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## **Author** Pandey, Shrina

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## A HISTORY OF ANDROCENTRISM IN AMERICAN CARDIAC PATIENT RESEARCH

## Shrina Pandey

Public Health and Health Sciences Undergraduate Laboratory at Berkeley

University of California, Berkeley

Androcentric beliefs perpetuate a worldview that men are the representative prototype of the species, to which women compare as deviant and faulty (Hibbs 2014). In the context of medicine, androcentrism persists in the examination of feminine and intersex anatomy as a physiological variant of the male sex, the usage of metaphors loaded with sexist symbols, and the historical justification of women as subordinate to men (Miqueo 1999). The historical consequences of androcentrism in 20th-century North American cardiac research were life-threatening and one-sided with impacts that ripple to the present. Unfortunately, medicine turned a convenient blind eye to the basic standard of survival as the rationale for equity in research and practice.

While significant work is underway to identify the parameters and solutions to androcentrism in clinical practice, millions of women experience the downsides of a historically accumulated dearth of clinical data for many cardiovascular conditions. This paper identifies the historical arguments and sociocultural biases of cardiovascular clinical trials and case studies in 20th century United States.

#### Atherosclerosis and Inequality in Cardiac Intervention

A prime example of androcentrism in cardiology is the juxtaposition of treatment provided to men and women experiencing atherosclerosis in the early 20<sup>th</sup> century.

Ruth Brewster Sherman, a graduate from the John Hopkins School of nursing spent years writing striking expositories that debuted publicly in papers in the *American Journal of Nursing* and privately in letters to the editor and her friends (Sherman 1908). Among a compendium of medical works, her 1912 report on arteriosclerosis which describes a general hardening of the heart, due to increased deposition of calcium that impedes blood flow, was especially revealing (Sherman 1913). She provided an analysis of the nature and demographics of reported clinical cases concerning sclerosis in the early 20<sup>th</sup> century:

Nearly all old people have become, or do become, more or less sclerotic, so that the condition is often found in elderly women. But we most commonly see it in men of fifty-five or sixty years, who, after lives of active work and mental strain, hearty eating and frequent alcoholic drinking, are suddenly stricken down upon beds which they too often never leave again. (p. 583)

Sherman's description of the pathological lead-up to arteriosclerosis demonstrated that health professionals were well-aware that women would succumb to the disease later in life, while males were more commonly observed with the condition in middle age. And her observations of sex-based demographical breakdowns match those of contemporary research.

Contemporary studies have found that the most common and important pattern of arteriosclerosis - atherosclerosis - is the leading cause of death of men and women in the United States and worldwide (Potru 2018; Lim et al., 2010; Brophy et al., 2017). Men and people assigned male at birth are more likely to develop and die from the disease at a younger age of 40-60 years (Roger et al., 2011). However, in individuals during menopause transition (MT), the endogenous hormone composition alters, creating adverse changes in body fat distribution, lipids, and lipoproteins (El Khoudary et al., 2020). Post-MT individuals are more likely to start developing atherosclerosis (Regitz-Zagrosek 2006). The observed result is that there are more women and

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individuals assigned females at birth who are "living with" atherosclerosis at an older age (Regitz-Zagrosek 2006; Villablanca et al., 2010).

Once contextualized, the 1924 article in the American Journal of Nursing by Dr. John Wycoff, M.D. is especially unveiling when he questions whether *senescent* heart conditions should be considered a disease (Wycoff 1924):

"Senescent heart disease is the type which is found in elderly people. It is really a question as to whether it should be called disease. Every species of living thing has an average length of life." (p. 529)

The rest of the article argues that there is an increased need to distinguish between different symptoms of *toxic* heart disease that occur earlier in human life and highlights that it is essential to enhance the care for affected patients (Wycoff 1924):

Fine judgment is frequently needed to determine whether a diseased heart needs more or less exercise (...) An intelligent understanding of what these causes are, how they can be avoided, and how remedied when they do occur is essential to the proper care of the cardiac patient. (p. 532)

Inherently, Dr. Wycoff's work advocated for tailored attention and care for the same diseases that are more susceptible to males at an earlier age. Historians Kathryn King and Pauline Paul argue that intentional or not, based on a pure statistical breakdown, Dr. Wycoff's argument implicitly suggested that some populations matter more than others, mandating the medical field's attention and care (Wycoff 1924; King and Paul 1996;). Furthermore, the arbitrary language of categorization reflects a deeply androcentric narrative. The same disease was classified as "toxic" in younger populations, where more men and people assigned male at birth tend to be affected, and 'questionably a disease' in older populations, where women tend to be more affected. At best, Wycoff's inattention to the accelerated risk of atherosclerosis reflects the medical field's ignorance of the sex-based breakdown of cardiovascular disease. At worst, he intentionally trivializes diseases whose susceptibility compounds once women cross menopause.

