

**Research on the Cardiovascular Health of Women:
Or the Lack Thereof**

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Introduction

Most of the research on cardiac medications has been, and is currently being conducted on male patients even though half of the people dying from cardiovascular disease are women. Heart disease is the leading cause of death in America for men, women, and people of most ethnic groups, according to the CDC (Prevalence of Heart Disease - United States, 2005, cdc.gov, 2007). In fact, one person dies from heart disease every 37 seconds in America, adding up to 647,000 people lost each year, or one in every four deaths in America. This is not a recent problem in our society either; the CDC admits that heart disease has been the leading cause of death for the last 80 years. With innovative advancements in technology in recent years, such as machines in Cath labs to help cardio surgeons perform surgeries and virtual image-based fractional flow reserve (FFR) technologies to more accurately measure the narrowing of coronary arteries during catheterization, why haven't health officials solved this problem yet? Considering how many people are unnecessarily lost to this largely preventable disease, American health officials and pharmaceutical companies must develop improved treatments and medications to defeat this epidemic. To do this, we need medications tailored specifically to the biological needs of men's and women's hearts in order to better treat and even cure cardiovascular disease in individuals, rather than in clustered general populations of people. Oncologists tailor their treatments to individuals who have cancer, which often results in better outcomes and fewer deaths of cancer patients, so why shouldn't cardiologists use the same tactic to treat their patients with cardiovascular disease? (Jiang Y & Wang M., 2010). According to the National Cancer Institute (Cancer Statistics, 2018), 606,880 people are expected to die from cancer in 2019 while a relative 655,000 people die of cardiovascular disease in America each year (Heart Disease Facts, 2019). Since the amount of deaths caused by both diseases are so

similar, it seems strange that medical professionals in the different fields take such drastically different approaches to treatment for their patients; researchers have been working on patient-specific treatments to decrease the death rate among Americans with cancer while cardiologists continue to use that same medications and surgical treatments on the majority of their patients with cardiovascular disease, regardless of many biological differences in these patients.

If cancer treatments are patient-specific and tailored to meet the needs of individuals, why aren't cardiologists treating their patients with the same level of specificity, especially since cardiac disease is the leading cause of death in the country? In fact, according to the Center for Disease Control, cardiac disease is the leading cause of death for women as well as men (Heart Disease Facts, 2019). Sadly, it is important to note that women make up only one-third of the people in cardiac medication studies (Complications From Heart Drugs More Common in Women Than Men, 2015). This lack in the research accentuates the need for additional clinical trials for all cardiac medications since the effectiveness and side effects are tailored mainly for men, but may not necessarily be the same for women. Females are being overlooked when it comes to treating cardiovascular disease, which could be a contributing factor in the large number of fatalities seen in women. If pharmaceutical companies, clinical researchers, and cardiologists work to create medications specific to women's biological needs, we may be able to better address and perhaps eliminate around half of the cases and deaths from cardiovascular disease, decreasing the prevalence of such a preventable and ongoing public health crisis.

Furthermore, patient specific treatments for heart disease may be more effective, especially because male and female hearts are structured differently. According to a study by Johns Hopkins University (Male and Female Hearts Don't Grow Old the Same Way, 2015), "In

both sexes, the main heart chamber, the left ventricle — which fills with and then forces out blood — gets smaller with time” meaning that less blood enters the chamber and, therefore, less blood is pumped throughout the body. In men, the cardiac muscle around the left chamber grows bigger with age, causing thicker heart muscle and a smaller chamber. But in women, the lower left chamber either gets *smaller* or stays constant. So, cardiologists prescribe medications to reduce the thickness of the muscle and increase the efficiency of the heart, but in women, this could be detrimental (Male and Female Hearts Don’t Grow Old the Same Way, 2015). If a woman’s left ventricle of her heart is already smaller and the cardiac wall is already thinner than usual, why would doctors prescribe drugs to further reduce its size? This seems counterproductive and harmful to the health of female cardiac patients. Although, research conducted by Harvard Medical School (Gender Matters: Heart Disease Risk in Women, 2006) revealed that Coronary heart disease “claims women and men in nearly equal numbers,” but considering women make up less than half of the patients included in clinical trials and research studies conducted for modern cardiac medications, it is not surprising that the medications do not affect women’s hearts adequately. Moreover, the research being conducted on developing medications to treat it is overwhelmingly focused on tailoring the medications towards men’s biological needs.

Methods

I initially chose my research question of how to best utilize cardiac medications along with other treatments to cure or prevent heart disease because it is a concern that hits close to home. My father and grandmother both have cardiac disease which has caused many concerning health scares in the past. My father was diagnosed with cardiovascular disease when I was just five years old and underwent numerous bypass surgeries, lifestyle alterations, career changes,

and began taking many new medications to manage his symptoms. My grandmother was diagnosed more recently, about two years ago, which was when I noticed that her cardiologists prescribe the exact same medications to her as those that my dad had received, regardless of their stark differences in gender and age. Some may think that medications for cardiovascular disease are universal in that they can mitigate the symptoms of the disease in any patient, but this is not the case at all. I easily discovered that cardiovascular disease manifests itself differently in males and females because their hearts are structurally different. So, how can one medication successfully treat symptoms the same ways in two hearts that differ in structure, and therefore differ in the execution of its functions? Even though teams of experienced cardiologists independently prescribed medications to my grandmother, an 86 year old female, and my father, a 65 year old male, most of the medications were identical between their two lists of prescriptions. They differed only in the daily doses allotted to each individual. If the heart's structure and function is fundamentally different in males and females, how could each medication have the same effect in patients that differ so greatly in age and gender?

