IG15: Human Rights, Professional Ethics and the Values of Medicine (Perfected Transcript)

Moderator: Frank Chervenak

We will have 3 lectures that will encompass a little more than half of our allotted time of 2 hours and then we will open for comments, questions and whatever you're comfortable with; we're very informal, so please, by all means, first names are fine.

It is a pleasure and privilege to convene this Interest Group 15 on human rights, professional ethics and the values of medicine; my name is Frank Chervenak and I'm Chair of Obstetrics and Gynecology here in New York at Lenox Hill Hospital and I'm also Chair of Obstetrics and Gynecology and Associate Dean for International Medicine at the Zucker School of Medicine at Hofstra/Northwell.

I'm joined by Jeremy Sugarman, who is the Harvey Meyerhoff Professor of Bioethics and Medicine at the Johns Hopkins University School of Medicine, Berman Institute of Bioethics.

It's a special privilege for me to present to you Renee McLeod-Sordjan; she's professor and Vice Dean of the Hofstra/Northwell School of Nursing and Physician Assistant Studies and adjunct professor of Graduate Nursing where she's the Chair. It's a special pleasure because Renee and I work in the trenches. We deal with a myriad of ethical issues. Not just academically, but real-world issues as they've come up, not just with COVID, but on a whole myriad of issues and I've come to admire her, not just for her wisdom, but for her practicality and her ability to deal with clinical issues. I can't think of anyone better who can discuss the lived experience of normative ethics in response to the COVID pandemic. Renee, we look forward to your presentation.

Renee: Thank you, Frank and I'm so pleased to be co-presenting with Ruth and Alex and I'm glad we're in a kind of intimate forum. I really have no conflicts of interest.

I also want to be cognizant that we are very, very thankful to all of the essential workers, not only that kept our hospitals and our care facilities afloat, but kept our lives afloat for really what's nearly two years of the COVID pandemic and I think we forget a little bit that we've been living with this.

So, as Frank said, my experience is in the trenches. Northwell Health is a conglomerate of 23 hospitals, mainly centered in Long Island, but also in Manhattan. And we have this meteoric rise of patient hospitalizations in New York during the first primary surge- I call it the 30 days of April.

One of the things that Frank also didn't share with you is that, in addition to having this academic background and heading up the division of medical ethics, I myself am a critical care and PA hospitalist at one of our hospitals as well. So, about March 16. We were seeing our first cases of COVID in New York, and I have two children that are in their 20s and they wanted to go to this little event, as 20-year-olds do, to see a rock band; and I said that probably isn't the best thing, guys, but here's masks to take because we're beginning to see COVID patients. The very next day New York state close down, and you can see our ICU hospitalization skyrocketed by four-time fold and a third of these patients were in the ICU.

The other backdrop of this is that there were two things that are going on for us to really discuss in normative ethics and human rights. While we were dealing with this global pandemic, we were also

seeing the moral injury and the social determinants of health play out in this pandemic, where black and brown were up to four times more hospitalized and three times more likely to die.

And we saw that play out in our hospitals as well where we saw patients with renal failure, diabetic patients, and overweight patients that were male more likely to die from complications related to COVID 19.

Well, another thing that we would be remiss if we didn't discuss in this forum was that 25% of the people that accounted for all of our hospitalizations were age 75 and older.

So, if we look at normative ethics as a way of how we should approach and look at the future then you're going to see we had really big problems. What we learned is that this pandemic laid bare all the structural and moral inequities that really needed fixing in American society. So, we have George Floyd playing out in the summer, at the same time, when in the summer, we were trying to find better ways of testing and getting into communities of color to slow this spread.

Well, the real reason why I'm really happy that Frank asked us to have this discussion is that, particularly in the Long Island communities, of which I was in the trenches with these patients, we had a public health perspective to get into the communities and test; and so, one of the things that we saw there that Dr. Stable, Director of the National Institute on Minority Health and Health Disparities, laid bare is that Long Island did something right. We acknowledged and addressed that there was moral suffering and moral injury to our communities of color. And that we could not approach ethics purely from a medical end without also addressing the social inequities as well. So, Frank asked me to really talk about the ethical impact of this lived experience.

Well, you're going to recognize this from how we dealt with flu, whether it was the Utah pandemic response, or the New York state pandemic response to flu - we decided that we could use a modified SOFA score to look at ventilators. As early as the beginning of the pandemic, Forbes asked the question about how doctors allocate medical resources and what we quickly learned was COVID wasn't the flu.

These increased flu cases that we thought we were seeing were actually COVID cases and these patients required 45 to 60 days of ventilator care. These patients got sicker more quickly; these patients were all of the others, whether we talked about older age, whether we talked about gender, whether we talked about low access to care.

So, in New York, we started an Empire State Bioethics Consortium so that all of the heads of bioethics departments would get together to look at best evidence, but also to share our stories.

Because the moral injury that we were seeing was not just the physicians at the bedside, the nurses at the bedside, but every healthcare worker at the bedside and particularly the ethicists and the chief medical officers that were asked to answer this question.

So, we're a group that looks at human rights and looks at normative ethics; and if I asked each and every one of us on this talk today to talk about how would we look at this, we always talk about the greatest good saving the most number of lives, taking into account, who could survive. And then, sometimes we talk about giving people the greatest chance to live through the most stages of life on a lifecycle mode; well, this didn't work for the younger people we were seeing, them as sick with COVID.

In fact, it didn't matter what your nationality, was it didn't matter what your economic state was, we were seeing people die.

I have to take this back into society and try to give you a little bit of levity. When I was younger, I loved Madonna and, of course, I love the movie “Desperately Seeking Susan.”

And my children were watching a TV show called “YOU” and yet every day there was someone at Lenox Hill, there was someone in health and hospitals, there's someone who we could recognize their names, whether it was on Broadway that was closing or anywhere else that were dying. Young people-30 to seven.

So, we needed to have meaningful public engagement to get around this.

Ezekiel Manuel put some of our thoughts to pen in his study that was published in the *New England Journal of Medicine*. The application to COVID wasn't as easy as what I showed you before because we needed to align and maximize slowing the spread.

