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## **#394: What's killing women? Sex disparity and the shifting landscape of age-related disease**

VOICEOVER

This is Up Close, the research talk show from the University of Melbourne Australia.

ANDI HORVATH

I'm Dr Andi Horvath. Thanks for joining us. Today we bring you Up Close to your health span. The number of years you live in the best possible health across your lifespan. The Global Burden of Disease Study is a comprehensive global research program that assesses the mortality and disability from major diseases and risk factors. Now the data shows a 10 year rise in global life expectancy which occurred between 1980 and 2015. Also deaths due to infectious and nutritional causes, as well as maternal and child health, have declined. But non-communicable diseases, the preventable lifestyle diseases have risen. For decades public health campaigns in many countries contribute a vital service in providing health guidelines including risks and preventative measures for living well as we age.

We've all heard the message of diet and exercise but it's not working on a global scale and it has its challenges for our health care systems. Our guest today on Up Close is Professor Cassandra Szoeki, a neurologist at the University of Melbourne. Cassandra is a chief investigator on a large Australian longitudinal study on lifestyles and aging and has led research programs in government and CSIRO the Commonwealth Scientific Industrial Research Organisation. Her work has focused on a particularly vulnerable group, women. She's the director of the Women's Healthy Aging Project and an expert in age related disability and disease with the view to improving the human health span. Welcome to Up Close Cassandra.

CASSANDRA SZOEKE

Thank you very much.

ANDI HORVATH

Cassandra set the scene for us regarding the global burden of disease. What has changed over a few generations?

CASSANDRA SZOEKE

So what we saw in the 2015 Global Burden Diseases Study was this definite shift where we're really winning in terms of infectious diseases and that shows how much has gone into that research. But the non-communicable diseases which were in western countries, inclining for the last decade are now across the global world on an increase.

ANDI HORVATH

Is it behavioural, environmental? What is it? What's causing this shift do we think?

CASSANDRA SZOEKE

There are many contributors to this but certainly in part it's our own success at finding cures for diseases and improved health, which allows us to live longer and chronic diseases by their very definition are diseases that take decades to develop.

ANDI HORVATH

Now how much of aging and aging well or longevity is due to luck of the genetic lottery, giving the lucky individual some resilience to really bad lifestyles?

CASSANDRA SZOEKE

Look it's certainly true that we know there are certain genes that make you more likely to get diseases and there are also certain diseases that make you more likely prone to vascular risk factors, which really account for a lot of the chronic diseases that we have today. Heart disease, diabetes, dementia; these have a big vascular component, but environmental components are just as important.

ANDI HORVATH

So are you saying that we are not just our genes, that we can be us with environmental input? We can be better than what our genes gave us?

CASSANDRA SZOEKE

We are a combination of both and in fact with some of the research you'll notice that in fact if you have a genotype that is an at risk genotype, lifestyle change is of greater benefit to you.

ANDI HORVATH

Now you've been focusing some of your research on longitudinal long term studies of aging in both the body and the mind with a particular focus on women? Why women? Isn't it one size fits all?

CASSANDRA SZOEKE

There's a lot of work done recently on gender disparity. So we have seen that whilst we did approach diseases with sex equivalency, in fact we're finding that diseases are quite different in men and women. So the heart disease example is a good one so I might talk about that, although it's true for many diseases. So, heart disease was thought to be a disease of men. Many men were dying of heart disease in the 50s. Most research was focused in men and then there have been such dramatic improvements in men's health. In about the late 80s more women than men were dying of heart disease and that is the case even today. More women than men suffer heart disease. There was a recent report actually done just last year in 2016 which showcased the fact that still more women are dying of heart disease than men in Australia.

In the USA in the 80s when they saw that more women were dying of heart disease, they did an awareness campaign. They had a red dress campaign. They tried to get people aware and they also mandated that women had to be included in cardiovascular studies. After this mandate, you can see a decline in women's heart disease and in fact awareness went from only 30 percent women aware that heart disease was a major killer in women to 70 percent awareness. After that you see an even greater decline in female heart disease in the USA. Five years ago in 2012 they did a study looking at Australian women's awareness and they found that in fact only three percent of women were aware that heart disease was a major killer in women.

