Wabash.

September 8, 2021

To: The Wabash Community

From: President Scott Feller

Re: Managing Risk with Data

In an earlier message, I mentioned that I will be providing educational resources on COVID-19 to the community at various points during the semester. My motivation is two-fold. First, I feel that we have entered a phase of the pandemic characterized by frequent gray areas that all of us are well served to understand. Second, I want to continue to provide transparency in decision making.

I want to begin with risk, and how we as individuals and as an institution assess it, mitigate it, and ultimately move forward by weighing it against benefits and opportunities. I know that talking about risk is uncomfortable, especially when we are talking about risks to the health of ourselves, colleagues, and loved ones. But each of us is making frequent risk assessments as we navigate our daily lives during the pandemic, even if we don't think of it explicitly in those terms. And I know that a day has not passed since March of 2020 when I have not thought about assessing and managing the risk to the Wabash College community.

For over a year, a key element in my assessment of risk has been the level of virus transmission on our campus and in the local community. We shared that data weekly all of last year and in dashboard form throughout the spring semester. (An enhanced dashboard with vaccination data will be rolled out following census.) Transmission in Indiana is at a high level and continuing to rise. And the situation in Montgomery County is even worse, with case numbers and test positivity rates moving us into the Red level. To give some perspective, the CDC recommends indoor masking for counties with substantial or high transmission, defined as greater than 50 cases per-week per 100,000 population. Montgomery County currently exceeds 600!

While there are ways that our situation is distinct from Crawfordsville and Montgomery County, especially being a universally vaccinated campus, the local community is a risk we must monitor, mitigate, and live with. We can all consider ways to avoid crowded indoor spaces in town and we can all wear a mask in public spaces off campus. Many faculty and staff have family members ineligible for vaccination, and transmission in the home is especially difficult to reduce. While a vaccinated employee bringing COVID to campus is a possibility, it is a certainty that we will continue to have staff and faculty unable to come to campus while caring for ill family members.

All of us have been dealing with exposure risk for a while and we can assess it fairly well by monitoring case numbers. But over the past six weeks or so, our attention has turned to a second question: Is the vaccine effective in protecting me if I am exposed? This is an important question in any risk assessment at Wabash right now, and unfortunately the news reports – and to a lesser extent the science – have provided conflicting information on the issue of breakthrough infections.

Much of the confusion arises from differing definitions of vaccine effectiveness (VE), i.e., differences in **what** is being measured. And the situation then gets much worse because of significant differences in **how** VE is being measured. Regarding the latter, it may be helpful to think about the difference between the vaccine clinical trials – where the vaccinated and unvaccinated groups were randomly chosen in a double-blind procedure – and the observational studies we must now rely on to compare outcomes among the two groups. The former gave us an apples-to-apples comparison of a population that differed only in the contents of an injection they received; the latter is often a comparison of two populations that have come to differ in every demographic variable imaginable.

Regarding what is measured, we are commonly reading reports of at least four different measures of vaccine effectiveness. The first is effectiveness against disease, i.e., how much does vaccination reduce the probability of developing symptoms of COVID-19. This is the quantity assessed in the clinical trials for vaccine approval in which the products from Moderna and Pfizer achieved 94-95% effectiveness (lower for Johnson and Johnson).

Because many cases of COVID-19 are asymptomatic, effectiveness against ***disease*** is not the same as effectiveness against ***infection***. While VE against infection was not measured directly in the clinical trials, it was subsequently examined in studies where vaccinated and unvaccinated cohorts underwent surveillance testing over several months so that rates of total infections (symptomatic and asymptomatic) could be determined, leading to an estimate of VE against infection of 90%.

Finally, effectiveness against hospitalization and death is of significant importance. The number of hospitalizations and deaths in clinical trials was too low to make precise determinations, but real-world comparisons of vaccinated and unvaccinated populations soon after approval suggested that vaccine effectiveness against hospitalization was 94%. Estimates of effectiveness against death are even higher, often approaching 99%.

