# DISRUPTING DEMENTIA: OVERCOMING SYSTEM-LEVEL HURDLES FROM DIAGNOSIS TO CARE

**Erin Brodwin** 00:00

I prefer these anyway. All right, we're good? Okay. Thank you all for coming. I am very pleased that you all are encouraged and want to disrupt dementia. Before we start, could I just get a show of hands to see how many people in the room are personally impacted by this topic? Wow. I don't know if I see a hand that's not up. Same here. I think a lot of the folks on our panel are as well. So, today's title is “Disrupting Dementia: Overcoming System-Level Hurdles from Diagnosis to Care.” I'm Erin Brodwin; I'm a health care journalist, and I'll be moderating today's conversation. We're at an extraordinary moment in terms of dementia research. We have new diagnostic tools, the first disease-modifying treatments for Alzheimer's, and promising advances in drug development. But there's a big gap between what science is making possible and what patients are actually getting. Today we'll be exploring that gap and what it's going to take to close it. I'm joined by four terrific panelists who bring very different perspectives to the panel. So, with me, I have Dr. Erin Angel, VP of global research and scientific affairs at GE HealthCare. Lord James Bethell, former UK health minister and chair of the BARBARA Alliance. Niranjan Bose, managing director at Gates Ventures. And Kasey Kissick Duarte, co-president of the Kissick Family Foundation. I'll let each of them talk more in detail about what they do. But I do want to start with one opening question for everyone. We've had more progress in dementia research in the last few years than in the decades before it. But if your parents started showing signs of dementia today, would their experience of getting diagnosed and treated actually look much different than it did five years ago? *[Crosstalk]* Don't make me call on you. Do you want me to?

**James Bethell** 01:58

Well, the short answer is yes and no. Bluntly, in the UK today, the NHS would not provide any support, probably wouldn't provide you with a diagnosis, would probably send you to a psychological track, which is completely irrelevant, and definitely wouldn't provide any of the groundbreaking drugs that are available in some countries. This is very dispiriting. But if you have a lot of money, you can go to Harley Street, which

is our private medical district, and have amazing treatments that would surprise many people in this room about how effective they can be, particularly if you catch it early. And they can be put onto treatments that include mental agility, diet, physical activity, sleep management, and also some pretty kickass medicines that will massively improve their prospects in the future. So, at the moment, the debate is an access debate, not just a science debate.

**Kasey Kissick Duarte** 03:02

Yeah, I can add to that. The title of this panel is “Disrupting Dementia.” We were asked to think about what does that mean to disrupt dementia. I think it just means treating dementia like any other disease. That we diagnose it, we treat it, and we talk about it. With dementia, it even starts with just recognizing that dementia itself is not a diagnosis. Dementia is an umbrella term that contains many different conditions that affects the brain in different ways. And in the same way that you would never accept cancer as a diagnosis, and you would push to understand what type, what stage, we need to expect the same for dementia. And also, we need to get rid of this cultural learned helplessness around dementia. Perhaps there's not approved treatments, but there are a number of very promising trials underway across neurodegeneration. And so, even if the option isn't an approved treatment, it's a trial, it's a research study, that this public sentiment that it's just old age, there's nothing that you can do about it, simply isn't true. That is changing, and I think that's an exciting shift that we're living through right now.

**Erin Brodwin** 04:20

Anything to add to that, Erin? Bose?

**Niranjan Bose** 04:23

I think it's definitely changed. So, the short answer would be yes. And I'd say, but depends on where you live. In the US, it absolutely depends on where you live. If you're in Indiana, you're in good shape. You'll get diagnosed early. If you're in Kansas, you're in good shape. Thanks to a lot of the health system work that's happening.

**Erin Angel** 04:47

Yeah, and I think I would add this. Up until very recently, most dementia diseases were both diagnosed and treated purely based on symptoms, and that's still true for several of the diseases. We have had a bit of a disruption in dementia for Alzheimer's specifically because there are two new drugs that target the disease itself, but they are not magic. They slow disease, they don't backtrack disease. So, is it different? Yes. Do we have a long way to go and a lot of potential? Yes.

**Erin Brodwin** 05:16

Let's talk about early detection for a little while. Bose, I have a question for you. Are we getting better at diagnosing Alzheimer's earlier than we are at actually helping people who test positive?

**Niranjan Bose** 05:33

The answer is yes and no.

**James Bethell** 05:37

You stole that from me.

**Niranjan Bose** 05:40

But it's a clear yes for the first question and no for the second question. We are getting really good at early detection. We've had this fundamental argument, like what does diagnosis mean? And what does early detection mean? If you don't have amyloid, it's not Alzheimer's disease. But what does it mean to go earlier than before amyloid detection? So, I don't want to get into that debate. Let's talk about how it matters to an individual. What do they want to know? Are they at very high risk of developing Alzheimer's disease? I think the tools are emerging. We have a confirmatory test, the two blood test or the multiple blood test, but I think we're going way upstream beyond that, even before the phospho-tau217 shows up, I think there's going to be promising biomarkers, including digital ones like speech.

**James Bethell** 06:33

I think that's such an important point because it is right that people should know what they're at most risk of. One person might be of one background and be at risk of diabetes. Another in my family, cardiovascular is by far the biggest risk. My wife is Asian, diabetes by far the biggest risk. Another might be dementia. Understanding that pre-symptomatic risk factor is so valuable for people. We've definitely understood what the drivers are. The Lancet Commission report on that is crystal clear, and that gives people choices about how they lead their life and what kind of early pre-medicine interventions they can make for themselves to reduce that risk.

**Erin Brodwin** 07:15

It does. On the other hand, it can also be somewhat debilitating for someone to find out that they're at high risk. For example, they have the two gene types.

**Niranjan Bose** 07:23

Four.

**James Bethell** 07:24

Yeah.

**Niranjan Bose** 07:24

Four.

**Erin Brodwin** 07:25

If you have all of them, you're at very severe risk. But if you don't know what to do about that, yes, you can make lifestyle changes, stop drinking, eat better, exercise, but we're all trying to do that.

