

DD: Describe yourself in three words.

JM: I'd say generous, outlier, and underdog.

DD: Hi everyone, welcome to Global Health Lives. I'm Delan Devakumar and today I'm joined by Professor Jaime Miranda, Director of CRONICAS Centre of Excellence in Chronic Diseases at the Universidad Peruana Cayetano Heredia. Jaime is a world leading researcher who's run large studies on a variety of chronic diseases and how they interact with each other. Jaime, thanks for joining me today.

JM: Thank you, thank you very much for having me.

DD: So, you were in the UK for a while, many years ago, and I remember hearing about this kind of mythical figure Jaime Miranda but I didn't know much about you or who you are or what you did, and then finally we met working on migration and health and it was lovely to put a face to the name. A lot of your work has been on strengthening of health systems with a focus on non-communicable diseases, and as we speak Peru has one of the highest Covid mortality rates in the world. From your work and your experience, why do you think Peru has suffered so disproportionately?

JM: Thank you, it's good to start with that question because we cannot escape that reality. Peru is in the unfortunate rank and leading the rank of excess deaths, which is a very telling story of how much the country is suffering. And I suppose it's a combination of multiple factors, it's years of political and financial problems, another statistic that 70% of the population is on the informal economy and people live on a day-by-day basis so they need to work and therefore, these containment measures are very difficult to sustain. Poverty and overcrowding, when you say 'isolate' there are some houses with four or five people, and that all knocks on and has these terrible effects on the health system and the pressures as well. So, even before the pandemic we had people on the hospitals lying on the corridors, before the pandemic we were at capacity. And, to me, the story of Covid in Latin America is that we've seen through all these macro-economic figures which are country averages, and we were growing with disillusion. Like having a cataract, having this blindness of the reality and the social weaknesses. Zero social protections, a lot of informality and a very weak health system, and when Covid arrived it's just like an abrasive removing of that cataract all of a sudden and seeing all the deficiencies that we're going through. So, there are many good things that are

happening, particularly vertical progress - the maternal, child health, many progresses. Maternal mortality - lots of protections going well there. Vaccinations - good effort. But when you move on to chronic care that's a challenge, it's a massive challenge, and I think Covid has shown us those deficiencies and is telling us another story which is, now, when I work on chronic diseases where we need people to engage with the system, now I'm realising, the more I do the research, I've found that there is the baseline of that interaction between health systems and communities have a divorce. And we're trying to make little by little interventions but we're not addressing that divorce which happens at multiple levels.

DD: Yes, we'll come back to this and how you structure a health system in relation to non-communicable diseases, but here in the UK and other parts of the world we've seen this and how Covid-19 mortality is higher in people who have other underlying chronic diseases, and how you really need the health system to function so that you can take care of this outbreak but on the background of everything else that's going on.

JM: Exactly, exactly.

DD: You described yourself as an outlier. You don't come from a rich family, you grew up in a small coastal town called Chimbote in Peru surrounded by your very large extended family, but your town and also Peru went through a number of these crises that you were mentioning, economic crises, political crises. Can you describe what effect this had on you and the community that you lived in?

JM: Yes, I grew up in this town, it's a small industrial town, and when I say I am an outlier, I'm perhaps an outlier in this professional world, but that opened my eyes to this diversity of people and needs. So, the town that I grew up in is a town that was entirely set up for the industry. (It) was a beautiful Pacific Bay that two major industries came in in the '60s, or in the late '50s I suppose, and then, yes, destroyed the bay. So, it was all about the industry. And the important part that I remember is living with my extended family, so this sense of freedom and tranquillity and interacting with, for us, the rich and the poor kids. My mum was a schoolteacher so a lot of people would pass by the street and say, "Hi, hi, hi, hello, hello." And I would finish my primary school and just go and pop in to see my cousins and play football in the street, come back, so you see the parenting that I received is entirely different to the parenting that I'm giving my kids now. But circumstances were very profound to me.

