

## Interest Group 16: Healthy Longevity

**Lynn Gerber:** Good afternoon, everyone, and thank you so much for joining us. It's wonderful to see so many familiar faces and some new ones as well. This is interest group number 16. Our topic is rehabilitation and human function.

This year, our subsection, that's 8C of the National Academy, decided we wanted to explore healthy longevity. For those of you who are members of the Academy, you know well that this has been an initiative and a significant financial commitment on the part of industry and the National Academy. We selected this topic, healthy longevity, for our IG presentation today. We have two world-class outstanding speakers, which you will hear about and from in just a short while.

I would like to give you just a little overview of the healthy longevity initiative that was started almost 2 full years ago by Dr Dzau when he presented the direction that the National Academy was going to take with respect to healthy longevity. It integrated global priorities and actions that needed to be addressed from a report that the Academy put out, hoping to reach these goals by 2030, optimize for all: health, function, and well-being. We don't have a corner on function and well-being, but we certainly identify with it. It has been one of our goals as an interest group and as a subsection to spread the word about function and rehabilitation; so we're taking that opportunity today.

Because of dramatic breakthroughs in medicine, public health, and social and economic development, there have been unprecedented extensions of the human lifespan. Globally, it's a real challenge. Today, 8.5% of people are over 65, and by 2050 that is thought to reach 1.6 billion people. The population of "oldest old," that is 80 and older, is expected to more than triple between 2015 and 2050. At the current pace, the population aging is poised to impose a substantial strain on our economies, our health systems, and social structures worldwide. But it doesn't have to.

This committee was formed under the co-chairpersonships of Dr Linda Fried and Dr John Eu-Li Wong to mount a grand challenge fundamentally to stimulate research through a process of jumpstarting young curious investigators. Once that got started, there would be a pyramidal effect to develop accelerator grants, which were substantially more than the catalyst, and then champion among those that were selected as the most outstanding. This is a major commitment on the part of the National Academy.

Basically, one of the goals highlighted and supported is function, which is the focus of this in this interest group. I would just define the word *function*, taken from our ICF classification—and many on this call have been leaders in helping to define, refine, and proselytize the utilization of this concept—*functioning* is defined as "a dynamic interaction between her or his health conditions, environmental factors, and personal factors." That is essentially what we have been working from as a professional society and as individuals.

Two contributors to functioning will be discussed today: (1) appropriate evaluations and measurement of function and (2) the other, physical activity and nutrition and dietary behaviors.

The title of one is *Function Frailty and the Implications of Screening for Risk* and the other *The Relevance of Nutrition for Functionally Successful Aging*.

Start your questions now in your own mind, and pepper our speakers as we go forward. Thank you once again for participating.

Let's hear it for Senior Women's Tennis.

**Amy Houtrow:** Thank you, Lynn.

I have the distinct honor and pleasure of introducing our speakers today. Our first speaker, Dr Jonathan Bean, will be speaking on function, frailty, and screening for at-risk in older adults. Dr Bean is a professor in the Department of Physical Medicine and Rehabilitation at Harvard Medical School and is a staff member at Spaulding Rehabilitation Hospital. He is the director of the New England Geriatric Research Education and Clinical Center at the VA Boston health care system, and he is the very first ever physiatrist to be appointed to this role. Dr Bean also serves on the editorial board for the *Archives of Physical Medicine and Rehabilitation*, he's served on the governance committee for the Association of Academic Physiatrists, and he's served as the liaison between the American Academy of Physical Medicine and Rehabilitation and the American Geriatrics Society. Dr Bean is internationally recognized for his expertise in geriatric rehabilitative care, having extensive experience in the conduct of clinical trials and the measurement of disablement outcomes. He has been repeatedly recognized for this expertise with awards from the Association of Academic Physiatrists, the Gerontological Society of America, and the American Congress of Rehabilitation Medicine. We are delighted to have him with us today to share his wisdom and expertise.

If you have questions for him, I encourage you to raise your hand once he's finished and engage in dialogue, or during the presentation, feel free to put them in the chat so that we can address them at the end of the presentation.

Thank you, Dr Bean, for your presence here and sharing with us your wisdom.

**Jonathan Bean:** I just want to confirm that everyone can see my slides, that I'm sharing the screen successfully.

I'll be talking about function, frailty, and as said, the implications of screening risk in older adults, which really is walking down the path of treatment. I'll be talking about a lot of the work that's been done in the field, and I'll also highlight some of the work we've been doing ourselves to address treatment paradigms and geriatric rehabilitative care that are focused on prevention.

We're going to cover the first part, screening risk for older adults, conceptualizing function as a guide for treatment, how do we deliver high quality care, and then rehabilitation as prevention. I want to acknowledge the support that I've had for some of the work that I'll be presenting here, and we'll get started.

I want you all to imagine that you are a primary care physician, and you have a busy practice, and you have a large percentage of older adults in your waiting area. In fact, the next patient is actually one that's going to undergo the Medicare-mandated annual wellness visit, a visit that's been designed to identify older adults that are at risk for adverse health outcomes and an opportunity to employ some

sort of preventative care measures. This is particularly important because, as you know, the oldest adults are the fastest growing segment of our population. When you consider older adults, they have very high levels of comorbidity, and you also know that using a specific care paradigm for a single disease does not really fit well for patients that have multiple comorbidities. The challenge is, what is the screening tool that best identifies people at risk?

As you're walking into the room it really begs the question, which vital sign is most helpful to you for identifying if this patient should or shouldn't be treated with preventative care? Actually, the vital sign that is best predictive of this is the one that wasn't measured, and it was the speed with which they walked into the room.

This is an article from *JAMA* in 2014. Along the  $x$ -axis as you go from the right side to the left side, gait speed gets progressively slower, and on the  $y$ -axis, what you're actually seeing there is actually predicting disability as the outcome via ADL-related disability or mobility-related disability. But, as it turns out, it doesn't really matter what outcome you put in there—you could put in hospitalization you could put in falls, you could put in mortality—and you'd still see the strong relationship between gait speed and its association with adverse health outcomes. It's so powerful that it has been advocated as a vital sign to be utilized in primary care for the exact purpose that I mentioned.

The real question is why is that? Why would a measure like gait be predictive? I think the best way to think about it is to actually think about an orchestra. If you think of each of the sections of the orchestra working together to produce a beautiful piece of music, you could also think, in contrast, where if there were certain sections of the orchestra that weren't working as well, that were maybe deficient in some way, that the resulting music would really not be very pleasant at all. It holds as well, if you think about that with regard to our body systems. If you think of our different organ systems working together to be able to enable us to walk normally or to walk optimally with the best-possible walking speed, when we start to see that slow, it's reflective of deficiencies in the underlying body systems that are contributing to that activity.

That really brings up the issue about frailty. When we think about frailty and how it's defined is that in the aging literature and geriatric literature, it's a state of increased vulnerability due to stressors that are caused by decreased physiologic reserves. It's really recognized as a way of identifying who is able to undergo a stress. Therefore, models of frailty have been developed to actually develop empirical measures for identifying who's at risk for various procedures, be it surgical procedures or be they other sorts of medical events, sort of characterizing their risk.

This really has tremendous relevance for all types of care. As you think about it from our standpoint of rehabilitation, it also is reflective of the opposite of resilience, the ability to withstand the stress. The empiric models that have been developed are generally based on the comprehensive geriatric assessment. It really looks at patients and their corresponding deficits in their different organ systems, going from head to toe, with also a regard for social setting as well as functioning. Both major paradigms that exist out there include counting deficits. I know Linda Fried was mentioned, and she really was a seminal figure in the development of frailty measures with the frailty phenotype, and also in Canada there's Ken Rockwood who has developed the Frailty Index and the Clinical Frailty Scale, which I will show you in a little bit.

When you think about operationally defining frailty, the frailty phenotype really describes five characteristics: weakness, slowness in the form of gait speed, reduced physical activity, fatigue or reduced energy, and weight loss. This was really based on the clinical experience and consensus among geriatric care providers, and then was proven empirically through work within a cardiovascular health study and many subsequent studies.

The Frailty Index takes a little different look at it. What it does is, it looks at a whole list of deficits that a geriatrician might evaluate in the context of their comprehensive geriatric assessment. What they've shown is that you could look at anywhere from 30 to 50 potential deficits in an individual; what you may do is then check off the ones that are actually deficient and from the number, the denominator, of the possible deficits to what's actually observed is actually an index that's calculated. What's been demonstrated through multiple studies and multiple data sets internationally, is that even if there's some variability in the number and the denominator of characteristics, that that index generally holds true at being predictive. The interesting thing about both of these measures is that both have been adapted for use with EMR data and have been used on a large scale to identify risk among larger populations.

