AJPH Podcast— June 2023
Population-based monitoring of SARS-Cov2, Covid-19, and beyond
Hosted by Alfredo Morabia

[musical introduction]

AM Hello and welcome to this new podcast of the American Journal of Public Health. I'm extremely excited today for this podcast for two reasons: First of all, Vickie Mays is my co-moderator and most always fascinating to have her, you know, perspective on public health issues, and hello, Vickie. And the topic is, as you know, very close to my heart and very central to the mission of the Journal and it's about survey and health monitoring and in particular the use of population-based survey, the use of random sampling and all its monitor[ing] health events in population *and* over those last years what happened with Covid-19. So, Paul Elliott, hello, welcome. Would you like to say a few words about who you are?

PE Yes, hi, great to be here. My name's Paul Elliott, I'm professor of epidemiology and public health medicine at Imperial College London; and I was leading the REACT program—stands for Real Time Assessment in Community Transmission—which was in the field for two years during the pandemic.

AM Thank you, and welcome Paul, and very impressive project and we'll be able to talk about it more. And, we have here from this side of the Atlantic, Natalie Dean who has been promoting this European surveys in the US but also has been speaking very carefully about how they could eventually be imported and what would this mean. Welcome, Natalie.

ND Hi, thank you, I'm really happy to be here. So, Natalie Dean, I am an assistant professor in the Department of Biostatistics and Bioinformatics at Emory Rollins School of Public Health, and I am a public health monitoring enthusiast. So, I'm excited to chat about these studies today.

AM Thank you, thank you for being here, Natalie. So, maybe let's start with you, Paul, because, you know, when the crisis started three years ago, everybody started to collect data that was convenient data from people who got tested, et cetera, and very few people had the courage to actually do the right work and go and do a random survey of their population, et cetera. Can you tell us how you did that? What led to REACT-1?

PE So, we, I mean like everybody else in the UK, there was very little testing happening; we were under-prepared. And I think with a lot of foresight, the government commissioned ourselves with a logistic partner, Ipsos, to run this large survey called REACT-1 to collect data on a random sample of the population of England to really give that situation awareness—what is actually going on, who's infected, where are they infected, which groups are infected, you know, how does it vary across the country, and what are the levels, and so forth. We started work on the study in April 2020, so this was actually during first lock down, and put together everything, you know, at double-neck speed. We had fantastic working arrangement with our ethics committee so that we could get permission to do this work and developed all the survey materials at double-neck speed, and then we were in the field actually at the beginning of May on the first of May. And our first survey was around 100,000 randomly selected people, and of course we were able to take advantage of the National Health Service in England because we were able to use the National Health Service list of patients to deliver our random sample. And that was a huge advantage.

AM And what did you expect you would get through a random sample that you wouldn't have gotten otherwise?

PE Well, the problem with the testing that was happening is that it was haphazard, it was happening at that time then people were getting tested in hospital but not outside hospital situations, and of

course it was also asymptomatic transmission, and those people wouldn't get tested. So really, there was no really idea as to the extent of the infection what was happening [to it]. And at that time during lock down, actually, we were seeing a decline, and of course later on we could pick out the new variants as they came along. We were able to estimate the, our number, during our surveys and that proved very, very useful, and we could see in real time the sort of turning point between falling infection, increase infection; at some stages it was happening more in the children; other stages it was then moving through the population more in older people. And then we were also able to link what we were seeing at the population level in terms of infection with future risk of hospitalization and sadly mortality, because we could see the lag in our data and we could tell what the pressure would be on the health services coming up based on what we were seeing in our survey.

VM Let me ask Paul a question. Paul, did you see any kind of difference in the cooperation of people than when you usually do surveys? Because I would imagine that the will of the people were to want to know this wonderful way of getting information.

