

AJPH Podcast—December 2024

Critical role of excess mortality in shaping public health decisions

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AM Alright, Vickie! This is a very complicated podcast we have today. So, I think you should explain some of the terms that they're going to need when they listen to this podcast. So, Vickie, first, what's comorbidity?

VM Morbidity, that's just illness. If you have morbidity, you have some kind of illness; and if you have comorbidity, not only do you have an illness but you have something else. If I talk about comorbidity, I might say I have asthma, but I have a cold so my asthma gets worse when I have a cold.

AM Got it! Finally, I understand it. Great, now a more complicated one: Random sampling. What's random sampling?

VM I want everybody to think about those annoying phone calls that they get. Would you want to participate in our study of—what they're trying to do is to reach you and they're reaching you because you have some characteristics that they randomly selected you. When you're randomly selected, we need your voice.

AM So now, what's a case-control study?

VM I want to see if whatever this person A has, which is a disease, I want to have somebody who's just like person A without the disease so that I can figure out as things happen to A is it just a disease process or is it that both of them are women so this happens more to women or both of them are—so it helps me to watch as some kind of disease progresses to just see the disease process, because the two people are exactly alike otherwise, so then I get to study just the disease. So, a case control study usually means I got a whole bunch of people over here and I have a whole bunch of people over there, and I'm, you know, monitoring both of them, watching the disease process.

AM Can you tell me what's a DID? It's difference in difference.

VM So, what happens is you want to see what happens to me in terms of as part of the treatment group. But you also want to make sure that later you look at that control group after you finished my treatment group and make sure did they get any changes? So you want to see the difference

in the difference. So, I want to ask you to talk about absolute excess measures and relative excess measures.

AM So, an absolute excess measure is when you look at the excess in terms of risk or rate, so that's why it's absolute; whereas if you have a relative excess measure, then you are looking at ratios and so instead of saying the excess is 10 per 1000 per year which would be an absolute excess, you would say the excess is four times larger.

VM That's great because what that does is it helps people to understand relative to what?

AM Let's turn the table again! What's a baseline life expectancy?

VM So, at a baseline, we have an expectation of how long people live, so this is a statistic that you can tell is very important.

AM They talk about co-specific path.

VM You talk about a disease or disorder to have a sense of its progression. Like for example, in Covid, if we'd had a whole bunch of things that happened to get you infected, we'd have been in a world of trouble being able to develop an intervention. So typically, when we're talking about case specific path, it means we think we know exactly how these things occur and ability for prediction is stronger and our ability to intervene can be faster. Last one's for you, and it's confidence in our estimates. How would we explain that to the general public?

AM Well, I'd say confidence means that our estimates or, you know, our measure is precise; and we're very used to it, especially now in those election days because we always have those ranges around estimates, you know?

VM I think what we can say there are some high schoolers and maybe even some early college students that we've turned into epidemiologists.

AM That would be our great action of the day, thank you!

VM Thank you!

*[musical interlude]*

AM Hello and welcome to this new podcast of the American Journal of Public Health. This is a very special podcast for us because during all the pandemic, most of the articles that passed review and were published about the impact of Covid-19 were based not on Covid-19's specific incidence of mortality but on excess mortality compared to the period preceding the pandemic. And so we wanted to have this discussion with people who have spent a long time thinking about this measurement that seems very obvious on some aspects but can be tricky too. And we were

lucky to receive an article written by Jan Vandembroucke and Neil Pearce about this issue, and we invited Andrew Stokes to write an editorial and introduce them to you briefly. Neil Pearce is a professor at the London School of Hygiene and Tropical Medicine in London, hello Neil, welcome to this podcast. Andrew Stokes is an associate professor in the Department of Global Health at Boston University, hello Andrew.

AS Hello.

AM Nice to have you. And Jan Vandembroucke is a professor at the Leiden Medical Center in the Department of Clinical Epidemiology in the Netherlands, Hi Jan.

JV Hi, may I just add, Alfredo, to your introduction, is that I also have an honorary position at the London School of Hygiene and a professorial position at Aarhus University in Denmark. So, I'm actually presenting three institutions so to speak.

AM Of course, very lucky to have my great cohost, Vickie Mays, an associate editor at the Journal and a professor at University of California in Los Angeles, UCLA. Hello Vickie.

VM Morning!

AM Andrew, is this new that people are interested in excess mortality? It seems that it's something we should have used for a long time. Was it discovered with Covid-19?

AS Absolutely not, this is a metric as old as the field of demography which has long been used to track the impact of natural disasters, heat-related emergencies, and other emerging pathogens. So, we've seen increasing sophistication of these tools but this is not the first challenge to which they've been applied.