**James Bethell** 07:36

I think we're on the brink of a mentality change about that. Listen, your point's fairly made, and I have thought at times that I was in risk of a certain disease, and I did find it debilitating. You're right. But hold on a second. In my pension plan, some of my stocks are at risk of crashing, and some of them are at risk of doing a bit better. I don't hide myself from that information. I do something about it. I sell my NVIDIA stocks and I buy more TSMC stocks. Likewise, my risks of diabetes are really low. My wife's are high, but my risk of cardiovascular is very high, and I jog around the Mount.

**Niranjan Bose** 08:19

I do want to add something to that. If you believe that amyloid accumulation is one of the big triggers, and you are at risk, I would urge you to reduce your amyloid accumulation. How do you do that?

**James Bethell** 08:33

Very hard.

**Erin Brodwin** 08:33

Was going to ask you the question.

**Niranjan Bose** 08:36

I think the answer's going to come out in the prevention study that's happening. If Lilly's prevention study reads out positive, and we can debate what that means, I think it's going to be a game changer. We're talking about disruption. That will be a disruption.

**Erin Angel** 08:54

Actually preventing disease, yeah. It'll be really important. We'll get a readout next year, I think, yeah?

**Niranjan Bose** 08:59

Early '27 is what I've heard, but I'm not on Polymarket yet.

**Erin Brodwin** 09:03

Do you want to explain that? What you just said.

**Erin Angel** 09:05

Okay. So, what's he talking about? In the brain, we have proteins that flow through the brain, like amyloids or taus are normal things in your bloodstream. And we have a system that cleans them, particularly when we're sleeping. It's called the glymphatic system, with a G, not lymphatic, but glymphatic. And it's very new science. We only learned about really the glymphatic system within the last decade or so. And what we do know is that it cleans your brain, particularly when you're sleeping. So, sleep is particularly interesting to study in this perspective. Yeah. What we don't know is if patients that progress to diseases with dementia have different cleaning systems. We suspect, that's the kind of ongoing hypothesis, that their glymphatic system is not cleaning those proteins out in the right way, but there's so much exciting science to really learn if that's the case. At GE HealthCare, we recently developed an MRI scanner, a super gradient MRI

scanner, that we believe could actually map out the function of this glymphatic system. So, we have two ARPA-H grants to look at can we potentially map out the features and really get to pre-disease and preventing disease as opposed to just treating disease. So, a lot of work still to be done, but exciting.

**Erin Brodwin** 10:21

Can you explain a little bit of the science behind how that works?

**Erin Angel** 10:24

MAGNUS, the MRI? It has what's called high gradients. High gradients allow you to see function of the anatomy better through diffusion. I'll skip diffusion, just not bore you with that. But basically, it allows you to see the function of the brain better. The hard thing about visualizing the glymphatic system is it's super slow. It's a very slow movement through the tissues of the brain. So, visualizing something so slow is actually really challenging. So, with these super high gradients, we hope that we can better understand the glymphatic system, because what's the ultimate goal in disrupting dementia? It's to avoid in the first place. So, can we understand what leads certain patients or certain humans towards dementia and others not?

**Erin Brodwin** 11:12

Yeah. Since we're on the subject of testing, blood tests obviously promise to democratize diagnoses. Patients still need specialists though, and imaging. Are we solving the access problem, or are we just moving the bottleneck?

**Erin Angel** 11:31

You probably want to talk, but I want to talk too.

**Niranjan Bose** 11:36

I think I disagree that we're not moving the bottleneck. I think we're solving for—

**Erin Brodwin** 11:40

It was a question.

**Niranjan Bose** 11:43

I think we're solving the problem in hand, which is if you had to go and get imaged or had a spinal tap, CSF drawn, I think that's a lot more harder. So, you've now reduced the hurdle by bringing blood tests, which are—it's not so much democratizing, it's easier. It's easier for the individual, it's easier for the family, the caregiver, because of lower cost and the system. So, I think it's a tide that's going to lift all boats. But now, it's not going to work for everybody. And the tests are not definitive by any stretch of imagination. Some of them have two cutoffs, so how do you interpret, et cetera. But we need to start somewhere. And this is a fantastic starting point.

**Erin Angel** 12:29

Yeah. A lot of promise in blood-based biomarkers, particularly because cerebrospinal fluid biomarkers are tricky, right? Lumbar puncture. But in a blood base, very easy to acquire. Where do they really play an important role is selecting those patients that definitely do not have Alzheimer's. By the way, only in Alzheimer's so far. In the clinical space, we'd love to get them to FTD, Lewy body, et cetera, but Alzheimer's so far. So, we can say who doesn't have disease. We can say who definitely does have disease. But here's the tricky thing. There's this sort of intermediate gray area that you're referring to, and those are the patients that may or may not have early disease, which are exactly the patients you want to find for these amyloid-targeting therapies. Because it slows disease, so finding it earlier in the disease pathway is going to be the patients that benefit most from it. So, I really think blood-based biomarkers in combination with imaging, because imaging is where you say, “Do they have amyloids? Are they likely to react positively from these drugs?” It's so important, that intermediate result. The tricky bit, though, is if you think about payers and how health insurance works and how new treatments like this work, there's some examples of not great in this space. So, for example, if a patient does not have Alzheimer's, great. If they have Alzheimer's, it's clear what path they need to take. But if they're in that intermediate, some payers misconstrue how to take the next step for that patient. They should go to PET, right, and get an amyloid scan to understand, to Vizamyl or whatever, to see if they need to go into treatment. But some of the payers are saying, “No, not until you're totally positive in that blood test,” and that's a really unfortunate approach that I think will iron itself out. These are new treatments, new standard of care, new pathways, but in the interim, it's a shame.

**Erin Brodwin** 14:17

What do you think it will take to get to that point? And then we'll go to you.

**James Bethell** 14:21

Yeah. Kasey.

**Erin Angel** 14:22

So—

**Kasey Kissick Duarte** 14:23

Go ahead, Erin, first.

