Global dialogue on LMICs: Transcript

The dementia landscape project

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Organized in partnership with Alzheimer's Disease International
Co-chairs

Meera Pattabiraman

Meera Pattabiraman is Chair of the Alzheimer’s and Related Disorders Society of India (ARDSI). She has been working in the field of dementia care, management and advocacy for the past 18 years. A post graduate in business administration, she entered the field of social work and dementia care because of her personal experience of being a carer for her father who had Alzheimer’s disease. Meera Pattabiraman was part of the editorial board that produced the India Dementia Report in 2010, which is now used by the Ministry of Health and the Ministry of Social Justice and Empowerment as the reference guide in all matters relating to dementia. She is also part of the national think tank to develop better healthcare for the elderly and has taken part in national health policy meetings.

Paola Barbarino

Paola is the CEO of Alzheimer’s Disease International. Prior to that, she was CEO of LIFE. Her previous senior positions include Cass Business School, Tate, British Library and IIED. She is a Trustee of The Postal Museum and Lauderdale House. Previously she was a Trustee of Shelter, the UK housing and homelessness charity and of MLA London. She is also the Managing Director of Opaline Limited, a consultancy company specializing in strategy and governance. She holds a degree cum laude in Classics from the University of Napoli Federico II, an MA in Field and Analytical Techniques in Archaeology and an MA in Library and Information Science both from University College London.
Speakers

Dr Paul Kiwanuka-Mukiibi

Paul Kiwanuka-Mukiibi is the Executive Director of the Uganda Alzheimer Association, of which he is also a founder Board member and the General Secretary. Until he took on his current role, he was Managing Director and Principal Consultant of PS Consulting (PSC), a health development consultancy firm he founded two decades ago. He is a research and policy specialist who has provided technical assistance to the Uganda Ministry of Health (MoH) and other line-ministries; national health programmes funded by Development Partners/Donors including the WHO, World Bank, USAID, UKAID/DFID, DANIDA, KfW, AusAID and Irish Aid, amongst others; other ministries of health, international and local NGOs throughout the region; and private health-sector organisations.

Professor Francisco Lopera

Francisco Lopera is full professor and Director of the “Grupo de Neurociencias de Antioquia” (GNA) at University of Antioquia in Medellín, Colombia. The GNA works in basic and clinical neurosciences, in developmental and neurodegenerative disorders. As a Behavioral Neurologist Lopera Works at the Department of Internal Medicine, Clinical Neurology Service at Medical School of the Antioquia University, He plays an active role in assisting patients with Alzheimer’s Disease, CADASIL, Parkinson disease, Huntington disease, Mild cognitive impairment, Fronto-temporal dementia, and other forms of dementias. Lopera has been working with a large groups of families with Familiar Alzheimer’s Disease due to a PSEN1 mutation (E280A) for over 30 years. He is the Principal Investigator in Colombia in Alzheimer Prevention Initiative program (API COLOMBIA) in collaboration with Banner Health Institute and Genentech/Roche.
Dr Vijayalakshmi Ravindranath

Dr Vijayalakshmi Ravindranath obtained her Ph.D from the University of Mysore in 1981. In 1986, after completing her post-doctoral training at the National Institutes of Health, USA, she joined the Department of Neurochemistry at National Institute of Mental Health and Neurosciences, (NIMHANS) Bangalore. In 1999, the Dept. of Biotechnology (DBT), Government of India sought her out to help establish the National Brain Research Centre (NBRC), an autonomous institution of DBT, Ministry of Science and Technology as a centre of excellence and to co-ordinate and network neuroscience research groups in the country. She continued as Founder Director, NBRC till May 2009, when she returned to Bangalore at the Indian Institute of Science (IISc) as Professor and Founder Chair of the newly created Centre for Neuroscience. She is currently Founder Director, Centre for Brain Research (CBR) at Indian Institute of Science.

Lenny Shallcross

Lenny Shallcross is executive director at the World Dementia Council. Prior to that he was Head of Community Engagement leading programmes across the UK to establish Dementia Friendly Communities. This includes the Dementia Friends programme which is the biggest health social movement campaign delivered by 10,000 volunteers that have recruited 2 million individuals through a community, digital and corporate offer. Before working for Alzheimer’s Society he worked in the UK government as a political adviser at DCMS and the DoH, as well as working in Parliament and for the Labour Party.
Good morning everyone. Let me just say welcome to you all. I am Lenny Shallcross, Executive Director of the World Dementia Council. I realise that some of you have participated in Council activities before but for those of you who are new, the World Dementia Council was set up following the London dementia summit in 2013. The Council is chaired by Harry Johns, President and CEO of Alzheimer’s Association in the US and there are 24 members of the Council. Alongside them there are a number of government members and OECD and WHO are also members.

At the London summit in 2013 the international community committed to make progress on research, care, awareness and risk reduction. The Council was established after the summit to support and challenge the international community to deliver on those goals. What we are doing this year is evaluating the progress that has been made and identifying how that can be accelerated. We will be producing a report on that later this year. To support that we are holding a number of workshops – virtually of course – of international experts to reflect on where we have come from, where we are, where we need to get to and what we need to do to get there.

After this meeting we will write up a transcript of the meeting which we will circulate to you and that will be followed by a discussion paper which we would welcome your input into. And all of this activity is as I said feeding into a report later this year which we will – and I know this might sound somewhat optimistic – launch at an in-person conference.
towards the end of the year where I can welcome you in-person rather than welcoming you virtually to my sitting room on what is a very sunny and pleasant London day.

Before I hand over to the co-chairs just to remind you to mute yourself unless you are speaking. As you will see we are recording the meeting, but this is only for the purpose of producing the transcript. Throughout the meeting we will have the chat function open so please use it to share your thoughts. There is plenty of opportunity to participate in the discussion live later in the meeting if you would like to do so please raise your hand virtually, put a message in the chat or just wave! We will be keeping a look out and Paola who is chairing the discussion will bring you into the conversation.

So with that I just want to introduce the chairs. Both of whom sit on the Council and I am sure you know them both. Meera Pattabiraman who chair’s Alzheimer’s and Related Disorders Society of India. And Paola Barbarino who is CEO of ADI and actually a neighbour of mine down the road, but right now in lockdown London down the road could be 100 miles away! Anyway she will be chairing the discussion later, but first to take you through the opening speakers I will hand over to Meera.

