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SEE ALSO: PUBLIC COMMENT AT END OF DAY (4-430 ET) (This document, page 47)

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Great opportunity for us learn about the implications and opportunities from her perspective about educating mount approval. So with that welcome Dr. Mooney, and I'll turn this over to you.

00:15

Thank you. I hope you can hear me. Okay. Okay. Well, thank you for inviting me to your meeting and also for having this opportunity to talk about few of the challenges we have faced over the past several decades really, and in the entire field of clinical trials in cancer. So I do have a slide presentation. I didn't know how that was going to I'm sorry, not being for the first time to your meeting. I didn't know if I had to do something or advance anything. Okay. We see it. Yes. Oh, actually, I clicked on the wrong thing, as usual. Sorry for that. To see it now. I'm gonna stop my video just to make it a little easier. Is that okay? Yeah. And just say next slide. And I'll advance the slides. Okay. All right. So first slide. For some reason, for some reason, Helen, I'm not saying that. I'm not sure why. I'm so sorry. For others seeing the overview slide. Yes, we see it tight.

01:23

I just

01:30

got this done.

01:40

Yeah.

01:43

Okay, I do I do see. Well, I did see it for a minute. I'm so sorry. I'm not sure what I'm doing incorrectly here. But, okay, if we could, actually that that's not the slides perfect. It's sort of in in small font. Doesn't seem to be the full spring. So I don't know if I have to do something.

PART 2

20210719 HHS ADU MTG 02.b

Mon, 7/19 1:42PM • 1:00:01

SUMMARY KEYWORDS

trials, clinical trials, patients, alzheimer, nih, question, oncology, treatment, fda, people, slide, results, approval, benefit, biomarker, conducted, terms, agents, opportunities, regulatory approvals

00:00

Um, if we could just go back one slide to the introductory slide. So when I was con, contacted by Helen and by Melinda Kelly about giving a presentation, part of what they asked me to talk about was the impact of new and emerging changes and standard of care that are brought about by new results from large well conducted, usually randomized phase three trials, and or from regulatory approvals of those trials, and how that affected the clinical research program that we conduct in oncology at the NCI. So the next slide, which is slide two and the overview, I'm going to talk just very briefly about how we're structured to perform national trials in oncology. Then just a little bit of information on the impact that we've seen in enrollment when we do get new information. And then I'm going to talk about how we assess and evaluate whether new results should change our research, focus and change our ongoing trials and the opportunities and suffering for new trials. And lastly, I'm just going to give some instances or examples from the past and one currently in front of us, of when new information comes out. Sometimes if there's uncertainty around some of the aspects of the trial result, how we think through those implications and their effect on the trials that doubt. So our national program is called the NCI national clinical trials network. This is a next slide, slide three. And the short form of that is nctm. It's been in existence since the 1950s, in some form, but over the past four decades, we actually have grown the entire clinical trials national program for cancer treatment into an organized network, in which we have five large us clinical trials groups, and one Canadian partner that lead various clinical trials in oncology across all types of cancers, as well as in both adult and adolescent, young adult and pediatric and adult populations. It's primarily a late phase clinical trials network. So we focus really on large randomized phase twos and phase three definitive trials. We do both treatment trials as well as large imaging trials. And our portfolio covers not just investigational new agents that might be conducted under ind and overseen by the FDA for a regulatory perspective, but also non ind studies. So comparing various options that are no longer considered investigational but different standards against each other to determine comparative effectiveness. We've also built an infrastructure where a centralized standing infrastructure to support a NCI central IRB, regulatory and administrative support. And among the five groups, and our Canadian partner that lead these trials, each of them have very well developed in an info standing infrastructure for operations for clinical trials,

statistics and data center, tumor banks and a large number of member sites we enroll about between 18 to 20,000 patients per year on our trials, we have approximately 200 active trials that are open for enrollment at any one time. And we have close to a little over 2000 sites both in North America and internationally that participate in our trials. So the next slides like forth.

03:40

So one thing that I was asked was to say what's the pool impact on our base with trials when we do have new and emerging data from trial results and regulatory approvals. Now we track accrual very closely in the standing infrastructure, we have all the groups do patient enrollments for one set portal, and that's available 24 seven, so we're actually able to track a pool really on a daily basis. And we've looked back at periodic times over the past two decades on an accrual to our trials. Normally, we're focusing on why trials don't accrue at all. And we did our first analysis of that between 2000 to 2007, and then updated it in 2014 to 2010. And we're about to look at the past step aid, as well. But when we look for the reasons for why our trials didn't meet their core goals, and we define that by not reaching at least 90% of the targeted approval in the protocol. The major reason was just we had an inadequate approval rate. And that was usually due to challenges with the randomization on but we found other reasons and one major another major reason was external information. And that really was defined by other clinical trial results that led us to stop our trials with Because the research question we were asking in those trials was no longer relevant. Now, we do know that, in addition to actually other new information, stopping about 5% of our trials during that period, they also affected many of our trials that were ongoing because we had to change the standard of care in some of our control arms through amendments, we're able to continue the basic research question or modify it slightly and continue during that period. We do track amendments, but we don't actually track the exact reason for the amendment. So I don't know exactly how many or trials were affected by the trial results that required us to change the design of existing trials. But I suspect it's probably in about the 10 or 15% range. And that reflects, I think, the vibrancy of the underlying scientific research culture for clinical trials in oncology. So next slide, which is slide five. So whenever we do have new information, and it really comes from three primary sources, one our clinical trials results are presented either peer reviewed publications, or at major scientific meetings, or else we do also have several organizations that provide practice guidelines for the oncology field are regulatory approvals, usually in conjunction with a with a welcome, large randomized clinical trial. And whenever we see those results come out no matter what source, they come from, the primary questions we ask, and there really are two of them, in terms of evaluating its impact on our research going forward, is whether the trials that we have open right at the moment, whether they're research questions, or for the research questions, does equipoise which really is whether that's still genuine uncertainty about the trials, different treatment arms that we're evaluating, in our research, clinical trials, whether there's still a question about which one of those is preferable, and therefore ecorys does echoboy still exist even when we have new information and new trial results? So we look at that both from the perspective of trials that are still open and enrolling patients, but also trials that may be close to enrollment, but are still treating patients because often new trial results come out to change the standard of care, even

for patients as their their trial may be closed for enrollment, but they're still receiving treatment and appear on the trial. And the second most important question, or I would say they're equally important. But the second question is, what do we really need to communicate to the patients who are on the study arm as well as to the investigators at the various sites who are participating with their patients on the trial. So on slide six, next slide, I'm just going to go over some of the considerations that we looked at and evaluating if the new results are affecting the equipoise of our existing trials. So probably the most important is the primary research endpoint for the clinical trial. So sometimes results from the trials focus really on results related to a surrogate endpoint. And there can be different types of surrogate endpoints in terms of the validity of the ability of that service for depth, or more firm clinical benefit. So service endpoints can be validated in some cases, in some cases are not validated. And in other cases, they might have been validated for certain types of treatments, but not necessarily validated when we introduce a new type or new class of agents such as such as when we went through the value of chemotherapy, which is the bedrock of treatments in oncology for the addition of immunotherapy. The second is in terms of endpoints as if there is a consensus clinical benefit. And that's usually something that everyone can agree on, like the value of prolong patient survival, or definite functional benefit makes it easier to understand how that might impact your clinical trial. And the other important aspect related to evaluate the endpoint is the clinical relevance of the magnitude of benefits that you actually see in the clinical trial. That can also the issues related to patient population, the demographics of the population, whether it was a local, regional, national or global trial and biomarker considerations. And then on the next slide, slide seven, the two other biggest aspects are the trial design with the new results and the trial conduct. I won't go through all of these, I think they're probably pretty well known to all of you who follow clinical research and clinical trials. But it doesn't matter what the clinical setting is the trial phase, whether it's a placebo or active control, the assessment of schedules for everybody who were on various treatment arms in the trials. And the same thing with trial conduct, where there are changes in the design during the course of the trial, how did that affect things, the impact of other secondary endpoints Most importantly, toxicity adverse events, the feasibility of the treatment and availability, and then of course, regulatory approvals and practice changing guidelines. On the next slide, slide eight. So we're usually faced when we get new results, with three really three options, really one, should we stop the clinical trial that we're conducting? Because there is no longer equipoise or really as a new standard? And our research question that we're asking is no longer considered relevant, relevant. The other is to put a temporary hold on new enrollments, the trial is still open to enrollment, in order to dress or incorporate that new information. Sometimes that is simply providing information. But sometimes it can mean that we're going to add new agents to our trials, because the standard of care, the control on in the trial does need to change. So there can be changes in design treatments, the statistical plan and informed consent. And the last, of course, is continuing our trial, because when we look at our trials, compared to the trial that has new results, there are significant differences. That means we that essentially, the standard is not is not changing for the patients who are on the particular clinical trial that we are conducting. And in all cases, there needs to be communication to the patients on the study, as well as to the trial investigators of these results, and the potential impact on them, even if we're not changing anything within the clinical trials that we are conducting.

11:29

So on the next slide, slide nine, I would also say with any new clinical trial results, and even with new regulatory approvals, whether they be through the accelerated pathway, or approval pathway or full approval, there's always continuing updates to clinical trials results, and a continuing scientific dialogue and discussion of the science in the clinical trial, as well as the regulatory approvals. So I just mentioned on this slide, a review that the FDA had published in JAMA in 2018, of their 25 year experience on accelerated approval and malignant, hematologic and oncology, drugs and biologics. And when they reviewed the course of their **accelerated approvals** and oncology before 1992 and 2007. They had 64 products and 93 clinical indications over that period in which they had accelerated approvals. And they were able to verify benefits and 55% of those 40% were not complete, or verified, and 5% was withdrawn. And so they concluded that only a small portion of the indications under that program failed to verify clinical benefit. But of course, there's always dialogue and discussion about those approvals and about what was chosen as a surrogate endpoint, which they thought was a good indication of a more firm clinical benefit. But also there's discussion around the relevance of the clinical bet the clinic clinical, I should say validated confirmatory clinical benefit that they're targeted, because I think on many of the endpoints, particularly on oncology, have changed over the years about clinical trials. And so it's often not always that a confirmatory endpoint will be something like overall survival. So I've just listed one analysis of the FDA experience that was also printed in JAMA in 2019, where they looked at those confirmatory trials over that 25 year period, and stated that only about 1/5 of those were improved, where the confirmatory benefit was overall survival. And that just led to a question about the continued dialogue, I think we all have to have about meaningful clinical endpoints and trials, and that reassessment may be necessary to obtain more plentiful meaningful information. So in the next side, I just wanted to also highlight that the set of the FDA accelerated approval process is in fact a pathway, it's a process to full approval. So sometimes they do with for all indications under the accelerated pathway. And this is just a slide that shows and this is slide number 10, excuse me, that shows for drugs and immune oncology, that were recently withdrawn that had received accelerated approval, but were withdrawn in late 2020 and early 2021. And they go across a range of different diseases as well as particular disease. patient populations, as you can see listed on the slide. There was also a recent, what we call odacc meeting, which is oncology drugs advisory committee that the FDA has as a standing committee that they used to help give them evaluate research and give them recommendations at the end of April of this year, to discuss an additional six indications that have been granted accelerated approval and to see what The Codex committee felt it was important to continue those accelerated approvals or not.

15:07

One thing that we have that I think is very useful in in oncology particulars in addition to regulatory approvals on the regulatory bodies, whether they be in the FDA or overtly elsewhere

in the world. So in the United States, there's also a national group called the National Comprehensive Cancer network, which is a nonprofit, which has been doing research and providing practice guidelines for over 25 years. And this is an organization comprising over 1600 group sessions and oncology researchers at 31 member institutions, and usually, cancer centers, and their panels look across all the various diseases and provide guidelines in various cancer types. And they include not just clinicians, but researchers and advocates as well. And what they help us do is define the practice the actual clinical practice of care based on clinical trials results, whether they be on trial results that have new agents that were overseen by the FDA, or trials that we conduct that are what we call ind exempt because they don't involve any investigational agents, but just different research strategies, or combinations of other agents. And they lay out different categories of evidence and consensus, as you see listed on the slide, and also empty. And they provide categories of preference for many of the regimens in particular cancer types. And so those practice guidelines are sort of another voice in what we use to determine whether new information should have us react, or we should react to it in order to change our existing clinical trials and trials that we have in development. So on the next slide, which is a slide 12, I'm just going to give some examples. It's really two examples in gi cancers, one from the very early part of the 2000s. And one recently, that we're still looking at in terms of new clinical trial results that had regulatory approval. In this case, they were both for approvals, and how those affected clinical trials that were done subsequently, and trials that we're considering or in the process of conducting now. So most state most changes in standard of care are really quite strong clinical trial results. And it often comes with full regulatory approval if the particular clinical trial involves a new agent or a new indication that was under FDA oversight. And the purpose of my talking about these two examples today is simply to to give a cautionary note that there can still exist uncertainty. And I think we all are pretty humble in the face of science and biology, of just realizing how complex it is. And even as we learn more and more every day, there's so much more we don't know, and we don't understand. And so how we try in some cases, to handle that uncertainty in the trials that we have ongoing and those in development when we're faced with new changes in the standard of care. So the two examples I'm going to bring up was one related to advance a metastatic pancreatic cancer in 2005. And a more recent one with an Ebola map, which is immune you know, therapeutic agent in advanced and metastatic, gastric g junction and esophageal cancer. So on the next slide, which is slide 13, a lot number was a targeted agent that was added to what was a basic component of chemotherapy treatment for patients with advanced pancreatic cancer in a clinical trial that was conducted in the early 2000s. And one of the major meeting for the oncology field in May of 2005. Results from a large randomized phase three trial were presented where survival was the primary endpoint. And what we were comparing in this trial is whether adding or wanting to drink side of the prolong survival or not, it may be difficult to read on the slide. But as you can see, the hazard ratio or the comparison between the two arms was point eight one, it was statistically significant. And it did have a statistically significant p value and a significant I get 95% confidence interval. But the issue that arose in discussion of these results was that the difference in the sort of median overall survival at one year between the two different types of therapy was a difference between 6.37 months and 5.95 months, which actually clinically translated into two or three weeks. And so despite the fact that this agent was fully approved to receive full approval from the FDA, because it was a very Important endpoint for overall survival,

and it was statistically significant. It was a large well done randomized clinical trial. Despite all that subsequent trials that were conducted in the period after these results and approvals did not actually make the standard of care and all those trials genocide of the plus placebo. And that was because there was concern over the magnitude of the endpoint, not the validity of the endpoint, which was survival. But the magnitude of the benefits seeing and subsequent therapies and trials were conducted with with other types of therapies, which eventually showed to be more beneficial. And two of those are listed, where they also received one of them FDA approval in September 2013. And the other one was a large global trial conducted by the French government with a combination of what I would say our standard of care, chemotherapy agents and other gi cancers that were combined together. And so it wasn't an investment new investigator agent, but a new combination of known agents that led to a significant significant approval and survival. And those two regimens have supplanted really in terms of our guidelines and practice guidelines on the use of gem side of being and Tarceva in advanced or metastatic pancreatic cancer. And as the guidelines noticed, even though the panel for the guideline stated that the combination of a lot of engine side of my side me, excuse me, was significantly improved survival, the actual benefit was very small. And that suggested only a small subset of patients benefited. So although it's considered a category one result, it is, you know, a survival benefit. It was the magnitude that led people to think we needed to search for new

21:50

combinations and new agents in this very deadly disease in which we continue to do so. And so this was not used as a control arm even in clinical trials that were conducted subsequent to its approval. The other example I'll just bring up is one that happened more recently. This is an approval by the FDA of nivaldo Mab, which is a chemotherapeutic agent, I'm sorry, which is a immuno oncology agent, in combination with chemotherapy, in what we call first line, advanced gastric g junction and soft geo adenocarcinoma. And this trial was conducted with dual slide. Oh, I'm sorry, this is slide number 14. Sorry. Yeah. So this, this is a nivola map plus chemotherapy in advanced gastric, esophageal and G junction cancer. And so this trial was also a very large randomized phase three trial conducted globally. But and it had dual primary endpoints of both overall survival and progression free survival. In this case on this slide shows the results from the recently published paper on the trial in June 2021, that chose the benefit of survival in the primary endpoint, which was in patients who had tumors that had a particular biomarker that had what we call a high expression, a score called CPS, which stands for composite positive score for a particular biomarker called PDL. One and I won't go into the science behind this, but simply to say that if you have your tumor had high levels of expression of that biomarker, then it was likely that you would respond to the immuno oncology Agent nivola map. And so patients whose tumors had scores over five were really part of the primary endpoint and survival and PFS for this trial. So on the next slide, which is slide 15, there was concern though about the benefit in different patient populations defined by that biomarker in the trial. So the statistical plan first tested survival, all the patients who had a high score greater than five, then then it looked at all randomized patients. So anyone who even had had any level actually have the biomarker or even negligible level. But the problem was that the majority of

patients in the trial had a high score and the trial investigators pointed that out in their publication that the relatively large number of patients who had the high level of expression in their tumors have that biomarker, that magnitude of the benefit for them, probably drove the benefit to some degree for sure. And patients who didn't have his tumors didn't have that high level or didn't have a neck they were had a negligible level. Despite all that information, and I shouldn't say despite it was also because there were a set other secondary endpoints in that trial that led everyone to say that perhaps there was benefit as well in the subsets of patients who had lower scores. These are v The molecular characterization of their tumors. And when the FDA gave approval of the agent in 2021, they did it without any limitations based on the biomarkers, or how much of an expression you had of the biomarker in your tumor. And on the next slide, slide 16, they did exploratory analyses, and this is from the FDA label for the drug in those other biomarker patient populations for the trial less than one in less than five. I won't go into the details here, but there was very little difference. Now part of that is because there were far fewer patients in those two categories, but also the 95% confidence interval, overlapped or went over one. So these were not statistically significant results, but with the other secondary markers, they thought it was suggested.

