Cardiovascular diseases are the leading cause of death among women, a fact widely recognized for years. Yet, the significance of heart disease in women has been underappreciated, and women are significantly underrepresented in cardiovascular clinical research. Women and men share common features in the manifestations and pathophysiology of heart and vascular disease, and understanding of those pathophysiological mechanisms is incomplete. At the same time, significant differences exist that have largely been neglected by regulatory, industrial, funding, and research policies.

In response to these unmet needs, the American Heart Association’s Go Red For Women was launched in 2004 to develop a strategic and integrated approach to the care of women with heart disease. In 2015, Nancy Brown, CEO of the American Heart Association, delineated the history of the Go Red for Women initiative, tracking its progression from an enterprise aimed largely at improving the awareness of cardiovascular disease in women to the development of risk assessment tools, management guidelines, and research focused on the influences of sex on all aspects of cardiovascular disease.1

Thirteen years ago, when the Go Red for Women initiative was launched, the landscape was much different than it is today. Perhaps because women have been historically underrepresented in research studies, little was known about the differences in biomarker profiles between women and men. Cardiovascular professionals and patients were struggling with the lack of recognition of the importance of identifying cardiovascular risk factors and developing appropriate treatment plans for women with heart disease. Little was known about the impact of pregnancy and its complications on subsequent cardiovascular disease in the offspring and mother. Defining the social determinants of health and contrasting their differential impact on cardiovascular outcomes in women and men had not emerged as an important area of research. The role of implicit, gender-based bias in influencing our care of patients was not emphasized in the literature.

This inaugural Go Red for Women issue in Circulation is a new effort to address the menace of heart and vascular disease in women. The issue celebrates contemporary research developments that guide care provided to women with cardiovascular disorders. Indeed, we can all take pride in the broad spectrum of high-quality investigation that now addresses the unique determinants, presentations, and outcomes of heart disease in women. We include studies ranging from the influence of pregnancy on cardiovascular risk to a deeper understanding of variation in outcomes by sex after myocardial infarction. We include an in-depth review of arrhythmias in women.

At the same time, the issue highlights challenges that remain. For example, preclinical research in animal models still fails to fully grasp the complexities of sex in heart disease. Women still represent a minority of faculty reaching the rank of professor in academic medical centers, another challenge we explore.

We hope you enjoy this issue of Circulation and will apply its messages to the care and management of women with cardiovascular disease and to ongoing investigative initiatives. We pledge to continue to explore and promote pathbreaking cardiovascular

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research in both women and men, leading the way to a future free of these scourges.

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FOOTNOTES
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Welcome to Circulation On The Run, your weekly podcast summary and backstage pass to the journal and its editors. I’m Dr. Carolyn Lam, associate editor from The National Heart Centre and Duke-National University of Singapore.

Today is special, special, special because here with me is the editor of special populations and that is Dr. Sharon Reimold from UT Southwestern, who is the editor handling the special issue for Go Red For Women.

Welcome, Sharon.

Dr Sharon Reimold: Thank you, Carolyn. I’m happy to be here.

Dr Carolyn Lam: This is so cool. Just us ladies chatting about issues that we need to be talking about.

Now first of all, this is the first time that Circulation is doing a focus issue for Go Red for Women. Could you tell us a little bit more about that?

Dr Sharon Reimold: Sure. The Go Red for Issue campaign has been around for many years. The editorial staff realized that we really hadn't had an entire issue devoted to cardiovascular issues in women. We decided several months ago to try to make this a reality and asked for submissions of articles and we’re delighted to see the interest that our cardiologists across the country had, as well as across the world, in submitting their research for consideration in this issue.

Dr Carolyn Lam: I know. There are seven original papers. There are review papers. There are research letters. It’s an amazing issue.

Dr Sharon Reimold: We had hoped to focus on a lot of different areas in which heart care in women is influenced. We're really quite delighted that we had papers on pregnancy, papers related to strategies to get women involved in trials. We were able to look at novel risk factors in women, and also, have an excellent review about arrhythmias in women versus men that I think everyone will want to take in.

Dr Carolyn Lam: Yeah. Congratulations once again right off, but let's jump straight into this set of twin papers that deal with post MI outcomes and sex differences. There've been quite a number of publications on this. What makes these two papers special?

Dr Sharon Reimold: I think these papers are special because they're trying to think more deeply into why women tend to get re-hospitalized after a heart attack more often and what are the reasons that they’re getting readmitted.

For instance, it seems that women, as we know, may get a variety of different symptoms that are their equivalent or anginal equivalent after they've been in...
the hospital and also before they were in the hospital. I, personally, suspect that when somebody comes to the hospital with chest discomfort and they've recently had a heart attack, then often times, they get readmitted and re-hospitalized.

These papers are starting to look at mechanisms, why this happens. I think this will be the bridge to the point where we figure out what can we about this, to hopefully, make men and women more equal in this regard.

Dr Carolyn Lam: That's so true and well put. I also found very, very interesting and important that paper that really highlighted the importance of coronary flow reserve and microvascular ischemia, not just obstructive disease. Can you say a few words about that paper?

Dr Sharon Reimold: Sure. It's been known for a long time that if you perform catheterizations on men versus women with similar presentation ... Women may not have as much obstructive disease. This particular manuscript explores coronary flow reserve and identifies this as being part of the difference between men and women in that regard. That, obviously, could have important implications for the clinical care of these patients.