**Meera Pattabiraman**
Chair, Alzheimer’s and Related Disorders Society of India (ARDSI)

Thank you, Lenny, welcome everyone. Today’s meeting on LMICs is part of a series of ongoing workshops and roundtables being held by the World Dementia Council. As Lenny indicated the purpose of this is to bring out a Dementia Landscape report by the end of the year. The other areas covered so far are research, care, prevention and technology. We thought it would be important to have a session exclusively on the challenges in LMICs. One reason for that is the majority of people with dementia live in LMICs. Dementia is the biggest challenge for the elderly population and the numbers living with dementia will increase very rapidly in the coming years. I am from a country with the highest number of persons with dementia in the world. I can tell you that although India is a young country at the moment in thirty years’ time, in 2050, one fifth of the world will be over 60. We will have about 30 million people with dementia. This scenario is similar in most other developing countries.

So are we ready as developing countries to meet this challenge of dementia? What is the situation and how is it different from the challenge in high-income countries? Firstly, dementia awareness and knowledge are very low across all our countries. And this is true of all sections of society, even among health professionals. And there is a lot of stigma and prejudice. And that is why dementia diagnosis is very low across all our countries. Also, we have scarce resources which limited diagnostic services and staffing. Care services and support for caregivers is also very low. And in most of our countries, dementia has yet to be acknowledged as a public health priority by our governments.

And so, moving on to research. Whether it is for epidemiological research, care services or clinical trials is this proportionate to the magnitude of the need in low- and middle-income countries? So, there is a lot of imbalance. Way back in 1998 the 10/66 grouping was set up to address this imbalance and research was started in developing countries and there was collaboration between developed and developing countries. And today what we have is a research programme called STRIDE. This was initiated by the London...
School of Economics and ADI is a partner in that. Seven countries are participating, and this research will help strengthen country level response to dementia. So what about clinical research and clinical trials? How much of the clinical research, especially for disease modifying treatments is happening in LMIC countries? Are more trials happening in high income countries rather than low-income ones? Is there disproportionate research taking place in high-income countries when compared to low and middle-income countries? And what is the reason for that and how could we address it?

So that is why we have a very diverse group of researchers and stakeholders to debate this and discuss it. I am sincerely looking forward to hearing your perspective and input. My co-chair Paola and I thought it would be great to have three different speakers from different background, so we have a diverse range of voices. So it is my pleasure to introduce the three speakers for today’s session.

First, we have Dr Vijayalakshmi Ravindranath founding director Centre for Brain Research (CBR) at Indian Institute of Science. Lenny said Paola is his neighbour. Viji is a neighbour from my neighbouring state. She is from Bangalore and I am from Chennai. Our second speaker for the day is Professor Francisco Lopera Director of Neuroscience at the University of Antioquia in Medellín, Colombia. And our third speaker is Paul Kiwanuka-Mukiibi is the Executive Director of the Uganda Alzheimer Association. I invite Viji to make her presentation on clinical trials in India.

Good afternoon everyone. Thank you Meera. In fact, Meera I was born in Chennai too and I live in Bangalore. I want to start off with a point Meera made which is how young most of these developing countries are, including India. Of course, my talk is very India-centric. Average age of Indians is 28.4 years, and we often talk about the demographic
But with increasing lifespan and a large population base we do see that we will have the number of the elderly will increase to about 20% of the total population of 1.6 billion – that is about 320 million by 2050. According to WHO projections, India and China will contribute maximally to the new cases of dementia and in general most of the new cases of dementia will come from low- and middle-income countries. So far public health systems in much of the developing world are focussed on managing infectious diseases, and rightly so, as infectious diseases contribute maximally to both morbidity and mortality. But as people continue to live longer, dementia will go from being a problem just for the elderly to a public health concern and of course a great economic concern.

**Unique challenges**

- Diversity in language/education/socioeconomic background
  - Urban workers (middle class)
  - Rural workers (lower socio-economic strata)

- Increasing prevalence of vascular risk factors
  - Diabetes, hypertension, midlife obesity, smoking

- Joint vs Nuclear families – differential cognitive engagement

- Genetic diversity?

- Longitudinal studies are needed to understand risk and protective factors.

- Such studies lacking from Low and Middle Income Countries

So, one of the unique challenges you have in these countries in Asia is the diversity in language, education and socioeconomic background. In India two thirds of our population lives in village, while one third are urban workers belonging to the middle class and are well educated. There is an increase in vascular risk factor both among the urban population but also interestingly among the migrant workers who come into the rural subjects now and we will have to work harder in our awareness campaign.

**Professor Adesola Ogunniyi**

Thanks Viji. The changing pattern of refusal is almost universal.

**Dr Viji Ravindranath**

Bert, I have presented the baseline data and it will take us a few years to get the longitudinal data.

**Dr Yuda Turana**

@Viji, thanks for great presentation, the big challenge in dementia research in LMIC, is the cognitive assessment in low education level subjects. could you sharing your experience in India? thanks

**Professor Ha Thi Thanh Huong**

I am also interested in how you tackled...
city to work. There is also tremendous change in the cognitive engagement of the elderly as we shift to nuclear families from joint families. And I think the current pandemic brought this to life very clearly. Of course, there is tremendous genetic diversity much of it not well understood. In fact, the whole genome sequencing from this part of the world is very limited except for Korea and Japan. More importantly we realise that our research with mice and cell lines can only take us so far and there is a need to study how people age to understand the risk and protective factors and then think about the right interventions and clinical trials. But such studies, including establishing cohorts and studying them longitudinally require the guaranteed resources to be given to researchers to run these studies. Personally, I can say I was trying for years to start these longitudinal studies.

Finally, I was able to start this research because of two extraordinary philanthropies. One is the Tata Trust that gave us a very generous grant that enabled us to buy a 3T MRI and put it in the Institute of Science campus and also giving us a complete platform, along with computational infrastructure, for doing genomic sequencing. With this we went on to study the elderly urban people in Bangalore. But we really could not go to the harder-to-reach rural populations, until Sudha and Kris Gopalakrishnan co-founder of Infosys, one of the big IT companies in India gave us a gift, and in fact it is the largest individual gift to scientific research in India. It allowed us to set up the Centre for Brain Research on the Science campus that you can see here. CBR will continue to be funded through this philanthropic gift. And through this we started to approach the more difficult task of researching out to our rural population.
Initially we started in Bangalore. We took people over 45. Although they reside in Bangalore our cohort comes from all over India. This was relatively easy to do because they were well educated, aware and accessible. We didn’t need to translate any of the cognitive tests. This is a very valuable cohort because they come forward willingly. They are prepared to spend hours with us, and it is a very engaged cohort.

