

**(TC: 00:00:01)**

**Dr Hazel Wallace: Hello and welcome back to another episode of The Food Medic podcast. It's me, Dr Hazel Wallace, host of the podcast coming to you from lockdown in London.**

**It is a common myth that heart disease is a man's disease, but here's the thing. Worldwide, heart disease is the single biggest killer of women and in the UK, it kills more than twice as many women as breast cancer every year. While heart disease can affect any person at every stage from diagnosis to treatment, women receive poorer care than men. For example, research shows that women delay seeking medical help and present to hospital later than men.**

**Women are also 50% more likely than a man to receive the wrong initial diagnosis for a heart attack and, following a diagnosis, women are less likely to receive timely reperfusion therapy like drugs or stents. To understand why this happens, today I'm joined by Chris Gale who is professor of cardiovascular medicine and co-director of the Leeds Institute for Data Analytics at the University of Leeds. Professor Gale is honorary consultant cardiologist at Leeds General Infirmary where he practices clinical cardiology with particular interests in general cardiology, post-myocardial infarctions, survivorship and chronic heart failure. He holds major research awards from the NIHR, British Heart Foundation and Horizon 2020, and has published over 200 research manuscripts in peer-reviewed journals including JAMA, The Lancet and the BMJ. Professor Chris Gale, welcome to the podcast. First of all, it would be great to hear in your own words a bit about your clinical and academic background, and what research and work you're currently doing.**

**(TC: 00:02:53)**

Professor Chris Gale: So, my name's Chris Gale. I'm a consultant cardiologist and professor of cardiovascular medicine at the University of Leeds and at Leeds Teaching Hospitals NHS Trust. I have an interest in how we care for people with cardiovascular disease, and academic interests really are specifically using population data, so that's large datasets in both randomised formats and observational formats to study cardiovascular care and outcomes. And that's mostly around heart attack, but also around heart failure and atrial fibrillation. And so we use routine NHS data and registry data from the UK, but also other countries. And we conduct trials. That's where we test interventions between two different sets of otherwise equal populations. And we also use a different methodology which is called 'observational', which is essentially just looking at the data and seeing what it tells us. So, my research is predominantly funded by the British Heart Foundation, but we also have substantive incomes from the National Institute for Health Research and Horizon 2020 and the Wellcome Trust. So, we have portfolio funding from a number of organisations to conduct what I call research for patient benefit. So, to study how we look after patients and to see how we can therefore improve how we look after patients and individuals with cardiovascular disease, and therefore reduce the burden of cardiovascular disease. And by that I mean mortality and morbidity.

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**(TC: 00:04:31)**

**Dr Hazel Wallace: Yes. And a lot of your research, or in recent years, you've been looking at sex and gender differences in heart disease. And let's start with the myth that heart disease is purely a man's disease and why this is untrue.**

(TC: 00:04:47)

Professor Chris Gale: Well, that's an interesting question and a really pertinent question. So, I'm going to push that back and I'm going to say, well, if we asked people or the public or even healthcare professionals to describe or imagine a person with cardiovascular disease, I suspect most people will say, 'Well, it's a man who's probably inactive, overweight, who smokes, doesn't have a good diet, doesn't necessarily exercise too much, but also has maybe high blood pressure and diabetes.' And it's a really interesting concept that the first thing we tend to think of is that, and that it's a man. But, what we do know is that cardiovascular disease also affects women and it's not necessarily just a man's disease. So, heart attacks and cardiovascular disease and stroke really does affect women.

**(TC: 00:05:38)**

**Dr Hazel Wallace: And on a basic, kind of, anatomical and physiological level, how different is a male and a female heart?**

(TC: 00:05:49)

Professor Chris Gale: Well, the underlying anatomy, that's the structure but also how it works, the function of hearts, are the same between men and women. So, the heart is a unique and really important organ in the body. It's essentially a pump and it's got four pumping chambers and valves to let the blood go through in one direction. And it's fed by little pipes or coronary arteries that supply the heart with blood so it can work, so it has the nutrients and the oxygen. And it's activated through electrical channels. So, it's a little bit like an engine in a way. It's a pump that has electrical stimulation and it contracts through muscle, and it forces blood around through these chambers in one direction. So, the structure and function is roughly the same between men and women, but what we know is that the weight or the mass or the size of the heart is slightly smaller in women compared with men, and that when the heart becomes diseased, it can become diseased slightly differently in women compared with men. So, the coronary arteries tend to be a little bit smaller in women than men, and when people have coronary artery disease, that is the small pipes or coronary arteries that feed the heart, when they become diseased or narrowed, the narrowing can sometimes be slightly more different in women than in men. So, even though heart attacks, for example, which are one of the forms of coronary artery disease, even though they're common and very similar between men and women, there are differences in terms of the heart attacks and the pathology between men and women.

