

LINDA P FRIED:

Good afternoon. Now, maybe for the next generation of the future and I'm delighted to welcome you to this next segment on health across the lifespan, Achieving Healthy Longevity for Women. We're three panelists plus JoAnn Manson who's about to join us visibly, oh, she's up there online and I will be introducing all of them to you. But let me take a couple of minutes for an introduction. So, we're now in this panel going to turn to focusing on the second half of a woman's life, which is often not in this audience, of course, the moment when many audiences leave. And what we would like to consider with you is what we now know and the opportunities to create healthy longevity for women and what its significance would be. So, I'd like to start with some good news with a few data points. The first bit of good news is that despite the bad press, we have created longer lives in the last hundred years. This is a product of societal investment over 100 years in human capital, in health, and education.

We extended life expectancy, which is 1900 at birth was 47 for whites and 37 for blacks. It is now 79 on average with a much smaller racial gap. And for women, life expectancy at birth as of a few years ago was 81, and for men 76 years. That's an astounding, unprecedented historic achievement of adding more than 30 years to human life expectancy. A whole new life stage we never had before. There's more good news. We now are learning scientifically that despite the negative press, as people get older, we actually as human beings learn a few things that we didn't know when we were younger. In fact, the expertise and experience that we accrue across our life course doesn't disappear the moment we change jobs or retire. In fact, we retain it and continue to accrue it. And on top of that, there's very strong evidence that as we get older, we develop other capabilities that we didn't have when we were 20 or 30 or 40, capabilities in terms of socioemotional stability, generosity, pro-social goals, a commitment to giving back and leaving the world better than one found it, and to assure that future generations are better off, highly altruistic capabilities and altruistic goals which get manifested in very specific things like older people being much better at conflict resolution than younger people.

So, with all of those assets, we have the potential for having a social capital of generosity and capability coupled by suggestive evidence in neuroscience and cognitive science that as people get older, they're capable of problem-solving in complex ways that they never could do before. How do we put that together? Well, it offers, for 20% of the population that is about to be 65 and older, a potential set of assets for society at a time when we desperately could use it. So, lots of good news about the potential for longer lives. And at the same time, we see the potential for huge concern. One is that life expectancy itself has been declining in the last several years, particularly for women and including particularly women of color with less than a high school education. We have seen that there is a large gap between the length of our lives and the length of our lives lived in health about on average, a ten-year health lifespan gap in the US. And we have seen that women in the US are living six years less than women in Japan.

And along with many other data that the US has racked up, life expectancy for women is ranked 30 out of 36 peer nations at the bottom. So, we're confronted with both great news and very concerning news. But we also have figured out that healthy life expectancy, healthy longevity is possible. And the recent National Academy of Medicine Global Roadmap for Healthy Longevity has laid out the evidence of what we've learned collectively, that it's possible to prevent a large proportion of diseases. It's possible for people to live long lives with health. It's possible to do it and the delivery has not been democratized. But those who have been the beneficiaries of the conditions in which health is created across the life course are demonstrating that this can be done. And we have learned that there is a gap and you've

heard that earlier today, so I won't recap it, in terms of what women live with and die from as they get older compared to men. Women live with more multimorbidity. They live with more disability, the same conditions that unfortunately men die from.

Women die from cardiovascular disease almost the third, cancers, lung disease, Alzheimer's disease. And the health outcomes that occur as we get older, expand and diseases become risk factors for disability. We have the appearance of higher risk for cognitive decline and for frailty as major health outcomes as people get older. And we have a number of societally constructed outcomes that particularly affect older women, issues particularly women over the age of 80, issues of loneliness which is highly socially constructed. Issues in the face of the loss of many of our social and intergenerational connections. Issues of isolation from social connection, social cohesion, and social engagement. So, today we have the opportunity to say what do we know about creating healthy longevity. Where can we go? And what's the cost of inaction? And we have an all-star panel who I am absolutely thrilled to introduce. And I'm gonna introduce them in order of their speaking. They're each gonna make remarks and then we'll have an opportunity for discussion among the group and then turn to you, the audience, for your questions and suggestions.

So, it's my pleasure to start first by introducing online, but very much present, Dr JoAnn Manson. Dr Manson is professor of medicine and the Michael and Lee Bell Professor of Women's Health at Harvard Medical School, and Chief of the Division of Preventive Medicine at Brigham and Women's Hospital. JoAnn, welcome.

DR JOANN MANSON:

Thank you so much, Dr Fried. Good afternoon, everyone. I apologize I can't be there in-person due to family illness, but it's a great honor to participate in this panel. I'll be talking about Lessons on Healthy Aging and Extending Healthspan in Midlife and Older Women: the Women's Health Initiative. I have no conflicts related to this presentation. Now, why the WHI? Well, the WHI is the largest set of randomized clinical trials and observational studies in postmenopausal women. It included more than 160,000 US postmenopausal women throughout the United States aged 50 to 79 with a mean age of 63 at enrollment. It included three large randomized clinical trials, the hormone therapy trial, calcium/vitamin D supplementation, diet modification, and a large observational population. It was a diverse cohort with follow-up now for 30 years. Now, the WHI trial findings were very complex and it would take well over two full hours to review them. I've only eight minutes total, so I try to distill the key messages down to the single slide.