PE So, at the beginning, Vickie, there, you know, people weren't able to get a test through, you know, routine methods, so we were offering a lot of tests; people were in lock down, so they were pretty much at home; so the response at the beginning was extremely high, over 27% which is really unheard of for this type of cold calling, sending people a letter. Later on, the response rate did drop a bit, but it never got below 15% which again is still high for this type of survey. And of course, what we were able to do, because although we had some differential response, we did collect data on all sectors of the population, so we were able to adjust our prevalence estimates for the differential response rate relative to what we knew was the population structure of the country.

AM And, Natalie, how do you react in 2020 and when you were seeing the type of data we were collecting here? I know you wrote in Nature and you raised awareness about the European project, but what was your reaction? Tell us.

ND Yeah, absolutely, I mean early on, in particular, there was such enormous need for basic epidemiological understanding about a new pathogen, and the sero surveys were so important, as Professor Elliott referred to. I mean, we didn't know the denominator, how many people were being infected, when you have such a range of severity and so many people who have little to no symptoms. And so really defining those basic epidemiological parameters early on was extraordinarily important, but then it also provides that situational awareness, so yeah there was extraordinary need for this information both at a sort of a global understanding of this new pathogen and also local understanding of what's going on in these outbreaks. And so one of the things I did on social media and other talking to reporters to sort of advocate for this type of monitoring and these types of studies—because there were a lot of sort of conveniently sampled data but it's really, you know, and that can provide sort of a quick and dirty estimate but it's these random samples that provide the most value.

AM Natalie, the proportion of asymptomatic cases, there's no quick and dirty estimate for that. I mean, there's no way to do that if you don't have a random sample or…

ND Yeah, well, I mean there's—so, right. I mean, people were trying to use blood specimens, [so] blood specimens from blood donors. I mean you can get, early on there was sort of Facebook-based surveys and things like that; there were people going to supermarkets and you know getting everyone at the supermarket or, you know, so I mean certain studies designs were able to provide a sort of order of magnitude when there was real substantial uncertainty about the

severity, but when it comes down to understanding like different subgroups and, um, really, really being able to interpret the reported data, you need that, to have randomly sampled data.

AM And frankly, for the case fatality rate, I just want to remind you that in 2020 according to what you had in the [denominator] as infected, it could change dramatically. You had 1%, 5%, you know, mort—it was, it could be huge without the type of data that Paul collected. So, Paul, just to make sure that our listeners understand what is a random sample, how did you, what did you do actually to get this random sample and to get the information about Covid?

PE Yes, so in England, in the UK, nearly all the population are registered with a primary care physician, a general practitioner, through the National Health Service. So, we were able to select our sample from essentially the population denominator of the country, and what we aimed to do –so the idea was to say can we find what the variation is by different demographic groups, so that included by geography. So, what we aimed to do was to find a similar sample size in each of the 315 [relative] local authority areas across the country. So we stratified the sample to obtain roughly equal numbers in each place, and actually that worked really well, but it obviously slightly over-sampled the rural areas and under-sampled the urban areas because of the way the population is distributed. After a period, we realized that we really needed more data in the urban areas, so we then moved to a population-size-based random sample. So, we switched during the study.

AM And you sent them actually kits so they could self-test themselves and send them back to you?

PE Yeah, I mean this was a great strength of the study because it depended on the participants themselves collecting the sample and also responding to a questionnaire. So, what we did is we invited people by letter; they were then invited to go online to fill in a registration, very brief registration questionnaire; and then if they wanted to take part in the study and they understood

the consent, they would be sent a swab kit and instructions as to how to complete the swab plus a link to a video to show them how to do this. They would then take the swab, and we asked them to put the swab in their refrigerator, and in the first part of the study we would then send a courier to their address to pick up the swab because we were concerned about deterioration of the sample. We did that on a cold chain, and then the swab went on cold chain all the way to the laboratory. We had a dedicated laboratory for our study, a commercial laboratory; and they then ran the PCR; and then with our colleagues at Ipsos we then fed back to the participants their result. And of course, we fed these results back to government almost in real time. I mean this whole thing happened very, very quickly.