One of the more subtle modes of androcentrism arises in androcentric language, whereby the gendered pronoun "he" is assumed to represent an individual of unknown gender (Hibbs 2014). Wycoff's work repeatedly attributed the word "he" with descriptions of symptoms and characteristics of cardiac patients that should apply to men and women. The usage of androcentric language transcends gender pronouns when Dr. Wycoff utilized "men" or "man" in every example of extreme cardiac conditions. And the possibility of the disease in discussion being sex-tailored is eliminated because he only cites general categories of diseases as opposed to specialized conditions.

Dr. Wycoff would have received considerable authority in the eyes of both the medical community and the general public. In the same year that he published this review, he played a key role in the formation of the New York Heart Association, becoming its chairman. Within the succeeding decade, he became the chairman of the association and then the president of the American Heart Association ("John Wyckoff"). The success met by Dr. Wycoff suggests that not only did his work meet the standards of medical literature, but it influenced readers with an authoritative ethos. The example of a leading practitioner in cardiac research and the inattention to the accelerated risk of atherosclerosis in individuals post-MT supports the qualitative

inference that and rocentric beliefs had a pervasive role in atherosclerosis research in the early  $20^{\scriptscriptstyle th}$  century.

#### Aortic Aneurysms and Bias In Research

The 1923 report of Dr. Lucke and Dr. Rea from Volume 81 of the Journal of American Medical Association (AMA) studied the "shape, size, position, direction, and effect on neighboring structures of aortic aneurysms." The researchers studied aortic aneurysms from 263 postmortem cases in the Philadelphia General Hospital and the Hospital of the University of Pennsylvania (Lucke and Rea 1923). The AMA bore significant medical authority even in the 20<sup>th</sup> century. Just 4 years after the data used in this report was published, the AMA Council issued the first list of hospitals approved for residency training (AMA History).

This paper, however, will focus on extracting all sex-based statistics – one of the several demographics peripherally listed in the study.

Aortic Aneurysm Location	Male Subjects	Female Subjects	Total Subjects	Total Cases
Ascending Arch	48	11	59	62
Junction of Ascending & Transverse Archs	19	4	23	23
Transverse Arch	39	6	45	46
Descending Arch	35	3	38	42
Entire Arch	17	2	19	19
Thoracic Arch	25	2	27	31
Abdominal Arch	32	6	38	40
Total cases of aneurysms	215	34	249	263

**Fig 1. Aortic Aneurysms Based on Anatomical Location and Sex**. The study reported more male cases of aortic aneurysms than females. The difference was statistically significant (Independent sample t-test, t(df) = +1.92, p < 0.037734, Table 1).

The sample revealed an expected sex-based difference found in contemporary literature - that men were more frequently affected by aortic aneurysms than women (Harthun 2008). Dr. Lucke and Dr. Rea's 1923 research studies the type, size, shape, location, and frequency of aneurysms from this largely homogeneous sample where the majority of cases were men (Lucke and Rea

1923). Conclusions drawn from data where males can offset women contain a subtle and unacknowledged bias of the male-centered paradigm. This androcentric perspective has historically led biomedical researchers to conduct their observations on males, such as anatomical shape and physiological severity. As a result, we have a dearth of information about women and individuals assigned females at birth (Upchurch 2020).

For example, Dr. Locke and Dr. Rea reported a large size of aneurysms in the thoracic aorta:

In the thoracic aorta the aneurysms are commonly large and extend posteriorly and to the left, eroding the vertebrae and ribs, and rupture into the left pleura and the lung. (p. 1170)

However, in current literature, several researchers have recognized that these descriptions of aortic size have historically disadvantaged women and individuals assigned females at birth, who are usually of smaller height and baseline aortic diameter (Chung et al., 2020). Specifically, a thoracic aortic aneurysm (TAA) of a 4.97 cm diameter in a woman was found to correlate with 6.0 cm in a man (Forbes et al., 2010). Indexing aneurysm size to body size or surface area was found to be more accurate for making clinical decisions to manage and treat TAAs (Davies et al., 2002).

The historically accumulated dearth of clinical data for women has direct repercussions (Upchurch). TAAs have an accelerated rupture risk even at smaller diameters in women and individuals assigned females at birth than men (Davies et al., 2006). The outcomes are also poorer with a faster growth rate, higher risk of acute syndromes, and smaller survival gains even post-treatment (Boczar et al. 2018; Mehta et al., 2012). Thus, despite the higher frequency of male aortic aneurysm cases as compared to women, the severity is lower, requiring practitioners to redirect their analysis and interventions by sex. Furthermore the current data suggest that there are significant differences in vascular anatomy, aortic wall stiffness, and hormonal milieu (Sweet 2011; Boczar et al., 2018; Ailawadi et al., 2004). Women and people assigned female at birth constitute more deaths from TAA and have worse rupture outcomes, underscoring a discrepancy in disease aggression (Cheung et al., 2017). The sex-based differentiation becomes particularly important at the level of describing aspects of the pathological description of thoracic aneurysms such as size and diameter, where rupture risk and health outcome are different by sex (Davies et al., 2006; Chung et al., 2020).

