SOCIETY to IMPROVE DIAGNOSIS in MEDICINE

WOMENHEART
THE NATIONAL COALITION FOR WOMEN WITH HEART DISEASE

From Errors to Solutions: Building a Research Agenda to Improve Diagnosis of Heart Disease in Women

A REPORT FROM A CONVENING ON MISSED AND DELAYED DIAGNOSIS OF HEART DISEASE IN WOMEN

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CONVENING
on Missed and Delayed Diagnosis of Heart Disease in Women

Heart disease is commonly assumed to be "a man's disease," yet it is the leading cause of death for women in the United States, with more than 400,000 deaths each year.[1] That misconception creates a blind spot for many patients, providers, policymakers, researchers and others; it also contributes to increased likelihood of missed and delayed diagnosis of heart disease in women. Furthermore, the risk factors and symptoms of heart disease for women can differ from those for men.[2] The challenges of heart disease combined with bias related to gender, sex, age, race and ethnicity, as well as systemic barriers to high quality care, result in diagnostic error and unequal care for women.

WomenHeart: The National Coalition for Women with Heart Disease and the **Society to Improve Diagnosis in Medicine (SIDM)** came together in 2020 to work toward advancing research to help find solutions to the difficulties women experience with the diagnosis of heart disease. With funding from the **Patient-Centered Outcomes Research Institute**, the two organizations formed a Steering Committee to plan an invitation-only convening designed to develop ideas for solutions-focused research about missed and delayed diagnosis.

The convening took place virtually on January 27, 2021, and included approximately 50 participants: cardiologists, nurses and other clinicians, hospitals, academia, professional societies, advocates, and patients along with experts from the Centers for Disease Control and Prevention and the National Institutes of Health. *WomenHeart Champions* — women with heart disease who are trained to provide peer support and community education — joined with other advocates and invited contributors in a one-day program of context-setting presentations followed by interactive sessions designed to generate potential research topics.

Background

Research shows that women with symptoms of heart disease are less likely than men to have non-invasive diagnostic testing at the initial point of care.[3] For many women, that results in delayed diagnosis, delayed therapeutic interventions and ultimately poorer outcomes. Women of color, especially Black women, tend to experience additional bias, such as trivialization of complaints and lack of respect from health care professionals, which further contributes to diagnostic error.[4]

Delayed and missed diagnosis of heart disease in women may also be due to inadequate clinical training of health care providers. In a national study, only 43% of medical students reported that their educational curriculum improved their understanding of sex and gender medicine and only 35% felt prepared to manage sex and gender differences in health care.[5]

It is within that context — based on research that describes the problem but is less robust at providing evidence-based solutions — that WomenHeart and SIDM convened experts, including patients, to propose research questions that could lead to improvements in timely and accurate diagnosis of heart disease in women.

A DISCUSSION BASED ON EXPERIENCE

Throughout the convening, participants discussed contributing factors that undermine timely and accurate diagnosis of heart disease in women. This included the lack of public education regarding the signs and risk of cardiovascular disease in women that may cause women to dismiss their own symptoms. Health care providers lacking awareness may discount the signs of heart disease in women and incorrectly attribute complaints to stress or anxiety. Age bias contributes to younger women being dismissed by being told that they aren't old enough to have heart disease. Lost opportunities include pregnancy, when women with complications are not informed that they remain at risk of serious cardiovascular disease well after childbirth. Inadequate health insurance and other financial strains put some women at further risk of poor outcomes. These biases and inequities are compounded for women of color. And women who live in underserved or remote communities face additional challenges to accessing timely, accurate diagnosis and the treatment they need.

STARR MIRZA
WomenHeart Champion
Silver Spring, Maryland

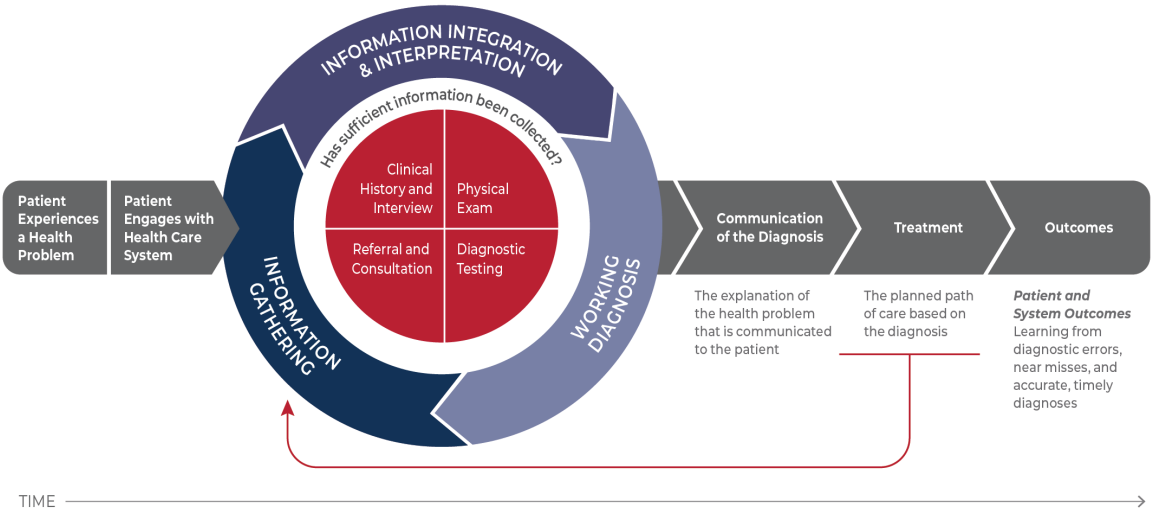
"I had a lot of cardiac symptoms as a teenager, but every time I went to the doctor, they just looked at me and told my parents, 'You know, given that she's a teenage girl, she's clearly doing this for attention.' And then at 22, I went into full-blown cardiac arrest."

Based on their experiences, participants agreed that many clinicians are not fully educated to understand sex differences in heart disease. They may not know that heart disease sometimes affects women differently than men, that certain heart conditions are more prevalent in women and that a patient's reproductive history can impact their future heart health. Furthermore, providers may lack easy access to decision aids or colleagues for consultation during the diagnostic process.

Challenges created by our health care system also became points of discussion. Health systems are often structured in ways that are difficult for patients to navigate, especially for those who are already having trouble getting help with a difficult diagnosis or who have limited resources. Rushed appointments limit the amount of time and attention clinicians can offer each individual patient. And, after decades

FIGURE 1. The National Academy of Medicine's conceptual framework for diagnosis[6]

(An interactive version of this framework is available on the SIDM website)



of perpetuating the myth that heart disease primarily afflicts men, medical schools, other clinical training programs and existing research are only now starting to catch up to the reality of how heart disease impacts women's lives.

A CONCEPTUAL FRAMEWORK FOR DIAGNOSIS

A conceptual framework developed by the National Academy of Medicine (NAM) provided a common understanding of the diagnostic process for the convening. The NAM's framework (Figure 1) reflects the complexity of the process. Diagnosis involves numerous team members, is influenced by the work environment and evolves over time. And the process should include learning from diagnostic errors and near misses, as well as from what goes well.

The framework explicitly devotes a step to communicating with the patient about the diagnosis. The NAM's definition requires clinicians to reach "an accurate and timely explanation of the patient's health problem(s)" and "communicate that explanation to the patient."[6(p4)] If the communication is lacking, a diagnostic error has occurred.

ENVIRONMENTAL SCAN OF AVAILABLE RESOURCES

Prior to the convening, WomenHeart, SIDM and members of the Steering Committee scanned published literature, social media, websites and other sources of information used by clinicians and patients to understand what is already known about the challenges of diagnosing heart disease in women. The preponderance of available information and evidence focuses on understanding problems related to disparities in diagnosis and treatment of heart disease in women. Substantial work has been done regarding the incidence of diagnostic errors; gender, hormones and pregnancy; comorbidities; special populations; and the experience of women with specific conditions,

such as heart failure and spontaneous coronary artery dissection. The environmental scan found very little research focused on how to fix those problems going forward. The purpose of the convening was to fill that gap by identifying areas most in need of research and developing a launch pad for further work.

Presentations From Experts

The Steering Committee met monthly to plan the convening. They focused on ensuring that those issues most pertinent to the missed and delayed diagnosis of heart disease in women were explored and featured in the agenda. During the convening, experts gave presentations that laid the groundwork for all participants to understand specific diagnoses, such as spontaneous coronary artery dissection and heart valve disease, as well as conditions such as pregnancy, that create particular diagnostic concerns for women. They also spoke about how the environment of the emergency department affects the process of diagnosing heart disease in women.

THE CHALLENGES OF SPECIFIC DIAGNOSES

In addition to diagnostic pitfalls that apply to all health conditions — cognitive preconceptions, socioeconomic barriers and structural biases in health systems and medical education — patients who have cardiovascular conditions not well understood in women face additional challenges. Because research and awareness are lacking, these conditions are more difficult to evaluate and diagnose in women compared to men.

Spontaneous coronary artery dissection (SCAD) is an acute event that occurs when a tear develops in a coronary artery, causing a heart attack. Sharonne N. Hayes, M.D., explained that it can occur in men, but more than 90% of SCAD heart attacks occur in women, often to women in their 50s, 40s and even younger, including mothers in the months following childbirth. SCAD events happen suddenly, without early warning signs and symptoms. Young women with SCAD, who may be fit and appear otherwise healthy, may be misdiagnosed because they do not match common expectations for what a heart patient looks like.

SCAD was considered an uncommon condition until recently because it often went unrecognized and undiagnosed. Awareness of SCAD has grown, but it is still a relatively new field of research, and the evidence base for diagnosis and treatment is slim. There are few standard protocols for diagnostic testing for SCAD, further contributing to missed and delayed diagnoses.

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Women's Heart Clinic
Mayo Clinic
Rochester, Minnesota

More than 90% of SCAD heart attacks occur in women, often to women in their 50s, 40s and even younger, including mothers in the months following childbirth.

Dr. Hayes also discussed coronary microvascular disease (MVD), a progressive condition most often seen in middle-aged and older women who develop shortness of breath or chest pain (angina) with exertion. MVD occurs when the tiny arteries deep in the heart muscle no longer expand to allow more blood flow when needed or become blocked with plaque. A confluence of factors makes this diagnosis challenging. Lack of sufficient blood supply due to MVD may not be identified through standard testing, such as stress tests. And even when stress tests are abnormal, these small arteries are not visible on coronary angiography. Without specialized testing during the angiogram, these women may be told that they must have had a "false positive" stress test and not receive treatment for their condition. As with SCAD, knowledge gaps, sex and gender differences, and the slow pace of evidence translation contribute to missed and delayed diagnosis of MVD in women.

In her presentation, Eileen Hsich, M.D., described other ways in which heart disease is different in women than in men. For example, while heart failure in women is most often caused by hypertension, in men it is usually caused by coronary artery disease. Chemotherapy agents used to treat breast cancer can also cause cardiomyopathies leading to sex differences in cause of heart failure. And cardiac amyloidosis is often missed in women, leading to delays in care, harmful treatment and a lack of research about this condition in women.

Dr. Hsich stressed the diagnostic opportunities that are missed when women do not receive proper diagnostic testing. She said, for example, that if medical providers looked at the voltage on an electrocardiogram while assessing the degree of heart thickening on an echocardiogram, this

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Too often simple diagnostic strategies are not utilized in women due to misconception that heart disease is a man's disease.

would help diagnose cardiac amyloidosis in women. Brain natriuretic peptide (BNP) testing is more reliable for identifying heart failure than a physician's clinical judgment and would aid in the emergency room when women present with shortness of breath. Too often these simple diagnostic strategies are not utilized in women due to misconception that heart disease is a man's disease. Dr. Hsich said, "If we standardize the process and use BNP for evaluating shortness of breath, we will identify heart failure more quickly which is cost effective."

Heart valve diseases also received attention at the convening. Rachel M. Bond, M.D., reported that women with aortic valve disease — especially women of color — tend not to be diagnosed in early stages of the disease, when they stand the best chance of having a good outcome. Given that 25% of women over the age of 65 have aortic valve stenosis, timely and accurate diagnosis of this disease would improve health care quality for a large number of women. In her research, Dr. Bond sees that women receive diagnostic testing and specialist referrals less often than men. Better

outreach to women in communities of color and in rural communities – where women may have more difficulty reaching providers and hospital facilities — may help close the access gap. Dr. Bond expects that increased use of telehealth will also help. She stressed the need for research into the relationship between underlying causes of heart valve disease and health care disparities.

Throughout their presentations, these experts noted the need for more professional training about heart disease in women. Using interdisciplinary teams, offering better diagnostic tools and devoting more resources to research were also featured as ways to improve diagnosis of these conditions.