They also did a study looking at clinicians in Australia, specifically obstetricians, gynaecologists and clinicians involved in women's health and only 70 percent of them answered all the questions correctly on heart disease in women. You can look up the Harvard Medical School website and they clearly show that the risk factors, the treatments, the management is different in women and men for heart disease. So

we can see from this example it's really important actually to look at sexes differently.

ANDI HORVATH

We'll come back to your work on women a bit later. But I'm curious, as young children we all heard the messages of healthy food and physical activity. The old chestnut of diet and exercise. We also know about the risks of substance abuse and many health issues. Yet we have these enormous numbers in lifestyle diseases which are essentially, as you've pointed out, either metabolic ones or the cardiovascular ones. Clearly unhealthy habits are not due to lack of awareness. So what's going on?

CASSANDRA SZOEKE

I think there are three things going on. The first is there is a bit of a lack of awareness. So it's a little bit like speeding and car accidents in young people. It's not that they don't acknowledge there are car accidents and you can die from that but there's this feeling that you won't have the car accident even when you speed. So, there is a bit of lack of awareness whereas I said if you think heart disease is a disease of men, women aren't going to get it. You're aware that lifestyle reduces heart disease but you think well that's not relevant to me.

So I think that's part of it. Also I think the nature of the advice. I give the example of a patient who actually came to see me for a cognitive assessment. He had diabetes and he was being referred for potential of dementia and for assessment. He had looked up all the websites and when he saw me he said look, I'd like to ask you a question. I looked up the diabetes website and the Alzheimer's website, just looking at what I could do to reduce my chances of getting dementia. I have a nutritionist. I have a very strict regime of my medication and my meals. I have standard three meals a day and so on and when I looked at this website for dementia it said you shouldn't have three major meals a day. It's healthier to graze. To him it was conflicting advice and he actually said to me, what's better to die from? Diabetes or dementia?

So if we're giving people that choice, that's the wrong choice. So I think there is an awareness issue in terms of you don't know exactly what you should do and you're getting conflicting advice. Then it's very hard to adhere.

ANDI HORVATH

Now these diseases are also related to aging. Now is this a correlation or a causation? Do we get them because we're old or do we get them because we don't step up the effort to look after ourselves as we age?

CASSANDRA SZOEKE

That's an excellent question and I think the research can't say conclusively the answer, because with chronic diseases and here's the difficulty, they develop over decades. So unless you follow people over several decades remembering funding cycles were three years and are now five years, I'm talking about a funded study for 30 years. We can't really do level A evidence which is saying whether or not intervention would change your development of disease. But by and large all the evidence suggests that it would reduce disease. Dementia was thought to be an inevitability of aging because every five years after the age of 65, the incidence of dementia doubles. So they were proposing that people over 90 more than 40 percent of the population over 90 would have dementia.

So this is a very disheartening kind of statistic. However there's a Danish centenary study that published in fact when they looked at people who'd made it to 100, they're not seeing those rates of dementia. So in fact it is not aligned with aging whilst that is a very strong risk factor because of the accrual of damage which happens over time. Age is an exposure of time. It is not inevitability of aging.

ANDI HORVATH

So we can prevent these diseases?

CASSANDRA SZOEKE

On that point as you said we know about healthy lifestyle. The message has been out there for a long time. Well in fact if we look at how many people have dementia now and compare that to how many people had dementia 20 years ago and this is being looked at in several of these really major international cohort studies, where they did a wave of assessments 10 years ago and a wave of assessments more recently. They actually showed less people are getting dementia now. So in fact those healthy heart messages look to have already had a positive impact in reducing chronic disease.

ANDI HORVATH

By cohort studies do you mean longitudinal studies?

CASSANDRA SZOEKE

I mean longitudinal cohort studies.

ANDI HORVATH

Cassandra what would it take for governments to really take longitudinal long term studies seriously, like for 30 years?