And there were two other things that we had to talk about in normative ethics- how could we give priority to healthcare workers and to the people that were participating in research for vaccination.

A study had come out and Harvard that said yes, let's give priority resources to those people who were engaged and getting vaccinations done. Well, the problem was we didn't have the resources to be able to give it to anybody as a priority when we were overrun in the hospitals and in the community; so, something that came out of this was to think about equity and equality.

So, from my lived experience, I want us to talk about four things that did go into some algorithm.

Equality. Thinking about how to reduce moral suffering and moral injury by giving every person some benefit, which means we had to look at algorithms; algorithms from precision medicine that really equalize the playing field to talk about who should have some priority. We had to think about utility which meant we had to upcode innovation and resources, but also think about creating responses that would do proportionality benefits and risks and we had to look at greatest need- prioritizing those that were sickest to get those ICU beds, which meant we had to create more beds quickly.

And so, in our own hospital system, we emptied out auditoriums; we emptied out places that were openings for cafeterias to turn them into ICU beds relatively quickly.

But also, we had to think about the essential worker; and calling on my colleagues like Dr. Tia Powell, we had a duty to safeguard, plan, and prepare, which meant that we had to allocate beds in a different way. Patients weren't just kept in their home communities, but we actually loaded patients into other hospitals that had more PPE and equipment.

And so, through this, I want to share with you a study that I did with Dr. Dolgin and Dr. Markowitz and Dr. Sanmartin where we did a mixed methods study looking at quantitative and qualitative results of how can we use ethics consultation as an approach to moral distress.

Well, one of the things we quickly found out is, thank goodness at least in our first surge in our health system, that triaging the use of ventilators never became a reality. We got extra ventilators that came into New York and we learned to use anesthesia machines as ventilators; so, ventilator allocation had the easiest solution.

The hardest solution and what I'm bringing to us now from a normative perspective, is how do we alleviate the moral distress of our overworked and understaffed clinicians. And so that transition from allocation strategy of ventilators occurred rapidly, as it became imperative to maintain a level of human capacity.

So, see- if these were some of the things- this was hellish. There was a total lack of preparation for handling the demands of this pandemic and that, while things were going on in Wuhan, China in December, here, in America, we were ill-prepared to either stockpile or look globally at what was happening and that it could happen here in America. We had the worst forms of nationalism, rather than globalism.

We needed the support from hospital administrators, from peers and we created these hospital clinical response teams as a way to alleviate the distress from the perception that we had to constantly make life and death medical decisions without familial support. Remember, families were not in the hospitals; the usual decision makers that we would rely on could not come up with these quick decisions. I myself saw patients that I was talking to at the beginning of a shift two hours later intubated, proned, unresponsive and without capacity. Things were happening rapidly that made decision making fall back on to the clinicians.

So, our CEO, Michael Dowling, wrote this story about leading through the pandemic and it really was the story of humanity and innovation; it's going to be our continued story of resilience.

What are some of the lessons that we learned? The burden on clinicians is onerous.

I'm really pleased to be at NSEM because what they talked about, even before the pandemic, was a clinical framework where we could reduce burnout and improve resilience. I challenge us as ethicists, to think about doing that.

There was also this potential obligation to look at triage and to look at allocation that might result in sacrificing one person's life or another. And we have to look at the increased responsibility and the moral distress that is going to lead through the next decade of how clinicians look back at the decisions that we made during this past two years.

So, my colleague Dr. Berlinger and the Hastings Center says that ensuring the health of the population requires limiting individual rights. How do we do that from a normative perspective, how do we do that from a moral perspective when there's this tension between the moral distress and what we know we have to do in disaster-based protocols.

So, these social determinants of health were amplified, and one of the things that we have to do is transition as IHI says to looking at moral determinants of health; there's a tremendous wealth gap.

The percentage of people who say they experienced fair or poor health was amplified during COVID.

And we have to recognize that that happened with individuals that are basically getting minimum wage-incomes that are less than $35,000. The work impact and the education disruption among black and brown were amplified.

The social determinants that we talk about - food insecurity, economic instability, education instability, community instability -are going to require social integration and community engagement for us to get back to some sense of moral health.

And so, what I asked us to think about is something I didn't see in my lived experience. We were so focused on equality, making sure that everybody had the same box that we have to now move into equity. We don't need the same box, we need to have the same view and so what that is going to require is different strategies to treat individuals according to their needs, rather than giving everyone the same thing. And so that is going to require a hyper-vigilance. What I think is four areas in ethics, that we have to look at.

-Access to care because we are going to have COVID long-haul syndrome, we have patients that spent 60 days on ventilators.

-Access to education, because we are going to have to equalize the playing field to put more income to education, so that we continue the innovation that happened during this time.

-Access to home ownership; because renters lost their homes; we are looking at recessions.

-Access to basic necessities: so that we can address one of the things that I haven't talked about- mental health issues. We saw an increase in mental health need in our community partners where we were looking at transitions to care; we now are looking at increase in suicidality, increase in depression, particularly around our physicians and clinicians.

And so. In this reflection as I end up my 20 minutes, I asked us to think about proactive ethics, upcoding trust. Are we better prepared now in our communities with that level of trust?

What should we do differently? Are there other reflections that we should be having, particularly for us that are in an interest group about human rights? And so, one of the things I want to leave us with is this, we still have a tremendous amount of people, including healthcare workers, that still have distrust about the basic thing- getting a COVID vaccination, so all these lived experiences that I've shared with you from being on the front line as an ethicist and ICU clinician hasn't stopped.

Because we still can't get those like me to say that we agree on the science of that vaccination; if we have hesitancy, what is our communities that are disenfranchised.

And so, I'm hoping that, as you listen to Ruth and Alex you keep this in the back of your mind, and thank you for just allowing me some of those thoughts in this time, thank you, Frank.

Frank: Renee that was wonderful and brilliant. But we need to move on well let's save questions and comments till after the two other speakers. you've given us so much you've given us a running start our program, but we need to move forward.

