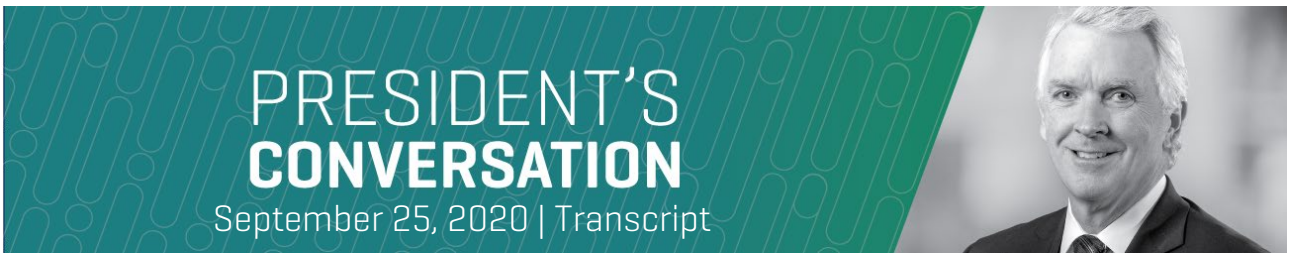

Tamsyn Theo [00:00:29]
Welcome to the president's conversation. Our presenters will be joining us shortly. Before we start, we have a few tips for using this video conferencing platform. You will have the opportunity to look in the second half of the event. Please use the Q&A tab on the upper right-hand side of your screen to add your questions. We'll answer as many as we can. If your internet bandwidth is not strong enough to stream the video, you can use low bandwidth mode. Note that you will still hear the audio, but you won't have video. To turn on closed captioning, click the settings button in the lower right corner of the web browser screen and toggle the closed caption slider. If you're having technical difficulties, our support staff can help troubleshoot. Please email events@fredhutch.org. Or call 2-0-6-6-6-7-1-1-1-9.

Dr. Tom Lynch [00:01:28]
Good afternoon and welcome to our Presence Circle discussion on how COVID-19 is impacting research and an update on where we stand at the Fred Hutch with COVID-19. My name is Tom Lynch. I'm the President Director of the Fred Hutch. And it's really terrific to have so many of you with us this afternoon. I'd like to start by sharing Fred Hutch as land, labor and justice acknowledgment. This is a statement that we've been using before all of our town halls and a way of grounding our discussion for the community that's present with us. And we found it's something that has resonated with a lot of the people who work at the Fred Hutch. And we know that our supporters and partners, as well as our patients, who benefit our reach research, understand why this work is important. So I'd like to start by reading our land and justice acknowledgment. We acknowledge that we work and live in the traditional lands of Duwamish, Tulalip Muckleshoot and Suquamish tribal nations. We thank the original caretakers of this land, who are still here. We support the ongoing struggle for justice against racist, sexist, xenophobic abelists, trans-antagonistic, and all oppressive violence. We recognize, with gratitude, those who sacrifice, struggle and labor make our freedoms possible and challenges us to learn, work and live justly.

So, again, thank you so much for being with us this afternoon. So what we're going to talk about today, is how the pandemic is changing biomedical research. And I think, this is something that is true, whether you're working in COVID or whether you're working in cancer. And as you know, while we probably have about 15 to 20 percent of our effort working on COVID at the Fred Hutch, we still remain a facility that is dedicated to searching for cures for cancer as well. Something that is very, very important. And I think as people, who support the Fred Hutch, I want you to know that we are still working day and night on cures for cancer. But we've also found is that because working on cures for cancer means understanding viruses better, that we were well positioned to work on COVID as well. And I think that's going to be important to our patients as well as to the people, who support the Fred Hutch. Today, we'll be talking with three Hutch researchers about how the pandemic is affecting the substance and process of their science. There are many facets to discuss from how open science is accelerating research. You know, one of the things that I think will be interesting to hear more from our participants is the fact that so much of science now is reported on Twitter, or reported in pre-review servers where people can read the science before

it's been reviewed. Well, that has great advantages, because it brings science to life quicker. On the other hand, it's got the problem, the fact that it hasn't reviewed and hasn't been looked at for quality and anyone can post something to a preprocess server. So, again, all kinds of interesting questions that we'll be talking about. Also, the public appetite for reliable size news has skyrocketed and you are likely consuming more science information as someone in the community than you ever have before. So I want to thank you for putting us at the Hutch on your trusted list of people for science information. And I really hope that what we're able to do today is increase your awareness and your understanding of COVID-19 and the impact it's having on science.

So, one key thing about the Fred Hutch, the Fred Hutch was founded in 1975 by Dr. Bill Hutchison as a living legacy for his brother, Fred, who was a baseball hero, who died of cancer. And again, people know us, because of our contributions to cancer research, including stem cell and immunotherapy. And we work very closely with this interface between what's happening in the laboratory, what's happening in patients. And folks just this week, we've opened up the Steam Plant. And I can't tell you how happy I was to be able to look out the window right behind me and see the moving vans come to our building and take laboratory equipment to the laboratories that are moving from here to the Steam Plant. And all the equipment's gone. It's at the Steam Plant and researchers are doing science in the Steam Plant again to advance our understanding of cancer and to develop new and new based treatments for being able to treat cancer, which is really incredible. None of this would happen without the supporters who are on this call today. And your generosity to the Hutch has been absolutely extraordinary. Thank you for it. I also point out that in this time of economic challenge, not only for the Hutch, but for all of us, your generosity and support to the ability that you're able to makes an enormous difference to us. And we really depend upon it as we move forward. We deeply appreciate the members of our giving clubs, current and former trustees, and board of ambassador members, who are present with us today. And as we've been having conversations like this for the past several months and will continue these through the end of the year. I hope you come back for more. They won't always be on COVID. Sometimes they'll be on on cancer itself. So I'd like to remind you that this event is being recorded. So if you have to step away, and want to come back and hear some of it later, you'll get a link tomorrow that will tell you how to access the information.