Here's an example of this, and this is specifically looking at the impact of COVID and survival with COVID. This is based on Rockwood's work, and it was the Clinical Frailty Scale. What was shown is that people with more severe frailty had a worse survival time after a hospitalization for COVID; this is a large-scale, multicenter, observational cohort study done in Europe.

Prior to that there were other studies that looked at the Rockwood Measures of Frailty, really showing that it could predict institutionalization and also mortality as well. These figures are actually showing the Clinical Frailty Scale, but there are other reports where they have the Index, and you see just about the same phenomenon. But I highlight the Clinical Frailty Scale because this was actually developed because Dr Rockwood's brother is an orthopedist, and as we know, orthopedists generally are not going to do the same sort of comprehensive assessment that a geriatrician would; they needed to have a very simple scale that would allow an orthopedist to be able to determine a patient's frailty. What they ended up looking at was really a scale of their physical functioning. At the top of the scale, you have someone who's very fit—who's very robust, active, and energetic—and at the lower end, you have people that are very severely frail or even terminally ill. It does also account for the manifestation of cognitive impairment in the scoring, but essentially it is predictive of these adverse health outcomes. But it also highlights an important issue that's been recognized with the large variety of frailty measures out there, which is that it's very difficult to differentiate frailty measures from disability measures.

This was a comprehensive review that was done and recently published where they looked at over 200 measures of frailty in the literature, and they found that over 50% had frailty relying on ADL items. When you speak to people that are really focused and interested in frailty predominantly, they have no problem with this because they feel like evaluating functioning is a really critical piece of identifying someone who's vulnerable to adverse health outcomes. But it does pose challenges from the standpoint of defining disability from frailty or when you're thinking about using it in different contexts; this was really highlighted in this article as well.

I'll give you an example of this. Here's another paper that looks specifically at the Frailty Index, and it used a functional performance measure called the "short physical performance battery." The short physical performance battery (SPPB) is the measure from which all the information about gait speed was

originally derived, because it's a composite measure of three tasks: (1) gait speed, (2) standing balance, and (3) chair-stand time. Each one is score between 0 to 4 with a maximal score of 12. What you see is that as you go from 12 to 0 in scores of SPPBs, you see a strong correlation between the Frailty Index and the corresponding SPPB scores. What this article actually showed was very similar data with the frailty phenotype as well, and the argument was made that the SPPB could be a crosswalk between those measures and really serves as a measure of frailty in and of itself. In a way, frailty measures are functional measures and are largely based on functional measures. I will add that, with the Frailty Index, when they've looked at and they've removed the actual functional parameters and looked at the more physiologic parameters, they still see that it has a predictive value as well.

Just to kind of summarize the frailty measures: They're particularly good because they can be used in EMR data, you can identify people that are vulnerable to stressors, and you can look at it on an individual basis and also on a population basis. There are the two measures that I described that are the predominant measures in the field; both can utilize the EMR data to predict risk across populations.

On the more challenging side, frailty is commonly conflated with function. That's very critical if, for example, you're going to use frailty as an outcome measure or you're going to target function in your treatment in that context, because you end up finding that function predicts function potentially; that's an important issue to consider. Another is that it lacks some dimensionality. Generally, it's focused on the patient and the corresponding deficits, and it doesn't really consider the interrelationships between disablement outcomes that we'll talk about in just a little bit and that are highlighted in the ICF model.

Next, I want to talk a little bit about how we conceptualize function as a guide for treatment. In order to do so, I want to highlight this image that I'm showing here. This is a woman crossing the street. You can't really visualize it very well, but it took her about 6 seconds to realize the light had changed. In the left panel, it says 54 seconds, and you can perhaps see on the right panel that it says 15 seconds; so it took her 45 seconds to cross the street, or 46. A year after I took this photograph, they reduced the time to cross the street to 35 seconds. Essentially, she's no longer able to participate in her life role and living in her community—this is in Brookline, Massachusetts. This is someone for whom treatment would be indicated. We'd want to think about, what would the ingredients of treatment be that would optimize her ability to walk as quickly as possible across the street? This really was something that guided a lot of our work and really guides the conceptual model of the ICF model. The notion is that you have deficits at the level of body functions and structures here on the left that are characterized as impairments. Activities such as walking speed, when deficient, are defined as limitations. Those are then related to participation in a life role, which when deficient is restricted. All of this is influenced by comorbidity or health conditions, environmental factors, and personal factors. As many of you know, this has been the conceptual model that has guided a lot of the World Health Organization and rehabilitative care.

Now, an important point that I want to emphasize is that when you start to look at these outcomes empirically, when you're based on the left side, those are largely determined by biologic factors. So when we look at what are predictors of impairments and body functions and structures, it can be based on cellular mechanisms, physiologic mechanisms, largely more biologic factors. But as you start to look at predictors of more distal outcomes like activities, you end up finding that, at the best, with biologic predictors you can describe about 50% of the variance in gait speed or in mobility tasks. There's a lot of social and behavioral factors that contribute to the various performance of activities. When you get to

participation, there it is even stronger based on social and behavioral factors. We might need to think about that as we design our treatment, which I'll get into a little bit later in the presentation.

The other important part is that this will be part of *ICD-11*, or at least that's the plan in the future, and so more than just rehab providers are going to need to be facile in understanding this conceptual model and being able to characterize their patients and their corresponding treatment accordingly.

I want to highlight some of the empirical evidence that we've developed over time to show these interrelationships and to potentially guide treatment. To do that, we conducted a longitudinal cohort study among 13 primary care practices from Massachusetts General Hospital and Brigham and Women's Hospital in the greater Boston area.

We looked at primary care patients that were older and at risk for functional decline, and we evaluated them on an annual basis over 2 years. What we were looking at, what we were primarily focused on is that from the literature, we could identify about a dozen different impairments that were identified as being relevant to mobility skills. We wanted to identify the subset that were most predictive of mobility decline over 2 years of follow-up. What we ended up finding was that there were really four attributes: limb strength, limb speed of movement, limb range of motion, and also trunk muscle endurance, which really gets at the endurance of our core and trunk muscles. In parallel, research, I want to highlight work done by Jeff Hausdorf and separately by Jennifer Brach that have also identified timing and coordination of gait as also important attributes that are predictive of this as well. What this really identified for us was that here's a subset of attributes that we could target in our care and potentially could drive improvements in mobility skills.

We were also interested in understanding whether it really held that there were these interrelationships between body systems, activities, and participation. What we were able to do is look at what predictors of participation and life roles 2 years later—to after 2 years of follow-up in our Boston RISE cohort—and look at these same attributes at baseline. What we found was that the majority of those actually acted through, in this study, mobility activities in their influence on participation. Leg speed had a direct effect, but also there may have been other mobility skills that were more basic that may actually have mediated that association. The take home was that there was indeed this interrelationship between body system impairments, activity limitations, and participation in a life role.

The other thing that is particularly important in geriatric research was the notion of comorbidity. I talked about the high rates of comorbidity where typically a primary care patient might manifest five or six chronic diseases at one time that are being managed by the primary care. There's a lot of debate in the geriatric literature about whether there were actually patterns of comorbidity or whether we should just consider counts of comorbidity. We looked again at the Boston RISE cohort, and we evaluated individuals based on their patterns of comorbidity. We were able to identify three different latent classes that we defined as a low burden of comorbidity, a high burden of comorbidity, and predominantly musculoskeletal comorbidity.

When we looked at those classes versus actual counts and looked at them in their association with the ICF disablement outcomes, what we found was that the latent classes were not significantly associated. But when we looked at comorbidity in terms of counts, it was strongly associated with impairments, limitation, and participation restrictions. What it really highlighted for us, in a way it makes it simpler for us when we're considering comorbidity and how we might account for it, that we may just look at the

overall burden in terms of counts than worrying about the actual classes; that was what was highlighted in this work.

We've also looked at personal factors as well. This was a separate clinical trial that was done; it was published in *JAMA* in 2014. It was a focus on patients that had completed care after undergoing a hip fracture and having had surgical repair for that. Many of these people under one subacute rehabilitative care, which we'll touch upon a little bit later. Once they had finished all their rehab, the outcomes are still quite poor for these individuals that survive, both in terms of survival as well as return to appropriate or prior levels of physical functioning. The purpose of this study was to have a treatment that was targeted to people once they finished all their rehab, and the control was an education program. The treatment was an exercise-based program that was delivered with two physical therapy visits and provision of a DVD, which had an exercise program on it. The exercise program focused on important impairments, as well as the optimization of functional activities, and also embedded in it was a focus on behavior change with a notion that that was critical for long-term benefits. What we saw on what's shown in the figure on the right, in this case looking at outcomes of short physical performance battery but also this was shown with patient-reported measures of functioning, was that there were robust differences at 6 months among those that were in the treatment versus the control.