AM And so, and [considering] Natalie, we have two models here: the model from the UK that Paul just described and the Spanish sero epidemiology cold survey, the national survey, they went, you know, they did the two-state sampling and they went actually to the house, called to the house, and then knocked at the door and got the information in a very traditional—I mean, in 1918, that's how the public health surveys did it, exactly the same. So what do you think both of you would be the design that probably would be most, be easier to import here?

ND So, some of my colleagues at Emory did undertake a random sampling survey in several states and it was building off studies that they had done HIV in the past, and you know but they did struggle with response rates. I mean, it was real issue and return rates as well, and so, I think, you know, whatever happens in the US, it will need to account for the local context of there's a real hesitancy about people coming, knocking at your door, and so you know figuring out kind of what works best in the US context. And there's still a lot of trust in people's doctors and so maybe something that aligns with people's physicians or, but yes, I think we'll need significant

behavioral science research into kind of what is a most acceptable way to approach people in the US, yeah.

PE If I may, so as you know as well as carrying out the study looking at the infection problems with PCR tests, we also did a sero prevalent survey called REACT-2, and again this was done at home with a self-test, an actual flow kit, and people really wanted to do it. The response rates in that study were uniformly high. People really wanted to know if they had antibodies, and again they were invited in, they could register for the study, they were sent the kit if they registered, and then they did the finger prick themselves, and then took a photo and that loaded it to the website. And we then did some machine learning to read those samples. Actually, people did pretty well, but actually machine did slightly better, so people were really willing to do this self-testing. We did a lot of public engagement, even during the early parts of the pandemic. We did a huge amount of public engagement to see whether this would be acceptable to people. As a result of that, we changed the lancet, we changed the design, but people really were very keen to do it. So I think this idea of self-sampling at home is really, really good; and obviously it massively reduces the costs because you don't have to send intrepid epidemiologists and public health people round knocking on people's door. Also, I mean the other thing is in, at that time, I mean you had to have social distance, so even the idea of someone could knock on the door, they had to stay at the door, they couldn't go in and take the sample.

AM But they had, they claimed 60% participation in Spain.

PE Oh yeah, yeah, no, the Spanish—yeah, yeah, no I think it was fantastic what they did in Spain. But for us, it worked really well to do this self-testing approach.

VM Well, let me just follow up with something you said, because I think it's the most interesting aspect of maybe what we can learn in the United States. You talked about the kind of

engagement that was necessary in order to get such a fantastic response. Can you talk a little bit more about that? Because that may be where we in the US—and Natalie, if you have some suggestions—that we in the US could really benefit from that.

PE Yeah, sure, so we had a longstanding participant engagement group through Imperial College and so we started with them, and then we did some pilot surveys where we did write to random samples of the population and we asked them to take part. In addition, we also sent—I mean we were now talking about taking fingerprint blood samples for the sero prevalence—and people, you know, so friends and family but also random samples of the population. We did that at scale, and we were able to, you know, adjust what we did; and we asked people, you know, what would you suggest, how would, can we improve it, and we got really good feedback. And that's how we were able to develop something which was very acceptable to the population, people wanted to take part in.

ND Yeah, I might add, too, that Covid-19 itself became very politicized. I think that was one of the, the major, the challenges over time. I mean I think willingness early on is sort of different from willingness later; but thinking about how we can depoliticize a little bit some of the public health monitoring and maybe by integrat—linking it with other diseases that are less hot-button issues—you know like other sort of systems that can exist that can have multiple functions that include monitoring for, you know, yeah, for, well who knows in the next pandemic what it will look like but, it's just something to think about, these multi-purpose systems.

AM And I think the point of Vickie is well taken. Probably a random sampling approach in the US would need to rely much, I mean very strongly, on grassroots organization on the community organization, people that really have access to some of the population that are minoritized and

usually difficult to access for the traditional public health structure. So, let's go to the other points. So what's the future of REACT-1 now that we are in the new phase of Covid?