So I'd like to begin by introducing Dr. Jesse Bloom. Jesse, welcome. Jesse has a background in chemistry, biology and computer science. He is a creative thinker who is helping us understand how viruses evolved to escape detection and and survive. Much of his work has focused on influenza, but the last several months, his team has done incredible work on the coronavirus, developing tools that help us predict how the virus might change to evade the antibodies our immune system produces to fight them. Jesse is an Associate Professor in the Basic Sciences Division at the Fred Hutch is an Assistant Professor in the Public Health Sciences Division and also a Howard Hughes Medical Institute investigators. Jesse, welcome. It's really terrific to have you today. I guess first question is you spent years building tools to understand influenza. How long how long did it take you to decide that maybe you should be working in COVID? And are the tools that you had to understand influenza, how are they helping you in being able to look at COVID?

Dr. Jesse Bloom [00:08:17]
Yeah, so like a lot of people, who follow viruses sort of in late January and early February, we were paying a lot of attention to SARS coronavirus2. And I actually have to credit a couple of the students in my lab, particularly Kate Crawford and Adam Vengeance, who sort of like pushing me, we should start working on this new virus. So we've spent a lot of time, as you mentioned, developing tools to study influenza virus. So one of the interesting things is when SARS

coronavirus2 emerged, initially almost nothing was known. So some of the first things that we did are really what you would consider sort of rudimentary advances if you were in the influenza field. But they were important first steps for SARS coronavirus2. So we set up good assays to look to see how serum, so the liquid can on it people's blood, is able to neutralize the virus. This is a measure of immunity. And then we also set up tools to look at how mutations, the key parts of the viral proteins, impacted both the function of these viral proteins and their ability to be recognized by antibodies. And I think this is sort of led to three significant beneficial things. One is by understanding the effects of mutations, this key part of the virus, the spike protein, which is being means, we've generated data on just how you can make the spike protein more stable and express that, which is really important because people are producing spike protein for vaccines. And we're now working with collaborators, who are engineering some of these mutations we characterized into vaccine candidates. Second, we've been able to look to see what are the viral mutations that could escape from antibodies. And so this is important because right now a number of companies, including, for instance Regeneron and AstraZeneca, Eli Lilly, are all developing monoclonal antibody treatments against the virus. And by knowing, which mutations in the virus could escape those antibodies, we can sort of monitor any of these antibodies that might be becoming affective and these approaches should also be useful for evaluating vaccine responses. And then the third thing that I think we're able to do is in collaboration with Keith Jerome, who's at the Hutch and UW lab medicine. We're really able to do some of the first studies looking at how neutralizing antibodies might actually protect humans against infection.

Dr. Tom Lynch [00:10:29]
And so, Jesse, so obviously there is a lot of discussion in the news, again, we're talking about how we're all reading much more about science than we ever did in the past in the popular press about the approval of convalescent serum as a therapeutic tool. What's your take on the status of convalescent serum? And then also want to get you think get your thoughts on monoclonal antibodies that are being developed? Because I know we developed some here at the Hutch in Regeneron, has some as well. And maybe you could for people define what those are, because we know with this kind of audience, we have an incredible mixture. We have some people on this call or executives of biotech companies, who understand this better than you and I might. And then there's other people on the call, who are poets and writers and artists and might not have that same levels. So try to walk that fine line so everyone can understand.

Dr. Jesse Bloom [00:11:24]
Yeah. So. So convalescent sera transfer is really a very old technique in medicine. And the basic idea is once someone's infected with the virus, they make an immune response to the virus, which includes making a lot of antibodies, which can help control viral infection. And so the notion is that you can take serum from someone, who has been infected by the virus and is willing to donate their blood and then infuse that, sera into some other person, who's just gotten sick. And those antibodies and then help protect the person, who just got infected because it's sort of like giving them a head start on their immune response. So there's a lot of work being done that that's exploring this. I think one of the challenges and convalescent sera transfer, I think it's a promising approach, but you're basically collecting blood and then isolating the sera from lots of different people. And there's a lot of issues in terms of quality controlling and standardizing that process. The monoclonal antibody approaches are sort of a I would call a next generation way of doing the same thing, where you basically identify a really nice antibody, really potent antibody that was made by someone, who was infected. And then you just produced that antibody as sort of a defined biological agent. And then you inject that instead. And I think most people believe that these monoclonal antibody treatments should, in principle, work better than the convalescent

sera transfer, because you can make the monoclonal antibodies extremely potent. You sort of are giving a defined product. I think the limitation with both of these approaches is simply, and this is a general limitation with drugs to acute viruses, like SARScoronavirus2 or also influenza, is that unfortunately people often don't become really sick and really feel sick and kill a lot of the viral replication that's already happened. So a big challenge with all of these approaches is that they're most effective if they're given early, but if people, you know, wait until they're sick before they get the treatment, which is quite common. Sometimes you're getting late in the window where they can be effective. So I think they're very promising approach, but that's probably gonna be a major element.

Dr. Tom Lynch [00:13:32]
And so, Jesse, we hear about this concept of neutralizing antibodies. Is that the same thing as saying that these are going to be effective in patients? And why couldn't the antibody be neutralizing and yet still not impact patients?