**Erin Angel** 14:24

Well, it just takes time with any new treatment and in every country to figure out what the standard of care looks like. And once that standard of care is accepted by specialists in the industry, then typically the payers follow that suit. But when things are very new, access to those newer treatments, it just, breakthroughs only matter if they really can impact patient care, and it takes some time. It's the reality and the complexity of health care.

**Erin Brodwin** 14:49

Go ahead, Kasey.

**Kasey Kissick Duarte** 14:51

I was going to take us a little bit even further upstream when you think about access. And there was some discussion of this in the opening plenary, which is these tests, new blood-based biomarkers, new imaging, they're game changers, but only for the patients who end up in the doctor's office. And just to speak a little bit to my family foundation focuses on and my lived experience, my dad passed away a little over two years ago from frontotemporal dementia, or FTD. And it is not what people think of when they hear the word dementia. It is not memory loss. Looking back at the early signs with my dad, his memory was totally fine. He actually aced all the cognitive tests he was given early on. He was brilliant, high-functioning. It was just subtle behavior changes, things like he was an absolute sports fanatic, actually grew up here in the DC area, was a major Washington, then Redskins, now Commanders fan. And seemingly overnight, he stopped caring about sports. He didn't care about his teams. He started to withdraw. He was an amazing mentor and storyteller, and then just started to withdraw from people around him. A lot of odd decisions with spending, with finances. We were just baffled. We were a family living in California, metropolitan areas with access to the best care in the world, but still it took us many months of searching for answers, lots of doctor's appointments, a misdiagnosis of Alzheimer's, and pushing to get us to an answer. And again, we were like, “This is not dementia.” We thought dementia was all memory loss. And so, yeah, and zooming out, this is true not just for FTD. Lewy body is often sleep changes that are early signs, can be hallucinations. These things that get patients to end up in, frankly, jail sometimes, in psychiatry offices, everywhere except where they need to be, which is a neurologist's office or specialized care. And so, I think when you think about access, it's even going further upstream, and it's really public awareness. And our foundation works both in scientific research and awareness for that reason.

**James Bethell** 17:13

Erin, to answer your question about the workforce bottleneck, I think Kasey's testimony is really, really powerful because we're brought up in a tradition of contagious diseases where a test might give a red light or a green light as to a yes/no answer. But with these chronic diseases, whether that's heart disease, mental health, or brain health, it's polygenic. There are a number of different factors that all have to be looked at at the same time. So, not only might there be several tests, a blood test or an imaging test, there might also be family history and genetics. There's also the observation of the carers, which in brain health is incredibly important and often more reliable than the patient evidence, frankly. And processing that quite complicated set of data is extremely complicated. I was in my cardiologist about three weeks ago. By the way, he's like the top in the country, and he has this huge desk. And he had my medical records spread all over the place trying to find my iodine. It was not very encouraging that he knew—

**Erin Brodwin** 18:17

2026.

**James Bethell** 18:19

—my polygenic risk score and what my prospects were going forward. I would have slightly have preferred him to have filmed it and put it in Claude, frankly. And there, I think, to your question, there's got to be some disruption in the way in which we process all the data. I'd be very interested in what the others on the panel thought of that. Patient confidence is quite low at the moment. They're not sure that doctors know what they're talking about. And I think that that's not unreasonable, because it is really, really

complicated. Something like the impact of your genetics on your risk score is not crystal clear, and so which algorithm are you going to use? And should the patient actually be involved in deciding which decision-making tool or approach is used? So, there is a workforce problem there because the person with a 10-year GMC-licensed medical degree may not necessarily be the right person to manage that quite complicated process. And by the way, we've got so much disease that we're going to need thousands and thousands of people engaged in this process, and that's far more than our medical schools can provide. So, there's a real challenge there. I don't know if others agree.

**Erin Angel** 19:35

Yeah, maybe if I can comment on that. So half the audience is going, “Well, my doctor has MyChart,” right? Good. Which is like EMR, but that doesn't really solve the problem, does it? Right? So, what we're seeing today is with the EMRs, electronic medical records, the MyChart that you have on your phone or whatever brand you use, with your doctor's office. It has your episodes of care, right? It can tell you, you went to the doctor a month ago for a cardiac reason or whatever, and the results of that, which is great. That's a great start. But what happens for doctors, particularly in the care area, cardiology, oncology, et cetera, is they need this sort of disease-specific view of everything relative to their patient. All of the biometrics that have been measured, every time they've been to another doctor, even if it's not within their health-care facility. And they don't need more and more data. Doctors are overburdened. They need just the really salient data relative to that patient. Also, their lifestyle, experience, all of the things that may impact their specific disease case. And AI has so much potential. Right? So much potential, but it's complicated. It's complicated for a lot of reasons. Clearly, top cardiologists in the world and still didn't have that kind of cross-disease view. Can we get there? Probably. Part of the problem is that—okay, so I'm industry. I'm going to give you that point of view—part of the problem is that, how does health care pay for that? So, there's no individual reimbursement for these AI tools that may help a physician better care for you. So, then how do these hospitals or health-care systems that are already running on almost zero margin find the margin to pay for that technology? So, what does industry do? “Ooh, who's going to pay for this thing? Maybe we won't build it.” So, it's kind of this cyclic, opportunity yet challenge.

**James Bethell** 21:30

No, it is. And EMRs have got so far, but the fact that Kasey's father was no longer supporting the Chieftains, go Chieftains, does not get captured in that EMR, right?

**Erin Angel** 21:48

Right. Yes.

**Erin Brodwin** 21:49

We will get to caregiving and AI. Yes, the two of those are together for a reason, I promise. So, we'll return to that subject in a second. I do want to talk about clinical trials, though, because I think a lot of people in the room are probably excited about those. James, I have a question for you. I did spend some time in the UK. There are a lot of things about its health-care system that are quite different from ours. Based on some of those things—

**James Bethell** 22:09

You don't pay for it is quite a big difference, yeah.

**Erin Brodwin** 22:10

Well. Also, based on a lot of those things, it should be one of the best places in the world to run a clinical trial. Particularly a dementia trial. Why isn't it?

