Dr. Naor Bar-Zeev

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Female: Welcome to Conversations on Health Care with Mark Masselli and Margaret Flinter, a show where we speak to the top thought leaders in health innovation, health policy, care delivery, and the great minds who are shaping the healthcare of the future.

Well, this week Mark and Margaret speak with Dr. Naor Bar-Zeev, Deputy Director of the International Vaccine Access Center at the Johns Hopkins School of Public Health. Dr. Bar-Zeev is collaborating with research scientists around the world all working towards development of a viable vaccine for COVID-19. He talks about moving into phase three trials for some leading candidates, and the huge challenge it will be to get it to the marketplace.

Lori Robertson also checks in, Managing Editor of FactCheck.org looks at misstatements spoken about health policy in the public domain, separating the fake from the facts. We end with a bright idea that's improving health and wellbeing in everyday lives. If you have comments, please e-mail us at chcradio@chc1.com or find us on Facebook, Twitter, or wherever you listen to podcast. You can also hear us by asking Alexa to play the program. Now stay tuned for our interview with Dr. Naor Bar-Zeev from Johns Hopkins Bloomberg School of Public Health here on Conversations on Health Care.

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Mark Masselli: We're speaking today with Dr. Naor Bar-Zeev, Deputy Director of the International Vaccine Access Center at the Johns Hopkins School of Public Health. He's a pediatric infectious disease physician and statistical epidemiologist whose research has focused into how to maximize vaccine benefits for low resource high mortality areas of the world. He recently co-authored a piece in the British Journal, the Lancet on the current race to develop a vaccine for COVID-19.

Margaret Flinter: Dr. Bar-Zeev is a Principal Director on a number of research protocols at the Bill and Melinda Gates Foundation and he's a Founding Member of Immunizing Pregnant Women and Infants Network. He led the Vaccines Research Group at the Malawi-Liverpool-Wellcome Trust Clinical Research Programme and was a member of Malawi's National Immunization Technical Advisory Group. Dr. Bar-Zeev, welcome to Conversations on Health Care.

Dr. Naor Bar-Zeev: Thanks for having me. Great to be here.

Mark Masselli: Dr. Bar-Zeev, I think it's fair to say that Johns Hopkins has really been out in front of this pandemic, building a robust scientific framework to address COVID-19. The world obviously is waiting with bated breath or any positive news about the vaccine. In the recent Lancet article, you offered some optimistic analysis of the phase one and two clinical trials of drugs in the pipeline. But you also caution there may be some potential roadblocks ahead, but I'm wondering if we could start off what's involved in a phase one, phase two and phase three vaccine development, and then if you could tell us why you're both optimistic and concerned about the development of the vaccine.

Dr. Naor Bar-Zeev: Phase one study looks at safety in a small number of people, and often tries to usually the first in human trial after some animal work or other work in that precedes in. It tries to generate an immune response at varying doses. Phase two similarly tries to get a little bit more detail on the right dose of an intervention, and again, looking at safety and usually in the case of vaccines immunogenicity. In other words, does the vaccine induce an immune response in the recipient? A phase three trial is a whole order of magnitude different. It's a much bigger trial and in the case of COVID-19, it will be very much bigger. It looks to see whether the vaccination reduces the infection itself, reduces the disease from infection and infection. It is looking also at the immune response, but it's not really worried about what the body does in terms of the immunity, worries about whether the vaccine actually provides clinical protection.

Now there are lot of reasons to be optimistic. First of all, we've seen a really big global effort, and there are many groups around the world working simultaneously. There’s funding that's available to drive that effort as well. We're seeing a broad range of vaccine candidates, which is really great because many fail, and so having depth of field is important. The initial findings are successful and have been good. But as you say, there are hurdles to come. The key one is always with any vaccine, but particularly now, the question of vaccine safety is crucially important, and will need to be addressed in ongoing studies. Even once we have a vaccine, we need to make sure that this distribution is equitable, that it's affordable, and it comes at a reasonable cost, and all of these are challenges yet to come.