Dr. Jesse Bloom [00:13:48]
So a neutralizing antibody means an antibody that directly blocks viral infection of cells. And for most vaccines, neutralizing antibodies are the corlett of protection. That doesn't mean necessarily actually much protecting you, but certainly the vaccines that do protect you elicit neutralizing the antibodies. And there's a lot of reasons to think that an antibody can keep the virus from infecting cells should be able to keep you from getting that. I think the main reason why a neutralizing antibody might not be effective is A.) If there's not enough of it, if you just can't deliver it in large enough amounts. And then B.) Is this issue that we often think, for instance, when we're infected with influenzas are SARSCOVID2, we often imagine that, you know, the viral replication in our body is tracking how sick we feel, but in fact, the viral replication often precedes the symptoms to some degree. The neutralizing antibodies can help control the viral replication, but in some cases, there may have already been a lot of viral replication before you have enough symptoms for getting the treatment. I'm not saying that that's going to be a killer or for these. I think they'll still be quite useful. But I think that that's going to be the major limitation that they have to be given early. And they're going to be more effective given early than in critically ill patients.

Dr. Tom Lynch [00:15:03]
And then again, that's one of the reasons that we're looking at them in trials to see if it can prevent infection. So that's another question. Yes. Is this it's Preventive agents as well.

Dr. Jesse Bloom [00:15:12]
The preventive agents are probably extremely useful. I mean, the challenge there is obviously you have a much larger target population.

[00:15:20]
Absolutely. So, Jesse, thank you so much. We're going to be back with you in just a second. So next, I'd like to introduce Dr. Neel Dey. And Neel is a physician. He's an assistant professor in the clinical research division at the Fred Hutch. He's also assistant professor at the University of Washington Department of Medicine. He's a gastroenterologist at the Seattle Cancer Care Alliance and he's a physician scientist, who is exploring the vast frontier of the human microbiome. The trillions of, more than that, of bacteria fungi, and other microscopic organisms that live inside our bodies. And he's studying the interactions between the bugs inside our body, our genes, and our diet. How all of these things together impact the risk for colon cancer. And so this is a really important area of research here at the Hutch. We've got a big program in understanding the

microbiome and trying to understand how this creates environments for colon cancer is able to progress. So, Neel, you spent the first few months of the pandemic seeing patients in the clinic and the hospital as a gastroenterologist. And one question that I get a lot is what's it like to balance your clinical life with your science life? And how did you do that in the pandemic? And what was it like being in the hospital during those early weeks and months the pandemic?

Dr. Neel Dey [00:16:54]
First of all, thank you for having me join the conversation today and for your question. You know, during the pandemic, there are a lot of mechanics of going to the hospital that were a little bit different, of course. But, you know, being at the hospital, I have to say I was really inspired by my colleagues, both at Fred Hutch as well as at our partner hospitals. Everyone really came together, worked together, in just incredible ways to figure out how we can best serve our community. And I have to say, one of the main emotional responses for me was just feeling a heightened sense of being part of an incredible community here. It is specific to being a physician scientist. You know, there were there were of some differences, of course, in the way we conducted our clinical work and the way we oversaw our labs. But I would say that, you know, for me, my training was really instrumental to this moment. During training, and I think this applies to both clinical training and research training, you know, one learns technical skills. Sure. But more importantly, one really learns how not to panic, how to troubleshoot a protocol, interpret unexpected results, deal with an unexpected immersion situation, and work together to solve those problems. And, you know, in my my role as a gastroenterologist, the most striking experience that I have is often getting called a panic call about, you know, somebody, for example, having a bleeding ulcer or something like that. And one of the things I notice really early on in my training was, you know, since I would arrive at the ICU or the emergency room, I could sense sort of a collective kind of calm. You know, people would often hear people say, hey, guys here, you know, things like that. I realized that, you know, I learned that just showing up and being there has tremendous value. I learned to grow into that role. And, you know, in both the clinic and in the lab during this time, I anticipated that my trainees similarly would experience a number of stressors and that I'd probably need to be there in more ways than simply scientific mentorship or clinical mentorship. And so my role as a mentor, I think, has also grown during this time.

Dr. Tom Lynch [00:19:09]
That's a terrific and thanks for sharing that part of it. So a question that came in, which is interesting, is this concept of how you define the microbiome. So the microbiome. Obviously, bacteria fungi for a part of it, are viruses considered part of the microbiome?

Dr. Neel Dey [00:19:29]
They are, yes. All of the microbes and all of the genes that are encoded in their genomes are part of the microbiome. And so within that, we can start to distinguish those different components, as you have done. And it's sort of distilling out, teasing out the effects of those individual components are very challenging. But, you know, we have so many so much great infrastructure and tools here, as well as funding for a lot of these efforts, some of which are donor sponsored.

Dr. Neel Dey [00:20:02]
And so, Neel, you have recently initiated a pilot project on COVID-19 and the microbiome. I want to just point out to everyone that this project, the funding for this project came from the people on this call. They came from philanthropic donations to the Fred Hutch COVID-19 research fund. And without you, Neel would not be doing this research. So Neel, do you want to tell us a bit about the research, what the project is, what the question is you're looking to answer.

Dr. Neel Dey [00:20:31]
Yeah. Love to. And I'd also just want to echo your thanks to our donors for really enabling this COVID-19 research fund. My lab is not a virology lab. We're not really a COVID lab. But we had some tools in place to start to look at whether the microbiome might impact a particular molecule, which SARS-Coronavirus-2 binds, and potentially that potentially would have implications for infectious risk as well as severity of disease. So with those resources in place, we thought, well, you know, it'd be really interesting to start to actually conduct some pretty straightforward, fast fail type experiments. And this COVID-19 research fund really enabled us to do that. And we're actually in the process of wrapping up a manuscript summarizing those findings that we hope to submit next week.