**James Bethell** 22:22

Oh, gosh. You're putting me on the spot. You're right, it absolutely should be, and occasionally it is. Just to break a few sort of secrets to this crowd, don't tell anyone. But although it is one system, it's actually 16,000 different organizations, and some of them jealously guard their own data and don't easily share it with one another. Now, there are ways to break through that, but it isn't quite as simple as—I can't from my office look up everyone's EMR or delve deeply into the records. So, that is a problem. It's also highly stressed, and so the investment in clinical trial nurses and into the amount of time that each doctor is meant to spend on research, which is roughly a day a week, has been chiseled down a lot, simply to try to keep up with capacity. There's also some clinical conservatism in the UK. We are not as adventurous as America. Some of that has spared us from things like the opioid crisis, but some of it is, frankly, just old-fashioned skepticism about innovation, and I think that there's a culture change. And then lastly, we're broke. And I think that there is a psychological terror, particularly in dementia, amongst clinicians, that if there was suddenly a breakthrough tomorrow, and there was a £10,000-a-year treatment for early-stage dementia, that would literally bankrupt the health system. And that then manifests itself into a resistance to ever finding a solution. And it leads to, and I've sat in the rooms and encountered this time and again, sort of clinical chiseling and resistance to progress that's really, really contagious. Now, the good news is our prime minister is all in on dementia. His father had Alzheimer's for a long time. He cared for him. He was himself a health secretary, so kind of knows how it works and where the bodies are buried. And I think that there is a new atmosphere in the UK, and we're definitely doing a lot to try to accelerate clinical trials in dementia in the UK.

**Kasey Kissick Duarte** 24:37

In the UK, and in worldwide, the economic case for investing in dementia research is there.

**James Bethell** 24:44

I know.

**Kasey Kissick Duarte** 24:44

This is an expensive, major problem across the world. It seems like from a policy perspective that there's traction there.

**James Bethell** 24:53

You'd think. But if you're a frontline clinician running an emergency department and you haven't got the money to update your fax machine—

**Kasey Kissick Duarte** 25:00

The fact that we're talking fax machines.

**James Bethell** 25:02

—then you are mentally terrified that the whole thing might blow the bank.

**Niranjan Bose** 25:09

So, I want to tie the first topic on early detection with clinical trials, and your comment, you're absolutely right that there's an economic case. But I think the lights are blinding, but I think I see John Dwyer in the room. We have an amazing pipeline, no doubt, in dementia trials including Alzheimer's disease, let's say 175-plus. To effectively enroll in all of those trials, I think John quotes a number like 50,000 or 60,000 individuals are required. But what do we enroll today? About 15,000. So, there's a massive bottleneck in trial enrollment. So, even if we do early detection and access is a system challenge, we absolutely can do better in enrollment in clinical trials. That's the only way we're going to solve this problem.

**Erin Angel** 26:01

But how can we do better at enrollment in clinical trials?

**Niranjan Bose** 26:06

Fantastic question. So, the first, I think, is understanding what some of the challenges are. And I can name a few. One, we require imaging as the entry point for clinical trials. What does that mean? You have to come the day before, take time off work, maybe a caregiver drives you to the place, et cetera. And a PET, again, has a half-life. So, you have to be there just in time to get it done, the whole day. Now, with a blood test, we're solving the problem one thing at a time. You can screen people at larger numbers. Now, you can do the confirmatory PET rather than screen by PET. I think the second part is we need awareness. Like, where do they send them? Do we even have that awareness built in the system? And we've got to do better. The third challenge is, and industry may not like this, I think we fish, and when we don't enroll them, we put them back into the system. Why can't we know what their status was and build a database or registry so we can avoid screening the same person multiple times? It seems logical to me.

**James Bethell** 27:24

That's a very good list. Can I add two to it? Firstly, in terms of participant data, we already have records of a lot of people who might be good for a clinical trial, and we don't use that asset nearly enough. I'm the chair of something called the BARBARA Alliance. That's what we're doing in the UK. And I think it'll be hugely successful. And huge thanks to Gates Ventures for supporting that with a very generous grant. Secondly, we are very squeamish about putting people with brain health issues into clinical trials in a way that we just wouldn't be with cancer. If someone had early-stage cancer, they are heroically brave about putting up with all sorts of noxious toxic chemicals and radiology. We put them through the mill in order to see if the tests work, and they are delighted, not delighted, but they are prepared. Their risk tolerance is huge because people want to survive cancer. But as Bose said, but with brain health, we have prophylactic MRI scans, which by the way, cost a lot of money and are difficult to book in, and the smallest sign of bleeding and the whole thing gets canceled. Why is it that we are so squeamish about health? I think that sentimentality needs to be lifted.

**Erin Brodwin** 28:44

Bose, I wanted to ask you a question about open data. We've heard for years that open data will accelerate drug discovery. Could you give me a concrete example of where data sharing has actually changed a research outcome?

**Niranjan Bose** 28:57

Yeah. Glad you asked the question. Let me give you the example of global health. And this is healthy birth, healthy growth and development, healthy pregnancy outcomes. The world has done hundreds of studies following pregnant women, birth outcomes, childhood outcomes of growth. But each one of those studies was done to the tune of 100, 200, maybe 500 women followed through pregnancies. But if we were to go to GE and say we want to do one ultrasound, in low- and middle-income country settings, even getting one ultrasound is hard for a woman who has to walk maybe 10, 15, 20 kilometers to get a medical checkup. But I can only give you one ultrasound image. With that image, can you tell me the baby's gestational age so I know if I can give steroids if it's a preterm baby? Because the mom likely doesn't know when the baby was conceived. She doesn't know the age, gestational age. The second, head circumference measurement, can you tell me, is this baby going to grow to have a normal, healthy life? So, how can we answer this when the numbers are 50, 100, 200? We can't really develop AI algorithms. So, what did the Gates Foundation do? They went and collected every single one of those funded studies and built a million-woman database, so almost a million birth outcomes. With that type of data, they were able to work with the GEs and the Philips of the world to say, “We give you one measurement, predict the outcome.” And that's been hugely successful.

