

“Book on Hysteria”

Unpublished

M. Darlington

Edited by

Michele Ford

Hi Nancy,

Here's the style sheet and copyedited manuscript for BOOK ON HYSTERIA. I edited mostly for proper punctuation and grammar, clarity, and accuracy.

#### **Medical terms and names of scholars**

- The author frequently misspelled the names of illnesses, like Briquet's syndrome, Yentl syndrome, and dysmenorrhea. I tried catching all of the misspellings, but I encourage an editor unfamiliar with this manuscript to do another look-over for any I missed.
- Several scholar/doctor names were misspelled. I did my best to catch all of them. For posterity, I added every scholar the author quoted to the style sheet.
- The author inconsistently used "Dr." to refer to the quoted scholars. I figured the author did this to avoid repetition, but it's worth checking in with the author to make sure. I did not change or add any instances of "Dr."
- It appeared the author did not fact-check her work. I found several books and organizations that were cited incorrectly. When working with this author in future, I suggest treating her quotations with care.

#### **Endnotes**

- I mentioned this in the style sheet, but it bears repeating: endnotes belong at the end of a sentence, at the end of a quotation, or, rarely, at the end of a clause. Also, endnotes should be in Arabic numerals, not Roman. The latter is a quick change; the former is a more intensive alteration the author should undertake.
- There's one footnote, my page 100, that can be removed from the manuscript entirely.
- I found several instances where the author seemed to be quoting from material or providing information that did not have a source. I queried where appropriate.

#### **Quotations**

- Several quotations had non-American spellings. I left them in to maintain the accuracy of the quotations.
- A few quotations from the author's interviews were improperly punctuated. I did my best to punctuate them in the most nonintrusive, elegant way possible.

#### **Tone**

- For the most part, I removed scare quotes. The author makes it clear that she disagrees with terms and phrases like "it's all in your head," and the overuse of scare quotes bogged down the manuscript. By removing the scare quotes, I hope the manuscript is more legible.
- The author overused italics as well. I left italics when introducing an unfamiliar medical term, but removed italics when used for emphasis.

There are some other, more specific items in my style sheet. Please contact me if you have any questions.

Best,  
Michele Ford

## Style Guide for Darlington

I have used the following reference materials for my editing:

- *The Chicago Manual of Style*, 16th edition (University of Chicago Press, 2010)
- *Merriam-Webster's Collegiate Dictionary*, 11th edition (2004 and online)

The following is a list of troublesome terms, including all names referenced in the manuscript. They have been checked for accuracy.

<p><b>A-C</b>            a priori (<i>not italicized</i>)            Addison's disease            American Autoimmune Related Diseases Association; AARDA            American Heart Association; AHA            anti-NMDA receptor encephalitis            antidepressant            Atkins, Chloë; Atkins            atherosclerosis            attention deficit disorder; ADD            autoantibody            Barbra Streisand Women's Heart Center            Black Woman's Health Imperative            Blount, Linda; Blount  <i>The BMJ (the British Medical Journal)</i>            Briquet's syndrome (<i>also</i> somatization disorder)            Beard, George; Beard            Bynum, W. F.; Bynum            Cahalan, Susannah; Cahalan            Charcot, Jean-Martin; Charcot            Chiamonte Gabrielle R.; Chiamonte            chronic fatigue syndrome            chronic obstructive pulmonary disease; COPD            Clarke, Edward H.; Clarke            conversion disorder            Corea, Gena; Corea            coronary artery disease; CAD (<i>and</i> obstructive CAD, nonobstructive CAD)            Crohn's disease            Croskerry, Pat; Croskerry            CT scan</p>	<p><b>D-F</b>            data (<i>plural, not singular</i>)            Dalmau, Josep; Dalmau  <i>Diagnostic and Statistical Manual of Mental Disorders; DSM</i>            diagnostic errors            dysmenorrhea            ectopic pregnancy            Edelberg, David; Edelberg            Edwards, Laurie; Edwards            Ehlers-Danlos syndrome            Ehrenrich, Barbara; Ehrenreich            Ehrlich, Paul; Ehrlich            English, Deirdre; English            electrocardiogram; ECG            electroencephalogram; EEG            Epstein, Steven; Epstein            ER            European Organisation for Rare Diseases            factitious disorder            fibrinolytic            Finger, Stanley; Finger            functional (<i>on its own, used similarly to somatoform</i>)            functional somatic syndrome            Frances, Allen; Frances            Freud, Sigmund; Freud            Freudian            fibromyalgia</p>
<p><b>G-I</b>            Gawande, Atul; Gawande            gestational diabetes mellitus</p>	<p><b>J-L</b>            Jacobi, Mary Putnam; Jacobi            Jutel, Annemarie; Jutel</p>

<p>Gilman, Charlotte Perkins; Gilman  Google (<i>verb</i>)  Graber, Mark; Graber  Graves' disease  Groopman, Jerome; Groopman  gynecology  Hamberg, Katarina  Harvard School of Public Health  Hashimoto's thyroiditis  HDL cholesterol  health care <i>as a noun</i>; health-care <i>as adj.</i>  Healy, Bernadine; Healy  heartsink patients  <i>Helicobacter pylori</i>  Hippocratic  Hoffmann, Diane E.; Hoffman  horror autotoxicus  Howell, Mary C.; Howell  Hunt, Harriot; Hunt  Hunt, Kate; Hunt  hyperthyroidism  hypochondria; -driac, -driacal, -driasis  hypothyroidism  hysteria  idiopathic low back pain  interstitial cystitis  irritable bowel syndrome  ischemic heart disease</p>	<p>Kennedy, Angela; Kennedy  Khan, Abid; Khan  Klonoff, Hope; Klonoff  knowledge-mediated bias  Ladd, Virginia; Ladd  Landrine, Hope; Landrine  Lasègue, Charles; Lasègue  Lennane, K. Jean; Lennane  Lennane, R. John; Lennane  Lipowski, Zbigniew J.; Lipowski</p>
<p><b>M-O</b>  M&amp;M'S  malinger  McGregor, Alyson; McGregor  medically unexplained symptom; MUS  menopause  Merz, C. Noel Bairey; Merz  mIU/L; milli-international units per liter  Micale, Mark S.  Mieres, Jennifer H.; Mieres  Mitchell, Silas Weir; Mitchell  Munch, Shari; Munch  myasthenia gravis  myocardial infarction  Nakazawa, Donna Jackson; Nakazawa  National Institutes of Health; NIH</p>	<p><b>P-S</b>  Pall, Martin; Pall  Pericarditis  PhD  Pollak, Thomas A.; Pollak  preeclampsia  primary ciliary dyskinesia  psych-out error  psychoanalysis  psychogenic pain disorder (<i>also</i> pain disorder)  psychosomatic (<i>also</i> psychosomatic medicine)  Ratner, Vicki; Ratner  Renaissance  rheumatoid arthritis  Rose, Noel; Rose  Roussel, Pierre; Roussel</p>

<p>neurasthenia  neurosyphilis  Nobel Laureate  nosological  O’Leary, Diane; O’Leary  O’Rourke, Meghan; O’Rourke  ob-gyn  open-heart surgery</p>	<p>Sanders, Lisa; Sanders  schizoaffective disorder  Schroeder, Rep. Patricia; Schroeder  Shomon, Mary; Shomon  Singer, Isaac Bashevis; Singer  Sjögren’s syndrome  Slater, Eliot; Slater  Smith-Rosenberg, Caroll; Smith-Rosenberg  somatic symptom disorder; SSD  somatization  somatizing disorders; somatizing patient  somatoform disorders (<i>different from</i> somatization disorder/Briquet syndrome)  Sontag, Susan; Sontag  Stekel, Wilhelm; Stekel  <i>stigmata diaboli</i>  Sydenham, Thomas; Sydenham</p>
<p><b>T-V</b>  Talley, Colin L.; Talley  Tarzian, Anita J; Tarzian  teratoma  Thomas, Laurie Endicott; Thomas  thyroid-stimulating hormone; TSH  triglyceride  troponin  type 1 diabetes  type 2 diabetes  Umeå University  undertreated  undifferentiated somatoform disorder  uterine  vulvodynia</p>	<p><b>W-Z</b>  Weetman, Anthony; Weetman  Weisman, Carol; Weisman  Wendell, Susan; Wendell  Willis, Thomas; Willis  WomenHeart Science &amp; Leadership Symposium  Wood, Ann Douglas; Wood  workup; workups  X-ray  Yale School of Public Health  Yentl syndrome</p>

**Abbreviations**

- Abbreviations were checked for accuracy and left in full caps. It’s the designer’s choice to use small caps or not.