AM Give us examples, please, of other situations.

AS Well, I think in our current era, this is a wonderful opportunity to use these metrics and to learn from our pandemic modeling to understand the impact of heat and other extreme weather events, you know, monitoring heat is much like monitoring Covid. We need spatially resolved estimates to identify hot spots where mortality is in excess of prior trends as heat-related emergencies occur. And so really a lot of the set-up, you know, methodological challenges that we've thought carefully about for the pandemic can apply to this other very important situation.

AM I see, like tracking the impact of environmental factors like heat or--

JV Yes, like, for example, within the peak of mortality it has been studied already for a long time in relation to temperature but also in relation to infections; it's also a type of excess mortality. It's an excess mortality between winter and summer. One other thing we were curious about given

that there's this long record of excess mortality is why did Neil and me think of writing this paper? We grew interested in it and several people started using it during the epidemic and all these early papers on excess mortality started in the same way. Because the [...] will be unaware, let us explain what excess mortality is. So, the first paper says it's a percentage. The paper said it's a number of deaths. The third paper said it's a rate; the fourth paper said well we need actually to transform it through [excuse]. We wondered what is it? Is it only a percentage? Is it always a rate? Is it always numbers as other people said? We found out it's all of them, and then we grew also interested in what kind of measure it is epidemiologically speaking. So, we actually wanted to look at excess mortality from the classical epidemiological field that we were educated in, what kind of measure it is, it's all kinds of measures apparently, but how is it set up, what can you do with it, what can you not do with it. It's a bit of an overview. That's we thought. And it will, of course, be a first or second maybe there have already been overviews but others will come. But it was a means of a more or less systematic theoretical description, that's what we found.

AM Great, Neil, what, can you give us the gist of this review? What did you find that you think was really relevant for people use that metrics that may not know this type of problem?

NP Well, maybe I'll make a couple of comments about what we discussed theoretically and then some practical examples. Theoretically, you find epidemiologists like to invent new names for old wine in old bottles. In fact, we'd been writing extensively on the test negative design which we realized was really just a particular type of case control study. So, it made much more sense to discuss in that context. And thinking about excess mortality, it's really a variant on the difference in differences design that if you can peer into countries you'll, essentially you're looking at the change pre-pandemic during the pandemic, post-pandemic in different countries and trying to find out something about the way that the policies have influenced those trends. So, that was the theoretical bit we write about that it was just probably easier and more rational to think about excess mortality in the context of difference and differences studies which, of which there's quite a lot of literature. And then the actual practical examples, I guess this is not new but it was striking in terms of Covid statistics that people could always find a statistic to, you know, support a particular point of view, so simply doing excess mortality was very informative but it didn't really solve the argument about which policies were best, and one example of that would be Sweden. Of course, you always end of talking about Sweden, but who

do you compare it to? In terms of total Covid mortality and excess total mortality, Sweden did slightly better than the UK. So, did that mean their policies were better or it did a lot worse than Norway so does that mean their policies were not so good? You've still really got to think about which comparison to make and then as Jan said, you really need to think about how you're talking about the absolute excess or the relative excess or just the number of cases, and we didn't have firm recommendations about that; we just basically said there's these different ways of doing things and different methods will be appropriate for different situations.

JV Age is a practical example of this and which we mention in the appendix of our [poll]. In the first year of the epidemic, Belgium and Bulgaria had the same percentage increase in that [...] so the relative 12% from both Belgium and Bulgaria. But the excess mortality rate was 110% and the other 190% excess mortality rate was almost twice to the one in Belgium for the same percentage increase, for the simple reason that the baseline death rates in Belgium are much lower than they are in Bulgaria. The question is, is this the same? Is this not the same? And did Bulgaria do worse or, if you have a higher death rate are you permitted to higher baseline death rates? Are you succumb to permit it if there's a pandemic to have relatively more deaths. Each time I start thinking about it, it's [...] change. It's a little bit like comparing the treatment of hypertension meaning also the treatment of hypertension in people with minor elevation of blood pressure and with people with severe elevation of blood pressure and a lot of all the disease that they have already. I mean when are we going to say it's equally effective? We were never going to reduce the one with the severe hypertension and severe comorbidity to the level of mortality and morbidity of the people with minor hypertension and nothing else.

AM Maybe this is a problem that in global health Andrew meets often. So, what's the solution there?