DIAGNOSING HEART DISEASE IN THE EMERGENCY DEPARTMENT

The emergency department (ED) was identified throughout the convening as an important setting for efforts to improve diagnosis of cardiovascular disease in women. Jenice Baker, M.D., explained that the first job of emergency physicians is to make sure to identify life-threatening diseases that will cause harm within 24 hours. In the context of cardiovascular disease, various conditions progress on different timelines, and how the diagnostic process plays out can depend on when in the disease process a patient presents. This means that women who present early on in their disease process may experience a missed or delay diagnosis or fail to receive referral to a cardiologist.

Throughout the convening, patients shared stories of having gone to the ED, sometimes repeatedly, for treatment of symptoms consistent with heart disease and been sent home without a diagnosis or with the wrong diagnosis. In addition to delays in the diagnosis, women often had been made to feel that their symptoms were either inconsequential or psychosomatic. As Dr. Baker explained, those types of experiences could be due to provider bias or to lack of medical knowledge about heart disease in women. However, with the right tools and resources, ED physicians have the opportunity to be integral players in the diagnostic process as they are in a position to refer women with less urgent or early symptoms of heart disease for further follow up and an accurate and timely diagnosis.

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Women with aortic valve disease — especially women of color — tend not to be diagnosed in early stages of the disease, when they stand the best chance of having a good outcome.

JENICE BAKER, M.D.
Chair of Emergency Medicine
Chestnut Hill Hospital
Philadelphia, Pennsylvania

ED physicians have the opportunity to be integral players in the diagnostic process as they are in a position to refer women with early symptoms of heart disease for specialized care.

PREGNANCY AND CARDIOVASCULAR DISEASE

Many women first experience cardiac symptoms during pregnancy, a time that illustrates vulnerabilities in the health care system for women with cardiovascular disease. In the past 30 years, the rate of pregnancy-related deaths in the United States has risen dramatically — especially among Black women. Overall, heart disease and stroke account for one in three (34%) pregnancy-related deaths.[7]

In her presentation, Afshan B. Hameed, M.D., pointed out that even normal pregnancy puts a pregnant woman's heart under stress. She said, "Being pregnant is like being on a treadmill for nine months," which is of particular importance for women with pre-existing cardiac issues or who face challenges accessing high quality care.

Some signs and symptoms of cardiovascular disease — shortness of breath, increased heart rate and palpitations, for example — are common in normal pregnancy, which complicates the diagnostic process. Pregnancy may also affect the results of diagnostic testing. Dr. Hameed emphasized that all providers, including physicians not trained as obstetric gynecologists, must pay close attention, listen carefully to patients, and consider cardiovascular disease in the differential diagnosis when pregnant women have common symptoms. Diagnosis can also be improved through the use of screening algorithms, decision aids and consultation with appropriate specialists.

Using mortality data from California, Dr. Hameed presented a timeline showing when pregnant or postpartum women who died from cardiovascular disease had been diagnosed. Nearly half (48%) were diagnosed postmortem,

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Santa Ysabel, California

"The emergency doctor didn't take any blood work or anything. He just said, 'My wife is eight months pregnant right now, and she's tired, too. You pretty much just need to suck it up and go home.' That weekend I literally was slowly dying."
Brandie was eventually diagnosed with heart failure and required a heart transplant.

AFSHAN B. HAMEED, M.D.
Professor of Maternal-Fetal Medicine and Cardiology; Director of Obstetrics, Quality and Safety
University of California, Irvine
Irvine, California

"At autopsy, their hearts showed us the whole story. When we went back and put all the pieces together, we could see that although these women presented with symptoms and abnormal vital signs, we were not able to catch them in time. It's very, very unfortunate and now must inform us for the future."

despite having displayed concerning signs and symptoms.

DIAGNOSIS AND SOCIAL DETERMINANTS OF HEALTH

Social determinants of health also significantly affect diagnosis and patient outcomes. In addition to employment and family status, where people live, learn, work and play affect health and quality-of-life. Biological, cultural and environmental interactions, as well as interpersonal and structural discrimination, may contribute to health disparities and have a profound influence on a patient's journey through the diagnostic process.

Patrice Desvigne-Nickens, M.D., moderated a virtual panel that discussed issues related to social determinants of health. The panel, which included Daniel Calac, M.D., *WomenHeart Champion* Florence Champagne, M.S.W., Keith Ferdinand, M.D., and Angela Richard-Eaglin, D.N.P., discussed how racial and ethnic bias exacerbates the problems that contribute to missed and delayed diagnosis for women of color. While all women are vulnerable to having clinicians dismiss their symptoms as psychosomatic or caused by anxiety, many women of color find their health risks and heart disease not taken seriously, which only compounds the harm.

Trust between patients and their providers is key to proper diagnosis and care for all women, especially those who face challenges in health care access or discrimination. If a woman feels undervalued or misunderstood, she will be less inclined to ask for help or provide needed information. Clinicians should work together with patients in the diagnostic process over a period of time, monitoring symptoms and navigating

FLORENCE CHAMPAGNE, M.S.W.
WomenHeart Champion
Upper Marlboro, Maryland

"But when you're weak, when you're sick and you're facing a doctor, you're looking for help. You're just looking for help."

testing and specialty consultations. All of these require a working relationship built on trust, as well as resources.

Throughout the discussion, convening participants stressed that listening to and supporting the patient should be the clinician's first priority. Dr. Calac urged all physicians to make sure patients have a simple and direct way to reach someone for help. "That's the connection our patients need," he said. Patient portals, email and other forms of after-hours access must be available to patients.

Particularly for women who face difficulties such as accessing and paying for care or a language barrier, a clinician who understands the patient's social and economic circumstances can add important dimensions to the diagnostic process. Dr. Richard-Eaglin encouraged clinicians to focus less on the business of health care and more on getting patients the care and services they need. Dr. Ferdinand stressed that, too often, women who lack insurance are not able to access appropriate diagnostic testing and specialists, leading to disparities in health and longevity for many women.

Empowering women with health information and connecting them to community resources are effective ways to engage patients as partners in improving their diagnosis and care. At the same time, women who are ill may need more direct help. A collaborative approach to care, one that includes social workers and other community connectors, as well as clinicians from different disciplines, can help improve outcomes for patients. The health care system and the care provided must be set up to meet women where they are, whether during appointments, visits to the ED or when patients return home.

Topics for Patient-Centered Research

Having shared their knowledge and experience about women and heart disease, the challenges women face accessing timely and appropriate care, and the underlying causes of missed and delayed diagnosis, participants met in small groups for discussion. Each group was asked to brainstorm patient-centered interventions to inform research questions which, if studied, could lead to improved diagnosis and outcomes of heart disease in women.

To help guide discussion, the groups were provided the following questions to focus their attention on patient-centered solutions:

1. What specific issues, if solved or improved, would lead to substantial improvement in health/health care quality and outcomes for women?
2. What interventions could be tested to try to solve these issues?
3. What outcomes (that are meaningful to patients) could be measured to determine improvement?

The discussions were structured to maximize exchange of ideas in a limited timeframe. The ideas and questions generated reflect the diversity of participants at the convening and the topics and themes identified by the Steering Committee as most important for discussion. They do not necessarily represent a comprehensive scan of all relevant issues. WomenHeart and SIDM believe that the convening and white paper provide support for future research in this area of growing interest.

CHALLENGES AND FACTORS THAT CONTRIBUTE TO DIAGNOSTIC ERROR

Ideas generated in the small group discussions are shown in the following two sections. First, Table 1 presents challenges the groups identified as contributing to missed and delayed diagnosis of heart disease in women.

Those challenges and the factors that contribute to diagnostic error segment into issues related to patients, providers and health systems. Many of the problems and pitfalls are shared across groups, with overlapping areas of influence and responsibility that contribute to diagnostic error. For example, factors that result in a patient not understanding the diagnosis could include the patient's limited English proficiency; the patient's limited access to online sources of information; the provider's lack of medical interpretation services; the provider's inability to communicate effectively with the patient; the health system's production pressure, which cuts time short for patient-provider discussions; and the system's patient portal, which is difficult to use.

TABLE 1. CHALLENGES IN THE DIAGNOSTIC PROCESS FOR WOMEN WITH HEART DISEASE

WHAT GOES WRONG?[1]	Why? Patient-related contributing factors	Why? Provider-related contributing factors	Why? System-related contributing factors
ACCESS			
PATIENT HAS SYMPTOMS BUT DELAYS ACCESSING OR IS UNABLE TO ACCESS CARE	• Isn't aware of the risk that heart disease poses to women • Unable to pay for care due to lack of insurance, underinsurance and/or financial resources; insurance denies coverage • Unable to access health care because of limited facilities and providers in local area or lack of transportation • Has been turned away from care in the past, diagnosed with anxiety or given erroneous information • Distrusts providers and/or health care system	• Not familiar with risks factors or symptoms of cardiovascular disease specific to women • Lack of screening or outreach for women with risk factors or symptoms of heart disease	• Patients may be underserved by the health care system based on their location, economic status, age, sex, gender, sexual orientation, race and/or ethnicity. • Lack of public health messaging to women about heart disease
HISTORY			
RELEVANT INFORMATION IS OMITTED FROM PATIENT'S HISTORY OR NOT CAPTURED EFFECTIVELY OR CORRECTLY	• Does not know or understand the details or significance of family medical history • Not familiar with known risk factors for cardiovascular disease in women • Language or cultural differences are barriers to communication • Has not been educated about the importance of accurate reporting of symptoms • Distrusts providers and/or health care system	• Lack of time and attention during clinical visit • Not familiar with risk factors or symptoms of cardiovascular disease specific to women • Is unable to gain patient's trust • Implicit bias based on patient's sex, gender, age, race, ethnicity, appearance	• Time pressure results in rushed clinical visits • Medical school training focuses on cardiovascular disease in men more than women • Insufficient research about aspects of cardiovascular disease that are unique in women, including the impact of racism and sexism on health

TABLE 1. CHALLENGES IN THE DIAGNOSTIC PROCESS FOR WOMEN WITH HEART DISEASE (CONT'D)

WHAT GOES WRONG?[1]	Why? Patient-related contributing factors	Why? Provider-related contributing factors	Why? System-related contributing factors
PHYSICAL EXAM			
SIGNS OF PATIENT'S HEART DISEASE ARE MISSED OR MISINTERPRETED	• Afraid of physical exam, anxious about disrobing, embarrassed about obesity or other aspects of appearance • Language or cultural differences are barriers to communication • Distrusts providers and/or health care system	• Not familiar with physical findings of cardiovascular disease specific to women • Is unable to gain patient's trust • Implicit bias based on patient's sex, gender, age, race, ethnicity, appearance	• Time pressure results in rushed clinical visits • Medical school training focuses very little on sex differences in cardiovascular disease • Insufficient research about aspects of cardiovascular disease that are unique in women, including the impact of racism and sexism on health
TESTING			
PATIENT IS REFERRED FOR IMAGING, LAB WORK, OR OTHER TESTING BUT DOES NOT OR IS NOT ABLE TO FOLLOW THROUGH	• Unable to pay for testing due to lack of insurance, underinsurance and/or financial resources; insurance denies coverage • Has not been educated about or does not understand the importance of testing • Fears pain, discomfort or rigors of testing (e.g., on treadmill)	• Failure to appropriately communicate the significance of the diagnosis, potential for treatment and/or possible prognosis	• Health system creates barriers when patients have to get care outside their doctor's office (e.g., from a lab or specialist) • Testing that is standard for men with heart disease may not be as accurate or relevant for women
NO TESTING OR WRONG TEST ORDERED	• Does not have sufficient information or understanding to know what to ask for	• Not familiar with appropriate tests for heart disease conditions in women	• Lack of research about heart disease in women • No effort has been made to empower women to ask about testing

TABLE 1. CHALLENGES IN THE DIAGNOSTIC PROCESS FOR WOMEN WITH HEART DISEASE (CONT'D)

WHAT GOES WRONG?[1]	Why? Patient-related contributing factors	Why? Provider-related contributing factors	Why? System-related contributing factors
TESTING (CONT'D)			
PATIENT DOES NOT RECEIVE RESULTS OF TESTING	• Is told and believes "no news is good news" • No computer and/or access to internet for connection to patient portal • Does not have sufficient information or understanding to know what to ask for	• No process for closing the loop on communication with patient and specialists • Some providers, e.g., nurse practitioners, do not receive test results because they are not considered to be primary care practitioners	• Lack of process for follow-up • Information technology systems and patient portals are not user friendly, underutilized by patients and difficult to adapt or customize
ASSESSMENT			
PATIENT'S CARDIAC SYMPTOMS ARE MISATTRIBUTED TO ANOTHER DISEASE OR ARE DISMISSED AS UNIMPORTANT OR THE RESULT OF ANXIETY OR STRESS	• Is not aware of the risk that heart disease poses to women • Is not empowered to question the initial diagnosis • Having symptoms dismissed, called "psychosomatic" or attributed to anxiety or stress can result in further avoidance of care	• Implicit or explicit bias discounts heart disease as possible diagnosis according to age, gender, race and/or ethnicity • Lack of knowledge about heart disease in women • Failure to use/lack of access to clinical decision support tools such as checklists, differential diagnosis list, especially those that account for sex/gender • Failure to consult with heart disease and other specialists	• Guidelines for assessment and treatment are based on research that does not reflect the sex differences and/or diversity of patients • Lack of interdisciplinary training for teamwork in diagnosis
REFERRAL/CONSULTATION			
PATIENT IS REFERRED TO SPECIALIST BUT DOES NOT OR IS NOT ABLE TO FOLLOW THROUGH	• Doesn't understand/is not informed why the referral is necessary • Unable to pay for care due to underinsurance, no insurance or lack of financial resources; insurance denies coverage • No logistical support, e.g., transportation, childcare, time off from work	• No process for closing the loop with patient or specialists	• Complicated health system creates barriers when patients have to get care outside their doctor's office (i.e., f rom a lab or specialist) • Lack of investment in exurban and rural health facilities