**Dates**

- Eras (BC and AD) changed to BCE and CE, caps, no periods. (CMS 9.35)

**Endnotes**

- Per CMS 14.21, endnotes should be in Arabic numerals (1, 2, 3...), appear at the end of sentences or occasionally at the end of a clause, and follow quotations.

**Formatting (text)**

- Commonly used Latin words and abbreviations are set in Roman type, not italics. (CMS 7.53)
- Pared down italics when used for emphasis.

- Spaces after paragraphs were removed silently. When viewing the markup, it looks like spaces were added after paragraphs; this is not the case. Turn markup off to view the proper formatting.

**Names**

- Names with initials will be open and with periods; *W. F. Bynum*. (CMS 10.12)

**Numbers**

- Spell out zero through nine; use numerals for 10 and higher, except in dialogue. (CMS 9.2)
- Avoid *and* in such expressions as “one hundred fifty.” (CMS 9.5)
- Large numbers, for the most part, are in numeral form; “12,000” instead of “twelve thousand.”

**Punctuation**

- All apostrophes and quotation marks have been changed to typographer’s quotes when applicable.
- Em dashes were replaced by commas when appropriate to avoid overuse.
- Commas inserted around “too” when used at the end of a clause or sentence to mean “also,” as in “it persisted when it came to more long-term pain management, too.”
- Ellipses will be marked with the proper glyph, not three spaced periods.
- Pared down scare quotes to avoid overuse; for the most part, the tone of the manuscript implies the author disagrees with the use of terms like “hysteria” and “‘typical’ heart attack symptoms.”
- Colons will be followed by a lowercase letter, unless the colon introduces a quotation or a list of items in full sentences.

**Quotations**

- Quotations with non-American spelling were left untouched.

## PART 2

### Invisible Women in a “Male Model” System

#### Chapter 3

#### Heart Disease

On a spring morning in 2008, Carolyn Thomas<sup>1</sup> was out for an early morning walk in her Victoria, British Columbia, neighborhood, when a pain—“a cross between crushing heaviness and a severe burning sensation”—hit her smack in the center of the chest, then wandered up into her lower throat. Suddenly sweating profusely, she felt like she was going to vomit. A prickling sensation traveled down her left arm. For about 20 minutes, she clutched a tree trunk and, frightened, fruitlessly scanned the empty block for any passersby who could help. Eventually her symptoms ~~had~~ let up enough to let her slowly continue walking ~~toward~~ home.

It was the arm that convinced Carolyn to stop by the local emergency room; she vaguely remembered hearing that left arm pain could be a symptom of a heart attack. And she’d literally be passing the hospital on her route anyway, so she might as well make sure it wasn’t a heart attack. In the ER, she was quickly whisked through the standard diagnostic protocol for patients with chest pain. But when the tests came back normal, the ER physician assured her that her heart was fine. He confidently told Carolyn, an active public relations professional who had

celebrated her ~~fifty-eighth~~58th birthday the day before, that she was “in the right demographic for acid reflux.” When she asked, “But doctor, what about this pain down my left arm?” a nurse reprimanded her for “questioning” him.

Flushed with embarrassment, Carolyn apologized to the ER staff for wasting their time and went home. But over the next two weeks, despite popping Tums like candy, her symptoms only got worse. Soon she’d have ~~to pause~~ to rest after just five steps, “~~but~~ hey, at least I knew it wasn’t my heart!” Finally, her symptoms became so severe on a five-hour flight home from a family visit back east that, upon landing, she went straight back to the ER. Even then, she didn’t think it could be her heart; the doctor, after all, had been quite definitive on that point. But this time, Carolyn was told she’d had two heart attacks on the flight. She was diagnosed with a 95 percent blockage in her left anterior descending coronary artery, the type of heart attack so deadly that doctors ~~—tellingly—~~ call it “the widowmaker.”

**Commented [MF1]:** Transition needed here; the reader jumps from viewing past Carolyn to hearing present Carolyn talk in the past tense. Could restructure the sentence to say “Soon she’d have to rest after just five steps, but at least she knew it wasn’t her heart.”

### How the Leading Killer of Women Came to ~~b~~Be a “Man’s Disease”

In 1964, the American Heart Association (AHA) held its first official conference on women and heart disease. Advertised “for women only,” it was called “Hearts and Husbands: The First Women’s Conference on Coronary Heart Disease.”<sup>ii</sup> Ten thousand women gathered in Portland, Oregon, to get tips on how to keep their husbands from developing heart disease and to care for them if they did. It would be another ~~twenty-five~~25 years before the AHA held a conference that was ~~actually~~ about heart disease *in* women. In 2016, the association released its first official



scientific statement<sup>iii</sup> on the topic; ~~over fifty~~more than 50 years after that first conference, ~~it~~the AHA declared that despite some progress over the last two decades, heart disease “remains understudied, underdiagnosed, and undertreated in women.”

Given this history, you could be forgiven for thinking that heart disease is rare in women. In fact, cardiovascular disease~~s~~s, which along with coronary artery disease~~s~~s (the most common cause of heart attacks)~~s~~s—includes conditions like stroke, heart failure, arrhythmias, and heart valve problems~~s~~s, has been the leading cause of death for women in the United States for ~~over~~more than a century. About one in three deaths among women each year is from heart-related causes, significantly more than from all kinds of cancer combined.<sup>iv</sup>

~~And~~Yet heart disease had become so thoroughly stereotyped as a “man’s disease” ~~in~~by the middle of the twentieth century that, back in 1964, nobody ~~really~~ batted an eye when that first conference geared toward women was all about preventing “your man” from getting it. The stereotype didn’t come completely out of nowhere. Rates of coronary artery disease, the most common cause of cardiovascular death, had spiked dramatically by the fifties, particularly among middle-aged men. Women, by comparison, seemed to be relatively protected until after menopause, when their rates of heart disease began to climb. Combating premature heart attacks that were striking down men in the prime of their lives was the growing concern. And the biomedical community responded with urgency, launching a concerted effort to study, prevent, and treat the disease.

**Commented [MF2]:** Weird switch in tone here. Maybe choose something like “husbands.”

By the late eighties, though, experts ~~were beginning to warn that, as like~~ Dr. C. Noel Bairey Merz, director of the ~~Barbara-Barbra~~ Streisand Women’s Heart Center at the Cedars-Sinai Heart Institute, ~~has put it, were beginning to warn that~~ the “diagnostic and therapeutic strategies, which had been developed in men, by men, for men, for the last 50 years, ~~...-...-~~ weren’t working so well for women.”<sup>v</sup> ~~Rates of~~ cardiovascular deaths among men had begun a steady decline, but among women, they hadn’t budged.<sup>vi</sup> The result: since 1984, more women than men have been dying of cardiovascular causes each year.<sup>vii</sup> And while ~~premenopausal~~ women ~~before menopause~~ are at relatively lower risk for developing ~~the~~ coronary artery disease than their male counterparts, they tend to have worse outcomes when they do get it: 26 percent of women versus<sup>viii</sup> 19 percent of men die within the first year after a heart attack, ~~or~~—a myocardial infarction; in ~~the~~ medical lingo. ~~And W~~within five years ~~of a heart attack~~, nearly half of all women, compared to about a third of men, have heart failure or suffer a stroke.<sup>ix</sup>

Meanwhile, the male stereotype associated with the disease seemed to lead physicians to underestimate women’s risk. In 1991, cardiologist Dr. Bernadine Healy ~~described named~~<sup>x</sup> ~~this~~ ~~problem~~ ~~as the~~ “Yentl syndrome.” Reviewing new research showing that women with symptoms of a heart attack were undertreated, ~~receiving and received~~ fewer diagnostic tests and lifesaving treatments, ~~she~~ Healy compared their dilemma to that of the heroine of Isaac Bashevis Singer’s short story, who disguised herself as a man to attend school and study the Talmud. “Being ‘just like a man’ has historically been a price women have had to pay for equality,” Healy wrote. “Decades of sex-exclusive research have reinforced the myth that coronary artery disease is a uniquely male affliction, and have generated data sets in which men are the normative standard.”