AS Yes, I would encourage our field to look at both absolute and relative measures; they tell us something slightly different. I think the relative measures of excess mortality are generally easier to interpret and communicate to lay people which I think is an important part of our work in public health, is to measure impact in such a way as the results are transparent and easily communicated as part of science communication efforts, and so the relative metric has an advantage there but as was said, not oftentimes we'll see higher relative excess mortality in countries that had a lower baseline to begin with, so in that sense the absolute measures are very complementary and should also be interpreted.

JV And there is even life expectancy. I mean, I have papers also about life expectancy and for example, both the United States and Russia had a decrease of life expectancy of two years in the first year of the epidemic. So, that seems equal. But the baseline life expectancy in the US of the time was roughly 76 and in Russia at about that time it was roughly 69. So, lowering it by two years is maybe worse in Russia than in United States. It remains a very difficult judgment.

NP Perhaps if I could mention one more which is the example in New Zealand which, as you know, I'm from there. I'm in the UK but I kept in touch with things in New Zealand throughout the pandemic, and they basically closed the country and locked down for about six weeks and essentially eliminated the virus, so for about a year and a half, I was talking in Zoom to my friends and relatives and they were living completely normal lives. They would go to a rugby game with 50,000 people and they could do anything they wanted. The only restriction was at the border, so actually they were locked down much less than many other countries except for the period at the beginning. The results are really interesting; they had negative excess mortality. They had no winter peak of mortality; they had no cases of winter flu. But they actually don't have the core specific results so you can really see apart from, you know, respiratory infections which are the causes were reduced, and I think it's an interesting research project for probably someone younger than me and Jan to look at in the next few years as the core specific data becomes available because it's quite possible that some of the things that had very low rates in New Zealand would also have been low in other countries, and excess mortality I think is the best summary measure but it probably conceals a few things that, you know, it includes all of the Covid deaths with classified, probably or not, but it may conceal the fact that some other causes of deaths may have actually reduced. You know, and one obvious example is in South Africa where they essentially banned alcohol and the rate of car accidents dropped. But there would be many other examples from other countries that are really worth exploring, I think.

AM So, let's go, you know, right into the core of this topic. Why didn't we use Covid-specific incidents or mortality to evaluate the impact of the pandemic, you know, between two countries, two communities, or whatever group that we wanted to compare?

JV My interest in excess mortality started with that problem. And as many scientific interests start, it started with something very personal. For the last 40 years, I'm living and working in the Netherlands; after a few months, half a year in the comfort in the Netherlands they said we're doing so much better than neighboring Belgium. You know, Belgium and the Netherlands are

two tiny countries off the North Sea and the continental face of Europe, and we're doing so much better than Belgium. They have twice the mortality than we have. The two capitals are like 150 US miles apart, but there was something very different in the Covid that registered. In Belgium in the preliminary registrations that were used for these preliminary statistics, very good judgment of a doctor sufficed, and doctor said well this was clinical a death by Covid, that sufficed. In the Netherlands, you needed to have a test, positive test, that was done before the person deceased. Early in the Covid epidemic, the large mortality was in nursing homes, and in nursing homes of course nobody was tested because all testing was ambulatory. So, dozens of people could die in an nursing home in Belgium and they would all be recorded as Covid-19-based. In the Netherlands, none of them would be recorded as Covid-19 deaths. That to us was a rather straightforward explanation of a rather seemingly huge difference in Covid mortality. It took a long time before we had excess mortality. It turned out that the Netherlands indeed did slightly better than Belgium, both countries being in the European average; to me this lesson made it abundantly clear to me that we needed to go to excess mortality and nothing else like you did in your journal.

AM Thank you, thank you Jan. Actually, it's not only Belgium and the Netherlands; I think it's most of the planet, right, Andrew? You have a global health perspective. I mean where did we have a measure of actually incidents and mortality from Covid-19 which would have been a valid measure of impact?

AS It's a great question. Unfortunately, many lower and middle income countries have very limited vital registration. The infrastructure may exist for all cause mortality identification but cause of death is challenging, and so developing a metric that kind of circumvents the need for cause of death data can give us a crucial insight into patterns and trends in much of the world where vital registration is limited.

NP So just adding to what Jan said, I think that the main reason for using excess mortality is for comparisons between countries, and they're very hard to do otherwise particularly in the early period of the pandemic. But the same thing applies to some extent for comparisons within countries for different groups, and one example of that from the UK was that for the first couple of months of the pandemic there were analyses of UK bio-bank and they found that healthcare workers were more than seven times likely to have a positive Covid test than the rest of the population. Of course the reason for that was that healthcare workers were being tested, so if

you looked at positive tests that were seven times; if you looked at death rates from Covid it was about 1.3 times; and if you looked at total mortality it was a little bit in excess. And we actually found it very useful to do excess mortality analyses as well which explained quite a lot. And what they showed was that, in the first couple of months of the pandemic, healthcare workers did have excess deaths at quite a high rate; but after that they had a lower total mortality than the rest of the population. And actually, being a front-line healthcare worker was one of the safest jobs to have because it was one of the few jobs that got proper protection whereas actually other healthcare workers, maybe people elsewhere in the hospital who were not front-line, they still carried on having excess mortality. So, there's quite a lot you can learn from excess mortality which is maybe not better than but it complements what we see when we look at Covid-19 mortality.