25:52

And therefore the approval was given across the board without limitations based on the biomarker.

However, in the nccn guidelines, they saw a difference between these two categories, people who had tumors with a score greater than five, and those with scores that were lower between one and four. So the question was really, how should trials that were conducting now be affected by this new information? and also whether the assessment with further follow up from patients with information on the trial will that change things over time? And so currently, we have a trial where we're just conducting chemotherapy. And the question in metastatic and advanced gastric and esophageal cancer was whether radiation therapy for people who had what we call a lot, sorry, several sites of metastatic disease was beneficial or not, but we didn't have immuno oncology agent in that trial. And so when this new information came out, the question came, how should we change that. And the approach that we're considering taking now follows more of the nccn guidelines in the sense that instead of saying the control arm should not just be chemotherapy, and in devala, nivola, Mab excuse me or a similar drug in that class, instead of changing the standard pair to that, or we're discussing changing that trial, so patients who have the high level of expression of that biomarker for them that would be mandated that they should give that nivo and chemotherapy, for patients who don't have that high level of expression in their tumors, they depending on discussion with their patients could choose to have nivola Mab added to their chemotherapy or not. And then the clinical trial, we would stratify them by that decision. And so we're proceeding to look at amending that trial and changing the informed consent. So on my very last slide, which is slide 18, I think I just wanted to bring up these

examples to say that evaluation of new trials, results on regulatory approvals and practice CAC practice guidelines really involves a broad community of investigators, patients, health care providers, and others. And there really is a need to look critically at the information that's provided to assess it against the research that you're doing and the research that you're going to continue to do in the future. Especially given the complexity of underlying biology of disease. And whether you modify trials, either that are open, or those that are in development really requires an in depth evaluation of the equipoise of the research questions, given the new information as well as their feasibility, I would say an oncology, because we've been lucky enough, I think, over the past 10 years to have had actually a number of new exciting agents introduced into the have the ability of us to provide new treatments to patients, we now design trials, new trials with sort of a very critical eye to the research that's going on globally, and sometimes put plans in place. So should results from other trials that are looking at certain aspects come into play, we can more easily change our trial, and keep it going. So for example, we might start a trial with three treatment arms, but drop one over the course of time, because we expect there will be new trial results affecting one of those arms in the future. And lastly, I would say the commitment on changing trials and doing clinical research in general really involves ensuring that patients are informed at every point in time of what's happening in the research area for the trial that they're on, and how any new results might impact not only the trial, but their care on the trial and the standard of care in general. So thank you for very much for having the opportunity to present today and I'm happy to answer any questions later in the panel. Thank you.

29:46

Thank you, Dr. Mooney, that was really spectacular right on spot and appreciate you doing your homework. Clearly the lessons that you laid out were so clear for us how to translate those as we think about treatment trials for Alzheimer's disease and related conditions and the application. So thank you. We understood that you had a hard step. Do you have time for a couple of questions now? And then we'll let you go? Or, actually, I can stay till two o'clock. So I don't want to interrupt your schedule. Now. We'll we'll go ahead and take the questions now. Okay.

30:15

I'll give you one quick one. And then I'll invite the council members to ask questions, just to remind people, **questions are limited to council members, the public is viewing but they have a delayed presentation**. The first question I have is that, you know, you're in the enviable position of having so many new drugs in the pipeline, we certainly are eager to get there. But I also am envious. My perspective is maybe wrong, but I'm asking for your input is that there's this expectation of cancer patients and cancer providers, that people are engaged in research, and we have a real difficult time getting, expecting that almost as part of the standard of care,

despite treatments that people don't think about getting enrolled in trials as robustly as we might hope, or they're Is that true? And what lessons should we be taking from you?

31:07

Well, I think, you know, I would say that, that an apology even today, even though people view us sometimes as having a community that's very committed to clinical trials and do it's not as widespread as we would like, on the patient populations, we try as hard as we can to make them as diverse as possible and as represented as representative of the patient population that gets the various types of cancer. And I think it's a continual process. And when I started in oncology now, almost 30 years ago, I would say right at the very beginning, um, you know, it involves really outreach to all communities or patients who get the disease to their families, or medical students who are who are in medical school right now. And then fellows and and interns and residents who will participate in our in the teaching environment, to really develop that entire culture. And we we have spent a lot of time I think, over the last 30 years trying to reach out not only within our own profession and our training programs, but also to patients communities and their families and trying to engage people in the research environment. But it's a continual process. It's not a process where you do something and then everybody's ready to join a clinical trial. It's a it's a continual process of outreach and dialogue.

32:32

Oh, fair enough. Thanks. We're on that journey as well. Let me ask my colleagues on the council, if anybody else would like to ask any questions.

32:48

Feel free to unmute yourself if you do. Well, while and for the sake of time and respect of your time, Dr. Mooney, thank you so much for joining us. Thank you. Really, really informative. With that, I'd like to introduce our next speaker, Dr. Marie Barnard, who is known to many of us she is the NIH is Chief Officer for scientific workforce diversity, where she leads NIH has effort to promote diversity, inclusiveness and equity throughout the entire biomedical research enterprise. Many of us know her from her prior position as the Deputy Director of the National Institute of aging. Needless to say, she is very familiar with dimension issues that the Napa council works on. ASO, she is well suited to discuss the equity application to the edgy Canyon map decision. Thank you so much for joining us today.

33:47

My pleasure, Dr. Levy, and I just want to confirm, can you see my slides? We can? Okay. Um, yes, I, when it was mentioned that this is the 41st convening of the Napa Council, I was thinking, Wow, I've been here for just about all 41 of them. But this time in a different capacity. What I'd like to do would be to talk a little bit about that acana map, you know, I know I'm preaching to the choir, you guys know all of this. But then to talk about barriers to equitable access and use things that and I am at NIH, as a whole are doing to make sure that there aren't those sorts of barriers and some of the things that we can look forward to for the future. So as we know, this was approved by FDA for an accelerated pathway based on the effectiveness and reducing amyloid plaques, that the trial was limited to people diagnosed with mild cognitive impairment or early stage Alzheimer's and that the labeling has been revised to be consistent with those trial criteria very recently. Houses associated with barriers Well, there is cost associated with this. Its list cost is $56,000 per year. In addition the There has to be a monthly infusion at a specialized center. You have to have PET scans or CSF tests to detect amyloid, you need to have an MRI at baseline and periodically to monitor for side effects. And so it raises the question about how accessible the drug will be given its criteria cost and the need for monthly infusions. And in particular, this has an impact when you think about a groups that are often underrepresented in scientific research. For instance, when you look at the real median household income among us adults, by race and ethnicity, you see that for black and African Americans they are at the lowest levels are Hispanics or Latinos are next, then all races and then non Hispanic whites and Asians are at highest levels in terms of meeting income, although income is relatively low as compared to the cost of this struggle. And honestly, you also find when you look at the Alzheimer's literature that underrepresented groups like African Americans and blacks and Hispanics will often have a Mr. Delayed diagnosis 41% of non Hispanic whites in the study by Lynette all versus 46% of non Hispanic black versus 54% Hispanics. So that has implications as well given the indication for the drug. And when you look at who actually participated in the attic kanematsu study, it was really not a very diverse group of 89%, white 9% Asian as compared to the prevalence of Alzheimer's across the country with a higher prevalence among African Americans and Hispanics than necessarily among non Hispanic whites and Asians. And it begs the question of things that might be genetic differences among groups, we know that a belief for in terms of predicting Alzheimer's is much higher among Asian populations and Hispanic whites than African Americans and blacks. We know that, for some drugs that have been looked at in the past, for instance, ACE inhibitors, the impact has been differential based upon race of African Americans and blacks as compared to white. So all questions that arise when you don't have a very diverse group of individuals. And it speaks to the role I have as the chief officer for scientific workforce diversity at NIH, because increasing diversity the scientific workforce is essential when you're thinking about developing drugs like this, for people who are thinking about the problems of these particular populations for people who can be involved in helping to recruit recruit these populations into studies. For instance, black and African Americans, Hispanics and Native American physicians are more likely than white physicians to practice in underserved communities. And those patients who have a choice are more likely to select those health care professionals of their own race, ethnic background and extrapolating that to clinical trials and clinical recruitment. You see, oftentimes an alignment between the race, ethnicity and background of the individual and the likelihood of people to participate.

38:18

So what are we doing at an IAA and at NIH to address these, these issues? Well, there's the national strategy for Alzheimer's disease recruitment that was unveiled here at the Napa Council in 2018. There is the NIH wide unity engagement Alliance was developed to address the COVID pandemic. There is an really neat funding opportunity announcement that was recently released by the NIH wide BRAIN Initiative. And then I would be remiss if I didn't talk about the NIH unite initiative that was unveiled and February 28, February 26 2021, in which I had the privilege of culturing with Larry Taebaek, the principal, Deputy Director of NIH and Dr. Albert Alfred Johnson, the deputy director for management. So, the national plan, as you recall, it's a strategy for clinical studies to engage a wider, more diverse pool of volunteers. It's meant to work in multiple ways, their funding grants to test and identify new approaches to recruit underrepresented groups of developing and testing recruitment messages and materials, and has developed this wonderful resource, the adore website, which is a repository of resources to help with recruitment and retention of participants and from multiple backgrounds. Additionally, as I said, there's the community engagement Alliance or the seal initiative that was put into place last year with the COVID pandemic and be an enduring resource because it's been very useful in providing trustworthy information. through active community engagement and outreach to people, hardest hit by the pope COVID pandemic. Now of course with the rates going up as they are among the unvaccinated, you may ask how truly impactful has this been, but it has really made a difference and bringing people in for clinical trials, bringing people in for vaccine trials. It has outreach across multiple states and the United States working pharmacies, state and local governments, faith based organizations, academic partners, community based organization and health care centers, and providers.

40:39

Additionally, as I said, the NIH wide BRAIN Initiative has put forward a funding opportunity announcement that for the first time allows the consideration of the diversity of the investigators as part of the scoring criteria, it's a plan to enhance diverse perspectives. This was developed because the brain investigators and the brain team recognized that the populations that were getting recruited for the Brain Initiative were not very diverse. And that there is value to having scientific leaders from diverse backgrounds and helping to think about that recruitment to help and bringing in subjects from diverse backgrounds. And we across NIH are really interested in seeing the outcome of this because if this proves to be impactful in the way it's hoped to be in bringing in more diversity among those scientists who are involved, it's something that will likely be replicated in multiple other funding opportunity announcements. And then as I said, there's the NIH unite initiative. This is something that was officially unveiled February 26 21. At a special meeting of the NIH Advisory Committee to the director. It is meant to address issues with structural racism, that provide barriers to scientists from underrepresented racial and ethnic groups from being fully at the table in developing scientific initiatives and clinical trials. We are

very aware from the events of 2020 that the ongoing reality of racial justice up continues to live in our country. And it was a sense that all of us have a responsibility to address this. So starting in June of 2020, there was a series of intense Institute and center director meetings and discussions to identify initial issues, discussions with a couple of self assembled affinity groups acre eight concepts, racial equity, senior African American and black scientists, the internal anti harassment steering committee and many others for candid discussions to inform next steps. And it led to a shared commitment to address structural racism. It was certainly further amplified after the unveiling this initiative with the killing of Asian women in Georgia in March of 2021, there was overall realization that we're at a tipping point, and we can't let this pivotal moment pass. So what was unveiled was something that's called unite five, interacting workstreams to address issues with regards to structural racism. Basically, we're stepping back and looking at everything that we do in terms of new research in terms of our internal culture, in terms of the extramural research ecosystem, to try to make sure that we do a better job of being inclusive of all sorts of scientists and all sorts of viewpoints. Some outcomes as a result of that, that would be of particular interest to this group. There's a common fund initiative that was unveiled a month after the ACD meeting, committing up to $24 million in the first three years to do transformative research and health disparities and advancing health equity. There was also a funding opportunity announcement led by the National Institute of Minority Health and Health Disparities and with 25 other institutes and centers, and offices signed on to address structural racism and discrimination and its impact on health. Additionally, being attempting to role model what we expect of outside institutions, the Office of Extramural Research recently released data about investigators who are funded by NIH by race, ethnicity, and disability status, added on to the already available data about investigators by sex and career stage.

44:50

We're also looking forward to additional activities as reported to the Advisory Committee to the director meeting on June 11. We stated We would develop programs to spur institutional cultural change in support of inclusivity and equity, that we would examine how our staff interact with applicants to make sure there's not bias and inequity in those very important interactions that can make or break a scientist career in terms of applying for funds, that we would develop programs to expand our interactions with and support of historically black colleges and universities, tribal colleges and universities and other minority serving institutions. And we have a very thorough summary of our reason for being interested in this and what we see as a way forward that was published in sell on June 10. I refer you to that document to get a clearer sense of things. These are the 80 plus individuals who are moving this initiative forward, I like to think of them as a Big Think Tank that's helping us to advance issues in this area. And if you want to see the very latest and thorough coverage of the things that we intend to accomplish, I refer you to the videocast from the June 11 Advisory Committee to the director presentation because I only provided you some very high level takeaways from that meeting. So what is it that we can look forward to? Well, we know that the pipeline of potential treatments for Alzheimer's has never been more robust or diverse. My colleagues from NIH share this, we have 56 therapeutic trials, 115 caregiving, 115, non pharmacologic trials, 84 caregiving trials 15.

Other trials, there is a lot going on in this space. And there will be a number of things that will come from these early stage trials or from the later state trials looking at different targets, and future discussions about drugs that come from that. I think the development of that Academy app reinforces the need for NHS commitment to additional research. This is a complex disease, and amyloid represents only one of the targets for therapeutics, as you saw from the slide that I just showed of the various targets that are being pursued. Um, there are many options and they are needed for the treatment of Alzheimer's and related dimensions, because the multiple pathways by which one ends up with that final common pathway of dementia. and enhancing diversity in clinical trial participation, and in the scientific workforce has the potential to result in stronger science that benefits us all. So I'll leave with our tagline great minds think differently, and encourage you to think broadly, when you're bringing people to the table to develop a scientific concept to develop a clinical trial when you're doing recruitment. And to think about the data that's derived from those studies and how generalizable and applicable it is. I will stop at that point.

48:19

Thank you Dr. Barnard. Really important. Obviously, we all need to be doing everything we can to help address the issues. And thank you for leading and really exciting united initiative. A lot of lot of great things ahead. Let me see if there are any questions from the council members.

48:41

Want Elena? Please go ahead. Cindy Carlson. Thank you, Dr. Barnard, for your presentation. I really appreciate that. And congratulations on your new role. So I guess one question, I know you've mentioned a lot of the work that NIH is doing. Do you have suggestions for academic institutions and healthcare systems that may be listening in on how they can help prepare their institutions, their healthcare systems for supporting diverse workforce, diverse patient recruitment? I know that you said that. And I just made launches and programs for the things that academic institutions and healthcare systems can prepare. So we can help reduce the inequity, not only scientific work, but also in the clinical care that most likely will be present with implement implementing some of these new therapies unless some changes are made.

49:31

Yeah, yeah. Thank you for that question. And yes, I skipped over some other content to try to save time. But there's a lot that outside institutions can do. One of the very first things is to step back and look at what you're doing and look at your data. Transparency is said to be the greatest antiseptic and when organizations stand back and look at the configuration of their staff, they often are surprised they Have a subjective impression that they're doing better than

otherwise they are. organizations also need to recognize that this is a value and have it clearly stated in their value systems and have systems aligned so that there are positive incentives for people doing the right thing. They need to be rewarded and acknowledged for doing things to enhance the diversity of the workforce of the clinical staff of the participants in studies. And that needs to go from the top down and from the bottom up. programs need to be developed to enhance diversity, and they need to be measured. And they need to be refined, as you're seeing impacts, whether it's positive or negative impacts. And you need to continue to focus on this on a regular basis. It shouldn't be, you know, this is the flavor of the month. This is the popular thing right now. And then it goes to the wayside. It needs to be embedded into what is part of just the normal operations of the group because it makes a difference in terms of the quality of the care in terms of the quality of the Clinical Investigation, in terms in the scientific setting of the quality of the creativity and innovation that's being done. It has value in and of itself that needs to be embedded into the systems.

51:43

Thank you very much. Any other comments or questions? Okay, well, thanks again, Dr. Barnard. We're at really important equity considerations. And then our final topic this afternoon on the edge Canyon map session is led by Dr. Robert eggy. Rob, thanks for joining us not only in your role as a council member, but outside of the Council. He is the chief public policy officer of the Alzheimer Association, and the executive director of the Alzheimer's impact movement. So he oversees government affairs, policy development and grassroots advocacy teams to work together to ensure secure policies to improve the lives and well those affected by dementia. So Rob, thanks for a few comments about opportunities in educating man princess.