What we also observed was that those improvements were maintained 3 months after treatment ended at 6 months; so treatment ended at 6 months, the DVD and the video player was taken away, but they still maintained their functioning 3 months later. Within a separate analysis, when that was looked at, it was shown that self-changes and self-efficacy were a major component of what was driving those long-term outcomes. There was indeed an impact on behavior change on those personal motivational factors that made a difference in their long-term physical functioning.

Next, I want to sort of highlight some empiric evidence related to the influence of environmental factors on these outcomes. I think that if we all pause for a minute and think about what we're experiencing with this pandemic, I think many of us have anecdotal experience of older individuals who, when they were under the conditions of lockdown, we were able to observe that their physical functioning, and maybe cognitive functioning as well, declined because of the lack of social engagement that occurred.

Prior to the pandemic, we conducted a study in Boston RISE. We were looking at an established relationship between cognitive impairment, in this case mild cognitive impairment, and falls. It was pretty well established that that was a predictor of falls; that mild kind of impairment was associated with a higher rate of falls than people that didn't have mild cognitive impairment. We looked at this in terms of the level of social engagement. When we looked at people with low social engagement, we saw that this relationship held, but when we looked at people with high social engagement, we saw that it was actually protected. Now, this was a cross-sectional study amongst a relatively small sample, and so it's hard to really generalize this more broadly; but it really begins to highlight the power of social engagement in predicting adverse health outcomes, such as falls. In separate analyses, we also saw this as well with regard to mobility overall.

I also want to highlight other work that's done by a colleague at Brigham and Women's Hospital, Amar Dhand, who's a neurologist. He's particularly interested in social networks, and the structure of social networks, and the impact on outcomes. In this case, he's specifically looking at stroke outcomes. What he was able to show in this paper in *Frontiers in Neurology*, which was published relatively recently, was that aspects or important characteristics of the social network of the participants were actually

predictive of patient-reported functioning after completion of stroke rehab—this is the Fugl-Meyer walk time, again, walking speed—and even scores of depression. So again, showing this relationship between the impact of social engagement, and social networks, and functional outcomes. I hope with this walk through some of the empirical evidence, it shows that the ICF model is not just conceptually based but actually empirically based as well.

I told you about the scenario of this woman crossing the street. The next issue is, how should we think about care for an older individual such as this? When we think about care in general, about value in care, there's a big focus on what matters most to patients. It's been actually defined that value in health care, in this article by Porter and Lee, is based on health outcomes achieved that matter most patients relative to the cost of achieving those outcomes; that represents value.

But then we looked at older adults, and we asked them, what matters most to you? There's many different things, but predominantly one of the biggest priorities for older adults seeking care with their primary care physician is actually maintaining functional independence. Function is actually a major goal of older adults and maintaining independence.

One of the other challenges that faces the world of geriatric care and this growing segment of older adults is how do we position health care systems to best serve older adults? One thing that the geriatric field has reflected on and recognize is that there will never be enough geriatricians to care for all of these older adults. So, they've been very active—and this is a photo of Mary Tinetti who is a leader with this initiative—where they've said, how can we train health care systems and health care providers to think like geriatricians when they're caring for their older patients? How can we get them to think of them in the same way? What's the lens that they can look through? They talk about the 4 M's. They talk about mentation, focus on cognition and mood; they talk about mobility, physical functioning, which we've talked a lot about; they talk about medications, be it too many medications or choosing the wrong medications for a given condition that put older adults at risk; and they also talk about what matters most as being really critical factors. This is being implemented nationally and a focus on each one of these M's has been shown to improve the quality of care for older adults; they're really advocating a focus on all four M's.

That's the age-friendly health care systems approach and that's geriatric care, but if we're going to think about geriatric rehabilitative care, we do focus on a lot on these four attributes to varying degrees; for sure we do. But we also focus on motivation. We think about motivation and behavior change, which I alluded to, but one of the first things that I was taught as a young physiatrist was first evaluating a patient's capacity to learn. Because so much of rehab relies on that capacity to learn, and be it practicing good nutrition or practicing any sort of preventative care paradigm, it's critical that the person is motivated to carry out those new behaviors. And so, you could think of it as one M for every finger of the hand.

Now I'm going to touch a little bit on how we've been focusing on designing rehabilitative care in order to position it as a model of preventative care for older adults in VA. One thing that we did was, we first said gait speed needs to be a vital sign. These are data from an early-stage clinical demonstration project that we did within a couple of primary care practices where we looked at older veterans that are 65 years and older. We measured their gait speed on their way to walking to the scale to get their height and weight checked. What we found was that 25% of them had a gait speed that was 0.8 m/s or slower, which is considered a threshold of high risk and one that's worthy of treatment in the literature. In fact,



the literature's even described 1 m/s, and that's probably 50% of the older veterans that we screened. This is one way that you can actually use gait speed to help pick how big a net you want to cast with your various preventative care paradigm.

Clearly, it was a prevalent problem and a concern for a large number of aging veterans in our health care system. So, we've developed the Live Long Walk Strong program. It was first developed before I moved back to the VA in 2016. It was started when I was primarily working at Spaulding Rehabilitation Hospital. What it's designed about is to reposition physical therapists to more optimally serve an individual that would be referred because they had a gait speed that was 0.8 m/s or lower.

The three components are: to focus on those core physiologic impairments that I highlighted, that we identified as being putting people at risk for decline; a focus on coaching and behavior change in order to optimize long-term improvements in order to engage people in the functional activities and be able to enable them to better participate in their life role; and then also case management, not only working with the primary care providers but also working with community-based programs to further reinforce engagement and participation in activities.

This is data from the initial clinical demonstration project that we did at Spaulding Rehabilitation Hospital. In total, we actually did over 400 individuals, but this is the data that we actually published; we had 363 referrals. These were people that had mobility problems, and this was referral for an outpatient physical therapy program of about 10 to 12 visits. It's understandable that 40% could not enroll because they had mobility problems themselves. We'll talk a little bit more about how we address their concerns.

What we found is that of those majority that actually enrolled in the program, over three-quarters completed the full program of care and about 25% partially completed the program of care with the program being interrupted due to health issues or other issues that it would occur.

This is the outcomes. If you look at this figure on the right, the gray area is representative of scores on the short physical performance battery, if you go from left to right in that little plot there, you see that 1-unit change is considered a very large, clinically meaningful difference in the short physical performance battery and, at the very bottom of the list, the bottom row shows the adjusted change that we observed among people undergoing Live Long Walk Strong. It was about 1.7 units, so this exceeded a large, clinically meaningful difference. But then we also analyzed to look at what are factors that could potentially mitigate improvement or engagement with rehabilitation to see how they influence the outcomes, because we designed the program to navigate and overcome those barriers—that could be advanced age, could be a history of falls, could be the manifestation of dementia, could be significant pain, or it could just be their stage of exercise changed their readiness to engage in exercise. What we found was that regardless of any of those factors, we still exceeded clinically meaningful differences when we looked at these factors individually so that we still were addressing the goals of our program overall, that even accounting for these potentially mitigating factors that we were creating improvements in physical functioning at the end of 3 months of care.

I mentioned the 40% that never engaged. That creates a challenge that we've been forced to address in COVID, but before COVID, we were very interested in looking at models or potential hybrid models of telehealth. What we did was, we were interested in an approach to care where we would take those physical therapy visits and make them more user friendly by reducing them down to six visits and giving the participant a choice, either have that at home or have that in an outpatient setting. We also gave

them an iPad tablet, where on the tablet was a video of the person doing their exercises, and they had prompts reminding them of their corresponding exercises. There was also a chat feature that allowed them to interact with their physical therapist. Treatment went on for 6 months that way, and then there were 3 more months when they could use the chat feature to further communicate with their therapist. At the end of 1 year, we evaluated outcomes. The comparison group was actually the Boston RISE study, those patients that were in that longitudinal cohort study, and the 75 people in the treatment groups were recruited in the exact same way as the cohort study, but they were actually treated.

What we found was that we actually had quite good adherence among participants really over the whole year but, in particular, there was a drop off after that 10-to-12-month period. When the chat feature was removed, adherence certainly dropped. But we saw good adherence where they were participating in their exercise program twice a week with over 60% over the course of the full year.

When we looked at our outcomes in mobility performance at the end of 1 year, we saw significant and clinically meaningful improvements in both gait speed and the short physical performance battery.

