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COVID-19 Challenges

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An Adaptive Response to COVID-19

John Nosta is the founder of NostaLab, a digital health think tank. He is regarded as one of the top global strategic and creative thinkers in digital health. He's also a member of the Google Health Advisory Board and a technology expert for the WHO. John is a contrarian with a sharp focus on the future, and it is this quality that makes him a defining force in dissecting and deliberating global events and trends. He has built his career on the science of innovation. ICU Management & Practice spoke to John Nosta on how the healthcare system has handled the COVID-19 crisis and the role data modelling, technology, and collective effort has played and will continue to play in combating this pandemic.

You've talked extensively about the need to develop an adaptive response to manage this crisis. What do you mean by this?

Developing an adaptive response has become even more important as time goes on, and we recognise a few central facts. Originally, I looked at the adaptive response as being a function of social distancing and risk evaluation to establish more personal, social, and economic freedom. Today, I think that we need to look at our response in an adaptive way. This applies to some of the modelling that's been done, as well as our clinical perspective in terms of patient management, and therapeutic modalities. We have to be adaptive as new knowledge comes to bear. Modelling is difficult; when we look at statistical models of large systems, we see it's made on many assumptions. Sometimes those assumptions are slightly off target, sometimes they are exactly right, and sometimes they are completely off the mark. This can push our modelling in ways that can cause significant changes in the projections. For example, if we look at the numbers out of New York state, where the initial projections are significantly higher than the current clinical need, this is a red flag. When we talk about social concern, psychological concern, stress, social isolation, and other important issues, we need to understand that the models have social and intellectual consequences. Therefore, when I talk about an adaptive response, I'm saying we need to be smart, but we might also need to be agile. We may need to look at modelling and medicines and be able to adapt as things come in through a clearer lens.

With respect to clinical information, we're seeing that COVID-19 may not be like a traditional nosocomial or a community-acquired pneumonia; it may be a systemic scenario that might be more akin to something like altitude sickness. The condition may reflect changes in damage to haemoglobin and oxygen transport. One of the manifestations of this is that the nature of the respirator settings, the force with which air is pushed into the lungs or settings, such as positive end-expiratory pressure (PEEP), may have to be modulated to accommodate some of the tissue damages in the lungs. Hence, for me, the key word is not only 'adaptive' but also 'agility' - the ability to be agile and modify in a circumstance that is evolving as we speak.

What about your two-pronged strategy? We all hear recommendations on flattening the curve, but is there another approach?

We all know the expression "flatten the curve" and flattening the curve is important. It talks about, in essence, what social distancing and social isolation can do to decrease the transmission of the disease.

But in certain instances, that really doesn't change the total number of people infected. In fact, what it does, it flattens the curve and the area under the flattened curve is similar to the area under the higher peak curve. It looks at the amount of patients getting sick relative to the capacity of our healthcare system. That's an important dynamic. But the other side of that equation (and this is where the wonderful global ingenuity of the life science industry is coming into play), is not only social isolation, but treating the curve and being able to use clinical practices such as having patients prone and face down to increase oxygenation when they're in the intensive care unit to drugs that treat the immune response. That could be Interleukin 6 (IL-6) or natural killer cells that can help destroy the virus in our bodies, and also the utility of hydroxychloroquine, as well as azithromycin and remdesivir. While there's a lot of controversy about that, the anecdotal evidence is very interesting. In those instances, p stands for patient, and what we need is p to stand for p less than .05. One of the greatest tools we have to combat COVID-19 is the ingenuity of the life science industry to treat the disease and to treat the curve. Among the therapeutic modalities that are entering the clinic today, probably the most important one is the use of vaccines.

When I talk about a two-pronged approach, there's a flattening of the growth from social isolation in some of the traditional modalities but, treating the curve, whether it be with hydroxychloroquine, IL-6, convalescent serum or with other treatments, is the essence of the two-pronged strategy. I would argue that therapeutic modalities may become the most important tool we have in our clinical armamentarium. Testing - for the virus and immunological status - is also critical.

I would also argue that the matter of hydroxychloroquine has become a political as well as a clinical discussion. I think in the U.S., it's distressing that we are arguing a therapeutic choice on the basis of a presidential election. Hydroxychloroquine can be a dangerous drug, as it certainly has an association with QT prolongation. But the drug has been around for fifty years, and it's being used extensively in patients with Lupus and Rheumatoid Arthritis. Where is the QT prolongation with this patient population, and why isn't it a tremendous public health issue that people are dying from ventricular arrhythmia when using hydroxychloroquine? I think that the data will speak loudly. There are many, many hundreds, if not thousands, of patients in a variety of double-blind controlled clinical trials so that information will be out soon. Further, because this is a short course of treatment, we may be able to see a clinical benefit sooner than later. I am hopeful that again, the p-value will switch from p equals patient to p is less than 0.05.

How close do you think we are to developing a vaccine against COVID-19?