We're going to hear about a very important topic from Alexander Capron. He's University Professor of Law and Medicine and Co-Director, Pacific Center for Health Policy and Ethics at USC. His topic is going to be research on therapies for COVID ethical foundations. Alexander, this is such an important topic, a topic around which there's been so much confusion and misinformation. We look to you to elucidate and shed some wisdom on this topic.

Alex Capron: Thank you, Frank and I'm pleased to be here with all of you.

As Frank said, I'm talking about research on therapies and I'm going to focus on the ethical foundations.

As an ethicist I begin with a disclosure I don't have any conflicts of interest, but I do want to acknowledge that this comes about in part from a committee of the Academy's that I have been chairing. Our report will be out soon, so obviously the presentation, you will hear is my view not necessarily that of the committee.

I also want to say that we were greatly helped by a number of speakers who were at our open sessions, and one of them, in particular, who talked about evidence generation and a pandemic, Dr. Christopher Seymour of the University of Pittsburgh Medical School I'm particularly indebted to, as you will see. The overview of what I want to do is the theme is the ethical imperative for therapeutic research and I put that in quotes because for 15 years I heard from my one-time colleague and friend, the late Bob Divine, that therapeutic research was a misnomer but we're talking about research, combined with therapy, with a therapeutic contempt.

The focus will be on seeing familiar concepts having new effects, the consequence, I hope, will be expanding the scientific practice of medicine and the objective of what is the lesson we can learn is fulfilling the duty of beneficence to population as well as to patients.

What's that familiar concept with new effects. Clinical care and research are actually quite separate and there are a number of reasons for this. At one level there are regulatory reasons, logistical, financial, professional, but given the focus of this Interest Group, of course, I'm particularly concerned with the ethical ones, and I will argue in fact that the ethical ones underlie the others.

So, on the regulatory side, research regulation primarily occurs at the federal level. You go back to the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which was set up, as you know after the Tuskegee study was revealed, and worked from 1974 to 1978. One of its main products was the Belmont Report which spelled out, among other things, ethical duties of beneficence, respect for persons, and justice and we're particularly concerned, right now, on the implications of that duty of beneficence. That was incorporated in the common rule which the Federal Government put out as the regulation for all federally involved research in 1991 and then updated in 2017.

The Federal Government does not have comparable authority over the practice of medicine and indeed in the national commission it very explicitly said we're not talking about and we don't want recommendations on research on experimentation novel treatments and innovation in clinical care. We're talking about research that can contribute to generalizable knowledge, not what is done to one patient, but what was done to an adequate number of patients to create research. And so, we leave decisions about care to physicians and even in the area that is very highly regulated the licensing of drugs and devices. That licensing and that control from the Federal Government stops at the moment of use. On the logistical side, most research takes place in specialized programs and academic institutions or other specialized institutions, like the Salk Institute and so forth and takes the form, ultimately, of randomized clinical trials. Also on the professional side, since this is a group about the medical

profession it's really different career paths between physicians who are in clinical practice and those who work for research organizations, even if they also do clinical care.

Financially, there's also a wide divide as healthcare insurance ordinarily doesn't pay for people participating in clinical trials, instead, the cost of research is borne by the government and industry. It's a collective good that the government supports, at least at the basic level, although NIH mostly focuses on the discovery side of research, rather than research that would take a new molecule and create a product take it through all phases of clinical trials so substantial support for that usually comes from industry to cover those logistical and regulatory complexities that I've already mentioned.

And finally, on the professional side I already mentioned a sort of a separate professional identity for physicians as opposed to physician investigators. But on the professional side, this is based upon the wishes of professionals to exercise their clinical judgment and a relevant example is, of course, the original Declaration of Helsinki. The World Medical Association created that declaration in its move to really replace the Nuremberg Code to have something that doctors had created, rather than judges based on medical principles, rather than on the law. And it recognized that, yes, for research, you needed informed consent (and this is 1964 at a time when informed consent was not yet getting the attention it got in the subsequent decades) but it also preserved physicians' discretion about whether and how they would have to explain any innovations that they were undertaking in experimentation, that is combined with clinical care, and so they really wanted that notion of clinical judgment to be protected.

So, all of those come into the ethical justification for that division and for the physicians' authority in exercise in clinical judgment in that patients can count on that judgment being exercised as an expression of the physicians' duty to put their interest first and that's that concept of beneficence - the duty to do what is best for the patient - and nonmaleficence, the duty not to harm the patient.

Physicians must do, as the Hippocratic Oath said, what in their judgment is best for their patient. So, what happened then when we faced COVID 19; obviously, at least at first, and to a certain extent, today, when we look at things like some of the pediatric cases, when we looked at long COVID, it's a poorly understood condition, there were very importantly, no known proven therapies that could be applied.

Now the duty to do what is best in the physicians' judgment offered two courses of action- the physician exercises clinical judgment or the physician enrolls the patient in a randomized controlled trial.

And on the first side, there is a strong impetus for physicians to say we've got to do something. I've got a very sick patient I've seen the course of this illness and other patients, we must intervene, what do we have of any possible relevance we've got to give it a trial.

A trial in this patient, that is, and it of course depends upon in individual judgment that doesn't mean isolated individual judgment. Doctors talk to colleagues, they see what other people are recommending, we ended up with a rather bizarre situation where those recommendations were being made in press conferences from the White House; but whatever the influences were, there was some exercise of individual judgments.

And, by acting, the physician knows that he or she is demonstrating their commitment to the patient's welfare. On the other side, a physician enrolling a patient in a randomized clinical trial is operating on the principle when doubt exists as to what will work, one must conduct a trial. And the ethical premise

is that randomization gives a patient a 50% chance of benefit or non-harm since one of the things, including the thing being tested, as well as whatever the control is whether it's a placebo or, more likely in these situations of severe illness whatever the standard of care would be, even if that doesn't include a cure, those are balanced by that randomization.

And, of course, there's the desire to help by producing knowledge there's also a relative desire to be recognized as the person who figured out something important and has that published, and this was very much encouraged in the COVID situation by the opening up the floodgates of publication and access to manuscripts through various pre-publication forums, so all of this feeds the understandable wish of investigators doing this work to be recognized.