**Commented [MF3]:** Just clarifying: “this problem” is the fact that physicians underestimate women’s risk of heart disease?

To get equal care, women first ~~they~~ had to prove that they were as sick as their male counterparts. “Once a woman showed that she was just like a man, by having severe coronary artery disease or a myocardial infarction, then she was treated as a man would be.”<sup>xi</sup>

Twenty-five years later, there’s more knowledge about sex/gender differences in heart disease than perhaps any other area of medicine. At the same time, there is a wealth of research documenting the gender disparities in diagnosing, preventing, and treating it that stubbornly persist.

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Since 2000 a few decades after men started seeing improvements, the number of women dying from cardiovascular disease has been declining a few decades after men started seeing improvements. Experts attribute the progress to an increase in awareness of the disease; among the public and health care providers alike, a greater focus on reducing their women’s risk factors, and the better application of evidence-based treatments. In 1997, only 30 percent of American women surveyed<sup>xii</sup> were aware that cardiovascular disease was the leading cause of death in women; by 2009, ~~#-that number~~ was up to 54 percent.<sup>xiii</sup>

Still, as recently as 2005, only 8 percent of primary care physicians, 13 percent of ob-gyns, and 17 percent of cardiologists surveyed in one study knew that cardiovascular disease kills more

women than men every year.<sup>xiv</sup> And a 2015 meta-analysis<sup>xv</sup> of ~~forty-three~~43 studies on women's experiences of heart disease since the early nineties concluded that the myth that heart disease is a "man's disease" remains pervasive. "The women described feeling invisible within a medical context that frames coronary symptoms within a dominant (male) paradigm," the authors wrote. "They thought physicians treated them differently than men and believed researchers paid little attention to heart disease in women. Women felt their risk factors and symptoms were not taken as seriously as men's."

~~The~~ research backs up these women's perception. In a 2008 experiment,<sup>xvi</sup> ~~to take just one of many studies documenting gender bias in the diagnosis of heart disease,~~ 128 primary care physicians in the United States, Germany, and the UK watched videotaped patients, played by actors, presenting with symptoms of heart disease ~~and~~ following an identical script, ~~and~~ ~~Then~~ ~~the physicians~~ were interviewed about what follow-up questions they would ask the patient, what test they would order, what diagnosis they felt was most likely, and what, if any, referrals or treatments they'd recommend. The doctors gave the women patients less attention than the men: they asked them fewer questions, were less likely to give them a possible diagnosis of cardiovascular disease, and were less certain about their diagnosis. "Although patients with identical symptoms were presented," the researchers concluded, "primary care doctors' behavior differed by patients' gender in all ~~three~~3 countries under study. These gender differences suggest that women may be less likely to receive an accurate diagnosis and appropriate treatment than men."

Gender disparities persist even when it comes to patients with the same actual calculated risk of the disease according to traditional risk factors for the disease. In 2005, the AHA tested<sup>xvii</sup> 500 physicians (300 primary care physicians, 100 obstetricians/gynecologists, and 100 cardiologists) on how well they could assess patients' cardiovascular risk and apply the association's new evidence-based prevention guidelines. The study found that, across all three specialties, when presented with male and female patients who, on paper, both had an intermediate risk based on various factors like age, smoking history, and family history of heart disease, ~~etc., they the~~ physicians were more likely to incorrectly judge the women as low risk. Because of this underestimation, they recommended fewer prevention measures to the women compared to the men. (One of the few exceptions to that rule: among the patients judged to have an intermediate risk, the women were significantly more likely than the men to be advised to lose weight.)

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Even women with family histories of heart disease tell of meeting resistance from their health care providers when they attempted to be proactive about monitoring their heart health. A woman in one study, concerned that the disease ran in her family, asked her doctor for a cholesterol test and was told, "But a young and healthy woman like you can't have raised cholesterol."<sup>xviii</sup> Another woman recalled, "I talked to the nurse practitioner and told her about my mother's history of heart disease and she just looked at me real funny, and I said, 'You think this is all in my head, don't you?' She said, 'I'm not saying it's all in your head, but your mind can make your body do things.'"<sup>xix</sup>

### **"She's Too Young and She's a Woman"**

Somewhat ironically, given that it was concern about middle-aged men dying that led to the focus on men's heart disease to begin with, today it's middle-aged women who too often slip through the cracks. The stubborn myth that younger women don't get heart disease lingers, it seems, because of the sex difference in rates of the disease according to age: women are typically older than men when they suffer a first heart attack (~~seventy-two~~72 years compared to ~~sixty-five~~65 years for men<sup>xx</sup>), and at every age up until ~~seventy-five~~75, men have greater odds of having a heart attack than women.<sup>xxi</sup>

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Still, more than 30,000 women under age ~~fifty-five~~55 are hospitalized<sup>xxii</sup> annually for a heart attack and about 16,000 of them die each year in the U.S.<sup>xxiii</sup> (Heart disease, in fact, kills more women at every age than breast cancer does.)<sup>xxiv</sup> And compared to men, ~~these women who do~~ get heart disease early fare especially poorly. Studies<sup>xxv</sup> in the nineties showed that younger female heart attack patients were about twice as likely to die in the hospital as their male counterparts—~~and this a~~ mortality gap ~~that~~ has just recently begun to narrow.<sup>xxvi</sup> In fact, despite the overall downward trend in heart disease mortality, in recent years, there's been a striking *increase* in cardiovascular deaths among women age ~~forty-five~~45 to ~~fifty-four~~54.<sup>xxvii</sup>

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Too often, health-care providers' perception of their middle-aged women patients' risk of heart disease appears to be overly influenced by how it compares to men's, as if the fact that it's even more common in men somehow means it's nonexistent in women—rather than being one of their leading causes of death. In one study, a ~~fifty-one~~51-year-old woman described what it was

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like to be told her heart attack was categorically impossible—while it was happening. “I can clearly remember the distress I felt when they phoned the ambulance from the hospital and asked them to turn round, because they were so busy: ‘She is too young and she is a woman,’ they argued. At that moment, I was horrified because I knew I was suffering from a heart attack.”<sup>xxviii</sup>

After she recovered from her own close call, Carolyn attended the WomenHeart Science and Leadership Symposium, a leadership training for women with heart disease put on by specialists from the Mayo Clinic, and started a blog called *Heart Sisters*. ~~(Her book, *A Woman’s Guide to Living With Heart Disease*, will be out in November 2017.)~~ As an advocate who now speaks regularly about women’s heart health, she’s learned that her experience is not as uncommon as she’d assumed. “I thought my story was pretty dramatic at the time, until I met so many women who, like me, had been misdiagnosed mid-heart attack and sent home.” Of the 45 other women in her WomenHeart class, a full third ~~of them~~ had.

Indeed, in a study<sup>xxix</sup> published in ~~*The New England Journal of Medicine*~~ in 2000, researchers looked at the records of thousands of patients who had presented to ~~ten-10~~ American emergency rooms with symptoms suggestive of a heart attack in the early nineties and determined what characteristics were linked to being mistakenly discharged. According to their calculation, the rate of misdiagnosis translated into at least 11,000 missed heart attacks per year in the United States. And women under ~~fifty-five~~<sup>55</sup> years old were seven times more likely to be sent home than the average patient. The consequences of the mistake were dire: being released from the hospital ~~early~~ nearly doubled the patient’s odds of dying.