CASSANDRA SZOEKE

I think that actually governments really do understand chronic disease and I think they have actually invested a lot of money in longitudinal work at the questionnaire level. So we have the Australian longitudinal study of women's health where thousands of women are filling out questionnaires every few years. That's been going for 20 years. We have the men's longitudinal study, so I think they understand longitudinal work. The Women's Healthy Aging Project that I run they have also funded now 30 years. So we are recipients of National Health Medical Research funding for that and that's a more detailed study. That is rare. So it's the only one in Australia and there are several internationally which has biomarkers, imaging, actually blood tests and physical measures.

So these women are seen by a clinician, rather than just questionnaire based data. That is much more expensive, much more complicated and I think we have to appreciate that the Global Burden of Disease Study in 2015 just raised this issue of non-communicable diseases, chronic diseases now coming to the fore. Lancet in 2016, publish the WHO statement that now the number one priority for the World Health Organisation is chronic disease. So I think we have to wait a few years for governments to then translate that into funding biomarker based studies to understand these chronic disease developments.

ANDI HORVATH

I'm Andi Horvath and you're listening to Up Close. In this episode we're talking about the global burden of age related disease and disability especially in women with neurologist Cassandra Szoeki. Cassandra you've done a major study on the health of aging of women aged 45 and over. What have you found, give us the numbers?

CASSANDRA SZOEKE

We've done a few things. So we did a big study looking at over 20,000 women in Australia just looking at awareness. So, we have already available preventative guidelines from our National Health Research Council and our government websites recommending levels of physical activity, fruit and vegetable intake, etcetera. What we did was have more than 20,000 women answer what was their body mass index. How much fruit and veg did they eat etcetera, etcetera. This was just published in 2017 and basically shows that less than 50 percent compliance with recommendations. In fact if you look at body mass index and physical activity, less

than 30 percent of people are compliant with recommendations. Given we're an island nation and most of our people live on the coast the guidelines to eat fish or legumes more than twice a week was only complied with with less than 15 percent of women.

Fruit and veg, five serves a day, complied with less than 20 percent of women. So clearly unhealthy habits persist. We were really winning as people aren't smoking, they're not drinking. They're looking after their blood pressure. They're reducing their fat fried food intake. However there are clearly areas that we could improve.

ANDI HORVATH

What was the methodology of the project? How did you make sure the data reflects an accurate status of women's health?

CASSANDRA SZOEKE

The Women's Healthy Aging Project has now been going for 30 years and really what I have to say the greatest part of the study is the women. Volunteering their time to come in every year and now every second year for four to five hours and undergo enormous evaluations and blood taking and testing for 30 years, I think that's the greatest contribution. What they have contributed to international global knowledge on women's health is astounding. So the early part of the study in the 90s, actually it was this cohort that defined the menopausal stages. Previously we thought of menopause as pre, early, late and post. More recently we understand post-menopause is a third of a woman's life and we have gone back and re-defined the various subsets of post-menopause and again it was this cohort that defined those now international criteria in combination with our American counterpart study.

So these women have really informed women's health incredibly and without them we wouldn't have the knowledge we do.

ANDI HORVATH

Just clarify for us the risk factors in women's health. What are some of the risks and what are some of the markets of ill health?

CASSANDRA SZOEKE

So, many of the vascular disease risk factors are associated with poor health. For example in 2016 we published a paper on the preventative factors for dementia. Now there's been a lot of work looking at prevention of dementia because to this day we have no treatment that alters progression of disease. Also we have a rising incidence

of dementia and it's now second leading cause of death in this country and also internationally. So, we took all the papers that had shown body mass index was related to dementia occurrence, cholesterol was related to dementia occurrence. This long list of 20 risk factors that had been associated with the disease. What we were able to do was put all of those in together to look at which ones were really associated with cognitive decline. What we found and published last year was that the number one influence on people's cognitive performance later in life was physical activity, getting enough of it, doing it every day. Having a good blood pressure, not being hypertensive and have appropriate levels of good cholesterol.