The social construct has positioned the male experience in medicine as central and universal, while the female and intersex experiences are understood as marginal, individual, and divergent from the norm (Hibbs 2014). These male-centered beliefs take effect in research by historically accumulating a deficiency in the medical understanding of the anatomical make-up and physiological activity of females. Practitioners thus have fewer resources to devise appropriate treatments and interventions. While TAA may be just one example, it is far from the only one.

#### Heart Attacks & Mating Status: The Conception of Female Domesticity

A woman's role in Victorian Society was predominantly childbearing and homemaking, with Evolutionary theory and medicine contributing to this prescriptive theory about the nature of women (MacPike 1989). The roots of androcentrism were inherently sown in the soil of theory that further supported the notion that women were inferior to men. It is this very belief that

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allowed the brandishing of Victorian society's hypocritical hold over women's rights to think, act, and love on their own terms.

On this battlefield waged by suffragists, medical men were some of the most influential adversaries since they wielded equally ardent arguments with the forceful blow of science and medicine. For example, Elinor Cleghorn argues in *Unwell Women* that for influential neurologist and asylum physician James Crichton-Browne – whose "whole career was based on upholding male physiological and psychological supremacy" – the evolutionary theory was particularly handy as irrefutable proof of women's mental and physical inferiority. He employed the Darwinist argument that the female human metabolism was supposedly anabolic and dedicated towards nurture and nourishment while the male metabolism was katabolic and thus biologically suited for activity, independence, intellect, and bravery. These remarks lead him and other theorists to conclude that women belonged to a "lower state of civilization" (Cleghorn 2021). In this manner, the theory of evolution and subsequent medical evidence in conjunction with the authority of a physician were actively utilized. Instrumentalizing these central and peripheral routes of persuasion, antifeminists continually propagated the Victorian standard of female domesticity in response to suffragists. This time science was the new pedestal.

Medicine was not only the tool for justifying the argument of the inferiority of women but it was actively utilized in areas that supported the domestic role of women and underutilized in areas that disrupted this presumptive norm. For example, the finding that valve disorder was "potentially fatal to pregnant women" was the "final catalyst for the exploration of cardiac disease in women" (King and Paul 1996). A 1927 study by Dr. Burton E. Hamilton detailed such a shift in the medical community's understanding of heart disease in women within a short span of 5 years:

At first sight, the care of women with heart diseases during pregnancy appears as rather a small problem. Study shows, however, that though this group of women with heart diseases is a small one among all pregnancy cases, it furnishes an astonishingly large percentage of all maternal deaths in pregnancy. Also, within the small group with heart diseases, the maternal death rate and disability rate and baby death rate tend to be discouragingly high. (Hamilton 1927, p. 173)

Concurrently, an analysis of the number of pregnant patients within the same longitude of this study (1922 to 1927) revealed that between 1922-1925, merely 66 pregnant patients with serious heart attacks were cared for and the mortality rate was just over 21%. But from 1925 to 1927, there were 114 pregnant patients of the same condition and the mortality rate had dropped to less than 5%. Dr. Hamilton explicitly noted that the "special care" that had been developed during this short span was able to "reduce greatly the maternal and baby death rate" (Hamilton 1927).

The stark difference in swift mobilization and dynamic innovation for pregnant individuals with cardiac disease can also be compared to the trivialization and inadequate response of older women experiencing atherosclerosis. The Victorian woman's role had been limited to motherhood in the sphere of domesticity. Thus, women beyond the stage of child-bearing were thought to have limited purpose and not in need of attentive care.

Additionally, while researchers galvanized efforts to include women and individuals labeled female at birth in clinical trials when a healthy pregnancy was implicated, they simultaneously

kept them out of other forms of clinical research. Their stated rationale was to protect these individuals from potentially "dangerous" procedures. This historical practice of benevolent sexism has placed barriers on researching diseases in women, especially for individuals of around childbearing age (UpChurch 2020). The cultural norm of benevolent sexism was even formalized between 1967 to 1973 when the United States Food and Drug Administration prohibited women from enrolling in early phases of clinical testing and further discouraged researchers from enrolling women in later phases (Czerniak 2001). As a direct consequence, there is considerably more data about the effects of pharmaceutical drugs and procedures on men than women (Sanfey 2005).