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## The Challenge of Overcoming “Knowledge-Mediated Biases”

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The myth that “younger women don’t get heart disease” points the danger of what Dr. Katarina Hamberg of Sweden’s Umeå ~~a~~-University has called a “knowledge-mediated bias.”<sup>xxx</sup> While an awareness that men or women have, on average, greater or lesser risks of certain diseases is important and useful up to a point, this awareness can lead to diseases becoming so stereotyped as a “man’s disease” or a “woman’s disease” that doctors are blinded to the individual in front of them—to the extent that the stereotype ~~actually~~ becomes self-fulfilling. And heart disease isn’t the only disease where this happens.

The history of chronic obstructive pulmonary disease (COPD) illustrates the ~~dynamic~~ well. The third most common cause of death in the United States, COPD is closely linked to cigarette smoking. ~~Accordingly, f~~For decades, the typical COPD patient was the typical smoker: an older white man. But beginning in the sixties, as tobacco companies began targeting women, the gender gap in smoking rates began to close—and the gap in COPD rates soon followed suit. Between 1980 and 2000, women’s mortality rates<sup>xxx1</sup> ~~from due to~~ COPD tripled. ~~And S~~Since 2000, more women than men have died from COPD each year. In a 2001 study<sup>xxxii</sup>, researchers suggested that COPD was ~~being~~ underdiagnosed in women due to the entrenched stereotype associated with the disease. They asked 192 primary care physicians to consider the case of a middle-aged patient, either a man or woman, with a chronic cough and a history of smoking. On

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first pass, 49 percent of the women patients received a COPD diagnosis compared to 64.6 percent of the identical male patients. Once test results pointing to COPD were offered, the gender gap narrowed but still didn't disappear completely.

As the researchers noted, some would argue that the bias demonstrated in the study wasn't entirely inappropriate given that "the risk of COPD is truly higher in men than in women given the historically higher tobacco consumption rates in men." But they point out that this is a circular argument: the accuracy of the epidemiological data that tells us how common diseases are in different groups is dependent on doctors making accurate diagnoses. If COPD was underdiagnosed in women, —as the study demonstrated it was, —who was to say that it was ~~still~~ actually more prevalent among men? And even if it were, that's irrelevant to whether an individual woman has it. Yet the image of the male "typical patient" was so strong that the doctors in the study overlooked COPD in female smokers, even though the only reason for men's historically higher rates of COPD to begin with was their higher rates of smoking. Today, despite ~~now~~ officially having higher rates of COPD than men throughout most of their lifetime, women continue to face delays in getting diagnosed. <sup>xxxiii</sup>

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"Knowledge-mediated" biases do affect patients of both genders. Studies ~~have suggested~~ that men are underdiagnosed with some conditions that are more common among women, including depression, migraine, fibromyalgia, and breast cancer. Still, this type of bias seems to be especially difficult for women to overcome. After all, when the diagnosis goes against what's statistically expected, a willingness to listen to the individual patient's symptoms becomes even more important to making the correct diagnosis. Many women with other diseases stereotyped as

“man’s diseases,” like autism and attention deficit disorder, report that doctors were absolutely resistant to the possibility—even when they suggested the correct diagnosis themselves.

**Commented [MF10]:** The possibility of what? Of women having traditionally “men’s diseases”?

It took Brenna<sup>xxxiv</sup> six doctor’s visits and 18 months to get someone to listen when she described her cluster headaches. Considered one of the single most painful medical conditions, cluster headaches are nicknamed “suicide headaches” for a reason. When Brenna’s attacks started, her husband, then a medical student who’d just learned about headache disorders, suggested she keep a record of when they happened and her symptoms. The level of pain and the pattern suggested that they might be cluster headaches, which, as the name suggests, tend to occur in episodes of a few weeks or months at a time, often striking at the same time every day. Brenna also had the watering eyes and droopy eyelid that often accompany the disorder; she never had the aura that’s common with migraines.

“But the doctors wouldn’t listen to me,” she says. “They heard the word ‘headache’ and immediately determined I was suffering from hormonal migraines ‘like all women.’” While cluster headaches are certainly more rarer than migraines and women are less likely than men to have them, the male-to-female ratio is not as high as previously thought: In the sixties, it was estimated at 6:1 but is now put closer to 2:1. And even if were 99:1, there would still be the one. Brenna showed her long-time primary care physician her spreadsheets, but it didn’t matter. — She was prescribed treatments for migraines.

She pushed to get a referral to one neurologist, then another. ~~By~~At this point, she was having multiple headaches per day; the migraine medications clearly weren't helping at all. "When I talked about the symptoms I was experiencing, two prominent neurologists, one from each major teaching center in our city, used a nearly identical phrase: 'You couldn't be experiencing that.'"

To Brenna, it seemed clear that the fact that *she'd* suggested the diagnosis was part of why the doctors wouldn't even consider it. "The first two neurologist were just like, 'That's not what you're feeling; you need to get off WebMD. They were looking for brain cancer before they would take my word that I had these headaches that followed this pattern.'" The sheer frustration of not being heard was almost as bad as the pain itself. "It was infuriating to be told I wasn't capable of even knowing what I felt. It was more infuriating than the headaches."

Finally, Brenna went to yet another neurologist and presented all the same information. "He just sat there listening to me and then said, 'You're right—this sounds a lot like cluster headaches.'" He offered an immediate solution that would both determine if they were indeed cluster headaches and, if they were, relieve her unbearable pain: an oxygen tank she should breath from when an attack began. "That was a miracle pill. By finally having somebody—my third neurologist—actually listen to me, I had an immediate treatment that worked."

Brenna had 92 untreated headaches while trying to get her diagnosis. She says she doesn't know what would have happened if she hadn't had a partner in the medical profession; or if she didn't live in a major medical mecca like Boston; or if she didn't have the financial ability to keep

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going to specialist after specialist. “I would probably still not have a diagnosis. And I don’t know how I could’ve lived through five plus years of that. I don’t think I could have.”

### Diverging from the “Textbook”

The stereotyping of heart disease as “~~man’s~~men’s diseases” is not the only reason for women’s under-treatment. It’s not just that doctors too often fail to follow evidence-based standards of heart care to women; it is also that the evidence base itself is skewed. The inevitable result of developing a model of disease based on research conducted almost exclusively on men is that women’s experiences—from their risk factors to their symptoms to the very definition of what qualifies as a heart attack—may be less likely to neatly fit into that model.

Even when properly applied, traditional risk scores—developed based on research on men—aren’t ~~as~~ accurate at predicting women’s odds of getting heart disease to begin with. While the major risk factors are the same for both men and women, there are some sex differences in their relative importance. For example, while high total cholesterol is a key predictor of future heart disease in men, low levels of HDL cholesterol—the “good” cholesterol—and high triglyceride levels are far more important in women.<sup>xxxv</sup> Having type-2 diabetes increases the risk of heart disease in women more than in men. ~~As~~ does stress and a history of depression.<sup>xxxvi</sup>

~~Meanwhile, n~~New research is starting to identify previously overlooked ~~“non-traditional”~~ risk factors for women. In 2011, the AHA declared for the first time that pregnancy complications ~~;~~ such as preeclampsia ~~and~~; gestational diabetes mellitus ~~;~~ ~~and pregnancy induced hypertension~~; can serve as warning signs that a woman is more likely to develop heart disease,<sup>xxxvii</sup> a link that many physicians still aren’t aware of. For example, when Carolyn had her heart attack, she was repeatedly asked if she had been a smoker, or had high cholesterol, or had a family history of heart disease. ~~—but s~~She had none of these “traditional” risk factors. She had, however, developed preeclampsia when she had her first child decades ago, which gave her double the risk of developing cardiovascular disease~~;~~; a fact she was neither warned about at the time nor asked about after her heart attack. ~~In the future, women’s risk scores may also incorporate whether they have disruptions in ovulation, inflammatory biomarkers, or a history of autoimmune disorders.~~

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**Commented [MF13]:** “Pregnancy-induced hypertension” is the same as preeclampsia.

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When it comes to the symptoms of a heart attack, too, women are more likely to diverge from the textbook. The “classic” symptoms, derived from research on men, are relatively well known: crushing chest pain and shooting pain down the left arm. An image of an older, slightly overweight, white man suddenly clutching his chest and slumping over in his chair has made its way into the cultural consciousness as the “Hollywood heart attack” and has, quite literally, been illustrated ~~in the~~ medical textbooks for decades.