And then I have two stories that are very present. One was this - in the first government of President Alan Garcia where it was this announcement which later became a 3,000-inflation rate overnight, and my job was to buy the bread every morning for breakfast. I arrived with my coins and everybody was in despair, I couldn't buy a loaf of bread. So, I couldn't understand, but actually for adults it was a massive, massive thing - all their savings, all their work, all of a sudden gone. The other one was when I moved to Lima, there was the years of terrorism, and the terrorism happened 'elsewhere' - this is the 'sensation' - that everything is protected and it's around Lima. So, all the good things are in Lima, there is a very strong separation of Lima with the rest of the country. And when I arrived in Lima, I knew about terrorism because there were people being killed up in the Andes and much closer to us, and when I arrived in Lima there was this bomb in the police station and them blowing the glasses of the bus that I was there.

DD: The bus that you were on?

JM: Yes, yes.

DD: Wow.

JM: And I was, "Maybe, well, it has arrived to Lima as well." So, people in Lima were scared and, for me, it was normal (from the) news. The point being of that story is that, when I talk about Peru, for me Peru is elsewhere other than Lima, and it is a different understanding for the rest of people. If you grow up in Lima where you have most of the resources, you don't connect with the rest of Peru. But I had this exposure, and also family's exposure, that there is something else out there, there are various groups of people and various needs as well.

DD: So then, at this very tender age of 15, you went to Lima, you started medical school a year later, and there you found public health and human rights and, almost by accident, you were following your new wife into these professions. This also got you into trouble with a senior colleague who told you to just become a 'good doctor'. Can you tell me about that early work, the broadening of your horizons and what is it to be a good doctor?

JM: That's very interesting. I have that very picture in mind because I get called to these very important offices with carpets and very fancy chairs and some of those you never expect to arrive to, and he's the Dean of the School of Medicine, and say, "Jaime, Jaime, what are you

doing?" And that point as an oddity, and again as an outlier, I ended up working in the ombudsman office. There was the story of female forced sterilisations, which was a plan of Fujimori for under the idea of family planning, it had a huge connotation of reducing poverty, but it ended up being badly executed and targeting the poorest women in the poorest areas. So, by working on the ombudsman and then having this angle of, *how come a health service health programme ends up committing these atrocities?* this world of human rights came into my world. And then I had the opportunity to travel supported by the university, so I travelled and presented this work on human rights, and I found other groups of people with similar interests. I came back and set up this group, and rather than setting it only within my school, through these new friends and because I was dating my wife who was studying psychology, I learned about interdisciplinarity and multidisciplinary early on in my career with an angle towards public health. So, all of that around the late '90s and early 2000s when I was doing my hospital work and Fujimori was still running for his third presidency. It's in that context when I get this call.

"Jaime, what are you doing? You have to be a good doctor." "Well, I'm working on human rights, it's important, our generation, people are on the street, the people- this is a dictatorship, and we are not seeing it, we as medical students are still in this bubble." And this idea that a 'good doctor', for my professors, was someone having good knowledge that could transfer to the patient in need in front of you. That didn't quite match with what I was seeing, so our relationship and responsibility with people and with populations in the provision of care is not only the transfer of knowledge, it's something else, and for me public health was opening those angles.

DD: So, my medical school was quite advanced in some ways but I don't remember ever doing public health, I don't remember it being a thing. We'd moved away from basic science to clinical care very early in medical school, but it was always within this health setting, there was nothing outside, there was nothing about how other factors can influence patients or people in general.

JM: And that's interesting because I do see the value, and by being good doctors, in a way, we're trying to be good people. But if we're disconnected from society, we're not doing our role, so that was my lesson. I remember this joke, so it was the '90s, HIV was exploding in Africa, my friends were reading about the discoveries of how this virus tricks the immune system around enzymes and their reproduction and the mechanistic things. I was reading that the president

of South Africa said that the virus could cross condoms because of the size of the, how it is weaved so it can go through plastic. And to me that was much more important because it had the relevance, if such a key living figure in a country could throw out all the lessons gained by all the mechanistics and the drugs and the discoveries. And my friends, now, when we look at ourselves backwards, they say, "You were a weirdo, why? You were reading those things back in medical school." Why not? Why not?

