From boosters to vaccine hesitancy, a biostatistician weighs in on the data

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When new Emory University faculty member Natalie Dean posted a primer on Twitter last year to demystify vaccine efficacy, she earned herself a fanbase outside the scientific community. Biostatisticians like

Dean are challenged to untangle complex data and project what happens next with the coronavirus, and she and others are adopting social platforms to try and dispel myths more quickly and more widely.

We talk with Dean, who's assistant professor at the Rollins School of Public Health, about this week's news of boosters, breakthrough infections, vaccine hesitancy and her path to infectious diseases research.

Why are the bulk of vaccine boosters being authorized only for select populations?

The Food & Drug Administration (FDA) has authorized Pfizer and Moderna boosters for Americans 65 and older, some adults with underlying health conditions and people at higher risk of exposure because of their jobs. I am glad the population was narrowed to adults with the greatest risk because for now the data are not there to support boosters for all.

Boosters are likely to provide a short-term benefit although durability is an open question. A booster given months later may ultimately perform better than two doses given only a few weeks apart. The latter strategy worked well to get people rapid protection during a pandemic, but it may not be as durable.

The bigger question is how valuable boosters are for younger, healthier people. I imagine that eligibility will expand in the future. It is critical that the U.S. and other high-income countries are committed to expanding vaccine access around the world. Vaccine inequities are astounding and these will contribute to prolonged suffering as well as increase the possibility for new variants.

Any takeaways on the mix and match booster approach?

It makes sense for the FDA to recommend the mix and match approach, especially for Johnson & Johnson despite less available data to guide this decision. A challenge for monitoring the performance of the Johnson & Johnson vaccine has been less real-world data than the widely used mRNA vaccines (Pfizer and Moderna), but Johnson & Johnson recipients shouldn't be left in the lurch because fewer people received it. The science, within the U.S. and abroad, supports the value of mixing and matching. Maybe it will end up being the best of both worlds. It remains to be seen.

[NOTE: Emory University was involved in conducting NIH-funded clinical trials to assess the potential for mix and match booster shots of COVID-19 vaccines.]

Some experts now say we underestimated vaccine hesitancy in the U.S. What do you think?

The level of hesitancy and how surprising it was to so many is a stark reminder of how important social science research is. Social science is often neglected in favor of clinical or laboratory science, but the real world impact of an intervention reflects both its effectiveness AND how willing people are to embrace it. Studying hesitancy, inequities and misinformation is complex science, and biostatisticians can play a role by mapping the networks we live in. We clearly need more of this research but that is not always mirrored in funding priorities.

If there were one thing you could say to someone who's still hesitant about the COVID-19 vaccine, what

would it be?

The current Delta variant is highly transmissible so if you are not vaccinated, being exposed to this virus is really a matter of when, not if. So, when you do get exposed to the virus, you want your immune system to be armed and ready so that it can either prevent you from infection altogether or protect you from getting very sick or dying. I would also highlight the extraordinary amount of safety data available, with over two billion people vaccinated globally. I would also encourage them to talk through any lingering questions with their doctor.

What do you make of COVID-19 cases in vaccinated people?

COVID-19 cases in vaccinated people are inevitable. First, vaccine protection is not one hundred percent. Second, respiratory infections are hard to avert entirely. The vaccines provided high levels of protection initially against infection. This protection has waned with time and with the emergence of the highly transmissible Delta variant. That said, vaccinated individuals are still much less likely to be infected than unvaccinated individuals. But the more frequently we are exposed to the virus—for instance, when transmission is high in communities—the higher the chance of a breakthrough infection. The key then is to determine whether those with breakthrough infections become very ill, and whether they go on to infect others who remain vulnerable. We have the most data on the first question, and thankfully vaccines continue to offer very high protection against severe disease.

What role have you and your colleagues played in this pandemic? Tell us about some of the big opportunities and challenges you saw.

I am part of a community of quantitative infectious disease researchers who have really leaped into action during this pandemic. While the core work remains research, many of us are also assembling crowd-sourced datasets, forecasting disease trends and working with public health departments. Along with some of my colleagues, I have been deeply involved in public engagement, through traditional media and Twitter. There has been a great need for scientists to digest new information and clearly communicate insights to reporters and to the public. I also served on the advisory board of The Atlantic's COVID Tracking Project. It has been an opportunity for biostatisticians like me to help steer an impactful conversation.

Tell us why you have adopted Twitter as a platform to disseminate information about COVID-19.

I am trying to help cut through the clutter as a sizeable chunk of the research in the news these days is not peer reviewed. I think it's important that we have experts who can look at these studies and discuss the strengths and limitations of the research approach and findings. Social media has also been helpful during the pandemic to break down discipline silos because of the urgency and speed that everyone is working at; for instance, biostatisticians like me are interacting more closely with clinicians and policy makers. Some of these questions are so big that it requires a multi-disciplinary response. Twitter has proven to be great at organically offering up a space to engage with people from different specialties.

Do you see signs of this pandemic abating?

I feel apprehensive as we move into the winter months about whether we will see another wave. Recent modeling predicts that the worst is behind us, but this virus has thrown us many curveballs. There are certainly

pockets of the country that could experience a surge. I am reassured by the high level of protection the vaccines afford against severe disease, and the knowledge that eventually this pandemic will end.

Regaining greater control will require an arsenal of tools—bringing vaccines to people, making testing affordable and accessible, masking where transmission is high and treating outpatients very early to prevent severe disease. Every country is navigating the same set of challenges, and so learning from other nations can be valuable. When you read about how cheap and widespread tests are in Europe, you can see the missed potential.

How could this pandemic help us more effectively respond to a future outbreak?

One of the great success stories of the pandemic has been very large randomized controlled trials, both for COVID-19 vaccines and treatments. The RECOVERY trial in the U.K. is a good example. It is extraordinary to see how much evidence a single unified trial platform can produce when it gets rolling, both for finding treatments that work well—the cheap steroid dexamethasone is an example of an unexpected winner—and definitively ruling out therapies that don't work. For vaccines, Operation Warp Speed in the U.S. oversaw multiple trials with shared oversight. I think it really challenges the traditional ways we do clinical research. Lessons learned on how to support common protocols and standardized decision-making will go a long way, whether it's for a global pandemic or for a regional threat like Lassa fever or Marburg virus disease.

Tell us about some of the research work that you are currently engaged in, and if you have been surprised with what you are finding.

I have worked with colleagues in several different research areas on COVID-19, including mathematical modeling and analyzing household studies. A special focus of ours is on the design of randomized vaccine trials and observational vaccine studies. This extends from previous work we have done on Ebola and Zika. Right now, my colleagues and I are thinking most about all the challenges and opportunities in real-world vaccine studies, trying to estimate vaccine waning and effectiveness against different variants. There are so many biases that creep into observational studies. Policymakers are using these analyses to guide real-time decisions, so it is critical to understand their limitations.

Provided by Emory University