TABLE 1. CHALLENGES IN THE DIAGNOSTIC PROCESS FOR WOMEN WITH HEART DISEASE (CONT'D)

WHAT GOES WRONG?[1]	Why? Patient-related contributing factors	Why? Provider-related contributing factors	Why? System-related contributing factors
FOLLOW-UP			
PATIENT DOES NOT RECEIVE APPROPRIATE MONITORING FOR HER CONDITION	• Unable to pay for monitoring due to underinsurance, no insurance or lack of financial resources; insurance denies coverage • Has not had the diagnosis or possible complications sufficiently explained • Is not informed about how to manage device(s) needed for home monitoring	• Failure to track patients in need of follow up • Lack of appreciation for patient's inability to pay for, maintain or use home monitoring devices • Does not have information about community resources available to patient • Does not provide adequate training for patient about how to use monitoring devices	• Lack of resources to assist with referrals, prior authorization and patient financial assistance • Lack of financial incentive to expand services in remote areas
PROVIDER DOESN'T LEARN ABOUT DELAYED OR MISSED DIAGNOSIS	• Does not know about medical error • Has not been informed of the value of providing feedback to providers • Knows something went wrong but is unable to gain enough information for full understanding • Doesn't feel empowered to or know of a mechanism for reporting back to provider about diagnostic error • Feels angry and betrayed; wants no further contact with provider	• No process in place for learning about diagnostic errors • Fear of legal action for malpractice	• Discourages sharing information about medical errors • No process in place for learning about diagnostic errors

[1]Categories are based on the DEER (diagnostic error evaluation and research) taxonomy, as described in:
Schiff GD, Kim S, Abrams R, et al. Diagnosing diagnostic errors: lessons from a multi-institutional collaborative project. In: Henriksen K, Battles JB, Marks ES, et al., editors. *Advances in Patient Safety: From Research to Implementation*. Vol 2. Agency for Healthcare Research and Quality Web site. 2005. https://www.ncbi.nlm.nih.gov/books/NBK20492/

SAMPLE RESEARCH QUESTIONS FOR IMPROVING DIAGNOSIS OF HEART DISEASE IN WOMEN

The small groups generated ideas for actions to address the challenges covered in Table 1. The following lists reframe those suggested actions as potential research questions. It is our hope that researchers will take them on as their own and help seek answers. Similar to challenges presented in the Table, the sample research questions naturally sort into actions focused on patients, providers and health systems.

Patients. To help ensure that women receive timely and accurate diagnoses, participants identified potential research questions related to enhancing patient services, providing tools patients can use to monitor their health and record personal health information, and improving access to health resources and support.

- Are patients who access information or support from other women with heart disease and/or from a patient-centered organization more likely to be accurately diagnosed or better informed about their diagnosis compared to those who do not access peer support?
- Among women who experience a long-term risk factor for heart disease during pregnancy (i.e., preeclampsia, gestational diabetes) and are informed about their risk, if/when they develop heart disease years later, are they diagnosed more quickly and accurately compared to those who are not aware of the risk?
- Do women who use a specific tool or resource to collect family history and to communicate that with providers get diagnosed more quickly/accurately than those who do not?
- Do women who self-assess heart rhythm, blood pressure or other biofeedback using wearable devices get diagnosed more quickly/accurately than those who do not?
- Do women who use a specific tool to track physical symptoms and/or receive education about the best ways to report and reproduce symptoms (e.g., learn how to track and report if their symptoms "get worse") get diagnosed more quickly/accurately than those who do not?
- Does access to a social worker for assistance with health insurance or other means of paying for health care lead to more timely diagnosis of heart disease, compared to patients who do not receive assistance from a social worker?
- Do patients who use a hospital system's patient portal to review their records and/or see the clinician's notes — and receive support in understanding the information — have more accurate and timely diagnosis than patients who do not?
- Are patients who receive an appointment reminder by text message more likely to come in for diagnostic testing than those reminded by telephone?

Providers. Ideas for improving diagnosis of heart disease in women at the provider level included interventions focused on decision support tools, communication, cultural competency and medical education and training.

- Do clinicians who have received comprehensive cultural competency and anti-bias training (and are held accountable for what they have learned) deliver

more timely and accurate diagnosis of cardiovascular disease in women compared to those who do not receive the training (or are not held accountable)?

- Do physicians who have been trained in the similarities and differences in how women and men experience heart disease demonstrate greater diagnostic proficiency than physicians who have not received that education?
- Does incorporating into clinical decision-making data from a registry that tracks patients' social determinants of health — e.g., employment status — lead to fewer missed diagnoses of heart disease?
- Do clinicians who utilize tools that allow them more direct communication with patients — e.g., scribes for charting support during the appointment or email and text for asynchronous communication — have greater diagnostic accuracy in women's heart disease than clinicians who do not?
- Does a decision support aid with specific sex and gender inputs result in more accurate and timely diagnosis than a traditional aid that is agnostic for sex and gender?
- Does using patients with heart disease as actors in simulation training programs improve the diagnostic accuracy of clinicians, compared to clinicians who do not receive such training?
- Does sharing the differential diagnosis with patients who have symptoms of heart disease lead to more timely diagnosis of heart conditions (than not)?
- Does the use of a cardiovascular disease risk score result in more timely, accurate diagnosis for women with heart disease?
- Do physicians who have participated in interdisciplinary training programs — e.g., ob-gyn and cardiology combined — deliver more timely and accurate diagnoses of cardiovascular disease in women compared to those who do not participate in such training?
- Do women with heart disease receive a more timely and accurate diagnosis when treated by a clinician of the same gender, race and/or ethnicity?
- Are obstetric gynecologists who received education about cardiovascular risks in women more likely to make accurate and timely diagnoses of heart disease?

Health systems. At the level of hospitals and health systems, participants in the small groups suggested interventions related to enhancing communication with patients, improving electronic health record systems and patient portals, effectively using telemedicine, fostering teamwork among clinicians and staff members, and increasing the diversity of the workforce.

- Do women seen in emergency departments using interdisciplinary teams experience fewer diagnostic errors related to heart disease than those seen in emergency departments using solo clinicians?
- Do women seen in hospitals that require admission after repeated emergency department visits have more timely and accurate diagnosis of heart disease than those seen in hospitals without such policies?
- Do women seen in health systems that use telehealth-enabled remote cardiology consultations during the diagnostic process

experience more timely and accurate diagnosis of heart disease than women seen in health systems without virtual cardiology consultation capacity?

- Do women seen in a health system using a women's cardiovascular disease "scorecard" experience more timely and accurate diagnosis of heart disease than women seen in a health system without a quality or safety scorecard for women's cardiovascular disease?
- Do women seen in institutions with focused training in obstetric gynecologist residency about the risk for cardiovascular disease experience more timely and accurate diagnosis of heart disease than women seen in institutions without such training?
- Does a health system with a universal diabetes/gestational diabetes protocol (such as the USPSTF guidelines for screening, diagnosis, and management of gestational diabetes) diagnose more cases of heart disease in women than a health system without such a protocol?
- Do women seen in health systems that analyze real-world data on women with heart disease and share that information with clinicians experience more timely and accurate diagnosis of heart disease than women in health systems that do not disseminate this type of real-world data?
- Would training that incorporates blinding of patients for diagnostic exams yield greater awareness and appreciation for gender and racial bias?
- Do women seen by clinicians or in health systems where value-based reimbursement payments are tied to gender/sex competency experience more timely and accurate diagnosis of heart disease than women seen by clinicians or in health systems without such payment approaches?

Conclusion

We anticipate that these and other similarly actionable research questions will provide tangible outcomes to improve diagnosis of heart disease in women. People who participated in the convening benefited from the opportunity to share their knowledge and stories about the challenges women with heart disease face. We expect they will continue to draw on this experience as they provide care and engage with patients. For the broader health care community, we hope this report will inspire research and foster solutions centered on women's experiences and needs.

All women deserve accurate and timely diagnosis when facing health concerns. It is important that patients are empowered to take charge of their health and that health care providers and health systems have the knowledge, tools and resources needed to provide high quality care, free from bias and barriers. WomenHeart and SIDM are committed to that value and will continue to work to promote patient-centered initiatives to improve diagnosis of heart disease in women.

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Appendices

Appendix A

The PICOTS Framework: A Path to Research

The PICOTS framework is a valuable tool for developing patient-centered outcomes research (PCOR) using a comparative effectiveness approach. The goal of the small group exercises was to move from discussions about the problem of misdiagnosis of heart disease in women and begin to identify potential solutions. There were four topics for discussion:

- Provider Education
- Patient-Provider Communications
- Addressing social determinants of health
- Pregnancy-related diagnostic challenges

THE PICOTS FRAMEWORK

- Patient Population
- Intervention
- Comparator
- Outcome
- Timing
- Setting

Each small group participated in four rounds, cycling through each of the topics, guided by the PICOTS framework, brainstorming and building upon the ideas from the group before.

In this process, the group starts with a focus area of discussion; in our exercise this was the topic area. The group then identifies a series of single issues that need to be addressed within the topic, from which possible interventions and solutions emerge. The final step is to take each of those interventions and develop research questions using the PICOTS framework.

LESSONS LEARNED

We created the expectation at the outset that we might not be able to complete each portion of the framework, but that we would address what we could. In the end we identified many interventions, with a sense of the population to be studied, the comparator and in some cases, the outcomes we were seeking. We were often unable to address timeframe or setting. Overall the list of research questions provided in the report is a good start for researchers who may wish to use the PICOTS model to flesh out their own research studies.

EXAMPLES

Focus Area

FOCUS AREAS
Provider Education

Rounds 1 and 2

SINGLE ISSUES	
1. From this large category of concern, what specific issues, if solved or improved, would lead to substantial improvement in health/ healthcare quality and outcomes for women?	Increase provider awareness of and recognition of heart disease symptomology in women
2. What interventions could be tested to try to solve these issues?	Leverage the value of lived experience of women who've experienced misdiagnosis
3. What outcomes (that are meaningful to patients) could be measured to determine improvement?	Improve diagnostic quality

Rounds 3 and 4

PICOTS FRAMEWORK	
P: What is the population?	Physicians and advance practice clinicians in the Emergency Department
I: What is the intervention?	A CME course using real patients with lived experience in training about diagnosis of women's heart disease
C: To what will you compare the intervention?	Standard/traditional training that does not involve real patients
O: What are the outcomes you are seeking?	Increase diagnostic proficiency of clinicians
T: In what timeframe?	(TBD in future discussions)
S: In what what setting?	(TBD in future discussions)

The PICOTS Framework: A Path to Research (cont'd)

EXAMPLES

Focus Area

FOCUS AREAS
Patient-Provider Communication

Rounds 1 and 2

SINGLE ISSUES	
1. From this large category of concern, what specific issues, if solved or improved, would lead to substantial improvement in health/ healthcare quality and outcomes for women?	Self-monitoring, increasing awareness among women of their own symptoms and risk
2. What interventions could be tested to try to solve these issues?	Wearables and other digital tech
3. What outcomes (that are meaningful to patients) could be measured to determine improvement?	Improve patient self-advocacy, ability to describe symptoms accurately, and ultimately, diagnostic quality

Rounds 3 and 4

PICOTS FRAMEWORK	
P: What is the population?	Women exhibiting symptoms of arrhythmia
I: What is the intervention?	Self-assessment of heart rhythm and other biofeedback using wearable devices
C: To what will you compare the intervention?	No self-tracking
O: What are the outcomes you are seeking?	Increased likelihood of timely diagnosis among these women
T: In what timeframe?	(TBD in future discussions)
S: In what what setting?	(TBD in future discussions)

Focus Area

FOCUS AREAS
Pregnancy-related Diagnostic Challenges

Rounds 1 and 2

SINGLE ISSUES	
1. From this large category of concern, what specific issues, if solved or improved, would lead to substantial improvement in health/ healthcare quality and outcomes for women?	Lack of awareness among providers of cardiovascular issues connected to pregnancy, lack of knowledge about how to address
2. What interventions could be tested to try to solve these issues?	Specific cardio training connected to OB/GYN training
3. What outcomes (that are meaningful to patients) could be measured to determine improvement?	Improve recognition of the issues and better diagnostic quality