PE So, REACT-1 was in the field for just on two years, so I said it started on May 1, 2020 and our last sample was picked up on March 31, 2022. So, we haven't been in the field for measuring prevalence for over a year. We like to joke slightly that we went out on a high because we went out just as the BA2 omicron really took off and it was the highest that we'd ever recorded, actually, was on that end of March. So, but since then, so we had the forethought, if you like, to ask people if they would wish to be followed up in the longer term, and we have two-and-a-half million people who consented for long-term follow up which involves both linkage to their health records through the routine health records and also the ability to go back and revisit people with questionnaires and so forth. And so what we've been doing since then is following up the population; we are carrying out a long-Covid study, so we're asking people about their symptoms, about persistent symptoms, and also we are undertaking a biological study a bit similar to what's happening in the US, actually, where we invited 10,000 people back for multiple blood tests, clinical exam, and so forth. And we're now carrying various [omics] including whole genome sequencing to see if we can find a biological signature that determines amongst infected people who goes on to get persistent symptoms and post-Covid symptoms and who actually recovers quickly or was asymptomatic.

AM This is fascinating, Paul, that you are scaring me! Is it turning into a cohort study? I mean, how public health monitoring aspect, where is the real time, et cetera?

PE It's a long-term cohort study, just by nature, I mean we have a natural experiment. The whole population has been exposed to a new pathogen, and we don't know the long-term sequelae because it's too early. We know the short and intermediate term, but we don't know the long

term. So I think it's really important we follow people up and see what happens over the longer term. As I say, we have a biological component; we have a social questionnaire component; we're also doing online cognitive testing because as you know patients who are suffering with post-Covid syndrome or long Covid complain of brain fog. So, I think it's really important that we do follow people up.

AM Ah, I totally agree, but where is the monitoring aspect, [anathema]? I mean, I hope that we would put in place some structure that would allow us to catch, you know, what else comes, what comes next, or learn what we've learned from Covid to other chronic diseases and other major public health issues. So, can we keep some of this and integrate it in our surveillance and health monitoring system?

ND Well, obviously an extraordinary amount of effort has been put into developing this, you know, this system, this survey, this study. And so, I know there's a lot of interest in thinking about how things can be scaled down and scaled back up and also how you can, you know, what are the, the things that the study can do, sort of in interim periods that add that value and justify the investment, because there's extraordinary upfront investment in how you keep that return on investment going. And so, switching to long Covid but then, you know, what other pathogens—that's why I would think these like multi-purpose systems that are monitoring all different types of respiratory pathogens or, but yeah, but keeping, but there's a lot of interest in how do we keep these studies warm so that they can be scaled back up.

VM You know, I was just wondering if you have the capacity as you're out now to, if new things happen to emerge, particularly towards the respiratory, are you collecting the kind of information that will be able to spot those early on?

PE So, we're not in—so, when we were in the field in the thick of it as it were, we were out, we weren't continuous but we were in the field like 17 days or so a month, and we were able to really spot everything that was happening, you know, when the new variants came in, we could see it, but we were also doing viral sequencing so we actually knew what people were infected with. And we did add flu actually towards the end of 2021, beginning of 2022. I mean there wasn't much flu but you know if there had been we would have been able to spot it. And we did do a brief look at other respiratory pathogens; but now we're not, you know, that, as Natalie was saying, I mean this is very, very expensive to keep that sort of level of intensity, so we're now currently in passive mode as it were in the follow up, more passive follow up, although we are going back and asking people about symptoms but, you know, on one or two occasions and not every month. However, if needed, we have a consented cohort, two-and-a-half million people, we could very, very quickly go back to people and of course these people have taken part already and, in our survey, so I think it would be possible to get back up to speed quickly if there were a need to do that and of course if there were funding to do that.

AM So, we're reaching the end of this podcast. I'm going to ask you just some final remarks, each of you. So I think with you, Paul, and again congratulations. I mean required quite a lot of courage and of presence, you know, to start such a project and that quick in 2020, and very few people on earth were able to do it, so that was fascinating. What is your main advice for other people in other countries, in other populations if they were to start a similar project? What's the main lesson you've learned?