These initial estimates of effectiveness were amazing, promising dramatic reductions in risk, nearly eliminating the risk of dying, and lowering the chance of even an asymptomatic infection tenfold. Furthermore, universal vaccination promised the additional benefit of reducing transmission by having fewer cases, i.e., your risk of exposure was reduced **and** your risk of acquiring the disease upon exposure was reduced. This is the reason that Wabash has a vaccination requirement for students, staff, and faculty.

While breakthrough infections were always understood to be present by health professionals – there is no argument that 90% is equal to 100% – rising overall case numbers in July raised the visibility of breakthrough cases. And at the same time, concerns were raised about reduced vaccine effectiveness from virus mutations like the Delta variant or waning immunity, or a combination of the two. This perfect storm led to concern among public health officials, extensive media coverage, and for many vaccinated individuals it led to a reassessment of their risk of disease.

Unfortunately, measuring VE in real time is no easy feat and several reports from July and early August likely overestimated any reduction in effectiveness. This had the effect of reducing confidence in the vaccines and in the science behind estimating VE. As an example, there were reports on VE against infection by Delta that ranged from 39-88% in the span of two weeks. We now know that some of this uncertainty arose by comparing infection and hospitalization rates among the vaccinated and unvaccinated populations in ways that did not account for demographic differences, primarily age.

If you are interested in the math behind this, I recommend this article evaluating the excellent Israeli data set on vaccine effectiveness against severe disease. The data shows that ignoring age differences leads to a VE estimate of 67%, while comparing age-based cohorts leads to VE in the range 85-92%. Breaking the cases down further into age decades shows that all groups under age 60 had a VE greater than 93%. This is an example of a phenomenon well known to statisticians called "Simpson's Paradox," though I readily admit it is the most dramatic example of the effect that I have ever seen.

Thankfully, an army of biostatisticians and epidemiologists made rapid progress, and by August we began to see more refined analyses of infection, hospitalization, and death data. You may have noticed that very recent reports from the CDC use terms such as "age-adjusted hospitalization rates." These tend to be significantly more positive assessments of VE against Delta, and are more consistent with earlier studies. But a recent survey suggests the ***perceived risk*** among vaccinated individuals has grown substantially, to the point that they are now twice as likely to be worried about becoming ill as the unvaccinated are.

The consensus view seems to be trending toward very strong vaccine effectiveness against severe infection – with notable exceptions among the elderly and certain immunocompromised individuals – and modest decline but still very good protection against mild infection. A large-scale, age-adjusted study of monthly data in New York state suggested that VE against infection has declined from ~90% to ~80% as Delta came to dominate infections. Those authors pointed out that it has become difficult to precisely estimate VE against infection because at this point the "control group" of unvaccinated individuals has many members with some level of immunity against the disease because they were previously infected. This confounding variable could well be artificially lowering the calculated effectiveness.

To summarize, the two big drivers of transmission risk at Wabash are the probability we are exposed to an infectious individual and the probability of vaccine failure in a situation where we are exposed. My view is that we should be worrying much more about the former than the latter at this time. In terms of off-campus interactions, we know that the probability of virus exposure is dramatically higher than it was a few months ago and it is clear that we should adapt our behaviors to reflect that. The diverging trajectories of the pandemic in high-vaccination and low-vaccination communities give hope that our on-campus situation will be different from Crawfordsville, but there is significant uncertainty around the transmission dynamics of a community within a community.

I have previously emphasized how much we learned last year, but unfortunately that past provides little guidance on what it means to be a universally vaccinated college within a broader world during a pandemic. I thank everyone for their diligence and patience as we continue to evaluate this evolving position.

Addendum: While I was in the process of writing this note, *New York Times* writer David Leonhardt published a column I recommend, which covers similar points and expands on the concept of personal risk. And if you have time, I also recommend a recent video interview with UCSF physician/scientist Dr. Monica Gandhi that goes into more of the science of breakthrough cases in an engaging conversation.