**Erin Brodwin** 30:43

Great. Not to jump back, but I'm going to jump back. Kasey, I wanted to go back to a point that you were making around economics and the case for research in dementia. In terms of FTD, are the economics of clinical trials for FTD fundamentally broken?

**Kasey Kissick Duarte** 30:59

Oh, that is a good question. Maybe. Sadly. FTD is classified as a rare disease. To be honest, I don't believe that it is a rare disease. I just think it's misdiagnosed so rampantly that it's missed, it's miscounted. But yeah, it's hard. Like any rare disease, it's hard to make the case to invest here. One thing to note with FTD is it's a complex disease, like many of different forms of neurodegeneration, but there's overlap with subtypes. Some of them have overlapping pathology with Alzheimer's, some with ALS. Many are mixed. We're finding more and more, there's a lot of mixed pathology. People can have more than one type of dementia. And so, I think, as a funder in FTD, we are often the squeaky wheel of like, “Hey, you're doing a trial with Alzheimer's? Don't forget about us. We want to be involved.” We recently supported a diagnostic accelerator program to bring FTD studies into this work that is ongoing to really look into diagnostics and to make sure that we could pull in FTD samples into that. So, some of it comes back to the awareness. I think people aren't recognizing the symptoms to get to the doctor. Doctors aren't recognizing what this is either. So, it's increasing awareness to increase prevalence, and then it's also making sure that we have that data, that we have a registry, that we know for sure what these counts really are. And then looking for areas where you can, I don't know, piggyback on other efforts that are underway. So, I think that's something that's going to be meaningful for FTD specifically.

**Erin Brodwin** 32:55

James, I want to go back to you. The US has more readily accepted, embraced new Alzheimer's drugs, definitely faster than the UK. Is the UK being too cautious, or is the US too willing to accept modest returns on its treatments?

**James Bethell** 33:12

No, I hugely regret the decision by NICE, the body that allocates drugs to patients, and their decision. Not only do I think it was the wrong decision, it was also done in a particularly brutal way that undermined confidence in the efficacy of the drugs. It was—

**Erin Brodwin** 33:31

What do you mean by that?

**James Bethell** 33:34

So, the trials that were done in the UK were far too complicated. They therefore loaded the process with a bunch of costs that, if you deployed the drugs realistically into the health system, wouldn't have applied. So, that was a way of kind of tilting the scales against the drugs. And secondly, it brushed off all of the improvements to the participants' health as though three, six, 12 months' worth of improved condition from dementia didn't really matter. That assessment would not have applied if it had been cancer. If someone had been given three, six, twelve months of good life from a cancer drug, they would have approved it. So, there was a snobbery or an aversion to approving a dementia drug compared to a cancer drug, partly because of the problem that they're terrified of the potential cost, and partly because dementia is still regarded as a Cinderella problem that people just think is a fact of life and bad chance rather than a treatable disease. There's been huge pressure since they did that to turn that decision around. I'm hoping that they are going to do that soon, and I hope that the protocol around doing further tests will be simplified. Bose alluded to this. We've got to make this stuff a lot more simple, and we've got to be less squeamish about the tolerance that people, particularly with advanced dementia, have got. Another way in which the trials that were done in the UK, I felt, were not proportionate is that they did the trial on people with advanced disease at quite an advanced age as well. Well, that's not necessarily where these drugs are going to have their greatest impact. It may well be that it will be at an earlier stage in the disease. I would love Britain to be at the forefront of clinical trials for these dementia drugs in the future, but we do need to get over that hump.

**Erin Brodwin** 35:33

Erin, new Alzheimer's treatments require quite a lot. They require imaging. We were just talking about this, scans, imaging specialists. We talked earlier about community hospitals. Can community hospitals realistically deliver this kind of care? Are we at risk of creating a two-tier system?

**Erin Angel** 35:51

Yeah. First thing is cycle back to the clinical trials for those community hospitals. One of the clear gaps, and I was hoping to set you up on this one, Bose. One of the clear gaps in clinical trials is we don't have clinical trial matching. So, how do you get into clinical trials? Do you go into an advanced clinical center,

advanced cancer center, et cetera? But do all patients that would be the right patients for those trials have the right access to the doctors that would get them in the trials? Absolutely not. So, what can we do to bring clinical trials to the community clinic that may not know what trials are otherwise available, and that their patient would be the right patient for that match? So, you were asking about imaging, as it relates to how do you get new therapies into the—

**Erin Brodwin** 36:41

Community hospital setting.

**Erin Angel** 36:41

—community hospital setting. It's challenging. It's challenging for a lot of reasons. Change management is challenging. The payer model is probably the most challenging. It's very hard for community hospitals to take on new therapies when they're taking a risk that they won't be paid for those therapies. So, that time that it takes from a therapy to be developed to the time that it's accepted clinically and paid by the health-care insurance, Medicare, Medicaid, et cetera. That is a time where there is just simply a gap in access to care because those patients aren't getting prescribed those treatments. I'll give you an example. It's more imaging, but forgive me for that. But in January 2025, CMS actually changed the way that we pay for the agents that we use in PET imaging. So, PET imaging is often used because it images the biology of the brain. It's often used in dementia cases, right? The problem is they were bundling the payments. So, if you did a payment for PET, you'd get one payment no matter which agent you were using, and the agents have different costs based on different diseases. So, those diseases that were higher cost agents, because it was one payment, hospitals just couldn't afford to give them the agent to look for the disease in the first place. So, CMS saw that issue and actually an example of good corrected for that issue by separating the payment for the agent, which is the thing you inject, the radiopharmaceutical, the thing you inject in PET versus the imaging itself, so that all patients could have access to that. So, it is financial many times.

**Erin Brodwin** 38:24

I want to move into a section that I previously said was called caregiving and AI, and there's a reason for that. I will admit I have a vested interest in this set of questions because my father had dementia. As we said, a lot of us have had a similar experience. But, this one's primarily for Kasey and for Bose. Millions of families are overwhelmed by dementia care right now. Why does so much innovation focus on detecting and treating disease rather than helping people live with it?