So, very briefly, the menopausal hormone therapy trial led to a sea change in clinical practice, a decline in hormone therapy use in the United States and throughout most of the world by more than 70%. A conclusion of the hormone therapy trial was that hormone therapy should not be used for prevention of heart disease, stroke, cognitive decline, trying to prevent heart disease, stroke, cognitive decline, or other chronic diseases. However, it still has a clinical role for treatment of menopausal symptoms. The benefit-risk ratio was found to be more favorable in early than later menopause. Now, the calcium/vitamin D supplementation trial, the conclusions were that CaD supplementation should not be routinely recommended for bone health or other purposes in generally healthy postmenopausal women. The calcium D findings, however, did support the recommended dietary allowances for women aged 50 and older for calcium, about 1,200 milligrams a day requirement, and vitamin D 600 to 800 IU a day, with supplements reasonable to fill nutrient gaps not met by diet but diet first.

Low-fat dietary pattern, that trial increase in fruits and vegetables, reduction in fat, this dietary pattern led to a reduction in breast cancer deaths with long-term follow-up, but it did not reduce cardiovascular disease. So, it provides one of many dietary options for midlife and older women, especially those at higher risk of breast cancer. Now, I want to move on to healthy aging more generally. And although I'll talk a lot about the WHI, I'm not gonna talk exclusively about WHI. I want to highlight the power of prevention and the strong link between several metrics of healthy lifestyle and lower risk of chronic disease found in the WHI and several other studies. Now, the metrics shown here is the American Heart Association's Life's Essential 8 and this metric includes four health behaviors, not smoking, getting adequate sleep - 7 to 9 hours, healthy diet and regular physical activity, and four health factors - controlling blood pressure, blood lipids, weight and blood glucose. Now, in WHI and in other cohorts, these healthy behaviors were linked to a reduction of greater than 80% in coronary heart disease, about 70% in heart failure and stroke, about 90% reduction in type two diabetes, 40 to 50% reduction in cancer.

And this was found in the WHI but also very similar results in other cohorts, including both men and women. Now, we looked at healthspan, specifically using the Life's Essential 8 metric. And this is healthspan-free of chronic disease, free of cardiovascular disease, cancer, diabetes, or dementia. And we found that actually, women following this metric did do even better than men with a healthspan extended 9.4 years in women and about seven years in men being in the high categories of Life's Essential 8 in the UK Biobank. And globally, in more than 34 countries similar results have been found. Now I'm going to just talk briefly about some of the findings by race/ethnicity. So, if these lifestyle behaviors could be made equally accessible, it appears that we would have similar health benefits by race as shown in this slide and the next. So, this slide shows that in the WHI, with higher amounts of moderate or vigorous activity as well as with time walking, we had similar stepwise reductions in the risk of cardiovascular disease in non-Hispanic white women, non-Hispanic black women.

This is for the total vigorous activity and this is for walking. In all of these cases, there were reductions in major cardiovascular events of 40 to 50%. In this slide, we look at type two diabetes. Now, diabetes is an even greater risk factor for cardiovascular disease in women than men and disproportionately affects underserved racial ethnic groups. However, in all of the racial ethnic groups looked at here, whites, blacks, Hispanics, Asians in this graph, there was a 60 to 70% lower risk of type two diabetes developing in those women who were in the joint categories of low BMI or BMI less than 25 and in the highest third or the highest tertile of physical activity. These women had very substantial reductions in type two diabetes. However, we know that healthy lifestyle isn't equally accessible across all groups due to disparities in access to safe areas, to walk, and to access to healthy and affordable foods. This has been touched on in the previous panels. But this recent study in Annals of Internal Medicine looked at the role of social determinants of health in explaining disparities in CVD mortality.

Now, in the nationwide NHANES cohort, more than 50,000 adults looking at CVD mortality, there's a 50% higher risk of CVD mortality in black compared to white adults. This is nationwide data. And adjusting for differences in behavioral factors, some of those listed here did attenuate. This excess risk actually led to a 40% reduction but not a full reduction. However, adjusting for social determinants of health, family income, food insecurity, unemployment, lack of home ownership, neighborhood factors, and others, there was a complete elimination of this excess risk of CVD mortality. So, the black-white differences in CVD mortality dissipated after adjusting for these social determinants of health in the US NHANES population. Now, just following up on what was mentioned in previous panels about pregnancy

complications, we know that there are tremendous implications for subsequent cardiometabolic health in the mother. Whether we're talking about gestational diabetes, pre-eclampsia, hypertensive disorders of pregnancy, preterm birth, or low birth weight, all of these conditions are risk factors for future risk of type two diabetes, hypertension, and cardiovascular events, including heart failure.