PE I think there are several aspects to this. I think really important, and Natalie mentioned this, is the situation awareness. We were able, because we were seeing the data in real time, we were analyzing it in real time, we were feeding it back to public health England and getting [it to] our

UK health security agency and to government in real time; and the other thing which think was extremely important is that we were very open about what we were seeing and we were rapidly publishing our results initially almost immediately as a preprint, as a full paper preprint, and then as a follow-on paper in scientific journals. So, the data were out there for our scientific colleagues to see but also for the public to see. And also accompanying every one of our reports, we did a press conference; there's an agency called the Science Media Center in the UK which acts as a way of scientists talking to the press and then talk to the public. And I think that was extremely useful, first of all to get out the message of what was happening and secondly that people felt really engaged with what we were doing and that the results were meaningful; and that, I think, enabled us to keep up a very high response in the public. It was absolutely full on for two years, so anyone who wants to take this one, clearly it's 24 hours a day, seven days a week. And the other thing I think, although there was a big organization behind this and we were working with a commercial company, we as a university couldn't have done this ourselves, so we worked with Ipsos which is a very big, well established research company, so they handled all the logistics, because the logistics were massive, in order to get the sample, to get the kits out, to get the stuff back. They sent us the results, we analyzed results, and we actually had a very small team, and that worked really well because the small team knew what they were doing and we knew we had to get results out, we knew we had to get the data out quickly. So, there was a huge effort whenever we got the data to get these reports out very, very quickly and, as I say, you know literally a handful of people were doing that work.

AM Great, thank you, Paul. And Natalie, I mean I can also congratulate you for your, to your thinking about this issue, your paper in Nature, and the one you just wrote for AJPH. And I practically lacked this idea and I would like you maybe to close with this, that when we actually

re-dimension those projects, we should think in terms of what's the most effective way to have a project that will impact policy, and can you say just a little more about that?

ND Yeah, absolutely. So, the editorial we wrote for AJPH extends from some conversations around the concept of value of information, and we're thinking about these studies as providing an extraordinary amount of information, but one of the dimensions of it that are really the most important for modeling policy making, individual decision making, I mean we talk about these extraordinarily large studies but what are the parts of it that are the most valuable at the end, and thinking about how we might, what we should add and what maybe we can trim, and so really taking a critical look at the value, how much more information leads to how much better of a decision. And I think it's something that economics does that I think we in public health could really benefit from a bit more, and so I think we're going to be studying these data from the pandemic for a long time. I think that will include how these sero surveys and population surveys were run and what we can learn for the future.

AM Yeah, and I though this idea was—I think because you know in the end, public health is policy and enforced policy, so that was very key. And Vickie, you know, I very few people who have a pulse on the public health system in the US as you, so are we going to be just jealous for the next years or can we use some of this and get rid of our fax machines and get some real time health monitoring in these kind of—what's your feeling? Are you optimistic, pessimistic? And these will be the last words of this podcast.

VM You know, I think our colleagues have given us a challenge, and I think this, and we what we're going to see is CDC and others needing to meet and deciding how to change. When we started, you said something I thought was so insightful and that is about the word, surveillance, and thinking about monitoring, and I think what's going to happen is in the US we're going to

determine this monitoring in a way in which we engage things, over time, real time basis, that we're going to see these models but it's going to take more time to get there, so all I can do right now is say I'm jealous but I also applaud my colleagues for the leadership because it really challenges the US to do it. We did try. Remember, we had the pulse survey that was using the APS data. We had some things, but the benefit of what the two of you really showed is something that I think is an aspiration for us in the US.

AM Thank you, Vickie. Thank you, Natalie, thank you Paul, thank you everybody for your time and for your great work and contribution to public health. I hope we'll meet in person soon. Take care, bye.

[musical postlude]