Dr. Tom Lynch [00:21:33]
Excellent, excellent, we'll talk more about that as we have a chance to get more deeply into talking about what the lab is doing. And Neel, thank you so much. We're now going to bring on Dr. Ruth Etzioni. Ruth is a biostatistician here at the Fred Hutch who creates computational models that, among other things, help guide recommendations for cancer screening. She is a professor in the Public Health Sciences Division at the Fred Hutch, and she is now the holder of the Rosalie and Harold Rae Brown, endowed chair at the Fred Hutch. Since the pandemic started, she's been helping the public really understand the nuances and limitations of modeling. She's very much a data scientist who understands data, big data and understands how to use it. Now, I've got to start off by asking you, I think of you as prostate cancer person. OK, how did you get into it COVID-19? I thought you were all about prostate cancer and screening?

Dr. Ruth Etzioni [00:22:33]
Well, I still am, Tom. Cancer research doesn't stop even though we're in the midst of this tremendous and epic public health challenge. But as as you mentioned, I'm a modeler. My work is all about getting the numbers right when it comes to cancer early detection and control. And in fact, I have some thoughts about the convalescent plasma question that relates to the data that was used in getting that emergency use authorization. But to answer your question with modeling, we're always trying to think clearly and we're trying to take the critical policy, the critical decisions that are being made and translate them into a form that can be addressed with mathematics and data. So as an example, in prostate cancer, one question that we've really been trying to gather data to address is the question of how best to screen African-American men, who have such a high risk should they be screened more frequently? That's a policy question. Can we gather data and formulate mathematically a response that would help guide policy? And when it comes to COVID, the exact same phenomenon is happening. We have tremendously critical policy questions locally, globally in our state. And can we, can we use data and models and mathematics to address those questions? In the beginning of the pandemic, there really wasn't any data. It was all models, and the models and everybody wanted to know, with so much uncertainty. What's going to happen? How bad is it going to be here? How much should we be worried? But the models were not consistent. They were a couple of dozen models. Now there's even more. And they were all giving different answers. But since I'm used to working with models, I started reading about them. It's always in the fine print with models and then trying to translate that to policymakers. And I began working with the Washington State Department of Health that has a COVID modeling team that advises the governor and was able to work with them to use my skills. Translating policy to mathematics and data, thereby got getting the opportunity not necessarily to make my own model, but to help translate the existing models and to get a crack at some of the data that is now

being collected for Washington state to anticipate and to navigate coexistence with the virus as we go forward.

Dr. Tom Lynch [00:25:12]
One of the things that's very interesting and I think is hearing your story, all three of you are people, who are doing incredible research in important areas that have all been able to shift into COVID and really be able to help the COVID area. And I want to just tell a story to the group. A good friend of mine named Giuseppe Mascarini, who is an economic modeler at Yale. He contacted me about how he was looking at economic modeling. Again, there's nothing wrong with epidemiology or health, but this is the economic model that's very prominent in this field. And he asked me some very detailed questions, and I knew that he really wanted to get to Ruth, because when they started going back and forth over the models, they very quickly eclipsed my ability to even read the emails, let alone understand them a lot of advanced mathematical modeling. But it was interesting to see how someone, who is an economist to be talking to, someone who's an epidemiologist about when school should open and when we should go from level two to level three. Very interesting to see that. So I guess I'll ask you the next question, which is how do we decide how to make the next question? Meaning right now we are at level two as a state, when do we go as King County, when do we go to level three? You advised the governor and others about that, what kind of data do you use? How do you make those decisions?

Dr. Ruth Etzioni [00:26:29]
We're using the data that's gathered by Washington State on cases, hospitalizations and deaths in the state. And I'll just say that, you know, the data is not straightforward here. For example, you might think that it's straightforward to count the number of deaths from COVID. But anyone who's tried to fill out a death certificate realizes that it's actually not straightforward, that there are several causes. And often, even if the person dies from COVID, the first cause on the death certificate is not coronavirus. It's the actual cause of death. And so different states have different rules about how to whether a death is a COVID death or not. And then when it comes to cases, for example, we can't find a case if we don't test. So the number of cases is very dependent on the amount of testing that's going on. And so in Washington State, we track all these things over time and across the state.

Dr. Tom Lynch [00:27:33]
So, Ruth, I want to thank you and I want to bring back Jessie and Neel to come into the discussion and we'll have a Q&A with all three of you. So, Jessie and Neel could come back and join Ruth and I that would be terrific. And to remind everybody, we have a Q&A feature as part of blue jeans. And you can enter your questions. Some of them we can try to have answered directly to you and then others will address to the group. As we as we talk today. So, I guess the first question that came in, I think is actually pretty interesting. And I'll address this one to Jessie to start. Jessie, how permanent do think that these kind of changes in research will be. Is this something you think we're gonna be we're going to be working with for quite some time? Tell me what you think about, is this going to be temporary? You know, I heard some of the other day say that COVID-19 is like a severe traffic jam. When you're in a traffic jam is the absolute worst thing you could ever imagine. But once you're through the traffic, you forget about it. Once we're through the pandemic. Will we forget about it? Or will this forever change science?