But women, younger women especially, are more likely to have other “atypical” symptoms during a heart attack and often in the days or even weeks leading up to it: pain in the neck, throat,

shoulder, or upper back; abdominal discomfort; shortness of breath; nausea or vomiting; sweating, anxiety, or a sense of impending doom; lightheadedness or dizziness; and unusual fatigue or insomnia. ~~Yet~~In 1996, a national survey<sup>xxxix</sup> revealed that two-thirds of doctors were completely unaware of any ~~gender-sex~~ variations in symptoms. And a 2012 survey of American women found that less than 18 percent knew the atypical symptoms of a heart attack.<sup>xl</sup>

**Commented [MF15]:** I went back and forth on this. “Gender” is a term for how one identifies, while “sex” indicates one’s genitals and DNA. My preference is to use “sex” here, but I’m not familiar enough with medical literature to make a firm call.

This difference in symptoms likely contributes to the longer delays in getting treated that women experience during a heart attack. ~~Certainly, it’s clear that~~Clearly, not having the hallmark symptom of chest pain at all can lead doctors astray. A 2012 study<sup>xli</sup> that tracked more than 1.1 million heart attack patients from 1994 to 2006 concluded that a lack of chest pain helped explain why 15 percent of the women died in the hospital, compared to 10 percent of the men. Patients who never experienced chest pain were nearly twice as likely to die, due in part to delays in getting lifesaving interventions. And women, particularly younger women, were overrepresented in this group: 42 percent of the women didn’t have chest pain, compared to only 31 percent of the men.

Perhaps the most glaring example of how a lack of attention to sex/gender differences contributes to women’s under-treatment is the fact that the standard test currently used to diagnose a heart attack—which measures the level of troponin, a protein released from the heart into the blood when it’s damaged—is less ~~sensitive-accurate~~ in women. In recent years, newer “high sensitivity” troponin tests have been developed that are able to detect the protein at much

lower levels, and have suggested there should be different cut-offs for the men and women. “It’s becoming increasingly clear with the high sensitivity ~~troponins tests now that are coming out~~ that the standard troponin level that we’ve used for years and years and years—which is the male standard again—misses about one in five heart attacks in women,” Bairey Merz says.

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A study published in *The BMJ* (the *British Medical Journal*) in 2015<sup>xliii</sup> looked at hundreds of patients with symptoms suggesting a heart attack and found that when the high sensitivity troponin test with sex-specific thresholds was used, the proportion of women diagnosed with a heart attack doubled from 11 percent ~~, according to the standard test,~~ to 22 percent. In contrast, among men, the two tests didn’t yield different results. The consequence: With the standard test, twice as many men as women were judged to have had a heart attack; with the new test, the rates for both genders were the same. The one-size-fits-all test, in other words, has been systemically under-diagnosing women’s heart attacks.

From one perspective, these are some of the more understandable reasons for the gender disparities evident in heart disease care. It is, after all, unsurprising that women are less likely to be treated aggressively for a heart attack if they are less likely to qualify as having had one ~~;~~ ~~period~~. As Bairey Merz says of the troponin test problem, “There are good and bad reasons why women are less aggressively treated. That’s kind of a ‘good’ reason in the sense that we can fix it. It’s just a lack of recognition that here’s an important variable where women and men differ and it’s making a difference in the diagnosis.” But, of course, it’s not a coincidence that women’s presentations are less likely to be “textbook” cases; the only reason their risk factors

are considered “non-traditional” and their symptoms are called “atypical” is that the norm has been a male one:—a fact there’s no longer any excuse for not recognizing.

### ~~“Doctors Think That Men Have Heart Attacks, and Women Have Stress”~~

~~Plus, t~~The knowledge gap doesn’t explain everything here. For example, in the study above that suggested atypical symptoms and the absence of chest pain contributes to women’s higher mortality, gender played a role independent of symptoms among the patients under age ~~fifty-five~~55: with or without chest pain, younger women had a higher mortality rate than younger men with similar symptoms. Indeed, most studies have found that while, on average, women do seem to have more symptoms; (which may confuse the diagnostic picture), the majority of people having a heart attack, including women, do have chest symptoms. And those women are also more likely than men to be misdiagnosed.

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~~In a~~ 2015 qualitative study<sup>xliii</sup> out of the Yale School of Public Health exploring the experiences of younger female heart attack patients, ~~for example, w~~ While the interviewees had a range of symptoms, ~~the vast majority of them (93 percent of them)~~ had chest pain. And yet, they told stories of unresponsive health-care providers and delays in getting timely ~~work-ups~~workups when experiencing both atypical and typical symptoms. One woman, for example, called her doctor to report chest pain and was told to schedule a regular appointment—five days later.



Even some women like Carolyn, suffering a picture-perfect “Hollywood heart attack,” report that their symptoms were initially brushed off. “I often say if that emergency room doctor had only ~~g~~Googled my symptoms at the time, there’s only one diagnosis that would have popped up, really,” Carolyn says. “Had I been a man who had presented with central chest pain, nausea, sweating, and pain down my left arm, there is no doubt I would have been admitted for observation”—even with normal cardiac test results, just to be safe.

In addition to finding their symptoms blamed on other, more minor physical conditions—acid reflux, ulcers, gallstones, and arthritis—many women were told ~~their symptoms~~ were related to stress, anxiety, depression, or “worry.” Forty-four percent of women with heart disease in one study said they felt health-care providers trivialized their complaints and attributed them to psychological causes. As one woman put it, ~~simply~~, “Doctors think that men have heart attacks and women have stress.”<sup>xliv</sup>

A series of studies<sup>xlv</sup> led by psychologist Gabrielle R. Chiamonte in 2007 vividly illustrated this problem. In one version, 230 family doctors and internists were asked to read two vignettes of hypothetical patients: a ~~forty-seven~~47-year-old man and a ~~fifty-six~~47-year-old woman with the same probability of having heart disease according to their ages, identical risk factors, and “textbook” heart attack symptoms ~~— chest pain, shortness of breath, and an irregular heartbeat.~~ Half of the vignettes included a note that the patient had recently experienced a stressful life event and appeared to be anxious. In the vignettes without that note, there was no difference between the doctors’ recommendations to the woman and man. Despite the popular conception

of the quintessential heart attack patient as male, in this quiz at least, ~~they-doctors~~ seemed perfectly capable of making the right call in the female patient ~~too~~.

But when the single ~~line~~ ke about stress was added, an enormous gender gap suddenly appeared. Only 15 percent of the doctors diagnosed heart disease in the woman, compared to 56 percent for the man, and only 30 percent referred the woman to a cardiologist, compared to 62 percent for the man. Finally, only 13 percent suggested cardiac medication for the woman, versus 47 percent for the man. The presence of stress, the researchers explained,<sup>xlvi</sup> seemed to spark a “meaning shift” in which women’s physical symptoms were reinterpreted as psychological, while “men’s symptoms were perceived as organic whether or not stressors were present.” The male patient’s stress not only didn’t detract from a heart disease diagnosis but actually seemed to support it; stress is, in fact, linked to greater odds of suffering of a heart attack and, in the men, it was “viewed (rightly so) as a risk factor.”

That was when the patients ~~did~~ experienced the “~~classic~~” heart attack symptoms. In the next twist on the study, the researchers asked 142 family physicians to assess a male and female patient presenting with atypical symptoms including nausea and back pain. This muddied the picture further: the woman was slightly less likely than the man to receive a heart disease diagnosis, but neither was likely to get one at all. And when stress was added to the mix, both men and women became even more likely to be diagnosed with a gastrointestinal problem instead.

If even a single line about the patient appearing to be anxious can spark such a dramatic “meaning shift,” it’s a wonder that women with diagnosed anxiety disorders are ever promptly and accurately diagnosed with heart disease. As Carolyn says, “It’s too tempting. As soon as they hear that, it’s very tempting for physicians to say, ‘Oh, that’s what it is.’” In fact, she heard from one woman who felt that her anxiety diagnosis was such a barrier to adequate care that she successfully fought to get it scrubbed from her medical records. “Women know that it is the label that follows you around from doctor to doctor and from diagnosis to diagnosis—that it’s always going to be a ‘problem list,’ as doctors call it, on that chart.”