What was really changing the literature in this field was being able to analyse it all together because we had all the detail of all these women. We could control for not just age education and genotype but also their social engagement; all those other factors that are influencing these to show it's really these three that, in our cohort, were the most significant on cognitive decline. The second thing we were able to do was to look at time, because that's the big question. Showing there's an association between a factor and disease if you don't know the timing of when that factor is influencing your brain. Now that we know dementia takes 30 years to develop you won't know when to target it. We were presuming that like heart disease, mid-life would be the most important time to target these risk factors, to prevent late life disease because that's what we've found in heart disease.

However we were surprised to find that in fact that cumulative exposure was most relevant for cognition. So in fact the good news is it's not too late because even people over 60 who were physically active had better cognition. But also every day you don't have good physical activity and you don't have normal blood pressure and you don't have normal levels of high density lipoprotein, the good cholesterol, it's a cumulative effect.

ANDI HORVATH

So by knowing these risk factors in dementia, essentially we know the predictive factors of cognitive decline. Now, I've heard you say that the instance of dementia in women could be significantly reduced and maybe even halved if preventative measures are in place.

CASSANDRA SZOEKE

So there was a Lancet neurology paper that was published in 2012 and the Lancet neurology paper looked at all the research that had been done on risk factors in dementia and they calculated a population attributable risk and they published that they could halve the cases of dementia if we intervened on these risks. But again in terms of level A evidence, we would like to create an intervention, then follow up for 30 years and see if this would be the case but of course we don't practically have the



capacity to do that.

ANDI HORVATH

What happens if risk factors compound? Like you've got more than one risk factor. Is it a road towards doom?

CASSANDRA SZOEKE

The answer is yes. So, certainly risk factors combine and there was a subsequent paper from that Lancet neurology 2012 paper where they actually looked at combined risk as well. The issues are not just in terms of risk factors, but once those risk factors give you a disease, if you have more than one disease that can also compound.

ANDI HORVATH

Cassandra, I want to know how much does stress play a part in women's health? Is it a really big impact?

CASSANDRA SZOEKE

I think stress plays a part in poor health in men and women and I think this is an area we haven't looked enough at. So in fact there's a lot of work showing stress and in particular chronic stress is very much associated with poor aging, poor health in aging and even poor health in young people. There's a lot more work done in depression. There's less work done in stress and in fact we're now understanding that not all stress is the same sort of stress. So first of all there's a big difference between acute stress and chronic stress, and secondly there's also a component of perceived stress. So you could have a major life event that others would consider extremely stressful, but if you don't perceive it as stressful then actually you won't have a negative effect.

ANDI HORVATH

How did women get into this position of jeopardised health? Is it the predicaments of being a woman in current society, meaning many women serve the needs of others rather than themselves?

CASSANDRA SZOEKE

I think that women used to live much longer than men in fact and men had much poorer health. Men were much more likely to die younger. So there has been a cultural change. Men were doing occupations which gave them asbestos exposure. They were more likely to smoke than women. They were more likely to drink than women. A lot of these toxic exposures were killing people. Infectious diseases were killing people. So there's been a change in what is harm. In addition we have had amazing advances in health. So again obviously across the board we've had advances but I'll use vascular disease as an example.

With heart disease we now can use medications to clear the cholesterol from people's vessels. Where there's cholesterol blockage in a vessel we can bypass that vessel. We can give you a new heart for goodness sake. So these kind of advances mean that what was killing men before is no longer. Women have different heart disease to men. This is getting a bit technical but where a man usually has a major vessel disease; a big blockage of a big artery which we can bypass, women have what we call micro-vascular disease. So all the vessels have a little bit of damage and it's not so easy for our current therapeutics to treat that. So firstly came awareness; remember that was after the 80s. So it'll take some time for medical advances to target women specific disease which is different from male disease in the heart. It's true for all diseases.