Dr. Jesse Bloom [00:28:41]
Well, it's really hard to predict in the future. I mean, I can certainly say this is not a scientific answer, but sometimes I like to think about, you know, events or get togethers I used to do, and I

get a headache just imaging how many people in one room. I'm sure there'll be a little, while that we all get accustomed to it, again. As far as whether we'll have really effective vaccines against COVID-19, I'm cautiously optimistic that we will have eventually, you know, hopefully within the next year, have vaccines that reduce the burden of disease. There's very little chance that we'll have a vaccine like the measles vaccine, which can actually provide herd immunity and suppress spread of the virus. I mean, based on what we know about other chronic viruses, it would be unprecedented to get that level of immunity against a coronavirus. But I also think we could easily have vaccines that induce enough immunity, that people are getting infected less often. And when they do get infected, they don't get nearly as sick. So I think I'm cautiously optimistic that two years from now, influenza will again, be a worse problem than SARS-Coronavirus-2, but I think it's, it's hard to say. And I think the research future of SARS-Coronavirus-2 obviously depends a lot of it on the course of the pandemic.

Dr. Tom Lynch [00:29:55]
Exactly. And the next question to come in, is it again, a really good question, I'm going to ask this one to Ruth. And the question comes down to the fact that we live in a time where information and truth is just not what it used to be, meaning one really has to question pretty much everything. Certainly anything on social media has to be taken with a grain of salt. Anything on at least half to two thirds of our regular media has to be taken skeptically, unfortunately. Ruth, where do you look for information about the pandemic? And where do you get information that you think that the people on this call today can learn from? What are the sources that they can trust to be able to understand what we're dealing with, with SARS-CoV-2?

Dr. Ruth Etzioni [00:30:48]
Well, that's a great question. I was thinking, I wasn't sure where the question was going, and we've been talking how the science has been changing. One thing that I find myself always thinking about more than I ever did was how my results will land. How will they be potentially politicized? You know, when working with prostate cancer, I've had many interactions with the media, recommendations for prostate cancer screening. And now I find myself really thinking about the messaging and how things are going to go out and how I can be as scientific as possible. So there are of course, there's many good sources, you know, social media. There's many good sources. And unfortunately, if I even if I give specific sources, I think that people would have an opinion about them. There's no source that's opinion free, let's say. But there's definitely bad sources. So your Facebook feed is a bad source. It's just, there's an algorithm there that's showing you things that are, and the way that things are scored and prioritized to show to you has nothing to do with their veracity. I'd be very happy to share some of my favorite publications. This is a little self-serving, because I've been writing for the Timmerman report, but my articles there, I'll stand by. And I think it's a local source.

Dr. Tom Lynch [00:32:25]
As you know, Luke Timmerman has been a great friend to the Fred Hutch.

Dr. Ruth Etzioni [00:32:29]
Right. And but I would have said that anyway, but he definitely has. And of course, you know, I think that publications that come directly from scientists or from institutional media. So, you know, Fred Hutch media, UW media or, you know, they have come, you know, one step removed from the scientists that are trying to do, you know, parlay their science into understandable pieces, you know, that can be understood by the lay public. So I think those are a couple of places to go. And then, of course, I have some sources are happy to share with anyone. Please feel free to

e-mail me. I think that Ed Young at The Atlantic has written some really outstanding articles, some of the best articles about the pandemic. And he started on Medium, but just wrote a piece on the New York, that was on the op-ed at The New York Times. Is Thomas PoyYo, I'm not sure I'm pronouncing his name right. Some very outstanding articles. And other than that, you know, our typical publications, Science, Nature. And other than that, I'm very happy to share. But I think it is difficult, but definitely not the social media feed, your Twitter feed are not included.

Dr. Tom Lynch [00:33:53]
OK, so people, who are on the call, just so you know, we will go ahead and try to get on and try to get some of these resources to you available so you can take a look at them. So Jesse, you're not as directly involved in some of the controversies on the modeling that Ruth is. Where do you look, just tell me not the local political answer, but the real answer, when you wake up in the morning, and you have all your media that comes into your computer, all of us, I know look to find out how the pandemic is doing. Where do you look to to get that answer?

Dr. Jesse Bloom [00:34:26]
So I look in two places, so particularly for the first three or four or maybe two or three months of the pandemic, I especially actually learned a lot from Twitter, because there's been a lot of great scientists, who are posting a lot about the coronavirus on Twitter. Now as time has gone on, and obviously the awareness that pandemic went up, there's still a lot of good scientific information on Twitter, but there's also now an astronomical amount of garbage. So I found the garbage information ratio on Twitter has gone way up. But I still look there. And then I read on the preprint servers. So bio archive and net archive, which is where papers are posted every day. I'll probably spend, you know, 50 minutes going through all the frequently posted and then, you know, potentially an hour or two reading ones that seem relevant and good. And I mean, I'm able to do that, obviously, you know, I'm not able to understand all the detailed epidemiology ones, but in terms of virology and viral immunity, I have a lot of sort of background knowledge, I feel like I can in general interpret those pretty well.

Dr. Tom Lynch [00:35:27]
And Jesse. Is there a place for the people, who are on the call, who might not be virologists and they want to just find out, are we doing better or worse in the pandemic the past week? The preprint servers are pretty rough to get through if you're not...

Dr. Jesse Bloom [00:35:44]
I mean, as far as real epidemiological updates, I think Ruth would probably be a better source of that information than me. I mean, I think at this point, I often just look at The New York Times front page case tracker. And as far as things that updates on vaccines, there's a number of people, like Florian Krammer is one of them, you know a variety of other people on Twitter, who are quite knowledgeable about this, who post a lot and I'll follow them up.

Dr. Tom Lynch [00:36:10]
So Neel, next question is for you. And this is come in from one of the people who were listening, which is which is, you know, your cancer research or you're wondering how the microbiome is causing colon cancer. Okay. And causing and impacting gastric cancer and other types of GI cancers where the microbiome seems to be important. Do you see what's happening with COVID, and the fact that look at these three fantastic scientists we have, who are now focusing on COVID. Does cancer lose out in that? How do we make sure that cancer is still front and center? And as a cancer researcher, how do you balance that?