Rounds 3 and 4

PICOTS FRAMEWORK	
P: What is the population?	OB/GYNs in their residency programs
I: What is the intervention?	Interdisciplinary training program during residency that includes cardiology with OB/GYN
C: To what will you compare the intervention?	Standard/traditional training
O: What are the outcomes you are seeking?	Greater diagnostic proficiency
T: In what timeframe?	(TBD in future discussions)
S: In what what setting?	(TBD in future discussions)

Appendix B

01.27.21
Agenda

TIME (ET)	TOPIC	SPEAKERS
10:00 AM	Welcome	*Celina Gorre, CEO WomenHeart*
10:10 AM	Misdiagnosis of Heart Disease in Women: Stories of Survival	*Lyn Behnke* *Rayette Brown* *Starr Mirza*
10:30 AM	Understanding Diagnosis: Mapping Diagnostic Error	*Kathy McDonald, PhD*
10:45 AM	Where do we go from here? Building on the Environmental Scan	*Suz Schrandt, JD*
11:00 AM	**PANEL:** How Race, Gender and Social Determinants of Health Impact Women's Care and Diagnostic Quality **Moderator:** Patrice Desvigne-Nickens, MD	**Panelists:** *Daniel Calac, MD* *Florence Champagne* *Keith Ferdinand, MD* *Angela Richard-Eaglin, DNP*
Noon	Break	
12:15 PM	**VIDEO SERIES:** A Focus in Specific Conditions and Challenges	
	Heart Failure	*Eileen Hsich, MD*
	Heart Valve Disease	*Rachel M. Bond, MD*
	Microvascular Disease/ SCAD	*Sharonne Hayes, MD*
	Challenges in the Emergency Room	*Jenice Baker, MD*
1:00 PM	Welcome Back A Heart Disease Story	*Celina Gorre, CEO WomenHeart* *Brandie Taylor*
1:07 PM	Focus on Pregnancy and Heart Disease: Diagnostic Challenges	*Afshan B. Hameed, MD*
1:30 PM	**SMALL GROUP WORKING SESSIONS** *(15 min break between Groups 2 and 3)* **Group One:** Provider education **Group Two:** Pregnancy-related diagnostic challenges **Group Three:** Patient-Provider Relationship/Communication **Group Four:** Overcoming social determinants of health	
3:30 PM	Report back and close	
4:00 PM	Adjourn	

Appendix C

01.27.21 Attendees

C. Noel Bairey Merz, MD, FACC, FAHA, FESC — Cedars-Sinai Medical Center

Theresa Beckie, PhD — University of South Florida

Biykem Bozkurt, MD, PhD — DeBakey VA Medical Center, Director of Winters Center for Heart Failure Research, Baylor College of Medicine

Rayette Brown — *WomenHeart Champion*

Joe Ann Burgett — *WomenHeart Champion*

Daniel Calac, MD — Chief Medical Officer, Indian Health Council

Justin Choi, MD — Assistant Professor of Medicine, Weill Cornell Medicine

Patrice Desvigne-Nickens, MD — Medical Officer, Heart Failure and Arrhythmias, NHLBI, NIH

Vasken Dilsizian, MD — Professor of Medicine and Radiology; Chief, Division of Nuclear Medicine, University of Maryland School of Medicine

Paul L. Epner, MBA, MEd — CEO, Society to Improve Diagnosis in Medicine

Keith Ferdinand, MD — Tulane University School of Medicine

Amy Friedrich-Karnik, MPP — VP, Advocacy and Communications, WomenHeart

Kecia Gaither, MD, MPH, FACOG — Director, Perinatal Services/ Maternal Fetal Medicine, NYC Health + Hospitals System

JoAnn Gerardo — *WomenHeart Champion*

Celina Gorre, MPH, MPA — CEO, WomenHeart

Martha Gulati, MD, MS, FACC, FAHA, FASPC, FESC — President Elect, American Society for Preventive Caridology

Afshan Hameed, MD, FACC, FACOG — Professor, Maternal Fetal Medicine & Cardiology, University of California, Irvine

Eileen Handberg, PhD, APRN-BC, FAHA, FACC, FPCNA — Professor Medicine, University of Florida

Ante Harxhi, MD — Medical Director, Johnson and Johnson

Sharonne Hayes, MD, FACC, FAHA — Professor, Cardiovascular Medicine, Mayo Clinic, Rochester MN

Brianna Harris-Henderson, Patient Advocate — Founder/CEO, LetsTalkPPCM

Heidi House, *Executive Assistant to Save The Mommies* — Illinois Representative for Save The Mommies, INC

(CONTINUED ON NEXT PAGE)

STEERING COMMITTEE

Jenice Baker, MD, FACEP
Chair of Emergency Medicine,
Chestnut Hill Emergency Department

Lyn Behnke, DNP, FNPBC, CHFN, FAACVPR
WomenHeart Champion

Kathy Berra, RN, NP-NC, FAHA, FAAN, FPCN
Co-Director, The LifeCare Company

Rachel M. Bond, MD, FACC
System Director, Women's Heart Health
Dignity Health, Arizona

Florence Champagne, MSW
WomenHeart Champion

Eileen Hsich, MD
Heart Transplant Medical Director,
Cleveland Clinic

Heather Johnson, MD, MMM, FAHA, FACC
Christine E. Lynn Women's Health &
Wellness Institute, Boca Regional Hospital,
Baptist Health So. Florida

Barry Liden
VP, Patient Engagement, Edwards Lifesciences

Kathryn McDonald, PhD, MM
Bloomberg Distinguished Professor,
Johns Hopkins University

Brandie Taylor
WomenHeart Champion,
Iipay Nation of Santa Ysabel

Attendees (cont'd)

Sue Koob, MPA — CEO, Preventive Cardiovascular Nurses Association

Janice Kwan, MD, MPH — Assistant Professor Medicine, University of Toronto

Starr Mirza — *WomenHeart Champion*

Jeanne Poole, MD, *Professor of Medicine, Division of Cardiology* — University of Washington School of Medicine

Tricia Regan — Filmaker Ms Diagnosed

Angela Richard-Eaglin, DNP, MSN, FNP-BC, CNE, FAANP — Assistant Professor, Duke University School of Nursing

Elena Rios, MD, MSPH, FACP — President & CEO, National Hispanic Medical Association

Stacey Rosen, MD — SVP, Women's Health Northwell Health / Katz Institute for Women's Health

Haley Stolp, MPH — Centers for Disease Control and Prevention

Suz Schrandt, JD — Senior Patient Engagement Advisor, Society to Improve Diagnosis in Medicine

Glenda Sexauer — *WomenHeart Champion*

Kelly Smith, PhD — Senior Director, MedStar Health Institute for Quality and Safety

Calondra Tibbs, MPH — Special Advisor, WomenHeart

Kaveeta Vasisht, MD, PharmD — Associate Commissioner for Women's Health/Director, Office of Women's Health, FDA

Mary Norine Walsh, MD — Medical Director, Heart Failure and Cardiac Transplantation St. Vincent Heart Center

Nanette Wenger, MD — Emory Univsersity School of Medicine

Julie Wright, MSNEd, RN — System Director, Clinical Risk Management, Intermountain Healthcare

Sheryl Zaworski, JD — *WomenHeart Champion*

Appendix D

Stories of Survival: Missed and Delayed Diagnosis of Heart Disease in Women

Our Stories

These stories from *WomenHeart Champions*, women living with heart disease, are just a few examples of the thousands of stories of diagnostic error related to heart disease in women.

WomenHeart, the Society to Improve Diagnosis in Medicine, and the many patients, clinicians, researchers, and other experts are committed to this effort to identify the greatest research needs in heart disease-related diagnostic quality, safety and improved health outcomes and lives of women faced with heart disease. Each of these stories reveals valuable lessons about how we can improve the diagnostic process and we are grateful to the women who were willing to share these personal accounts.

Brandie's Story

Brandie was diagnosed with cardiomyopathy and congestive heart failure at the age of 32. When she was about eight months into her pregnancy, Brandie began having symptoms of shortness of breath and fatigue, but was initially only prescribed inhalers and sleep medication to address her symptoms at the local Indian Health Clinic. She felt that something was wrong, and it wasn't asthma, so her mother later took her to the nearest hospital, an hour away, where her symptoms were dismissed as pregnancy-related and she was told to deal with it. After continuing to have symptoms she was taken to another hospital where she was immediately placed in the intensive care unit because she was going into heart failure. Brandie believes that because of the delay in diagnosis and appropriate treatment her heart was weakened and led to her need for a heart transplant.

Dianne's Story

Dianne initially presented to her allergist, due to a history of asthma, with symptoms of shortness of breath and fatigue. After a monitored walk, lasting only three minutes because she was out of breath, she was sent back to her primary care doctor for follow-up. She was unable to see her primary care provider the same day, so she made an appointment for the following day. Danne's primary care provider found a "little anomaly" after doing an EKG, then referred her to a cardiology practice. Dianne got an appointment with the "first avalaible cardiologist" the following day where a next day stress test and echocardiogram was ordered, but her insurance denied the claim. Only after the cardiologist intervened was she able to get her test the following Monday. During her stress test she passed out and was immediately admitted to the hospital and scheduled for a heart catherization the following day. She coded in the cath lab and underwent open heart surgery for a blocked left anterior descending artery and damage to the mitral and tricuspid valves. The total time between the onset of symptoms and the cath lab was only two weeks, however no one ever communicated the urgency of her situation throughout the process.

After reviewing her medical records, Dianne realized that her doctor had recorded test results that were warning signs and risk factors for heart disease, such as high blood pressure, high LDL and low HDL, obesity, and pre-diabetes, however she was not told of the danger. She "did not know to ask for copies of [her] test results and trusted [her] doctor to advise her of risk factors."

Stories of Survival: Missed and Delayed Diagnosis of Heart Disease in Women (cont'd)

Florence's Story

Unemployed and uninsured, Florence went to the emergency room for nearly a year experiencing symptoms of chest and upper body discomfort, shortness of breath, fatigue, backache, and pain radiating down her arm. She was finally referred to a cardiologist, after she saw her primary care doctor, but she had to borrow the funds to pay for the visit. Florence found out that an essential test, a cardiac catherization, was never done for her because she was uninsured. Her cardiologist assured her he would "find a way for [her] to get the proper test" and sent her to a colleague for the cardiac catherization, where they found that her left anterior descending artery was 99.9% blocked and rushed her to the operating room to save her life. Florence's diagnosis delay was not only impacted by her lack of insurance, but also because no provider believed there was a problem. She also believes that her race and gender played a role in delayed diagnosis. In addition to Florence's diagnosis delay, she was unable to get the follow-up care and therapy, such as cardiac rehab, that was necessary for her recovery. She then "had to try to recover, breathe, walk, and regain strength to improve and reduce [further heart disease risk] all on her own."

Glenda's Story

Glenda went to her obstetrician/gynecologist because she was experiencing shortness of breath, nausea, fatigue, weight gain and a "gurgle" in her chest and thought she was going through menopause. But after her symptoms didn't improve, she saw a different doctor and was evaluated for thyroid issues. Later, she went to the doctor thinking it might be pneumonia. By the time she got to her last doctor, because the "pneumonia" wasn't clearing up, she was sent to the emergency room and diagnosed with congestive heart failure. Four days later she went into cardiac arrest. Each time she interacted with a health care provider she was treated exclusively for the symptoms she presented, and there was no follow-up by providers.

After her husband insisted she continue to seek care, she mentioned to a doctor that she had gained weight and he ordered an EKG, which helped lead to the correct diagnosis. She believes that doctors and patients share responsibility in the diagnostic process. She admits that she may have misled her providers by only giving them the information specifically asked or that she thought was important.

Gwen's Story

In 1988, at age 32, Gwen was diagnosed with heart disease. She knew she had a family history of sudden cardiac death and had experienced some chest discomfort and shortness of breath. When she finally went to the emergency room while experiencing severe premature ventricular contractions and dizziness, she was treated for a non-existing heart attack and referred to a cardiologist. She got the right diagnosis of hypertrophic cardiomyopathy once she got to the cardiologist. But for years after, she felt there was limited information about her condition, particularly among emergency room, EMT and general nurse professionals. She was initially told that she would "have a shortened life expectancy" with no further information on what that meant nor provided any support for the emotional impact the diagnosis had on her life. In many cases, she's had to educate providers about her condition, what it felt like and how foods, drugs and treatments can trigger adverse reactions.

