COVID Information Commons (CIC) Research Lightning Talk

Transcript of a Presentation by Kristen Miller (MedStar Health National Center for Human Factors in Healthcare), September 22, 2021

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Kristen Miller CIC Database Profile

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Transcript

Kristen Miller:

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Great. Thank you. I'm Kristen Miller. I'm the scientific director of the Medstar Health National Center for Human Factors in Healthcare, but I am representing a much larger project today that includes multiple healthcare systems.

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This is a project actually funded by the CDC. A two-year award, again, includes lots of different health care systems. I think, really, the beauty of this project is a number of different features where we are engaging with the community but to look at the spread of Covid-19 in a number of different ways. We have participants that are participating in daily syndromic surveillance, so you can imagine folks that maybe are experiencing some symptoms but don't rise to the level of requiring clinical care. We have participants that conduct monthly serology tests, and so in that way we're capturing participants that perhaps are asymptomatic. We have symptom and serology triggered virology data, and then we have linked electronic health record data. So, in that third component, the EHR data, we're actually capturing patients that are hospitalized, so we're able to get asymptomatic all the way up to hospitalizations.

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There are a number of different sites. I represent Medstar Health in the mid-Atlantic, but there are six sites that were funded by the CDC: Medstar Health at University of Maryland representing that mid-Atlantic area, Wake Forest who's leading this project, and Atrium Health representing North Carolina, and then in the deep south, University of Mississippi and Tulane. There was at the same time a project funded through the Cares Act for the state of North Carolina, so that includes Atrium Health and Wake Forest in both cohorts and then other health care systems in the North Carolina area.

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So again, really two key components here. The first is daily syndromic surveillance, and you can see some screenshots at the top. Every day folks get a request to complete this daily status through their email or through a push notification on their smartphone. It asks questions like “Do you consider yourself healthy?”, “Are you experiencing any symptoms?”, “Are you wearing a mask?”, “Have you had any exposures?”, and then collects information about test results for COVID. We've also added information, of course, about vaccines, and now specifically the flu vaccine as well, and then there's the monthly serology tests. These are at-home kits which we thought were pretty important during the pandemic to make sure that this could all be from the safety and comfort of one's home, and those are blood spot kits that you conduct in your home, and then mail back. So, collectively here we're able to capture symptoms. We can look at social distancing and personal protective equipment like masks, access to health care, and then more objective measures, like prevalence of antibodies and also vaccine related outcomes.

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We have more than 60 000 people that are participating in this study, obviously, around the health care systems that I mentioned, but we have at least one participant in every one of the states, and we even have some international participants as well which is quite exciting.

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Just as a summary of how much information we've been able to gather over the last year or so, we have more than four and a half million daily symptom updates. We have more than 150,000 serology results, and that's most of what I'll focus on, sort of the preliminary findings that we have right now. Then, across all of the different sites, we have more than 17 million electronic health record data elements, and this includes a number of things, so demographic information, behavioral information, like smoking and alcohol use, vaccine-related information, and then general information about a primary care visit,

an urgent care visit, or hospitalization. We capture medications, vitals, lab results, active problems, diagnoses, and anything else that happens in the encounter or in an outpatient procedure.

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This is the distribution. For the gender distribution you see all the way on the left, these are the males and females participating in the study at large, meaning the daily syndromic surveillance. Then we took a subset of those participants and asked them to participate in serology, and so you see there's a sampling strategy here. You see the gender on the left and then age on the right, so we've oversampled different populations to try to get some more information.

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You see that most relevant here is when we look at race and ethnicity, so the total bar is everyone that's in the study. The darker green shows the sampling for serology, so you'll see that we've over sampled four minority populations on the left.

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Of all the things that I'm sharing today, I think the piece that I'm most excited about, and perhaps most proud of, is the results of the serology testing in terms of participation. This is Medstar data specific. We have over 8,500 participants, and again, this is a monthly blood spot test and we have almost 45,000 kits that have gone out. There's about a thousand people who received a kit. They said they wanted to participate but never returned that first kit, but outside of that, that means there are 7,500 people that have been doing this. More than 50% of those people are in at least their sixth kit or their seventh kit, and that's pretty incredible community participation. So, 78 % of all the kits, more than 34,000, are representing people who have returned at least five kits, so you can imagine since we're looking at antibodies over time, that continued participation is quite important.

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I'll share with you some of the antibody results. What we did is conduct two different antibody tests in our study. We're trying to figure out if people are developing antibodies from natural infection, natural transmission, or from vaccination. Essentially, you develop antibodies about one to four weeks after infection or vaccination, and the spike protein antibody starts to rise if you've been infected with the virus. The nucleocapsid antibody will also rise. In people who have been vaccinated, they won't have that nucleocapsid antibody, and we can see how long it takes for them to develop and how long it takes for them to decay. Based on these different tests, we're able to see how many people had a coping

vaccine, how long antibodies lasted after vaccination, whether someone who's been vaccinated can get infected. We're looking at those breakthrough cases with and without symptoms: how many people who have been vaccinated get infected, how long antibodies last after detection, and whether people with antibodies after infection can get infected again for a second time.