Dr Carolyn Lam: I like that. All these papers really took what we may have known a bit before, but took them to a deeper level and in a very novel way. So important. You mentioned some of the novel aspects that were also explored in the issue, the pregnancy related factors, in fact, novel risk factors that we should be taking note of in women. Do you want to comment on a few highlights?

Dr Sharon Reimold: The relationship of pregnancy complications to long term, both maternal and offspring health has been around for a while, but really, we don't know very much about it. We, certainly, have known previously that women with preeclampsia, or those who have significant hypertension, or diabetes in pregnancy may have later problems when they are in middle age or older.

What we are learning from some of these new entries into the research domain is that women who have premature labor and delivery are also at risk for having complications, and this sort of fits in the middle. It's not just preeclampsia, or hypertension, or diabetes. It's that you delivered earlier. Then moreover, we have a couple of research focused letters that describe arrhythmias in pregnancy and what happens to those women during pregnancy. I think we all have seen young women come in and have symptoms, but we really don't know what their outcome has been because any single physician probably just sees a few of them. This highlights arrhythmias as a issue in that population.

We also looked at other articles that focused on other risk factors for heart disease, ranging from breast arterial calcification to traditional biomarkers that we may be drawing in hospital, BMP, troponin, and such. There's a nice manuscript that focuses on hormone changes in women and how they're
associated with development of cardiovascular disease. So a fairly broad look at a variety of different risk factors that we don't think about when we're simply asking, "How old are you? What's your blood pressure? What's your diet? Do you have diabetes, and do you have lipid disorders?"

What I would hope that we would get out of this is to open all of our minds and our approaches to patients to think about asking about their pregnancies, did they have any complications, figuring out if they have any hormonal issues, and then being free to consider whether or not the woman that you have in front of you actually has obstructive disease or perhaps has issues with abnormal flow reserve.

Dr Carolyn Lam: Exactly. I would, actually, add to that, also, looking at our commonly used cardio metabolic biomarkers with the lens of realizing that there are important sex differences in all these biomarkers. That was a very nice paper, corresponding author, Dr. James de Lemos. All these papers are just so practical.

I'm actually going to switch tracks now, Sharon, because I really want to talk about this final paper. All I need to do is read the title of the editorial and it'll be self-evident. "Women are less likely than men to be full professors in cardiology. Why does this happen and how can we fix it?" I love that you invited this editorial. Could you tell us a bit about the paper that sparked this editorial and your thoughts on this?

Dr Sharon Reimold: Yes. The original article has as its first author, Dr. David Blumenthal. It's an article that's one of a series of manuscripts that looked at academic cardiologists and looked at faculty rank where they were able to gather data on sex differences, clinical productivity, research funding, publications, et cetera. They have looked at other disciplines other than cardiology, but this particular manuscript focuses on cardiologists. What it demonstrates is that we are getting, perhaps, a little bit more women in at the assistant professor level, but there's still a significant lag at the full professor level.

In fact, in many centers if you query development offices, there's probably at least a seven year lag between women and men in terms of making it through the whole spectrum. While perhaps, this is not new conceptually, I think it does quantitate it for us and it highlights the concept that this is an issue now, similarly to what it was 25 years ago when I was a cardiology fellow.

The interesting compliment to this is the editorial by Dr. Karns and Dr. Bairey Merz which tries to go into why does this happen and how can we fix it. They took a very academic approach to their editorial in terms of looking at data and then talk about implicit bias and how even a very small degree of implicit bias will cause men to be promoted, perhaps more in a faster manner than in women, and also bring up some things we don't even think about. One of the best ones was the concept that you advertise for a new position as a cardiologist. If you advertise for someone and you list the skills you want and
what you want to build, then that's a more gender neutral way to approach a job. If you advertise for a dynamic, outgoing, I don’t know, vigorous sort of person, and there are ads out there that read like that, you are, inadvertently, advertising for a man, most of the time.

Dr Carolyn Lam: Male characteristics.

Dr Sharon Reimold: Yeah. They talk about that. Then they obviously end up with how can we fix it? I think that's a real challenge.

There are some data within the field of literature for development that suggest that mentoring and coaching are important, but that they don't necessarily push people up the ladder very rapidly. There are some places, for instance, our University of Texas system now that is very interested in the concept of sponsorship. That someone sponsors another individual, could be male or female, to get involved and pushes them ahead, not pulls them, so that they have opportunities for faster career development and success. In any event, I think this compliment of paper and editorial really highlights an issue that, while not necessarily affecting female patients, certainly affects cardiology as a destination career.

Dr Carolyn Lam: I agree. I think part of the how to fix it is simply by being aware and acknowledge the issue. That is exactly what we’re doing in these papers. I love that they are academically written. Like you said, you read a lot about these gender biases in the popular press, but it's so refreshing to see it addressed in an editorial, in a beautiful paper, in circulation.

Sharon, congratulations on just this excellent, excellent issue. Is there anything else you may want to highlight about the issue?

Dr Sharon Reimold: I think that's the major thing. I think we moved a long way from the beginning of Go Red For Women as a campaign where we really wanted patients to be aware that hypertension or elevated cholesterol levels were an important issue. I think now is a time where we move forward. We’ll learn more about differences between men and women and we figure out how we can treat or account for these differences as we strive to make health care for all and cardiovascular care for all improve over time.

Dr Carolyn Lam: Thanks Sharon. Everyone of you listening to this, go pick up this issue. I’m sure we’ve peaked your interest.

Thank you for listening to Circulation On The Run. Don't forget to tune in next week.