Dr. Neel Dey [00:36:47]
That's a really great question. Undoubtedly, COVID-19 has impacted clinical trials in terms of recruitment, but in terms of our collective focus on cancer, I have to say anecdotally, I've been as part of as many conversations on cancer research projects now as I had before, and looking at the literature, looking at New England Journal of Medicine, you know, we're looking at all the high impact journals, I'm still seeing really hard hitting cancer research coming out issue after issue. So my sense is that our collective progress, aside from the clinical trial recruitment issue, is still, you know, still moving forward and individual for myself specifically, I would say that I think it's invigorated our lab to expand, not necessarily divert our attention.

Dr. Tom Lynch [00:37:43]
And so, Neel, just tell me a little bit what's happening in your lab right now. Who's coming in? Are experiments being done? Because we are, one thing I've been very proud of at The Hutch is how we maintain our productivity in the laboratory. But it's not the same thing as having you coming in and walking around the benches. Or maybe you're doing that. Tell me how you're interacting with your people and making that work?

Dr. Neel Dey [00:38:06]
That's a great question. It is not it's not the same thing. You know, prior to the pandemic, I would stroll around the lab every day and just chat, just chat with folks. And now we we are trying to still be as distanced, as remote as possible. You know, all of our lab bitting meetings are still virtual. Our sub-group meetings are virtual. But people do come in when they have experiments to do, if they have samples to process or sequencing. And I've encouraged my lab members to basically come in just for their discrete experiments and to feel totally comfortable with doing analysis, writing everything now.

Dr. Tom Lynch [00:38:48]
So how do you, the question is, OK. So that's great for someone, who is a postdoc, who's experienced. How do you teach a graduate student to do a new technique, or how do you teach a physician scientist how do sequencing if you can't be their hands on to show them?

Dr. Neel Dey [00:39:04]
Oh, that's yeah. That is a huge challenge. Absolutely. I think for for my lab specifically, I was fortunate to have trainees, who are a little farther along, so I did not have to worry about the basic molecular biology protocols. As far as some of the computational work that was pretty feasible to discuss progress, discuss implementation of new strategies, virtually as well. On the clinical side of things, yes, that, I think the trainees did suffer initially, but now that we have brought back some of the procedures as needed, you know, I think we are getting that opportunity to do that hands on teaching of what's a colonoscopy, which we would not able to teach virtually.

Dr. Tom Lynch [00:39:54]
I would imagine that. So Ruth, a question that has come in for you, which I think is a good one, people have talked about the fact that in the influenza outbreak in 1918, that October was the month that had the largest number of deaths. And we're now four days away from or five days away from October 1st of this year. And I guess the question to you is, do you see things in the models that might suggest a similar trend here? Or tell me your thoughts about what the coming fall means in terms of of this pandemic.

Dr. Ruth Etzioni [00:40:38]
That is a great question. It's difficult to model, but I will say that we are concerned, because what has happened, at least in Washington state, what we can see, and it's very interesting, if you look at mobility patterns, mobility went right down very, very fast in March and April and has been coming up slowly and and yet the infection, the transmission, the ambient infection rate in Washington has not come up. We've been doing a good job, and that's because we've been clearly interacting, we've been moving around and interacting, but interacting safely. We've learned how to interact safely. And that has two parts to it. There's the leisure part, which is the decision to interact safely, which is under your control. But then, of course, with essential workers, that's much less under their control. And, you know, they have to be protected. And it seems that when you look at, for example, the rates in Yakima, which were very high and have come down, that practices seem to have been, you know, preserving the ability to interact. But that has at least been facilitated by the ability to be outside. When we come in, we have to be even more cognizant, which will happen simply because of seasonal factors. We have to figure out how we can continue to interact safely, if we want to keep the lid on the on the virus in Washington state. We're simmering and we're in a transition period and we're very close to the edge. But we have to consider that as much as possible, if we can interact safely indoors, which also involves limiting interaction, rigorous masking outside of the home, that maybe will be enough to help us get through what is anticipated to be a more challenging time in terms of controlling infection.

Dr. Tom Lynch [00:42:54]
One of the questions that's come up on the on the feed has been the question of what role does the Hutch play in vaccines? And I'll give a little bit of a plug for the COVPN, COVID Prevention Network. So, Larry, Corey, who used to be the President Director, is one of the world's foremost virologist. Larry Corey is the principal investigator of the COVPN, the COVID Prevention Network. And what Larry did, great example of exactly what the three of you were talking about, this ability to pivot and to adapt one's science to a current crisis. Well, Larry was able to do all the work he was doing in HIV and creating HIV vaccines and pivoted to COVID. And so by creating this large network, the Hutch is coordinating five large Phase 3 trials globally, not just being done here, they're being done all over the world globally to help look at vaccines. Those include the vaccines that are RNA based. Those include the vaccines that are more traditionally based, not just messenger RNA vaccines. And those are all being coordinated from here. One of the big challenges that Larry had, and Dr. Wallace, who works in his group, is working on is making sure that the patients, who participate in the vaccine trials are reflective of the diversity of the people, who are suffering from the virus. Ruth, you mentioned Yakima and you mentioned how difficult it is, I know the Yakima agricultural workers don't have the luxury that Neel's laboratory staff has, in terms of how they isolate themselves in the laboratory. In a food processing plant or a meat processing plant, it's a lot harder to isolate yourself physically. And so making sure that the vaccines include patients from those backgrounds that we can see efficacy data, I think is going to be very important in terms of how we go from there.