**Kasey Kissick Duarte** 38:58

I can take a stab at it. I don't know. I'll start with there. But no, I can speak to some sort of bright spots. The thing about AI, obviously, I'm sure it's come up in every single session at this conference in some capacity. But, one, it's only as good as the underlying data, but I think it's going to revolutionize everything from early diagnosis all the way to streamlining reimbursement. Our foundation recently supported an exciting initiative that is on the caregiving side and leveraging AI. It's an organization called Foreguard, which is really just looking at using AI to help families navigate public and private insurance. There are so many families who spend tens, if not hundreds, of thousands of dollars on dementia care who have no idea that actually they're just leaving money on the table. They're qualified for public benefits that they don't know about. And so, this is a tool that's meant to help families understand what are they eligible for and to help them get that coverage. So, that's something that I think every family, it will help tremendously,

especially for diseases like FTD or other early-onset dementias that strike earlier in life. It's often when people are in the prime of their careers, and so that's transformational. Bose.

**Niranjan Bose** 40:26

I'll build on that and say, I think it's fundamentally a payment issue, right? Where's the money to be made? I think it's on prescribing tests, diagnostics, and treatments. Caregiving, what's the reimbursement code, so to speak? I think it comes down to a complexity of those issues. I'll draw two analogies for you. One is, eight years ago when we started the diagnostics accelerator with the Alzheimer's Drug Discovery Foundation, we went around, asked VCs why they were not investing in blood tests. The blunt answer was, “There's no money to be made in this.” Mm. Until you see treatments come in, no one's going to prescribe the blood test. And that, unfortunately, is the reality. So, somebody had to de-risk the development of the blood test, and that's, I think, where philanthropy has a role to play in caregiving and leveraging AI advances. Until it becomes mainstream, I think philanthropy will have to play a role in catalyzing some of those tools. And we're attempting to do that.

**Erin Brodwin** 41:29

Here's a question.

**James Bethell** 41:30

Sorry. Do you mind if I just come in on that?

**Erin Brodwin** 41:32

I do have one question for Bose, just to ask real quick. Yeah. Why not invest $100 million in caregivers than in another drug discovery initiative?

**Niranjan Bose** 41:41

Oh, in terms of caregiver support? It's not an either/or game, unless you told me it's only $100 million and I get to make my bet in one place or the other.

**Erin Brodwin** 41:53

Let's do that.

**Niranjan Bose** 41:57

I'm glad I walked into that.

**James Bethell** 41:58

Yeah. You did.

**Niranjan Bose** 42:02

If it's a zero-sum game, I would say investing in upstream innovation is going to solve the problem for all caregivers down the road. So, if you do an NPV calculation on the ROI on that $100 million, I would still put it upstream because if you have a game changer, it's going to have a longer-term impact.

**James Bethell** 42:25

Well, I would agree with that. I think that it was never meant to be like this. I hugely regret, and I've been a caregiver, the huge pressures that are put on millions and millions of people who are caring for people with dementia. It is a huge burden on society, and individually, they sacrifice time, love, energy, money to do it. But the idea in the old days was that people died before they got dementia, or that they didn't carry the same metabolic risks that have led them to get dementia, and so the economics hasn't worked out. Ultimately, a lot of this is about the same old drivers of heart disease, of cancer, of dementia. They are the same upstream causes, and ultimately, the answer is to bend the curve and to get a reduction in the total amount of dementia. I am hopeful that, in the UK we're running at about 40 percent of people will have about between five and 10 years of dementia at the end of their life. That's a huge burden. I think that number could come down to 10, 5 percent within certainly my children's lifetime. And that's what we should be striving for.

**Erin Brodwin** 43:40

I'm supposed to remind you all to submit questions. I believe I'm supposed to be able to see the questions on this tablet here. I cannot currently see them—just as a warning—but if you would like to submit questions, I might be able to see them pending some tech developments. In the meantime, AI is supposed to transform dementia care. I would love to hear some concrete examples, specific examples, because I know AI can get very broad and very confusing, where it has.

**Erin Angel** 44:12

I'll tackle one. There's so many. AI changes pretty much everything we innovate today. But, um—

**Erin Brodwin** 44:19

Can we think about both patients and caregivers, just since—

**Erin Angel** 44:22

Yes. I will start with caregivers, since I usually start with innovation. My sister is a nurse advocate. Nurse advocate is someone that kind of helps to fill that gap between what the doctor is prescribing and then coming home and figuring out how to put your pills in the right pillboxes so that you take them at the right time, or thinking about making sure you have the right materials near your couch if you're not able to get up from your couch. Just that translating from the diagnosis and care to the family world life. It's great for those patients that can afford it, right? But not all patients can afford or are lucky enough to have the family that can afford the time to care for them. So, there's definitely gaps there. Can AI help? Yeah. She alone is using AI all the time. Every patient has a booklet, right, of their disease and their care pathway and what medicines they take, et cetera. That's just very simple AI. But is there more opportunity to help these patients with AI? Yes. Not without a human component, though. It's AI-assisted human care. Okay, now I get to go to technology? Great. So, with these drugs, I'm going to use the two amyloid-beta-targeting drugs for Alzheimer's. With these drugs, there are very serious side effects. Brain swelling and/or brain

bleeding can happen in some subjects, and so we use MRI scanning before and during treatment to monitor these patients for disease. It's not an easy MRI to read. It really does require an expert radiologist, and there are not enough expert radiologists in the globe to read that many MRIs for ARIA. ARIA is the name of the brain bleeds that you're looking for. So, what can we do, and what have we done about it? We purchased a company called icometrix that actually developed AI models off of the MRI images to help any radiologist. So, sometimes the reality is it's a body radiologist reading a brain for ARIA. That's the workflow-burdened world that we live in. And so, it helps them do that ARIA read in a level that would be more similar to that of an expert because we don't all live next to an academic health care institution. So, it kind of brings up that level of care as we think about access to care and bringing the best care to all.