Now, what are the weaknesses of that existing duality between the standard care and the randomized trial? Well, on the exercising clinical judgment side, the intervention that was chosen may cause harm and we had lots of examples of that. That is direct harm that made the patient worse, but there's also the indirect harm that occurs when you keep a patient from receiving another more beneficial intervention. There are also lots of biases in how you decide, and any particular patient, to use an intervention. What else you do with that patient affected by your judgments about the patient, clinical differences about patients and so forth. All of that is perfectly appropriate on the clinical side, but it means that when observational studies are published and as again just to remember that works, a lot of publication of this or it doesn't really add anything to the evidence base, because the observations are either quite inexact or they are subject to all these biases.

Now, on the RCT side, unfortunately, setting up an RCT is even when you have all hands-on deck, is a time-consuming process; there's a lot of logistics; there's a lot of regulatory stuff you have to do.

It's also very difficult to recruit patients and convince their physicians that this is the right thing to do, because randomization is, frankly, uncomfortable, even though we know, as I already remarked, that it gives that 50% protection that you're not on the wrong side of receiving something which is going to turn out to be harmful. It is an uncomfortable process.

There's competition for money for support for this and patients, with the result that a lot of research that was carried out was not carried out to the usual methods of outside funding but in academic centers, people were trying to use their existing resources to carry on research and then the question was who gets access to the patients, which are many who are desiring many investigators, desiring to test out one treatment or another, are going to be the ones who have access to a group of patients.

A further result is that many of these trials that went forward were small in number and they were based at an institution, so they had, whatever the profile of the patients of that institution, rather than being more generalizable; and, at best, with those low numbers they became uninformative. And most typically they were a standard randomized control trial that that was looking at a single intervention against the placebo.

So, it's here that we see an alternative, and that alternative is one that can overcome the regulatory, logistical, financial, and professional barriers. But the real question is, does it do a better job of meeting ethical obligations.

And so, before the pandemic, there were already ongoing several multi-institution adaptive clinical trial platforms that could be used to look at a number of alternative conditions and examine a range of

interventions for them. One of the ones that has picked out a lot of attention because it was pressed into use for COVID was REMAP-CAP which stands for the Randomized, Embedded, Multifactorial Adaptive Platform which had been established to conduct treatments evaluation for Community acquired pneumonia and it was quickly pivoted to using this platform to test drugs for COVID and the advantage of that was the institutions were already on board. They already had approval for the use of the novel methodologies here, they had physicians in the hospitals who had relationships with their clinicians who were used to the notion that this was the right thing to do, for Community Acquired Pneumonia. And during the process of dealing with COVID a number of additional adaptive trial programs were developed, including the Solidarity Trial from WHO and the COVID Trial in the UK. So why is this superior on the research side, and here I do draw directly on Dr. Seymour's work.

First, if we look at the existing ideas behind REMAP-CAP you can see, if we have the notion of a pandemic, we can see first the pandemic starts. And then, it takes a little while, while the number of patients admitted to the ICU is rising, the study is designed, the ethic application is submitted, and in Dr. Seymour's experience what would then happen is you've actually reached a peak of the patients in need of the ICU treatment patients who are dying because of the condition and only after that you move over to where the ethics approval is obtained and the study opens at sites. This is not just hypothetical and indeed in the situation we faced with Ebola about five years ago it was only the preventative treatments and the potential curative treatments only were being rolled out towards the end of the pandemic on this downward slope and again what that meant was that particularly as to the preventative things, it would be hard to know whether you were having the effect because the number of people who were being exposed was already reduced.

And this is Dr. Seymour's representation of when an adaptive trial platform exists before a pandemic, all of these things happen can happen more quickly in this early stage of the pandemic before you get that huge upward movement of the number of patients, not needing ICU treatment.

So then, why is it more ethical? We can see logistically why it's superior because you get into the process of providing your interventions in research more quickly, but why is it more ethical. well, it produces the greatest value in terms of knowledge from patients' participation in the trial. And so, if you look think back at what I said about the randomized clinical trials if those are uninformative than the patients who were recruited for those well-meaning trials were not contributing to knowledge, just as those observational studies which were not conducted as trials, but we're just throwing something at the patient let's do something and then we'll write up the results; also weren't contributing to knowledge and that really is part of what we promise patients when we enroll them in research; you're well-meaning being asked to be a participant in research and the reason is, we don't have an answer to something.

Your involvement may help us answer that and that wouldn't have been true in those other formats. The larger size is more informative, the greater speed is means that the benefits are conveyed to other patients more quickly, it can investigate multiple intervention simultaneously, it can be informative about what happens as these interventions are possibly combined with COVID both things which are anti-viral and those which are anti-inflammatory can be used in combination and it can detect intervention effects it incorporates the knowledge immediately the way the trial is set up with the feedback mechanisms and as part of our whole idea about self learning healthcare systems more generally it.

Patients are randomized preferentially to the most promising intervention so over time if you start off with three or four things that you're investigating, some of them are going to move up in terms of effectiveness, some move down. And you have a Bayesian design would predefine statistical triggers for moving proportionately if you start with an even proportion of people in the different interventions.

That you move proportionately towards more those that are showing the greatest effects and at some point you cross a line to say, this is a proven effect and, conversely, this one drops off because it hasn't been proven. And why is this more ethical on the clinical side- it reduces the risk of harm and maximizes the chance of benefit. And this comes about, for a number of reasons in part of the design, but it's important who is involved.

The academic and research physicians are more likely to be familiar with the things that are going to be tested, they have a superior knowledge base compared to the average clinician and they have resources that will be helpful in making sure that the interventions are used in the best way and with the best monitoring support of patients.

The rapid incorporation of the knowledge increases all patients' likelihood of getting the beneficial treatment because your disproportionately moving patients toward that treatment and the movement of the competitor of the control will go towards whatever is the most established effective intervention, instead of just sticking with placebo or, probably at the beginning of the pandemic, the ineffectual standard of care.