Margaret Flinter: Well, Dr. Bar-Zeev, you've been on the frontlines of vaccine

development for years and we really appreciate the focus that you've had particularly on vulnerable sectors of a population and pregnant women and children. But you have this unique challenge of we've got to get to safety, and at the same time, we know that people most affected by COVID-19 have been vulnerable, particularly members of some minority groups and people with other coexisting chronic illnesses. Maybe you could share with our listeners some of the unique challenges that are encountered in the developing of vaccine that will be safe and will be safe for, in particular, those populations who are really at most risk from the disease itself.

Dr. Naor Bar-Zeev: There are a number of challenges in developing a COVID-19 vaccine, and partly they're related to generating protective immunity. Given that we don't really even know yet what level protective immunity is, we don't know how much antibody we need to have in the body to prevent us getting infected. We've seen from trials that there's good immune response and that's great. We've also seen T-cell mediated or cellular mediated response, and that's even better, and that's really reassuring, but we'll have to see the phase threes really tell us. The other challenging thing is that the risk group as you've alluded to are older adults, and older adults particularly older-older adults have a phenomenon where they don't respond even in logically as well as younger adults or indeed children. We call that phenomenon immune senescence.

Developing a vaccine that's particularly effective in older adults can be quite challenging. It may require more than one dose. It may require specific adjuvants or other formulations that are unique for adults. At the moment, from the initial studies, we can't say very much about adults. The phase three's trials are going to include adults up to the age of 85, specific groups around the country and elsewhere overseas working on specific older adult vaccines and there may be a range of products out there in the end, so that other problems are going to be generating long lasting immunity. We want immunity to be there a year after vaccines and several years after.

But underlying all of this beyond the vaccinology really is the demographic question. Till now we've had a total of six people of African descent in the Moderna trial and the OXI trial, for example. They're very preliminary trials, the numbers are small anyway, but that's really a tiny number. The phase three trials are going to have to be in the tens of thousands and be as inclusive as possible so that we can infer both safety and efficacy in these population groups because the people who

want to receive the vaccine in the end want to know that it's safe for them. We won't know that unless they're in the studies.

Mark Masselli: Well, let me pull the thread on that, we're heading into this phase three, we might see -- I heard the number up to 30,000 people obviously the ability to reach out to a much broader and diverse population. As you just said, there's only a small fraction of minorities being counted among the current participants and those numbers were small. We happen to be part of the initial IRB process for the All of US initiative at NIH. Dr. Collins really set out to create a study that really represented our whole country, and we here in the United States have a very diverse populations as you know. Is there a sort of a custodian of these phase threes that say, you're the quarters you should be in, in terms of representation, or is Moderna and others allowed to sort of determine that on their own?

Dr. Naor Bar-Zeev: Well, it will be up to the regulators really. One of the advantages of things being at, so called, warp speed, it's not so nice to go and things warp speed because I think the population thinks that their corners are being cut, but they're not. One of the advantages of doing things in a somewhat more overlapping ways that in the routine course of events, the company that wants to produce a product for the market in those kinds of capitalistic terms, if you like, goes off and does its work and then gathers all the data and presents it to an independent regulator to review. Here, because we want things to be successful first time, we don't want to just send companies back to the drawing board because we as a society can't afford to lose time.

Regulators are participating and not in the production of the data, obviously, they need to retain independence. But they are already laying out what trials really need to look like going forward. Part of that comes from societal expectations. I think scientists are just human beings. Even though the methods that we use is scientific, the questions that we ask are often based not on science, but on issues or on societal issues. The more we argue and the more we advocate for inclusive trials, pragmatic trials, the more I think those will occur. Human beings are not perfect specimens, and what we want are trials that are pragmatic so that we can infer from those trials to what the real world result will be. We want a efficacy results from trials that are much more closely reflective of what we might expect in effectiveness. We don’t -- the perfect specimens in the trials, we want everybody in the trials.

The All of Us example that you gave, that's a great example of the breadth of data that are required. I think if you want to understand the data are useful in a couple of ways. First of all, obviously, they tell us what we can know, but they only tell us those things if we measure them. [Inaudible 00:10:04] that data can tell us what we don't yet know, and where we need to try to look. I think that those gaps are important when it comes to developing trials.