This bias is obviously most dangerous during the acute emergency of a heart attack when, as cardiologists like to say, “time is muscle.” A 2014 study<sup>xlvii</sup> that tracked over 1,000 heart attack patients ~~under younger than fifty five~~55 years of age, at ~~twenty six~~26 hospitals in Canada, the United States, and Switzerland found that less than half of all patients got access to cardiac testing and care within the benchmark times set by experts, and women experienced longer delays. The average time it took for men to get an electrocardiogram was ~~fifteen~~15 minutes, compared to ~~twenty one~~21 minutes for women; the gender gap was ~~twenty eight~~28 to ~~thirty six~~36 minutes for fibrinolytic therapy to break up a clot and ~~ninety three~~93 compared to 106 minutes to implant a coronary stent. The researchers noted that while some factors, ~~—~~like an absence of chest pain, ~~—~~contributed to a delay in both men and women, there was one that seemed to pose a problem in women only: anxiety. Women with high scores on a scale measuring anxiety symptoms were less likely to meet the ten-minute benchmark for ECG than women without anxiety; in men, it didn’t matter.

And it's not just women who have been diagnosed with an anxiety disorder, or who seem to be anxious, or who mention a recent stressful event that are at risk of having their symptoms dismissed as psychological. ~~It's~~ Simply being a middle-aged woman may be sufficient. That's what was suggested by a 2009 study<sup>xlviii</sup> in which 128 internists, family practitioners, and general practitioners viewed different versions of a video of an actor presenting with signs and symptoms of coronary artery disease and offered their diagnoses. The doctors were least confident in their diagnosis of heart disease in the 55-year-old women patients, and those patients were twice as likely as their middle-aged male counterparts (31 percent compared to 16 percent) to receive a mental health diagnosis instead. The combination of their gender and age, the researchers concluded, "misled physicians, particularly toward mental health alternative diagnoses." They warned that "physicians should be aware of the potential for psychological symptoms to erroneously take a central role in the diagnosis of younger women."

#### **"Hysterical Females Who Come to the Emergency Room"**

The tendency to misdiagnose women's, especially younger women's, heart symptoms as anxiety, particularly in the ER setting, is often explained by pointing to the relative probabilities. Chest pain is the second most common complaint that brings patients to the emergency room, accounting for eight million<sup>xlix</sup> visits in the United States each year, but only about 20 percent of those who are admitted are found to be having a heart attack or other cardiac problem. Meanwhile, there is

symptom overlap between a heart attack and an anxiety or panic attack<sup>1</sup>, and younger women are at relatively lower risk for the former and higher risk for the latter. Given this reality, “triage personnel might initially dismiss a cardiac event among young women with anxiety,” as the 2014 study discussed above concluded. One cardiologist put it<sup>1</sup> more bluntly in a media interview: “In training, we were taught to be on the lookout for hysterical females who come to the emergency room.”

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It’s not entirely clear who all these mythical “hysterical females who come to the emergency room” actually are, though. Certainly, many people experiencing their first panic attack do go to the ER, convinced ~~it’s their heart~~they’re having a heart attack; but trained professionals can do a decent job of differentiating between a genuine panic attack and a heart attack. And panic disorder is not so common that it can explain all but a fraction of women’s chest pain visits. Instead, the perception that women’s chest pain is likely to be “anxiety” or “stress” seems to stem from a more general sense that they’re hypochondriacs prone to blowing minor ailments—like ~~say,~~ acid reflux, as in Carolyn’s case—out of proportion and talking themselves into believing they’re having a heart attack.

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<sup>1</sup> A panic attack, a feature of panic disorder, is a brief episode of acute fear and intense physical symptoms that comes on suddenly and unpredictably. An “anxiety attack,” while not an actual medical term, is usually used to refer to less extreme episodes of anxiety, whether due to an anxiety disorder or stress, which comes on more gradually and persists longer.

And there's no reason to think that women do that. ~~It's~~ exactly the opposite ~~in fact~~: research has pointed to women's tendency to delay going to the ER when they're ~~actually~~ having a heart attack as one factor that may contribute to their worse outcomes compared to men. Chest pain is one of the symptoms for which the assumption that women seek care more readily than men do just doesn't hold up. While survival rates increase by half if patients are treated within an hour after their symptoms begin, few patients, of either gender, get to the hospital that quickly,<sup>li</sup> and multiple studies have shown that women wait longer than men do before seeking treatment.<sup>lii liii</sup> According to a 2014 qualitative study<sup>liv</sup> by researchers at Harvard School of Public Health, when chest pain ~~struck~~strikes, men and women ~~went go~~ through a similar progression of stages, starting with uncertainty and denial, before finally reaching a "symptomatic tipping point" that ~~compel~~led them to seek out medical treatment. But women were one and a half times more likely than men to wait for their symptoms to become worse or more frequent before seeing a doctor.

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Carolyn suggests that it may be women's caretaking tendencies that explain why men, despite their reluctance to seek treatment, still seem to get to the doctor more quickly. As she puts it, "You've got the wife thing. Many men having a heart attack have wives who say, 'You're going to the hospital, and that's all there is to it.' Whereas when husbands say to their wives, 'Honey, you don't look good. I'm calling 911,' the wife will almost always fight and say, 'No, no, no, if it's still bothering me tomorrow, maybe I'll go.'" In fact, Carolyn generally finds women to be so much more willing to raise the alarm about heart attack symptoms in loved ones than they are in themselves that, in her talks, she often urges them to simply imagine if it were someone they

cared about experiencing the same symptoms: “Demand the same kind of help that you would demand if it was your daughter or your sister or your mum.”

Of course, one reason for women’s delay in seeking treatment may be that, misled by the myth that heart disease is a “man’s disease” or confused by “atypical” symptoms, they simply dismiss the possibility that they could be having a heart attack. That certainly seems to be part of the story, according to the 2015 qualitative study<sup>lv</sup> from Yale School of Public Health. Some of the women under the age of ~~fifty-five~~55 interviewed by the researchers explained that they had hesitated before coming ~~in~~ to the ER because they figured that they were too young to be having a heart attack, or they attributed their atypical symptoms to other health problems.

But the study identified another worrying trend: some of the women had, in fact, immediately suspected they were having a heart attack but had waited until they were sure because they were worried about being seen as a hypochondriac. “Not wanting to make a fuss, or not wanting to be embarrassed ‘in case it turns out to be nothing and I would feel like a fool’—that’s hugely pervasive in women’s reasons” for delaying care, Carolyn says. “Even in the middle of very severe symptoms, we talk ourselves into thinking that it’s probably nothing.”

Of course, all too often this fear proves to be entirely justified. Once they finally sought help, many of the women in the Yale study encountered health-care providers who treated them precisely like the hypochondriacs they feared they were—until they overcame the ~~Yentyl~~ syndrome and proved they were ~~really~~truly sick. Indeed, while there are many cultural forces that may contribute to

women's fear of being seen as hypochondriacs, their previous experiences in the medical system are one big one. Many of the interviewees reported having had "poor physician-patient relationships, feeling rebuffed or treated with disrespect, and being denied care." And it had made them reluctant to seek medical attention even before their heart attack; they reported having "limited and sporadic" routine doctor's visits because they didn't want to be "perceived as complaining about minor concerns."

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Patti is one woman<sup>lvi</sup> whose fear of being *that* woman, that "hysterical female" clogging up the ER, nearly cost her her life more than money. A concussion after tripping on an uneven step had marked the beginning of two months of "nothing but health care—just one thing after the other." Two weeks after the fall, she'd suddenly developed blinding double vision while driving. A month after that, she'd woken up to severe vertigo that put her work as an author and writing teacher on hold for weeks. "I'd never experienced anything like it in my life. The room was completely spinning around me." Then there was a "hard, hot burning" in her leg that her husband thought might be a blood clot—and yet another trip to the emergency room revealed it was indeed he was right.