So, what are the remaining ethical problems? Convincing practitioners that this is the way to fulfill their ethical obligation of beneficence to patients. I know I don't have quite the depth of frontline experience that Renee has, but I know at USC working with the researchers in trying to convince clinicians was often an appeal thing the notion of enrolling a patient in a trial, even of this sort on a trial platform with all the advantages that I've described.

It wasn't an always an easy sell because of that issue randomization it just felt to clinicians who are not familiar with this, that they were abandoning their obligation to use their clinical judgment, even if they didn't have much to go by. And what they may have had to go by, is their observational experience and so forth, and that's subject to all sorts of heuristic biases, as we know.

So, getting this clinical judgment and the idea of doing something to be replaced by having it be recognized that the more defensible course is to get them get the patients into one of these randomized adaptive trials. The other remaining ethical problem is establishing these trials platforms and having them ready, like everything we do when we're thinking about health crises and pandemics, we forget the lesson about an ounce of prevention being worth more than a pound of cure. We are much more oriented towards rescue than we are towards all the planning that has to go in, of a public health source sort but also, in this case of the research in the research area and having these platforms.

In place being used for current non epidemic conditions but widespread conditions where you're going to have a lot of enrollments.

And having them in high-income countries and in low-income countries on a collaborative basis with that cross fertilization and support of the more resource rich settings helping the others in establishing their part in the platforms is all very important for one we face another global pandemic. So, I thank you very much, and look forward to the discussion.

Frank: Let's move on now and we're going to hear from someone who is known to all of us Ruth Faden, who is the Berman Institute Founder and the Philip Franklin Wagley Professor of Biomedical Ethics at Johns Hopkins University School of Medicine and she's going to talk to us on vaccine ethics in the pandemic.

Ruth, we're so happy you're with us, I quote you when I speak on the topics in obstetrics and we look forward to your perspective on this important topic; welcome Ruth, the floor is yours.

Ruth Faden: I'm going to zero in on vaccines; obviously that's my topic for today. I want to start, though, by reinforcing what Renee and Alex's comments to me illustrate which is this recognition, I think that many of us feel, that bioethics, that our field has never been more relevant nor, more widely recognized as important. And I mean recognized by public health policymakers, by clinicians, by researchers, by the public; I don't think we've ever gotten as much attention.

And I hope it's the case that the contributions that we've actually made to the real world match the reputational benefits that that bioethics has by and large gotten. And I hope in the discussion we can have a conversation about both how much difference we think people in our field have made, and how we would know it, right? So how would we know what will be the metrics; can we tell.

Certainly, listening to Renee my heart breaks and listening to Alex, the best of our analytic a talent.

And yet, at the same time, I just want to leave it out as a challenge right, how will we know how well we have done in addition to spending a long time articulating what that doing could be cashed out to be so I'm going to go through this pretty quickly. I'm going to begin with a few comments about my own experience, which I think is just yet another data point to support the case that bioethics is making a difference, but we shall see. And then I'm going to make some observations, maybe some questions and in the five areas you see here. First, let me start with the WHO process with respect to vaccines

So, for those of you who are not familiar, which is, I think most of us until recently with how the WHO operates with respect to vaccine policy, they had something called the Strategic Advisory Group of Experts on immunization which is referred to as SAGE; I think it's a great acronym that SAGE adopted for itself. SAGE's standing body is composed of people who are experts in the range of relevant vaccine sciences and policy and practice.

It is the convention of SAGE to name a working group when they have a particularly difficult and large issue to take up. That working group is composed of members of the parent group but also additional people who are named to the working group, because they have particular expertise that bears, for example, on the disease or on the vaccine technology so there's a working group on COVID 19 malaria vaccines, for example, and there is now a stage working group on COVID 19 vaccines. That working group was set up in the late spring of 2020 and I was asked to join it and was told that I would be the first ethics person ever to participate in the SAGE process on the inside.

So, that was going to be interesting. Among other things, the working group set up a public health objective subgroup which I had the honor of chairing with Dr. Sonali Kochhar in the beginning and then Saad Omer for the bulk of the time.

We were charged with filling in something new for SAGE. So, I'm not going to go into what COVAX is, we can talk about it in discussion, but I'm assuming that most of us in this conversation know COVAX and its global place in terms of allocation, especially to low- and middle-income countries.

The SAGE process worked orthogonally with COVAX and it was for the first time in the context of this pandemic that stage, which is I've mentioned this, the principal advisory group to who for vaccines and immunizations decided that it needed to have an explicit statement of its underlining value underlying values in order to make global vaccine recommendations.

So, we were charged to come up with a values framework and ethics framework for SAGE, which once adopted, became the values framework for vaccine.

For WHO and then, building on the values framework to develop a roadmap to assist countries, especially low- and middle-income countries that rely on WHO recommendations more than wealthier countries for how to prioritize vaccine during the period when supply constraints are severe to moderate, which remains the case sadly in many parts of the world based on which specific recommendations would be made.

This is just a screenshot of what the values framework goal and principles look like; I won't go through this, but you can see some familiar principles; nothing here will be surprising. It took us a long time to get to the over-arching goal, but it became the sort of the medical for the whole of the work.

And I'll just read that the overarching goal for is for COVID 19 vaccines to contribute significantly to the equitable protection and promotion of human well-being among all the people of the world. What is significant to me about that goal is that it talks, not just about health but about human well-being more broadly as part of what vaccines are supposed to help secure and, obviously, that it speaks about global equity for all the people of the world; and then you see human well being equal respect, global equity, national equity, reciprocity, and legitimacy as the core values commitment.

What happened next is after the values framework went through its approval process through the stage process and up to The Director General, we were then charged to come up with this prioritization roadmap. And the way the prioritization roadmap is designed considers scenarios based on the stage of the epidemic, so community-wide transmission to zero cases, and also availability of supply from severely constrained say, less than 10% of the population, through to 50% coverage.

What I want to illustrate here is the crosstalk between the values framework and the prioritization roadmap; I don't expect you to be able to read this. But basically, for every scenario, for every combination of epidemiological scenario with a supply constraints scenario, there is a listing of the groups that are prioritized in rank order and in each of these groupings, there is a justification back to the values framework, so there is a legend that works backwards to the values framework, and then the values framework forward back into the prioritization roadmap.