What do we do? We look at socio-demography, deep clinical assessments including psychiatry and neurology. Cognitive assessments. We use the whole cognitive battery as well as a couple of other batteries. Detailed blood investigations, whole genome sequencing and brain MRI. And they come back for follow-up. Soon we will be starting to measure the blood-biomarkers and optical coherence tomography. All of the data is collected in a digital manner and the computational analysis is done. We have a group of data scientists who help us with the analysis.
When we went to the villages it was a different story. Here we chose a group of villages in a part of a district called Kolar, north east of Bangalore within that we work in a subdistrict called Taluk and are hoping to reach out to 65 villages. But here the strategy was very different.

Here what we needed to do was work with public health officials as well as the village leaders and most importantly ASHAs – those individuals you can see in the pink saris. These are the health workers who are the bridge to the community, and they are main focal point for helping us getting going with the study and recruit volunteers. So, whether we do longitudinal observational studies or clinical trials linking with public health officials and the villages is going to be crucial to reaching this group of people, who form the majority of the population in most LMICs.
This is just a slide to show you how we collect the data. It is all digital. Interestingly even though there is low literacy our rural cohort, they adapt very easily to doing cognitive tests on a touch screen. Those are important things to remember as we move onto clinical trials. They are eager to get into the MRI. I think this is a very nice way of planning these studies and all of the data flows back into our Institute and we have set up a good computational architecture.

So, what is the big difference and why do we need to look at these two populations? One is their low literacy. Low socioeconomic strata. They have had low lifestyle changes which is very different from the urban community, which is where they are middle class, well-educated and have experienced major lifestyle changes.
What we see is both MCI and dementia if you look you see the rural cohort has much higher incidence much earlier on.

And what we see which is really worrisome is that most of this early burden is in the females rather than in the men. And I think I would end with this. It is important to look at both populations. The gender differences are extremely stark. We need to collaborate and share. Learn the lessons from western studies. And within LMICs I would urge the need for more cooperation and more sharing. Thank you.

Meera Pattabiraman
Chair, Alzheimer’s and Related Disorders Society of India (ARDSI)

Thank you Viji for that excellent presentation. We learnt how difficult it is to get resources and sometimes we have to depend on our philanthropists. And also you brought out how important it was to do studies in rural and urban areas in India as well
as collaborations between other LMICs. It is my pleasure now to introduce Professor Francisco Lopera and he will be talking about clinical trials in Colombia and South America.

Professor Francisco Lopera
Director, Grupo de Neurociencias de Antioquia, University of Antioquia
Colombia

Autosomal dominant Alzheimer’s
a window to understand and reduce
apparently non-modifiable risk factors for dementia

Francisco Lopera
francisco.lopera@gna.org.co

Thank you very much for the opportunity to share with you this presentation. Autosomal dominant Alzheimer’s Disease is an exceptional window to understand and reduce apparently non-modifiable risk factor for dementia.

common problems that can be solved through collaborative networks

Professor Francisco Lopera
I Think we can look these population by electronic methods, we are doing it in Colombia now

Professor Ha Thi Thanh Huong
Thank you Viji, that is a good idea.

Professor Adesola Ogunniyi
Great to have George join us.

Professor Ricardo Allegri
Thanks George, very important information for ours countries

Professor Paulo Caramelli
Thank you for these very nice presentations, Viji, Francisco and Paul
In Antioquia Colombia we found and have been studying for the last thirty-six years 25 big families with autosomal dominant AD.

They have more than 6000 members. And 1119 of them are carriers and are alive with dementia or they are going to develop dementia in the next few years.
This is the natural history of the disease in this population at median ages. The clinical phase of the disease at forty-four with MCI, dementia at forty-nine and they died at fifty-nine. The pre-clinical phase has several phases. Phase 0 to 24 when they have a high level of AB42 in CSF and high levels of NFL and p-tau in plasma. Phase 1 from 24 to 28 when we can see amyloid positivity in the brain. Phase 2 from 28 to 32 when we can see for the first-time cognitive decline in memory task, without complaints of memory loss. Phase 3 from 32 to 38 years when we can see from the first-time tau positivity in the brain. And phase 4 from 38 to 44 when there is MCI. Then the question is where can we treat? The treatment depends on the stage of the disease. We can do palliative treatment in later stages of dementia. We can do tertiary prevention when they have MCI. We can do secondary prevention from 28 to 44 when they have amyloidosis without symptoms and primary prevention when they do not have amyloidosis among people younger than 28 years old.

**CLINICAL TRIAL**
**API COLOMBIA**
**GN28352**
**(CRENEZUMAB)**

Conducted by Neurosciences Group of Antioquia:
supported by NIA, Banner, Genentech & Roche
Launched 2\(^{nd}\) half 2013

asking Viki what are the barriers to such collaborations

George Vradenburg
DAC is also building a global clinical trials platform and is looking for sites in Africa and Latin America. We have many sites volunteering in many Asian countries

Dr Sonia Brucki
We could initiate collaborative studies with the same tests. Do you think to use visual stimuli to minimize education factors?

Meera Pattabiraman
Infrastructure already exists in the big cities in India

Professor Adesola Ogunniyi
I am an advocate of the DAC initiative for bringing researchers in LMICs together
We are doing now a clinical trial supported by NIA, Banner, Genetech and Roche. We started the clinical trial seven years ago and it is going to finish next year.

We have enrolled 252 members of the 25 families with autosomal dominant Alzheimer’s disease. All of them are healthy people. 168 of them with the mutation. Of that group 84 are receiving crenezumab and the same number the placebo. There are also 84 healthy participants in the trial without the mutation and they are receiving the placebo. In all of them we are looking for biomarkers including cognitive, CSF, plasma and other biomarkers.
At the beginning of the clinical trial, we did a public information campaign in the country. And this campaign was in order to look for other members of the family in branches with the mutation. We received over 1000 blood samples coming from people with early onset dementia but only eight were positive for the Paisa presenilin1 mutation.