The risks are largely mediated but not fully explained by traditional risk factors. So, we need much more research on how to prevent these risks. Now, I'm going to just mention very briefly because Dr Kantarci will be focusing on cognition, that we found many risk factors for cognitive decline in WHI, strongly supporting the concept that what's good for the heart is good for the brain. So, all the major CVD risk factors, that short sleep duration, air pollution was strongly linked to cognitive decline in WHI through geocoding that was done. Also, late initiation of hormone therapy at age 65 or older, but not if hormone therapy was initiated in early menopause. And then several social determinants of health were related to higher risk of cognitive decline, as well as a number of biomarkers. Now again, very, very briefly Dr Cheng will be discussing some of the biomarkers. But we found many biomarkers in WHI that predicted exceptional longevity and extended healthspan. And these include, of course, polygenic risk scores, epigenetic clocks or DNA methylation metrics, telomere length, clonal hematopoiesis of indeterminate potential or chip strongly linked to healthspan, metabolomic, and proteomic signatures.

So, in conclusion, the WHI randomized trials have addressed pressing questions to improve health in midlife and older women, including the risks and benefits of hormone therapy, calcium/vitamin D supplementation, and a low fat/high fruit vegetable dietary pattern. And we know that lifestyle behavioral factors have a powerful role in preventing chronic diseases, as well as extending healthspan. However, social determinants of health and neighborhood factors are also contributing enormously to inequities in both the prevention and treatment for vulnerable groups. Reproductive and pregnancy-related factors are a window into a woman's future cardiometabolic health. And additional research, especially on translation and implementation, improved health care, and overall health policies and social changes are needed to achieve health equity. So, thank you so much for your attention. Thank you to the panel, and thank you to WHI and other research study teams. So, I'll stop sharing my now.

CROWD:  
(APPLAUSE)

LINDA P FRIED:

JoAnn thank you very much. When I was in training as a geriatrician, the argument among my betters was whether prevention would be relevant for older people. And you just did an elegant summary of some of the answers, which are pretty consistent. So, it's now my pleasure to turn to Dr Susan Cheng. Dr Cheng is the Director of the Cardiovascular Population Sciences and of Public Health Research, and the Erika J Glazer Chair in Women's Cardiovascular Health and Population Science at Cedars-Sinai Schmidt Heart Institute. Susan, welcome.

DR SUSAN CHENG:

(INAUDIBLE) for having me. Is this working OK? Sounds like it is. So, I first just have to say that it is really because of the trailblazing work by Dr JoAnn Manson and colleagues on critically important studies like the WHI and similar studies that we're starting to appreciate, not only why it's so critically important to study women over their life course, why it's also important to appreciate how women age differently than men and put all of this together to better understand the differences that we see in clinic. And what do we see in clinic? For those of us who are clinicians, we see that women continue to outlive men, as Dr

Freud just mentioned so elegantly. And yet while they're continuing to outlive men pretty consistently across geographies and still across historical times, even in this age of extending longevity, they tend to still consistently carry the greater burden of chronic disease with aging. And that difference between men and women as they age that we see in the clinic is one that expands and gets more and more complex with the advancement of age.

And this is just a relatively short list of the differences we see in clinicians, their age-related diseases. Some are less apparent in older versus younger, long Covid syndrome being one of them that we see more predominantly in younger and middle-aged women compared to their age-matched men. And so this has really led us, those of us who do clinical science as well as population science, to what's really a simple two-part thesis, a two-part thesis that I think a lot of us in the room have thought about. And that is, where do these differences come from? The first part of the thesis is that sex differences. So, differences between females and males really start from the beginning. They are present in health, you see them in normal anatomy and physiology. We have different growth charts for our babies who are born either female or male, pink and blue, growth charts for height, for weight, and so forth. And those differences really start with the genetic code, as David Page and others have taught us.

At the level of genetic code, there are sex differences, gene expression, sex bias, and gene expression that translates to sex differences in molecular traits, cellular traits, phenotypes, and outcomes. And those are the outcomes that we see in the clinic. The second part of the thesis has to do with the fact that in the context of having sex differences in health, sex differences in normal anatomy and physiology, that's really a setup for actually having differences in response to exposures and response to stressors that accumulate over the life course. As a clinical cardiologist and as somebody who is also a part of a team that has tried to study this phenomenon and try to test this hypothesis, this thesis, if you will, using clinical data, using population data, I can now share with you a little bit of what we've learned with respect to just looking at blood pressure - blood pressure being accrued, yet accessible measure of vascular aging. So, what we've done to date and this is really the work that has culminated over a series of several studies, is we just looked at systolic blood pressure, the top number you get from seeing your doctor in the clinic.

Systolic blood pressure, this recapitulated decades' worth of cross-sectional data you see on the top left. We found from looking at data from over 30,000 participants of US cohorts that not only are women starting at a lower baseline systolic blood pressure, but the top right, you see that the blood pressure increases over age, it increases at accelerated rate, and that increase actually starts early in life. And the bottom panels just show you that when you compare males and females, the relative rise in blood pressure is different, is much larger in the setting of cardiometabolic risk factors. And those risk factor traits include obesity, diabetes, hypercholesterolemia, and current smoking. Importantly, work not by our group but by other groups have shown us that the difference in blood pressure that you see over the life course, over aging and males versus females, particularly in the females, is actually there not just in association with traditionally, conventionally measured cardiometabolic stressors, it's there in response to other types of stressors that are critically important.