Dr. Ruth Etzioni [00:45:00]
As a postscript, Tom, vaccines, as well as preventive measures that, you know, rigorous preventive measures in, those are essential working situation. I mean, know this is where we get our food from, from Eastern Washington and, you know, protecting those workers. You know, we all have a stake in making sure that there are policies in place to protect them and that those are monitored and enforced.

Dr. Tom Lynch [00:45:26]

And that's absolutely, absolutely true. Jesse. Questions come in for you. Since you've done so much of your work in influenza and I know everyone's about to get their flu vaccine, we start our program here at the Hutch this coming week. What are your predictions for the upcoming flu season? So will the things Neel and Ruth talked about in terms of masking and PPE. Will these precautions keep the flu season at bay? And so that's one question. Second question of the same relation is I understand that there's been an uptick in some viruses. So is that true? And what do we know about flu, about the flu season?

Dr. Jesse Bloom [00:46:11]
So as far as the influenza season, it's certainly been the case that in the southern hemisphere where they have their flu season in their winter, which is our summer, the flu season was minimal. There were very, very few flu infections compared to normal. And the reason for that is believed to be the same social distancing measures that people were taking to protect against SARS-Coronavirus-2, are also limiting the transmission of flu. And in fact, there are women in the transmission of flu even more than they were of SARS-Coronavirus-2, because at least right now when there's no population immunity of the SARS-coronavirus-2, it's actually probably more transmissible in most populations than influenza. So based on that fact, I can never be sure, I would extrapolate that if people maintained pretty rigorous social distancing up and in our country, for instance, there's going to be a pretty reduced influenza season, and that would probably be the case as long as people, I mean there'll still be influenza, but it'll be a lot less, and that'll be the case as long as people are maintaining social distance. I do think we have to worry that whenever people stop maintaining social distancing, there might be an especially large influenza season, because there'll be less immunity from prior infections. You know, there's also the question of what would be the impact, the clinical impact of the SARS-CoV-2 infection? I don't know for sure, but it probably wouldn't be good. And then, yeah, there have been, I've heard the same level you were describing that certain places have found an uptick in rhinovirus infections, which could indicate that conditions are becoming more permissive for respiratory virus infection. I haven't looked at any of that primary work, so I can't really comment more. But we do know that most respiratory viruses, including at least other coronaviruses, rhinoviruses and influenza viruses all tend to transmit a lot more in the autumn and winter months then during the summer. So probably that will be a trend.

Dr. Tom Lynch [00:48:08]
Yeah. Thank you, Jesse. And so, Neel, in your world of the clinic, asking to pull back your clinical hat again, we've had a number of people who said, you know, in fact I was talking with someone this morning who said, you know, I think this is COVID-19 is really not as serious as we thought it was. And it looks like the cases are more mild now. The death rate seems to be going down. You're in the hospital. You've seen patients with this disease. Tell us what you think about that line of thinking.

Dr. Neel Dey [00:48:42]
Oh, that's you know, that is such an important question. At the present time, I would say to that person if I were face to face, you know, I can understand why you might feel that way. You know, we as human beings have evolved to be really great at assessing sort of short-term risk, immediate risk, but not really long-term risk or medium term. So, you know, weak line incubation or chronic symptoms those are difficult to wrap one's head around and further, our risk assessment is really based on a set of senses that don't include the ability to use viruses or to appreciate, know epidemiology or genetics, and certainly not to appreciate the scale of 30 million people worldwide being infected, et cetera. And so that's why I would one out emphasize, that's why the work being

done by Ruth and Jesse's groups are so important. They're so critical in enabling us all to see the world using senses that we don't naturally have to really appreciate the gravity of what's happening. So I guess in sum, I would certainly affirm they're very human response, which might also include denial as a way of coping with something that's very overwhelming. But, you know, I then take them through the things that I've seen in the hospital, the data that are published online, for example, the UW, IHME sites, and journals that were discussed earlier. And, you know, I wouldn't really take the time to go over that. You know, it's certainly not the case that this coronavirus is not serious. It is serious. It is a big deal.

Dr. Tom Lynch [00:50:26]
And Ruth, I'm going to ask you this question, because I know there probably a few people we are more critical of data, I don't mean critical in a negative way. Critical that you really do look at all the different sides of the data and you interpret whether or not the data is legit. As someone in the community with lots of contacts and family members, we're going to turn to you. And inevitably, the fact that you're at the Hutch, they're going to say, Ruth, should I get a COVID vaccine? And what are you going to tell them and how are you going to make that decision to advise your loved ones and your friends as to whether the data is supportive or not? And that question has come up at least four or five times in the Q&A feed as we've been talking today. How do we look at the data for the COVID vaccines, as it evolves?