Then we decided to do total genome for all the blood samples and we discovered ten other different mutations in our country for the presenilin1 gene. Seven mutations coming from Europe, one from Africa and three from Amerindian. We were thinking that we had only one mutation – the Paisa mutation – for three decades. And in one year we discovered we had many more mutations in the presenilin1 gene!
And also, we discovered different families with frontal-temporal dementia with tauopathy. With causality genes of tauopathy.

**RARITY OF AUTOSOMATIC DOMINANT FORMS OF DEMENTIA**

- 1. There is no active search for these forms of dementia
- 2. Family history and genealogy are not done

Then the rarity of autosomal dominant forms of dementia is because there is no active search for these forms of dementia and because family history and genealogy is not done.

**PREVENT BETTER THAN CURE**

The challenge is to PREVENT an incurable disease

How to do it?

**Acting on the population at high risk**

The challenge is to prevent an incurable disease. How can we do it? Act on the population at high risk.

@ Lenny: I believe Finger is a fantastic initiative, but we should not forget the local contexts.
How can we act before genes of causality and susceptibility and prevent their action? By developing prevention strategies for populations with high genetic risk and doing primary and secondary prevention clinical trials.

We propose a method to prevent Alzheimer’s Disease. Read and learn from Nature. This is a paper we published two years ago. We have discovered that a form of apparently non-modifiable AD, such as the autosomal dominant form, can be naturally delayed for up to thirty years, which in practice is equivalent to the cure of the disease.
A method to prevent AD: Read and learn from Nature

We have discovered that a form of apparently non-modifiable Alzheimer's disease, such as the autosomal dominant form, can be naturally delayed for up to 30 years, which in practice is equivalent to the cure of the disease.

Then how to find the population at high risk and open windows for prevention. This is the proposal. (1) identify cases of early onset dementia or late onset dementia but with autosomal dominant form. (2) always doing family history and genealogy (3) look for AD/dementia causal mutations (4) look carefully for carriers with resistance to AD/dementia (5) read and learn from nature in order to do imitation of nature.

**How to find the population at high Risk And open windows for prevention?**

1. Identify cases of early onset dementia
2. Always family history and Genealogy
3. Look for AD/Dementia causal mutations
4. Look carriers with resistance to AD/Dementia
5. Red and Learn from Nature

Dr Graciela Muniz-Terrera
Viji: that was exactly my point, the intervention needs to be culturally adapted

Dr Andres Damian
Hello, I agree with Andrea. It would be great to have this information. Some Soth American countries are currently classified as HIC but the reality is very different from developed countries.

George Vradenburg
DAC not limited to LMIC. We want to understand different Alzheimer’s pathways in racially and ethnically diverse global populations and is using UK Biobank
Thank you for that great presentation. It was a fascinating study for us. 25 families with early onset. As you say prevention is better than cure. And to learn from nature! That is a wonderful thought. Thank you again. We now move on to the final speaker Paul Kiwanuka-Mukiibi who will talk about the need for global trials in LMICs.

Dr Paul Kiwanuka-Mukiibi
Executive director, Alzheimer Association Uganda

Thank you for that introduction. What I am going to address in regard to clinical trials in low- and middle-income countries, using Uganda as an example, is the lack of clinical trials and give a background to why we are currently in this situation. Interesting; when you gave your opening remarks Meera and when Viji was speaking, I remembered a Canadian bought a formula one team, Force India, and he has recently bought Aston Martin. They have just announced they are going to shift all their vehicles to electrical ones starting this year. The UK has said by 2030 there will be no diesel and petrol vehicles and Bentley have said there will not be any by 2025. I will get back to why I am saying this later, with reference to clinical trials in a country like Uganda.

To give you a background, very similar to what Viji said, we are a very young population. Our median age is 16 years old - just over 16 years old. We are a very young population! The population above 65 is 2.5% of the population and over 80 fewer than 0.5%. Because of that, quite obviously, economic and health policy does not have a primary focus on ageing, and that is also true of political focus.

Looking at Alzheimer’s and dementia in Africa as a whole, a study estimated a prevalence of 2.4% among adults over 50 years old. Significantly at the time it was published in Journal Global Health 2012, a literature review on Medline and other places only found ten relevant studies, post 1980, on Alzheimer’s and dementia in Africa. Let’s fast forward to ADI’s report ‘Dementia in sub-Saharan Africa: challenges and opportunities’, from 2017. What this report showed us was they discovered 12 studies done in sub-Saharan Africa – so two more studies than almost a decade ago - including six in west Africa and one in east Africa. The prevalence estimate was 7.2%.

However, since that particular report by ADI there has been a paper published about some research recently done in southwestern Uganda, and this has been published in BMC geriatrics; the study was called “Prevalence and correlates of Alzheimer’s disease and related dementias in rural Uganda”. This cross-sectional population-based study had a sample of 400 people aged 60 and above of which 20% screened positive for dementia in southwestern Uganda. The reason I am bringing this up is that, although we are getting more and more information now, we still have widely varying data, statistics and other forms of information across the continent about what is happening as far as prevalence is concerned.
Now on clinical trials, and I will go back to my Aston Martin, across most of this continent we already have the challenge of diagnostics as far as conditions like Alzheimer’s and dementia are concerned. To be quite frank, apart from using the tool that Mbarara University used - and they used the Brief Community Screening Tool for dementia - apart from that, from a clinical basis everything that has been mentioned by previous speakers (MRI, PET and amyloid and tau markers), the reality is that over here that is not available. How does that relate to clinical trials? Well, if clinical trials are to be standardized across board, and we are all using the same markers in order to share our information, the first constraint is the reality of the African scene.

Using the example of clinical trials that are currently going on. According to the NIH, 46 of theirs are at the early stage, 123 are non-pharmacological intervention trials, and 84 are care and care giver interventions. The reason I bring this up, and I am going to relate it to a conversation I had with the Assistant Commissioner for Non-Communicable Diseases in our Ministry of Health. The structure of our Ministry is, at the very top you have Top Management, the ministers as well as the directors: Director of Clinical Services, Director of Planning etc. After that you have the senior managers that is made up of the technical people including the assistant commissioner whom I spoke to yesterday.