But what was also very exciting was that, we weren't we weren't planning to power our study to address these outcomes, but we saw a 73% reduction in the rate of emergency room visits among people that were treated compared to those that were in controls. Hospitalizations, we were not powered to evaluate that as an outcome, but what we did see was that the effect size was in the hypothesized direction; and so it really highlights that there's an opportunity to do more work in this area, with the potential of this approach to care.

What we've done since then, and have been influenced a bit by COVID as well, is that we've now adapted our Live Long Walk Strong program to subacute care and VA, which is a major focus of care in VA and outside of the VA, as I mentioned before. We've adapted the program to treat patients during the inpatient stay and then to also have a series of follow-up visits over 4 weeks, once their transitioned to home care.

If we look at the components of our treatment, the coaching and behavior change occurs in all of those visits across the board. The focus on physiologic impairments is more heavily weighted during their inpatient stay, and the focus on case management is more focused in the latter stages.

There were delays in the implementation of this clinical demonstration project because of COVID, but some of the early findings that we found is that at the end of the stay within—the CLC is really the sniff, this subacute nursing setting—we saw that the level of improvement in physical functioning, which is measured by the AM-PAC in this case, exceeded clinically meaningful differences and that also those differences are still observed 3 months after they're discharged from the subacute care setting. However, if we look at the magnitude of improvement that occurs once they're discharged from the subacute setting, it's really negligent, it's really minimal, and so there's really an opportunity for us to address this in a better way in the future.

What I really would like to conclude with is that hopefully I've highlighted for you how we could think about older individuals, how we can recognize how measures of function and frailty are highly related and are able to identify individuals at risk, how we might use the ICF model as a way of conceptualizing treatments, and how if we think about geriatric rehabilitative care and geriatric preventative care we want to think about the five M's as well.

Thank you very much.

**Amy Houtrow:** That was just remarkable, Thank you so much, Dr Bean.

I would like to ask a couple of questions, and I think there may be some in the audience as well. Let's take Gerold—Dr Stucki, do you want to start us out?

**Gerold Stucki:** If you allow me so. I'm really excited about this presentation. Congratulations, you really have demonstrated that using the ICF conceptual framework may help us to structure research not only contextually but also empirically; so it goes both ways, and also the structure that it invites.

I think this was a model presentation that should be given to many other communities that are caring for other populations, maybe not 80 but, any other populations. You could basically use your approach as a model, so I really congratulate you and thank you for showing this.

I have one comment and one question, if you allow. My comment was that you very clearly pointed out the problem of distinguishing what is for the functions, and if you go for the capacity, and we should not conflate it necessarily with measures that go into people's performance in their real lives because one is the outcome and one is a predictor in, for example, in outcomes research. One way to overcome that would be to basically consider capacity versus performance in an activity that can really distinguish measures of a person's capacity for a daily activity versus what they actually do.

My question, then, is frailty versus functioning—isn't frailty some another animal in the sense that frailty is more close to a syndrome at the...? I mean, you put together an arrange of things—it's not a health condition, it's not a disease—but it's something close to what the health condition may entail. How do you capture it through your approach of assessing a person's function, capacity, interaction with environment? Frailty and functioning—more health condition versus how you're assessing?

**Jonathan Bean:** Thank you, I really appreciate your comments and, obviously, your seminal leadership with the ICF model in general.

We do use measures that I believe you would call "capacity measures" in terms of patient-reported measures of functioning. We use those a lot. I just was limited in my ability with a presentation to show all the different types of work that we're doing. We do rely on that a lot. The AM-PAC is a measure that we use quite frequently in that regard; we've used the late-life function disability instrument.

There's a lot of debate. I work with a lot of geriatricians, some of whom are very active in frailty. There is a tension that we have within our conversations, a friendly tension. Some of us would like to distinguish frailty from disability or frailty from measures of physical functioning, but I'm starting to sort of move in their direction in a sense of saying that frailty for older individuals represents a state of vulnerability to stressors; that's a really critical thing that we need to evaluate and consider as we're planning out our treatment paradigm.

If you have someone who's a 20-year-old who maybe grew up with CP, it may not hold that their gait speed is going to be predictive of how well they're going to do if they undergo surgery or whatever. Amy can speak to that much better than I can. But, I think that for older adults, those relationships hold pretty true. There is a significant amount of overlap, but I think that when I try to work with my geriatric and gerontology colleagues, it is to understand the nuanced differences between impairment, limitation, and restrictions, because you can't call them equivocal.

The other thing that I will say that we really focus on is that this is very much based on—I know John Whyte's on the call— notions of enablement theory in terms of treatment. We also have done specific work looking at targeting those specific impairments, showing that we have a treatment that can address those impairments, and that also that can then directly impact functioning as well.

**Gerold Stucki:** Thank you.

**Amy Houtrow:** I would like to ask Lynn to the mic so that she can ask her question.

**Lynn Gerber:** Thank you. Jonathan, a wonderful presentation and lots of suggestions for research going forward.

We think of ourselves as specialists across the lifespan, and prevention is in our DNA or our mRNA; because it is, I wonder when prevention starts. There was a very interesting slide that you presented in which the group that was between age 65 and 74 had the greatest improvement with your intervention compared to the older population, which isn't always the case with respect to an impairment improvement. I think that's really, really critical. Are the risk factors universal? So if my gait speed starts falling off at age 50 as opposed to 95 or whatever, do I use that as the step-in for engaging in a more preventive or early interventive strategy? Thank you.

**Jonathan Bean:** Thank you for that question, and that's exactly what we're doing in VA. One thing that has been recognized with veterans is that if you age-match veterans, they're more functionally limited and more impaired than their civilian counterparts. A lot of that may have to do with not only their exposure to maybe injuries in the military and so forth but also that it's recognized trauma from their military experience and also other social and behavioral factors that preceded their military experience. Regardless it's recognized. With some of the clinical trials that we're doing, we're actually starting to look at individuals that are 55 years and older, and so I qualify for my own studies by age.

Also, there's some really nice data from researchers at the University of Indiana where they've actually looked at more less-privileged parts of Indianapolis, and they looked at people in their 40s. What they found was that the SPPB still helped just to cut points that were a little bit different, but if you looked at them from a population standpoint and you developed cut points, you still saw the same risks.

I do think that these higher-risk populations, these relationships, still hold. You may have to adjust your cut points.

**Lynn Gerber:** That is so critical for issues of health disparities and for other important social factors, which tend to be looked at in the participation rather than in the impairment or in the performance metrics. We may have to shift our thinking a bit to accommodate for that. I think this is a really important point.

Thank you very much.

**Amy Houtrow:** Well, Jonathan, you said his name, John Whyte, and then he raised his hand. So, John, you want to come on?

**John Whyte:** Thanks, Jonathan, excellent. I agree that your presentation was excellent along with everyone else.

You sort of alluded to this, but it seems like gait speed, for example, is a good indicator to some degree, because it catches variants from a lot of potential impairment sources. The analogy to the orchestra—we know the orchestra sounds bad, but they're still going to be the question of intervention; which section has to practice harder.

Presumably we don't just practice people walking faster and that will solve everyone's problems, so one strategy involves sort of trying to unpack the impairments that lead to this particular person walking slowly or failing—whatever screening it is—and now this one is going to get strength, or this one's going to get cardiorespiratory training, or what have you. Given also the relationship to more participation things, another possible way to go, is the notion that greater activity involves walking faster and breathing more, so that the macro-intervention may, perhaps somewhat dumbly, address a bunch of different underlying impairments at the same time.

Do you have any guidance about how to go from screening to thinking about what the specific interventions need to be more?

**Jonathan Bean:** I can give you a couple examples that reinforce your question.

Linda Fried, who has done amazing work over the course of her career, led this program in the city of Baltimore called Experience Corps. What they focused on was less affluent individuals living in the city of Baltimore and maybe economically disadvantaged in other ways. What they did was they actually engaged them in a program of volunteering in schools. Embedded in it was a physical activity program.

What they ended up finding was that indeed their mobility overall improved, even though it wasn't the primary focus of what they were doing because they had to get up, get dressed, get moving, get the bus, go down the stairs, fill in the blanks. So, you're absolutely right.

However, within those programs, when you look at some certain aspects of physical functioning, they may not have as significant improvements across the blend of physical functions; so that's one issue. The other is another study. There's a famous study that really focused on the prevention of cognitive decline

that was done in Finland. It was called The Finger Study, and they did a multifaceted treatment where they looked at engagement, activity, nutrition, exercise, and so forth. They were able to improve cognition or show blunting of cognitive decline, but what they didn't show was improvements in physical functioning because they weren't really prioritizing it and targeting it. I think there's some combination of that.