DD: Exactly. And to me, I guess I'm biased, but it should be the other way round, you read about politics of South Africa first.

JM: Exactly.

DD: So, then you moved to the UK, to UCR, for a while, where you worked on medical electives. So medical elective is a period in medical school where students get to visit another setting, often travelling to other countries. There are lots of discussions about this, about the ethics of this kind of work, particularly when going to a very different health setting to your own. You were organising these electives for UK students; can you tell me about what you did and what you set up?

JM: At that time there was an International Health and Medical Allocation Centre being set up which was the very early origins of what is now being called Global Health, but that was in the early 2000s and it was this visionary group trying to introduce the concepts of international health, power politics, health systems, human rights and so on to medical students, which had a profound effect on their training. And that's where I work, Tanzania, India and Cuba. What we want is to be a good package in the sense of having a preparation, you may have one set of views but your peers or your partners will have a different set of views, time commitments and priorities, and so on. So we had this preparation with a few courses expectations and then they went and came back and had a briefing. That was good. And the other thing- we were very keen that on, it had to be a bilateral programme, so in the same way that the UK students will travel to a place, we will receive and host people from that place. And we had people from Tanzania and Cuba and it was fantastic, fantastic to have this horizontal, bilateral, mutual learning process.

DD: So, then you completed your PhD at the London School of Hygiene and Tropical Medicine on rural to urban migration looking at cardiovascular outcomes. At the end of that you got

a call from your colleague Bob Gilman, a professor at Johns Hopkins University but who works a lot in Peru, he contacted you about NIH funding to set up a centre of excellence, and that was the birth of CRONICAS. Describe what CRONICAS is and what your main goals are.

JM: That's a very- another interesting story. So I was writing up my PhD and I was meant to hit submit by December and I got this call in October. So what it was, I was writing my PhD between 2005 and 2007, it was early in the days where people were not yet paying attention to the important problem of chronic conditions. Up to that point, you may remember, the global discourse was extremely focused on HIV, malaria and TB, with this enormous attention through the global funds and funding and so on. Yet, in the back of the settings a couple of things were happening in terms of population - people were ageing more, there were more people turning to the 40s, 50s, life expectancy was changing, and the appearance of chronic diseases, particularly in poorer countries, was starting to become visible. And the signs for that were seeing a stroke- that's something else that caught my attention - seeing stroke cases at 40 when the book says, English books says, that it's around 60, *what's happening?* That caught my attention as to *let's start doing something*. Bear in mind that in the university I come from, but also in Latin America, most of the research that receives attention or funding is on the infectious diseases area, so when Bob said, "Jaime, give me your PhD." I said, "Bob, I haven't submitted it." "Give me your PhD, give me whatever you have." "Bob, I still need." You know, the perfectionist, "No, I still need, let me go through chapter seven." "Send me whatever you have." So, I sent my draft PhD which made the case to study chronic diseases in lower income settings. And that was the basis for the grant, we obtained the funding to establish this centre of excellence that we label CRONICAS in Peru. And CRONICAS for two things, for the chronic disease bit of the area of research, but also because *crónicas* in Spanish means chronicles, tell a story, tell a narrative. So we wanted to tell the story of this new group of diseases in our country.

DD: And which diseases are you-

JM: So, we started with cardio-metabolic, particularly hypertension, diabetes, yes, and certainly obesity being the key driver. So we got the funding to establish the centre of excellence. An interesting funny story was that that was the largest rebuttal letter that I have ever written.

DD: Oh, right.