AM Thank you, but was it possible if we had for example random sample of the population that would have allowed us to track the progression of the pandemic in the reliable way, would it be possible to have actually Covid-19-specific indicators of impact? Wasn't it because we lacked all those types of random sampling? We were basing our reasoning essentially on convenient sample. Wasn't this the main reason why we used excess mortality rather than Covid-19-specific mortality?

NP I think that the lack of random population surveys was as key problem early in the pandemic, and Jan and me and a couple of other authors published something in your journal about this early in the pandemic. And that was pretty crucial because without knowing what the underlying infection rate for the population was, it was very hard to work out what the real infection fatality rate was, and that was quite crucial in terms of which policies to adopt. But I think even if you have those random population surveys, there's still a problem with the outcome and the measurement of the outcome. So, you're still going to need to look at excess mortality and at least some analyses.

AM Is this, you know, the ability to track actually the impact of the pandemic related to how the different countries have been allocated their resources for public health?

JV I think there must be an anecdote, a personal anecdote, like the way that testing and tracking was set up in Denmark where they immediately put out tent camps to have people tested and the whole system of tracking. And almost in the real time could connect people who test positive with whether or not they are hospitalized and the outcome of hospitalization. That I see



happening in Denmark; I think it happened in some other Scandinavian countries, there may be some countries I don't know, maybe other places of the world, I just don't know. But it was a far cry from what I saw happening in the Netherlands where the services were so overloaded right at the beginning the epidemic that people think well maybe we'll stop tracking, so in the Netherlands they stopped tracking at a certain point in time because they need everybody for the testing. In between Europe, within Europe, within two high-welfare countries, yes they still was a difference.

AM But for example in the UK, there was the react study which was a kind of random sample of the population in survey which allowed you to track the pandemic. So, wasn't there an alternative or a complement to excess mortality?

NP Certainly it was a complement; I don't think it was an alternative. There were actually two large studies in the UK; one was react and the other one it was just the Covid-19 survey. And I think the Covid-19 survey we got tested once a month for a couple of years and there was something, 150,000 people or something, and it provided fantastic information on underlying infection rates but it didn't actually our data to mortality, as far as I know. The mortality data was still just based on national data. So, maybe within that country it might useful that between countries you still have these big problems with what gets tested by those Covid deaths and what doesn't.

VM You what really worries me as we're talking is that it's almost like either we need epidemiologists police or epidemiologist ethicists, because during the time of an epidemic, what you do with that data, particularly if you're equipped to be able to produce it can really cause a country to go in a particular direction, and the thoughtfulness that you're discussing, sometimes we don't have that in an epidemic. And I guess I'm wondering who is to kind of monitor this. Should it be us reviewing the papers, should it be the public health system that, you know, challenges answers that they seek quickly? Who should be the, you know, the ethicists in this and making sure that it's thoughtful, that it's reflective of true conditions, it isn't the you know chicken little the sky is falling, so the worse that the data could be the more attention it gets. What are your thoughts about that?

JV There is a standard answer from infection and disease epidemiologists. We say whenever people have been educated in combating infectious diseases, okay, like the disease detectives, they say that whenever there's an epidemic my first job is to wipe it out. That's a standard medical

response, I think. When there is disease, we want to wipe it out. And then the question becomes how and when and why.

VM I think we're in a time of lessons learned, so that's why I think this session is so important because I think what we're learning is by any means necessary didn't work as well, and we had different countries doing different things. You know it's almost like the lesson for epidemiologists is maybe not first looks, you know; it's kind of like step back and be thoughtful and say what question am I answering? Is it really the most pressing question or am I just out the door with data? Because I think that, you know, resources, policies, they get created sometimes out of first-out data, and I don't know. You all are scaring me this morning, so I'm not sure in terms of, you know, as a reviewer I'm going to think twice now when I read papers. So...

AM I think Vickie's very right, because we're discussing the limitation, interpretation, the relative, the absolute difference, and what it means, et cetera, but at some point someone has to decide in order to make decisions, and this in the heat of the pandemic or the crisis. And so shouldn't we have more precise accurate recommendations?