Vaccine trials are a bit different to clinical trials, and I think the general public isn't aware of these things. But a clinical trial, let's imagine a new treatment for cancer, well I need to go to patients who have cancer, they're already sick, and perhaps they'd be willing to tolerate some degree of risk to cure their cancer with a potential cure. A vaccine trial isn't like that, vaccine trial is given to healthy people, and it's given potentially with the view that it would be given to all the target population, all people, in order to prevent a condition, not to cure an existing condition. The bar of safety has to be much, much higher. I mean, we really have to demonstrate safety in vaccine trials even more than in usual therapeutic clinical trials.

As in all trials, particularly here, the individual who is participating the trial has to be fully informed and has to consent. That's the foundation of ethical conduct of trials, and that implies trust, and it implies openness, and the reason for that is that you need voluntary participation. I mean, I think the All of Us thing is fantastic. But it's not enough just to go to communities and observe them. We need communities to be participating in the trial. It's not just with the company that makes the product. Now this is a different kettle of fish. We need all of humanity to come together and participate in these activities so that we can have a vaccine for their communities as soon as possible.

Margaret Flinter: Well, Dr. Bar-Zeev, I wonder if you could comment on another -- I think a concern that we've had that maybe there's other crises in the making here, and that is that we saw the tremendous drop off in people getting primary care at all and with a real drop off in childhood immunizations over this course of time. That's really gone on for about five months now, and we have the flu season coming up, right. Now we're telling other people avoid crowds and avoid putting yourself in places where you can't social distance, and yet we have the huge potential for the risk of people are not getting the influenza vaccine. I'm really curious have you seen any spikes or crises? How are we going to message to this for the fall to

get people to come and get that flu vaccine even when we're telling people avoid crowds?

Dr. Naor Bar-Zeev: Sure. Look, there are good data already available from around the world. I mean, in the US in the first quarter of 2020 at least some states have reported a reduction in childhood vaccination coverage of over 20%. In an analysis World Health Organization conducted showed that at least in 68 countries, which covered about 400 million under five children, and coverage reduced between 15% to 50% in some settings, and that's work that was done here at Johns Hopkins, so these are real crises. They don't want to even wait till we have another measles crisis or [audio cut] the fact that we have low coverage is a crisis. It's not just children who are at risk of reduced childhood vaccination rates, it's the rest of us. We've seen adult cases of measles occurring a year ago when we have the measles outbreak because of reduction in childhood vaccination.

Colleagues of mine from around the world are telling me stories that people that they know are being turned away from accessing healthcare when they're about to birth a baby because of lockdowns and whatever, let alone with a mother seeking to vaccinate her child. The key issue is that we really have to ensure access to everybody. This really is an opportunity to build the systems, rebuild the vaccine systems in a way that's robust and flexible, adaptive and responsive to community needs, to family needs.

I've seen in places around the world that vaccinators really make a big effort to reach every child. It's like they go far in the back of a bike but then they have to carry the bike on the back to cross the mud or in the Pacific where people are adding little dinghies going across from island to island. That kind of flexibility and outreach has to happen even in high income settings. We need to value what vaccines are.

In terms of the question about flu, I think it's a great opportunity to have a dress rehearsal for COVID vaccine. If we build the right kind of mechanisms to reach all older adults with vaccines and make -- flu vaccines, I mean, before the coming winter and make them available and engage with communities to make that happen, we can learn a lot from that. We can learn how we can engage with the communities, we can learn how we can reach optimally older adults, and that would be great lessons to then implement when it comes to the availability of COVID-19 vaccine.

Mark Masselli: We're speaking today with Dr. Naor Bar-Zeev, Director of the

International Vaccine Access Center at the Johns Hopkins School of Public Health. He recently co-authored a piece in the British Journal, the Lancet on the current race to develop a vaccine for COVID-19. You know Dr. Bar-Zeev, you and your colleagues at Johns Hopkins recently held a press event addressing the race to a vaccine, which you feel could be ready for some kind of deployment next year. But you say the federal state and local governments must start acting now to really to develop a comprehensive strategy to prepare the public and the need to participate on the COVID-19 vaccination.