**(TC: 00:07:25)**

**Dr Hazel Wallace: Yes. And so, kind of, looking at the research, there seems to be this gap at every stage when a woman versus a man has a heart attack. And I think, starting from the beginning, what are some differences in how a woman might present with a heart attack versus a man?**

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(TC: 00:07:45)

Professor Chris Gale: Yes, well, I suppose the important thing here is, whilst we think that there are differences, when heart attacks do happen and when we look at the data across populations, in general the heart attack symptoms and signs tend to be very similar between men and women. I think that's the first learning point. And the symptoms and signs of a heart attack really are of sudden onset chest pain that's central in the chest. It may go up to the throat or to the left shoulder or to both shoulders, or even down to the left arm. And with that, you can feel sickly and sweaty and breathless and light-headed. But, there are also some differences between men and women in terms of the frequency or how common these symptoms are. And recent studies have suggested that women can have slightly more atypical-, I don't particularly want to use the word 'atypical', but slightly different frequency of symptoms. And so women can sometimes present with more breathlessness or palpitations or collapse, and maybe less typical chest pains. But, that in itself is not the commonest way to present with a heart attack. The commonest way is, as I said earlier, these main classical symptoms.

(TC: 00:09:00)

**Dr Hazel Wallace: And do you think even when women are presenting with the, kind of, classical textbook symptoms, that because we perhaps hold these biases in our head, that we're less likely to pick it up when they come through the door in the hospital?**

(TC: 00:09:15)

Professor Chris Gale: Well, I think you're absolutely right, Hazel. I think there are misperceptions and biases at a number of levels here. So, again, going back to that concept of who we think would have a heart attack when we're asked to describe someone, when we describe that it's a middle-aged or elderly gentleman, if you were, for example, a woman who was experiencing a heart attack, you would, number one, perhaps think, 'Well, this shouldn't be me,' or, 'These symptoms can't be a heart attack.' And there may be a situation where you're thinking, 'This just can't be a heart attack and therefore I will wait perhaps a little bit longer to see if it goes away,' or attribute it to something else such as indigestion. And what we've found is, as a result (TC 00:10:00) of that, we know that women can present later when they present to hospital with a heart attack. So, I think there's a systematic bias in society as to what we perceive as the characteristics of a person with a heart attack, and that needs to be recalibrated. We need to re-educate ourselves about heart attacks and that it's not just a man's disease.

(TC: 00:10:23)

**Dr Hazel Wallace: Yes, absolutely. And I think there are two things going on there, whether it's, kind of, female sex and the biological basis, and then there's the gender as a woman and the social biases that we hold. And I guess they both affect how women are diagnosed and treated.**

(TC: 00:10:43)

Professor Chris Gale: Absolutely. So, when women do present to hospital with-, we know from our research, our BHF funded research, when we have looked at the UK national heart attack registry of several hundred thousand patients who come to hospital with heart attacks, when we look at that and we quantify or we

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measure what we call the performance of hospitals and care according to specific metrics or indicators, consistently we found that women tend to fare worse than men. Now, that's not to say that the care in the UK is bad. Overall, when we looked at these metrics, NHS care for heart attacks was very, very good. But, there were marginal differences and systematic differences between men and women. Those differences were in standards or metrics or indicators such as how timely you get certain treatments, or whether you even get certain treatments or investigations, and they seem to be consistent across women compared with men.

(TC: 00:11:47)

**Dr Hazel Wallace: Yes.**

(TC: 00:11:47)

Professor Chris Gale: And then the issue is, well-, so, what if you don't get these care interventions? Well, heart attacks are a medical emergency. They require urgent and specialist and evidence-based treatments. And we know that in particular for certain types of heart attacks, what we call ST elevation myocardial infarctions, that time really is of the essence and emergency surgery, keyhole surgery to unblock these blocked arteries, is absolutely crucial. So, if, for example, you presented late or you had delayed treatments, then there'd more heart muscle damage and therefore greater morbidity and greater mortality. And this is what we found in our studies. Women had higher mortality rates than men.