**Erin Brodwin** 46:44

How does it do that?

**Erin Angel** 46:46

Sorry?

**Erin Brodwin** 46:47

How does it do that?

**Erin Angel** 46:48

It trains on experts. I don't know exactly how their model works, to be fair. But usually models like this, because there are many, they train on experts to take what used to be a qualitative thing, an image, right, a picture of the brain, to something more quantitative like a blood test. So, it's training on experts to learn how to do the right measurements, find the right metrics to get to something more like a blood test off of that image. It's not doing any radiologist's job for them. It's definitely an assistance. But it does help bring up that level of care to closer to that expert level of care for all that have access to it.

**Kasey Kissick Duarte** 47:27

I might build on that a little bit. This is, again, I spoke about caregiving innovation AI with the insurance navigation. But on the research side, and again, the lights are blinding, but some friends from the 10,000 Brains Project are in the crowd, I think. And there's a whole lot. They're doing amazing work to leverage AI across neurodegeneration. One project that we supported that I'm particularly passionate about is just to digitize brain slides. So, we, and many families, make what for us was actually not a difficult decision, but it can be, to decide to donate your loved one's brain. I was completely aghast to find out, from Pat Brannelly, who's somewhere in here, that the brain that we donated to ALLFTD up at UCSF, the slides were just sitting in desk drawers, not digitized, just sort of in this one office in the desk. And it gutted me because I'm like, “We donated that. It was so meaningful to us to use that to advance science.” And so what their team is doing is, it feels very simple, but they're digitizing all this really rich information, and then can leverage AI to combine that with family history, clinical history, genetics, all these things, and pull it together. And hopefully it will lead to some new clues that will get us to some breakthroughs.

**Erin Brodwin** 48:57

Anyone have anything else they want to add?

**Niranjan Bose** 48:59

I'll add one example. This is about Clinical Dementia Rating scale, which is an interview along with a caregiver.

**James Bethell** 49:06

Yeah. With the caregiver.

**Niranjan Bose** 49:08

And AI is going to revolutionize using digital voice. It's a conversational bot. You call a phone number, it has a conversation for however long you want. It can go on and on for hours. Patiently engages with the caregiver and the participant. There's no rater bias. You can scale. Cost effective.

**James Bethell** 49:30

Really nice. I have a more mundane piece of agetech which I got my auntie, which is a pill container with a speaker and AI built into it. Obviously, it's to make her take her pills and not fall over, and it records my voice, and it says, “Hi, Auntie, don't forget to take your pills this morning.” And then if she doesn't take her pills, it says, “Susanna, you've got to take your pills.” And then if she still hasn't taken it, I won't do it now, but I blow my top and say, “For God's sake, Susanna, take your bloody pills.” And she normally gets to, because you can see on the thing, it takes to the third bollocking that she actually takes her pills. But the incidence of her taking her pills has gone up a lot. And I tell you what, that's had more impact on her health than really—

**Erin Brodwin** 50:21

I was going to say, does that work?

**James Bethell** 50:22

Just taking the pills every day does make a big difference.

**Erin Brodwin** 50:26

Really? Okay.

**James Bethell** 50:27

Oh, God, yeah. You bet.

**Erin Brodwin** 50:28

Are you measuring the improvement?

**James Bethell** 50:29

Yeah. It's all on the thing.

**Erin Brodwin** 50:30

Okay.

**James Bethell** 50:31

Yeah. She's now totally accountable. It's dank, yeah.

**Erin Brodwin** 50:33

My pad hasn't lit up yet. I have some audience Q&A that is not from the audience it is from me, because I can't see your questions. We can move to mic-based, I can take questions. So, can I just give you my, I don't see anyone to help me.

**Erin Angel** 50:48

There it is.

**Erin Brodwin** 50:49

Okay. I'll just do this.

**James Bethell** 50:51

Nice.

**Erin Brodwin** 50:51

I'm just going to give you guys this.

**James Bethell** 50:55

Nice.

**Audience Member 1** 50:56

Thank you very much. It was a really terrific panel discussion. I have one question. I haven't heard you say one word about hearing loss. So, one of the things that annoys me is when I hear of all the biomarkers and how we're diagnosing earlier in stage, no one talks about doing a hearing test to say to what extent is hearing loss contributing to what appears like dementia, and in fact, it's not, it's hearing loss. Case in point, I have a friend whose mother was put into hospice because she stopped engaging and was told that she's dying of dementia. Turns out she lost her hearing aids. And when her hearing aids were put back on, she was back to her normal cognitive behavior and social engagement.

**James Bethell** 51:39

Wow.

**Erin Angel** 51:40

Yeah, I'll share, you called out a true reality here. We're mostly talking about Alzheimer's, FTD, and Lewy body, but is that all of dementia? Absolutely not. Or is it all of the things that may present as dementia? Absolutely not. Stroke, vascular issues, there's a huge spectrum of different diseases that may present or be misdiagnosed as dementia, and hearing loss is certainly one of them. We just can't cover everything.

**Kasey Kissick Duarte** 52:08

No, it just speaks to the complexity of diagnosing these things, and so real promise and excitement at better biomarkers. But I think, again, for me, it does come back to awareness building as well of we should talk about that, that that happens. I think our foundation is we're invested in a number of things on this front, films, documentaries, even theater, to bring sort of stories of what dementia actually looks and feels like. And then we're also building a public awareness campaign, it's called Beyond Memory, to shed light on the lesser-known symptoms, the early symptoms of dementia. But I think this type of misconception is exactly what we want to shed light on, of if you were talking to a friend, what would you be describing? You'd describe hearing loss. But to be able to have a place where you can start to untangle these, people don't think in clinical terms, they think in what they're seeing in front of them, but how to untangle that and then get routed to the right doctor and push for answers and the right tests. So, it comes back to awareness for me.

**James Bethell** 53:19

And certainly for the BARBARA Alliance, we've got a fund to help support interesting diagnostics. Of course, some of those will be images, some of them will be blood, most of them will. But we're open to all comers. That includes people looking at pee, poo, dogs, speech, any number, and I'm a champion for that, not so much because I think that they will be medically more confident and secure, but because some of them may suit the patient much more. And we've got to be open to the idea that there are going to be different ways in to the dementia diagnosis journey.