I think we also have some of the challenges for a much larger movement that seems to be growing about people who are opposed to vaccine. But we're still seeing a very disjointed message out of the White House on some of the basics use of mask, trying to make sure they're talking about proven remedies versus unproven remedies. What kind of messaging would you recommend for the government's to really be conducted right now to prepare the public for really a very important campaign that's going to go on trying to control the pandemic?

Dr. Naor Bar-Zeev: Look, I think it's important to remember that we're seeing a brand new, and we're learning a huge amount very quickly. What we're actually seeing is science unfolding, mainly blossoming in real time. With [inaudible 00:16:01] glorious uncertainties, we don't know everything in science and that's good, that's what science is about, it's about exploring the unknown. Our obligation is to provide as best available data, the best cutting edge science to the population as quickly and definitively as we can, but also humbly to admit what we don't know and to be prepared to change course if new evidence emerges. Hydroxychloroquine example which perhaps you were alluding to or others, is a good one. I mean, we thought that -- there was some suggestion, there was some evidence, and then the evidence was undone, and so the messaging was changed, and that's okay.

The public maybe feels uncomfortable about that because people in our society, we live in this kind of a post -- well, let me just say like this, that people put a lot of stone on what science has to say, and science seems to be the doing of some kind of objective truth, and that's not the case. Science is just human beings exploring the unknown. I think as long as we are clear about that, but messages have to be empathic and they have to be real, with their feet on the ground, they have to know what communities are feeling. They shouldn't be

patronizing. They shouldn't pontificate. It's especially true for vaccine safety, just saying vaccines are safe, and the saying that vaccines are safe doesn't make them safe. The evidence that vaccines are safe is hard one, and it's challenging to get and it takes a lot of effort and diligence.

I think the best way to speak to people is to be frank, open, honest, listen as much as you speak, speak with people not to or at people, and listen to their concerns. If people have concerns about vaccine safety, so do I. I don't want to give an unsafe vaccine my aging mother, I want to be able to give her a safe vaccine. Now we're all in the same boat, the scientific community, the vaccine community and the general community, and I think that that's the foundation in which we would need to discuss with people rather than message at people.

Margaret Flinter: Well, let me ask you to address another what I just see as enormous challenge. We've never had anything in my lifetime that I can remember that we've said we would want to get this to every person on the planet or as close to that as we can. Now we're talking about a manufacturing process of just like enormous proportions, and now we're talking about a logistics, if you will, operation of enormous proportions. I appreciate the point about using our flu clinic this year as a kind of a dress rehearsal. But this is on a factor a few hundred times larger. I'm really curious at the center at Johns Hopkins, is there somebody in charge of scenario planning, thinking about just the scale of what we are all going to try and accomplish when a vaccine becomes available?

Dr. Naor Bar-Zeev: There's not going to be one solution that's suitable for all locations. The detail has to be focused ground up not planning from the top. We have to be listening to what people want and understanding how countries prioritize. For example, the COVAX Facility which is a combination of CEPI which is pandemic preparedness organization, GAVI which is remedies to deliver vaccines globally, and the WHO conducted 136 country consultations just now finished to really understand where countries are at, what their planning requirements are. It's one thing to give a country a whole bunch of doses, but it's quite another if they don't have the culture and capacity, I mean where am I going to store my vaccines?

When new vaccines were introduced in 2011, and 2012, for example, in Malawi, there was a lot of very proactive planning by the Ministry of Health to their very great credit, they thought about this very carefully in advance, and they built the

culture and capacity right through system to accommodate just the storage of the physical vaccine. That has all happened in advance. There's no point having a vaccine and then not being able to deliver it. What we're doing here at Johns Hopkins and the International Vaccine Access Center is developing the tools that countries can use that that the National Immunization Technical Advisory Groups can use to implement and to plan for implementation and delivery.