52:45

Thank you very much, Alan, and thanks for the honorary degree. I appreciate that. I'm going to tell my kids appreciate that very much Alan introduction and the invitation to speak. I want to start out with a disclosure. So I have no personal disclosures. the Alzheimer's Association received 0.15% of revenue from Biogen and ACI this past year, ever received less than 1% total 8.8 excuse me, 0.89%. From the life science sector, that's pharma, biotech medical devices together, I just want people to know that now these contributions have or ever will affect the decisions the Alzheimer's makes Association makes them these kinds of issues. But I thought the disclosure was important. So to start out, I was asked, as Alan indicated to discuss opportunities, I mean, immediately was worried that it would sound like I was out of touch and talk about only opportunities. When this introduction has been we all know so controversial. But as I briefly chatted with Katie and Alan about this, what's apparent from the other presentations already is, if you're optimistic, you look at things as opportunities. And if you're not so optimistic, you can frame the same things typically as challenges. And I'm an optimist by nature, so happy to take this on. There have been challenges, no doubt about it. And one of those to start with

has been the data assembled. That was the basis for approval, and that people are interpreting now for coverage decisions. The whole to the studies beside futility analysis has created true challenges and complications. But it leaves a lot for us to think about in terms of opportunities, I've decided to keep this presentation free of slides, and make it more of an informal survey and opinion in survey all admit up front, but survey of issues that among many other issues that are going to be things that the officer Advisory Council has the obligation but also I think the opportunity to grapple with in the years ahead, and I'm only a bit sad that I won't be part of this group to do so because there'll be very important issues to be thinking through together. So there are good things that a group opportunities for consideration. One of them is generally speaking now recognition from the recent news that, and I'll start broadly here that Alzheimers is a serious public health crisis that needs to be addressed. Now, in some cases, the way things have been framed hasn't looked so much at what the underlying state of the world is with Alzheimer's and dementia today. That's not from any ill intent by anybody, no doubt, but just the way the stories have been discussed. But it is important for us to keep thinking about opportunities to recognize that just the challenges within Ulzheimer within this treatment, and what to do about it. But more broadly, an example of that is costs. So there are significant challenges and thinking through what the implications are for addressing the costs of this new treatment as they're anticipated to be. On the other hand, in terms of opportunities, one of the only viable ways long term to address the cost curve, which is set to grow, as I think we've all heard many times, and rightly so over the years to come is through treatments, I don't think add you home is the treatment that will do that. But as Alan and we've heard otherwise, a as we look at the pipeline, that is the route to bend that cost for the future. So it gives us an opportunity to continue to work along those fronts. Another overarching example of opportunity through this approval has been just that the the approval gives us the opportunity to move faster. And this is again, a framing issue. There's no doubt that there's uncertainty about the clinical drug trial data, and what it will mean, who will respond, how they'll respond, and what ways

56:48

the choice that the FDA made with accelerated approval, as I see, it has meant that in the face of that uncertainty, and a recognition, the science that is established and the unmet need, that it is better for us to err on the side of speed. I personally see, as we've heard from so many commenters over the years, he's 41 or 42 meetings, that this is an you can think of as a rescue operation, that there is speed involved in getting treatments to people as soon as we can. And if it turns out, when all of a sudden done, the treatments didn't work as well as we hoped that will be really disappointing for everyone, probably no more so than those patients and families who use those treatments. On the other hand, if we were to delay and find out after the fact that it could have made a really meaningful difference to people, that would have been, I think, the more regrettable choice to make. And so maybe a good decision was made with opportunities to keep that speed moving in terms of accelerated approval. But again, these are all debatable points to be sure. So let me move on then to class of drugs. Again, we've heard some things about this. And just some quick high level observations here. I'm not trying to be Dr. ag in this case, I'll leave that to the two doctors. But first of all, we have an opportunity to frame this in

terms of what we've seen in other conditions. And there's no guarantee based on that what will happen in Alzheimer's, but we do recognize, as we look at, for instance, HIV AIDS, as we've discussed, as a council together in the past, that the first treatments in that case, were not what was hoped for. And that was recognized up front, just as we recognize that with this treatment now approved, not what we hope for in terms of where we want to go. But it did set in motion was part of that unfolding story, that pathway to come about where we needed to head. And there's reasonably we'll see the same in this for and I'll just mention a few points that that I'm I'm many of us have heard discussed recently. One is that, although it's framed up in that there's been a series of amyloid treatments that have failed and that is true. That's a fact. What is missed sometimes in that discussion is what's been learned along the way. And how important that's been in terms of as we look at that this particular class of drugs in particular, as we look to the future, that's better targeting engagement as different ways have been explored to engage with unclear amyloid proteins, better trial recruitment, fundamentally to make sure that those who are in a trial for amyloid clearance have amyloid when they enter the trial because of PET scans and other ways that that is possible the past into the future. And then applying the trial population earlier and earlier in the stage of the disease. And that is another area with great with very serious challenges, but very exciting opportunities looking further down the road that may be really relevant to the Advisory Council and what you're thinking about. We've we've heard this discussed again many times at the Advisory Council, but the

PART 3

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good reason to think just as this trial has moved earlier than some of the past ones in terms of the trial population now in the revised label recognized that way, there's reason to think that could be even stronger benefit moving before any clinical symptoms for MCI, that's speculative. But if it is the case, evaluating that, in the first instance, in dealing with it are going to lead to some very significant opportunities and challenges. The other point I'll make on the research side is combination therapies. So I was surprised to be reminded with education map that really the the idea crystallized in the minds of some researchers about 15 years ago. So we think about this in terms of let's let's look at this, just in terms of their recent, so important increase in Alzheimer's research funding by Congress in just the past recent years. This, as you can imagine, as as the idea came together and was initially developed, predates all of that, we have so many opportunities, as we just heard from Dr. Barnard, in terms of the range of things that are now funded, that can be combined with as they have been other disease states into combination therapies that can we explore that together, perhaps will give us the kinds of benefits that we are hoping and looking forward anticipating. So looking ahead, then to some quick points about access. Yeah, the first one I think we should start with is, and this goes back to the point about, you know, will we say as a country, the cost of this disease is the cost of Biogen, we've been very clear, the Alzheimer's Association is saying we think is unacceptably high. We call for that price to be lower. And that is important for a number of reasons. But the first and foremost is, I think, what again, although Dr. Barnard didn't linky, quite this way, we saw in some of our early slides, and she didn't comment on this. But I'm going further than she did in, in making this point that the price that was cited was surprising to many, and will create real problems in terms of access for many. So that is an opportunity. It's a challenge. Now it's an opportunity to lower that price. Looking also then to coverage that the next big set of decisions we know will be with CMS. I think they seize an opportunity with what they did what they announced last week, the way Time flies these weeks, I never quite sure if I said last week, it really was last week, but I'm pretty sure it was last week with the announcement of a national coverage determination process. That was a very good decision and argue and I think probably universally regarded as a very good decision to create the right context, especially when there's so much debate about this, to really have an informed decision where everyone can participate and think through methodically, what are the best coverage decisions to make? From a CMS perspective, that process is made easier? I'm, I would imagine quite competent by the revised label, which addressed one of the most important challenges, I think, in the early days and thinking about that this treatment, how would we be clear about coverage where it's appropriate in terms of a clinical trial population, that issue has been resolved, which is very good. So the NCD a national coverage determination, which is a jargon for this process that we're undergoing for about the next nine months, doesn't need to address that issue in a way that was perhaps anticipated weeks ago. But there are still important questions that need to be addressed in that context.

03:40

What other opportunity there in terms of how coverage should take place? Well, let me just mention one few quick points about NCD. We're very briefly in passing. So by having a

nationwide approach to coverage, to potential advantages that are really important, first of all, it will supersede would be the default approach of region by region, making these decisions and that kind of consistency can be extremely important for issues of access for issues of health equity, and so on. And also beyond that, then it takes away It has the potential take away a lot of the uncertainty, case by case in the absence of either regional coverage decisions. So that's why one reason why we're very pleased with the NCP is the NCD decision is to have that sort of level playing field across the country for everyone in terms of how coverage works. Beyond that, though, there's an opportunity, but how it's done would be very important for what's called coverage with evidence development to accompany three announces an outcome of this national coverage determination process. Sometimes, we're called coverage coverage, evidence development. And we've talked about some examples of the council over time. that can take place almost like a clinical trial with a placebo or control arm. In this case, the FDA with accelerated approval is has already called for that and that commitments made and we urge for that process and other opportunity to go as quickly as it possibly can. Some of the timeframes discussed to seven or nine years simply won't produce clinically relevant information in our view soon enough. So there's an opportunity to think how to speed that up by the CMS will not I'm sure want to duplicate that work. It's one of their principles for coverage with evidence development, it still leaves opportunities for determine whether coverages being applied appropriately. And this can take the place of looking for issues of safety or equity, and generation of real world evidence. So again, important opportunities in that regard, that may make sense to pursue. In the meantime, there are opportunities to make sure during this nine month process that for those that could benefit from this treatment, in the shorter term, that these next nine months are facilitated just as well as they can be. So that x is for those who decided for their doctor that this is the right treatment for them. And it's in their qualified as such that they have the opportunity to benefit from this treatment, as they may quickly be moving through this window of the trial population. And then finally, we recognize that there are very important issues for private payers to consider or recognize that challenge. But we urge private payers then that to approach us as they have other diseases, we just heard about oncology, for instance, and to be consistent in the framing of these issues. So finally, let me just wrap up with a few points on providing care for these therapies. And this echoes back to a lot of our discussions, including our most recent one, there are a lot of issues that are very relevant from just what we discussed in our most recent meeting. So first of all, though, we've discussed about the reluctance at times to seek help by those who worry about what they may be seen in themselves or in family and loved ones, there's an opportunity here, done rightly that this approval of treatments and those two come will really help encourage people to initiate the right kinds of conversations. As soon as they as soon as they identify worries and concerns with their healthcare providers. That's extremely important and and that opportunity, perhaps that the council can find ways to accelerate. A second one is in the context of detection diagnosis. With this treatment at trial population, it's extremely important to be looking at detection early on. That's the challenge of MCI and even early stage dementia many times is to have that early detection. Moving into a diagnose diagnosis process, we heard some great examples of how that could potentially be done. In our most recent meeting, and I think reflected our recommendations that we're going to consider later today. This detection is to be very sensitive, we heard in, in our research meeting two meetings ago about exciting developments, for

instance, in plasma and ways to detect perhaps in a much, much more cost efficient price point that it wouldn't be for PET scan. And again, this is especially important if we're able to keep moving treatment earlier and earlier in the process, we'd really need such a solution. So it's exciting to see that rapid progress being made on that front CSF and in plasma, and to consider what can be done to move that as forward as expeditiously as possible.

08:41

Also, we know that when people come in for these treatments, there'll be some time, if ever before there is the cure, right. And so that's the history of many different conditions, is incremental progress. And just as today for all the progress in oncology, and it's been so encouraging, there's so much more to do there. But it's been so encouraging about that. Cancer Care, of course, continues to be an extremely important issue. And that's just to say that dementia care will of course continue to be crucial whenever the advances are in treatments, given my most optimistic scenarios, for years and years to come. It's not just in the healthcare setting, but in community as well. And so the kinds of models that we discussed in our last meeting of comprehensive dementia care are going to be all the more important and if more people come in, and they may find, for instance, that they talk to their providers, they do have MCI, but it's not due to Alzheimer's, and this treatment in particular would not be appropriate for them. It's so important that we have the right infrastructure for they for those who move beyond it who do have Alzheimer's that have moved beyond the early stage and committed and late stage that we have the best possible supportive care. So those models are not shouldn't be just models for long we have to move them as quickly as we can into care available to everyone equitably across the country. And that will bring with it workforce issues. We heard from Dr. Boris, in our last meeting about the importance of the role of primary care physician and others. And it isn't just about moving people on into getting PET scans, you made that point very convincingly. But in the case of this treatment, as we've already just have already talked about, we do have that obligation to find out is amyloid present. And that may lead to workforce pressures that we haven't experienced to date. And that's what specialists for instance, I can, that primary care physicians can refer people to, for that work. And their availability by location as close to people, especially underserved populations, and others will be very important with these advanced practice and the practitioners, whether it be physicians, physician assistants, nurse practitioners and others. So that's a quick tour of some of the issues, they'll no doubt be more, I would have mentioned this later removed a bit better here are political care committee thought about trying to address some of these early on, we recognize that our existing recommendations do to some extent, but the very specific work of what is to be done about this treatment, the opportunities, the challenges, and how to address them is a challenge left for meetings to come. So with that, Alan, I'll turn it back to you.

11:27

Rob, thank you so much for those thoughtful comments, really appreciate it. I think I will accept that as your oral presentation of your doctoral thesis and your your diploma will be in the mail. So congratulations, Dr. ag, that might have been a low bar, but I appreciate it. So although we're behind a bit for time, this is such an important issue, I definitely want to make sure our council members, feel free to comment and ask question. So please either raise your hand, if you know how to do so in the zoom reactions button, or just unmute yourself, or feel free to write something in the chat to share. But

12:08

Rob, I was thinking about the statement that I heard once a few years ago during an advocacy experience that the first survivor of Alzheimer's disease is going to be enrolled in a clinical trial. And that really struck me. And I think as we have discussions today about how to diversify our research enrollment, how to engage people at earlier stages, what I hope that the presence of educators have the approval of advocate map sparks for our larger community is this idea of wanting to engage with clinicians and researchers and the opportunity to participate in research that there's hope that there's a treatment available. And so that's what I hope it brings for families. And I just want to say I appreciated your presentation. I'm sure that was difficult to prepare.

13:08

Well, thank you agree, agree more with your point, Katie, that is a great point about an opportunity I had. So thank you.

13:32

Okay, I think zoom is made everybody quiet, a little reticent to speak up. But again, thank you, Rob, for that and so much more. Appreciate it. Let me turn this over to Helen. And I'll let you help manage the net section of the meeting.

13:49

Great. Thanks, Alan. And thanks to our great presenters, it was great to hear from everybody and hear these different perspectives on the latest updates in the field. So we're now at the point of the agenda where we do federal updates, but because we're a little bit behind, I'm going to propose that we skipped the oral presentations of the Federal updates today. And just post the slides that our federal colleagues we're going to present. However, I know, some folks do

want to present their slides and flags don't have all the information on it. So if there are any Feds that would like to present their slides, please let me know. And I would be happy to advance the slides for you.

14:32

And Helen, can you just remind everyone, where will we be able to see the slides from the federal updates?

14:39

Oh, that's a great reminder of what was in our slides. So as we got a new website that went live at 5pm on Friday, the old link will redirect you to the new Napa website. We had to wait a little bit to make sure we got everything up and running in time. So starting tomorrow, we will have the slides available on the usual The website and what we will do is send out an email to the listserv with the link to all of the presentations from today's meeting, including the federal slides. And we will give our make sure our feds have time to update anything that they need to update there. And then it looks like Lisa has a quick announcement.

15:20

I do I wanted to let the council as well as those watching know that through the bold programs initiative, we were able to award seven new awardees, and they have received their notice. So they know they're getting your award. It's public, but please don't reach out to them yet because they can't start working until September 30 with this award, so it's the South Carolina Department of Health. Idaho Department of Health, Boston Public Health Department, Louisiana Department of Health, Tennessee Department of Health, Arkansas Department of Health and Connecticut Department of Health. So we want to congratulate and welcome those seven new awardees and they will be joining the other 16 awardees for bold and if my math is right, that's 23. So thank you very much.

16:20

Thanks, Lisa. Anyone else? Okay, and with that, I'm going to turn it over to Dr. hotas to present the bypass budget and I will do your slides. So just let me know when you're ready.

16:39

Okay, so anytime. My Give me a second screen. Well, that didn't work. The quick version of federal updates. Oh, no, I went too far. My apologies, everyone. Okay, ready? Thank you. Well, thanks for the opportunity to go through with you again, this year's bypass budget request. This is for FY 2023. Next slide please. As a reminder of the origin of this bypass budget language, it comes from appropriations law here that requires the n i h director every fiscal year through 2025. prepare and submit directly to the President. For interest middle to Congress. The bypass budget is commented upon by the this committee by the administration department president, but bypass reflects the fact that the language goes directly to Congress as an expression of the annual budget estimates for what is needed in terms of funding personnel staffing, in order to add maximum opportunity and efficiency, address the goals of the national plan. Next slide please. So this outlines the process with input begin through 20,012 through 2020 series of meetings, notably including but not limited to the summit's that we have on an annual basis generate from academics from private sector from publics from constituents from interested populations, a set of criteria for reaching goals, a set of milestones that need to accomplish those goals. And on the basis of this at NIH, there is a staff discussion which looks at those milestones that come from all this expert, national and global input and estimates, the inclusion of them in a national plan and what price it would cost that is what funds will be required to achieve each of those milestones. So building, not an abstraction, but very concrete estimation of priorities and what's needed in the way of research to achieve these goals into a final budget estimate in this case for fiscal 2023. Next slide, please. The framework for this categorization of goals is cadra. That's a common Alzheimer disease research ontology that was originated with niha in collaboration with the Alzheimer's Association, as a way to categorize our research efforts so that nationally and globally we could have in a single place a registry of the research that's ongoing that would be a way to inform identify gaps, avoid unnecessary overlaps. And this is the framework that again that is used in both the I drop the national database, but also for the budget formulation. Next slide please. So this is the illustration then released now for FYI, 2023. In each of these cadrul categories, these major research categories of the finances needed the day to what's already been invested to achieve the goals of the national plan, you can see that they total if you read down to the third from the bottom that number 376 million approximately, that's the sum of those areas. Now, because this plan and our research expansion has been in place for a number of years, certain projects have already been successfully completed. And so funds from those previously completed projects become available, can be applied to these new needs. And therefore, if you will, or subtract from the net request for additional funds, in this case, they subtract is $150 million dollars, which means that the request for additional funds is $226 million for FY 2023. Next slide, please. This shows the breakdown needed by categories you saw in the form of table the pie diagram lets you look at the categories by components of this donut from year to year. They vary because the milestones and their achievements from year to year, the course of their progress will vary. But this is an illustration for this year, you've seen similar prior years. And estimate again, the total cost these projects are $376 million, which translates with that subtract for funds from successfully completed projects, an additional $226 million. Next slide, please.