AS You know, and taking the United States as an example, as the pandemic evolved, unfortunately it became a highly partisan topic and there were, you know, debates and disputes over under versus over-counting. You know, I think it's our ethical obligation as researchers to provide the best data possible. We can't guarantee what will be done with that data, but certainly you know the advantage of our work around excess mortality has been that it's harder to dispute the all-cause death numbers versus the cause of death numbers. So, it's more insulated from partisanship versus the not getting into what is certified versus not certified as a Covid cause.

NP I'd just like to add one other point which is something I tend to talk about whenever given the opportunity. I think in the UK and the US, we're not very good at learning from the experience of other countries. We tend to think we're the best in the world and we just do it. And the reason countries like New Zealand did so well is that they actually read the WHO reports, they realized this was not like flu, it was a corona virus, they read what other countries like China were doing, and they thought we can stop this thing. Doesn't mean you could do it in every other country, but I think in general—and it's not just for Covid and not just for infectious disease—the thing we're really lacking epidemiologically is international networks and international studies so we can actually coordinate and do things in a standardized way. And there's probably many things we need to for the, to prepare for the next pandemic, but having the skeleton of international

networks including the capacity to look at excess mortality internationally in real time would be a real valuation resource, I think.

VM Yeah, I think Neil's point is great, but even though I think we can coordinate data, we can have policies, it's like countries have their own set of cultural behaviors and tolerances. So, you know, shutdown in one country is accepted and shutdown in another country is, you know, grounds for the politicians not getting re-elected. So, we've gotta think about, you know, can we make the case that allows people to change their behavior in the face of what we could tell them, that if you don't this is what happens. So again, we get back to the truth of the numbers and how we connect that up so that people will have trust in the public health, you know, advice. Because Andrew's point is so well taken that, you know, the partisanship, if we looked within the US, those places that had deaths, sometimes they had to do with partisanship and less with the solidness of the data. We still got a problem.

NP I agree and I didn't say it was easy, I just said it was necessary. So, it's always going to be difficult, but you're still better to have the data than to not have the data.

AM And I insist that it's not always an issue of political partisanship, because we in the Journal grow to the US the experience of the Spanish national study on Covid-19 which was a careful random survey of the population and we broke react which was not well known, et cetera. So there is a need for international cooperation on those issues and it would be very well. Alright, we're getting to the end of this podcast, and I would just want you to conclude with what is your main recommendation for people that are going to use excess mortality in the months to come. What is your one and single most important recommendation.

NP I would say the first thing is just to have the capacity set up to do it. And also you referred to the react survey and I referred to another UK survey—for future pandemics, we need to be able to get those set up very quickly in as many countries as possible. So, I think if you don't look at excess mortality for ten years and then suddenly you have to do it, it's very hard to get geared up. So, I think you need to have the capacity to do it, the record linkage to do it, and the technical expertise to do it so that it can be done very quickly when the next pandemic comes along.

JV For me, the most important thing to ask oneself is what is my precise [...] question? What do I really want to know? What do I want to know and why do I want to know it? What I'm going to do with it? What will it change if I know it? So what do I really want to know, what do I do, and what will it change? And then, to me, the rest derives from that.

AS You know, we've seen during the pandemic that excess mortality has become a very popular indicator to understand the impact. I think we're at a point where, you know, there's no textbook for excess mortality calculations. A lot of the work has been ad hoc and without proper coordination. I think we're at a time when we ought to be asking as a research community to better understand when this measure is helpful, under what assumptions we can give it a causal interpretation, and what decisions can influence the results of an excess mortality analysis. All very important to increase the competence of our estimates and prepare for future pandemics.

VM I think very much like Neil, I think we should be working right now to strengthen our data collection infrastructure, our toolbox, you know, teaching our upcoming infectious disease individuals about ways in which, when there is an epidemic, to think about it. So I think we need to modify some of our teaching to emphasize what you can do under restricted, by restricted I mean you don't have quite enough data that you want, you have to make decisions. Now's the time to do those things so that when the next epidemic hits which we know it will, that we have some standards of how we want to provide the data; we have, we know that we can get the data; and lastly that we're willing to do comparisons and accept other countries may be able to provide insights into, you know, the decision-making that a country is making.

AM Thank you, and I think we showed to our listeners and our viewers that excess mortality may not be the simple and straightforward index that it looks like. There are issues when you start comparing the index that you use with comparison that you do, et cetera. And so I invite you all to read the article by Jan and Neil and the current by Andrew. Thank you all very much, all of you, thank you for your time, for your expertise. It's been a great moment. And thank you, Vickie.

VM My pleasure.

ALL Thank you very much.

*[musical postlude]*