Every country will have different priorities, there needs to be block parties as mentioned around safety and around financing, there's going to be ethical questions about which population and subpopulations should we prioritize first. There are questions about demand and hesitancy, and how do we address those things. Again, I can try to deliver, but if the population doesn't want to receive, then I need to address that in advance. All of these things are facets of sort of a complex matrix, a Rubik's cube, if you like, that every country has to think about implement and evaluate. Just as an example for, let's say healthcare workers in the United States, they're probably will be in the first round prioritize. That probably could be vaccinated through their places of work.

Older adults, as I said before, we need to think about the infrastructure for delivery. But think about people with comorbid conditions. How do we even identify them? Maybe there's a diabetes registry or whatever, but how do we identify everybody who's obese or everybody who's got high blood pressure? How do we reach them? These are very complex. The question of resistance or hesitancy, again, we need to address that right at the outset through the whole process with inclusion, openness, honesty. I mean, the large bulk of people in the middle who share my vaccine safety concerns, not extremists, but normal people who have reasonable concerns, and they need to be engaged in the process in order to be successful in delivery.

We are hopeful that some of these new vaccine products and vaccine platforms are scalable. We'll get through those hurdles, they're not insurmountable. It's good to know that some of these companies that are investing at risk [inaudible 00:21:29] with not knowing that the vaccine be definitively efficacious, and are investing the infrastructure that's required to produce these vaccines to massive scale, billions of doses.

Mark Masselli: Dr. Bar-Zeev, we've been fortunate to have a number of thought leaders who have joined us recently Dr. Eric Topol and Dr. Zeke Emanuel. It seems to be some unanimity on one

hand, the lack of federal leadership in this really incredible time of crisis, the muzzling of the CDC that's been going on. But they also marvel at the accelerated level of scientific collaboration that's occurring really all over the globe. As you sort of look at all the investment that's going in, what are their collateral discoveries might be hastened or unleashed because of this really massive scientific endeavor.

Dr. Naor Bar-Zeev: Yeah, look, I mean, there's always reasons to be optimistic, and especially now there are many reasons. I think the science is cutting edge. We've shown ourselves as a community, scientific community, that we can really band together and move things forward. The vaccine platforms that are being developed and novel, obviously, we need to demonstrate their safety and effectiveness. But they're not just novel, but potentially adaptable for the future and that's really important because this isn't going to be our last pandemic. We're fortunate that this is a very infectious pandemic, but with a relatively modest mortality, if we were to combine in 50 years from now or in 15 years from now a coronavirus pandemic with the infectivity of this one and the mortality of the MERS one that happened in 2012, that would be medieval like plague all over again.

We need vaccine platforms that can be developed quickly and rapidly and adapt to new emerging threats, and that's happening right now and that will become normal going forward. The other opportunity is to heal ourselves as a society as we build better health systems, responsive health systems and inclusive health systems. More than a science it's our ability to gather together with all of our differences and all of our divisions to really celebrate the division. Those divisions are just all many parts of the unified whole that we're healing and strengthening in response to this pandemic.

Margaret Flinter: We've been speaking today with Dr. Naor Bar-Zeev, the Deputy Director of the International Vaccine Access Center at the Johns Hopkins School of Public Health. Learn more about their important work on COVID-19 by going to www.jhsph.edu/IVAC or go to www.jhsph.edu/covid-19. Dr. Bar-Zeev, we want to thank you for your commitment to advancing this vital area of scientific discovery and for providing a sober but, I think, optimistic voice in this ongoing crisis and for joining us today on Conversations on Health Care.

Dr. Naor Bar-Zeev: Thanks so much for having me.

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Mark Masselli: At Conversations on Health Care, we want our audience to be truly in the know when it comes to the facts about healthcare reform and policy. Lori Robertson is an award winning journalist and Managing Editor of FactCheck.org, a nonpartisan, nonprofit consumer advocate for voters that aim to reduce the level of deception in US politics. Lori, what have you got for us this week?