What we've tried to do with our program of care is use it as a sort of jumpstart for people that are at risk to get them to a certain level, and then it's really kind of up to them. They may do a very impairment-specific exercise program that they like, or they may end up, rather, going to a sewing class they have to travel to and do that. That's where the "what matters most" comes in. We'll try to tailor—that's the sort of case-management component where we go long-term with them to meet their needs and what matters most to them.

**Amy Houtrow:** We have time for one more question. I see George has his hand up. Do you want to jump in and ask your question?

**George Alleyne:** Thanks very much. I'm very conscious at my age, very conscious of this concept of frailty. So the question I have is, you speak about those who are already old or near to being old. What is the message you're going to give to the young to stop them from reaching that stage? I think through the life course, what method, what messages are you going to give to the young to stop them from needing your treatment?

**Jonathan Bean:** I think that it's about practicing healthy behaviors. I don't really work with... When you say you, me personally, we're very focused on geriatric care and so forth, so I'm not really working with that population. But for primary care providers, it would be about eating well, drinking in moderation, all the sort of healthy behaviors that we would want while maintaining physical activity as well.

It would be those sorts of preventative approaches that are well recognized at helping people to maintain their function and independence and health.

**George Alleyne:** So just a general nostrum and nothing specific, you're suggesting.

**Jonathan Bean:** I'm not saying anything specific with regard to that, with respect to frailty.

**Amy Houtrow:** That was great. Thank you, Jonathan. There's one more question in the chat, which I am hoping you'll be able to answer quickly in the chat as we move on to our next presenter.

I have the distinct pleasure of introducing Dr Jürgen Bauer, who comes to us today from the Center for Geriatric Medicine and the Network for Aging Research at Heidelberg University in Germany. Here's a bit

of trivia for you: Heidelberg University is Germany's oldest university and was founded, you know, just yesterday in 1386.

We're really lucky to have Dr Bauer. He is an internationally respected leader in geriatrics. In September of 2016 he assumed the newly established Chair for Geriatric Medicine at his institution and prior to that that had served as the Director for Geriatric Medicine.

His record of service to national and international medical societies is really more than laudable. I'll share just a couple of examples. From 2007 to 2015 he served as a member of the Executive Board of the European Geriatric Medicine Society; he's currently a member of its academic board and served as President in 2018. He's also served as the President of the German Society for Geriatric Medicine and was awarded that society's honorary prize in 2007. And if he wasn't busy enough, since 2015 Dr Bauer has been a member of the Committee for Scientific Advisors for the International Osteoporosis Foundation.

As the title of his presentation alludes to, Dr Bauer's research focuses on nutrition and exercise in older persons. In the past 3 years alone, he has published 74 peer-reviewed manuscripts on these topics. We are just incredibly honored to have him here today to share his wisdom.

After his talk, we'll take questions either by raising your hand and engaging in dialogue or by putting your questions in the chat during or after his presentation.

Thank you, Dr Bauer, for joining us for this session.

**Jürgen Bauer:** Thank you very much for this very kind introduction. I really feel honored to give a presentation to you tonight. Let me know whether you can see the slides properly, and also the change of the slides. Is it changing for you? Thank you very much.

Yes, I think Jonathan has really prepared the ground for me where I can easily start from. As you all know, aging is a universal phenomenon. You see here on the left side, in 2015 the countries that had a percentage of about 30% of 60 years and older—it's only Japan—and this will move up until 2050 in many more countries. I would like to let you know that Germany is one of the fastest aging societies in the world, so we're really concerned about the demographic shift, about the social implications, etc.

It's very difficult not to talk about COVID if you give a talk these days. This is a very recent publication from the *International Journal of Epidemiology*. We're talking about longevity and its implications. What you can see here—let's focus on the age 60 group—that during the period between 2015 and 2019, you see this on right side, in nearly all Western countries there is a prolonging of life; there was longer lifespan.

And then, considering the change in 2020 with different relevance and different amount of losing lifespan is COVID, so the pandemic really set us back several years. It will take quite long time to achieve the longevity prognosis again that we've lost during the last, let's say, 18 months. There was a relevant decrease of lifespan in the older population above age 60, and there is, as you all know this has been addressed before, there's a worsening physical conditioning in the older population between 50 and 80 like shown here, based on a representative online survey of 2,006 US adults. This is also causing worsening mobility. This as a consequence causes more falls. What we are concerned about is that we

already have an aging phenomenon which really will stress society with regard to long-term nursing care, for example. We already have a shortage of those kinds of nurses in our country. The numbers will go up steeply, and the pandemic has done this even worse.

What we're not focusing on now as geriatricians, it's not lifespan anymore. We are focusing on functional optimal span, or best span, or health span; that's what we are addressing. Olshansky in 2018 addressed this issue that society has to be concerned much more with health span than on lifespan.

With regard to functionality and independence, the older individual is vulnerable. You've seen it before. Frailty is, like Jonathan said, it's a concept of vulnerability; I think it's an equivalent of biological age and originally has been multidimensional. The physical frailty is only part of the larger concept of frailty. Frailty is integrating a lot of influences. I think it's a difficult concept with regard to functioning because it's nearly going beyond that, but this would be a separate discussion. I cannot go there, of course.

We as geriatricians want to keep those older people as long as possible physically active independent, but this independency is threatened by the interaction between sarcopenia and, we'll address this later on, frailty. All of it is connected somehow; that's one of the problems of aging. You never meet, or hardly ever meet a condition on its own; it's all interconnected. This makes things sometimes very complicated, and there's sometimes not an easy solution towards keeping people independent.

I also have to focus somehow with regard to scientific evidence. I will leave out cognition, because cognition, like we've heard before, is also highly relevant for keeping older people functionally active. I want to focus very much on mobility, giving us some kind of additional perspective on the training we've just heard before.

What is the background? Let's start very easy. It's body composition change. If you look at large statistics, you see you have a plateau of weight around about age 50 to 70 and then you have, on average, you have a slow degrees of about 450 gram in males and about 200 gram in females with regard to body weight; you see this here. It's quite an old slide, but it's still relevant; no change there. Unfortunately, these 450 or 200 grams in a rather healthy population is caused by a decline of fat-free mass, which is mostly muscle. In parallel, the fatness like you see below here in yellow, it goes up. We have this proportionate effect between muscle mass and fatness.

This is illustrated by the slide on the left side. You have in about a 25-year-old a CT cut through the thigh muscle, and you see on the right side, you see the change with age 80. You see much more fat subcutaneously and intracellular in the sector; so much more fat, less muscle. This is a difference of about 40%, and that's a background we're talking about.

If we want to talk about interventions, and we have to consider this is a lifelong perspective. It's really important how far you've trained when we're young, how active you've been up there, how your maximum was—maximum muscle, maximal peak bone mass—you have to set your level high up, because then, most probably, it's a very individual progress. If you raise your maximums, then you have more to rely on when the this goes down with old age. The muscle mass goes down, but of course, also strength goes down.

It goes down in everybody that you start from a different level, and if you're lucky enough, and this has been shown in the last slide, you don't reach the level of disability. This is true for the upper extremities, which you see on the lower half of graph, and it's true for the lower extremity for both genders like you



see in the upper part of this slide. Loss of muscle mass and loss of strength is the concept here that we have to tackle if we want to keep people active, functioning, and mobile in old age.

I think a concept, which is also overlapping with frailty, and I personally think frailty is more a risk assessment like said before, if you really want to focus on function, I think the sarcopenia concept is maybe more suitable in many regards, because it's much closer related to muscle function. Gait is a complicated thing; there is a lot of neurological input with regard to gait speed, so if you stick with muscle, sometimes things get a little bit easier.

Sarcopenia means a combination of the muscle mass, low muscle mass, lower than average muscle in an older population; it's part of the older population and the combination with a muscle strength-of-function parameter that is mostly directly connected to the muscle.

It's a complex etiology, of course, if you look at sarcopenia. What I want to stress here, and then we really move right into the main topic of this talk, which is nutrition. It's not nutrition only, but nutrition—it's a much more important player in the older population than in the younger population. We talk a lot about obesity, about malnutrition in young individuals, in patients with chronic disease, that's true. But we have vulnerability in the older individual. This vulnerability is about reduced reserves, which is reflected in the change of body composition like I've showed you before. You have to keep your reserves as long as you can, and if you lose reserves, you have earlier functional impairment if you lose muscle mass. That's a complete change if you look at younger population, not the most serious ill, like people on hemodialysis you see accelerated aging in this patient group but that's not in general. You find this vulnerability with old age, so you have to keep a really close eye on the nutritional factors if you want to keep your older individual functionally active.

It's not about malnutrition only that's very closely related to a decline in muscle, and function, and strength, but it's also very important for prevention. If you want to be on the upper level of functioning, you have to check nutrition for a long period, and you have to follow preventive rules.