Stories of Survival: Missed and Delayed Diagnosis of Heart Disease in Women (cont'd)

JoAnn G's Story

At age 55, JoAnn presented with symptoms of chest and upper body discomfort, shortness of breath and fatigue. She finally got the right diagnosis when her current cardiologist listened to her and thoughtfully reviewed all her test results. Prior to that, JoAnn felt other doctors made a lot of assumptions before thoroughly reviewing all the test restults. She has been diagnosed with angina, aortic aneurism, broken heart syndrome, heart attack and spontaneous coronary artery dissection. The lesson in her diagnosis journey was that "it is very important to chose your words carefully when describing your symptoms."

Joe Ann B's Story

Joe Ann was first diagnosed with heart disease at the age of 52 years. She went to an urgent care walk-in clinic with symptoms of chest and upper body discomfort, shortness of breath, nausea, jaw and neck pain, backache, and a persistent dry cough, and she was told that she had anxiety and acid indigestion. The provider even remarked that her medical record should note that she is "morbidly obese," which was the cause of her symptoms. Worse yet, her general practitioner agreed.

It wasn't until a friend intervened after her symptoms had significantly progressed that she went to his cardiologist and was diagnosed with heart disease. She believes that because her doctors didn't believe that women could have heart disease and judged her by her appearance, she wasn't taken seriously. She says that "every time [she] asked [her] doctors about a specific symptom they minimized it and misdiagnosed it." And even when she did get to a cardiologist, when she asked questions, she was told "you're a smart woman. You will figure it out." She believes her life was saved when she attended the WomenHeart Science and Leadership Symposium – other women listened to her and the doctors at the Symposium provided suggestions to improve her treatment.

Judy's Story

Judy was diagnosed with congenital heart disease and heart valve problems at the age of 10 years. She got a diagnosis when she went to the emergency room after seeking treatment for being hit in the forehead with a bat. She had surgeries at a young age to fix defects in her heart and later received a bovine heart valve in 2006. She was actually one of the first children to survive surgeries to repair her interventricular septal defect in the late 1950's. Her accidental and early diagnosis allowed her to get the right treatment and ensure her health.

Lyn's Story

At the age of 50, Lyn began having a "funny feeling in her neck, [that she] couldn't get rid of." She was referred for a stress test and was later diagnosed with congestive heart failure, coronary artery disease and peripheral arterial disease. After bypass surgery she developed blockage in the right coronary. It was also thought that she had a bad left internal mammary artery (LIMA) graft. While trying to fix the blockages, her artery was ruptured and she went into cardiac arrest and had a subsequent balloon pump. Her cardiologist overlooked previous films that could have compared the blockages and LIMA to determine the right course of treatment. Lyn felt that when entering care, she was only seen as an overweight, Native American woman, not as someone who is a nurse practitioner who participated in cardiac rehab daily.

Stories of Survival: Missed and Delayed Diagnosis of Heart Disease in Women (cont'd)

Rayette's Story

At 34 years old, Rayette was told that she didn't have heart disease, that it was all in her head. She kept going back to her doctors for a whole month with symptoms of chest and upper body discomfort, shortness of breath, nausea/vomiting, fatigue and other symptoms – being very persistent – until finally learning she had heart disease. She was diagnosed with angina, atrial fibrillation, coronary artery disease and small vessel disease. At each ER visit prior to getting her correct diagnosis, her EKG and blood tests would come up "normal," and she was told it was a virus, she was having anxiety, and she was even given a pregnancy test because of the nausea and fatigue. She felt that doctors had been too quick to diagnose and attempt treatment of the simple symptoms, not getting to the cardiac issues soon enough. She has had to be an advocate for herself and never gave up on getting the right diagnosis.

Sheryl's Story

Over the course of four years of "normal" results on cardiac diagnostic tests, despite ongoing chest discomfort and jaw pain, Sheryl was diagnosed with panic attacks and potential dental issues. While her cardiologist suspected microvascular disease, they simply prescribed a "heart healthy" diet and lifestyle changes and talked her out of getting certain diagnostic tests, warning her that they were expensive and complicated. After a severe instance of her ongoing symptoms, Sheryl took charge of her health and scheduled an appointment at the Mayo Clinic where an angiogram finally confirmed her diagnosis of microvascular disease.

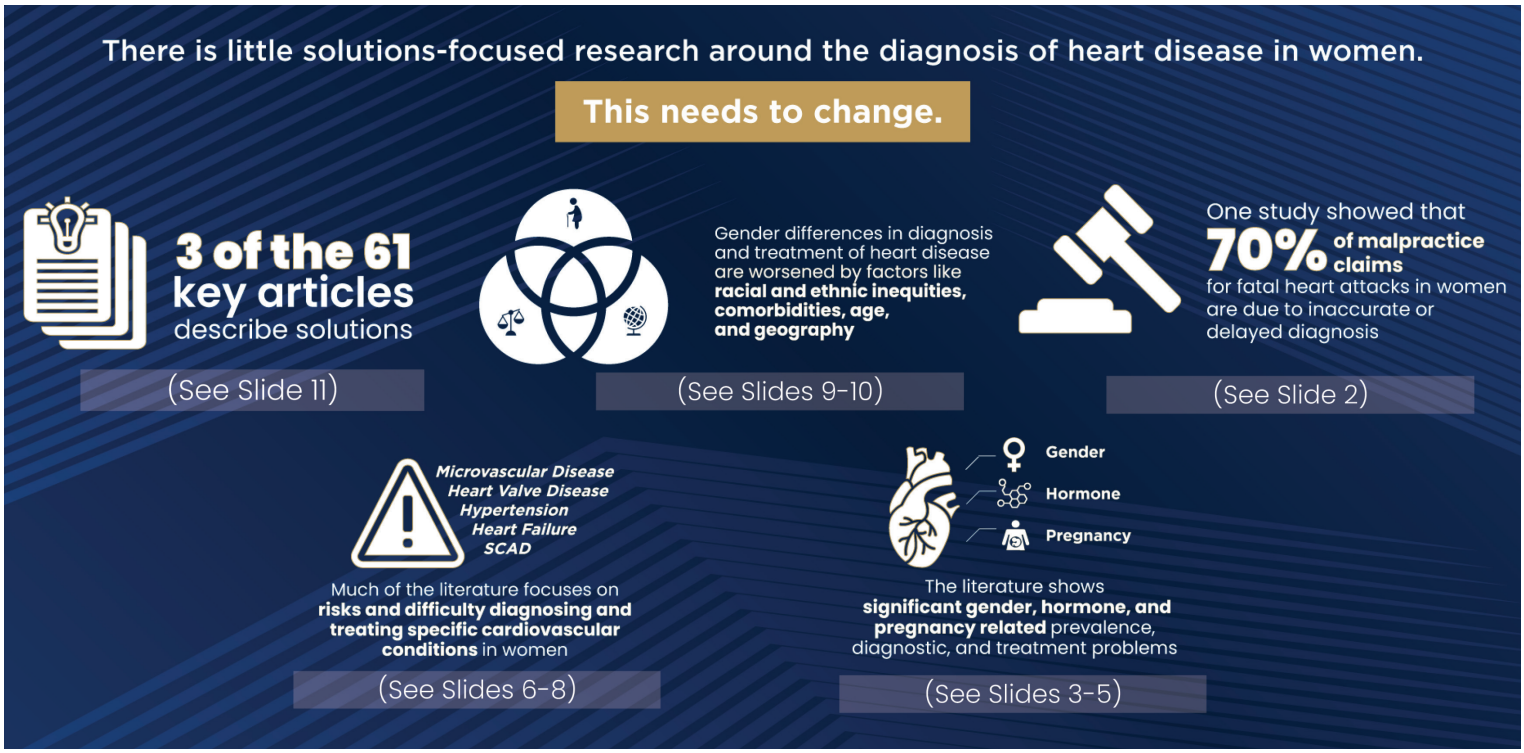
After diagnosis, Sheryl was then provided with several treatment options that had never been suggested by the network cardiologist and invited to participate in a Mayo Clinic research study. In this study, Sheryl's own stem cells were harvested and placed in her left anterior descending artery (LAD) with the hope of improving the endothelial tissue function in her heart. As a result, her chest and jaw pain symptoms have been greatly reduced. Sheryl thinks that "even well-meaning primary care physicians and cardiologists may not be educated on the finer aspects of how heart disease presents in women" and the combination of lack of awareness, medical research, dissemination of findings, and gender bias contributed to the delay in her diagnosis.

Starr's Story

After years of various symptoms, such as discomfort in her upper body, shortness of breath, episodes of pre-syncope, and visual impairments, it took going into cardiac arrest at 23 years old to "prove" that Starr was sick. Throughout her teen and young adult years, doctors told Starr she had anorexia, bulimia, was suffering from panic attacks, and that she was a hypochondriac. Because she was so young, she was never given a cardiac examination. She attributes her delayed diagnosis to the fact that she was a young female and had little or no health insurance. She has since been diagnosed with prolonged Q-T syndrome, arrythmia-induced cardiomyopathy which led to congestive heart failure, and multi-valvular dysfunction.

Appendix E

Environmental Scan



Diagnostic-Error Specific

FINDINGS	CITE	FINDINGS	CITE
This feature article on ACC's website discusses findings from The Doctor's Company Foundation's work that shows that 2/3 of women who die suddenly from a heart attack had no previous symptoms. From the study: "...in 70 percent of claims the patient died when her heart condition was not correctly diagnosed and 28 percent had heart muscle damage from myocardial infarction."	Taking the Risks to Heart: Misdiagnosis of Heart Disease. Access at: https://www.acc.org/membership/join-us/benefits/additional-member-only-benefits/acc-and-the-doctors-company/the-doctors-company-updates/2017/02/20/12/55/taking-the-risks-to-heart-misdiagnosis-of-heart-disease	Landmark study released by David Newman Toker analyzing medical malpractice claims data to show that three main causes of diagnostic error related death. The first category is cancers, and the second is a multitude of CVD related errors. See Appendix M for infographic.	David E. Newman Toker , et. al. Serious misdiagnosis related harms in malpractice claims: The "Big Three" vascular events, infections, and cancers. Diagnosis Volume 6: Issue 3. DOI: https://www.degruyter.com/document/doi/10.1515/dx-2019-0019/html. Published online: 11 Jul 2019.
This article on the AHA website discusses findings from the Brush et. al study published in February 2020 exploring symptom differences in women's heart attack and the need to expand clinician training and awareness.	Changing the way we view women's heart attack symptoms. Access at: https://www.heart.org/en/news/2020/03/06/changing-the-way-we-view-womens-heart-attack-symptoms	Maya describes a variety of factors in missed and delayed diagnoses of numerous conditions affecting women. From the article: "There's a general lack of knowledge about women's symptoms, bodies and conditions that disproportionately affect them... that's the legacy of decades of women being underrepresented or excluded from the research."	Maya Dusenberry, in ACHJ blog post about her book, Bad Medicine: The Truth About How Bad Medicine and Lazy Science Leave Women Misdiagnosed and Sick, Harper Collins Publishing, 2018. Accessed at: https://healthjournalism.org/blog/2018/11/women-more-often-misdiagnosed-because-of-gaps-in-trust-and-knowledge/

Appendix E

Diagnostic-Error Specific

FINDINGS	CITE	FINDINGS	CITE
Conclusion: Multiple opportunities for future research aimed at improving detection and treatment of this population remain. Work aimed at creating the design/application of clinical decision rules, educational campaigns designed to educate young women and emergency medicine providers, and consideration of preventive strategies that might be applied in the ED (i.e., young women with hypertension, smoking, obesity) may ultimately lead to interventions that can improve outcomes in women with ischemic stroke. Ultimately, a multidisciplinary approach aimed at improvements in the identification and care of young women will increase our understanding of the pathophysiology of ischemic stroke as well as improve outcomes for patients served in the ED.	Bernard P. Chang MD, PhD Charles Wira MD Joseph Miller MD Murtaza Akhter MD Bradley E. Barth MD Joshua Willey MD Lauren Nentwich MD Tracy Madsen MD, ScM . Neurology Concepts: Young Women and Ischemic Stroke Evaluation and Management in the Emergency Department. 24 June 2017 https://doi.org/10.1111/acem.13243	Conclusion: Middle aged female patients were diagnosed with the least confidence, whether for CHD or non CHD conditions, indicating that their gender and age combination misled physicians, particularly toward mental health alternative diagnoses. Physicians should be aware of the potential for psychological symptoms to erroneously take a central role in the diagnosis of younger women.	Maserejian NN, Link CL, Lutfey KL, Marceau LD, McKinlay JB. Disparities in physicians' interpretations of heart disease symptoms by patient gender: results of a video vignette factorial experiment. J Womens Health (Larchmt). 2009;18(10): 1661–1667. doi: 10.1089/jwh.2008.1007

Gender, hormone, and pregnancy-related concerns (cross-condition)