I think if you've read the news recently, you know what's happening around the world. And here's an example of men and women, their blood pressure is measured in war-torn western Africa. And you can see you don't actually have to adjust the y-axis here. You don't have to adjust or normalize the charts. The women have blood pressure that is responsive to psychosocial, psychological, and environmental

stressors in the setting of a war-torn region of the world that is much more pronounced than men. And normally these charts are reversed. Normally, men have higher blood pressure than women. That's what we've seen across all of our Western-based contemporary data. But this obviously looks very different. And how does this translate in terms of outcomes? It translates relatively directly. We and others have found that when you look at blood pressure-related cardiovascular outcomes, at a starting at a very much lower threshold of relative blood pressure elevation, women start to have a very statistically significant elevation in heart cardiovascular outcomes, be it myocardial infarction, heart failure, and stroke.

And so I've just used blood pressure as an example of a crude yet accessible measure of vascular aging that we deal with day to day in the clinic. We have this measured across all year chart data, population cohort studies. And really at the end of the day, we recognize that blood pressure as a measure of vascular aging is really just one piece in what's really an intrinsically integrated complex multi-organ system. And we see that's really just one part of the story that we're still trying to unravel. So, we and others and we hope that generations of scientists will be motivated to continue this work. We're now in a position where good news... We talked about bad news and good news. Good news is that we not only have more data, but we actually have more advanced data science tools, molecular profiling tools. Unfortunately, I don't have time to go into some of the molecular profiling data that we've looked at. But we have the tools, the techniques, the approaches, and we have the talent in the room and beyond our trainees and our colleagues to be able to address these questions that are pretty persistent and hopefully will be answered and addressable over time with more effort.

Thank you.

LINDA P FRIED:

Thank you very much.

CROWD:

(APPLAUSE)

LINDA P FRIED:

So, now it's my pleasure to turn to Kejal Kantarci. Kejal is a consultant in the division of Neuroradiology and the Catherine B Anderson Endowed Professor and Director of Women's Health Research Center, and Associate Director of the Alzheimer's Disease Research Center, and Director of Building Interdisciplinary Bridges in Women's Health K-12 program at Mayo Clinic.

KEJAL KANTARCI:

Thank you. Do you all hear me? Probably not. We will use this microphone. Hopefully, this is active. There you go. Perfect. So, my topic is menopausal hormone therapies and what they may mean in midlife for late-life cognitive health. And how do we use imaging biomarkers to perhaps measure the effects of these hormone therapies on the brain? Now, we know that there is more women living with dementia than men, about two-thirds of dementia cases are women. And women are also caregivers to a majority of dementia patients, which is also a risk factor for developing Alzheimer's disease and dementia later in life by itself. So, the social and economic implications of dementia is greatest in women. And this is in part because women live longer. Therefore, there are more dementia cases in women than men. However, there may be some sex-specific and potentially modifiable risk factors that can help us reduce the risk in women. Now, as Doctor Clayton mentioned, menopause is a time when we

see inflection of several chronic diseases, including perhaps cognitive influences and later cognitive health.

Now, two-thirds of the women have subjective cognitive difficulties during menopausal transition. When measured clinically, though, their cognitive function is intact. This cognitive testing with neuropsychological tests, shows subtle and temporary decline in cognitive processing speed, verbal encoding and verbal episodic memory. However, these resolve during post-menopausal period. So, this is very transitional. Yet 13% of women report having at least one adverse work outcome due to menopause symptoms in one year. Now, when we think about menopause, we have to also understand menopausal hormone therapies. As Dr Manson mentioned that menopausal hormone therapies in the Women's Health Initiative may have adverse effects on cognitive function if administered later in life. Based on that knowledge and based on some of the observational studies which show that if menopausal hormone therapy is administered early right after the menopausal transition, may actually have beneficial effects. There were two studies, clinical trials, that were initiated to test this timing hypothesis.

One of them is the early versus Late Intervention Estradiol trial, which looked at early at 56 and late at 65 years of age of women who were administered hormone therapies and showed that in the early group, there was a slowing of atherosclerosis. And they did not find any cognitive effects on hormone therapies based on the timing of exposure. Another one, the Kronos Early Estrogen Prevention Study or KEEPS trial which we will talk about a little bit more, were administering hormone therapies in women who were at 53 years of age, and they did not find any slowing of atherosclerosis, neither they found any effects on cognitive function in women who were administered hormone therapies compared to placebo. So, really no effect on cognitive function at the end of treatments. But when we look at the ages of women, we might think is this too early to see these cognitive effects because they're in their early 50s. We're talking about cognitive decline later in life. Now, one way of looking at cognitive function is to see how pathology evolves in the brain.