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This first result is focused on antibody development. How long does it take for antibodies to develop the test? On the left is the Euroimmun. This is a research grade test, so it's much more sensitive. It's much much more specific, and you can see consistent with what guidance we're getting from the CDC, about two weeks after vaccination, you start to see those antibodies rise. This is looking at different age groups, and so it's taking longer for an older population, generally, to develop those antibodies. The test I'm showing you on the right is the Inovita lateral flow assay, and this is more commercial grade. You might be wondering for a CDC-funded research study, why we are using a test that's less sensitive and less specific? I think we really want to think more pragmatically about this. If folks in the community are using this community level or these commercial level tests, are they getting the right results, and how might that be impacting their behavior or the policy? In this less sensitive test, we're seeing a similar trend. It's taking longer for older people to develop antibodies, but we still see them around that two-week period. We're not detecting as many, again, because it's not as good of a quality of a test.

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Then we can look at zero prevalence, so zero conversion means you didn't have antibodies and then you do. On the left, we're looking at the national cohort, so the site's funded by the CDC. We didn't start doing this as early as we would have liked, so you would have expected to have seen more natural infection, but that's just because we didn't have as many of those tests going out. It is interesting to see when the vaccine was available just how many people were vaccinated. You see just a tremendous uptake in antibody development. Another interesting piece here, looking just specifically at the North Carolina cohort, is the difference between non-healthcare workers and healthcare workers. We see different levels here of that zero conversion, so pre-vaccine, lots of natural infection, and then for healthcare workers, we see a spike because they were one of the first in line to get the vaccine, so we saw more antibodies develop.

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One of the things, I think, top-of-mind and in the media right now is antibody decay, and so we're looking at that as well as how long we can detect antibodies after infection. These graphs are showing not vaccine induced antibodies, but natural transmission, and so you're seeing on the left this decay in antibodies. For folks that had that natural transmission, we're seeing the antibodies start to go away

after two or three months. One other interesting finding, which is this graph on the right, is that for the folks who had pauci or asymptomatic COVID, they didn't have as many symptoms, and they weren't as sick, those antibodies go away a whole lot faster than someone who had a higher severity case of COVID. I want to make sure I'm not contributing to misinformation here. These are not quantitative tests. We're either detecting antibodies or we're not. We're not calculating how many antibodies we're able to see, but it is interesting. The body is just pretty amazing in terms of how it responds, so you might not have detectable levels of antibodies, but because of your B cells and T cells, they might immediately engage and react when they meet the virus. You might also have detectable antibodies and still have those breakthrough cases, so this is in no way a perfect test to say whether or not you would get infected.

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We're also looking at symptoms, which has been really interesting. Thirty-five percent of folks that zero converted, meaning they didn't have antibodies, and then they did, either from natural infection or from the vaccine, reported symptoms in that month prior to the blood test that they had returned. In a lot of those symptomatic cases, you're seeing about 65% were asymptomatic or didn't report anything in their daily symptom reporting. We can also look at different clusters of symptoms, so you see on the right, folks that are presenting with congestion and loss of taste and smell or headache. Those are associated with having a positive antibody test, and then you see combinations like diarrhea, shortness of breath, nausea that those are less frequently associated with having developed antibodies. The thicker the line, the stronger the association, and so this has been interesting for us to look to see what are the symptoms that you would expect to see for a COVID case.

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Lastly, we're looking at symptoms reported amongst folks that had seroconverted in the long term, and so again, it’s really important right now to think about long COVID and the type of symptoms that folks are reporting. Here, you see a really significant amount of time. Time zero is when we have that zero conversion, so for the week before that there are some heavier symptoms in the first couple weeks of infection, and then we see some of them continuing 30 to 40 weeks after having that infection. Then, this is a natural infection not just vaccine related.

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We're also able to deploy some supplemental surveys. In that daily symptom reporting, we're able to sneak in a few of these other surveys to get more information from folks that are participating. There are some interesting findings here. We released a survey around Thanksgiving and then another around the winter holidays. We had more than 20,000 respondents, and not surprisingly folks were gathering

with people outside of their household, some for Thanksgiving, even more around the holidays. Only 30 to 40 percent of those folks wore masks, and less than one fifth of them were tested prior to gathering. You can see those public health type behaviors in the top right. Then, lastly, we looked at vaccine attitudes. Of course, we're interested in things like vaccine hesitancy. In one recently published report, this includes just folks from the North Carolina cohort, more than 20,000, we did see vaccine hesitancy noted in specific subgroups, specifically African Americans, folks living in more suburban areas, women, and folks with prior infections. So again, we're thinking about some of the misinformation about protected immunity, and that having infection protects you for a long amount of time, which we've demonstrated it does, the main concern being about safety and a lack of testing in the vaccine. We did follow those people over time, and so by May, we had seen most of them had been vaccinated, including more than 50% who initially expressed resistance.

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So, ongoing and future activity. I'm focused right now on breakthrough infections of course and variants of concern, so following Delta and looking at some of that virology to see how that spread across the country, especially trying to inform the need for boosters. We'll continue the serology tests and be able to see some of that antibody decay. We're also looking at the EHR data, so like many other folks really interested in the long-term sequelae, and the total burden of the pandemic on the health care system. Right now, we are really focused on immunocompromised patients: what their experience has been, are they developing antibodies, and are they experiencing any vaccine hesitancy?

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Thank you. This is an army of people behind this work, and it's really led by the community and their participation, so thank you for your time. I'm happy to answer questions once all the speakers are done.