Sex factors play a significant role in assessing stroke risk factors; women's risk factors include HDP for ischemic stroke, late menopause and gestational hypertension for hemorrhagic stroke, and oophorectomy, HD , preterm delivery, and stillbirth for any stroke. Hysterectomy possibly protective against stroke	Poorthuis MHF , Algra AM, Algra A, Kappelle LJ, Klijn CJM. Female and Male-Specific Risk Factors for Stroke: A Systematic Review and Meta analysis. JAMA Neurol. 2017;74(1):75–81. doi: 10.1001/jamaneurol.2016.3482	This is a discussion of guidelines on treatment of pregnant women at risk of developing CVD, particularly those with specific comorbidities.	Perrone G, Brunelli R. Prevention and treatment of cardiovascular disease in women: the obstetric gynecologist's point of view. Ther Apher Dial. 2013 Apr;17(2):162–8. doi: 10.1111/1744 9987.12022. Epub 2013 Mar 1. PMID: 23551672.
This is a UK based piece focused on the diagnostic challenges related to identifying CVD in women.	Tracey Keteepe Arachi and Sanjay Sharma . Cardiovascular Disease in Women: Understanding Symptoms and Risk Factors. European Cardiology Review 2017;12(1): 10–3 DOI: 10.15420/ecr.2016:32:1	"We are absolutely convinced that only an accurate knowledge of the sex specific pathophysiology may allow determination of the appropriate diagnostic instruments and to implement tailored treatments of CVD in men and women."	Mercuro G, Deidda M, Piras A, Dessalvi CC, Maffei S, Rosano GM. Gender determinants of cardiovascular risk factors and diseases. J Cardiovasc Med (Hagerstown). 2010 Mar; 11(3): 207–20 . doi: 10.2459/JCM.0b013 e32833178ed. PMID: 19829128.
Data gathered from 1993–2014 shows trends in prevalence in pregnancy related HTN (up), Post partum hemorrhage (up), and DVT (up) or PE (down).	Data on Selected Pregnancy Complications in the United States, CDC webpage at: https://www.cdc.gov/ reproductivehealth/matern alinfanthealth/pregnancy-complications-data.htm	"Among young individuals, high CVD risk was almost as common in women as in men. It appears that the high risk situation is not always recognized and treated adequately in young women."	Lehto HR, Lehto S, Havulinna AS, Jousilahti P, Salomaa V. Gender differences in the prevalence, causes and treatment of high cardiovascular risk: findings from the FINRISK Survey. Eur J Prev Cardiol. 2012 Oct;19(5): 1153–60. doi: 10.1177/1741826711422454. Epub 2011 Sep 2. PMID: 21890534.
Despite widely recognized association between pregnancy and the development of later CVD issues, there are no specific guidelines to manage or detect such problems.	Emmanuel Bassily, MD,a Cameron Bell, MD,a Sean Verma, MD,a Nidhi Patel, MD,b Aarti Patel, MDb. Significance of Obstetrical History with Future Cardiovascular Disease Risk. The American Journal of Medicine (2019) 132: 567–571	There are multiple female gender-specific factors that play a role in women's CVD that are chronically overlooked. Researchers, clinicians, and patients themselves all need to be more aware of and vigilant about these issues. See Appendix F for excerpt/summary table.	Clare Arnott, MBBS, PhD, Sanjay Patel, MBBS, PhD, Jon Hyett, MBBS, MD, Garry Jennings, MD, Mark Woodward, MedSci , PhD, David S. Celermajer , FAA, DS. Women and Cardiovascular Disease: Pregnancy, the Forgotten Risk FactorHeart, Lung and Circulation (2020) 29, 662–667. doi.org/10.1016/j.hlc.2019.09.011

Appendix E

Gender, hormone, and pregnancy-related concerns (cross-condition)

FINDINGS	CITE	FINDINGS	CITE
This bulletin describes prevalence, cause, and provides guidance on effect of heart disease among pregnant/postpartum women. It includes recommendations for care for postpartum/pregnant women with new or existing heart disease and a comprehensive-care plan for pregnant women with heart disease.	The American College of Obstetrics and Gynecology Practice Bulletin on Heart Disease and Pregnancy https://www.acog.org/clinical/clinicalguidance/practice-bulletin/articles/2019/05/pregnancy-and-heart-disease	"This review examines how physiological adaptations during pregnancy can provoke cardiometabolic complications or exacerbate existing cardiometabolic disease and how cardiometabolic disease can compromise the adaptations to pregnancy and their intended purpose: the development/growth of the fetus."	Ramlakhan, K.P ., Johnson, M.R. & Roos Hesselink , J.W . Pregnancy and cardiovascular disease. Nat Rev Cardiol 17, 718–731 (2020). https://doi.org/10.1038/s41569-020-0390-z
This study explored patient frustration with their provider's (perceived) lack of knowledge of or attention paid to their concerns about heart disease. Patient-centered communication approaches may be particularly important in overcoming shortcomings in women's CVD care.	Agnes E. Berg Gundersen, Tore Sørlie & Svein Bergvik (2017). Women with coronary heart disease making sense of their symptoms and their experiences from interacting with their general practitioners, Health Psychology and Behavioral Medicine, 5:1, 29–40, DOI: 10.1080/21642850.2016.1263574	Abstract: The maternal cardiovascular system undergoes profound changes to support the increasing demands of fetal growth during pregnancy. An accumulating body of evidence has shown that common pregnancy complications, including gestational diabetes mellitus, preeclampsia, low birth weight, and preterm delivery, can be associated with future cardiovascular adverse events in mothers. Factors such as glucose metabolism, hyperlipidemia, inflammatory markers, and large and small vessel stiffness/functionality have been linked with these pregnancy conditions. Critically, there are no established guidelines to account for these maternal factors when considering future cardiovascular disease risk, one of the leading causes of female mortality.	Emmanuel Bassily , MD, Cameron Bell, MD, Sean Verma, MD, Nidhi Patel, MD, Aarti Patel, MD, Significance of Obstetrical History with Future Cardiovascular Disease Risk. The American Journal of Medicine (2019) 132: 567–571.
This is a comprehensive review of the various risk factors unique to women and a discussion of the many shortcomings in the prevention, diagnosis, and treatment of CVD in women. See Appendix H for excerpt.	Mariana Garcia, M.D., Sharon L. Mulvagh, M.D., C. Noel Bairey Merz, M.D., Julie E. Buring, Sc.D., and JoAnn E. Manson, M.D, Dr.P.H. Cardiovascular Disease in Women: Clinical Perspectives. Circ Res. 2016 April 15; 118(8): 1273–1293. doi: 10.1161/CIRCRESAHA.116.307547	Conclusion: Women exhibited substantially more variation in unique symptom phenotypes than men, regardless of whether the symptoms were derived from structured interviews or abstracted from the medical record. These findings may provide an explanation for the higher missed diagnosis rate in young women with AMI and may have important implications for teaching and improving clinicians' ability to recognize the diagnosis of AMI in women.	John E. Brush Jr, Harlan M. Krumholz , Erich J. Greene, Rachel P. Dreyer. Sex Differences in Symptom Phenotypes Among Patients With Acute Myocardial Infarction. Originally published17 Feb 2020 https://doi.org/10.1161/CIRCOUTCOMES.119.005948
This is an editorial from the Editor-in-Chief about the clear disparity in women's heart disease and the battle to figure out why it exists.	Shader, Richard, Women and Heart Disease. Clinical Therapeutics. Volume 41, Number 2, 2019.	This article provides examples and arguments for both biologic and bias based disparity in women's heart disease.	Wenger NK. Gender disparity in cardiovascular disease: bias or biology? Expert Rev Cardiovasc Ther. 2012 Nov; 10(11):1401 11. doi: 10.1586/erc.12.133. PMID: 23244361.

Gender/Hormonal Differences in Treatment Response and Efficacy and Diagnostic Procedures or Interventions

"Response to drug administration is a primary determinant for treatment success. Sex and gender disparities play a role in determining the efficacy and safety of the most commonly used medications suggesting the need for a sex tailored approach in prescription."	Raparelli V, Pannitteri G, Todisco T, Toriello F, Napoleone L, Manfredini R, Basili S. Treatment and Response to Statins: Gender-related Differences. Curr Med Chem. 2017; 24(24): 2628–2638.	Better understanding how social and environmental factors contribute to CVD risk factors like inflammatory response will help create more focused prevention, diagnosis, and treatment options for people of color. See Appendix I for excerpted infographic.	Karen L. Saban, Herbert L. Mathews, Holli A. DeVon, Linda W. Janusek. Epigenetics and Social Context: Implications for Disparity in Cardiovascular Disease. Aging and Disease. Volume 5, Number 5; 346–355, October 2014.

Appendix E

Gender/Hormonal Differences in Treatment Response and Efficacy and Diagnostic Procedures or Interventions

FINDINGS	CITE	FINDINGS	CITE
By comparing/contrasting American and European guidelines for statin use, this research showed that the standard of care is only appropriate for about 1/5 of the population because of the prevalence of risk factors not taken into account in prior research.	Pavlovic J, Greenland P, Deckers JW , Brugts JJ, Kavousi M, Dhana K, Ikram MA, Hofman A, Stricker BH, Franco OH, Leening MJ. Comparison of ACC/AHA and ESC Guideline Recommendations Following Trial Evidence for Statin Use in Primary Prevention of Cardiovascular Disease: Results From the Population Based Rotterdam Study. JAMA Cardiol. 2016; 09 01; 1(6): 708–13	CVD has decreased more in men than women, and yet women are less likely to be prescribed statins. When women are given statins, they are likely to get less "intensity" statins, and are less likely to achieve treatment targets.	Moreno Arellano, S., Delgado de Mendoza, J., & Santi Cano, M. J. (2018). Sex disparity persists in the prevention of cardiovascular disease in women on statin therapy compared to that in men. Nutrition, Metabolism and Cardiovascular Diseases, 28(8), 810–815.
Survival of mitral valve replacement surgery in Finland has improved from 1997 to 2014, even though patients were older and had more comorbidities. We need to understand how/why.	Myllykangas ME, Aittokallio JM, Pietilä A, Salomaa VV , Gunn JM, Kiviniemi TO, Niiranen TJ. Population trends in mitral valve surgery in Finland between 1997 and 2014: the finnish CVD register. Scand Cardiovasc J. 2018 Feb; 52(1): 51–57. doi: 10.1080/14017431.2017.1405068. Epub 2017; Dec 3. PMID: 29198154.	In this Denmark-based study the use of Doppler to evaluate coronary flow reserve is being studied compared to other methods in women with angina but not coronary obstructive disease.	Eva Prescott, MD, DMSc, et. al., Improving diagnosis and treatment of women with angina pectoris and microvascular disease: The iPOWER study design and rationale. Am Heart J. 2014; 167: 452–8
In premenopausal women, especially those with specific risk factors, coronary angiographic imaging should be done as soon as CVD is suspected to avoid misdiagnosis and to facilitate prompt treatment.	GWICC Abstracts 2010, Clinical and research medicine: Coronary heart disease: The analysis of clinical and coronary angiographic characteristics for pre menopausal women with coronary heart disease. Ting Wang, Peiling Cong, Xiaofei Sun.	Cardiovascular Disease Assessment in Pregnant and Postpartum Women tool. This is an assessment framework and algorithm for identify CVD issues in pregnant and postpartum women.	California Department of Public Health and California Material Quality Care Collaborative, available at: file:///C:/Users/Admin/Downloads/CVD%20Disease%20Assessment%20in%20Pregnany%20and%20Postpartum%20Women.pdf

Specific Conditions: Heart Failure, SCAD, Hypertension, Microvascular Disease, Valve Disease

Recapture of data examined in 2017 guidelines for HTN management that did not do a deep exploration of gender differences. See Appendix A for more detailed findings.	Beth L. Abramson, MD, FACC; Kajenny Srivaratharajah, MD; Leslie L. Davis, NP, PhD, FACC; Biljana Parapid, MD. Women and Hypertension: Beyond the 2017. Guideline for Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. July, 2018, ACC website at: https://www.acc.org/latest in cardiology/articles/2018/07/27/09/02/women-and-hypertension	This study found no difference in control of HTN between men and women, but issues of obesity, cholesterol, and low HDL are more prominent in women and women have more risk factors for HTN in general than men.	Kwok Leung Ong, Annette W.K. Tso, Karen S.L. Lam, and Bernard M.Y. Cheung. Gender Difference in Blood Pressure Control and Cardiovascular Risk Factors in Americans With Diagnosed Hypertension. Hypertension. 2008;51: 1142–1148. doi.org/10.1161/HYPERTENSIONAHA.107.105205
There are significant differences between men and women in the natural history of HTN, and in response to treatment. Practitioners need to take gender and hormonal variances into account when diagnosing and treating HTN in women.	Ahmad A, Oparil S. Hypertension in Women: Recent Advances and Lingering Questions. Hypertension. 2017 Jul;70(1): 19–26. doi: 10.1161/HYPERTENSIONAHA.117.08317. Epub 2017 May 8. PMID: 28483918.	While rates of HTN are the same in men and women, and this study found men to have more severe risk from HTN , work up of CVD concern should be as aggressive in women as in men.	Tziomalos K, Giampatzis V, Baltatzi M, Efthymiou E, Psianou K, Papastergiou N, Magkou D, Bougatsa V, Savopoulos C, Hatzitolios AI. Sex-specific differences in cardiovascular risk factors and blood pressure control in hypertensive patients. J Clin Hypertens (Greenwich). 2014 Apr;16(4): 309–12.