Lori Robertson: New York Governor Andrew Cuomo made the over the top claim that if the Trump Administration, "had done its job, the virus wouldn't come here," meaning New York. Cuomo pointed to a study that suggested government officials could have better mitigated the spread of the Coronavirus in New York City, but it didn't say they could have stopped it. Cuomo made his comments in a July 16 CNN interview. The governor referred to a study by the Centers for Disease Control and Prevention in saying, "Trump is to blame for the virus coming to New York," and that's what the CDC just said.

The study found that genome sequencing of positive Coronavirus cases in New York City mostly resembled sequences in Europe, but the US government's travel restrictions on Europe were implemented too late to mitigate the introduction of the virus. Those restrictions were implemented on March 13th. By March 15th community transmission was widespread, but the CDC didn't say that Trump is to blame for the coronavirus coming to New York or that the federal government could have stopped the virus from coming to New York as Cuomo suggest.

As we've written before, the research on international travel limitations shows they can delay the path of the spread of diseases, but do little to contain them. The CDC report used specimens collected by the New York City Department of Health and Mental Hygiene from March 1st through the 20th at six hospital emergency rooms from patients with influenza like symptoms, who had tested negative for influenza. Of the 544 specimens, the CDC found 36 tested positive for the Coronavirus. The CDC then used genetic sequencing and found the positive specimen mostly resembled the genetic sequences of the virus circulating in Europe.

The study suggests the virus spreading in New York City in March largely wasn't affected by the federal government's restrictions on travel from China, which were implemented on February 2nd. Limited testing availability and strict testing criteria harmed the ability to detect cases and slow the spread, the report further said. That's my fact check for this week. I'm

Lori Robertson, Managing Editor of FactCheck.org.

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Margaret Flinter: FactCheck.org is committed to factual accuracy from the country's major political players and is a project of the Annenberg Public Policy Center at the University of Pennsylvania. If you have a fact that you'd like checked, e-mail us at www.chcradio.com, we'll have FactCheck.org's Lori Robertson check it out for you here on Conversations on Health Care.

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Margaret Flinter: Each week Conversations highlights a bright idea about how to make wellness a part of our communities and everyday lives. September is suicide prevention month, and it's a particular interest to the Veterans Administration. An estimated 22 veterans per day are taking their own lives in what's being described as a post-war suicide crisis. With a lack of behavioral health clinicians available for every veteran who's experiencing difficulty, the VA has launched a campaign aimed at all Americans who know veterans who may be struggling to be aware that they can make a difference just by reaching out. It's called the Power of One campaign. The idea that one person reaching out to one veteran in a caring manner can make a difference.

Dr. Caitlin Thompson: The Power of One small action, one conversation, or one phone call can make a difference in the life of a veteran going through a difficult time. For free 24x7 confidential support call the veterans crisis line or the military crisis line.

Margaret Flinter: According to Dr. Caitlin Thompson, Deputy Director of VA Suicide Prevention Program, it takes only a moment and just one small act can start them down the path to getting the support they need. The VA has launched a new suicide prevention hotline. It's now collaborating with community groups across the country to prepare them to better address the needs of these veterans, many of whom don't know how to ask for the help they need. Veterans, service members and anyone concerned about them can call the veterans crisis line 1-800-273-8255. They can chat online at www.veteranscrisisline.net/chat or send a text to 838-255 even if they're not registered with the VA or enrolled in VA health care. All veterans' crisis line resources are optimized for mobile devices. A dedicated program aimed at reaching out to veterans across the country, empowering community groups and individuals to find ways of offering support to getting

veterans to help they need before it's too late. Now that's a bright idea.

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Mark Masselli: You've been listening to Conversations on Health Care. I'm Mark Masselli.

Margaret Flinter: And I'm Margaret Flinter.

Mark Masselli: Peace and Health.

Female: Conversations on Health Care is recorded at WESU at Wesleyan University, streaming live at www.chcradio.com, iTunes, or wherever you listen to podcasts. If you have comments, please e-mail us at www.chcradio@chc1.com, or find us on Facebook or Twitter. We love hearing from you. This show is brought to you by the Community Health Center.

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