The ER doctors had instructed her to follow up with her regular doctor in a few weeks, and so ~~now~~ she was she did, this time with a new worrisome symptom to report: for the last couple days, the slightest exertion would bring chest pain and shortness of breath. "I was so winded just getting up and going to the kitchen. It felt like one of my lungs had collapsed."



Her doctor had a medical student shadowing him that day, so after Patti relayed the last months' events, she was treated to the opportunity to hear him spell out his thinking about her case to his trainee. As if Patti weren't in the room, he explained to the student: "What we really are dealing with here is anxiety. Because it is anxiety that would take her to the ER on a Saturday with what might be a blood clot. Most people would wait until Monday and call here to get an appointment, but she went to the ER. We can tell from that that she's overwrought about her health and all she needs is anxiety medication."

It was not the first time Patti had felt this particular doctor didn't take her symptoms seriously, nor was he the first in the line long of health-care providers she'd seen during this recent saga to suggest that it was all in her head. The ER doctor who had examined her when she came in with sudden double vision put down "~~anxiety~~" in her chart—even as she told Patti to follow-up with a neurologist about an abnormality on her brain scan. Similarly, the fact that Patti's "anxiety" about a blood clot had been warranted—she actually *did* have one—somehow didn't detract from her primary care physician's analysis. Neither did the fact that Patti had no history of an anxiety disorder—which, having been her regular doctor for years, he knew—"and I don't come across as a very anxious person." Indeed, when we talk, her voice, with a gentle Southern accent, is remarkably calm even as she says, "I was so furious." She can't imagine her doctor saying the same thing to a male patient. "My husband would have gotten very different care. He would have immediately been hooked up to an ~~ECG~~ machine in my doctor's office—I'm sure of it."

Two days later, as a snowstorm engulfed her home in the North Carolina mountains, Patti was hoping a hot shower might make it easier to breath. Minutes later, she yelled for her husband to call 911. Taken by ambulance to the ER, she was diagnosed with a heart attack and eventually had a stent placed. Like Carolyn, she'd had a widowmaker; the artery was 90 percent blocked. "I was lucky that I paid attention to my own intuition. Had I not told my husband to call 911, I'm not sure I would be alive; I probably wouldn't be." She did, in part, because her father had died of a heart attack when he was just 53—three years younger than she was at the time. "Because of my dad, I'm perhaps more aware of heart attacks—with good reason, it turns out."

Still, "in the back of my mind, I was thinking about what my doctor had said," she recalls. Laid up for a week in the hospital recovering from a complication from the stent procedure, she wrote a Huffington Post piece about what had happened: "The sad fact is that I waited. I waited because I felt shamed into feeling like a hysterical female, shamed into feeling like I was just anxious. JUST anxious. Like anxiety is something to be ashamed of or embarrassed by." In fact, a healthy dose of anxiety had saved her life. "This was not something to be calm about. Calm people are dead people, when you're dealing with a heart attack or anything life-threatening."

### **Undertreatment in the ER**

Though it's been the focus of the most research, a heart attack is certainly not the only acute, life-threatening condition for which women are treated less aggressively in the ER. Dr. Alyson McGregor, an associate professor of emergency medicine and director of the Division of Sex and Gender in Emergency Medicine at the Warren Alpert Medical School of Brown University, recently co-authored a new medical textbook *Sex and Gender in Acute Care Medicine*. "It's amazing and really alarming to see that cardiac arrest, stroke, conditions of sepsis—in almost all of these conditions, women receive less intense care," she says.<sup>lvii</sup>

Indeed, in 2014, the first large-scale study<sup>lviii</sup> of the misdiagnosis of stroke in the United States, based on medical records of 187,188 patients in over one thousand hospitals nationwide, found that up to 12.7 percent of people later admitted for stroke had potentially been erroneously sent home from an ER in the thirty days prior. At that rate, the researchers estimated that there are between 50,000 and 100,000 missed strokes each year. Typically, the misdiagnosed patients had come in complaining of dizziness or a headache, and left with a diagnosis like inner ear infection or migraine, or no diagnosis at all. Women were a third more likely than men to be misdiagnosed.<sup>lv</sup> Prompt treatment can lower the risk of a repeat stroke by as much as 80 percent.

Each year, over 300,000 people suffer a cardiac arrest in the United States. A cardiac arrest, though it can be caused by a heart attack, is not the same thing: it occurs when a malfunction of the heart's electrical system causes it to suddenly stop beating, and death can occur within minutes if CPR isn't started. Few people even make it to the ER and of those who do, nearly two-thirds ~~still~~ aren't saved. Though in-hospital survival rates have been increasing for patients

of both genders in the last fifteen years, this improvement has been relatively ~~less~~-lower in women. A 2016 analysis<sup>lix</sup> of the records of a sample of cardiac arrest patients in over a thousand United States hospitals between 2003 and 2012 suggested that's at least partly because women are treated less aggressively than men. After adjusting for other factors,<sup>lx</sup> women were 25 percent less likely to have an angiography to check for blocked arteries, 29 percent less likely to undergo angioplasty to open them, and 19 percent less likely to be treated with hypothermia to lower body temperature, which increases odds of recovery.

“What we’ve done over the past couple years is really gather this type of health disparity data,” McGregor says. “Our next step is to identify why, then to educate people and health-care providers to improve and to decrease this gap.” As with heart attacks, the reasons why may include both bias and biology; perhaps women have more “atypical” symptoms or are less likely to test positive on the diagnostic tests to detect certain conditions. But surely part of the reason is they’re just not taken as seriously. When I asked McGregor why she thought women’s symptoms in an urgent care setting often didn’t seem to be met with the same level of, well, urgency, she suggested that the fact that women might be more open in displaying the emotions that pain—or any sudden alarming symptom—often provokes may mislead doctors. “Women may be more likely to express that they are anxious that they’re in pain, so oftentimes physicians translate that to ‘this patient is anxious,’ when they’re actually anxious because they’re in pain.” But, as we’ve seen, sometimes women are perceived as anxious regardless of whether they express it, while men are perceived as in pain regardless of whether they’re anxious.

## “Female Pattern” Heart Disease

When women’s heart experts say that our knowledge of heart disease has been based on a “male model,” they’re not just talking about how women’s symptoms or risk factors may differ, or how tests and treatments—from troponin tests to stents—were designed for a male norm. One of the most important findings to come out of sex- and /gender-specific research in the last two decades has been the discovery of a whole new form of heart disease—previously unrecognized and, to this day, largely undiagnosed—that’s more common in women, called ischemic heart disease. In a 2014 AHA scientific statement, cardiologist Dr. Jennifer H. Mieres explained<sup>lxi</sup>: “For decades, doctors used the male model of coronary heart disease testing to identify the disease in women, automatically focusing on the detection of obstructive coronary artery disease. As a result, symptomatic women who did not have classic obstructive coronary disease were not diagnosed with ischemic heart disease, and did not receive appropriate treatment, thereby increasing their risk for heart attack.”

Here’s how the classic (~~read: male~~) model of coronary artery disease is thought to work: over time, plaque builds up in the arteries that deliver blood to and from the heart (a process called atherosclerosis) and causes them to narrow. If a patient begins to experience chest pain, they might be given a stress test that indicates they’re getting reduced blood flow to their heart, (~~known technically~~ as ischemia). If ~~that’s the test is~~ positive, they might get an angiogram: an ~~ray~~X-ray image of the heart’s arteries. If one of the major arteries of the heart is revealed to be more than 50 ~~to~~ -70 percent blocked, they’ll be diagnosed with obstructive coronary artery

disease (CAD). Treatment is focused on preventing further narrowing of the arteries and, if they're already severely blocked, reopening them with ~~procedures like~~ an angioplasty, a stent, or, in the worst cases, bypass surgery. The hope, of course, is to detect the disease before it causes the life-threatening event of a heart attack. Under the classic model, a heart attack happens when a plaque obstruction suddenly ruptures and causes a blood clot that completely cuts off blood flow to a part of the heart, which, deprived of oxygen, rapidly begins to die.