I told him about the forum I was speaking at today and one aspect was clinical trials, and his immediate reaction was how are we going to do that? Thereafter, as we discussed how Uganda Alzheimer Association and the Ministry of Health can collaborate in relation to Alzheimer’s and other dementias, and bringing this onto the table, he actually said that as a division within the Ministry of Health they have the very big constraint of literally being ‘an orphan’. Viji has said the primary focus in countries like ours has been infectious diseases. In Uganda we have had – putting aside Covid-19 – Ebola, HIV/AIDS; there is malaria, childhood respiratory diseases, all of which are the biggest killers. That notwithstanding, when we have a country where a senior member of the ministry requests a person like myself to come and make a full presentation about Alzheimer’s Disease and dementia to the senior management in the Ministry, so that we understand the situation we face, this underscores and encapsulates the challenge that we have on this continent when (it comes to) keeping up with clinical trials in the rest of the world.

Now to close, coming back to my Aston Martin. Aston Martin, UK and European car manufacturers are moving toward entirely electrical cars. Those cars are not going to be viable on this continent – whether they are affordable or not – simply because we do not have the infrastructure to be able to charge the cars, let alone the roads to drive those cars on. If you look at clinical trials it is an analogy. The way they are done elsewhere in the world, we will not be able to do them here.

Meera Pattabiraman
Chair, Alzheimer’s and Related Disorders Society of India (ARDSI)

Thank you for a very inspiring talk and you highlight how Africa is not ready for clinical trials under current circumstances. But it also highlights the fact that we need to step
up and carry out trials that are being carried out in other parts of the world. And with that I will not invite Paola to take the conversation forward and to chair the rest of the discussion.

Paola Barbarino
CEO, Alzheimer’s Disease International (ADI)

Thank you very much Meera and thank you very much to all participants for being here. It is a pleasure to see so many known faces and so many new ones as well. It is a pleasure to be managing this particular conversation and I would like to invite you, while I am making my opening remarks, to please send questions on the chatline. The reason we are doing this is to get your input as experts. Just to remind you what we have talked about, our presenters have done a miracle in condensing so many complex studies – in particular I am thinking about:

- Viji’s amazing study on genetic diversity which has uncovered so many points. And one of these is the existence of such great disparity between men and women in the study. How long will it be before the full impact of a longitudinal study of this magnitude can be revealed?
- Francisco with whom we sat together in other circumstances, telling us about the fantastic work he is doing in Colombia, in particular looking at the genetic diversity of the populations and with a message around prevention that resonates very well with some of the other work we are doing.
- And finally Paul, I am looking forward to reading this article you mentioned that could update some of the very harsh truth we uncovered in our study of sub-Saharan Africa three years ago, a study which would certainly benefit from some update. But there is still so very little published from Africa. And I have seen in the chatline that someone else was commenting on some studies happening in the Congo. Do let us have your studies so we can update our work at ADI.

During the presentations there has been a very healthy conversation going on we have someone from Johnson and Johnson, Bert Herzog. You were asking Francisco specifically whether his work was using electronic patient records or other databases. now This is a very interesting point. We are working on dementia registers right now. Can you share your thinking on the topic? I think it is interesting to hear someone from industry given we have heard from academia and medicine. Bert over to you.

Dr Bert Hartog
Senior Director, Clinical Trial Innovation Group, Janssen

Thank you, Paola, for asking, and very happy to share what I was thinking. In industry we do a lot of clinical trials and we think a lot about the efficiency of clinical trials as much as the science of trials. We want the trials to go as quickly as possible and be as patient friendly, or participant friendly, as possible. That helps get the results quickly, but it also helps keep people in the trial. There is nothing worse than inviting someone...
to participate in a trial and then lose them halfway before you reach your end point because the trial is too burdensome. So, we pay a lot of attention to this. And one way we prepare is by understanding natural behaviour we see in electronic patient records. Longitudinal measurement of people as documented in electronic health records. That helps us find potential trial participants, it helps us design clinical trial protocols based on what we see happen, it helps us understand potential conflicts in the inclusion/exclusion criteria where the science may ask for particular criteria but in reality, creates conflicts. So long story short these electronic patient records are a goldmine to design and execute our trials.

The problem is that, and this is why I was asking the question, most of this is done in western countries. In hospitals with large databases on their patients or related to their patients. I think this would translate to LMICs provided there is an infrastructure in place. If the infrastructure is not there that might call for a different type of investment to help start building the infrastructure. In light of the 2050 dementia pandemic problems in countries like India and China we need to start investing now to do the research in ten or twenty years.

So two thoughts. Can we already learn from some of the LMICs where the electronic infrastructure is already present? And second, is it worth thinking about investments in the infrastructure to allow electronic patient record research in the years ahead once the infrastructure is in place.

Paola Barbarino
CEO, Alzheimer’s Disease International (ADI)

Thank you very much Bert. This is a very good point. We are not debating this further at this stage but I would encourage people who have been stimulated by your point to contact you directly. I do think, and we at ADI think, that the lack of sharing data is making delays. Because if we do not share data then it means people are repeating things again and again and again. There is a great question in the chatline, and I would like to give the floor to Paolo Caramelli, he would like to know whether our speakers think it would be possible to establish a research network between Africa, Asia and Latin America to develop a collaborative project. Could I ask Paul, Francisco and Viji to give a thirty second reply to that question and Viji you first.

Dr Vijayalakshmi Ravindranath
Founder director, Centre for Brain Research, Indian Institute of Science

I would say definitely yes and where we could start is sharing the data we have from our studies and having more interactions. The pandemic has taught us to have zoom calls. And definitely to share and analyse our data together.
Professor Francisco Lopera
Director, Grupo de Neurociencias de Antioquia, University of Antioquia
Colombia

Yes of course we can collaborate with all countries in this idea. Someone was asking about the possibility of electronic studies. I think this is a very good idea. The experience we are doing in Colombia is one. We are proposing to the population we are interested in doing primary and secondary prevention studies in the next ten years. Then we are looking in the database for all people who have a family history of dementia and this is a good way to find a population at high risk. Because once a person has been identified we can contact and talk with all the family group and this is a way to recruit a population interested in clinical trials.