So if we look at the chronic diseases of aging, osteoarthritis; more women than men. Depression; more women than men. Dementia; two-thirds of people with dementia are women. What are our top killing diseases? Heart disease and dementia. So the Alzheimer's Association did this brilliant study focusing on women given two-thirds of dementia is women. When they looked at it they asked women ?what are you really worried about dying from?? and they said breast cancer. So then they looked at the statistics and they showed this beautiful graph where basically the chances of dying from breast cancer in your lifetime are half your chances of dying from dementia. So women do not realise actually what the real diseases that will impact them in their aging are. So that was done in 2014, in 2015 the UK did a report and they showed exactly the same. Double the chance of getting dementia in your lifetime compared to breast cancer and then the World Alzheimer's Association published a compilation of that data.

ANDI HORVATH

Cassandra what does it mean to die from dementia? Just clarify that for us.

CASSANDRA SZOEKE

Speaking of lack of awareness, that's an excellent question, because in fact dementia is a terminal disease. However, it's what we call a neurodegenerative process. So cells die in the brain. I am a neurologist so I'm biased here, but the brain is everything. So your breathing is controlled by the brain. Your heart pumping has

got its own neuronal network, but is also subject to control by the brain. So what happens is people often die of pneumonia, lack of nutrition, wasting, other things but the underlying cause of that reason for death is the degeneration.

ANDI HORVATH

I'm Andi Horvath and our guest today is neurologist Professor Cassandra Szoeki. We're talking about understanding and enhancing wellbeing in aging societies and factors especially applicable to women right here on Up Close. Cassandra whilst we sense it's important to have meaningful connections and social connections with people, what exactly is the impact of wellbeing on aging individuals?

CASSANDRA SZOEKE

Social connections are really important in aging and there's been a lot of research showing that social disengagement, that is more likely to occur in aging because you have, with your colleagues dying you have a smaller cohort and social isolation is associated with poor aging. We did some work looking at social engagement and cognition, and social engagement and healthy aging and certainly found that people who were more engaged had better mood and had better health and in fact had better cognition. We even looked at grand parenting. So people who looked after their grandchildren had much better verbal episodic memory than people who didn't. However social engagement is not easy to research because it's not a simple yes no kind of variable. What we found is where social engagement was causing a demand or a stress getting back to your earlier question on stress; in fact the stress component of that engagement could undermine any health benefit and in fact end up with a health deficit.

ANDI HORVATH

Cassandra I'm keen to discuss your work on grand parenting and its effect on aging people. How did you measure this and what is the effect?

CASSANDRA SZOEKE

So we asked people ?did they have grandchildren??. If so, how many and what were their ages etcetera. Then we said do you look after your grandchildren? Because what we were noticing in our social engagement questions with the women was they were not necessarily doing your standard volunteer work or employment that people usually ask about. They were doing questions that aren't in your standard questionnaires, like grand parenting or caring for friends or in fact had people living with them. So we do a household questionnaire where we say who's living with you and there were all these people living in their household we didn't expect to find

there. So we looked at that on that basis and we looked at how often they looked after their grandchildren each week.

We've looked at a range of outcomes and one of the most recent papers we published in 2016 looked at cognition and showed that those people who were looking after their grandchildren were more likely to have higher cognition than those people with grandchildren who were not looking after their grandchildren. However if they were looking after their grandchildren five days a week they had worse cognition than anyone. Then we did an analysis of the stress questions we asked them and found sure enough in our demand question, that they were feeling a high level of demand from their children and this was associated most with that decline in cognition. So we have to be careful all of us I think at every age on how much we take on.

ANDI HORVATH

I imagine that geriatric depression is of also concern around the world.

CASSANDRA SZOEKE

Yes it is an I think this is another area that's under represented because you're relying on people reporting that and being treated for it and I think there's a lot of people who have depression and not just in the geriatric population. I think across our entire population, who have depressive symptoms and disease from that, but don't get counted I guess in the statistics. One of the areas of research we're moving into in 2017/18 is looking at positive mood, because there's been such a focus on disease and depression and really in our program our focus is health. It looks like positive mood is actually even more important if you're talking about quality of life in aging.

ANDI HORVATH

Cassandra where do we start to mitigate the age related disorders for the next generation of aging individuals? Whilst I hear prevention is the key, but we need another line of attack. Could it be earlier detection of some of these age related diseases? Where do we go?