For the first few decades that we were studying coronary heart disease, it was this form of the disease—obstructive CAD—we were focused on. However, it's long been known that a large proportion of patients have chest pain that suggests heart disease, ~~and~~ an abnormal stress test, but when an angiogram is done, it shows that they don't have obstructive CAD. In some cases, their arteries appear to be perfectly “normal,”<sup>2</sup> with no visible narrowing. In others, there is some mild narrowing but it doesn't reach the greater than 50 percent blockage that typically qualifies as obstructive CAD; this condition has been labeled “nonobstructive CAD.”<sup>2</sup> In men, this is exception, but in women, it is in fact the norm. Studies suggest that 60 to 70 percent of women undergoing an angiogram because of symptoms and signs suggesting reduced blood flow to the heart are found to have normal or nearly normal arteries, compared to just 30 percent or less of men.<sup>lxii</sup>

These patients posed a baffling dilemma. They seemed to have reduced blood flow yet in the classic model of the disease, if there wasn't a visibly blocked artery, it wasn't clear what was to blame. So, initially, they were considered “false positives.” If the angiogram showed their

arteries were clean, perhaps the stress test was wrong. Instead of taking the existence of these perplexing patients as evidence that the model wasn't adequate and needed to be adjusted in order to explain their symptoms, some of the evidence was simply thrown out so that ~~they~~ patients would fit into the existing paradigm. This happened despite the fact that these women not only had the subjective symptoms, namely, chest pain, but also objective signs of ischemia measured by a variety of different technologies including electrocardiogram, PET imaging, and contrast cardiac MRIs.

Eventually, the evidence of ischemia in the absence of obstructive CAD was accepted but the poorly defined condition, (sometimes called cardiac syndrome X<sub>2</sub>) was thought to be a fairly harmless ~~one~~. Small observational studies since the sixties had suggested that these patients weren't at increased risk of suffering a heart attack or other life-threatening cardiovascular condition.<sup>lxiii</sup> So while they often continued to have ongoing and debilitating symptoms, they were offered nothing more than reassurance that they did not have heart disease.

In 1996, the National Heart, Lung, and Blood Institute launched the Women's Ischemia Syndrome Evaluation (WISE) study,<sup>lxiv</sup> a groundbreaking research project to correct the decades-long focus on men's heart disease. It confirmed that the mysterious condition was hardly a benign one in terms of quality of life and economic costs: About half of women sent home "reassured" that they had "normal" or "nonobstructive" arteries still had chest pain five years later; many returned repeatedly for diagnostic testing and largely ineffective treatment, and one in five had been were rehospitalized. Over the course of a lifetime, the researchers estimated, the

health-care costs<sup>lxv</sup> of women with nonobstructive CAD were over \$750,000, not that far below the \$1 million price tag that women with obstructive CAD faced.

Furthermore, by the mid-2000s, results from the WISE project began to reveal that, contrary to the conclusions of those earlier small studies, which experts now believe were poorly designed and didn't have a long enough follow-up period, these patients actually *do* face increased cardiovascular risks, ~~having~~ and have two to four times higher odds of suffering a heart attack, heart failure, or stroke within five years than individuals without ischemic heart disease.<sup>lxvi</sup> Yes, that prognosis is better than those with obstructive CAD, but only by a matter of degree. After ten years,<sup>lxvii</sup> 6.7 percent of the symptomatic patients with “normal” arteries, 12.8 percent of those with nonobstructive CAD, and 25.9 percent of those with obstructive CAD had died from heart-related causes or had a heart attack.

Indeed, while most people who have a heart attack have obstructive CAD, a minority of them—~~more-most~~ of them women—don't. The WISE study<sup>lxviii</sup> found that 10 to 25 percent of women who experienced a heart attack didn't have evidence of obstructive CAD, versus 6 to 10 percent of men. Autopsy studies<sup>lxix</sup> also show that while about three-quarters of fatal heart attacks in men are due to plaque ruptures, only 55 percent of women's heart attacks are explained by ruptures; instead they have more evidence of plaque erosions. Turns out the classic model, in which a heart attack is caused by a rupture of an obstruction, doesn't tell the whole story for a significant number of women.



Research like the WISE study has now identified several other abnormalities that can cause ischemia in the absence of obstructive CAD. The most common one seems to be coronary microvascular disease (CMD). Undetectable by traditional angiogram, it's a condition that affects the small arteries or the inner lining of the main arteries leading to the heart. Among the WISE women, nearly half<sup>xx</sup> of them had evidence of microvascular dysfunction.

**Commented [MF21]:** The AHA abbreviates this term as "coronary MVD." OK to change?

Despite this emerging knowledge, ~~at this point,~~ a comprehensive search for other causes of ischemia, once obstructive CAD has been ruled out, is still not the norm. As McGregor explains, "When you come to the emergency department with chest pain, all of the protocols that we undergo—what happens to you, what tests we do, whether you get admitted, whether you get further testing, what medications you're on—they're all designed based upon a male pattern of disease, the obstructive disease." If you have non-obstructive heart disease, there may be a delay in getting put on the "rule-out-heart-attack protocol" because your symptoms may be more "atypical." And once on that protocol, "none of those tests are designed to test for ~~it,~~ so you might go through this entire medical system and be discharged, and we'd never detected the type of heart disease that you actually have. That's what's happening to women more often than men."

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When I learned about this "female pattern" heart disease, the puzzle of why doctors seemed to have the impression that there were countless hypochondriacal women rushing to the ER for every slight chest pain, despite the fact that, in reality, women are *more* reluctant to seek care

when having a heart attack, suddenly got a whole lot clearer. Here, finally, were those mythical “hysterical females” coming into the ER: the millions of mostly women patients—perhaps three million in the United States, by the WISE researchers’ estimate—who have heart disease and all its symptoms but, until recently, have been told that they do not. A 2015 study of patients with chest pain but no obstructive CAD,<sup>lxxi</sup> 77 percent of whom were women, found that over three-quarters had other coronary abnormalities, such as CMD. According to a 2016 article<sup>lxxii</sup> by emergency room physicians, in their experience, microvascular disease may explain the symptoms of as many as 40 percent of patients, the majority of them women, coming into the ER with recurrent chest pain; yet “applying the current standard of care, most patients with microvascular angina remain undiagnosed.”

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No wonder doctors might unconsciously ~~come to~~ take women’s chest pain a bit less seriously when the reality is that women make up the majority of the patients they see that, in the end, don’t have any obstructive CAD to account for their symptoms—not, ~~primarily~~, because they’re more prone to anxiety but because of medicine’s own failure to recognize the forms of heart disease they do have.

Just as the “male pattern” of obstructive CAD is not unique to men, CMD, while apparently more common in women, doesn’t just affect them. And it’s not an either/or scenario: the same person may be affected by both. Indeed, the growing recognition of alternate mechanisms that may cause ischemia is helping to explain<sup>lxxiii</sup> a number of other previously perplexing realities

about heart disease, including the fact that nearly a third of patients with obstructive CAD who've undergone procedures that successfully opened up their blocked arteries find that their symptoms inexplicably persist.<sup>lxxiv</sup>

That's what happened to Carolyn. After her "male-pattern" widowmaker heart attack, she had a stent implanted in her clogged main artery. But her chest pain, shortness of breath, and crushing fatigue didn't go away. At first, her cardiologist suspected a blockage inside the new stent, but another angiogram showed that her arteries were "pristine." "I actually cried when I heard that—and not happy tears," she remembers. "If it wasn't stent failure, what the hell was causing these debilitating symptoms?!" Thankfully, her doctor was familiar with CMD and suspected it might be the culprit.

Many others aren't so lucky. As Bairey Merz, who is lead investigator for the WISE study, said in a 2011 TED talk, "We've been working on this for fifteen years and we've been working on male-pattern disease for fifty years. So we're thirty-five years behind."<sup>lxxv</sup> That thirty-five-year knowledge gap means awareness of "female pattern" abnormalities like CMD in the medical community is currently variable. "I think more physicians are paying attention to it. I'm getting more referrals," Bairey Merz says. "Is it widespread? I would say not quite yet."<sup>lxxvi</sup> Indeed, Carolyn heard from a woman whose cardiologist told her, "I don't believe in microvascular disease.' Like it was Santa Claus or something."