21:20

As we put that in another context for FYI, 2021, the inactive level for ADHD rd research across NIH is $3.2 million dollars. We don't know of course, what our F 22. appropriation will be, but we assume that as the base for this request for 2023, the request for additional $226 million would bring the total 2023 resources needed for ad ADR, the research for $3.4 billion. Next slide, please. But that budget also importantly, in addition to these figures as a narrative, and includes examples of many of the advances across science and multiple topics, ranging from basic science, translation, clinical care, and caregiving. This is the link to that now public and I encourage all of you to have a look. his nails, illustrating, illustrative and gratifying indication of the progress is being made across many of these domains, with input from Napa, from the many committees and importantly, with the support bipartisan support this come from Congress from a series of administrations to provide the resources needed for these initiatives. Next slide, please. To look at implementation and tracking, you can look in and near real time by looking at I drop, that's a list of all of the funded awards. And then web based tools for tracking based on achievement of milestones. You can see with links here happy to make available to you a way in which any audiences can help to join in the population of those of us who are interested in tracking research and contributing to the ideas and priorities you have to come. Thank you. Thank you, Dr. Harris. Are there any questions?

23:17

I can just make a quick comment. Just thanks in for all the work along these lines, you know, which goes into I'm really appreciate it. Thank you. Thank you, Rob, for your support and the association as a partner.

23:30

Thank you also, Dr. Hotez. You've been giving this yearly and MSA every time it gets better. I know it's a complicated process. But you've done a great job distilling and making it very clear for us. So thank you for that. I guess. One, one question for you just just more broadly, is, as the as the council has been looking forward, there's more and more need for implementation research for public health awareness and dissemination? Are there adequate mechanisms to ensure the bypass budget is developed, thinking about other agencies that might be in you know, necessarily funded appropriately?

24:10

It's a great point is summarize the bypass budget is a requirement for report from NIH. And it is that and that has to be put as you're alluding to element in context in order and other agencies could contribute. The I drop, that is the database of supported research includes that supported by other agencies, organizations and other nations for that matter. But yes, I think Napa and the

role we're all playing here, serves to integrate what comes with the bypass budget NIH initiative as one of the many partners and agencies that we're very gratified to be a part of. Thanks. I guess I should add the implementation. Implementation Science, as you will know, is a part of research and one which you're not ignoring. So in addition to looking for Answers to Questions looking for interventions that work. It is also a part of the research we support. identifying what in terms of behavioral and policy kinds of approaches is important for implementation. As we increasingly know, there are important areas in which that is an important next step.

25:26

Brad, do you have a question? I see you're unmuted and anyone else? All right. Well, with that, I'll say thank you again, for that great annual update. It's so exciting to see where the research funding is right now, compared to when we started this effort. 10 years ago, it's hard to believe that it's come this far, but it's really amazing and a great sign of the partnership between the federal government and Congress and the advocacy community in advancing this research. So with that, and relatedly, I'm going to turn it over to rob to just give us a quick update on what's happening on the hill and legislative proposals that are currently active or that our members should be watching. No, thanks.

26:17

I'll do this very briefly. So so far in the appropriations process, apropos a conversation we just had. So it wouldn't be for the fiscal year that we just heard discussed, but this coming fiscal year, the house now has taken action the Senate is yet to do so. And the highlights from from the house, or work on appropriations in the in the Appropriations Subcommittee and full committee relevant to this group are first of all, they call for an increase in their bill $200 million for Alzheimer's research activities at NIH. That would bring it from about 3.2 billion today by their belt to 3.4. CDC, another increase of 4.5 million in this case was in call for for bold, bring it to 19 point 5 million if that's sort of become law, in addition to ongoing 5.5 million for the Healthy Brain Initiative that we often discuss an increase an ACL to $34.7 million dollars would be the total amount then that would be called for in this bill. On that side, the Indian Health Service would have a $500,000 increase this very new program, new program this year, bring it to 5.5 million for that work that we've heard described here. Level funding for dia de at 15 million and for DOJ on their work on the Kevin avantis law. And it was God it was for that peer reviewed Alzheimer's research program. In the new Congress, several bills have been introduced. Some have been reintroduced and quickly go through those. There was a reference by Dr. RUBIN our last meeting to the comprehensive care for Alzheimer's act that's now introduced into Congress and off to a good start in both chambers on a bipartisan basis to ask Center for Medicare and Medicaid Innovation CMMI to implement Dementia Care Management models to customer effectiveness. Also the equity and neuroscience of Alzheimers clinical trials or enact Act has been introduced now for the first time in the house in the Senate. And it's really addresses and

complements, I would say the work that we heard described by Dr. Barnard by outreach underserved communities, and enhancing diversity of clinical trial staff and reducing participation burden. And then two bills that have been reintroduced the highlight. One is the Alzheimer's caregiver support Act, which provides grant grants for training and support services for families and unpaid caregivers to ACL, at least a 2% 10% excuse me that grant funding must go to underserved communities. And then the change Act has been reintroduced. That has been spearheaded by us against Alzheimer's. that change is an acronym for concentrated high value Alzheimer's needs to get to the get to an end. And this has broad focus on encouraging Early Assessment and diagnosis of Alzheimer's through better utilization, the Welcome to Medicare initial exam and medical excusing Medicare annual wellness visits, and other important elements of that bill. And then finally, I'll round out with just mentioned to broader bills with quite a bit of implications for the work we often discuss. One is called referred to as cures 2.0. You may remember several years ago, the first cures bill. This is now a bipartisan effort and includes 77 initiatives such as funding or authorization of ARPA H, which is a new model that would be within NIH that would complement the work We've heard discussed in many different disease states, potentially Alzheimer's as well, if that were to be funded and implemented. And then also, a number of calls from the administration for work on community support infrastructures only could describe it now includes 400 billion for home and community based services HCBS to keep people in their homes and increase wages for the caregiver workforce was part of the American jobs plan to the administration. And then from the administration's American families plan. It was called for the creation of a national paid family and medical leave plan to ensure workers remain employed while caring for themselves or a loved one, which of course could include those with dementia. So that's a quick Roundup, I'll turn it back to you.

30:50

Thanks, Rob. I love all the acronyms. I don't know who comes up with them, but they're very creative and a skill that I don't have. So great work. Um, any quick questions for Rob? All right, hearing none, I will turn it over to Katie to introduce our next section of the agenda.

31:10

Thank you, Helen. And thank you, Rob, and Dr. Hotez, those are great updates and thinking about how we're making progress. And it takes more than one group, right, we need to learn to well, we already do this to work together. And that's how we're moving forward. I'm especially excited about the presentation of next the risk reduction recommendations and voting. Think about how in 2020, our counsel had three cross cutting recommendations. One of them was a focus on risk reduction. And so out of that recommendation, came the work of this ad hoc subcommittee. And so as we're listening to the presentation today, I just want to remind all of our council members that at the end of the presentation, there's going to be an opportunity for question and answer. But there's also going to be an opportunity for voting, and we're gonna

vote on two things. First, we're gonna vote on the opportunity for the permanency of this subcommittee with the council. And second is we'll vote on the recommendations from this ad hoc subcommittee. So I just want to prep everyone with that before the presentation. So were listening with our eagleeye equally. So now I get to turn it over to Lisa McGuire. Lisa is the lead epidemiologist at the CDC. She is leading the also risk disease and healthy aging program. She is a seller council member. And she has chaired this work with tenacity and collaboration, which I know she will share with all of us. So Lisa, I turn it over to you.

33:00

Great, thank you so much for that introduction, Katie, and also for setting the stage. And I'll wait a second for Helen to get our slides up.

33:16

Great, you can just go to the next slide, Helen. Well, Katie did an excellent job of cueing us up today and really helping us remember one of the reasons why there is this ad hoc committee for risk reduction. And so the objective that we were charged with, you can see here is to develop a national goal to reduce the burden of risk factors in order to prevent or delay onset of Alzheimer's disease and related dementia. You can see the rationale that we looked at. And we thought about, as we were considering this charge, this very, very hefty charge. And you can see some of the advances, there are advances in the science related to risk factors that we really needed to consider. We also wanted to think through some of those preclinical stages of the disease, as well as the heterogeneity of the pathologies, the cause dimension. We've heard quite a bit about that today. In our previous presentation. Next slide, please. Katie mentioned that we did this with a strong partnership. So as being charged with this activity, I reached out to my colleagues in the field I reached out to Matthew bomb guard from the Alzheimer's Association who is the vice president of health policy, as well as the principal investigator for the bold Public Health Center of Excellence on risk reduction. I also reached out to Kelly O'Brien, who is the executive director of brain health ecosystem project at the US, US against Alzheimer's and who's done a lot of work in this area as well. And I figured with their energy and tenacity, we could get anything done. So you will see the next slide please. This is the timeline that we were working under. So this timeline looks like we forgot some months. But this timeline really is a reflection of the bulk of the work that happened. So from the last, from the beginning of this year, we spent our time thinking about who else we wanted to invite to join us, and why and thinking about trying to create a very diverse subcommittee, not just based on race and ethnicity, but also on G geography. Also, different types of experience and expertise, trying to invite a variety of people from different fields. You can see a list of the other parts of the timeline. And I will go on to the next slide for the sake of time and show you who we selected for our subcommittee chairs, and also who the subcommittee chairs invited to join the workgroups. So our first subcommittee, we refer to it lovingly as Group A, which they investigated obesity, diet,

sleep and traumatic brain injury. So when I'm saying these names of the risk factors, they might have more a little bit. Over time, it may have changed from diet to another terminology that you'll see. So our sub committee chairs were jewel Marlon and Josh Chodos, and you can see the workgroup members who so eagerly volunteer to do a lot of work very quickly. The next slide shows us a workgroup B which examined physical activity, tobacco use and alcohol. It was co chair by Laurie weitzel, and Karolina coats. And you can see they had a little bit larger of workgroup membership. We allow each of the subcommittee chairs to invite as many people as they wanted, or as few people as they wanted, and to organize and run the group as they saw appropriate. Next slide.

37:12

Group C, was focused on social isolation, depression, hearing loss and cognitive activity. And that was Marilyn Elbert, and Joe, Tom were our gracious co chairs. And you can see the folks that who participated on their workgroup. The next slide is Group D. And this group looked at some heavy topics, they looked at hypertension, hyperlipidemia, and diabetes. And we had Rebecca gutsman. And Karthik, Schumacher, who also served as our co chairs of that subcommittee, and they also invited another great group of individuals to serve on their working group. So the way the next slide is showing us that we operated, we figured these are huge fields. There's lots of science involved, there's so many different facets and aspects that that a workgroup could explore and examine. And we wanted to help them stay focused on what was going to help us to make a recommendation and for the next steps. So we had a series of framing questions. So in other words, we wanted to know to what extent and they had a rating scale, did the potential risk or Protection Factor have strong evidence for from a population based perspective? Then the second thing we were interested in was did that factor was it right for public health action? So in other words, were there public health interventions and actions that are either currently available or could be available rather quickly? The third framing question is we wanted to find out if there was intervention wouldn't have a strong public health impact. And the fourth is we wanted to know if this risk factor protective factor if there was an intervention or an action that an individual healthcare provider or teams could actually recommend to their patients. Next slide, please. So at our we refer to as our outputs meeting, we had each of the groups report out on their findings after they had a couple months of workgroup meetings and deliberations. Next slide. And all of their outputs were numeric, and they were put into a scoring system. And you can see the output of the scoring system here. So what this is showing us here is the size of the circle is showing us the greatest. So that's potential for public health impact. And then we can see our axis so the top is looking at the strength of the evidence, and the left side is looking right for public Public health intervention. So in other words, those items that are up in that right hand quadrant are those that have the strongest evidence, most right for public health action, and the larger the circle is there's greater public health impact. The next slide is based on that meeting, we drafted a report on and with a recommendation and strategies that was set to the napal, Napa advisory council members and the CO chairs, all the subcommittee members, the workgroup members, then we had a list of researchers, professional organizations, other people out working in the field, we explicitly

sought tribal expertise, as well as a group of individuals had volunteer. So there was about 100 people total that had an opportunity to review and comment. And then we, as a group incorporated those comments. And I today am here talking about step three. We are where you're presenting our recommendations to the Advisory Council, and then we will submit a final report. I'm going to turn it over to my colleague Matthew bombard and my co steering committee chair. I think the next probably slide one or one more. Great. All right, Matthew.

41:27

Thank you very much, Lisa. And Hello, everybody. Glad to be with you today. So from the outputs meeting, that was the meeting with the word had the grid with all the colorful circles in the end the matrix from that output meeting. We Lisa Kelly, and I look to decide if we could make a recommendation to the council if there was sufficient evidence, and if there was sufficient public health action where we could make a recommendation to the council and if so, what that recommendation would be. So we decided, in fact that we could make a recommendation. And if you go to the next slide, please, we set our recommendation into kind of three tiers. The first is the goal. The second is, what a recommendation on what to focus on in order to address the goal. And third, what are the strategies to employ to achieve the goal. I'm going to talk to you for a few minutes about the first two the goal and the focus and then Kelly will come on and discuss recommendations on strategies. The next slide. So at the high level, we are recommending that a sixth goal be added to the national plan. But you see it there on the screen to reduce the burden of risk factors for Alzheimer's disease and related dementias. Have one comment on this. As many as you will know, the first goal includes the word prevent, prevent and effectively treat Alzheimer's by 2025. However, that goal as you know, is research focused in trying to find the research or investing in the research that will result in evidence to support Prevention's that evidence definitely feeds into our recommended Goal number six. But Goal number six is really about driving action then on those Prevention's or those risk factors. Next slide. So from that output meeting, once we decided that we could make a recommendation for moving forward, we identified 10 potential risk factors to recommend as the focus of the of the plans effort in order to achieve the goal. That's selection was based on those framing questions that we had posed to the workgroup that Lisa talked about. So we selected the 10 areas of focus, based on the strength of the scientific evidence, their rightness for public health action and the potential for impact both in the community at large and or in particular, diverse communities. And we wanted to set something aggressive to kind of tee up strong actions and strong strategies. And so we are recommending that to achieve the goal of reducing the burden of risk factors, that we reduce the prevalence of these potential risk factors by 15% by 2030. In my conversations with public health experts 15 a 15% decline is doable, but it is very aggressive and we did want to set an aggressive target.

44:54

Next slide.

44:55

So what are the 10 risk factors that we recommend is the area is a focus. You see them on the screen now of the first one has a slight typo and that's my fault. It should say unhealthy alcohol use not abuse. So it's unhealthy alcohol use, depression, diabetes, hearing loss, midlife hypertension, physical inactivity, poor diet quality, obesity, poor sleep quality sleep disorders, tobacco use and TBI. And as Lisa had mentioned, when the workgroups were looking at the potential risk factors that had been assigned to them, she noted that some of the wording has changed in these in these wording reflects what they have discovered in their view of the scientific evidence. So for example, on alcohol, it was it was recommended that it be changed to unhealthy alcohol use, as one example. So we also wanted to know, once we settled on these 10, we wanted to just kind of what does this mean for the adult population in America? What are we talking about here. And so if you go to the next slide, to give you an idea of the scope, we did an analysis of the 2009 data from the Behavioral Risk Factor Surveillance System, if you're not familiar with the brfss. That's a public health survey that's conducted every year in all states and territories supported by the CDC. And that data from 2019 showed that two thirds of American adults have at least one of these risk factors. But we also wanted to know what impact this could have if we were successful at addressing the risk factors and reducing the prevalence of the risk factors. So we made an assumption that all of these risk factors are causal, and not just correlative. And then we use the population attributable risk model, the next slide. And what we found was that an aggressive 15% per decade reduction, so that's slightly different than what what we recommended, or recommending as an aggressive effort to achieve a 15% reduction by 2030. But if you were to continue that aggressive 15% effort, the modeling assume that it would continue for a decade 15% reduction in the prevalence of these risk factors, it could result in as many as 1.2 million fewer people with Alzheimer's dementia in 2015. In 2050, sorry, again, two points. That's assuming these are causal in nature. And it assumes that there are no other changes that would cause a reduction in the prevalence, for example of therapy, that might that might reduce prevalence, but all other things being all other things being status quo. Based on the baseline projections of prevalence in 2050, as many as 1.2 million fewer people could have Alzheimer's dementia if we were successful at a very aggressive effort to address these risk factors. So with that, I will next slide into my last one. Thank you. And I'm going to turn it over. So we made the recommendation on the goal. And we've recommended the areas of focus, and the aggressive focus. So how do we go about doing that? What are the strategies, and for that, I'm going to turn it over to Kelly O'Brian.