The genome was determined almost instantly, and we have the methodology in place to create vaccines. But that's the short side of the equation. The longer side of the equation is dosage, safety evaluation, and clinical efficacy, and moving into phase-three trials. This could take a year. It's being explored extensively by pharma and being funded by governments and the Bill Gates Foundation which is donating a lot of money to drive this idea forward. Probably the solution with regard to vaccines may not be for this pandemic; it may be a modality for the recurrence of this virus at another time.

What we've seen in European countries like Italy and Spain and what we see in the U.S. is that most global healthcare systems were not prepared. Why do you think this has been the case?

This is a very complicated question because it touches on everything from clinical preparedness, to financial capabilities and even human nature. Number one: I think people are optimistic, and they tend to look the other way. I also think that the economic constraints put upon countries have also let us reprioritise preparation for more current or urgent needs. The question is, how do you pick the issue that you need to be prepared for? Pandemics are reasonably high on the list. But there can be many others. How do we pick the appropriate emergency to begin to build readiness? As a first responder, we've always done drills, we've always tried to be ready. Prioritising is a difficult job, but I think our first job is to prioritise what represents an urgent risk. This involves a little bit of science and a little bit of guessing.

The interesting thing is when you look at dollars spent, and we look at the EU in particular, Italy had one of the highest healthcare spends per capita than any of the other countries in the EU. It wasn't an impoverished country. It was a country that had a reasonably robust and qualified healthcare system. So even some of the best systems can be overwhelmed in certain instances. Was it multi-generational living that caused things to get out of control in the northern region of Italy? Is it the economic relationship that Italy had with China in terms of manufacturing, particularly associated with the Wuhan district, and tremendous travelling back and forth? Or was it some other unknown factor?

If you look at the U.S., using one data set is sub-optimal. The U.S. has many regions. We're looking at New York, California, Washington, and New Orleans as well as some of the Midwest states that are not as populated and have a much lower occurrence of the condition. We also see a younger population in Spain, a similar hotspot. This is an epidemiologist's dream. We are generating so much data, and it is going to be extraordinary. I predict that we'll find some surprises. We may find that certain drugs worked or didn't work; we may find that some elements of social distancing were more effective than others, or wearing masks was extraordinarily effective or completely inappropriate.

What do you think is the most important lesson that we should learn from COVID-19?

That is a tough question because we're seeing things change on a daily basis, and we're seeing the models themselves change by tens of thousands of people. We're seeing curves shift, and we're seeing a peak or flattening in a variety of countries. I think the lesson learned is to be open-minded, follow the data, and recognise that in today's data-based, analytical driven AI world, we have a tremendous opportunity to advance human civilisation in new, important, and exciting ways.

Do you think that virtual reality could have any role in combating such a pandemic?

We are seeing the empowerment of technology from areas as functional and practical as telemedicine to eLearning in schools. I believe that a new human connectivity will emerge, and whether it will be traditional chat-based, or something richer, virtual reality, is certainly going to play a role. I think that virtual reality is probably at the wrong spot in the continuum for today. Six months ago, virtual reality was relevant. It drove a sense of empathy. It allowed a caregiver to understand what macular degeneration looked like for another person. It allowed someone with a movement disorder to walk in a patient's shoes. I think that today, we're taking a step back and looking at some of the functional realities of video conferencing and telemedicine, but the expanded world of virtual reality might have actually been a bit compromised at this stage of the game.

Could there be a second wave of COVID19?

Yes. It is important to question whether the virus is going to be eradicated. Will the virus develop a seasonal nature? What is the nature of the mutation or mutations? It was originally assumed to be a slow mutating virus that bodes well for vaccines, but if there is a second peak, the question is, how high will that peak be? Is it regional? Are there local hotspots? Is it a pandemic? We may get a hotspot in Italy or New Orleans, or we may find local areas where the virus emerges. But I don't think it's fair to apply the vast global response to that wave. I think that again, we have to be adaptive and agile. The recurrence of this virus may occur on a regional and local level but we might be better prepared to manage it and to implement social distancing quickly in ways that are highly effective. Maybe we'll have drugs that we can use and other treatments. I think that any second wave would have to be looked at in the context of the first, but also how, where, when, and why it's happening.

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We've seen different countries using different approaches to containing COVID-19. Do you think that the strategies are sufficient or effective? Do you have any examples that could have been more successful?

Let me ask that question rhetorically. Are the strategies we're using to treat cancer effective? Are the strategies and tactics we're using today to treat high blood pressure appropriate and effective, recognising that most patients don't stay on drugs or aren't even diagnosed? I think that, in the context of human nature and clinical medicine as it exists today, it is difficult to say that what different countries are doing is enough or is appropriate. The answer would be no, they're not. The question is, where does it fit on the continuum that will often find countries doing a variety of strategies and tactics? Some might be experimental; some might be optional. There may be a cultural dynamic; others might be absolutely fundamental. The use of quality care insights around respiratory care when these patients are severely ill and hospitalised in the intensive care unit and the use of certain drugs or therapeutic modalities certainly can be a checklist. But unfortunately, in today's world, I think that there are a lot of question marks in boxes versus hard and fast checklists.