There is this preclinical phase where there is pathologic involvement emerging in the brain without any effect on cognitive function. And later in the course when there is a certain threshold is reached, the individual starts showing decline in cognitive function and after a certain threshold is reached, the diagnosis of dementia is given. Now, this pathologic enrollment starts decades before we start seeing cognitive decline. We have imaging biomarkers that are sensitive to this early preclinical stage and one of the... Probably most important developments in the Alzheimer's field has been to image Alzheimer's disease pathology in the brain before we see cognitive symptoms. For example, amyloid imaging, as you can see on the left-hand side, can show us the amyloid protein deposited in the brain with molecular imaging, radioligands, and PET imaging. And by measuring the amount of amyloid or tau proteins in the brain, we can tell whether that individual is developing Alzheimer's disease many years before they start showing cognitive symptoms.

So we administered amyloid imaging in women who participated in the KEEPS clinical trial after three years of the menopausal hormone therapies, when the menopausal hormone therapy stopped. We waited three years. And what we saw was, in the transdermal estradiol group, so there were two treatment groups, oral conjugated equine estrogen, similar to what was given in the Women's Health Initiative, and the transdermal estradiol group. Now, the transdermal estradiol group showed lower levels of amyloid deposition when we looked at the whole group compared to the placebo. However,

when we look at APOE epsilon 4 allele carriers, which is the well-known risk factor for Alzheimer's disease, we see this effect more pronounced in that group, but not in the APOE 4 epsilon allele non-carriers. So which demonstrates that there may be an increased risk in a specific group of patients. Now, we also found relatively preserved dorsolateral prefrontal cortex, which is one of the areas that is responsible for working memory function, more in the transdermal estradiol group.

So as the brain cortex thickness was declining due to aging, the transdermal estradiol group preserved this region better than the placebo. Yet, we did not see any change in cognitive function that was different between hormone therapy groups and placebo groups. So these were all structural changes that were identified in the brain. So this study showed that effects of early menopausal hormone therapy on biomarkers of cognitive health differed by formulations and administration routes. They are modulated by the APOE epsilon 4 allele that increases the risk of cognitive decline and Alzheimer's disease. And that has important implications for individualized approaches to prevent Alzheimer's disease in women, particularly carriers of this allele, who are the most vulnerable. However, we need to think about long-term outcomes. So what we were looking at were women in their early 60s. How about the long-term outcomes? So we initiated this study called 'KEEPS Continuation' in multiple sites that were involved in KEEPS ten years after the hormone therapy trial.

And now the women are at their age of 67. There are longitudinal cognitive, cardiometabolic outcomes evaluated, and there is also imaging in this study. These are results that were presented a couple of weeks ago at the Menopause Society meeting. We are not seeing any effect on cognitive function in various domains of cognitive performance. They are remarkably similar across the groups. The only thing that determined cognitive change over time was the baseline cognitive function. The hormone therapy does not play a role in the decline or change in cognitive function. Looking at the cardiometabolic outcomes, we did not find any evidence of cardiovascular metabolic benefits or any evidence to suggest that there were adverse effects. Now, we need to emphasize that KEEPS women were all quite healthy when they started menopausal hormone therapies. We don't know what the outcomes would be in women who are not healthy cardiovascularly. And we still need to look at the brain imaging data. So here are some future perspectives.

Now, we studied in this KEEPS cohort women who were cardiovascularly healthy. We don't know what would happen to women with poor cardiovascular health. And also, we need to understand better social determinants of these outcomes. And we had a relatively racially, ethnically diverse cohort. However, we cannot really individually test differences in these cohorts. And we need to understand the effects of race and ethnicity better in this cohort. Now, we also need to study women who undergo early menopause. So there is a cohort of women who undergo bilateral oophorectomy at a young age, particularly those who have their ovaries removed at the age less than 46 are at a higher risk for dementia. And we need to understand why. Is it Alzheimer's disease or is it vascular disease that's increasing the risk? And how about those who are undergoing premature and early menopause at a young age spontaneously? And what's adequate hormone therapy to treat these individuals? And how long should the hormone therapies last?

We still don't know whether they would be harmful if they last longer. Now that's all I had.

LINDA P FRIED:

That's fabulous. Thank you. (APPLAUSE) So now, to pull it all together, I'll turn to Ramsey Alwin, who is the President and CEO of the National Council on Aging. Ramsey.



RAMSEY ALWIN:

Thank you, Linda. And it's my pleasure to be with all of you. This is one of our favorite topics at the National Council on Aging, talking about the gift of longevity. We're deeply committed to making sure everyone gets not just those quantity of years but quality of years as well. So my honor to be with this incredible panel today, to really share some of our insights from our practice and policy perspective. So, the National Council on Aging, for those of you that don't know us, we have been around for over 70 years. We were the first national aging organization working with the vast network of aging network professionals across the country with a deep commitment to ensuring all can age well. We believe aging with dignity shouldn't be a stroke of luck. It shouldn't depend on your gender, your zip code, your education level, or any factor out of your control. We truly see aging and aging well as a social justice issue. It's an issue that impacts all of us, and the cumulative advantages and disadvantages, the disparities we experience over a lifetime all compound in old age.