48:30

Thanks, Matthew, and Helen, I'll just share my screen to make it easy here. Thank you. And I just wanted to before I dive into the strategies and how to get some of this done, I really want to

take a second to thank Matthew Vaughn garden and Dr. McGuire, it's been such a pleasure to work with you all. And despite the look of our three different logos on the slides, suffice it to say that I support mathy slides, and I'm pretty sure you support ours. And we're all together on this. So I'm just really had a great team effort and also wanted to mention Eva Jeffers from Lisa's team who was just instrumental in making this happen. And thank the Napa, you know, chairs and the Council for catalyzing this effort in the first place. It's a really big step after 10 years, I think there's an incredible accomplishment that Napa can claim that we're at this place where we're recommending an additional goal be added to the plan. So thank just thank you for all of your help and support and input. I'm gonna I know time is short. So I will probably talk really fast. I'm not going to read all of these things, you all have a copy of the recommendation. I'm just going to go through them at a very high level pretty quickly and comment on some of these. The the strategies were developed, really consistent with the structure of the original Napa plan, which included goals, strategies and tactics and the inputs on the strategies and tactics. Really We're directly from the workgroup members themselves. And, and also from the reviewers, more than 50 people commented on this. Now I know what it feels like to be inappropriate. But it was, you know, I said, not everything is in here, but hopefully the structure is is recommend is in place in a way and recommended in a way that can incorporate these things down the line. So, um, and one of the thing I will say is that the other cross cutting recommendation that the council made was around health equity last year, and that is reflected, I feel strongly together throughout all of this. In every effort, we tried to incorporate a health equity and the social social determinants of health throughout this throughout this recommendation. So there's four key strategies, identifying priorities and milestones, accelerating public health action, reducing risk and early intervention. And, of course, more research. The birth strategy, really does recommend that we wait, I'm going to go back for a second, identifying the priorities and milestones toward goal through a health equity framework, much in line with Dr. Hotez talks today about the bypass budget in the effort that naa goes through, and NIH goes through to develop clear milestones with a line of sight to budget. That is the model that we had, I think in mind, when we're thinking about how do we keep ourselves on track? How would the council continue to to track progress? The first recommendation is that the risk reduction subcommittee should be formalized within the Advisory Council to help Shepherd this work through. And again, similar to previous efforts through the the Napa plan that a summit should be convened, that would really focus not only on some of the barriers and challenges for marginalized communities, but engage diverse stakeholders, one of the things that the commenters and the reviewers, I think it was one of the most frequent comments was about the structure and about how Napa was intended to be a national plan, not just a federal plan and how important it is. And this is probably not relevant just for the risk reduction work, but for Napa itself, to incorporate input from private sector and other organizations outside of the federal government. So that's a tough cookie, but others have done it. And that is reflected here in this recommendation that we need to find a way to engage diverse stakeholders in this process. And we also recommend that federal agencies should identify and coordinate implement strategies and report on these within the national plan. And note where there are gaps. One of the things that I'll highlight here is just again, it is difficult through the process, now to identify a line of sight to budget. So we, the council members, I mean, the risk reduction, subcommittee members recommended that there be a process to identify the amounts proposed for advancing the Napa

recommendations in the federal budget, some line of sight to enable transparency around how the Napa council recommendations and work are being implemented through the federal budget process and the resources that are needed.

53:26

Strategy B is focused on public health and by public health. The subcommittee addressed this broadly, not just CDC, although CDC is central, but thinking also about state and local community based in home and abroad array of stakeholders that come to play when we talk about accelerating public health action with a focus again on addressing those interventions that could greatly impact those at greatest risk. I think there's broad agreement from the subcommittee and the world at this point that public health infrastructure needs to be strengthened. So this is reiterated here. And again, that the social determinants of health are critical to this process and should be a part of all of these discussions. Again, targeting communities of greatest need both with the highest prevalence of risk factors low longevity rates, high prevalence of ADR D. There is a good amount of data out there. I'm proud that us against Alzheimer's has a national Alzheimer's disease index where we began to track this by place but others exist. So this is definitely possible, and also that it should be a collaborative process. There are other federal initiatives and public private initiatives such as Million Hearts and diabetes prevention programs that could be leveraged in both directions to help advance these recommendations. And finally in the public health at CDC and has already done a great deal of work. In this they have laid the track and many of their recommendations in the roadmap for this and also for Indian Country reflect a lot of the recommendations here. And so we want to make sure that these would be aligned with any actions, strategy see clinical care. Often when we think about public health, and community based in our interventions, we're forgetting about what can happen in the healthcare system itself. And many of the recommendations from workgroup members reflected on comments. That could be improvements that could be made in the health care system. So um, both inside and outside of the federal government, but particularly CMS hersa. The VA, I just, the subcommittee recommends clearly that they take a more comprehensive look to identifying opportunities to reduce risk, particularly by looking at the Medicare annual wellness visit, improving uptake of that visit, thinking about how to do more frequent and improved clinical screenings, and identifying existing benefits already related to risk factors that could be supported around the risk factors that Matthew reviewed, and potentially any gaps that exists in that coverage. improving access to care, other subcommittees have mentioned this meeting to accelerate strategies to improve access to primary care, there's an opportunity for pilots and CMMI and probably other agencies as well. workforce training, the Milken report most recently clearly outlined the workforce shortages and needs that we have to improve primary care in particular, and then coverage gaps. And this is a recommendation to Congress to really look at some of the areas where we have coverage gaps, I understand they're considering hearing right now. Also, mental health, a depression and unhealthy alcohol use are two areas where Medicare's coverage has not kept track with the private sector and encourage Congress to take a look at that. And finally, strategy D. NET last, but of course, never least is research, we always need more research. And Dr. Hood has outlined, as others have

Dr. Barnard so many good things that are already happening. Much of this, I'm sure is reflected in this recommendation. We all agree that research needs to be advanced through an equity and inclusion framework. And that we need more to identify more clearly the causal pathway for a lot of these risk factors as well as intervention. And some of the interconnectedness of the risk factors and co occurring disorders that we all know happen. Finally, that CDC, or an also, I should say, AHRQ, together should think about ongoing updates to update the list of key risk factors. And focus on that are the efforts focusing the efforts to achieve this goal and a modify as additional research becomes available. And that is a very speedy run through of those recommendations. And again, I just I want to say thank you, to everyone for the opportunity to present this and participate in this really gratifying process,

58:19

energy and enthusiasm behind the steering committee and committee. It amazed me as we were reaching out to people with this very ambitious timeline. How many people said yes, I mean, it was almost we were probably at 90, some percent of people agreed to help us because they thought this was extremely important. And then the last thing I will say is a big, big shout out to Eva Jeffers, who is a fellow on my team, who really kept everybody going strong and straight and kept us organized. So thank you, I know you're watching.

58:59

Well, this is a really exciting step forward among the people who said yes, Lisa, you were the first. So thank you for saying yes. When Katie and I asked you to consider leading this process, you've certainly brought more than we anticipated the beginning and you've done it with extraordinary success. So congratulations. I'm personally thrilled to see this six goal, the national plan be considered for adoption by the Council. You know, I also want to thank Matthew and Kelly, who I know we're partners in crime with you and the scores of other people that you enlisted that who you mentioned, you know, all of you really accomplished a huge amount of work in short order, which now expect this to be a foundation for the Advisory Council in the future. You know, I think all of us in the field realize the risk factor mitigation is undoubtedly going to be more and more important as the Science Advances and it's going to need to continue to advance and particularly it's going to be important to have structure so that

Part 4

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scientific advances can be made actionable. So clearly sciences illuminating our understanding of Alzheimer disease and related diseases as chronic diseases with a life course full of behavior and lifestyle choices, exposures, the medical comorbidities, we know well, such as hypertension, the critical social determinants of health, for which we still have a lot to learn, and other factors that may be modifiable to reduce the risk of disease and possibly even bring forth prevention. Now, so again, just thank you all for really incredible work. And with that, we have ample time for questions and comments from the council to to the three of you.

00:45

Ellen, I have a few points if it's okay. Please go ahead Sunday. So thank you, Lisa, Matthew, and Kelly, for your great work on this risk reduction strategies. I just want to thank you again, because it makes us realize that, you know, within the clinical care, long term care and support services and the research arm, there's really a gap in thinking about public health initiatives. So not everyone's going to get into the physician or the clinician into the clinic setting to get those preventive measures addressed. And so having a public health initiative to really fill that important gap is really important. So thank you for addressing that. And I think a few points to that you mentioned, you know, working across You know, there are a lot of overlapping themes, of course, that we see the clinical care the need for research, I think, working with the other subcommittees and trying to think about what are the cross cutting themes like health equity, social determinants of health? What are the things that should be done in a Babak set public health sector, what should be done in the clinic, to helping to work across federal agencies, private sector, I think there's another important point your team brought up that we need to have a collaboration across these groups work across public health clinical in the cross cutting research so that we're really looking at what are the actionable items? What are the what's the

science behind implementation sector hood is spread out early earlier this week, and really good, not just educational programs put out there but effective educational programs that change practice? So it's really when applied, you're working bringing this to the forefront today.

02:32

always hard to know how to bond but I'll just add to what Cindy said, Cindy, I think you you read my mind and and but added in a more articulate way. So I really agree this spectacular way of pulling together a very disparate set of data. And really, there are implications, not just from from the public health point of view, which of course, are a really, really strong, but drilling down to every little bit. So, you know, how does hypertension synergize or not with the ongoing pathophysiology, other neural system dysfunction disorders and so forth. And so I think it really leads to enormous opportunities to reframe some of the questions that have been in sort of little, you know, there's an amyloid lab and a tau lab and a vascular lab and or whatever lab and really think about it in a much more cross cutting setting, which is Napa at its finest. So, you know, please thank you and the whole team, really spectacular job

03:54

of it, if I may ask a question. It looks to me like there was a decision made to focus specifically on Alzheimer's disease. Is that true? I mean, I could see the relevance of much of the work you all presented to vascular dementia. But was there a conscious focusing of this recommendation on Alzheimer's disease? Matthew, do you want to take that one?

04:20

Yes, sir. So Deborah, the answer is actually no. One of the things that we wanted to really focus on and recognize at the very outset is the the different pathologies that result in dementia. I think, I think Lisa mentioned that is kind of one of our core rationales at the very beginning of the process was not to focus just on Alzheimer's. And in fact, the the evidence, for example, in traumatic brain injury is actually about the strongest evidence is actually about other forms in dimension on actually Alzheimer's. And of course, you noted so many of the risk factors Are vascular related. And so there's a very strong connection to vascular dementia. The one the one thing toward, you know, toward in my presentation where he's talking about the impact, or the potential impact of this on what could could happen if we were really aggressive in addressing these risk factors that was limited to Alzheimer's because the model, we don't have prevalence estimates, and we don't have prevalence projections of other forms of dementia out to 2050. And so when we did the modeling to try to figure out what potential if we were really, really successful at this, what would the potential be in terms of reducing prevalence of out in mid century, we were unfortunately limited in that model to Alzheimer's dementia because of what

data exists in terms of prevalence. But in terms of the work up to that point. Nobody else was nobody else really ever talked about Alzheimer's, and only Alzheimer's and it was always about what are the there are multiple pathologies here and we we need to make sure that that's taken into account.

06:09

Right. Thank you, Matthew. Older Do you have your hand up? So I want to thank the group for work on this project. So ni NDS has really been interested in this for quite a while we do have a public health campaign that we've been trying to get out there for the last couple of years, which has its focus most recently on midlife, hypertension and African American males, because that's actually the risk group that seems to be most is disproportionately affected by the bad effects of hypertension on brain health and

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00:00

Which has evidence of Alzheimer's and vascular disease combined. It's it's probably in the elderly, the more common pathology is a mixed pathology as opposed to one or the other. But the evidence, as you rightly pointed out, is strongest for midlife hypertension, which is an area

that is never really been pushed very much. Most of the work on hypertension has been to try to get people with 65 to get their blood pressure control, and it's much harder to go for people in midlife. So it's a real challenge, but I think it's very important. And with that being said, Sprint trial where we did do you know, aggressive blood pressure control, reduce cognitive impairment. And people who were elderly too. So it's important to just don't hypertension is never good for your brain. And, but but I get midlife. hypertension, I think is really important. But it's actually very challenging. So I just compliment the folks on the work. And I put some, some of the references in the chat if people want to look at the ad some of the public information campaigns that we have going on, always happy to work with others to get the word out. Thank you for that.

01:34

Yeah, thanks. I'll just comment on that briefly and say, I think that's one of the perfect opportunities for collaboration. And AARP just came out with a wonderful study about stigma that showed, you know that people really would take some of these lifestyle changes and make some behavioral changes if they thought it might help their cognition. I think there's just an incredible opportunity to sort of leverage the work that you all are doing and others are doing at earlier ages and across different conditions towards mitigating dementia. So thanks for that. That's a really good present. It's true.

02:11

Yes. And I think what's the point, the point you made about you call that midlife hypertension, because we we specifically had that parameter put on it. But almost all of these are life course.

02:29

Risk factors and, and well, midlife. hypertension is a particular issue, I think is from a public health standpoint, not something we ought to be waiting, whether it's physical activity, or diet, or sleep or any of the others, we should not be waiting until people are 65 from a public health perspective to be dressing these respecters that they really ought to be addressed across the life course. Good point. Yeah. Other comments, questions?

03:16

Okay, well, hearing none, thank you, again, Lisa, Matt, and Kelly, for really extraordinary work. That point, I guess we'll wrap things up and let us vote.

03:27

I just have to pause for a moment and talk about how our agenda today has included information about risk reduction, and also potential treatments. And how representative is that of the work, the breadth and the depth of the work that the council has done? working with our partners as well. So it just wanted to say thank you all for the work and the presentation today. And I was just I'm just really inspired by acknowledging that. So now we get to move forward to some action. I want to remind everyone that only non federal members of the council are able to vote. So that's good as we embark on all our voting for today. And Helen, can we talk about how a council member can can mark their vote? Should it be in the chat?

04:25

Should it be verbal? Should it be with a raised hand? Did we decide that? That is an excellent question, because we've done this before and I cannot recall what we did. I think maybe a raised hand if everyone can find the raised hand

04:42

emoji next to your name. Right, so we'd be under reactions. So folks see that reaction face at the bottom of their zoom screen and then there is a raise hand button. So I would like to make a motion to permanently accept the risk reduction subcommittee as a subcommittee of the Napa Advisory Council. And so if you're in favor of that, you can raise your hand.

05:25

And I will be happy to second the motion before we go. Just That's right,

05:28

Alan, I forgot about the second. Thank you very much. Thank you,

05:37

Brad, did you want to make a comment? Yeah, I was just willing to second it. So Brad thirds, it okay. Yeah, no, we've we've been in too many committee meetings out.

05:52

And Helen, you can let us know. When it's been sufficiently tallied.

06:01

Yes, everyone who's voting please vote if you would like. Okay,

06:14

I think we're good. So then you can go back to the reactions button and lower your hand. And I would like to make a motion to accept the risk reduction recommendations. I will second that. Okay. And so then Council, non Federal Council members may vote through the raised hand function. Okay, that's it. Okay, great. So, Ellen, I'd love to turn it back to

07:08

you. Okay. Well, thank you, Katie, and council members for that. So our next phase will be reviewing the rest of the recommendations. And they just wanted to just make a comment. You know, following on the heels of the exciting progress we just had saw with the risk reduction committee, we need to remind ourselves as I know, all of you know that there are millions of people that are currently affected by Alzheimer's disease and the entire spectrum of related disorders. And, and moreover, we have to remind ourselves that there are nearly 50 million people Americans alone today who have Alzheimer disease pathology, which is in the silent preclinical phase, not yet causing symptoms. So clearly, the research the translation into the clinic and into public health practice needs to be aggressive. And I know all of you on this Advisory Committee, I wholeheartedly agree. We've heard many times on this committee that there are also urgent needs to ensure better practices care and support for those who are symptomatic. And were enthusiastic about the recommendations ahead, to make sure that we're comprehensive in our perspectives on on all aspects of dementia. Moreover, we're all Cognizant as we reminded ourselves about the challenges ahead to still prepare, transform and operationalize the clinical practices that are going to be necessary to enable early recognition, diagnosis and deliver the new generation of disease modifying treatments that is almost certainly head, as well as the behavioral and lifestyle modifications that are needed that we just heard about. And to make sure that all of these actions in the future are, are actionable for all,

including the underserved segments of society that we heard about from Dr. Bernard and who are most of the highest risk. So it's that I'm doing this over to our snowboard here to review commendations. Again, thank you for being bold and aggressive. The advice that we encourage to provide the Brad with that, let me turn it back over to you to review the research subcommittee recommendation.

09:21

Helen, I'm hoping you have the slides. Okay, and there's noise in the background. I don't know if

09:41

one of our support personnel, they could go on mute. I just tried to meet them. So we'll see if that worked. Thank you, Katie.