In discussion, I'm happy to talk about whether to what extent this is actually assisting countries as far as we can tell and also talk about the efforts and energies that have gone into thinking, whether and how to revise the framework as the epidemic changes and vaccine supply changes as well

That's by way of backdrop just to tell you where I'm coming from and to add another data point where we could argue anyway that bioethics is finding its way into, in this case global public health policy, and I

should add that there are other committees of the WHO working groups, tasked with dealing with ethical issues in the pandemic and with reporting out guidance through the WHO and also in the professional literature.

So, here's my five topics again what I want to bring for us really quickly: pandemic justice, vaccine R&D, regulatory science, legitimacy of state action, and public health reality. First pandemic justice, and this is a territory where I'll come to at the end, but where I would say, we have had Zero impact, but the question is whether we could, as people who work on ethics and justice theory generally have been expected to have any impact basically going forward, we need a special understanding.

Of the demands of global justice in a pandemic sound oh man, I have come to talk about this is pandemic justice, we need a new way of thinking about pandemic justice we need hard stopping rules for vaccine nationalism or but we need hard stuffing rules, we need to think about global equity differently. We have been thinking about global equity in terms of a very critical metrics vaccine doses per hundred thousand population and that's the way the trackers UNESCO and Our World data report vaccine equity visualizing for us and they're important work.

But it's not only the doses that are critical- its which vaccine products are available to whom around the world. We have known from early days suspected from early days and have known for some time that these vaccines are not equal in terms of their effectiveness and also, they are not equal in terms of their adverse event profiles and we need to be thinking about global equity from the standpoint of vaccine products, as well as vaccine doses. And going forward we need clear global ground rules for global obligations to prevent, prepare, and respond to the next pandemic. An awful lot of energy is going into the space right now, but there's no shortage of issues that continue to need to be worked on so next, please.

This is a whirlwind tour so I'm going to go quickly next; space to stop and visit is vaccine R&D, and here I want to make 2 points really; the first is that, as we are thinking through the ethics of the research plan that vaccine developers are putting to gather and submitting to stringent regulatory authorities, like the EMA and the FDA it's going to be increasingly critical to recognize that the ethics of who and where, who is involved in the trials or otherwise, in the evaluation R amp D and where the trials are conducted will have significant impact has had significant impact on equity and vaccine access there's a direct line between the evidence is generated early on and who gets access to vaccine when vaccine is rolled out.

I want to just illustrate this by a quick segue as Frank mentioned, and thank you for the kind words I've been worried with many wonderful colleagues over the years, around equity in evidence for public health and clinical management in pregnancy. This is the commit tracker, commitglobal.org, that some my entire colleagues with Karen and Kelly crew and Aaron have working on for months now, and this tracker is ongoing it monitors for over 200 countries in the world what the policies are for access to vaccine by pregnant women.

We update this on a cyclical basis every three weeks and we also do this specific to particular vaccine products, what I want to draw your attention right now is even today is fairly recently people refresh there are 40 countries in the world that effectively deny pregnant women vaccine that have vaccine available right now and that's, despite the fact, and I would turn to Frank and others who are more directly expert in the space, despite the fact that the evidence base is becoming almost incontrovertible

that pregnant women face elevated risk of severe disease, severe outcomes, with COVID 19 disease, as do of their offspring.

So, despite the evidence going in a very devastating direction for pregnant women, we still have 40 countries that are not allowing pregnant women to be vaccinated. At least in some cases there is sufficient supply to do so, and the reason that many of these countries are giving for not vaccinating and not allowing vaccination in pregnant women the absence of evidence, the absence of developmental and reproductive ecology studies and the scientific known sub studies with pregnant women have reported out anything; many have never been conducted

Again, this is to illustrate that direct connection between how R&D happens, who's in the evaluation plan for a new vaccine in an emergency public health epidemic context and who gets access to those vaccines; older adults were very well addressed as a priority group in the US, supported Pfizer and Moderna and J&J age trials, they are absent entirely from the initial work done to evaluate the Chinese vaccines that enrolled no one over 60.

So, we have to think globally, as well as nationally, in terms of needing to link the ethics of R&D, design and development, with its implications for equity down the road.

The other point I also want to make here is that the ethical issues and R&D don't end when the initial trial design is put in place and implemented. I'm sure everybody here remembers the controversies around unblinding in January, especially and in February as vaccine became available; Astra Zeneca in the UK context and the Pfizer and the jury trials be unblinded given the fact that vaccine was now being rolled out to population groups at scale.

There are also evolving research questions as the pandemic progresses, with respect to getting an evidence base and then boosters and federal outlets and finally, there are a bunch of ethical issues around the evaluation of next generation vaccines. It would be interesting to have a conversation about adaptive clinical trials as Alex was presenting them this context it's getting an awful lot of attention around the evaluation of next generation vaccines as well.

This connects up to a territory that I think is increasingly important, and that we have spent far less time I think in bioethics thinking about and that's the ethics of regulatory science. The use of, and it's kind of connected line also to the ethics of public health policy; it's all of a piece the prominent role of that emergency use authorization as a mechanism for the FDA and its analog with the EMA With the AMA and also at the WHO and in national and regional regulatory authorities globally, the role of the EUA called different things in different contexts in putting forward it's something like 500 some odd therapeutics, diagnostics, and of course the vaccines has really caused all kinds of challenges with respect to research ethics, also with respect, more importantly, to public trust. I'm going to stick with vaccines right now evidence is emerging, about the extent to which it's not great evidence, but it's coming up the extent to which the some of the people who have not yet been vaccinated or have only recently been vaccinated in response to mandate, some of their concern was actually linked to not wanting to be vaccinated until a vaccine received for regulatory approval.