JM: It was, like, 56 points. Two of the comments said the PI is too junior and our responses were, "If you were to turn the country upside down you won't have a PhD in chronic diseases. So you have to get on with it." And that's why I said the underdog. And when we set up CRONICAS and were navigating these routes of research, we had to ask the question, *What glues us together? What are our values?* And we came up with these four values that have been very useful in guiding our work, generosity, innovation, integrity and quality. Certainly, innovation and quality are very much important for any research endeavour. Integrity, just do you want to do the right thing? Generosity is something that is very pressing upon me, so I know of the very privileged position where I am now but I want for more people to have it. I have these policies of open doors, come and share, and we'll do the extra effort to support the younger ones. So, generosity is a key one for us. What do we do? We started with epidemiological studies, so we said rather than turning into intervention we still need to describe the pattern of chronic diseases in Peru. But we evolve over time by doing health system research but also interventions, and we use the term CRONICAS as an umbrella. We don't describe ourselves as experts in particular conditions or disease but rather as connectors between a number of them, being either mental or physical chronic conditions.

DD: Tell me about some of the epidemiological work you've done. So you've run these large cohort studies, and this is where you follow up a group of people over time and observe them in multiple assessments. And one of the main studies was on migration within Peru and this idea of 'multiple Peru's', and also personally for you migration has always been important - your parents migrated within Peru, you've moved and lived in many parts of the world, your wife is a third generation Japanese Peruvian, we have similarities there, my wife is Japanese Brazilian. Tell me about how migration affects chronic diseases.

JM: Yes, that's why we get along very well, Delan, our wives know [laughter]. To me, migration is fascinating because it's a natural experiment.

Maybe a recommendation for anyone listening to this is that when you see any statistic, or any point estimate as we call it technically, is it's a national average, and then you say, "Well, what is behind the average?" And, for me, coming into Lima, coming towards medical school, coming towards university, and so this idea of movement and lived experience it cannot be captured in a single national average. So, Peru, we have the Amazon areas, so we have very isolated populations and hard to reach populations, we have the Andes that divides the country from North to South, and we have the desert coasts where most of the biggest cities

are in the small valleys in these deserts in Peru. So the three biggest cities are somewhat in the coast or close to the coast. So when I see any number about Peru this number cannot capture what is Peru, so are we talking about the Peru in the jungle, in the Amazon, are we talking about the Peru up in the mountains, are we talking about the Peru big cities or the small coastal cities, what exactly? And then the other thing that kind of triggered my curiosity was the scientific discourse, and it's very obvious that there are clear differences in the epidemiology and in the patterns of disease in urban and rural areas. That's not new. But migrants were receiving this label that for the most common cardiovascular diseases they become, or they behave, like the urban people, but how? And that's why we set up this study. So, most of the difficulty with these migrant studies are *who are these migrants? Where do they come from?* And then you lose the comparability because, therefore, migrants are very diverse. And here was the uniqueness of Peru, back in the '80s terrorism put enormous pressure for pushing people out from the Andes, because there were lots of killings, and for survival or fear or wellbeing they moved to Lima, to the capital. So, I could have the perfect experiment whereby these migrants were from the same place of origin as the rural group and the urban people were second or third generation migrants from the same Andes as well, so we can remove all the questions about genetics, and the migrant will serve as the needle when we look at different outcomes. Now, with more of the genetics, epigenomics, you can see these are kind of living laboratories which will tell us how do they express disease. So, Peru is multiple Perus and we capture that heterogeneity in these different Perus. How? So, we chose sea level areas and high-level areas. By high level I mean 4,000m above sea level. And there is the border with Bolivian Peru where Lake Titicaca is, where it's very commercial and is a point of entry, so you have a city at 4,000m above sea level, but also you have rural villages. And then we have Lima, like the sea level highly urbanised area, and then Tumbes in the border with Ecuador, more tropical, we call it semi-urban, but sea level, and that also told us another picture. There's one particular slide that I use a lot where we say, "If you were to be the Minister of Health and I show you this as a profile of six major chronic conditions, what would you do?" And it's impossible to give the one size fits all, in some particular areas you have the problem of alcoholism and depression being strongly pronounced, in others it's the combination of hypertension and diabetes, so to me that's the uniqueness and what motivates me about going beyond the national averages.