09:55

Great. So we have the you know, several page document that outlines in detail their research recommendations. What I'd like to do now is just spend a few minutes identifying sort of the high end themes that are important looking forward into this next year, and then in the next several years, of course, and then open for some discussion. So the themes are listed here. The first is to encourage a robust medical and, and holistic strategy. As Katie pointed out, this is very much aligned with the Napa mission as a whole, to join the both federal and non federal strategies for biomedical research, as well as keeping a close eye on what the societal needs are. His second recommendation is to encourage Congress to continue its generous support of these programs, given the urgent public health needs, and the devastating effects of this disease. Right. Would you like me to fast forward to the slides with the full recommendations? Are you going to go into more detail? No, I'll go into some more detail with each the site I just want to give an overview here. Thank you. The third is a consistent terminology. Even in the presentations today, we heard the term Alzheimer disease used to connote all dementia in you know, no matter the underlying pathophysiology, versus very specific plaque, untangled driven disorders of consciousness and, and even preclinical states in which those legions don't lead. And we need to make sure that when we're communicating with each other, that we're using clear terminology, there's, in fact, a committee to it to try to sort that out and make the terminology clearer, and more easy to communicate. We need to continue to develop our efforts to recruit people with the highest risk for research. The discussion this morning on cancer research, I thought was fascinating. I do believe that the cancer field is a little bit ahead of us in terms of learning how to recruit from the community, individuals to participate, both both clinicians and patients to participate in ongoing trials. Now, we're a little bit behind but but moving forward in that direction. So ethical data sharing, I think it goes to that's saying that, that the community as

a whole benefits that from having access to data, although clearly there are limitations in terms of privacy, and so forth, to the extent that we can encourage data sharing, and do so in a fair way, benefits everyone. And finally, an inclusive role for the dementia community. The participation of those individuals who are at risk for developing dementia, and in fact, are already having some symptoms from the Alzheimer's and related disorders, critical to keep that in mind and to hear their voices and to continue to engage them as research programs go forward. And so those are the broad themes. And now how and if we can move on slide by slide to the individual recommendations. So the first recommendation is to encourage a sense of urgency about providing a robust, comprehensive, collaborative and transformative scientific roadmap. And here This suggests listening to the summit listening to the research community and re evaluate each year. as we learn more and more, perhaps, change the goals slightly or, or as some milestones are achieved, move on to the openings that that that are created from that research.

14:23

Next slide, please. The second recommendation is to remain to keep in front of Congress, the urgent need to increase annual federal research funding sufficient to meet the goals because of the devastating nature of this disorder. And in a new edition this year, that the analysis should explicitly include a response to other public health emergencies and disasters. That especially impacts people with dementia as we so sad learned with COVID-19 taking its toll on individuals in long term care facilities. Next slide, please. The third is emphasis, to have a standardization of terminology across multiple fields. And across both clinical and preclinical types of disease. This is important to make sure that we're communicating with each other, clearly, that the research goals are clearly articulated. And that we're able to not only within the research community, but also translating that the clinical community and the long term care community, and perhaps most importantly, to the public, and to our patients. Exactly what what we think is going on. And right now there is, in fact, a wide variety of the you use of commonly used terms like Alzheimers disease, and we just need to be able to do better than that. And there's been a lot of progress in this in the last year. I'm optimistic that in the coming year, we'll be able to have some recommendations on these along these lines. Next slide, please.

16:20

She's been

16:23

a major emphasis by all federal agencies involved, the national plan should be enhancement for recruitment efforts for research involving those with or at least or at risk of developing

Alzheimer's disease. And here the the nuance that's new this year, is the emphasis on those individuals who are at risk of developing a dementing illness. Next slide, please. The next is is again, an emphasis on strategy and infrastructure to increase open sharing of access to and utilization of both research data and research samples. The NIH certainly taking the lead in this, along with the ni NDS, creating neuro biobank, the altarum C's research centers, multiple programs, the center in Indiana and so forth. But more has to be done to look for gaps in tissue availability, and biomarker sample availability, how to link those to the relevant clinical data, while at the same time being very, very conscious of the privacy issues that are involved in order to make sure that consent, for example, is obtained in in the appropriate way. Next slide, please. And finally, that all Alzheimer and Alzheimer disease related disease research should make an attempt to engage persons living with diseases, their families and caregivers, both in research and on decision making, and care planning. And that we believe that that emphasis on this is renewed this year, and important to communicate across the research community, as well as to our clinical colleagues and to the long term care and planning groups. So those are the top line six recommendations that the research committee generated. I want to thank my colleagues in the committee who have reviewed each of these discussed in the multiple meetings, and bring them forward for your consideration.

18:50

Thank you.

18:57

Thank you, Brad, that was great. I'd like to offer the opportunity for any questions that council members may have at this time. So Brad was able to prevent present the CI prevention on the brain, it's great, you know, was able to present for the research subcommittee, and then we'll have clinical care and long term services and supports and so we want to just allow a q&a if necessary, in between each one before our voting.

19:39

If there are no questions and if something comes to your mind, you know, put it in the chat or feel free to ask it after one of the next presentations. So if there are no questions, then we will move forward. I'll turn it over to rob Aggie for our clinical care recommendations. Thank you. Alright,

20:07

so in terms of themes, let me give you a big picture from this slide. And that is the, for the first four there are listed that we'll go through in a bit more detail in just a moment. They're largely the same as last year, as we reviewed that we made some minor changes. But fundamentally, we thought they merited inclusion, essentially, as they were for another year as a recommendation. The Advisory Council, there's one other last year's five that we dropped, but for good reasons we were came to believe that it is now really well, institutionally ingrained, that was a reference to the they care summit of the three summit rotation by NIH and FDA. And the recommendation just to refresh memories was basically about making sure that recommendations and presentations coming out of that summit were reflected then in terms of appropriate agendas. And convinced that that was taking place, we decided that we could remove that recommendation at this point. And nearby, have the focus more on some other issues that includes those first four repeated, then the final one will tie when just a moment, but just to highlight it here is a new brand new recommendation. So moving ahead to the next slide. The first one focuses on as you see educating the public about early detection, diagnosis of ADHD, person centered and family centered care planning and the importance of in ways to enter into research. So combines a number of different issues here, many of which were already discussed today and presentations, which to get confirmation of the track the committee was on with this recommendation continued this year. Moving on to the second recommendation, and this one is to enhance the current and future workforce through education to better address the needs of persons living with ad and ad rd, and their caregivers. So again, now, this workforce emphasis continues across a broad spectrum of issues under that category. Moving ahead, your recommendation three. So this is about essentially about practice guidelines. If I were to summarize it in a few words this way, so professional groups should determine a process for those groups and non federal stakeholder holders to reach consensus on definitions of the best practices, including the integration of new biomarkers for comprehensive care per ad and ad rd at all disease stages. Again, some things that are enduring for years and some that are especially important in terms of the presentations we started with today, such as integration of new biomarkers, as we look to the future. recognition for this is to encourage further development, evaluation and use of health care models for ad rd. Ad slash ad rd, that align performance measures the experience of care by persons living with AD AD rd and their caregivers and with payment. And so this amplifies the one panel that we had at the most recent meeting where we focused on comprehensive care models and our encouragement as a committee to move those into evaluation. And finally, recommendation five. This is focused on all this the first panel from our most recent meeting that you may recall, I'm sure you do focused on the two year waiting period for younger individuals living with Alzheimer's and related dementias and who have been deemed eligible for Social Security Disability Insurance SSDI to have access to Medicare. Now at this point with as we thought about the most productive way forward is to focus on the next building block of what we thought was needed to advance this conversation knowing that we require legislative action. And knowing that the Advisory Council can of course update this recommendations, we make progress on these points. And so what we embraced was the recommendations by Leslie freed in her presentation to us at the last meeting, where she met we agreed that the emphasis should be on building the knowledge the data that we need to understand the case for doing so since we know it's a it's a heavy left and and do you use that then to build from there in terms of gain momentum for this proposal to be

addressed legislatively. So the next slide like Just as Brad did, thank you very much all the members who contributed to this non federal partners and federal partners like

25:08

Matthew.

25:13

Thank you, Rob. That was great. Does anyone have any questions for Rob or the clinical care subcommittee? Deborah, I see are unmuted. Okay. Well, with that, I will turn it over to Deborah. The chair of our long term services and support subcommittee, Dr. Deborah cherry.

25:50

Thank you, Katie. And Helen, if you could bring up the slides. Appreciate it. I'm going to note that consideration of long term services and supports is often the last thing we discuss as we go through our Napa recommendations. But of course, that doesn't mean that they're not essential. These are the services that family say they need in order to carry on. So the recommendations that we are presenting seeks to strengthen our nation's long term services and supports system in a manner that is culturally competent, and that responds to both the person's needs. And those are the family. Next slide, please. These are our themes. I'm not going to cover them here because I think each one will come up as we discuss our recommendations. So let's go to the next slide. Recommendation one addresses the need to expand home and community based services particularly for people living with ADR D who are marginalized, historically underserved, are disproportionately affected by dementia. And our committee found four ways to expand access and utilization when addressed them in this year's recommendations. This is arguably our most critical set of recommendations. So I'm going to elaborate the most here. We're going to start with expanding access through Medicaid, which as you know, is our primary public vehicle for funding long term services and supports, but it doesn't serve the middle class, and it has a bias towards institutional care. The 2021 recommendations as Congress to make home community based services an entitlement under Medicare, bypassing appropriate legislation, and rebalancing Medicaid funding at the federal and the state level. The second part of this recommendation is looking at Medicare, which can also expand access to home community based services. We recommend that CMS monitor Medicare Advantage health plans, encouraging them to offer benefits that meet the needs of people of diverse people living with different forms of dementia, and addressing social determinants of health. We also asked Congress to authorize CMS to implement successful models of dementia care that were already proven through the CMS Innovation Center to be impactful. Then beyond Medicaid and Medicare, there are other federally supported long term services and supports programs for

example, and I'm just selecting a few of the many in our recommendations. We recommend that Congress increased funding for the administration on Community Living Alzheimer's disease program initiative 250 million dollars. And we also ask the funding for Older Americans Act programs be doubled prioritizing pro services for people living with ADR D and for caregivers. Finally, they protect financial security of people living with EDR D and their caregivers. We recommend and this is an audacious recommendation, but we recommend that building on past efforts and on actuarial data. Congress should pass legislation to finance long term services and supports. Congress should also expand the Family Leave Act. And together with States Congress should make tax credits, long term care savings accounts, and other options available to the American public. No one should need to impoverish themselves in order to access long term services and supports that they need. On to the next slide, please.

29:59

Recommendations to focus on ensuring that people living with ADR D receive clinical care that's coordinated with home and community based supports. This means that clinical settings will be able to design person and family centered care plans. It means that they will be able to identify a caregiver where appropriate, and assess that caregivers needs and to provide or arrange for culturally competent disease education and home and community based supports for people living with these conditions and their families. settings should include providers that reflect the racial and ethnic diversity of the community served much as we heard, was a move in the research environment. We also agree that it should be a direction for staffing in long term services and supports. Finally, we would like to encourage CMS to formulate or adopt quality measures that encourage healthcare systems to implement these recommendations. Quality quality measures can drive improvements in care. Next slide, please. Record recommendation three focuses on quality and on making long term services and supports more person and family centered. We ask that the department of health and human services provide training and guidance on the development of person and family care plans that use a shared decision making process to engage those concerned in setting the plan and have plans that address social determinants of health. We also asked federal, state and private its entities to expand the availability of evidence supported dementia interventions. While the level of evidence supporting these interventions may not yet be as high as the level of evidence that is used for pharmacological clinical trials, many of these interventions demonstrate impact on outcomes meaningful to people living with a dr. D and their caregivers. They need to be made more available. Next slide please. Recommendation four deals with workforce development. numerous reports have documented the shortage of dimension capable long term services and supports workers recognizing that high staff turnover and its contribution has a contribution on to quality of care experienced by the people that this Advisory Council cares about. to better prepare for increasing numbers of people who will be needing long term services and supports Congress, federal agencies, states and others should recognize that workforce compensation, recruitment, retention, and training are challenges that should be addressed. Specifically, we recommend that Congress allocate funding to federal entities for the training of the long term care workforce in culturally competent dementia care. We also asked corsets to create a lot of

workgroup that better defines the role of dementia care managers. They're the staff who frequently connect people to long term services and supports. And we asked that Congress address the root causes of staff turnover in long term services and supports including this workforces need for living wages for health and for family care benefits and for paid time off. Next slide please. Recommendation five addresses behavioral and psychological symptoms of Alzheimer's disease and related dementias across care settings. The Committee recommends that federal agencies provide funding to their grantees to train care providers to deliver evidence informed non pharmacological interventions that are dementia capable and culturally informed. Next slide, please. Finally, recommendation number six seeks to improve and expand long term services and supports emergency preparedness so that these services can better address the needs of the ADR D community.

34:43

As some of my colleagues have mentioned, the covid 19 pandemic has highlighted the vulnerability of our population, especially when they are low income, socially isolated, or living in congregate. settings. The people for whom we advocate are especially at risk during emergency events. This year, the long term services and supports committee added a set of recommendations to support people living with ADR D during such events. And these include recommendations that FEMA, in coordination with the Department of Health and Human Services and the Department of Justice develop specialized training for dementia care for emergency personnel. We also ask that the Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response developed protocols for use by long term services and supports providers for when a caregiver becomes unavailable during an emergency. And finally, we accept federal agencies do provide dementia capable emergency preparedness training for the community, for caregivers, and for health care providers. Last slide, please. I really want to thank my committee, this committee for its passion and for its contributions to the recommendations. I ask for your forgiveness, if the necessity for being quick, cause me to condense something that you care about deeply and lead to admissions. It's been a pleasure to work with you all for these past four years. Thank you.

36:33

It is. It is worth noting here that Deborah has had the leadership position of Chair of the ltss subcommittee for all four years of her council tenure. And Deborah, that is tremendous. Thank you for your leadership. appreciate it very much. Does anyone have any questions related to the ltss recommendations?

37:11

Matt is celebrating I love that. I want to take a moment and thank all of the subcommittee chairs and members for working to incorporate the cross cutting recommendations of our 2020 recommendations related to emergency preparedness, health equity and risk reduction into this year's recommendations. I think that that was incredibly important. And you all did that beautifully. If there are no further comments or questions, then I would like to make a motion to vote to adopt all of the recommendations put forth by the research, clinical care and ltss subcommittee.

38:05

I'm delighted to second that motion, Katie. Also reminder that the voting is for the non federal members.

38:13

That's right, non Federal Council members fully. Okay, the vote is recorded. Okay, thank you, everyone. So, at this time, I would like to acknowledge the council members who will be rotating off of the council this year, making way for new voices and fresh perspectives to work towards meeting the goals of the national Alzheimer's plan. I will try not to be emotional in my remarks. But I am included in this group of council members whose appointment is coming to a close. Many of you know that I represent the caregiver seat on our council. I came to this position because of loss in my life. My husband Michael died at the age of 33. After living with behavioral variant, Frontotemporal dementia. My father was diagnosed with Alzheimer's disease. At the age of 5912 years later, I continued to be his caregiver. becoming a member of the Council and serving as counsel co chair has allowed me to be a voice in honor of my late husband and advocate in support of my dad and an ally in support of all families living life with dementia today. When FTD tried to have the last word in Mike's life and in our family's story, my role on the council played a big part in my resilience to turn the page and start a new chapter. I am grateful for this opportunity and the support that I have received from my fellow council members, Helen, Emma, and all SV staff, and my director at massgeneral, Dr. Brad Dickerson to fully engage in this critical work. When I was 16 years old, my mother gave me a book as a Christmas gift. And inside she wrote an inscription on the cover, Katie, Sunday, you'll have stories of your own to collect that will give you inspiration, write them down, we all need to be reminded that love is out there. Love mom. My journey to the council has been an unexpected love story in my life. Through this role, I have been inspired by the love stories of others, authentic voices of persons living with a diagnosis and caregivers, friends and loved ones who wished for a different conclusion. families who are waiting for the final pages to be written in a new way. I would like to say to every council member here to the today to those who have come before us and those who will come next, know that you are the authors of future family stories. There is no one individual or entity that will solve the problem of Alzheimer's and related dementia. Our collective work is what builds hope that the cure of tomorrow is not so far from

the care of today. Keep being tenacious. Let love be the gas in your tank to move forward. Your work is making a difference.

42:02

So that's my message, I decided to take a breath. so appreciative that everyone here. And now I would love to take the opportunity to recognize the wonderful council members who are also in this rotation to rotate off to allow that space. I'm gonna start with Deborah cherry. So Dr. Cherry is currently the executive vice president of Alzheimer's Greater Los Angeles. For more than 25 years, she's been an effective advocate for persons with dementia and their families. The thing that I will remember the most Deborah about working with you is your consistent message. That while we of course, as professionals and council members must be realistic. We also need to be aspirational. Use the word audacious. Today, there's nothing audacious about saying that people should get what they need to care for themselves and their loved ones. And so I want to thank you for encouraging me to be aspirational. And allow you to take a moment to say something if you would like

43:21

I think You took the words right out of my mind. And if I were going to leave any kind of legacy to this group, I think that that

43:31

blend of

43:32

strategy and aspiration is critical. If you only are strategic and you don't have the aspirational part to what you're doing in mind. You missed the heart of reaching the goals of the families, we want to help if you're only aspirational. You sort of miss all opportunity and you fall flat. So if I leave with any words, aspirational, strategic advocacy is where it's at. And it's been a pleasure to work with all of you.

44:05

Thank you.