This slide shows you this interrelation between comorbidities, immobilization, medication, which is also highly relevant for appetite. Appetite gets more vulnerable in the older individual. You have vulnerability with regard to reserves, but you also have less appetite. This is more often impaired by medication, by immobilization so you really meet somehow a difficult condition always at risk of losing appetite, always at risk of losing weight, which is a characteristic of the older individual, let's say beyond age 75 or 80. You have to get a clear understanding that nutrition is highly relevant in this patient population, also in the nonpatient/pre-patient period of this population, and you have to be more preventive with regard to nutrition than with any other age group. Because you want to keep your reserves. That's what I wanted to illustrate based on some slides that underline the concept of sarcopenia—keeping muscle mass, keeping strength, keeping function in this population.

This is a very famous slide. It shows you the hallmarks of aging. And yes, we are moving closer to a pharmaceutical therapy of aging. You may be aware of the TAME study with metformin, which tackled some of those hallmarks of aging and which wants to stop degenerative age-associated diseases and functional decline. We'll see whether this works. There are other substances that are tested already now, some in animal experiments but some already in human population. We'll see about that. What still is highly relevant to focus on those hallmark processes is, as shown on the left side of the slide is,

exercise, which is the best thing to overcome anabolic resistance of aging, but also diet; and that's what we want to talk about now.

Let's start with prevention. Fortunately, it's not about process. It's about tasty food, it's attractive food, it's Mediterranean diet. There's some molecular work, there's some clinical work that Mediterranean diet has a lot of qualities that tackles the aging processes like the oxidation, the chronic low-grade inflammation, which is relevant for mass loss and all the population, maybe a favorable acid–base load, which is also helpful, and by these mechanisms, it may reduce the muscle loss and may reduce the deterioration of muscle function. That's the content, but does this work?

There has been a study already published in 2011 by Luigi Ferrucci among others, you will be very much aware of him; he's the director of National Institute of Aging in Baltimore. They could show, and you already are aware of the SPPB, they had, if you followed strictly at, if you adhered strictly to the Mediterranean diet, in an Italian population in the InChianti study, there is really a rather well-performing population in in Tuscany around Carrara, which is the King County region, and they could show, for one, that you have a higher SPPB score if you have a higher adherence during the study's 9-year follow-up. Even more importantly, if you have a high adherence, your risk of mobility disability is significantly reduced by around 50% during the 9-year follow-up. This was the first indication that the relevance of following the Mediterranean diet for improved functionality over 9 years' follow-up.

Recently Karlsson published data from Sweden. You don't have to live in Italy to have a protective effect, a preventive effect from the Mediterranean diet. I recently talked to colleagues from Hong Kong, and they also score for Mediterranean diet components there. If you follow, if you have a high adherence they could show, again, with the concept of sarcopenia—a combination of loss of muscle mass and mostly loss of strength—that you have, in 16 years, a 50% reduction of incident sarcopenia in the Swedish population. This goes towards the same observation.

Can you do badly as well? Yes, you can, if you follow The British diet. The British diet, you may be aware of, is not a healthy diet; it's really fatty. You see some components of the British diet on the right side, and I think you can easily understand that this is not a healthy diet. On the on the left side, you'll see DP2 is the traditional British diet and, if you look at baseline at the 3-year prevalence, this is quite highly significant, you have about a 2.6 higher risk of being sarcopenic if you follow a fat-rich diet. In an older population, extremely older population, [[WEBCAST CUTS OUT]].

Can you do something, if you have a lifelong perspective, can you do something if you're middle-aged, if you're 45–50? Lynn also asked me to speak about prevention on not only the older population but midlife. For the 40–50 etc., yes, you can. This is quite a recent publication coming from the US, the Baltimore Longitudinal Study of Aging. They tested diet scores based on this tool, which is mentioned in the title. If you improve your diet based on these categories here, you can get a better result during a long-term follow-up with regard to functionality, based on the SPPB that has been introduced to you by Jonathan.

Underlining the positive effect of a healthy diet, a long-term effect mostly; it's not a short-term effect. If you do prevention towards aging, in my perception, it's longer intervals, big studies, long follow-ups; it's never done quickly. You may be aware of the DO-HEALTH Study, which has been recently published in *JAMA*. They tried to do a lot of preventive measures, and they didn't result in approved functionality. I

think you have to have long intervals, and it's helpful to really go for higher age or for a population at risk.

Summarizing this first part of my talk, I would say, yes, if you go to natural food components, there is a positive effect which is related to food quality. Which is also relevant not to include components of the nutrition that may impair metabolism, may cause inflammation like saturated fatty acids, for example. If you have high-quality foods rich in vitamins and minerals, etc., you get a positive effect with regard to function and, which is also relevant, it's protein. If you have protein-rich foods, this may also stabilize muscle loss in older age; that's the second part I want to talk about.

I want to talk about protein intake and the muscle in the older population. On this slide you see some healthy and less-healthy components. You see beef; you don't serve a T-bone steak now after this talk to your older patients in the hospital. You don't do that; you have other sources.

What's the problem protein? You may be aware of that quite a percentage of older individuals don't have adequate access to good protein sources; that's one part of the story. But there's a phenomenon many, many researchers in the world are now really supporting this concept; it's the concept of anabolic resistance. There's a reduced ability to use the protein that you ingest to build the muscle, to support muscle protein synthesis.

There are also, of course, inflammatory conditions that may cause a greater need for protein. In it, if you have less protein, you have a greater loss of functionality, which concerns the muscle and the bone. Muscle, as you are aware, is your rehabilitation specialist. The interaction between muscle and bone is it's one system, so we have to think about it very closely together. We also see more data coming up that support with regard to bone quality, higher protein intake.

Here you see the problems in the older population with regard to insufficient protein intake. You see about 20% of older individuals don't reach a threshold of 0.8, which is currently still the WHO recommendation. If you want to have an optimal protein intake in an older, possibly distressed population, you should move it up to at least 1.0; this percentage increases up to 40%–45%.

Is this based on science? Is there enough evidence? This is still discussed, especially in the US, but there are data from the US, like the first study from Houston, which has been highly relevant for the field. This study showed that if you are in the lowest quintile of protein intake, in a large population this has been served during a 3-year follow-up, you have a higher decline of muscle mass; if you are in the top quintile with regard to protein, you have 40% less muscle loss in the same population.

This is muscle and function. It's a difficult issue regarding methods. We want to assess muscle mass is not the whole story, because there's not a close relationship between muscle mass, loss of muscle mass, and loss of function. Therefore, it's very important to support these data that loss of muscle mass is less with higher protein take, with functional data. This has been done by the same group published in 2017, and they could show that with higher protein intake you have less incidence of mobility limitations. You're better off with regard to gait speed, strength, if you have a higher protein intake, possibly always beyond 1 gram of protein per kilogram of body weight.

This has also been shown in clinical populations that are also part of the rehab setting or rehab population, for example in a population with knee osteoarthritis. The majority of the subjects with knee osteoarthritis had a protein intake that was lower than the recommended daily allowance. Lower

protein intake, again, was associated with lower upper leg strength. The preventive effect of higher protein intake was underlined once more.

Like I told you before, there's the concept of anabolic resistance with aging. This can possibly be overcome by higher protein intake, but it will certainly be overcome by exercise. This is mostly strength training, where it should get could be shown to be most efficient. Some molecular data supporting this concept: If you want to reach the maximum plateau of muscle protein synthesis, it's a different threshold if you compare younger men with older men. If you are older, you move right on the scale, you have to invest more in protein to reach these plateaus, and this is underlining the concept of anabolic resistance for the older population.

Our expert group started in about 2013 to ask for a higher protein intake for the older population as a preventive measure against muscle loss and loss of muscle strength in the older population. We called this "optimal protein intake," because it's not on the same level like protein allowances. We know in the population that is getting older and older on average, we have a higher risk of functional decline with older age, and we want to counteract this development by increasing protein intake like shown before. There are much more data out there, which are unfortunately mostly observational. There are not that many intervention studies that focus on milk protein, for example, unfortunately. But if you raise the protein intake, you can expect positive effects. If you have overt sarcopenia or frailty, if you are beyond the rescue, if you're affected by these geriatric syndromes like we call them, then a high protein intake up to 1.4 gram per kilogram body weight per day is recommended, but be aware, don't go far beyond that. If you increase protein intake beyond 1.4, you might have a negative effect on appetite. If you have an [[WEBCAST CUTS OUT]] by the protein, you may have a problem with the overall caloric intake. Because the caloric intake in the older population is always the first target you have to meet. You always have to meet the adequate caloric intake, and only the next step is the adequate or optimal protein intake. So never forget about this. If you go up too steeply in an older individual with protein intake, you might have a negative effect on the caloric intake and this might overcome the positive effect of the higher protein intake. That's very, very important to have a really differentiated view on the macronutrients that are indicated for at-risk older populations.