Women are a central focus to our work. Last year alone, through our service delivery efforts, we reached nearly 6 million older adults, improving their health and economic security. Over 70% of those individuals raising their hand for help, finding jobs, gaining access to programs that can help with food and medicine, and other basic needs, requesting help to navigate their chronic conditions, prevent falls, and access life-saving vaccines were women. The vast majority of individuals struggling in old age are women. Today, our goal is to improve the lives of 40 million older adults by 2030. We're focusing like a laser beam on what the challenges are and the solutions that we know work. So focusing on women is critical for us because aging is a woman's issue. Women enter retirement at more disadvantage and more likely to age into poverty. Women, especially women at the intersection of race and ethnicity and socioeconomic status, have earned less in their careers due to pay gaps, occupational segregation into low-wage work, and time off for caregiving.

And so many of the programs we all rely upon to age well don't recognize that reality. That means women have lower Social Security benefits and fewer savings to draw upon as they age. And why does that matter when we're talking about health? Because your wealth so often determines your health, and your health is a critical factor to your ability to continue to work and accrue that wealth. So we see health and wealth being inextricably tied. And in a recent analysis our team did, we looked at the true cost of chronic conditions. Our analysis demonstrates 80% of older adults have two or more chronic conditions. And we wanted to better understand the real cost of chronic conditions. So we looked at the cost of treatment, non-treatment, and lost wages. In doing so we found that older women represent two-thirds of those with the highest annual cost burden. At the same time, older women have the lowest household income and the highest out-of-pocket medical expenses. So the bottom line is that women have higher health costs and less money to pay for them.

Absolutely unacceptable. And we're addressing it at the National Council on Aging through policy and through practice. So what are we doing? We are in communities all across the country. We work with a vast network of community-based organizations, senior centers, area agencies on aging, councils on aging, faith-based organizations, and others. We are working with them to educate women through evidence-based health promotion programs. It's truly impactful work that benefits both the older women and the health care organizations. For several decades now, NCOA has run two national resource centers whose goal is to spread the use of these evidence-based programs nationwide. We actually certify the evidence-based health programs on behalf of the Department of Health and Human Services. With funding from the Administration for Community Living at HHS, we support this vast network of

organizations in running programs that help women prevent falls and manage their chronic conditions such as diabetes, hypertension, obesity, and so much more.

We know these trusted, community-based organizations with peer-led self-management educational trainings make a difference and a real difference on the health system. When we talk about true cost, let's talk about falls, for instance. Falls can have a devastating effect on an older woman's health and finances. When we look at the most recent data, nonfatal and fatal injuries are most likely to come from falls. Falls cost the system \$50 billion on average annually. And yet there are evidence-based health promotion programs that can prevent falls, but they're not available in every community. Even though these programs are proven, they are held hostage to the existing appropriations and availability of resources. So your availability, your opportunity to benefit from evidence-based programs currently depends on your zip code. So while we've made great strides in terms of spreading these programs, there are some critical next steps we need to do. First, few healthcare providers know these evidence-based programs exist, so very few will make the referral to the patients.

We need to better educate providers about these resources in their communities. Second, as I mentioned, the programs are hostage to a funding level, specifically through the Older Americans Act, which is chronically underfunded by Congress. We need more resources so we can scale what we know works. And third, these evidence-based programs are not reimbursable under Medicare yet. Even though we've decades of research to demonstrate the effectiveness, and some Medicare Advantage programs are even starting to cover programs, original Medicare, traditional Medicare hasn't kept up. And this needs to change. So what are we doing at the National Council on Aging when it comes to policy? Well, we're working to address the insidious nature of ageism that often prevents these programs from being supported and scaled. And we're continually advocating for the Older Americans Act programs. In addition to the health programs I mentioned, there are other older adult programs that provide meals, transportation, other social services that can address the social determinants of health.

And we're building the case that these evidence-based programs should be reimbursed by Medicare. And we're also recognizing we're long overdue from addressing all the programs we rely upon to age well. Social Security, Medicare, Medicaid, and the Older Americans Act were all created at a time when women were not engaged in the workforce in ways they were. We weren't enjoying the longevity trends we are today. So we're advocating to make sure we strengthen and expand the programs we all rely upon to age well. And then building the political will and the public awareness to do so. We recently administered a public opinion sentiment survey, 'What Women Say'. We surveyed women 25 and older because we know aging well starts well before retirement years. We asked the women with an oversampling of Black, Latinx, and white low-wage workers what they think could help them age well. And what we found was sobering. We heard, regardless of generation or party affiliation, that women believe government has a role to ensure they can age well.

94% said they supported making the Social Security cost of living adjustment more accurately reflect the true cost of health care and housing later in life. The same number said they support providing a tax break to family caregivers to help cover out-of-pocket costs providing care. And on and on it went in terms of the policy proposals we put forward with bipartisan, multigenerational support. At NCOA, we know a woman's ability to age well starts early, not just when she retires. And women of all ages and life stages are finding it challenging to age well. We have to make sure we take a more holistic life course approach to our current systems. That's why we need transformative solutions supporting women across

the lifespan so that that quantity of years can be coupled with quality of years. We believe that means getting more women, especially older women, in the room where the decisions are being made. Thanks, Linda.