Appendix E

Specific Conditions: Heart Failure, SCAD, Hypertension, Microvascular Disease, Valve Disease

FINDINGS	CITE	FINDINGS	CITE
Despite the impact of HTN on women, major gaps exist in knowledge including the role of pregnancy in contributing to later issues, postpartum issues, and optimizing management of PE and of BP in the elderly. See Appendix B for excerpt.	Nanette K. Wenger, MD, a Anita Arnold, DO, MBA, b C. Noel Bairey Merz, MD, c, et. al. Hypertension Across a Woman's Life Cycle. J Am Coll Cardiol 2018;71: 1797–813	"CMD is associated with a nearly 4-fold increase in mortality and a 5-fold increase in major adverse cardiac events. Future studies are needed to identify effective strategies to diagnose and treat CMD"	Mark A. Gdowski , Venkatesh L. Murthy, Michelle Doering, Andrea G. Monroy-Gonzalez, Riemer Slart, and David L. Brown. Association of Isolated Coronary Microvascular Dysfunction With Mortality and Major Adverse Cardiac Events: A Systematic Review and Meta-Analysis of Aggregate Data. Journal of the American Heart Association. 2020;9 https://doi.org/10.1161/JAHA.119.014954
Reference numbers for measuring BP were found to be incorrect for women, indicating a need to revise current BP measurement guidelines for women and men.	Hermida RC, Ayala DE, Mojón A, Fontao MJ, Chayán L, Fernández JR. Differences between men and women in ambulatory blood pressure thresholds for diagnosis of hypertension based on cardiovascular outcomes. Chronobiol Int. 2013 Mar;30(1-2): 221–32.	"A shared pathology across multiple organ systems highlights the need for a collaborative, multidisciplinary approach among medical subspecialties caring for women with these diseases…It is essential that providers caring for women obtain a complete history with a focus on microvascular disorders, including a detailed pregnancy history, as standard of clinical care."	Patel H, Aggarwal NT, Rao A, et al. Microvascular Disease and Small-Vessel Disease: The Nexus of Multiple Diseases of Women. J Womens Health (Larchmt). 2020;29(6): 770–779. doi: 10.1089/jwh.2019.7826
Women, especially older women and women of color, are not represented in clinical trials which makes applicability of CT findings limited. Future research needs to focus on studying these populations where possible or identifying parallel data collection opportunities where not.	Monica Colvin, MD, MS,1,1 Nancy K. Sweitzer, MD, PhD,2,1 NANCY M. ALBERT, RN, PhD, et. al. Heart Failure in Non Caucasians, Women, and Older Adults: A White Paper on Special Populations From the Heart Failure Society of America Guideline Committee. J Cardiac Fail 2015;21: 674e693	Adding other diagnosis SCAD Spontaneous coronary artery dissection (SCAD) is an understudied but very worrisome issue, especially in young women without traditional risk factors.	Hayes SN, Kim ESH , Saw J, et al. Spontaneous Coronary Artery Dissection: Current State of the Science: A Scientific Statement From the American Heart Association. Circulation. 2018;137(19): e523–e557. doi: 10.1161/CIR.0000000000000564
A how-to guide for HF nurses working with heart failure patients. See Appendix C for excerpt.	AAHFN Heart Failure (with preserved EF) talking tips sheet: available at aahfnpatienteducation.com	"Spontaneous coronary artery dissection (SCAD) is an under recognised and important cause of myocardial infarction in young women."	Main T, Prakash R, Starovoytov A, Sabbaghan A, Aymong E, Mancini G, Saw J. Characteristics of extension and de novo recurrent spontaneous coronary artery dissection. Eurointervention. 2017;13: e1454–e1459. doi: 10.4244/EIJ-D-17-00264
Heart failure is difficult to diagnose and categorize because of a number of complex and confusing factors; current guidelines and schematics are not adequate and moving forward, research should focus on subspecialty populations and more specific definitions and treatment approaches.	Marc A. Pfeffer, Amil M. Shah, Barry A. Borlaug. Heart Failure With Preserved Ejection Fraction In Perspective. Circ Res. 2019;124: 1598–1617. DOI: 10.1161/CIRCRESAHA.119.313572	"Gender and age bias complicate the evaluation of women with acute coronary syndrome (ACS) …conditions like spontaneous coronary artery dissection (SCAD) are often missed. SCAD is an infrequent yet important cause of myocardial infarction (MI) with a predilection for young to middle-aged women. The condition is thought to be under reported, likely a result of both low-index of suspicion as well as an unfamiliarity with SCAD's angiographic variants.	Lebrun S, Bond RM. Spontaneous coronary artery dissection (SCAD): The underdiagnosed cardiac condition that plagues women. Trends Cardiovasc Med. 2018 Jul;28(5): 340–345. doi: 10.1016/j.tcm.2017.12.004. Epub 2017 Dec 11. PMID: 29275928
This discusses various aspects of heart failure unique to women and concludes that significant underrepresentation in clinical trials is a huge barrier to our knowledge.	Bozkurt B, Khalaf S. Heart Failure in Women. Methodist Debakey Cardiovasc J. 2017 Oct–Dec;13(4): 216–223. doi: 10.14797/mdcj-13-4-216. PMID: 29744014; PMCID: PMC5935281.	Conclusion: HF is associated with increased risk of maternal mortality and morbidities. During hospitalization, high-risk mothers need to be identified and surveillance programs developed before discharge	Mulubrhan F. Mogos, Mariann R. Piano, Barbara L. McFarlin, Jason L. Salemi , Kylea L. Liese, and Joan E. Briller. Heart Failure in Pregnant Women: A Concern Across the Pregnancy Continuum. Originally published 12 Jan 2018. https://doi.org/10.1161/CIRCHEARTFAILURE.117.004005

Appendix E

Specific Conditions: Heart Failure, SCAD, Hypertension, Microvascular Disease, Valve Disease

FINDINGS	CITE	FINDINGS	CITE
This article provides an overview of the gender differences in how valvular heart disease manifests itself, is diagnosed, and treated.	Nitsche, C., Koschutnik , M., Kammerlander, A. et al. Gender specific differences in valvular heart disease. Wien Klin Wochenschr 132, 61–68 (2020). https://doi.org/10.1007/s00508-019-01603-x	Poor maternal and fetal outcomes—including death—are possible in women with moderate to severe valvular disease.	Ducas RA, Javier DA, D'Souza R, Silversides CK, Tsang W. Pregnancy outcomes in women with significant valve disease: a systematic review and meta analysis. Heart. 2020 Apr;106(7): 512–519. doi: 10.1136/heartjnl-2019-315859. Epub 2020 Feb 13. PMID: 32054673.
This is an expert treatise on management of pregnancy in women with valvular disease. "Given the complexity of valvular heart disease in pregnancy, women with congenital and acquired heart disease should be managed with a multidisciplinary approach before and throughout pregnancy."	Kathryn Lindsley, MD, FACC, Valvular Heart Disease in Pregnancy. Feb 12, 2018. ACC Website, accessed at: https://www.acc.org/latest-in-cardiology/articles/2018/02/12/07/29/valvular-heart-disease-in-pregnancy	Excerpt: Indeed, that unconscious bias of what a heart attack victim looks like helped keep SCAD off the radar screen for so long. "A lot of patients I see with cardiac symptoms were hesitant to seek care in the first place because they felt they wouldn't be taken seriously," says Lewey. "So, they often have to become advocates for themselves to get the care and attention they need." Among the growing field of advocacy and support organizations are the SCAD Alliance, a network of SCAD survivors, researchers and clinicians; SCAD Research, Inc., a volunteer, grassroots group that has raised hundreds of thousands of dollars for research; and WomenHeart, a patient centered organization that serves women with heart disease.	Randy Young, SCAD: Not Your Typical Heart Attack: New Findings & Increased Visibility AreChanging How Spontaneous Coronary Artery Dissection Is Diagnosed & Treated. Randy Young, July 11, 2019, Coronary Intervention & Surgery. Accessed at: https://www.cardiovascularbusiness.com/topics/coronary-intervention-surgery/scad-not-your-typical-heart-attack-new-findings-increased

Appendix of select findings/excerpts

A.

Beth L. Abramson, MD, FACC; Kajenny Srivaratharajah, MD; Leslie L. Davis, NP, PhD, FACC; Biljana Parapid, MD. Women and Hypertension: Beyond the 2017 Guideline for Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. July, 2018, ACC website at: https://www.acc.org/latest-in-cardiology/articles/2018/07/27/09/02/women-and-hypertension

	Female sex/gender-specific factors
Pathophysiology	•Vascular protective effects of estrogen: up-regulation of NO pathway & downregulation of sympathetic pathway, RAS and endothelin production • Menopause – change in estrogen levels • Pregnancy related vascular risks such as preeclampsia and gestational hypertension • States of estrogen imbalance such as polycystic ovarian disorder, premature ovarian insufficiency and infertility •Inconclusive data on progesterone
Epidemiology	•Lower hypertension rates in premenopausal women •Two-fold increase in risk of hypertension with menopause •~80% of women aged ≥75 have hypertension
Screening and Diagnosis	•Hypertensive women have more non-traditional CV risk factors •More variability in ambulatory BP measurements in perimenopausal and menopausal women •Postmenopausal women more likely to exhibit non-dipping pattern of blood pressure
Treatment – Pharmacological	•Diuretic therapy may be more beneficial in postmenopausal women with osteoporosis •CCB may be more beneficial in women for stroke prevention •Women may experience more antihypertensive side effects
Treatment – Non-pharmacological	•Salt restriction may benefit women given possible upregulation of RAS after menopause •Weight loss after midlife weight gain •DASH diet plus weight loss may have incremental benefits on BP lowering •No more than one standard alcoholic drink/day •Combined aerobic and resistance exercises reduce arterial stiffness and BP in postmenopausal women

B.

Emmanuel Bassily, MD,a Cameron Bell, MD,a Sean Verma, MD,a Nidhi Patel, MD,b Aarti Patel, MDb. Significance of Obstetrical History with Future Cardiovascular Disease Risk. The American Journal of Medicine (2019) 132:567–571

Table 1. Association of Pregnancy Risk Factors with Incidence/Mechanism of Future Cardiovascular Disease Risk

	Incidence in Pregnancy	Mechanism of Cardiovascular Dysfunction	Increase in Lifetime Cardiovascular Risk
Preeclampsia	1%-5%	Blood pressure, lipid levels, large/small vessel functionality	Yes
Gestational diabetes mellitus	2%-5%	Blood pressure, lipid levels, large vessel/small vessel functionality, fasting insulin levels	Yes
Preterm labor/birth	5%-8%	Unknown	Yes
Low birth weight	5%-8%	Unknown	Yes

Numbers presented vary based on ethnic group, population studied, and diagnostic criteria utilized (Sattar & Greer, 2002).[32]

C.