(TC: 00:12:36)

**Dr Hazel Wallace: Yes. And going back to what you mentioned when it comes to the heart and how women have perhaps maybe smaller coronary arteries or it's the smaller vessels that are affected, do you think that when it comes down to diagnostics then we're looking in the main arteries and we are perhaps missing out other causes for chest pain?**

(TC: 00:12:56)

Professor Chris Gale: Yes, I think there are a number of things to unpick here. One is how good are our diagnostics? And our diagnostics include biomarkers and there's an argument for using sex-specific cut-offs for biomarkers. Our other investigation is to look directly at those coronary arteries that feed the heart, the pipes that feed the heart, and that's through an angiogram, as an emergency angiogram. And we tend to see detail that's millimetres or several millimetres across, but anything below that level is difficult to visualise. And coronary artery disease is not just what we call macrovascular, it can be microvascular as well. Equally, we do know that when the coronary arteries, these pipes that feed the heart, are diseased when they're atheromatous, when they have fatty deposits in them, it's not necessarily the burden or the extent of the coronary artery disease, which is an important factor, but it's how vulnerable those fatty deposits are. And we're still uncertain as to how to identify the vulnerable plaques. On that note, we do know that when women present with certain types of heart attacks called MINOCA, myocardial infarction with non-obstructive coronary arteries, they can have diseased arteries, but not sufficiently diseased for us to unblock them with a stent. We tend to unblock arteries when they're moderately or severely diseased in critical areas. But, when you have a coronary artery that is modestly or minimally diseased, really there is no benefit from popping a stent into that artery to try and open up the blood supply. And so there's uncertainty

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as to the treatment. And this has been actively investigated, so I'm working with colleagues in other countries where we're undertaking a large international trial of patients with MINOCA to see whether types of standard heart attack treatments, so medications and tablets, change the outcomes in these patients.

**(TC: 00:15:02)**

**Dr Hazel Wallace: Yes, interesting.**

(TC: 00:15:03)

Professor Chris Gale: And because there's an area of uncertainty in terms of our diagnostics and treatments, that may be, or may explain, some of the differences in the outcomes that we see between men and women.

**(TC: 00:15:14)**

**Dr Hazel Wallace: Absolutely. Just to circle back, you mentioned you've seen different or sex-specific cut-offs for markers such as troponin and that's one of the key diagnostic blood tests that we use when it comes to heart attacks. What are your thoughts on this, and how close are we to using sex-specific, kind of, reference ranges?**

(TC: 00:15:35)

Professor Chris Gale: Yes, that's a good point. So, these markers, these troponins, are increasingly important, in fact nearly the cornerstone of how we study myocardial injury and therefore heart attacks. Although it's a little bit more complicated than in terms of we need other clues as to whether someone is having a heart attack or not. But, nonetheless, troponins are a core component of diagnosing heart attacks. And we have different thresholds or cut-offs for that to help us diagnose heart attacks, and there is information or evidence from what we call observational studies. So, when we look back at treatments and the use of these, that if we lower the threshold for men and for women for these troponin cut-offs for diagnosing a heart attack, we can diagnose more heart attacks more effectively in women, but not necessarily in men. And why is that important? Well, if we lower the threshold and you get a classification of a heart attack, then you're more likely to be seen by a cardiologist, a specialist. You're more likely to have the right treatments and, theoretically, you're more likely to have better outcomes. So, there's an argument for having sex-specific cut-offs. But, when we look towards the guidance, and in particular NICE, there is now a recommendation that research is done in this area so that we can really provide robust evidence to inform our practice. But, it's certainly something we should be considering.

**(TC: 00:17:12)**

**Dr Hazel Wallace: I think so. Absolutely. And thinking about modifiable risk factors, again, unmodifiable risk factors, are there certain risk factors which impact men and women differently? Such as, you know, the classical risk factors that we're all aware of. Smoking, high blood pressure. And, second to that, do sex-specific risk factors exist which increase the risk for women?**

(TC: 00:17:36)

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Professor Chris Gale: Well, the important thing here is that we're all aware of our potential risk factors and our modifiable ones. You know, the non-modifiable ones such as age and our family history, we can be aware of but can't do too much about. But, modifiable ones, as it suggests, are something we should be aware of and we can do something about. And these are important in men and women, first of all, and they include smoking, as you suggested, high blood pressure, diabetes, high cholesterol or the fats in the blood, and diet and exercise. And there is some evidence that these risk factors, albeit very important both in men and women, have a different, sort of, penetrance or effect in women compared with men. And perhaps things like smoking, which we know is also more common among younger women, may have a more detrimental effect. But, the bottom line here is that you should know your risk factors, your cardiovascular risk factors, you should be proactive in being aware of them, and ensuring that they are as low as possible, that they're minimised. So, that you know your cholesterol, you know your weight, and that your weight is within normal parameters, you have a healthy diet, you're exercising regularly, and that you know your blood pressure and that you've been checked for diabetes. And if you do have a strong family history of premature cardiovascular disease, so people have it with heart attack and stroke and heart failure in their middle and younger ages within your family, and certainly within your first-degree relatives, that you actively seek screening for that from your primary care physician or specialist.