A related and very important public policy lever, has been the implementation of employer-based mandates both by the employer and now with the force of the Biden administration's regulatory requirement about to be put into place where there was hesitance, no I won't use that term has been

none, there were there were many institutions, employers and including the military that wanted to wait until the vaccine had gotten for regulatory approval before imposing a mandate. There is just a real conceptual and ethics sort of confusion about what it means for a product to have quote “merely only emergency use or the relation, while at the same time being rolled out and put into the arms of 10s of millions of people around the world.” How are we supposed to think about this, how should we think about this from an ethics and public policy perspective.

This takes me, of course, to a whole set of ethics issues and vaccine policy having to do with the legitimacy of state action to mandate vaccines in one context to another, and just want to make two quick points, which is that when we think about these issues we need to be thinking about them, not only in terms of the way vaccine mandates or vaccine passes of one sort or another intrude on and arguably are justifiable intrusions on bodily integrity and privacy, but also freedom of movement, association and religion; we have to think broadly and lot more work needs to be done cashing out what kind of intrusion into each of these called civil liberties right now is at stake with vaccine mandates in different contexts. I want to underscore, by the way for some who have thought that this was a singularly American obsession around respect for autonomy and individual liberty, I’m sure everybody here is familiar with the turmoil that is going on in Germany and France in Greece, and most recently in Italy vaccine mandates, imposed by the government and the introduction of vaccine passes in Israel as well, but I think right now the battlegrounds is in Europe and, especially, and in the southern states in Europe. So, there's that to think about and with respect to vaccine mandates, I want to emphasize that it's really important to think about them in principle, but also in practice.

And there is again also wanting a building evidence base I’m sure everybody here is familiar with it, that, in fact, a vaccine mandates quote work that we are seeing sizable numbers of people become vaccinated in response to employer-based mandates, even though the rhetoric in prospect, was that huge numbers and the workforce would refuse and the headlines, for example what is happening in Chicago with respect to the police force and by and large mandates quote “work” that does not mean alone that it is sufficient to justify them but it's important to fit that to fit that in there.

Finally, just a couple comments on vaccine ethics and vaccine reality, and I think the scores a little bit connects up to what Alex is talking about, but not maybe exactly we have this maximum ethics right and good ethics demands good facts only in the context of a pandemic; we don't have good facts right.

Renee can speak to this and did already as well, we don't have facts, we don't have good facts right now; in fact, we don't know anything with certainty we had just have an enormous amount of uncertainty and it is the fact that policymakers have to make decisions, clinicians have to make decisions about how to proceed with vaccines, in the absence of a lot of really critical evidence about the pandemic. Now we knew enough, for example, very early on, about something that Renee did show a slide on which is the association, the really stark association, between severe disease and death and age and this pandemic.

That resulted in an awful lot of conversation about how to think about age in the context of vaccine policy in this allocation scarcity period and the pandemic in which most much of the world still remains, and if we have time and conversation we can talk about the challenges that the advisory committee on immunization practices faced and trying to understand and square some conception of equity in relation to systematic disadvantage and preexisting systematic disadvantage as well as ongoing with respect to the burden to the pandemic and the disproportionate burden of the pandemic in terms of its health consequences on older people. And finally, I just want to make a point about how easy it is for people

who get invested in trying to think through the ethics of a problem, whether it's what to do with ventilators in the case of scarcity, or what to do with vaccines in the case of scarcity, the end up with overly complicated ethics guidance that ends up for collapsing on its face.

We saw this in in the US in January, February and March with the 50 states responding in very different ways, with different kinds of roles and prioritization that kind of defied comment or ordinary understanding. And we can contrast that with some of the simple strategies that were adopted in other countries that it first seemed less, perhaps, equitable but ended up arguably in a better place, and I'm thinking about the UK is very simple age descending strategy or when they on.

With the exception of healthcare workers, high-risk healthcare workers, which were at the very top of the list they went age descending right in the UK from their oldest old 80 plus down as a way of more efficiently distributing and they're distributing their vaccine and other European countries and other parts of the world followed suit.

So, there's my sort of world wind tour of some ethical challenges and issues in the vaccine space last slide please, I want to close by returning to global inequities and vaccine access that tragically persist and the need for a new pandemic justice way of understanding how to think about the world. This is a fairly recent heat map from our world and data, I think probably everybody here is well familiar with it, but it seems to me that we could clearly conclude, along with the question I started with, that the work of people in ethics and global health and ethics and global justice didn't have any impact in this pandemic. Now you could also say, in fairness to our little tiny field and a sort of a bunch of arcane scholars like me where I put myself, that the geopolitical forces and the national forces at play that are responsible, along with the global structural unfair fair patterns and power, an advantage that defines the global order that these forces are so enormously strong that you know even a perfect theory of pandemic justice is not going to make a dent.

I think that would be that would be fair, but at the same time I don't think it gets us off the hook. I don't think when and when we do our own after-action assessments of how much contribution our field and defines our incredibly hard-working practitioners in the field and policy advisors in the field have done, I think we have to just say squarely, we have to figure out a better way to contribute to global justice in vaccine access going forward. So, I'll stop with that. Thank you, Frank and everyone.

Frank: Ruth this was wonderful we have so much to discuss I'm going to take the liberty of making the first comment because there's so much, I agree with you Ruth and in this especially poignant area of pregnant women.

And then we'll go to Michael Katz, our most senior Member, will let him have the floor and then, the floor is open to everyone.

One area that I know Ruth is the theory of pregnant women, is so important because there are high-risk group and they haven't taken up the vaccine, the latest figures, only about 40% nationwide have accepted the vaccine and going to Renee's point and black and Hispanic women it's much less than that.

One area that has this been neglected, is what Larry McCullough and myself call physician hesitancy, not patient hesitancy, but physician hesitancy to recommend the vaccine. And there are three core areas of

this and Ruth you touched on one of them; they are clinical misapplications of important aspects of professionalism, one is therapeutic nihilism. This is an important aspect of medicine; it has its basis from the time of Hippocrates where we avoid doing bad things to patients.

And it's especially true in pregnancy; we're ignorant of so much, we have the examples of Thalidomide and DES, and we need to be humble; I can give many examples, but it's misapplied here.