Dr Paul Kiwanuka-Mukiibi
Executive director, Alzheimer Association Uganda

Very briefly, I do think there is a lot of room for collaboration. One of the ways we can do this is an approach of asking who can do what where. For example, if it was Uganda, I would not at this particular stage (and here I link to what Bert said about not just the scientific rigour but the infrastructure) I wouldn’t at this stage try and do what Viji is doing or what Francisco is doing. But there is other quality of life studies you could be doing. And with us in Uganda, having a more static population and a rural population - Bert you talked about being able to retain your study recruits - with our more static population this is an area where we as a continent could contribute greatly to the sum of knowledge, working collaboratively.

Paola Barbarino
CEO, Alzheimer’s Disease International (ADI)

Thank you very much Paul. Very, very brief as you promised. There has been a number of discussions around the Davos-Alzheimer’s collaborative project on the chatline. Can I ask George Vradenburg who is on the call today, to tell us about it? But George briefly if you can, I know it is difficult because it is a complex project, but could you say something about your aspirations and where should people contact you if they want to know more.

George Vradenburg
Co-Chair, Davos Alzheimer’s Collaborative

Yes Davos-Alzheimer’s collaborative was launched in January 2020 at the Davos meeting. It is intended to be a six-year effort. $725 million to invest in cohorts in low- and middle-income countries and then to connect them, invest in them, to bring them up to a minimum data set across omics as well as digital, phenotyping of the populations and
then automatically linking them through the AD workbench techniques of the Gates Ventures. So, this is now beginning to operate. We are looking for volunteers in Africa and South America. We have any number of volunteers in Asia. But are still looking for people who are willing to cooperate and participate.

Paola Barbarino  
CEO, Alzheimer’s Disease International (ADI)

Thank you, George it is a fantastic initiative, and George has put his contact details in the chatline for people who are interested. Not There are a number of strands of conversation in the chatline. I can see one on the FINGER study and Miia Kivipelto who is the lead and is not with us today. Can I remind all participants that we are going to do a FINGER webinar specifically for ADI members in the next three weeks so keep an eye for that if you are a member of ADI. Would anyone like to comment who is involved in the FINGER study. I know almost everyone in Latin America is! Would anyone like to raise their hand?

Dr Vijayalakshmi Ravindranath  
Founder director, Centre for Brain Research, Indian Institute of Science

We are part of the FINGER network and have been engaged in conversation with them. We are interested in an intervention trial. We will start with an urban cohort. It will be a different cohort. But we are still grappling with adapting the FINGER trial approach to make it fit to India, especially the elements around diet and exercise. We are also part of the FINGER network post-covid survey. So yes, we work with them very closely.

Paola Barbarino  
CEO, Alzheimer’s Disease International (ADI)

Thank you very much. Ricardo you would like to comment on FINGER?

Professor Ricardo Allegri  
Head of the Department of Cognitive Neurology, Neuropsychiatry and Neuropsychology and Director of the Ageing and Memory Centre at the Neurological Research Institute Raúl Carrea (FLENI)

Yes, thank you. Very nice meeting. Very nice presentations. I think that the project ww-FINGER is very important for Latin America because one of the biggest challenges for our countries is the lack of control of vascular risk factors: hypertension, diabetes, cholesterol, obesity, and physical inactivity. Latin America has more vascular risk factors than developed countries. At the end 2020 LatAm-FINGER was launched in 13 countries from Latin America. This is a very interesting platform to work together in risk reduction and prevention with patients across Latin America.

African component will include a survey and validation to some extent of the CSI-D and a number of other measures.

Dr Lucia Crivelli  
LatAm We are collecting MRI and DNA and serum samples to correlate with neuropsychological performance. This is being funded by the Alz. Association

Professor Huali Wang  
Is there any ethical guidelines on recruiting people from underrepresented areas in LMIC countries? Could ADI lead to develop one set?

Professor Ha Thi Thanh Huong  
Hi Huali, may I know what the concerns might be with this population that are different from recruiting patients in urban areas?
Thank you very much Ricardo it is an amazing effort. FINGER is a very important study, I cannot praise it enough and praise its efforts to bring together LMICs. Now there is a really interesting question from Thomas in the chat he asks the group what you think is the role of training health teams, especially primary health teams, in dementia care, especially considering increasing prevalence and the lack of specialists. As you all know, we have been discussing for some time about the importance of increasing the knowledge of primary health care professionals. Our survey on stigma and attitudes to ageing in 2019 pointed out the 62% of health care professionals globally still think that dementia is caused by normal ageing. So, Thomas you put a very good question to everyone. Would anyone like to raise their hand and comment on this? What do you think about training health teams? Any of you found yourself in that position?

Professor Huali Wang
Professor and Chair for Clinical Research, Director of the Dementia Care and Research Center, and Associate Director of Beijing Dementia Key Lab, Peking University Institute of Mental Health

Thank you, Paola. Yes, this is a very important question. We have been working to train primary care physicians. We have found that after training the motivation of physicians to be involved in prevention screening and early diagnosis has been improved. So I would encourage the LMIC working groups to try and encourage promoting training for primary care physicians. Last year we published a series of books for physicians. Thank you.

Paola Barbarino
CEO, Alzheimer’s Disease International (ADI)

Thank you Huali. I knew this would excite ADI members. Petra du Toit from South Africa please.

Petra Du Toit
Executive Director, Alzheimer’s South Africa

Thank you, Paola. Yes, here in South Africa it is a very big need to train health care professionals and primary caregivers. Because there really is a lack of knowledge. We find in Alzheimer’s South Africa that there is a real need to reach out to clinics in rural areas. But even in the developed areas health care professionals also have poor knowledge. So it is a major task, but we need help to do that. There is a very big need in South Africa to train health care professionals and primary caregivers. There is a lack of knowledge on dementia amongst health care practitioners and their training should include

Dr Sonia Brucki
We ave in Brazil a very simple test for episodic memory with 10 black and white drawings that show through experience in many settings and other countries to be a very useful battery - Brief Cognitive Screening Battery - Nitrini et al. Researchers in Norway and Turkey are using it with success, as well in Latin America. It is very good for screening and for epidemiological studies.

Professor Andrea Slachevsky
Concerning caregivers, one of the main problem is the access to
modules on dementia. Alzheimer’s South Africa should be empowered to train health care professionals, primary caregivers and other interested parties on dementia within communities.

Paola Barbarino  
CEO, Alzheimer’s Disease International (ADI)

Thanks Petra. Andrea you were also a person to put your hand up. Lovely to see you from Chile.