DD: Thank you. So, the other landmark study your group conducted was a trial on salt reduction to reduce blood pressure. And this, to me, is like a textbook example of a public health intervention. Can you tell me what you did and the results that you've had?

JM: It's interesting you ask. During one of my Masters I was listening to this concept of population wide interventions. I used to fall asleep in my classes but in this one I was awake [laughter], but that was in medical school, I sat in that class and I saw that slide and I said *I want to do one of those studies one day*. Because, at medical school, most of our medical interventions we need to be efficient and one way of becoming efficient is to single out and to separate those who are very sick, so you can have more opportunity or offer them treatment. That is called the high-risk approach, if you're very obese, if you have hypertension, if you have diabetes, we need to capture you because your chances of you progressing to something- you're already there, and you progressing into something worse are much higher than in the general population. But yet, the other way of looking at population benefits, or benefits in general in health, is looking at the population as your unit of intervention, and in there you are not selecting people who may are may not have a condition, you are not screening people, you are not giving treatment, but you are focusing on the population determinants of a given condition or risk factor. And the concept there is that you try to shift the curve of that risk factor, and if you shift the curve of the entire population you decrease that negative risk factor in the entire population and it's assumed that the benefits will be not only for the entire population but by shifting them all the benefits also get observed in the high risk group.

DD: So, you're trying to reduce the blood pressure of the whole population?

JM: In this case, yes, that was our target, blood pressure. But why hypertension matters, because hypertension is one of the most powerful risk factors for a variety of conditions. Strokes, when you get disabled, dementia, renal failure, and what's there? Salt. So a lot of talk there, so if you have hypertension you have to reduce salt, you have to do this, you have to take your pills. Is there anything wrong with reduced salt at a community level? No. What's our competition? There's only one salt that is in the market, so can we compete with that? Our intervention was a social marketing approach where we use a low-sodium salt and we knew that most of the discourse at that point was for salt reduction, it was government led or regulatory or industry. But in Peru, still, people cook and in many poorer countries people still cook on a daily basis, so that was our opportunity to get in there. Not to remove the habit but by supplying this low-sodium salt, so we embarked on this very innovative design which is a step-wedge trial in a way that, rather than having parallel groups you start giving the intervention on a sequential basis. Let's imagine that- we have five fingers on our hands, so on my left hand, all of the fingers are the villages to be intervened and all of them start and we measure the blood pressure, nothing has happened, we just measure blood pressure. Let's

start village number one, one finger, this village will turn, flip, towards receiving interventions and continue with the intervention. The others, we make sure the others are still under control then, at a given point in time, the village number two flips towards the intervention, then village number three and sequentially and so on. All villages have the benefit of receiving the intervention.

DD: And so, what did you find?

JM: We found very modest reductions in blood pressure, as suspected, because it was in the general population. Two things here, very modest I'm talking about 1.2-1.5 unit of millimetre of mercury in systolic blood pressure. You say, "That's nothing. Why one, does it matter?" Yes, because our study, we had people from the ages of 19 years old all the way to over 60s and, obviously, the people, the 19-year-olds, they don't have problems with their blood pressure, so the chances of seeing a large effect are not there. And the start point of the systolic blood pressure was 113, if you look at country rankings there are countries in Africa and Asia whose mean blood pressure is 130, so 113 to start with was very low, so it's very healthy, so we didn't have that many chances of having a large effect. But even despite that, despite these modest effects, we found key findings that this- what is the populational average of 1.2-1.5 got enhanced in the high-risk group, so you bring benefits for the entire population but also for the high risk groups. The people who were hypertensive to start with will show larger decreases in blood pressure and the people who are older, the elderly population, will show larger decreases there. That was one thing. The other crucial finding was- *but what happened with the new cases? Will new people become and receive the label of having hypertension?* And here was the surprising thing, that the transition towards new cases of hypertension was reduced by half. A 50% reduction of new cases of hypertension, and that is massive because these people won't need to go to the health system, won't need doctors, won't need medications and so on.