In most Western societies, you have the highest protein intake during the evening. You have a very skewed balance of protein intake of the day. Many researchers at the moment think that this should be more balanced. The perfect intervention would be if you pass over the plateau that I've shown you before for muscle protein synthesis. During several meals during the day—which would be breakfast, which would be lunch, and which would be dinner. One main target could be to increase protein intake at breakfast because, this is shown here, it's usually, the lowest protein intake of the day is during breakfast. Maybe this can be a target. This has been shown already in several studies that you can raise the overall protein intake over the day, the summation of the protein intake, if you target breakfast.

Another thing in the context of prevention and possibly therapy is vitamin D. This has been something which was a hype, we have to say. We didn't expect a lot of effects from vitamin D, we did expect that vitamin D, based on the current evidence, didn't meet the expected. What we can say now, the effects of vitamin D supplementations are very, very minor and obviously, with regard to strength, muscle strength, there is some effect, small effect, only if real vitamin deficiency is present. In this population, you might see an effect. But you don't see it if you're already beyond that; if you have a normal level of

vitamin D, there is no linear correlation between strength effect and vitamin D levels. This has been a failure, and this has been the wrong expectation, and this was not met.

This is very clearly, now shown, this is a very, very good study done by Shea, done in men and women beyond age 60. They had rather low vitamin D levels; it was easily shown that you can raise the vitamin D by 800 IU/d. But there was no effect if you go from low to high in this study on any strength of functional parameters. Vitamin D is part of a healthy diet, and of course we have a higher risk of vitamin D deficiency, which clearly should be corrected, but there's no justified expectation that high vitamin D supplementation is justified by the effect on the muscle mass of function.

Something else that we've shown (sorry for this mix-up), that obviously it's helpful for increasing the effect of protein to counteract a vitamin deficiency. If you have a protein intake, high protein intake, this is helpful for muscle protein synthesis if you correct, first, vitamin D deficiency.

(Sorry for this.) This is again very important, just underlining this. I told you before, this is the DO-HEALTH study, which was coordinated by Bischoff-Ferrari from Syria, and she did several interventions in quite a large data set. I think a quite difficult study design, multinational study, and they did vitamin D supplementation, omega-3 fatty acid supplementation, strength training exercise, but they could show no effects, no effects on function, SPPB, again, no effect on cognition, no effects on fractures, no effect on infection, no effect on blood pressure. This was rather untargeted. If you do intervention studies, most probably, it's good to focus on real address population. This population was quite heterogeneous and, unfortunately, this was very disappointing.

Coming back once more, and then finishing this part of the talk. Vitamin D supplementation—how much? Don't go beyond 2000 we now recommend 800 IU to 1,000 IU a day, and this would be safe. If you start to correct a deficiency, probably after hip fracture, you start at maybe 2000 IU for 4 weeks or 8 weeks, then go back to 800–1,000, but don't keep up the high doses for longer periods. Don't do positive vitamin D shots every 3 months or 6 months; there are several studies showing that you increase the falls rate in this population if you do 3 months or 6 months shots of high vitamin D doses. I think that's a very important message, because obviously, it might counteract the rehabilitation efforts.

Can you do more? Can you have the best protein possibly and get a stronger effect on the muscle? Yes, obviously you may if you target the right population. We are not talking about prevention, nor are we talking about the sarcopenia population. Leucine is a high volta amino acid that acts as a *katalysator*, we say in Germany, *katalysator* [catalyst], maybe it's the same word in English—I hope so—it strengthens the effect of the other proteins that are ingested in parallel with leucine. You don't give leucine on its own; you always combine it with other proteins. It always has to be a mix. If we have a high-leucine supplement, a whey protein for example, then you get, possibly, the best effect. It's easily digestible; you get a strong effect, a very quick effect on muscle protein synthesis. What we could show in a rather large study with about 400 participants, all with a worse sarcopenia on the European Sarcopenia Criteria, we could show a positive effect on muscle and a positive effect on the chair-rise test. Simply by this supplement, which is something which is not a routine, of course, in a sarcopenia population because, always, training is the key intervention. And usually it's strengthening as a basic requirement in this population. Don't forget, you have sarcopenia patients that cannot train because they don't have access; some of our patients that have pelvic fractures and sarcopenic hip fractures, being sarcopenic they start rehabilitation. We can discuss this later on, but it takes a while until they reach a plateau of the strength training, of the mobility, of the flexibility training, etc., that stabilizes the muscles. We are

not allowed to underestimate the negative effects of the early postoperative phase in patients with hip fracture and in all those patients that are pain-associated or immobilized after pelvic fractures. I think this can be an indication, not only for high protein but possibly for supplementation with leucine.

Coming back to what I said before. We do it in a in a post hoc analysis of our study, we saw that those patients that had a larger increase of muscle mass that started with a higher vitamin D level, that were not deficient. Therefore, we think it's good to correct the vitamin D deficiency if present and combine it then with protein. You get a better effect on muscle protein synthesis, which results in a higher muscle mass.

Is this our study only? Unfortunately not. We definitely did the largest study, but other researchers contributed to this field. They could show that if you combine high-quality protein with vitamin D, you get a, in this recently published meta-analysis, you get a positive effect on handgrip strength and also a positive effect on sit-to-stand time. But you don't get a significantly positive effect on walking speed. Again, walking speed is a complicated issue. That's why it's such a good indication of risk, because there are more systems going into the parameter than only the muscle. Even a stand-up performance is not only the muscle, of course, but obviously gait is even a more complicated, functional process than a stand-up mechanism is. At least, that's our concept. We can discuss this later on.

What we should be aware of is that also in geriatrics, like malnutrition, which is multi-etiological, it interferes directly with sarcopenia and vice versa—from two sides. It's not only malnutrition causing sarcopenia, but it's also that if you have difficulty climbing stairs you have a higher incidence of malnutrition, because you have less appetite, you have problems to access better nutrition, etc. So it goes in two ways, and this may of course cause a vicious cycle.

Well, very briefly, it's not only the US; it's also Germany. I show you some really bad data on obesity and old age in Germany. You see here for women and men, you see we move up beyond 30% in the age group of 70 and 79, and that's very, very unfortunate. Because if we look at a long-term observational study coming from Finland, then of course obesity in age 50, 60 is causing frailty, pre-frailty in later life. Obesity may be another challenge to society in an aging society. If we are not training early in life, if you are not keeping physically active, then this really may cause serious problems. This also is a trick of disability in old age, like shown here—high BMI having a higher percentage and a higher risk of a lower activities of daily living.

The worst thing is maybe if we have obesity in combination with sarcopenia but, unfortunately, there have been no agreed definitions of this geriatric syndrome sarcopenic obesity, the combination of sarcopenia and obesity. Those two conditions shouldn't combine, because they have really bad outcomes. They have, also, higher fracture rates; that's what has been shown. At the moment, international experts group still work on definitions and are trying to agree on diagnostic criteria for this special condition.

What can be said today is that obesity is impairing physical performance in the older population, causes more frailty during long-term follow-up studies, decreases quality of lives, and increases dependency. We have to keep our eye on malnutrition. Clearly, we have to focus on sarcopenia, we have to be aware of obesity and, very often, we have a mix of it all, and that makes things, very often, very difficult.

As you are definitely aware of, the best remedy, the best trunk against the aging process is physical activity. It has been shown in a large number of experimental studies that this really tackles quite some hallmarks of aging. What we can see is that you have to change, possibly. You weigh how you train when you get older and that's—I want to state this briefly—if we want to tackle sarcopenia, the muscle loss, if you have the muscle still as one outcome parameter, you have to do resistance exercise because aerobic exercise and flexibility training does not increase the muscle like shown here. Skeletal muscle doesn't increase with these. So if you want to really go for the muscle, for the strength, you have to do resistance training. This has to shift between age 50, 60, and 70 towards the older population 80. You have to change, possibly, the percentage that you want to invest in this population, and you have to increase the percentage that you invest into resistance training when compared to aerobic exercise.

Coming to an end. Like Jonathan said, it's a combination; you never go for one intervention alone if you want to successfully age. If you want to be a good agent, then you have to combine the physical exercise, the training, you have to combine with nutrition, and with your social interaction.

That's the last study I want to show; I love it. It's about art, life, and death. This study, published in the *BMJ, British Medical Journal*, looked at a 14 years' follow-up of consuming art. It's not making art, which I couldn't do, but I like to consume art. Even if you're very much engaged with art and consuming art, going to galleries or to concerts, you have a higher survival rate. I think that's a good message for finishing this talk.