Professor Andrea Maria Slachevsky  
Professor, Corporación Profesional Alzheimer y otras Demencias (COPRAD), Chile

I have a comment about training. Last year we launched training in dementia, and it was a surprise for us because a lot of people who did the course were not physicians, they were people working in primary health centers, people such as a nurse, occupational therapist. People said training in dementia was useful to help them follow up people with dementia and also raise the suspicion of dementia in people without previous diagnosis. I think when we talk about training, we focus a lot on the physician but actually they often do not pose the diagnosis because of time constraint. When we talk about training we need to think of primary care as a multidisciplinary team and include health workers, eithers professionals and not professionals. Expand training in primary care centers could contribute to facilitate access to the diagnosis of dementia.

Paola Barbarino  
CEO, Alzheimer’s Disease International (ADI)

Thank you, very good point. And we all know training is complicate in different cultural settings. I am going to ask Jean to speak who has his hand up.

Dr Jean Ikanga  
Assistant professor at the university of Kinshasa School of Medicine, Democratic Republic of Congo

My experience is a little bit different because what I did first was create a neuropsychological test so we can make a diagnosis. Then what I did was train medical students who were resident because Congo was very big, and it is now those are training in universities those who are about to become physicians. This is the way we have been training because one of the things is there are not many neurologists in the Congo. Now we are collecting biomarkers so we can correlate the biomarkers with neuroimaging and neuropsychologist test. This will assist physician to make clinical diagnosis of AD with a neuropsychological test.
Thank you, Jean, great point. And I remember seeing a very good example in Costa Rica where a local organization was training primary care physicians, but it takes a lot of time and effort. A bit like what Huali is doing, taking advantage of the specific way Chinese society is structured, I was so impressed when I saw that in Beijing. So I just want to move the conversation. Agustin, I see you have a really interesting point about socioeconomic factors that you want to put to our three speakers.

Dr Agustin Ibanez
Director, Cognitive Neuroscience Center and Senior Atlantic Fellow, Global Brain Health Institute (GBHI)

Thanks for the excellent presentations. It is a great inquiry to assess countries' socioeconomic differences, but it is also very challenging. We have so many different circumstances, such as socioeconomic status, social determinants of health, or other cultural-relevant factors. Sometimes there are straightforward and shortcut measures like zip code to assess socioeconomic levels. However, developing a harmonization methodology to compare disparate cultural and economic settings is not an easy task. Even with different genetic backgrounds or physiopathological presentations, we need to rule out and control current environmental differences. I think this is an enormous challenge to make regional comparisons in this regard. We are beginning to do that in the ReDLat consortium, although we don't have a clear pathway to do it globally and be locally and culturally sensitive. So if you have any thoughts on that, it would be appreciated.

Dr Vijayalakshmi Ravindranath
Founder director, Centre for Brain Research, Indian Institute of Science

So having cultural and socially adapted tests?

Dr Agustin Ibanez
Director, Cognitive Neuroscience Center and Senior Atlantic Fellow, Global Brain Health Institute (GBHI)

No it is how to make comparable the results when the data has come from so many socioeconomic backgrounds. Not the cultural patient background, and of course that is critical. But how to make a standard comparison in performance, in affect on clinical trial, when you have so many socioeconomic differences.
Dr Vijayalakshmi Ravindranath  
Founder director, Centre for Brain Research, Indian Institute of Science

So we adapted a lot of questionnaires and tests. So actually, there is a Hindi adaptation of MMSE which is what we used it is called HMSE. So this is a very important point. So, what I am hoping is that we are also part of ADI and we will be participating and putting in our data. I am looking to our data and computational people to help make this comparison between oranges and apples. Which is why I have my urban cohort. This cohort is closer to western cohort then the rural cohort. And since the bulk of the population is in that lower socioeconomic cohort especially in LMICs you have no choice but to study and compare. So, you can definitely measure white matter hyperintensity, grey matter loss. There are certain parameters that could be measured across. Cognition is harder but the rest of it yes, we could and look at the burden in terms of CBR. But by throwing open the data and sharing it for analysis and giving everyone a chance to look at it. That is also another reason why we in the LMICs need to come together where we can have more overlap with the other cohorts in terms of socioeconomic factors as well at literacy.

Dr Paul Kiwanuka-Mukiibi  
Executive director, Alzheimer Association Uganda

Yes, I don’t have much to add to what Viji has said. She has addressed it very comprehensively. How is it being done, and should it be done, as you asked Agustin? And my answer is ‘absolutely’! In Uganda we have many different ethnic groups and we also have socioeconomic divisions not just between urban and rural but also within them. How would it be done? Again, I defer to what Viji said. Cross-continental or cross-country collaborations. I go back to what I said earlier because there are many differences between countries as I referenced.

Paola Barbarino  
CEO, Alzheimer’s Disease International (ADI)

Graciela would you like to come in here because you are nodding vigorously?

Dr Graciela Muniz-Terrera  
Senior Lecturer, Biostatistics and Epidemiology, Centre for Dementia Prevention

I think it is important to share the data, but I believe that we need to think about how to fund the development of methodological tools that would enable us to do a fair comparison of results across different countries. That is an area where it is really difficult to get funding for. And much as I like the idea of comparisons unless we do it in a fair way the results are going to be misleading.
There was a particular question about whether it would make sense to develop materials for patients that would enable you to manage distress in particular with relevance to LMICs, there is information on the ADI website on this actually. Again, I encourage everyone to read the chatline, there is a lot of material there. Now there is something from Lucia Crivelli on their effort to collect MRI and DNA and serum samples to correlate with neuropsychological performance, funded by the Alzheimer’s Association. The Alzheimer’s Association has been a big funder of research in Latin America. I wonder Lucia if you would like to tell us a little bit more about this project.

Thank you yes. This is part of the project during the project we are collecting serum samples and DNA samples and MRI images from 13 countries in Latin America, and we are building a biobank for this. This will be done at the beginning of the trial and the MRI will be repeated at the end of the trial. It is a very big initiative to collect all these samples across South America. So all the centres will collect their own samples and send the samples to five leading centres across Latin America: Mexico, Argentina, Colombia, Brazil.