Dr. Ruth Etzioni [00:51:22]
It's a great question and I'm going to answer it. But I want to broaden it because it's not just about the vaccine, right? It's about all of the interventions that we have, including treatments. And so I'm I'll say something, General, then you asked me about what I would do. The convalescent plasma is an excellent case in point. Paper appeared on med archive that was not peer reviewed. It was taken up by the media, who couldn't possibly understand that, just to review, the result there was, one of the results, the key results was that patients treated earlier did better, I'm sorry, did better than patients treated later, for example, as it as evidence that convalescent plasma was effective. We never compare patients treated earlier with patients treated later, because they're apples and oranges in order to be treated later, you know, you have to survive, to get to be treated later. This is a well-known bias, right. And of course, the media couldn't recognize that this was a very flawed comparison. And so, the first thing is that, you know, there are people, who want to get the message out, who want to get the numbers right, like myself. And it's it can be quite difficult to do that when you when you learn, you know, when you have something that you want to put out there and you learn that Jamma is completely overwhelmed and they just don't have time to even look closely at what they're getting submitted about COVID that the that the avenues to really get the right information out are limited. So we try and and this is part of a lot of the work that I'm doing. Part of my publishing on the Timmerman Report and other efforts to publish this translation and what people can believe in. As for the vaccine, though, the first thing we have to recognize is there's going to be more than one vaccine. And it's the same thing with diagnostic tests. It's the same thing with antigen tests, even PCR. Right. There are different flavors, different versions. And so we want to understand what we're getting. And we have to, so my feeling is to wait, because I think that there's a rush to get to a result. I'm concerned that early results will have the same problem, early problems will have the same problem as the convalescent plasma situation. And I think that, as you know, I would trust people like Jesse, who really know this area for myself as a scientist, and to the layperson, I would just say wait and see. Recognize that there are multiple vaccines and we need to understand how well they work. And you can find that out, but you need to know to go and look for it. And the same thing, if you get an antigen test, if it comes from a company, you need to find out what's the false positive rate, what's a false negative

rate. You have to may have to do some snooping to understand whether you're getting a lemon or not.

Dr. Tom Lynch [00:54:46]
Then, Neel, I'm going to pass it to you as the physician. I'm also a physician. I don't know how comfortable I feel with Ruth saying to wait. Meaning if Peter Marks and the FDA tells us that the vaccine has efficacy and it's safe, it has been safe in the randomized trials. I want to get the vaccine as soon as I can. Neel. How do you interpret this data?

Dr. Neel Dey [00:55:08]
Yeah, I you know, I agree with you in assuming that the trials have been not short circuited and that we have reliable data. I agree with you. And I think for us it's a dual sort of responsibility, not only for personal protection, but we're also just like with the flu shot being mandated, we're also trying to protect the patients with whom we interact, whom we're trying to care for. And so I think with a dual obligation, it for sure tilts the balance for me, as with you, and probably would tilt the balance, I would imagine, you know, for Ruth as well. You know, if we're now thinking about patients.

Dr. Ruth Etzioni [00:55:43]
Right. I'm not saying to wait very long. It's time to digest the data and time to learn about. And I think that we need to say a vaccine, you know, and I would, I would definitely go to a clinician, a virologist to figure out which vaccine. Right. Because they'll be different versions and, and definitely not wait long, but just to be able to digest the results and make sure that they are valid from a statistical standpoint.

Dr. Tom Lynch [00:56:16]
Well, one of the interesting things also about this is that there are people now weighing in who say that people other than just the FDA should be looking at this, which as a drug developer, which is what I done for much of my life that's a little unusual. I have to say. And so, for example, last week I was watching Anderson Cooper's TV show and he mentioned he asked Sanjay Gupta if he was going to be reviewing the data, because there had been a report that Sanjay was going to be asked to review the data, which, you know, I probably would believe most things that Sanjay would say, he is incredibly reasonable physician. Very thoughtful guy. And then Cuomo, Governor Cuomo came out and said that he feels the state of New York is going to need a separate panel to review the data on the vaccine to see if it's efficacious. Now, perhaps Governor Cuomo can create a separate panel that could possibly do this, but what does it mean, Jesse, that we've lost faith as a society in our FDA, which has professional, lifelong people who look at this kind of data, and yet so many people are losing faith in our ability to make these decisions.

Dr. Jesse Bloom [00:57:32]
Yeah, I mean, it's certainly not good. I mean, obviously, I'm not, my specialty is not, you know, vaccine epidemiology. But my understanding is that the actual vaccine trials, which are, you know, double-blind placebo controls are very well designed. And if those trials run, they have large numbers of enrollments, if those trials run sufficiently long, we'll get really good answers to these questions and we should feel 100 percent comfortable. I think that the question is there's been, you know, in some cases pressure or discussion of trying to draw conclusions very early in the case of the Pfizer vaccine trial, I think there's an interim evaluation point there. There have been thirty-two cases observed total among the 30,000 people enrolled. And that's that's an early interim point. There may be reasons for having that early interim point, but the question is then, would

there be pressure to based on those initial three cases, try to short circuit or bypass, sort of like letting the trials go further. And I think that's something that we should be worried about. So, I mean, my impression is that the trials are extremely well designed, the question is, is simply will the decision makers, in this case sort of wait for trials to play out as long as they should? Or is there going to be pressure to sort of draw up early or premature conclusions based on the stress?

Dr. Tom Lynch [00:59:04]
OK, we've got 60 seconds. I'm asking for one date from each of you. No discussion behind it. I don't want a justification. OK. One date I'm going to ask you. I want to know what's the date back to normal? We can go to a crowded restaurant, go to a crowded bar, feel comfortable, go to see the Seahawks play, Patriots play, the Cowboys, whoever your team is, and feel part of everything. When is that going to be? Neel, what's the date?

Dr. Neel Dey [00:59:38]
February 14th, 2022.

Dr. Tom Lynch [00:59:41]
February 14th, 2021. Jesse, what's the day?

Dr. Jesse Bloom [00:59:46]
June 15th, 2021. Ruth, what's the date?

Dr. Ruth Etzioni [00:59:51]
Well, I'm with Jesse and I would say not back to normal, but better than normal, because we will have learned a lot and hopefully we can translate it into positive change in the way we live, and the way we live in the world.

Dr. Tom Lynch [01:00:04]
What a way to finish. I want to thank all of you for a fantastic discussion. I want to thank all of the people who been with us for the past hour. Thank you for everything you do for the Fred Hutch. And we look forward to seeing you next month.

Post-event correction of Dr. Neel Dey's estimated date from February 14th, 2021 to 2022.