is something we have seen throughout history, though it worsened from 1957 to 1961. In Europe and Australia, thousands of women took Thalidomide to manage morning sickness. Later, it was revealed that the drug caused severe birth defects in over 10,000 children (Unachukwu, 2021). As a result, policy makers capitalized on this fear to justify excluding women from clinical trials. In 1977, the FDA introduced regulations to prohibit all women of

childbearing age from participating in clinical trials, unless they had a life-threatening condition. The objective of this was to protect women's fertility; in reality, researchers wanted to test medications without thinking of or unintentionally harming any woman's reproductive system (Jakubek, 2024). This perpetuated the mindset that the biologically male body was the easier one to work with and that the female's reproductive system was a burdensome complication. This gave researchers permission to cater their studies toward males, without adapting research to females too.

It took until 1993 for the NIH to identify and attempt to reverse this injustice. The NIH Revitalization Act of 1993 required all clinical trials that receive federal funding to include "women and minorities" (Mazure, 2015). Even though this is a positive step forward, there are still significant barriers in improving equity in clinical trials. For example, the government funds most clinical trials, but approximately 40% of clinical trials in 2017 were funded by private, for-profit companies (Hokoum, 2017). This means that not every drug that enters the market must follow these equity standards. Additionally, while the provisions of this act apply to all future testing, it does not change the past. Many prescribed drugs on the market now were approved by the FDA before 1993, and do not need to undergo retesting. Even though there have been significant strides forward, especially with better female representation in Phase III clinical trials, we must recognize that there is still underrepresentation, especially in Phase I and Phase II studies (Fultinavičiūtė, 2022). Dosing regimens used in Phase III are based on pharmacokinetic data from Phase I and Phase II, meaning exclusion from any phase of the clinical trials is harmful.

Despite efforts to increase the enrollment of women in clinical trials, progress has stalled. A study by Contemporary Clinical Trials looked at federal data covering over 300,000 participants. Despite being the leading causes of death

for women, only 41.9% of participants in cardiovascular research and 41% in cancer research identified as women. The disparities are even worse for mental health: 60% of people with psychiatric disorders are women, but women only make up 42% of clinical trial participants. This signifies an improvement from the late 1900s, but still shows opportunity for growth (Blakemore, 2022).

Because of this history, women are more likely to be overmedicated or face adverse side effects from medicines in the market. Males and females metabolize medicine differently due to differing sex hormones. These hormones, which can be impacted by menstruation, pregnancy, menopause, or oral contraceptives, affect how the body breaks down medicine. Without equivalent testing, there is no definitive way of knowing how a biologically female body may react to a medicine. For example, Irving Zucker, a professor emeritus of psychology and integrative biology at UC Berkeley, and Brian Pendergast, a professor at the University of Chicago, conducted a study on the sleep medication Ambien. They revealed that women experienced stronger side effects than men in over 90% of the cases and experienced adverse effects at twice the rate of men (Pratt, 2020). Additionally, Zucker and Pendergast found that there were sex differences in how the body broke down 86 different medications, including aspirin, morphine, and sertraline (Lerner, 2020).

These shortcomings in research contribute to inequities in health access. Consider cardiovascular disease: the number one cause of death for men and women in America. Women die at higher rates from cardiovascular disease than men, but the warning signs are analyzed through a male perspective (Unachukwu, 2021). During a heart attack, both men and women will likely identify chest discomfort. However, women are more likely to also identify nausea, fatigue, and breathlessness. Since heart attacks are a condition more commonly studied on men, people who present these other symptoms are thought of as “unusual cases.” In

other words, the way a heart attack manifests in a woman is “unusual” compared to a man’s presentation, which is the socially constructed norm. As a result, in an emergency room, women with chest pain wait 11 minutes longer than men to receive treatment, are less likely to receive an electrocardiogram, and are less likely to be hospitalized. With this information, it is not surprising to learn that between 2010 and 2017, women made up only 27% of research participants in studies concerning coronary artery disease (Corliss, 2022).

Our understanding of the human body and medicines has grown tremendously, but that knowledge is not spread equitably. We know that there are differences between biological males and biological females, and instead of embracing and learning more about these differences, researchers have attempted to ignore it. I am still enduring the impacts of taking a medicine that was not tested on women; I still hold onto the helplessness I felt in high school, the feeling like no medicine was made for me; I still hold onto the frustration I had at my provider when my new symptoms appeared, but now an understanding that she had no studies or trials to reference. Without equitable access and participation in clinical trials, women will continue to face adverse impacts. We must work to ensure that clinical trial access is available to all people, regardless of sex, gender, race, religion, and socioeconomic status.

There is no easy band-aid for more complicated medical problems, and that is okay. But it would be better if the band-aids we gave women to cover their cuts did not give them bruises too.

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