AAHFN patient talking tips sheet at: aahfnpatienteducation.com

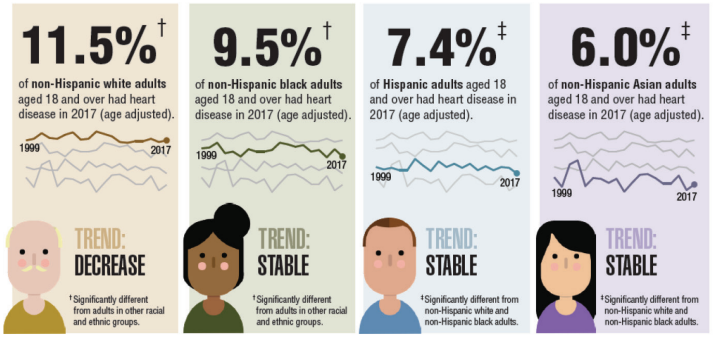
Patient teaching:

- Self-monitoring of symptoms is critical in managing heart failure
- Treatment of patient's comorbidities and risk factors for heart failure are associated with improved outcomes
- Salt reduction, exercise/staying active, weight loss and medication management are important self-care strategies
- Review all medications the patient is taking including OTCs and supplement.
- Advise patient to avoid non-steroidal anti-inflammatory drugs (NSAIDS) as this can worsen their symptoms
- Counsel patient to take all medications as directed and to communicate intolerances to their provider
- Encourage patients to keep all follow up appointments
- Teach patients the symptoms they need to report to their provider
- Close collaboration among caregivers is also recommended

Appendix E

Appendix of select findings/excerpts (cont'd)

D. Health, United States Spotlight Racial and Ethnic Disparities in Heart Disease, 2019



F. Clare Arnott, MBBS, PhD, Sanjay Patel, MBBS, PhD, Jon Hyett, MBBS, MD, CVD Risk in Women

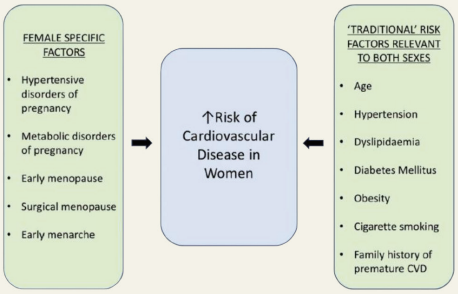
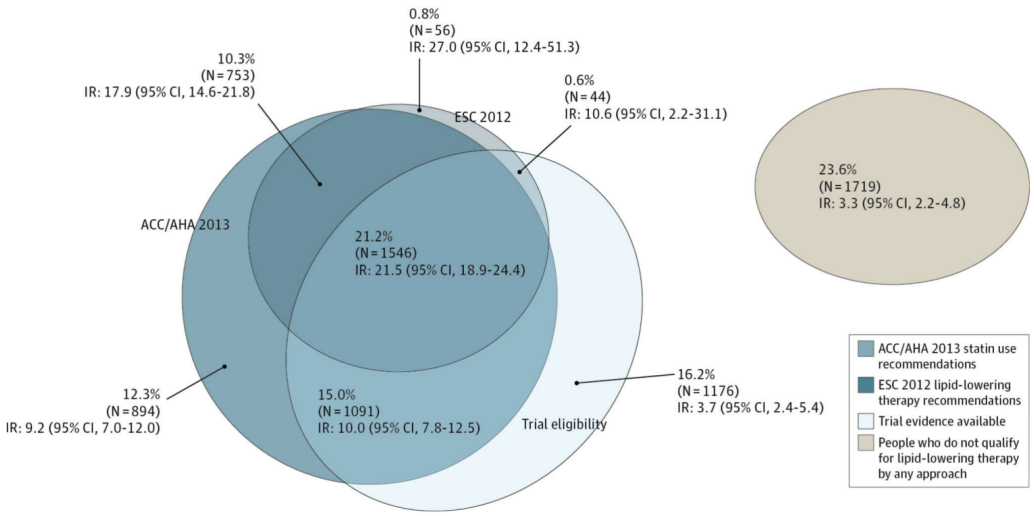
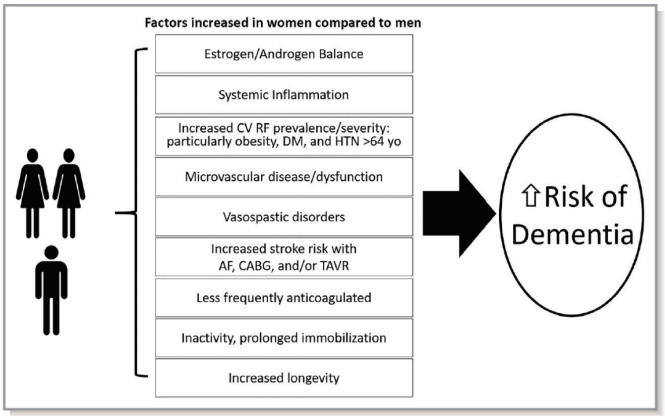


Figure 1 Cardiovascular risk in women. Traditional and female-specific factors related to the risk of cardiovascular disease in women.

E. Venn Diagram of AHA/ACC/ESC Applicabili
Comparison of ACC/AHA and ESC Guidelin
Recommendations Following Trial Evidenc
for Statin Use in Primary Prevention of
Cardiovascular Disease: Results From the
Population-Based Rotterdam Study. Pavlo
J, Greenland P, Deckers JW, Brugts JJ,
Kavousi M, Dhana K, Ikram MA, Hofman A
Stricker BH, Franco OH, Leening MJ. JAMA
Cardiol. 2016 09 01;1(6):708-13



G. Volgman, et. al, Cognitive Impairment and CVD in Women



H. Mariana Garcia, M.D., Sharon L. Mulvagh, M.D., C. Noel Bairey Merz, M.D., Julie E. Buring, Sc.D., and JoAnn E. Manson, M.D, Dr.P.H.. Cardiovascular Disease in Women: Clinical Perspectives

Table 2 Pretest probability for Coronary Artery Disease by Age, Sex and Symptoms
Reused with permission from Gibbons et al. [215]

Pretest Probability of Coronary Artery Disease by Age, Gender and Symptoms[1]					
Age (y)	**Gender**	**Typical/Definite Angina Pectoris**	**Atypical/Probable Angina Pectoris**	**Nonanginal Chest Pain**	**Asymptomatic**
30–39	Men	Intermediate	Intermediate	Low	Very low
	Women	Intermediate	Very low	Very low	Very low
40–49	Men	High	Intermediate	Intermediate	Low
	Women	Intermediate	Low	Very low	Very low
50–59	Men	High	Intermediate	Intermediate	Low
	Women	Intermediate	Intermediate	Low	Very low
60–69	Men	High	Intermediate	Intermediate	Low
	Women	High	Intermediate	Intermediate	Low

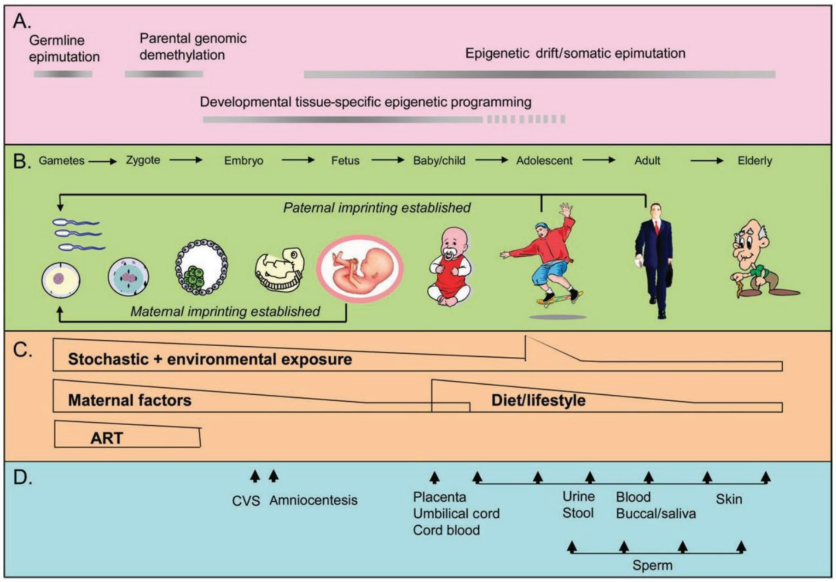
High indicates >90%; Intermediate 10–90%, Low <10%, Very low <5%

[1]No data exists for patients <30 or >69 y but it can be assumed that prevalence of coronary artery disease increases with age. In a few cases, patients with ages ages at the extremes of the decades listed may have probabilities slightly outside the high or low range.

Appendix E

Appendix of select findings/excerpts (cont'd)

I. Karen L. Saban, Herbert L. Mathews, Holli A. DeVon, Linda W. Janusek, Epigenetics and Social Context



J.

Figure 3. The Robert Wood Johnson Foundation action cycle for improving a community's health. At the core of the action cycle are key stakeholders for taking action. Each step on the action cycle is considered a critical component for creating healthier communities and offers a guide that describes key activities within each step that includes suggested tools, resources, and additional reading. In this action cycle, Work Together and Communicate are distal because they are needed throughout the cycle. Reproduced with permission from the Robert Wood Johnson Foundation County Health Rankings & Roadmaps Action Center, 2017; Take Action Cycle. http://www.countyhealthrankings.org/take-action-cycle. Copyright © 2017, County Health Rankings.

K. Leigh JA, Alvarez M, Rodriguez CJ. Ethnic Minorities and Coronary Heart Disease: an Update and Future Directions

Table 2

Race/ethnicity makeup of major cohort studies in cardiovascular disease [10–14]

Population group	MESA (%)	ARIC (%)	HCHS/SOL (%)	Jackson Heart (%)	CARDIA (%)
Non-Hispanic white	38	73	0	0	48.5
African-American/black	28	27	0	100	51.5
Hispanic/Latino	22	0	100	0	0
Asian/Asian-American	12	0	0	0	0

MESA Multi-Ethnic Study of Atherosclerosis, *ARIC* Atherosclerosis Risk in Communities, *HCHS/SOL* Hispanic Community Health Study/Study of Latinos, *CARDIA* Coronary Artery Risk Development in Young Adults

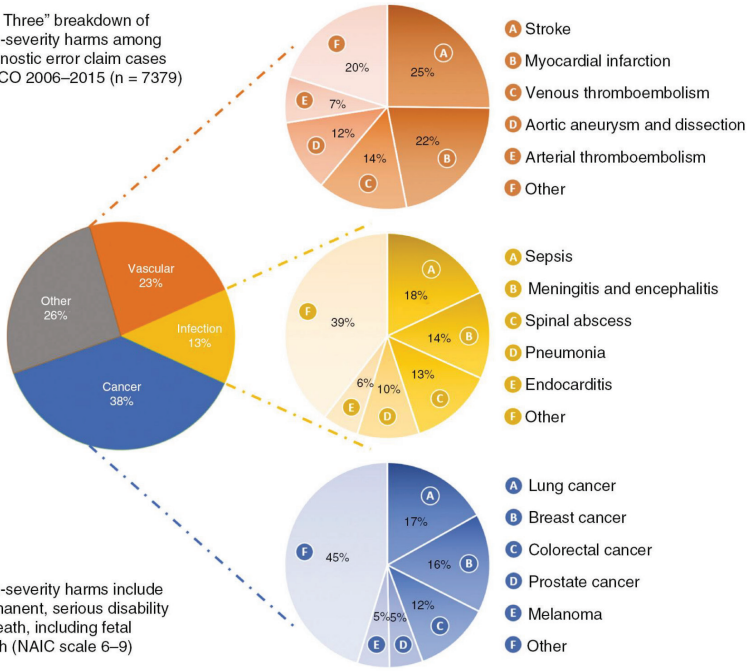
Appendix E

Appendix of select findings/excerpts (cont'd)

L. Factors Identified by the HCNI Team Members that Contributed to a Successful Community-Academic Partnership (CAP)

Strengths	Partnership Accomplishments
Characteristics of the Partners	
Consistent and committed leadership with shared vision	•Kept the study team focused on the needs of the community •Helped community partners and residents navigate through some of the challenges of research from a community perspective.
Many of the original team members continue to partner, and there are generally several representatives from each agency/institution involved in the project	•Maintained continuity •Presented a consistent face to the community •Depth of agency/institution involvement meant that leadership changes did not destabilize the partnership
Transparency about needs of the community	•Kept the needs of the community foremost •Used the strengths of the community to enhance partnership, study design, and data collection. •Pursued extramural funding for future opportunities
Transparency about needs of academic partners	•Addressed the needs of the academic partners •Pursued extramural funding for future opportunities •Supported publications and other deliverables for academic promotion
Transparency about the partnership	•Maintained a high level of communication and copied team members who were not present so they do not feel excluded •Agreed that information on working group activities would be shared with the larger group at a given periodicity •Minimized small group conversations that can be destructive and bring to the entire group as soon as possible
Several individuals (both community and academic partners) had prior experience with (CBPR/CPPR[5])	•Created a more efficient process •New or less experienced members mentored by community and academic members with more experience in CBPR/CPPR
Characteristics of the Partnership	
Trust within partnership	•Pre-existing partnerships grounded in trust helped study team work together with similar assumptions, which provided a foundation for a more committed partnership; •Helped to navigate with balance between trust and skepticism
Peer Governance and Egalitarian Processes that were informed by group discussions, presentations by "resident" experts from community and academia, and invited presentations from other individuals when outside expertise was needed	•Improved operations and reduced tensions and hierarchies •Allowed team to make informed decisions regarding study design, protocols, data collection, and ethical issues within the study team
Built trust within the community	•Strengthened community support of the project, enhanced participation of stakeholders, and facilitated honest feedback and engagement of community members
Emphasis on a non-deficit, asset based approach to working with community	•Demonstrated respect and regard for community being served •Synthesized information on community resources that could be shared with residents, local agencies, and academic institutions
Commitment to ethical behavior within the partnership	•Developed an expectation of fair, equitable, and respectful treatment of and by all members of the partnership
Identified benchmarks and celebrated interim successes	•Enhanced the engagement of individual participants in the process •Highlighted achievements of individuals, organizations, and the HCNI team
In-kind funding from CAP despite initial limited funding	•Staff time •Space for project activities •Project materials •Administrative support •Obtaining local funding to support the partnership
Recognition of mutual benefits	•Recognized these needs also had relevance for community members whose employment prospects could be enhanced

M. "Big Three" breakdown of high-severity harms among diagnostic error claim cases CRICO 2006–2015 (n = 7379)



High-severity harms include permanent, serious disability or death, including fetal death (NAIC scale 6–9)