44:09

Can someone please write that down? aspirational, aspirational, strategic advocacy. It's recorded, Katie. Thank you, Alan. I'm going to recognize you last. Okay. Rob Aggie is the Alzheimer's Association chief public policy officer and executive vice president government affairs and leads the associations Public Policy Division based in Washington, or maybe from his home. He's been the chair of our clinical care subcommittee these past two years. And Rob, I would say that the takeaway that I have from working with you is so often when you would talk to us about how we could take Action, that, of course, there were so many things that we could recommend or suggest as good things to be thinking about. But what could we suggest that had real traction to make movement? So I want to thank you for that message. And allow us the opportunity to say a few words, if you would, like.

45:23

Thank you, I'll pick up the opportunity to do that. But as Deborah said, thank you so much for you open this session. And that leads me to thanking all the people, as I've heard already said today, who've commented, taking the time to comment publicly, to the committee over the years has been so important to us. And to my non federal members been great working with you and to the federal members. You've been out in a long time, many of you some of you have come in with your responsibilities. Some of you have been here for I think I'm counting now like a month and a half straight of meetings. Oh, at 40 some. So it's a big investment. And I I've thought about Helen here at the start. And some names some of us might remember like Don molds at HHS and Jeff Crowley as little nostalgic this morning. Thank you by the 10 year anniversary happens to be this year of his work and how this has been a vehicle to accomplish many great things. So thank you all who are continuing on and looking forward to seeing the work you do.

46:29

That's wonderful. Rob, thank you so much. Becky Kurtz currently directs the aging and independent services group within the Atlanta Regional Commission, and is widely regarded as one of the most innovative Area Agencies on Aging in the nation. It's great tackling previous previously, she led the long term o budman. program both at the state and federal levels, and provided legal services to low income elders. In each of these roles, Miss Kurtz has served and advocated for individuals living with dementia, their families, and caregivers. Becky, I want to say that being able to work with you on the long term services and support subcommittee has given me so much information about what we could do, how to navigate the challenges of learning about government policy, and how our voice could be really effective to make movement in those areas. So I want to thank you, I feel like I always learned something from

you every time we interacted. And I want to give you the opportunity to say a few words, if you would like.

47:40

I'd love to Katie, thank you. And thanks to everybody. Both the federal members, the non federal members and the public member individuals who've commented for your commitment to this work. You each of you bring heart and mind and soul to this work. And it's been just an honor to be on this group. I want to I want to say especially how much I appreciate HHS is a willingness to have an area agency on aging director on this group. We deal with dementia nonstop, whether it's in Home Services, or caregiver support, or providing social determinants of health, meeting those needs, we're doing it non stop. And it's the first time that an area agency on aging director was part of this Napa council when I came so I was thrilled that HHS saw that opportunity. And whether it's you Older Americans Act or whether it's through Medicaid funding or whether it's even connecting people to private pace or resources. We're a piece of that puzzle at the local level. So really pleased to represent Area Agencies on Aging in this work, as well as my previous work with the Ombudsman Program and the ability to work on quality issues and long term care, such an important work that this committee does. And I wish all of you that remaining on it. All the best. And it's just been a joy to work with each and every one of you. So thanks so much for this opportunity. And big shout out to all the ltss Committee folks, you're you really have been tremendous. Thanks, Deborah, for your leadership, especially.

49:36

Thank you, Becky. Before I recognize Alan, I wanted to take a moment as we're acknowledging retiring council members to thank Gloria Owens for her role on the council. She retired earlier this year. And Gloria fulfilled the seat on the Council of a person living with a diagnosis I want to say that I know that our counsel benefits tremendously from the voices of the lived experience. And I know that we will continue to do that, for the folks who have volunteered and agreed to take on these roles, to thank them for their bravery, and for allowing us a window into their journey. So now, Dr. Alan levy is the director of Emory University's also Mr. z up. Go ahead, Alan,

50:35

I want to have the last word candy. So I would like to give Brad Hi, man the opportunity. Oh, yes. You know what? He's your boss.

50:43

Brad. I think I did just forget, you know, Brad's not my boss. He just we're working in the same department, but Oh, my goodness. Thank you. Nobody. Who's your boss, Katie. Brad, thank you so much of I would love to take the moment to introduce you and thank you, Alan, for catching that misstep. Dr. Brad Hyman is a world renowned neurologist, neuro pathologist, neuropathologist and neuroscientists with extensive experience in basic and translational neurosciences of Alzheimer's disease and related dementias. He has been the chair of the research subcommittee, and he is a colleague of mine, at Mass General Hospital within the memory disorders unit. Brad, one of the things that you have done is show me how a clinician with an incredible acumen for science can also bring that warm heart and bedside manner that our families need so much. I think that your work, both on the council, and in our clinic at Mass General shows how clinicians can build relationships with families that can lay the foundation for trust and participation in research. I want to thank you for your mentorship and allow you a few moments to speak if you would like.

52:16

Katie, thank you, you know, it's really a privilege to be able to care for patients with dementia is it's it's an honor to, to honor my own father who passed away have dementia, Lewy Body disease, to end in order to do that, and also to, you know, be able to have had the excitement of doing research for many years in this field. Because the need is so, so great. And the satisfaction of being able to even make small contributions is huge. And I have really been honored to be part of the council to interact with the federal and non federal members to really see how how things evolve, and how we can really make a difference. But what I want to close with is is not just all the thank yous, but a look to the future. First, I'm so proud of what's been accomplished by the field in the last four years. And second, I'll speak for myself, but you know, Alan, we'll get the last word in. But But I'll speak I think for everybody else who's who's rotating off. It's hard to get rid of us. So please feel free to reach out to, to you know, we're still part of the fight. We're, we are absolutely deeply committed to helping however we can. If there's anything that I can do, please, please, please just no, whispered. No, be there. Thank you, everybody.

54:00

Thank you, Brad. That was wonderful. So now, before I turn it over to Alan, I just like to take a moment and talk about him a little bit. Dr. Alan levy is the director of Emory University's also most Disease Research Center and chairman of the Department of Neurology. He's widely respected among providers and researchers in this field. Dr. Levy is a practicing neurologist, in addition to his work on neurodegenerative research, and brings an important dual perspective to this role. I would like to say Ellen that to be co chair with you a caregiver and a clinician, a

caregiver and a scientist. I think it has been a wonderful model about the way that we hope families will approach, care and care planning to work in partnership. You have always made me feel like I'm a full partner. In our co chair role together, and I have appreciated your perspective and everything that I've learned from you, in the four years of being on the council, but especially in the past two years as co chairs together, I'd love to allow you to close out our meeting. And thank you for your partnership today.

55:23

Wow. JD, thank you so much. It means a lot. And thank you and every one of our colleagues on the committee, you know, again, federal and non federal members, you know, like, like everyone you've heard from, I have really been honored by this opportunity to work with you all, I've really enjoyed it. And especially pre COVID days, when we actually had the chance to get to see each other and get to know each other personally a bit more. I also came into this, you know, with a career, spending my time, as Katie mentioned, seeing patients and doing research and in like Brad and Katie, also a caregiver with family member, both parents affected by neurodegenerative disease. You know, I don't I didn't realize four years ago, when they joined the council, how much more there was to learn. But it's because of all of you that I've learned so much. So thank you for that. You know, the ability to work with like minded people that are passionate. dasia says we've heard about all because we want to do the right things for patients. You know, you've all brought amazing expertise experience from your different perspective. So working with you all has just been truly a joy and great opportunity. Katie is particularly grateful to you, your leadership. And I would say you clearly are the better half of this co chaired partnership for that committee. I'm deeply grateful. Your commitment as a leader and a voice for patients and families. Your voice continues to be heard loudly and thank you for doing so. I also want to reiterate earlier, grateful appreciation of Helen and the Ask B team Emma and Gavin have done a lot of behind the scenes t so you're going to be a great addition to ask me just was so looking forward to what all of you accomplish going forward. So your support for helping Katie and I guide the council along with the council members is really meant a lot. To me personally, I certainly know I needed the direction, the patience and encouragement that you've shown us as we've learned how to help work with the group. So I'm absolutely confident that this council is going to continue to do great things and it's such an exciting time in the field as we move forward and was yet was so much more to do. So on that note, I am thrilled to announce the new chair of the Advisory Council, Dr. Cindy Carlson. Cindy, congratulations. As you all know Cindy has been a great addition to the council since joining and as the chairwoman of the Council for the next term. She just brings extraordinary leadership as a researcher and a clinician. For those who don't know, Cindy, I just love the opportunity to work with her for the members that are forthcoming. Cindy is a Lewis a Holland senior endowed professor in Alzheimer's disease and the director of the Wisconsin Alzheimer's Institute, as an aside something that my mother was involved as a patient. She's a clinical core leader and co leader for the biomarker core and the Wisconsin's Alzheimers Disease Research Center. She's also a member of the National Institutes of Health is today an aging Alzheimer disease centers, Alzheimer disease Center's clinical core steering committee and the clinical Task Force.

Moreover, she chairs several NIH and then I review committees for grant reviews. So she obviously is keeping busy and the advisory councils should be absolutely thrilled and will be to have her leadership going forward to make time for this amongst other activities. And most importantly, addition to her research leadership her perspective as a geriatrician i think is never more needed as we move into a new era of clinic implementation of the research advances that she understands as Cindy also brings a really important perspective from primary care. So congratulations, Cindy, thank you for your past contributions and best wishes for great success and continued rapid progress. like Brad I remain available fully available and eager to help however I can. And like all of you I remain fully committed to working on behalf of patients to accelerate the research and help

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00:00

translate these advances into clinical care. Cindy, I am privileged to now officially pass you the baton. Thank you, Alan. And Katie. Again, I'm so honored to be a part of this group. And I think as a lot of us have alluded to, you know, it's not just ourselves as members of the council, but who are representing the patients, the families, the other clinicians, the other community workers who we've interacted with. So hopefully, their voices are being heard through what we're saying as well. But I do want to really thank again, Katie Brandt, Ellen Levy, Deborah cherry, Rob eggy, Brad Hyman, Becky Kurtz and glory Oh, and for their work over this past four years. Again, it has been mentioned, they've contributed so much to leadership of this group, and again, bringing those voices to the forefront. And then again, I really want especially thank

Katie, Brandon Allen levy for your leadership during this unusual past year, again, with the COVID pandemic, the heightened awareness of the ongoing racism and health inequity in our country. And I think your efforts to really help us to move some of these big events we've we've we're going through into our recommendations and recognizing bringing the voices of the vulnerable, bringing their and their research needs to clinical needs long term care needs to the forefront have been really impressive. So thank you for your work on that. And I think it's been very evident through their discussions today, their their words, again, Katie, as a co chair, you've been a role model leader, that you've made sure that we have the authentic voices in front of the front of the room that they're being heard. So I really appreciate your compassion, your advocacy, has really set a strong role model that I think will continue with the council. So I appreciate your efforts. And Alan, for your work in trying to really move the clinical care and science forward to make sure that we're looking at good treatments, that they're distributed equity, their equity equally, and that the public health efforts are moving forward. So I think you both I think, as you mentioned, Katie, I think you have great complimentary expertise, it all needs to be represented here. So thank you for your leadership and your commitment, your wisdom. And I look forward to partnering with the ongoing members, and also the future members. As Katie mentioned, I think bringing different perspectives to the table is really important, and the people that they interact with as well. So with that, I thank you for this opportunity to serve as chair and look forward to the next several years. And with that, Helen, I think I'll turn it back over to you. And also, as we hear from public voices. Thank you.

02:38

Thanks. Thanks, everyone. It's been amazing for years working with Well, actually, I've only worked with you guys for three years, but amazing and crazy. And it's in this weird time warp where it doesn't seem like it's been that long, because I think we only had one or two meetings with you all in chair roles, and then we transition to the virtual format. But I think it's been a great transition for us an opportunity to build on the work and keep working while we're farther away. And to get more engagement from folks in our virtual meetings. People who couldn't always come or the audience that maybe couldn't make it into the meeting can now see our meaning. So I'm excited to keep working with this team sad to say goodbye to our friends. But as you'll see, even our former council members still come in and sometimes make public comments. So we'll have an oldie but goodie bag today as well.

PUBLIC COMMENTS

Um, I'm going to start with the public comments now a few minutes ahead of schedule, but I think almost everyone has joined for public commenters. Please speak when I when I call on

you. And if I miss anyone, I'll go back through at the end. And I asked others to mute themselves for our members. If you have the opportunity to to turn your video on. I think it'd be great for the public commenters to see to see your faces and to see that you're listening to their comments. So our first public commenter on my list is Arnold bearish. I'm hope I'm pronouncing that correctly. And Arnold is presenting with Beth Nolan. So Arnold and Beth if you would like to kick us off the floor is yours.

04:14

Thank you. My name is Arnold bearish, mild cognitive impairment with early onset dementia. I'd like to believe that this new drug by Biogen was my ticket out but instead I'm discouraged by the findings. This drug has twice been rejected by the FDA in November 10 of the 11 panel members voted that there is not enough evidence to show that this drug could slow cognitive decline. It has now been passed in its third presentation. And since its introduction on June 7, has had to revise neuro the patient base that it can be used for there was not convincing evidence that it slowed down the patient's cognitive decline, but instead it based its approval on the drugs ability to reduce levels of amyloid protein in the brain. It does not treat, nor does it cure. Unfortunately, the cost is estimated at $56,000 per year. This cost is not included administration of the drug or the ancillary costs such as multiple MRIs, and PET scans to monitor the effects, excuse me, of the drug on the brain and make a difference in the patient's cognition. The medication has not been tested. At this time on a population of patients with comorbid conditions such as diabetes and heart disease. We were starting to now see that hospital systems are pushing back on the drug and starting to say that they will not administer it. Insurance companies are already restricting the use of the drug. There has already been a call for congressional investigation about the approval process for marketing and pricing and their controversial drug. We all want hope, need hope. But this is not the panacea. cost estimates will break the back of Medicare as well as private insurance, people will demand the drug because they know which there will be very frustrated when they are told they don't qualify for medication. I thought this would help people with dementia, I'd be the first in line. But after what I've read and heard, I just don't think so there needs to be more research done, though this may be a stepping off point. I don't think it's the drug in the future. Thank you. So guys, I

06:24

want to thank this committee and the opportunity to bring the voice of people living with dementia. My name is Beth Nolan and I work for positive approach to care. Some of you notice cheapest knows positive approach to care. We advocate for people living with dementia to their families and for providers. But mainly our work is education. And we have spent the last weeks fielding calls from families and providers, really providers as well, with regard to educating you have the daily changes that are coming out. People are confused and they're Deaf desperate, without a proper infrastructure around the disease modifying protocols that are going to be

coming out, hopefully over the next Well, hopefully in my lifetime. So we ask this committee to not only to continue to support the amazing subcommittee work recorded on today, but to advocate for public health in two areas. One, we really could all agree on this call that we are not just talking about Alzheimer's, it's confusing to the public. And it's not good leadership, I would accept I would ask that this committee show leadership by using consistent nomenclature. And for simply by changing the name from Alzheimer's to dementia, it's the beginning. And second is advocate for public health services funding to identify best practices to build infrastructure around disease modifying protocols, specifically with access to diagnoses, infrastructure around dissemination of enrollment and finding as efficacy of trials. But even more so and that would totally have helped us and people like Dr. bearish over the last couple of weeks and months would be infrastructure and creation around dissemination around practice guidelines to establish some sort of standard of care for disease modifying protocols, specifically with regard to cause benefit language for providers and families with an emphasis on meaningful clinical outcomes, especially with regard to magnitude of benefit. That sort of language and leadership can truly be heralding many many less stressful nights for so many people that every single one of us care about. Thank you.

08:18

Thank you, Arnie Abbess our next public commenter is Sue Bunning and follows solving Sue will be Seth killer.

08:29

Okay, good afternoon,

08:31

everyone. My name is Sue bunting and I am the industry director for pet drugs at mitre. My thanks to the Advisory Council for allowing my dad to comment today. With the encouraging FDA approval of Agile helmet becomes even more important that the appropriate patients those who have amyloid plaque that the drug is targeting, get identified and to go on treatment. FDA approved amyloid and tau imaging pet agents are available today to detect the Hallmark pathologies of Alzheimer's disease. amyloid pet imaging was used in the most extensive Alzheimer's disease study ever conducted the idea study and resulted in a change in a patient's disease management over 60% of the time. And in 36% of the cases, there was a change in diagnosis as a result of the patient's PET scan results. 77% of patients in the study had a diagnosis of Alzheimer's disease before the PET scan. But in over 3100 patients, the PET scan was negative meaning no amyloid pathology could be detected in the brain. But amyloid pet diagnostics are currently not uncovered by CMS. And we encourage CMS to immediately open

the noncovered reconsideration request that was submitted last September to prevent a delay in patient access to the first ever disease modifying treatment. With regard to Medicare payment, the current inequitable package payment methodology make these new targets diagnostic radiopharmaceuticals a financial liability to hospitals particularly acute in some states that limit PET scanning outside of hospital outpatient departments. A recent GAO report highlighted the enrollment challenges to the new idea study, which examines Alzheimer's in the minority population. The enrollment challenges are a direct result of the CMS packaging policy, which results in significant losses in the Medicare outpatient hospitals. As an update to the GAO report, I can say that only a handful of hospitals invited to date have accepted the invitation to participate in new ideas. We urge support for rational coverage and payment policies for pet amyloid diagnostics to help ensure the right patients are selected to receive edgy help. Thanks, and thank you for allowing me to comment.