CASSANDRA SZOEKE

Look that's another excellent question. If you look in the field of dementia, all the studies were done on people over 65. Because of the disease focus, the disease was only occurring in people over 65. So now if you look across the world, what knowledge and information we have on cohorts of dementia and cognitive testing all

those cohorts are aged over 65. So we can't answer what would happen in younger people. Five years ago, in 2012, this really started being discussed in the dementia forum as many of our therapies were failing and the pharmaceutical companies were getting less interested in pursuing dementia, because of the poor return on investment. The thoughts were perhaps these treatments that were given to people with dementia or with mild cognitive impairment might actually have benefit if they were given earlier.

So just in 2015 the new study giving a dementia therapy to people who don't have dementia yet was designed and implemented. We won't get the results of that study yet, but that shows you just how recently we've been thinking about this. So to have earlier detection you need to have measures 30 years before these chronic diseases manifest because we know it's in those 30 years of exposure that they're developing. In fact I would say that healthy aging is from birth to beyond.

ANDI HORVATH

Alright, in a nutshell what is prevention? Give us a to-do list.

CASSANDRA SZOEKE

At the moment a lot of research is disease focussed. Because it's disease focussed, there are different preventive targets for each disease. One of the key things that we're looking at in our program and we made an application to the NHMRC for a centre of women's healthy aging. We want to take what we call a multi-morbidity approach in that centre. What we want to do is look at these risk factors holistically around lifestyle and socio-demographics and look at a multi-morbidity, quality of life, healthy aging, unified outcome to provide a shopping list that's relevant to quality of life and aging rather than being a disease specific risk profile.

ANDI HORVATH

Cassandra do women prioritise their health differently?

CASSANDRA SZOEKE

There's not been enough work done in this space but there's certainly been research studies that have looked at heart health for example. There's very clear guidelines on risk prevention, and when people have a heart attack they go into a program where they're given a special diet, told about exercise and so on and so forth. There's some interesting findings from that work where they have shown that where they take a cohort of people who've had a heart attack they get this advice and then they looked at them at 12 weeks follow-up, a year and so on. When they told the men to eat a

certain diet, in fact they found at follow-up men were a) adhering to the diet and the entire household had started eating that diet, the heart healthy diet. Whereas in the women in fact they were cooking two meals. One was their diet, one was the other diet and when you look out to one year the compliance was much lower.

ANDI HORVATH

Cassandra I know we've got to look after our physical health, keep our brain in check, follow a healthy diet and enjoy social activity but who do I listen to? It's so confusing what information is out there.

CASSANDRA SZOEKE

Yes I understand that and that's one of the reasons why we're trying to pull together this centre that focuses on multi-morbidity because for example there might be advice for something that prevents a single disease. But that doesn't necessarily prevent all diseases or several diseases. What we now know is that people over the age of 50 don't have one disease. In fact people over the age of 50 with a disease two-thirds have three or more. So it's actually irrelevant to look at one disease if you're over 50 and have any disease because unless someone's done a study looking at three and your three, how's that specific advice relevant to you? So it's an excellent question. I think multi-morbidity is something we have to look at. Look speaking as a clinician, GPs at the coalface do this every day.

None of their patients have one disease. So this is something that doctors are doing that when we look at our research which has been quite disease focused and that's been why we're so healthy now and living so long because of those great advances in disease focus where we can really understand the development of disease. Looking at chronic disease in older populations it's not one thing.

ANDI HORVATH

Cassandra thanks for being our guest on Up Close.

CASSANDRA SZOEKE

My pleasure.

ANDI HORVATH

We've been speaking about understanding aging with the view to optimise our health span in our life span with Professor Cassandra Szoeki from the University of

Melbourne. You'll find a full transcript and more info on this and all our episodes on the Up Close website. Up Close is a production of the University of Melbourne Australia. This episode was recorded on 20th April 2017. Producer was Kelvin Param. Audio engineering by Gavin Nebauer. I'm Dr Andi Horvath. Cheers.

## VOICEOVER

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