The initial research findings indicated that clinical trials for these medications in cardiac patients did not contain as many women as they did men. One important revelation in the research is that men overwhelmingly outnumber women in clinical trials for cardiac medications! Female patients make up about half of the population with heart disease but are being overlooked since their medications are not tailored to their biological needs, as seen through the excessive amount of negative side effects they experience compared to their male counterparts. After researching various specific medications that are common for all cardiac patients to take, it became clear that commercials and other advertisements have been misleading Americans about many of their medications, including one as common as aspirin. Pharmaceutical companies are

taking advantage of older individuals with heart disease by publishing misleading advertisements for their medications. Since clinical trials for most cardiac medications do not include an equal number of female patients as males, although females make up half of the population with cardiac disease, the medications produced by pharmaceutical companies in America do not account for the biological concerns, symptoms, and side effects of women. In response, more clinical trials need to be conducted that include female patients for all cardiac medications in order for them to be considered effective to use in all patients. This will hopefully show that pharmaceutical companies need to develop medications tailored to the biological needs of women.

Cardiac Medications

Since cardiac disease is the leading cause of death for all genders and races in America, as it has been for over 80 years, according to the CDC, one would think that the medications to treat the symptoms associated with cardiac disease would be diverse enough to meet the biological needs of everyone (Prevalence of Heart Disease, 2007). Yet, this is not true of medications for heart disease; pharmaceutical companies, physicians, and credible research facilities in the United States have tailored the effectiveness and allowed the side effects of these medications to meet the needs of men, not women. This highlights the fact that, even in recent modern day America where gender equality is supposed to be present in our society, women are being overlooked when it comes to things as personal as their health and well-being. Although men and women are being prescribed the same medications when diagnosed with the same diseases, their effectiveness differs from person to person mainly depending on gender and age. For example, in men, aspirin prevents heart attack, but in women, it prevents stroke according to

a Harvard Health Newsletter (Aspirin and Women - Age Matters, 2014). A medication as common and as widely used as aspirin does not metabolize the same way in women as it does in men, causing its effects to differ between genders. Now, you would think that this is the only difference in the effectiveness of this widely accepted drug, but it also differs with age.

“Although in men under 65 years old, 100mg of aspirin every other day significantly reduced their risk of a heart attack, it does not prevent heart attacks in women under 65” according to The New York Times (Duenwald M., 2005). Furthermore, a research study conducted by Harvard Health (Aspirin and Women - Age Matters, 2014) revealed that “a daily dose of aspirin is helpful in preventing heart attack and stroke in women over 65 years of age, while it is harmful to women younger than this as it increases the risk of bleeding complications.” This indicates that the effectiveness of cardiac medications differs between age groups, biological genders, and individual people throughout their lifetimes. Henceforth, American pharmaceutical companies must create medications tailored to each specific gender and all age groups in order to help people live longer and maintain their usual lifestyles.

One common type of medication prescribed to cardiac patients are statins, which are “a type of medication that treats high cholesterol, helping reduce the risk of heart attack or stroke” says Dr. Joseph A. Hill from UT Southwestern Medical Center (2019). It is thought that statins like Atorvastatin (Lipitor), a common medication prescribed to patients with cardiovascular disease, are effective at treating cardiac disease in women and men. A 2012 review of statins that included 18 clinical trials led by Dr. Kostis from Harvard Health (Statins and Women, 2012) involving “40,000 women found that statins prevent heart attacks and deaths from coronary artery disease in women just as well as they do in men, including women with risk factors for coronary disease who have not yet had a heart attack.” Results further revealed that statins are

effective for both primary and secondary prevention in women; that is, women with and without existing heart disease were benefited by the use of statins in these clinical trials. Although, Dr. Kostis did mention that women are being underrepresented in clinical trials for statins in her article “Statins and Women” (Harvard Health Publishing, 2012) published in the Harvard Medical Journal when she disclosed, "it is the unfortunate truth that many large clinical trials still don't have great representation of women," and “the lack of evidence may be why women aren't prescribed statins as often as men, despite our high risk for heart disease.” Since statins have different effects in women’s bodies than they do in men’s bodies and in older versus younger individuals, pharmaceutical companies need to create medications that are specific to the biological needs of various genders and ages. One medication is not effective in treating all patients of cardiac disease and, therefore, should not be used as a “cure-all” for this disease. If we want to reduce the amount of people that die in the US from cardiovascular disease, the leading cause of death in America, we must create more personalized medications.