The impacts of the past, ripple to the present. Even though there is increasing awareness of the need to study heart disease in women, the historically accumulated scarcity of data on women still results in limited information on optimal treatment and intervention patterns for these groups.

#### Myocardial Infarction and The Yentl Syndrome: 21st Century Androcentrism

Androcentrism perpetuated through centuries of heart disease research and persists even today, only under a new name - The Yentl Syndrome. Originally the title of a movie about a woman who had to disguise herself as a man to attend school, Yentl was later coined in the medical context by Dr. Bernadine Healy. In her 1991 article, she cites a prospective postinfarction intervention trial that determined that women had angina before myocardial infarction (heart attack) as frequently with more debilitating effects than men, but underwent cardiac catheterization only half as often. Only when women presented with myocardial infarction, were they as likely as men to undergo interventions such as cardiac catheterization and revascularization (Healy 1991).

Being different from men comes at the price of being treated less than equal for most of the recorded time in cardiac treatment (Healy 1991). Women and people assigned female at birth have to present the same symptoms as most men to receive equal treatment, i.e., severe myocardial infarction. Ultimately, these individuals are misdiagnosed and sent home from the hospital during heart attacks at rates seven times more often than men (ACC 2015). And heart attacks remain the leading cause of death among women (CDC 2022).

Furthermore, in *Medical Sexism*, Dr. Jill B Delston describes two disparities that run in tandem. Women and individuals labeled female at birth die at higher rates because they receive worse care and are misdiagnosed (Delston 2019). The driving cause is that their condition is not as well understood. These individuals are severely underrepresented in the statistics that inform treatment and intervention practices (Healy 1991). Clinical trials also significantly underrepresent women of racial and ethnic minority populations relative to their disease burden (Brown et al., 2022; Michos et al., 2021)

Historically, drug therapy was determined based on extrapolating male data to women (ACC 2021). The danger of such practices is the assumption that women and individuals labeled female at birth are physiologic versions of those assigned male at birth. In reality, pathophysiological composition and outcomes are complex and reported to be affected by molecular and hemodynamic differences (Solimene 2010; Sokolis and Iliopolus ; Mitchell et al., 2010). The

lack of representation can have disproportionate life-threatening consequences for women and individuals labeled female at birth, and sex-specific data is necessary for effective and equitable care.

#### **Paths Forward**

Despite differences by sex in clinical presentation and treatment, the clinical approach to men and women has historically remained homogenous (Banco 2021). Women and individuals assigned female at birth are still misrepresented, mismanaged, and misdiagnosed, culminating in greater misfortune across the CVD spectrum (Henry 2021).

A response to the deficiency in data is gynocentric research. Gynocentrism attempts to recenter female experiences by not necessarily replacing a male-centered worldview but challenging its presumed objectivity (Hibbs 2014). In the context of medicine, this could mean devising clinical trials targeted toward women and individuals assigned female at birth, especially for conditions that adversely affect them. Gynocentric research would aim to identify the molecular and physiological changes that occur with aging, hormonal composition, body size, and other female-specific biological risk factors. This is valuable and overdue in a field where the average cardiovascular disease trial enrolls 85% men (Dougherty 2011).

Practitioners must address why women tend to be under-enrolled in clinical trials having greater contact with healthcare service and utilization of its services (Bertakis, et al. 2000; Crews, et al. 2018; Kim et al., 2008). Part of this question will involve understanding mechanisms of how ageism, lack of trust, and logistical barriers such as childcare tend to affect women significantly more than men (Cho et al., 2021). These steps are necessary to generate evidence-based social, cultural, and legislative solutions for the underrepresentation of women in cardiovascular clinical trials.

Additionally, the lack of diversity in clinical leadership is a significant barrier that directly impacts enrollment of women in clinical trials, with clinical trials with women leadership consistently enrolling a larger percentage of women participants (Dougherty 2011; Cho et al., 2019; Reza et al., 2020). However, more than half of the recent cardiovascular trials had no women on the leadership team and only 10% of clinical trial leadership committees are composed of women (Denby et al., 2020). Efforts to change cardiovascular leadership are an important step toward achieving gender parity in clinical trials (Brown et al., 2022).

Historically pervasive androcentrism is confounding because medicine is fundamentally a science, which we expect to hold to the standards of impartiality, justifiability, and ethicality. However, in practice medicine is also deeply rooted in sociocultural factors as much as it is scientific. In this social sphere, men have broadly held the balance of power in patriarchal cultures (Hibbs 2014). However, the medical implications of inadequate treatment must compel practitioners to improve equity in clinical research and representation. Women have unique medical problems, and they must be addressed sex-specifically.

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