So the simplicity and the power of population approach is most demonstrated by that, that you shouldn't be captured by the smaller effects because we are so used to clinical trials large effects, large effects, large effects, but the population benefits and the health system benefits as well.

DD: Fantastic. I mean, that's just a wonderful example of how population benefit from this very small reduction but it has these massive health benefits, and health systems and economic benefits, more broadly, as well.

JM: Indeed.

DD: So, finally, I just wanted to ask you about your recent sabbatical. You took a year off and you travelled with your wife and three children around South America. Can you tell me about this experience and also the sad trigger that led you to doing it?

JM: Yes, we did this travelling in 2018. It's crazy, people were looking at me, "Are you crazy, you are at the cusp of your career, you're going to let it go?" But there were triggers. We were entertaining the idea with my wife for a number of years, and at that time we had our smaller kids, and we said, "Well, maybe, maybe when he's bigger so we don't have to be much more on this parenting of this small kid." But my mum passed away, and my mum passed away suddenly, within five days, and at that point I was travelling a lot, I was receiving grants, I was publishing, I was seeing the world as a professional, it was good, but always looking back at my family and the picture that I had when I left home for the April was a picture of tranquillity and, to me, of happiness. So, to me, doing this work of research and being on the international environment was feeding my ego, but then when my mum died, I felt like an amputation, like a sudden amputation, and I didn't grieve properly, I suppose, and it took me a number of years, I'm still kind of learning, but I wasn't happy. I wasn't happy in the sense of how come this perfect vision of- I felt I had attained at that point in time, just this picture of my kids having a very intense, substantial, emotional relationship with their grandparent. I think there was a very good driving force, something in me telling me it's the right thing to do. Everybody else keeps telling me that it's not the right thing to do but, you know what, life is too short. Life is too short, and I think we're reflecting on this, if you were to die tomorrow would you be happy or will you- what would you like to have in your pocket? And then this idea, *no, I need to accommodate work and I need to accommodate that and I need to then this and then the schooling*, and if you wait for the perfect time, for the perfect moment, to accommodate everything, it won't happen. It won't happen. So, we did it, and something that we see in pictures and we see in Europeans or the profile of people, we say, *let's give it a go*. And we left Lima by December of 2017, by New Year we were crossing the Atacama Desert into Chile, all the way down to the Chiloé archipelago in Chile, and then Argentina, Uruguay, the tip of Brazil and then Bolivia and Peru by December again, a year after. And it was a massive learning

experience, I'd recommend it. I mean, I suppose that was our preparation for Covid, nowadays, living with yourself, with your kids, what do you do? The first four or five months were terribly slow, so we didn't know how to travel, how to live with each other, and then we became much more efficient, the kids become very independent with their school course, and they finish earlier, their own education programme, we had extra holidays, and we also were staying in these farming camps and farming houses doing some volunteering work, and it was the beauty of having a headache that has to stop when the sun stops, because I couldn't do more. And then, just, you had to disconnect. Just disconnect. And I miss that, now with the technology being all the time, I'm relearning how to sleep as well, going to sleep. Going to sleep doesn't mean falling asleep, I thought when you're too tired you drop, that's not good I've been told. But in those days, we would say "Okay, what is it to do?" No, let's go to bed. 7:00PM we were in bed watching the stars.

DD: Fantastic, thank you. So, thank you Jaime for joining me today. There was a *Nature* medicine article that described your group as the model of interdisciplinary research that is scarce in any part of the world. You've really shown the power of public health research to both understand and improve health. Thank you very much.

JM: Thank you, thank you very much, Delan. Pleasure to be here.

DD: Thank you to my guest Jaime Miranda. The episode was produced by Shruthi Mahadevan and myself, the theme song is *Paper Stars* by Liam Aidan, this is a Global Healthwise podcast, thank you for listening.