**Audience Member Catherine** 54:00

Hi, good afternoon. My name is Catherine Buell, and I run a firm called Wellness Real Estate Innovations. And we're trying to build DC's first dementia village. And one of the things we've learned, we're modeling this after De Hogeweyk in the Netherlands, is how much places make a difference in patient outcomes, and having appropriate care settings, having trained professionals and the like, and that social interaction. And so I'm curious from you all, if you all are seeing in the United States place-based models that actually work to address the symptoms of dementia, and are also places where people can go to get help.

**Erin Brodwin** 54:38

Great question. I am not suited to answer that, but you all are. Go ahead.

**Niranjan Bose** 54:46

I don't have much knowledge about this.

**Kasey Kissick Duarte** 54:50

I think you're onto something that's a gap. I feel like this is a real need in the space. I mean, I can't tell you, especially with FTD, there are often behaviors that are socially inappropriate, hard to manage. All you want to do as a family is isolate, but that's not good for the patient. That's the last thing that you want to do from a health perspective. So, I'm really excited about the dementia village concept, and I think it's great if we can find ways to scale that here just to let people have dignity and be in community and socialize, but to do so safely. So—

**Niranjan Bose** 55:30

I do want to—maybe we should not be calling them dementia villages to begin with. If we believe that it's a stigma, and we want to remove that stigma—

**Kasey Kissick Duarte** 55:42

It's part of our society.

**Niranjan Bose** 55:43

I think we've got to come up with a different way of talking about it.

**Erin Brodwin** 55:47

From very limited personal experience, seeing a loved one through a series of locked hospital doors is not really the best way to go either. So, it's a super interesting concept. Any other audience questions? Yes, sir. Oh, right there. You next.

**Audience Member 3** 56:12

Thank you all. So, there's a lot of noise. You were talking a little bit about upstream drivers of health, and there's a lot of noise in the news about what kinds of things prevent dementia. Can you name the top three lifestyle changes you think that prevent dementia, as where the research is right now?

**Niranjan Bose** 56:29

Absolutely. Hearing loss is a big risk factor. I wouldn't say it's the biggest. It's one of the big risk factors. Social interactions, goes hand in glove with hearing loss, and the third would be, for me, diet and exercise. It all depends on context. People talk a lot about Mediterranean diet, but I think it's going to be culturally whatever the right diet is.

**Kasey Kissick Duarte** 56:58

The shingles vaccine.

**Niranjan Bose** 57:00

Yeah, shingles vaccine.

**Kasey Kissick Duarte** 57:00

Has been amazingly shown to—

**James Bethell** 57:02

I know. But there'll be others. Obviously, it's going to be—and that was a chance observation, right?

**Niranjan Bose** 57:08

From Europe.

**James Bethell** 57:09

I know, from Wales. Amazing. Are there going to be more of those kinds of connections, particularly to our immune system, isn't there?

**Niranjan Bose** 57:18

Absolutely. But I think people will argue is it correlation or causation?

**James Bethell** 57:24

I don't care.

**Niranjan Bose** 57:24

Can you show me through a randomized controlled trial? But I think if we're truly talking about lifestyle modification, get the shingles vaccine when you turn 65.

**James Bethell** 57:33

Oh, I had it already. I went early.

**Erin Angel** 57:35

At 50.

**Niranjan Bose** 57:36

50?

**Erin Brodwin** 57:37

Age 50, I believe it is.

**Niranjan Bose** 57:38

Oh, shoot.

**Erin Brodwin** 57:39

We only have one minute left.

**Niranjan Bose** 57:39

Maybe I'm—I need to go get my shot.

**Erin Brodwin** 57:41

It's all good.

**Kasey Kissick Duarte** 57:42

You've got to go.

**James Bethell** 57:42

Come on, Bose.

**Erin Brodwin** 57:44

We're going to wrap in one minute, so closing thoughts.

**Erin Angel** 57:49

Just on that one, and sleep. We don't know for sure, but we believe that good, solid sleep is critical for dementia, and I hope we can prove that in the upcoming years.

**Niranjan Bose** 57:59

I think we have the much-needed boost in optimism. People needed that hope. And I think we have it. We need to capitalize on that moment and accelerate things.

**Kasey Kissick Duarte** 58:10

Yeah. I think, dementia, there is still stigma associated with it. It is still scary, but again, there's real reason for optimism, in the science and where we're headed, and I think we're going to see some real breakthroughs. So, I'm excited.

**James Bethell** 58:30

I think that there is real hope. Our politicians were terrified of talking about dementia. It's so encouraging that in the UK, we have a prime minister who's leaning in. Someone used the phrase, "We have 'Star Wars' medicine, and 'Flintstones' health systems." I thought that was cute, so I'm going to steal it.

**Erin Brodwin** 58:49

I think it's "Star Trek" medicine.

**James Bethell** 58:51

Okay, “Star Trek.”

**Erin Brodwin** 58:51

As a Trekkie, I would like to correct that.

**James Bethell** 58:53

I like “Star Wars,” though.

**Erin Brodwin** 58:54

Sorry.

**James Bethell** 58:55

I like “Star Wars.” Either way. That's just so true in this area, and I think this discussion, by getting under the skin of some of the practicalities, has illustrated what a struggle it's going to be for our health systems to adjust to this revolution.

**Erin Brodwin** 59:16

Thank you.

**Erin Angel** 59:17

I'd say we're just at the tip of the iceberg of this. We're learning there's 158 dementia trials underway right now. So, yeah, we have two accepted. Great. What else is coming, and are we ready to translate it into maybe not the Flintstones health care hopefully in the future?

**Erin Brodwin** 59:30

Wonderful.

**James Bethell** 59:31

Thank you.

**Erin Brodwin** 59:31

Well, thank you all so much. Thank you for coming. Appreciate it.

**Announcer** 59:35

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