Thank you, Lucia. The Alzheimer’s Association has done a lot to help kick start research in Latin America which is great to see. There is a point from Huali. Huali asks whether there are any ethical guidelines on recruiting people from under-represented areas in LMICs and whether ADI could develop any. Yes, there is something, but we could do better so perhaps this is something we could pick up after this discussion thank you. Now Sonia Brucki I cannot see you on the screen maybe you are on the other screen can I ask you to come in because you have been very active on the chat the latest one on memory tests.

I have commented on a simple test (the episodic memory task of Brief Cognitive Screening Battery). It is ten black and white drawings that have to be learned, and with
a delayed recall), we have used it in many studies here in Brazil with good results both in high and low educational levels. Nowadays, it is used in many Latin American countries, Norway and Turkey, with low education populations and immigrants. It is useful for epidemiological studies in low- and middle-income countries. I can share with you many manuscripts with validation data from this battery.

Paola Barbarino
CEO, Alzheimer’s Disease International (ADI)

Thank you, Sonia and thank you for participating in the chat. There is a great question around diagnosis from Andrea and it allows me to tell you that the next World Alzheimer’s Report that we will be launching in September will be on diagnosis. We are going to look in 2021 at diagnosis and in 2022 at post-diagnostic support. The survey for clinicians and health care professionals is currently out. If you are connected with me on LinkedIn, you will see we are asking clinicians to participate in the study which is available in four languages so please do take part in the survey and do disseminate it. You know this is going to be a critical year because there are disease modifying therapies on the horizon but as Andrea says if there is not a diagnosis you cannot access that. And there are so many governments that are not aware of what you can do about dementia or that it is a challenge in their countries, and we have to do something about that. Now I would like to bring in Daisy Acosta could you give us your view of the discussion so far.

Dr Daisy Acosta
Principal investigator of the 10/66 Dementia Research Group center in the Dominican Republic

Good morning everyone and thank you Paola for inviting me to speak. It has been an excellent discussion. Very productive. I have learnt a lot of things that are being done in different parts of the region. Also Meera thank you for being here. It is great what is happening in India with all these studies and in Africa. I thank you all for being here and for inviting me.

Paola Barbarino
CEO, Alzheimer’s Disease International (ADI)

I am glad you found something new despite having so many years of working in the field under your belt. I have found Viji’s interventions quite fascinating. Can I ask now Cleusa Ferri would you like to give us your view on the proceeding so far.
It has been an interesting meeting; we have been talking about low- and middle-income countries and about lots of different topics because of the numbers and diversity of these countries. I know this is just a short meeting to raise a few issues and put them on the table, but I feel that each of these subjects needs a much deeper and separate conversation. It would be interesting if we could come together in another opportunity to discuss the strong/weak points of the many different ongoing cross-country original studies involving LMICs, such as FINGER, 10/66 DRG, HCAP, among others.

Thank you for your point of view. Before I conclude I would like to call in another person who I have not heard from so far and that is Yuda Turana from Indonesia.

Thank you they were wonderful presentations from the presenters. The thing I would ask about it the challenge of cognitive assessment especially in low education populations. I think it has already been answered about the validation of the instrument. But I think low- and middle-income countries and especially in the village there is a lot of bias in the reporting of cognitive assessment, and this is the difficult part in assessment. That is my point of view.

Thank you very much that picks up a number of points that have been made in the chat. I would ask our speakers to say one thing to say that they have learnt in this conversation just as a wrap up.
Thank you. Well I think this is one of the first occasions that we have had a chance to meet and talk. We have common problems especially as was mentioned in adapting cognitive tests to the social and cultural milieu and to the low levels of literacy. It is a challenge that we all face. And of course we need more studies to understand our population to know where the risk lies and where the burden lies before we approach clinical trials and interventions. Again, I would say we need to work together and take a leaf from each other’s experiences. And I really hope that the DAI that George mentions could be a platform. If we could get funding that would enable LMICs to exchange ideas, it would be of such a great help. It is a lonely space, and I am sure most of you will agree, because the burden will only increase – and as Meera said it is already high. So, I hope that through the WDC we could have a forum that would help and promote cooperation and collaboration through the LMICs.

Thank you, Paola, and thank you everyone else. This has been eye opening absolutely eye opening. It is as Viji just said a lonely space, but this has shown me that there is so much more avenue that exists for collaboration and working together. One is not as much alone as one might have thought! If the World Dementia Council can continue to bring us all together, we will make great strides. There is a lot more to do in bringing us all together.

The final comment is related to the proposal I am doing. We need to understand how to control for the non-modifiable factors and to do that we need to find the population with the genetic risk factors, we need to work together to find those populations because I think if we do, we will be able to control it.

Well, I thank everyone our time has come to an end. I thank Lenny and Josh and the World Dementia Council who invited Meera and I to chair the group. It has been a great discussion. And I will now hand over to the Meera but before doing so I remind you to do the survey which Huali has very kindly posted in the chatline.
Thank you, Paola, for leading the conversation and getting everyone to participate. It was a fascinating and absorbing discussion. So we had discussed every aspect of it. The paucity of fund was something so the information from George who is a member of the World Dementia Council about the Davos-Alzheimer’s initiative was really very encouraging. And as Viji and Paul said it is a lonely space for us. So we are all looking forward to high we utilise those funds. Do get in touch with George he has given his details. And Huali’s experience of how to train primary care physicians was a great learning experience for all LMIC countries. For a big country like India it is a major challenge it is important because primary care centres are the main access points. The support and training of doctors there will be very beneficial. And the final take away of course was collaboration. Though we may be at different levels we can support each other and learn from each other. So with these closing remarks I thank everyone and Lenny and Josh for having this roundtable and now it is over to you for your closing remarks.

Thank you. And thank you for chairing to both Meera and Paola. As I said at the top we will be sending round a transcript of the discussion and the chat. It has been a very lively group and we will check that you are happy with us sharing your contact details with each other so you can carry on some of these discussions. Just to wrap up there has been a lot covered in this meeting and there is a lot going on in the field. As Paola said the ADI survey is out there at the moment and I’d particularly like to thank ADI for helping get a lot of you together to help us work on this report and shape the conversation. We will be following up next week with a transcript but wherever you are, have a good rest of your day. Thank you.
The World Dementia Council (WDC) is an international charity. It consists of senior experts and leaders drawn from research, academia, industry, governments and NGOs in both high-income and low- and middle-income countries, including two leaders with a personal dementia diagnosis. The WDC has an executive team based in London, UK.