LINDA P FRIED:

Thank you. (APPLAUSE) So we got a bit of a late start on this session and don't have more than a couple of minutes for our group discussion. But while I try and summarize what I think has been presented, I'd like to invite people who want to ask questions to come up to the microphone. So what I've heard across each of your wonderful talks is that there is a gap, a large gap between life expectancy and healthspan, that it's possible to dramatically increase healthspan through prevention. That the exposures that occur across a woman's life are cumulative, and that there is a need for prevention at every age and stage of life to create health futures for that woman into the oldest years. I heard you say that much of prevention needs to occur outside of medical care, and we need those systems to deliver it. Ramsey, excuse me, you focused on community-based organizations, but going back to some statements that Dr Dzau made this morning, there is a huge need to also look at our public health system, which was not designed for a population of long lives, and take all of the science that you all have prevented, and think about how a public health system designed to deliver health into every community could do that.

What I also heard across the first three presentations is that there are shared risk factors across many outcomes. We all know smoking causes 14 diseases, physical activity is responsible for most. Education is important for every health outcome, as is precarity. And the list could go on and on. So how we develop a prevention agenda going forward that finds the best buys for healthy longevity and then how to deliver the most effectively to everyone is going to be critical. With that, I'm going to turn in the interests of time, unless anybody on the panel wants to add to what I just said, you're welcome to. But I think you've made a compelling case about both the opportunities for healthy longevity and the need for system change in, really, every system to deliver it. So I can't quite see who's at the mic, but please introduce yourself and ask your question.

SHARI BARKIN:

Good afternoon. My name is Shari Barkin from Virginia Commonwealth University. Thank you very much for the panel. And you all mentioned that this starts early. I know Dr Johnson talked about the life course, and I so appreciate Dr Fried mentioning that. I'm a pediatrician, so early is a lot earlier. And if we look at fetal programming as well as the early days, we know that that sets you up for health across the lifespan. And so my question to you is if you look at each of your areas, whether that's policy, research or genetics, what would it look like to ask this question starting from childhood?

LINDA P FRIED:

Go ahead, Kejal, yeah.

KEJAL KANTARCI:

OK, well. the microphone is active now. Well, cognitive health really starts with education and occupation. That goes through the whole lifespan. And what we have learned in Alzheimer's disease research is that a healthy brain, a brain with lots of reserve is resilient to pathology. So imaging has provided that window into how the pathology is evolving in the brain and how a person is exhibiting cognitive impairment or difficulties with cognitive function. So what that research has shown that people with higher education, more cognitively engaging occupations tend to be resilient to more pathology, keeping their brain functioning well until a certain level of pathology is reached. Of course, they can't be

resilient after that stage. And then you start seeing cognitive decline. And I think that's an important consideration for even childhood where those kinds of resilience-related factors need to build up over the lifespan.

LINDA P FRIED:

I can't resist adding one of many connections between the opportunity of a child for healthy longevity and climate change. And on your example, one example is it was cited earlier today that air pollution is associated with cognitive decline in older people. There's also compelling evidence, as I'm sure you know, that pregnant women who inhale significant particulate matter from air pollution while they're pregnant, their offspring actually have impaired neurocognitive development in the first years of life, which sets them up for exactly the kinds of problems that Kejal is talking about. And of course, climate change worsens air pollution. Thank you. Any other comments?

SHARI BARKIN:

Thank you.

ALEX CAPRON:

Alex Capron from USC. We have heard so many important developments in science and genetics and therapy. But I'm concerned with the fact that, right now, longevity in the United States lifespan is decreasing. And again, this is one of those ways, and we've heard of other ones, maternal mortality and so forth, that sets us apart from the rest of the developed world. I want to ask a question about a concern that while we have associated that decline in lifespan, mostly with deaths of younger people in their middle years, often termed deaths of despair, that we may be on the brink of seeing deaths of despair among our older population, the people to whom you all are trying to give a healthy lifespan, a healthy longevity. And I think there were statistics from the National Council on Aging that talked about the fact that women retirees have half the savings, about \$60,000, a little bit less than that, something like that compared to men. That's the average. The median retiree in this country has no savings for retirement.

They're dependent upon Social Security. And as your questionnaire to people revealed, most people who are dependent on Social Security know that that is not adequate. And when those diseases - and I think I heard the panel say that the average person in older age has at least two chronic conditions, when those diseases add to costs which are not being covered even when we have proven therapies for them, as you remarked, how are they going to live? Where are they going to live? Will they be in nursing homes, which we know today are even more understaffed than they used to be, etc? What is the life that will be worth living? Are we going to see people who either can't afford or who just give up on their medications or whatever, because of the conditions of their life? What are we thinking about of that larger social determinant of the way in which our society puts all these efforts into increasing lifespan but leaves a lot of people unable to enjoy it?

LINDA P FRIED:

Well, I was just going to comment that these are critically important questions, and they exemplify what the Global Roadmap for Healthy Longevity said, which is that we sit in the interregnum between having created longevity and not having redesigned our society and our systems to support it. And I'll ask Ramsey to comment.