I want to summarize. The relevance of adequate nutrition for functionality increases dramatically, in my view, with age, because it's a vulnerable population. Positive preventive effects of healthy diets like the Mediterranean diet on muscle mass in muscle function have been documented; of course, we always need more study. Nutrition is never an easy focus of science; it's very complicated because of the interaction of other lifestyle factors with nutrition. An optimal intake of protein is effective in sarcopenia prevention, possibly also in therapy. Vitamin D deficiency has to be corrected, but over supplementation has to be avoided because of possible side effects. Obesity in our populations with less physical activity is a serious threat, especially to those with less education; this comes becomes very prominent in higher age. The concept of successful functional aging has to be multidimensional, cannot be nutrition alone, and it has to incorporate nutrition, physical exercise, and social interaction as equivalent components.

Thank you very much for listening. These are four photographs from a German photographer. It's a book he published. He did photographs in all continents, and all those pictured here and all the people in the book are far beyond age 100. I think these pictures show how quality of life can be retained in an older population. I think it's a positive end of this talk. Thank you very much for listening.

**Amy Houtrow:** Well, thank you, that was absolutely fantastic. You're getting a round of applause, and I see Walter has his hand up to ask the very first question. We have about 10 minutes for questions, so take it away, Walter.

**Walter Frontera:** Thank you very much, fantastic talk. The importance of combining exercise and nutrition, optimal exercise and good nutrition, is clear. I guess I completely believe in that, and you have provided strong support for that idea.

One question that I have here regarding the level of protein intake has to do with a recommended daily intake. You mentioned up to 1.2 or 1.4. My question to you has to do with this idea that people who are physically active may require more than the standard recommendation. How would you recommend evaluating that additional need and providing that additional protein if needed?

**Jürgen Bauer:** Well, I think those that are training well are not the at-risk groups. I think we see these data from Netherlands, for example, we have a lot of countries that are beyond 1.0 regularly. It's the regular intake, especially in milk-drinking countries, is quite high. The problem is much greater, for example in Asia, as the diet is much different originally. I think we wouldn't adapt the recommendation based on the activity level. I think I would target first 1.0 on a more general level, and in the at-risk population during exercise, I would possibly supplement in the rehabilitation period, moving them up to 1.2. I'm not a big fan of any extremes with regard to anything in the older population. I always would start moderate and only be very intense in a very small percentage of this population. That is really suitable for these more sophisticated training, for these higher supplementation, so I would always play it safe.

**Amy Houtrow:** Wonderful. Lynn, do you want to come in and ask your question?

**Lynn Gerber:** Thank you. First of all, thank you so much. I think we think of nutrition and macro- and micronutrients as an afterthought. Just as we condemn our fellow health professionals of just referred to PT, we say refer to nutrition. I think the time has come where there's lots of data that we need to know about.

On that, I actually have two questions. The first one is, can you elaborate a bit on the factors that may contribute to anabolic resistance? Clearly aging and age is one of the biggest, as is activity, but are there physiological and other risk factors that we should be more attuned to and possibly target?

**Jürgen Bauer:** Well, this is the complicated thing. You have different levels; you have the general physiological aging process, and I think the chronic low-grade inflammation that is associated with aging may be a key player here. It's only part of it, and we don't know exactly.

We have some good cohort data on the relevance of chronic low-grade inflammation, but it's, again, only one part of it. Another thing is, we have shifting hormonal levels, and we have low testosterone. Low testosterone is some kind of risk factor for even lower performance level and lower muscle mass. It's definitely low-grade inflammation, it's definitely hormonal factors, and what we've missed on, we have definitely also changes in innervation. But in looking at the neural part of it has been quiet. There was not a lot of research in patient population or sarcopenia population tackling the neural side of it. I think those are only three examples that we're looking into it at the moment.

Another thing, and we have first compounds trying to work on this, is mitochondrial dysfunction. I think that's the current kits on, new kids on the block. I cannot tell you which one is the one we can overcome



and then create patient-relevant effects, but I think we're moving faster now from molecular analysis to where it's meaningful, possibly pharmacological or supplementation intervention. I think this is going much quicker in the years to come than we've seen in the last 10 to 15 years.

**Lynn Gerber:** We are looking at a secondary sarcopenia in our patients with fatty liver and NASH, and we have begun to sort out things like biological groupings of proinflammatory markers, growth factors, so insulin growth factor-1, and myokines CCL-1 and -3, and also looking now, recently, to your point at neuropeptides. What is the role of the chromophant cells and serotonergic systems tryptophan pathway, etc. It's very complicated; I'm with you 100%. But I was thinking you could send me down the right pathway.

**Jürgen Bauer:** I would like to add, I think geriatric medicine, and I think it's a very similar picture in Europe and the US—it's not an easy discipline. It's something like a stigma, I have to say, several reasons for that. Which is now really happening is the concepts of frailty and also sarcopenia is going far beyond geriatric medicine. American Society for the Study of Liver Disease has recent guidelines and recommended screening for malnutrition, sarcopenia, and frailty in all patients with liver cirrhosis.

One example, and it goes towards pulmonology, heart disease—the concept of muscle loss and functionality as a major determinant of the quality of life. That's the story that's entering the general field of medicine. I'm very pleased to learn about this, but I believe, that we have to analyze, someday, the individual key players of the process. We have to see if it's a history or if it's ongoing. And if it's ongoing, this would tackle them, the phenomenon rightly; but we're not there. We're looking there. This may be very complex, but I would love to have sarcopenia biomarkers that would identify the key player of the sarcopenia development.

**Lynn Gerber:** Does it matter if you consume plant or animal protein?

**Jürgen Bauer:** That's a huge story.

**Lynn Gerber:** Sorry. You mean, no yes or no to this?

**Jürgen Bauer:** That's difficult because, in principle, I think data are out there that especially in the younger population, it's equivalent in many respects, on consumed plant or milk protein. But in the older population, there are some data that, obviously some reserves of digestion are not optimal, and they benefit possibly more from the easily accessible animal protein more than from the plant protein. And, the bulk associated with plants can impair appetite, possibly, if you go towards higher plant-associated protein intake in a sarcopenia patient. There's already a vulnerable appetite situation. So

that's why we recommend more milk protein, etc. But that's a problem in India, Thailand, and other Asian countries that are not consuming milk.

**Lynn Gerber:** Thank you, thank you.

**Amy Houtrow:** Well, we just have a couple more minutes, and I'd like to hand over the Mic to Gerold, who will take the last question with you before we wrap up.

**Gerold Stucki:** Thank you very much for clarifying also the vitamin D issue; I think you made it very clear.

In rheumatoid arthritis, we have kind of a similar starting point, creatine supplementation. You can increase muscle mass, you can may even increase muscle strength, but it does not translate into people's functioning. My question is, beyond inflammatory diseases, what do you think—is it worthwhile to look for creatine phosphate in a population, at least to supplement to a normal level? Because what we found is that some people that actually had a lower level could get a bigger level, and maybe that could translate into better functioning.

**Jürgen Bauer:** Well, there's definitely something good in creatine supplementation as well, I think, in this population. Unfortunately, the literature is very scarce on creatine supplementation in the older population. I think, to be honest, that the big studies are driven by the industry and, obviously, the interest is different between the leucine-supplementation concept and the creatine-supplementation concept. Unfortunately, it cannot be said at the moment which kind of supplementation would be the best approach.

In principle, we should not over-expect these effects, especially on a short-term basis. It's not the perfect tool; it's just an add-on tool in a highly at-risk population. That's what I see with the supplementation. And also limit it for maybe 2 to 3 months. It takes a lot of talking to the patient and the caregivers, because otherwise, they just don't take the supplement. We have to limit this subscription to certain patients, definitely. This goes for the creatine and the leucine, etc., as well, in my perception at least.

**Amy Houtrow:** Thank you so much for being here. I'm going to give Lynn the last word as we out close out the session. Thank you very much, and thank you, Jonathan if you're still on as well.

**Lynn Gerber:** Thank you so much to our outstanding speakers. This will be recorded, and we are hoping if everyone is willing, that we can come up with a summary document.

It was absolutely groundbreaking and eye-opening for many of us, even those of us who've been around for a while, so thank you so much to our speakers and an exemplary audience obviously engaged, and

connected, and challenging. We very much appreciate that. We would like to thank you on behalf of the National Academy of Medicine for tuning in today. We hope that you would like to join for the award ceremony, which follows this at 4:00. Your link should get you to that as well for those of you who have registered.

We encourage you to participate in our future interest groups. It will be exciting and interesting going forward—every year, a different topic.

Thank you, again, for your interest in rehabilitation in human function.

Bye bye.