10:56

Thank you, Sue. Seth, you're next and following Seth is Chris Lightman?

11:01

No, thank you, Helen. Do you hear me? Yeah, thank you very much. I appreciate coming back to speak in front of the Council. For those that may or may not remember me. I'm Seth Keller. I'm a developmental neurologist. I work as the CO president alongside your council colleague, Matt janicki. I'm also the chair of the American Academy neurology adult section of adults with IDD. And I just wanted to briefly bring up the attention of advocates to those with IDD specifically Alzheimers in people with Down syndrome. And I had submitted information that a core group of us as advocates have come together to to voice or questions concerns, voices about add to Canyon Mab and people with Down syndrome. And as everyone knows, that people downstream have a huge prevalence of early onset Alzheimer's. And so certainly when the word came out that add to canyamel was approved. people in the community in the Down syndrome advocacy world were like, excited and excited about it. And because of the controversy and the fact that people in the studies really were not studies because we were down syndrome, it really led to a lot of questions whether or not as you can imagine Helm would be appropriate. So we had formed a group within the national task group called the Agile helmet Down syndrome Medical Advisory Group made up of a number of national leaders to pull together some aspects of thought that we absolutely believe needed to be thought of and carried forward to look at medications such as, as a canyon Mab or any future medication that might be also looked at certainly markers. And we really were also pulling together support from a lot of the advocacy groups too. So I'm really representing a different a lot of different groups. And we really were calling for the inclusion of participants with down syndrome. In ongoing and further clinical studies and research, asking for research inform appropriate oversight over its usage, safety data on aggi Canyon Mab determine the optimum age for possible prophylactic

usage of therapeutics. And surely because the the early time in which a lot of people are developing development of amyloid in their early age, the questions of them getting therapeutics early in their age as compared to other populations as we've looked at, and absolutely the protocol developed and disseminated gotting to practitioners like myself as neurologists, and other family doctors and other assessment assessments is so interesting and different as as you as I'm sure many of you can appreciate intellectual disabilities, lifelong cognitive impairment. And the studies that are being done now for tools looking for neurotypical population don't match the same for people to IDD and Down syndrome and this leads to everything in terms of how we can gauge appropriateness or outcomes decision making very much very apropos and IDD populations. And this is something very important caregivers, family members, decision making, and absolutely just finally, providing orientation and education to caregivers. That's a lot of that we do in our in our organizations. I mean as a physician neurologist, providing staff and then the aftercare. So again, we really definitely appreciate you know, all the attention of what it is that we're doing with Addy, can you map it physically for Down syndrome in the population and definitely equity of care. I know the term equity and access to services is huge, but certainly people with with a Down syndrome definitely a fairness of getting accurate care. We do know and appreciate other or other efforts going on by the NIH funded Alzheimer clinical trial research are our colleagues, Mike Rafi and his work and other colleagues work in that realm. But we definitely want to draw attention and again, I would appreciate having the opportunity to speak in front of the council and definitely appreciate all the work that you're doing and will continue to do and for those that are leaving Best of luck to you. And thank you for what you've done. Thank you.

14:56

Thank you fast. Our next commenter is Chris Liebman. Followed by Hanna mama Sokka.

15:03

Good afternoon. My name is Chris Lightman. I'm an Alzheimer's researcher and lead up the patient access and value organization at Biogen. And it's a real pleasure pleasure to have the opportunity to give comments to this council this afternoon. As I know you're all aware and have been speaking about today, the past five weeks have certainly been historic with the approval of Agia. Home under the accelerated approval pathway based on reduction in amyloid plaques. A biomarker that is reasonably likely to predict clinical benefit. Add to Home is an amyloid beta directed antibody indicated for the treatment of Alzheimer's, as our label guides treatment with Agia home should be initiated in the earlier stages in patients with mild cognitive impairment or mild dementia stage of the disease. This is the population in which treatment was initiated in our clinical studies. We do not have any safety or effectiveness data on initiating treatment at earlier or later stages of the disease and then were studied. And of course, continued approval for this indication is going to be contingent upon verification of clinical and confirmatory studies which

we are working on with urgency. And the real reason I want to make comments is I do believe this is a historic juncture in the treatment of Alzheimer's disease. Having worked in this area of research for nearly two decades, I'm truly honored and humbled to be here to speak not only to this first approval, and also the research that has brought us to this point over the last decades, but also to what we believe this has the potential to mean in the lives of people with Alzheimer's disease their caregivers, their families, friends, and the doctors, nurses and so many others in healthcare, as well as to the scientific community that can build on this now moving forward. In other innovations. This is the first treatment, it most certainly is not the last. It's not a cure, it is not a silver bullet. But we do believe that Alzheimer's now is on a path that diseases like multiple sclerosis, and many areas in oncology have been before where the first treatment was approved. And then we start to see and sparked further innovation that builds on the scientific understanding where we are now. Our focus now needs to be on working together to support patient access to care for the right patients, and work on future innovative treatments to change the overall course of disease. It's truly a privilege to be part of this moment that we believe is likely to catalyze a new era and future Alzheimer's disease treatments. Today, Alzheimer's is a very much a progressive disease. But as the field continues to innovate, our hope is that one day it'll be very different. Thank you for the opportunity to speak to you.

17:38

Thank you Chris Hanna, you are next followed by brandy Matthews

17:44

so much. My name is Hannah Mischka. I'm CEO of Alva 10. I'm like a biologist by training but an avid 10. We create economic models to incentivize development of diagnostics. And I think that's really a critical thing that we need to focus on Katie Brandt correctly stated in her opening remark, but it's critical that we build a foundation and infrastructure so that when the treatments come for neurodegenerative diseases, we are ready, and Dr. Moon River reviewed many of the advances we've made in oncology with targeted agents over the past 20 years. And central to her descriptions were the focus on diagnosis, both of the pathological and molecular level. In 2021, a patient's not just diagnosed with cancer, but with EGFR positive alq, negative non small cell lung cancer and the treatment is based on that specific diagnosis. But we don't do that neurodegenerative diseases, really, in Alzheimer's disease. Most patients are diagnosed by roulotte tests when they present with dementia and other memory complaints. We use cognitive function testing, mental status testing, neuro psych testing, and laboratory testing to rule out metabolic disorders and vitamin deficiency. Then we use imaging to rule out hemorrhage, brain tumors and stroke, which also allows for the imaging of amyloid plaques. None of those give a definitive diagnosis. None of those are true biomarkers of disease as we think of in oncology, they're really surrogate markers to indicate that some disease is present. But as we know, patients can have dementia without amyloid, and they can have amyloid without severe

dementia. And they're really two problems. One, none of these tests are adequate to diagnose and differentiate between different types of Alzheimer's and the way we do in oncology, especially in early stages. Maybe the bigger problem is that they're frequently not covered by insurance. Even if they do give an ability to distinguish between dementia, if they're not paid for it creates a massive disparity in care. Even Medicare payment allows patients to leave with a presumed Alzheimer's diagnosis unless they're able to cover some of these tests on their own. And last, none of these give an indication if a patient is likely to respond to a class of drugs, whether it be disease modifying therapy or something that's in a clinical trial, and this is not for technical lack of ability to do so. The technology is very But if we really want to truly make progress in Alzheimer's and other neurodegenerative diseases, we need to invest in and find ways to pay for the diagnostic tools to definitively define and subtype these diseases in the same way that we've done in oncology. Thank you so much.

20:18

Thank you, Hannah. Our next speaker is Brandy Matthews and after brandy will be cafard peers if she was able to join.

20:26

Thank you. Hi, Brandy Matthews, behavioral neurologist representing Eli Lilly and company. Liz Lilly is excited that meaningful change for people living with Alzheimer's disease is upon us, however, hoped from the availability of current and future approved amyloid plaque reducing therapies can become reality only if patients have timely and equitable access to both diagnostics and therapies. In addition to informing treatment duration, existing and emerging diagnostics can identify the patients who likely will and will not benefit from these therapies. existing data suggests approximately 40% of clinically diagnosed ad patients are actually negative for amyloid plaque by amyloid PET scan. amyloid negative patients are highly unlikely to benefit from amyloid plaque targeted therapies, so patient burden from unhelpful therapies would be minimized and economic resources could be saved if these tools are readily accessible and reimbursed. To minimize unnecessary resource utilization. CMS needs to establish appropriate coverage and payment rates for Alzheimer's diagnostics, including amyloid and tau pet. class based access decisions for therapeutics are premature at this time, because amyloid lowering agents may have different degrees of amyloid plaque reduction, trial entry criteria, dosing approaches and duration of treatment. CMS coverage policies on Alzheimer's therapeutics should evaluate each product based on its own label clinical trial design and results. limitations placed on the first product should not automatically apply to future products. Lily supports postmarketing confirmatory trial commitments for products under accelerated approval. Such commitments should be guided by the FDA rather than CMS. Establishing sufficient coverage for the patients that is consistent with the study populations is necessary when we does not support class based coverage with evidence development as the

only form of coverage for all new beta amyloid targeted therapies, because each new treatment has its own benefit risk profile, and CEED alone would be too limiting to current and future patients. We urge providers, payers and policymakers to work together to provide access to Alzheimer's diagnostics and therapies for patients who are most likely to benefit. Let's together ensure we are helping patients rather than hindering progress.

23:05

Thank you.

23:07

Thank you, Brandy, with Katherine piers able to join Shayla lon. Okay, if not, I'm going to read her comments. She was worried about bad weather and losing her connection today. So her comments begin. Good afternoon. My name is Katherine Pierce, and I am the CO vice president of the National Task Group on intellectual disabilities and dementia practices. The MTG the NTG urges the Advisory Council to develop policies that will expand dementia capable care to a group of individuals that to date has received little attention but they've faced significant challenges as they age and face the risk of developing Alzheimer's or related dementia. Aging individuals with autism spectrum disorder, a topic that one writer in 2016 described as a black hole. In fact, it is such a black hole that I am unable to even tell you how many adults with ASD There are over the age of 65. to say nothing of how many adults with ASD have Alzheimer's or related dementia. In 2014, the MTG developed a national model training curriculum on dementia capable care for adults with intellectual disabilities. To date, over 55 workshops have been held in 25 states across the country with over 3000 participants. A consistent question at those workshops is what can you tell us about how dementia impacts adults with ASD? The answer very little. Here's what we do know. The first individuals formerly diagnosed with ASD were diagnosed in the 1940s. And those individuals are now at the age of risk for developing dementia. We also know that people with ASD have a range of health conditions that place them at special risk of developing dementia, such as an increased risk of Parkinson's disease, depression, social isolation and long term anti psychotic medication use that can raise the risk of diabetes and heart disease. Additionally, we know that many people with ASD are being supported by aging family members. And then what and when that family support system is lost, they will require alternative placements and support for the remainder of their years. Finally, we know that pre existing sensory processing issues along with verbal communication and behavioral challenges that characterize ASD make diagnosis of dementia challenging which can lead to inappropriate treatment. Consistent with strategy to age of the national plan to address Alzheimers disease, we urge you to consider the following First research on aging with ASD and the specific risk of dementia. Next, develop a validated clinical intervention specific to aging adults with ASD and dementia, development of education and training curriculums for health care providers and community service providers who lack understanding of an expertise in the

problems of aging with ASD. And finally, studies on the efficacy and safety of pharmacological interventions in aging adults with ASD, especially regarding colon histories, inhibitors and anti psychotics. Thank you for the opportunity to speak today about the challenges faced by aging adults with ASD who are at risk for web develop Alzheimer's disease or related dementia. The ntj greatly appreciates the effort and actions that the Advisory Council has taken today to raise the visibility of the needs of all aging adults with intellectual disabilities. And then our final two comments are from Matt sharp and Angela Taylor. So Matt, the floor is yours.

26:27

Thank you, Alan. My name is Matt sharp. I'm with the Association for frontotemporal degeneration. Thank you for another opportunity to offer input from the perspective of FTD. One of the related dimensions FTD strongly supports adding the six called the National Alzheimer's plan. reducing the burden of risk factors for Alzheimer's disease and the related dementias is a vital and and achievable goal. As scientific understanding of modifiable risk factors for dementia grows, it is increasingly important that the nation's response as expressed by the National Plan include public health and policy steps to address these risks and potentially delay onset and reduce the prevalence of ad rd. We greatly appreciate the work of the risk reduction subcommittee and the attention given to all forms of dementia. The majority of the research on modifiable viable risk factors for dementia has understandably focused on Alzheimer's disease. That seems fair to assume that reducing the 10 modifiable factors that the subcommittee identified will benefit those living with FTD and other forms of dementia. However, with an estimated 60% of FTD cases considered to be sporadic, and without more focused research on non genetic risk factors for FTD. We will only be able to make that assumption. There's great need for more research on risk factors associated with non Alzheimers dimensions. aftd strongly supports the addition of the sixth goal, along with the strategies and recommendations made by the risk reduction subcommittee, but urge the subcommittee to be more explicit in their recommendations for additional research to do to determine whether and to what extent modifiable risk factors for dementia affect non Alzheimer's dimensions, including FTD, Lewy Body and mixed image. Thank you very much.

28:16

Thank you, Matt. And our final public commenter is Angela Taylor, who as you all know, is a former council member. So maybe we'll see some of you back. Me public comments in a few years. Angela?

28:28

Hi, Helen. Can you hear me? Yes. All right. Wonderful. I'd hate to just get started and find myself still on mute. First and foremost, I need to say hello to all my friends on the council. I really really was inspired by today's meeting. What a robust agenda. What passionate farewells, breaks my heart. It's wonderful to see the continued work that this council is doing and the new ground that you guys are breaking. For all of the people that are on the in the extended virtual audience who don't know me. I'm Angela Taylor. I'm the senior director of research and advocacy for the Lewy body dementia Association. Excuse me, I lost my father to LBD and I am co chairing the dimension nomenclature initiative, which was mentioned earlier today. I wanted to share an update from the Lewy body dementia associations perspective as it pertains to edge Academy. We've certainly received our fair share of questions about this new treatment from the LBD community. Our scientific advisors urged us to create a position statement because there's, you know, over half of the people who have LBD have some code testing Alzheimer's disease, and that that mixed pathology results in worsened outcomes for those people who have just than those who have just done Lewy Body disease alone. So it's really important to our community that when there are disease modifying treatments for Alzheimer's disease available, that we also The Lewy body dementia community. So we are in very close collaboration with our scientific advisory council put together a position statement, and it's very short and I just wanted to share it. People with LBD can have severe medication side effects that are not common in people with Alzheimer's disease. As such clinical trials are needed to determine if edge acana map is safe and effective, and people with LBD who also have coexisting Alzheimer's disease. So that's the position statement from our organization. To be clear, we really strongly advocate for the study of edge can map in the LBGT community, specifically in people who have coexisting Alzheimer's disease. There are some extremely important unanswered questions about safety and potential long term benefits, not just in Alzheimer's disease, but also in LBD. That has to be answered. Ib da supports a network of experts in LBD through our Research Centers of Excellence Program. And so if there's a decision to conduct a study of edge kanematsu in LBD, our Research Centers of Excellence Program is prepared to participate. I wanted to make a few specific points about the importance of looking at individuals with coexisting disease pathologies. Because we know that the majority of people who have dementia have more than one underlying disease process behind their symptoms. So we need to take that broader look to see who may benefit from potential disease modifying treatments. What we know from autopsy studies is that about half of the people with Alzheimer's disease have some degree of Lewy Body pathology. And without assessing for those other disease processes using biomarkers, clinical trials for Alzheimer's disease may be confounded. So it's important that we begin to look for opportunities to use those biomarkers that are emerging for Lewy Body disease, to enrich ad study populations, those are very highly sensitive and specific now, both in CSF and in tissue skin tissue. Lastly, I'm what concerns me the most, though, is that, because I've been personally affected by Lewy body dementia, is that people with LBD, who have coexisting Alzheimer's pathology may never have the opportunity to benefit from disease modifying therapies for Alzheimer's disease. Because once we get an approval, often we stop there, and the studies don't go on to look at other diseases that may not be as profitable, there may not be motivation to move beyond that. So what I really hope to see is that we take that in an intentional approach to moving past looking at clinical trials for a single disease population or a single syndrome, we really need robust study designs that are that will

accommodate multiple types of dementias in a single study. And with that, I'll conclude my comments. And thank you so much for the time.

33:15

Thank you so much, Angela. And thanks to all of our public commenters today. Thanks to everyone for such a robust meeting. It really points to the progress we've made under Napa, I just looked in my notes. And our first meeting of the Napa Advisory Council was September 27 2011. So our 10 year anniversary coming up. And it's amazing to think about how much progress we have made since then, and also to look at our next four years towards the 2025 goal. So I hate to say goodbye. But I won't say goodbye. But thank you to our retiring members, especially Katie and Alan for their leadership and friendship over the last couple of years. And to all the members for their leadership on the council, as been said before, you know, you sort of get into this and you don't know what it's about. And it's real opportunity. And then you're asked to step into a leadership role. And you really all have stepped up into that role. And it's, it's visible in the work that we have done. So looking towards the next couple of years going forward. Our next meeting is on October 25 will be virtual or in person will we'll see it'll be focused on long term services and supports and we'll have a new set of members. And we hope that even if you're not a member anymore, you'll still tune in and stay engaged with our work, though. Thank you, everyone. Thank you, Helen. Thank you. Thanks, everybody. Thank you, everyone. Thank you guys. Thank you. Thank you