(TC: 00:19:17)

**Dr Hazel Wallace: And then, kind of, thinking about things that would affect women specifically, the menopause is one thing that comes to mind, but I guess different times across the lifespan for women when hormones are fluctuating, pregnancy's another example, but we do see this increase in cardiovascular disease particularly after the menopause.**

(TC: 00:19:39)

Professor Chris Gale: Yes, absolutely. We know that women who present with a heart attack, for example, tend to be older than men, and I suspect there is a strong component there of post-menopausal effects where coronary artery disease and these risk factors become more aggressive in women as they age. It's being mindful that we (TC 00:20:00) should know our risk factors and know that, you know, at every stage of our life, we are exposed to these risk factors, but they may become slightly more dominant at certain times.

(TC: 00:20:11)

**Dr Hazel Wallace: Absolutely. And one of the, kind of, areas of research, I think, that seems to be growing is the link between the mind and the body, and the link between mental health conditions and physical conditions. How do conditions such as depression and anxiety impact the heart?**

(TC: 00:20:27)

Professor Chris Gale: Well, I am pleased you've asked that because I think this is really important and is often sidelined or not discussed. We know from a study that we're doing at the moment and have published on, and funded by the British Heart Foundation as well as the NIHR, when we looked at people with heart attack across the whole of the UK, so over 10,000 people-, we were following these patients, these individuals, up for quite a number of years. For a decade, we've followed them up now. We studied their

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heart attack care, their heart attack outcomes, but we also looked at their quality of life and we found that at the time of heart attack, people can have a range of different levels of quality of life which includes not just mobility, but also their mental wellbeing. And we found that people who had lower levels of quality of life at around the time of their heart attack tended to do worse in terms of their recovery of that quality of life. And one of the important discoveries here is that those who had the worst trajectories for quality of life and had the lower baseline, these people tended to be the people who are comorbid, so had other ill health problems, but were also older and were women. And so there is really a need to study this in much greater detail because I think there will be a link between quality of life and other traditional outcomes such as death and morbidity. And that may well be driven through other mediators such as health-seeking behaviour, how we approach our lifestyle, whether we take our medicines and so on. And so this is an active area of research in terms of our recovery from cardiovascular disease.

The other area, which I think you may have been alluding to, is how mental health can serve as a precursor or even a trigger for cardiovascular disease. Earlier we talked about these traditional cardiovascular risk factors, but we didn't really mention mental health, and I think, well, we certainly know that people with anxiety and depression and with mental health problems are at a greater risk of cardiovascular disease. The mechanism behind that, I am not entirely sure about and could easily be explained through a higher preponderance of risk factors, but I do suspect there are other factors as well at hand. But, it's an active area of research and it's something we shouldn't be dismissing.

**(TC: 00:23:04)**

**Dr Hazel Wallace: No. And obviously, you know, it's interesting how the research is moving and the different things that we're looking at now. Particularly, again, going back to sex differences in heart disease but in lots of other conditions, but how do you think we can improve outcomes for women when it does come to heart disease, research aside?**

**(TC: 00:23:27)**

Professor Chris Gale: Well, I think the critical component here is improving the awareness of cardiovascular disease. So, in particular, heart attacks and the risk factors for that. If we can get that message out, if we can educate society, the public, individuals about their risk factors for cardiovascular disease, so the risk factors we discussed earlier, then I think we'll go a long way forward in terms of reducing the burden of cardiovascular disease. In addition to the education of people about these risk factors, we certainly need to remind ourselves, re-educate ourselves, about the symptoms of heart attack and how cardiovascular disease presents so that we do reach out to the emergency services who can help us should we be in that position of having a heart attack or a cardiovascular event. So, this is about education. This is about spreading the word about our risk factors and the symptoms of heart disease.

**(TC: 00:24:30)**

**Dr Hazel Wallace: Yes. And the British Heart Foundation have lots of resources about that on their website as well.**

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(TC: 00:24:36)

Professor Chris Gale: Absolutely. And I would encourage your listeners to tap into that information.

(TC: 00:24:42)

**Dr Hazel Wallace: Yes, I agree. And the more we talk about it on podcasts like this, the more awareness that we'll raise. So, thank you for giving us your time today in a very busy time for everyone.**

(TC: 00:24:53)

Professor Chris Gale: Thank you very much, Hazel. It's been an absolute pleasure.

(TC: 00:24:58)

**Dr Hazel Wallace: Okay, guys. That was a really important conversation and hopefully it helped you to understand and recognise the symptoms of a heart attack and also how heart disease may affect women differently. I encourage you to share this podcast and start a conversation with your friends, your mum, your auntie, your girlfriend, your patients, all the women in your life. Little by little, we will raise awareness and we will start to understand and tackle the barriers that prevent women from receiving the same quality of diagnosis, treatment and rehabilitation as men do. That's all from me. Until next time, take care.**

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