Carvedilol, or Coreg, is another medication prescribed to both my father and my grandmother by separate cardiologists regardless of their age and gender differences. According to the Mayo Clinic (Carvedilol Oral Route, 2020), Carvedilol is in a class of drugs called beta-blockers which “work by affecting the response to some nerve impulses in certain parts of the body.” This medication decreases the workload of the Sinoatrial Node, the part of the heart that generates electrical impulses to stimulate heartbeats, which in turn, decreases the heart's need for blood and oxygen and helps the heart to beat more regularly since it doesn't need to work to supply so much blood to itself. The lack of research distinguishing the effects of this medication on women and men leaves a gap in the research as it is unclear how many women compared to men participated in clinical trials during the development of Carvedilol. A study by

the National Library of Medicine on The Effects of Carvedilol (n.d.) instructed 415 patients to take low daily doses of carvedilol for two to three weeks and engage in a six minute walk each day. After six months of this treatment, half of the participants were randomly chosen to cease medicinal treatment and take a placebo instead but continue their six-minute walk for the next six months. The study revealed that the six-month treatment with carvedilol “improved left ventricular function and maintained exercise performance at a lower rate pressure product, but symptoms assessed by functional class were slightly worsened.” The details of this study did not reveal the number of women and men that participated in the trial nor the age differences between participants. However, since we don’t know how many women took part in this study, it seems that Carvedilol is an effective medication for use in cardiac patients overall, disregarding gender and age differences. Currently, it is unclear whether Carvedilol is more effective at managing symptoms of cardiovascular disease in men than in women or if the side effects from this medication are more manageable for males than females. Thus, more studies need to be conducted to reveal the true effectiveness of Carvedilol in women and men since many other cardiac medications have been proven to metabolize themselves differently in these two genders, rendering them less effective.

Another medication usually prescribed to most cardiac patients regardless of gender or age is Clopidogrel, or Plavix, which “is given to reduce the risk of heart attack, unstable angina, stroke, and cardiovascular death in patients with cardiovascular disease. Plavix works by decreasing the activity of blood cells called platelets, making platelets less likely to form blood clots” (Center for Drug Evaluation and Research, 2017). Plavix is very useful in preventing stroke and heart attacks after a person has already had one of these episodes, but it is worthy to note that “some patients do not convert Plavix to its active form [due to low CYP2C19 activity]

as well as other patients. These patients may not get the same benefit from Plavix and are known as poor metabolizers.” In fact, research by Dr. Dean from the National Center for Biotechnology Information (Dean L., 2018) indicates that individuals who carry two nonfunctional copies of the CYP2C19 gene are classified as CYP2C19 poor metabolizers. They have no enzyme activity and cannot activate clopidogrel via the CYP2C19 pathway, which means the drug will have no effect. Approximately 2% of Caucasians, 4% of African Americans, and 14% of Chinese are CYP2C19 poor metabolizers. This is just one instance that highlights the need for patient-specific medications for people with cardiovascular disease. Although the effects of Clopidogrel do not differ by gender or age of the person taking it, pharmacists and cardiologists need an alternative option for their patients who are CYP2C19 poor metabolizers. Surely medical professionals do not ignore the needs of these patients, but I could not find any alternative medications that cardiologists might prescribe to their patients instead of Clopidogrel. This instance highlights the need for more clinical trials on CYP2C10 poor metabolizers in order to find medications that meet their biological needs.

Conclusion and Point

Cardiovascular disease is partially hereditary and partially caused by poor lifestyle choices such as eating a fatty diet and not engaging in brisk exercises overall, but after a person develops heart disease, there is no going back. Patients can regain partial function of their heart muscle and partially clear their arteries of plaque using various surgical and natural remedies, but people diagnosed with cardiovascular disease will never be undiagnosed; the symptoms and reality of the disease can improve, but patients will never be fully cured. Even though cardiovascular disease is equally as prevalent in women as it is in men, pharmaceutical companies continue to develop and distribute medications tailored to men’s hearts and biological

needs. This could play a large role in the massive amount of deaths from cardiovascular disease each year. One medication might not cure the disease of a muscle that is anatomically different in women and men. Since women's hearts are smaller overall and function fundamentally differently than men's hearts, it is likely that the medications designed to alleviate symptoms and improve the function of the heart in men do not have nearly the same effect on women's bodies. If pharmaceutical companies and researchers developed medications tailored to women's hearts, then there is a possibility that many of the unnecessary deaths from cardiovascular disease each year could be prevented. In the modern world of supposed equal rights, one would expect health-related gender disparities to be long gone, but women continue to be largely underrepresented when it comes to the matter of their healthcare! Pharmaceutical companies must develop and distribute medications for cardiac disease tailored to women's hearts, women's needs, and women's bodies if we want to curb the mortality rate of cardiovascular disease in America. Average American people, especially those with low socioeconomic status who are most likely to develop cardiovascular disease, must be aware of their risk and armed with information and strategies to prevent themselves from developing it. If we want to slow or stop the prevalence of cardiovascular disease, the leading cause of death in America, pharmaceutical companies must develop medications and treatments tailored to individuals' biological needs which includes that of women.

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