We can talk about countries like New Zealand and South Korea squashing the curve, but what drugs have come out of these countries and what is the contribution to global health provided by them? From my perspective, these are almost cultural issues. When you look at the South Korean population, it's easier to align them with a social goal. It's the nature of their society. Now, when we look at other countries where they have a greater spirit of independence or entrepreneurship, you may have a harder time getting people to adopt social distancing at the snap of a finger. If you look at the curves in New York City, it has been doing surprisingly well in relation to the predictions. Look at Sweden and the emergence of the idea of herd immunity, and how it may or may not be working. Clearly, Sweden took a more contrarian approach - and that in itself is very interesting. It's easy to point to success stories when the underlying factors are complex. Successful models make many assumptions. That being said, I tip my hat to South Korea, It has taught us some very important things that if we can act collectively, we could get on top of the COVID-19 spread.

For how long do you think it's practical and feasible to implement social distancing?

This goes back to your first question, which I think is really at the heart of what we're

doing now. The notion of an adaptive response, as was originally articulated, was the notion of reopening life, of reestablishing some level of social and economic connectivity. If there was a recurrence of the disease, we would have to go back to more controls and more constraints. It's a balancing act between suppressing the disease and returning to normal societal activity. Society is a complex structure and to look at the clinical implications, without looking at social, economic, financial implications, will not do the problem justice. Prioritising health, safety and wellness is extraordinarily important, but we have to prioritise it in the context of running the country, of our businesses, and of our livelihood.

How long can it go on? That's a really interesting question. What I'm seeing is in terms of the curves, flattening of peaks, of decreased deaths, decrease in admissions into the ICU, decrease in hospitalisations makes me optimistic. I put my hope in what society is doing and what our brave and bold healthcare providers are doing, and what the life science industry is doing in terms of therapeutic treatment choices.

If the pandemic continues, how should healthcare decide who gets what resources if there is a shortage?

We have a lot of what-if questions to be answered. We could wonder if you have a shortage of respirators, say where you have 100 patients in a hospital, and you only have 50 respirators, what happens? Well, first, as a mechanical engineer, we know that we can split respirators, and there are options where we can use respirators in other interesting, effective ways. I see extraordinarily interesting opportunities for Tesla, for Dyson, to build respirators. Yet we cling to the notion of catastrophe as a defining element. When we plot the curve, we have to make assumptions that are aligned with the data. Some people plot the curve, and then they fill in the data, because they have pre-existing notions about where it's going. But what we're finding is, after we draw the curve and we plot the data, we're seeing significantly different scenarios. I think that the potential issues of not having enough medicines, or enough respirators are going to be handled on local levels. Number one: I think that problem is not as big as it has been suggested. Number two: I believe in the technological ingenuity of many people to repurpose respirators in a two-to-one modality or someone squeezing an ambu bag for a few hours until we can get the technology in place. Again, I tend to be optimistic and am driven by the data rather than emotion. It's important to recognise that all these ideas need some strategic focus. We need to channel our intellectual capacity to key areas of need and future need.

Let's look at both perspectives. If we look at the negative perspective, we could potentially have hundreds of thousands of people in the intensive care unit with 20,000 respirators. From a U.S.-centric perspective, I have seen an extraordinary amount of effort going into moving respirators, using stockpile, driving corporations to make new devices, whether it be Tesla or the auto industry or Dyson. I think this is a human miracle that is rising to the occasion. We live in a unique time in human history. Never before have we had the opportunity to have scientific, technological, and manufacturing opportunities to rise to the occasion. If you go back to the Spanish Flu (1917 to 1918) and look at the data from that time, you will see some very different modalities. It's a very different time, whether it be the ability to communicate through the internet or the ability to sequence a genome to test drugs and develop technology like respirators.

Are we doing enough to protect brave healthcare workers?

Healthcare workers are heroes. The Person of the Year in Time magazine should be the healthcare worker. The Nobel Prize should be the healthcare worker. They walk into danger every day when they go to work and then they go home and bring that danger with them. When a soldier comes home, he or she is embraced with a hug. But when a healthcare worker comes home, they very well may be bringing the danger into their own house. For me, they are at the forefront of this physical and psychological war.

Are we doing enough? I think that we are struggling to understand this in the context of a new global pandemic. Healthcare workers are overwhelmed, the system is overwhelmed, medicine is overwhelmed, and society is overwhelmed. I think that we have to push forward with an adaptive response. If we can decrease viral shedding, if we could decrease the likelihood of hospitalisation or the need for intensive care or the need for respirators, then we can shift the burden off the healthcare system. That comes right back to the idea of flattening the curve, the ability to lower the clinical need to match the capacity of the healthcare system. This may be the most important way that we can help our healthcare workers. I believe that they can manage an appropriate caseload. It's when the caseload supersedes capacity that errors occur. I'm overwhelmed personally by the sacrifice that these people are making for the system.

Is there anything else you would like to say?

What bothers me is that these issues have become political. I believe that there are some people who wish that the system could be reset to accommodate their political and social perspectives. I think that there is a sense of social responsibility and that we have to be fair. Sometimes I'm criticised by trying to look at issues more broadly but my voice is one of my perspectives, and it's by far from definitive. Some voices have positioned themselves behind a set perspective and they can't see outside of that box. We need to change that. ■