RAMSEY ALWIN:

Well, the alarm bell is ringing loud and clear. The decrease in life expectancy in the United States, coupled with the fact that the most recent census data once again saw an increase in poverty among older adults for the third year in a row, for the third year in a row. The reality is this do-it-yourself retirement, DIY retirement to manage and navigate your own health needs as well as your own financial needs is not working. Other countries that also saw a decrease in life expectancy due to COVID have already rebounded, yet we have not in the United States. So we really need to build the public awareness and the political will to have some tough conversations about the realities that all the programs we rely upon to age well, as well as the social contract of work hard and then retire has outlived its utility. It's now time for a new conversation about healthy longevity. What does it take? What are the multisectoral collaboratives that need to happen? What's the role of the private sector, the public sector, nonprofits, and individuals in changing mindsets and systems to make sure we can truly experience the gift of healthy longevity?

Otherwise, we're on a trajectory for decline. Globally, we are an outlier, though. There are best practices around the globe that we can draw upon, in Singapore, in Japan, in Germany. We can learn from others, and we can put ourselves on a better trajectory. We need the political will.

LINDA P FRIED:

Ramsey, could you also comment on the increasing reports of an increase in homelessness among older women and what's being called the forgotten middle, of the lower half of the middle class, of older adults, and the similar straits that they're in?

RAMSEY ALWIN:

Sure, well, we saw this anecdotally before the data sets even caught up. An increase in older adults generally, but older women in particular, couch surfing, living out of their cars, because they came to the National Council on Aging asking for help finding a job in their 70s and 80s came saying, "Social Security is not enough. I would like to get a job to make ends meet and to get out of my car." Now the data is starting to catch up from HUD, and it's clear we have quite a crisis on our hands. We have an increasing number of older adults retiring with a mortgage, and for those that can't afford the rent or the mortgage, homeless.

LINDA P FRIED:

So this takes us into another set of social situations which create a whole different realm of precarity. What we see is that many medical care systems are groaning under the increase in older patients making appointments, because they need to talk to another human being. The rates of loneliness are escalating, and the only person they can think to talk to, even in the face of medical care, is a clinical provider. Clinical providers are experiencing what we have seen in most communities which is the decay and disinvestment in the social fabric of the organizations, of our communities which create social connection and cohesion and support our pro-social identities and well-being. And in the face of that, I'll go back to my opening comment, which is that what we know about human development in the second half of life is that people seek, just as we do when we're younger, meaning and purpose and the opportunity to stay engaged, committed to a better future and to give back. But we do not have the roles, whether it's in the paid workplace or in volunteering for older adults to remain engaged, to be wanted by a workforce that could deeply benefit from them, or to stake, to be able to enact their commitments, to leaving their communities better off.

A huge gap. Additionally, because that kind of social connection and the ability to fulfill a desire to make a difference in whatever realm one desires actually is hugely important for healthy longevity. Thank you all very much. Yes, go ahead. Oh, I'm sorry, I can't see you there.

JOIA CREAR-PERRY:

I'm sorry, I thought we still had time for questions.

LINDA P FRIED:

Yeah, no, go ahead.

JOIA CREAR-PERRY:

Great.

LINDA P FRIED:

I have the light in my eyes and I can't see anything.

JOIA CREAR-PERRY:

I was learning, so it was fun. So I'm Joia Crear-Perry. I'm an Ob-Gyn and the founder and president of the National Birth Equity Collaborative. And I feel like we have very similar problems. So the work that we do in reproductive justice, we've been trying to explain that we need the full range, not just access to abortion. When the 12 Black women who created the framework, the point was that we need to be able to have children. So if we want to have ten kids, we can. Not have children, that means if we exist as a human being and never have a child, we still are valuable and important. And we should be studied and researched and be able to also parent our children in safe and sustainable communities. So that's the whole social determinants conversation. So how can we do that in the last part is be able to have personal bodily autonomy. And with the overturning of Roe, we're clear that that has not been happening. So the similar problem we're having is that we spent a lot of time talking about the need to see race as a social construct.

So since Bill Clinton came out and said we've done the entire human genome, there is no biological basis of race, and we're still having that same conversation since 2001. Many researchers in all these buildings are still looking for a biological basis of race. And then when it comes to sex, you all have proven that there are biological basis of difference in sex when it comes to aging and menopause, and yet we still have to keep proving that there is a biological basis around sex, that there are actual things that happen and be able to differentiate what's the difference between - I'm standing here as a Black woman, but my genetics are equally Irish and Nigerian. So my social identity has very little to do with my genetics. So when we think about how does one think about sex differences across aging and be able to see that clearly there are genetic things that make me a woman that you can't necessarily - I have ovaries and things, but my social expression of that also plays into my outcomes as well.

So how do we come all together to say that we no longer want to keep arguing about the fact that there's clearly a biological difference between men and women, and yet it's also tempered by gender norms, those other things exist as well, and that there is no biological basis of race. And so when you put those things together, what are we supposed to do as a community to solve our problems?

LINDA P FRIED:

Thank you. You just did a fabulous job of summarizing the day and saving me from having to do a closing. So thank you. I would say that what I hope is that this very rich set of knowledge, information, and

discourse can take the lid off the invisibility of the opportunities and needs for women's health and the necessity to move out of what President Johnson said, which is thinking about women as a niche issue. Thank you. (APPLAUSE)