The demand for too much information, randomized clinical trials, and Ruth you gave the example 40 countries today won't permit the vaccine, they want more information. This is a mistake. I agree with you, Ruth, in your writings that they should have been admitted to the randomized clinical trials, but the fact is, the fact is, you make clinical judgments based on the best available information. Alex, the sad truth is in obstetrics unlike many other fields, most of the decisions we make are not based on randomized clinical trials that's the state of the art today.

In clinical obstetrics but good or bad that that's the reality and we make our judgments based on the net clinical benefit versus the net harm. And that the net clinical benefit is overwhelming of taking the vaccine.

We don't have time to go into a clinical discourse there no documented harms to the pregnant woman the fetal patient and the medical benefits are overwhelming; therapeutic nihilism doesn't apply.

Shared decision making: this is so important in clinical obstetrics but it's not a universal dogma. When evidence is overwhelming, we make recommendations. If someone has an acute appendicitis I hope the surgeon, is going to say you need to do an appendectomy.

If I have a patient with acute fetal distress, I tell my residents you don't offer a caesarean, you recommend it; it's a misapplication to say that you use shared decision making, if it's defined is offering not just recommending in all clinical situations. In the third I'm going very quickly. The dogma these such an important principle of respect for autonomy so important. One of the bedrocks of ethics that Ruth and Alex you've pioneered for so many years, but what do we know.

That women have reported and our group has documented this, the most important factor in a woman's decision is what the physician recommends and to just brush aside that the physician's recommendation is unimportant is a misapplication of respect for autonomy.

What I'm saying is when the evidence is decisive, we need to make recommendations now, why is this important our professional societies, let us down.

They were at least six months behind the realm here and they should have come forward with this much, much earlier and I think this has somewhat hurt us here. There's so much more to discuss Michael your hand was up next and then we'll open this up.

Michael Katz: Thank you, this is, I attend this meeting, because I am a member of the Committee on Human Rights of the National Academies and the issue of human rights and ethics is obviously very closely related.

And the you might say that twin issues but they're not identical twins.

My impression is that the concept of triage was developed during the Second World War, it may have been done earlier but that's as far as my own memory and experience. And the issue of triage does require some moral violations so we say the issues that those who are on the safely injured can be left alone to wait, those who are extremely severely injured and probably will die or ignored and the middle ones are cared for. How do we did deal with ethics like with the issue of ethics under those circumstances?

Frank: Renee, you want to tackle this first.

Renee: Thank you, Michael I think one of the issues with COVID is that, yes, as frontline clinicians and emphasis, we felt like we were in a war-like situation. However, the illness that we were dealing with didn't respond to those cut and dry categories of emergency preparedness that we were taught.

So that that ability for us to see a person and say that they don't deserve any help, leave them alone was a misnomer, and we quickly figured that out. One of our patients that we cared for spent 65 days in an ICU when we were trying to figure out whether it was ethical or not to have anesthesia and ENT perform tracheostomy. The patient was 49 years old and at day 75 got a tracheostomy and at day 80 walked out of our hospital back to her 14-year-old son.

So, I think that is one of the problems and we quickly moved away from calling these triage committees so you notice, I called them response teams. And those teams were really there to help bring what we knew was ever changing to the bedside into the clinician who had to make these decisions. So, resource allocation in this regard didn't follow the usual war-like emergency preparedness and required us to bring a lot more humanity to the bedside and to the clinicians who were making those decisions.

Michael: I accept your point absolutely except there was a situation where there was a limited number of respirators, and that is much more like the war situation beyond your control because you couldn't just create them.

Frank: Michael Thank you Susan Wolf is next, please.

Susan M. Wolf: Yes, thank you. I actually co-chair the Minnesota COVID ethics collaborative which sounds similar Renee to what you were describing in New York, and we are in the throes of the fourth surge we have multiple institutions reporting zero or near zero staffed ICU beds available.

And what I'm seeing, and I wonder whether, others are seeing this in other contexts, is a what to me is a very concerning and fundamental challenge to patients' regional authority and the way it's arising is, we have no declared crisis standards of care, in fact, our governor's emergency powers are no longer in effect.

But clinicians are so stressed that they are invoking the cluster of concepts- feudal care, potentially inappropriate care, non-beneficial care- many of you are familiar with this cluster of concepts to basically say enough already we're going to decide who gets what treatments and who gets what treatment and who remains in the ICU. I worry about this and I worry about its persistence beyond times of stress as a real shift in the needle toward more authority, solo, among the clinicians and less decisionional engagement and authority among patients, so I wonder if others are seeing that and have developed approaches, starting with you Renee.

Renee: It Susan I'm glad that you brought that up because that was our biggest fear that the dirty F word of futility was going to be involved. One thing I do want to say to you is that we did have to have a community approach among hospitals. And that's one of the things that came out of this was that the private hospitals needed to help the state and city hospitals and we had to get together to load these patients across health systems and across regions, so that we could get some resources that was one of the first things. That really did help some of that clinician distress. But the second thing that you're bringing up is the voice of the patient and the voice of the family. We didn't list chaplaincy, social work, to begin to have conversations with family and make people more human. One of the things that I worried about was exactly as you said, as used or tried to use as Ruth said these complicated things could we just keep it simple. And by keeping it simple really go back to what we would do in normal circumstances, even though this was abnormal but really look at the totality of the patients.

When things got the worst, we were getting 55 calls a day, particularly at night, from our younger residents, younger clinicians, advanced practice providers, we stopped that. In order for these decisions to be made, they needed to be made by the senior attendant and senior clinicians The second thing is that, when we got through the second surge, we went back to re-educate and I'm proud to say that, a year after, when we look at consultations and when we look at palliative care and ethics did get a lot more calls, but we are not seeing that unilateral I'm going to mean futility. In fact, what we are seeing from our clinicians is going back to that humanism, a lot of reflective writing a lot of pictures of patients, of what they look like before.

A lot of the discussions of going around and having patients come back for short rounds, so I believe, like Ruth said, that resilience comes in and humanity did show, so we didn't have the shift towards death squads like we were scared of; instead, more what we had was a shift back to looking at empathy and resilience.

Frank: Excellent. We have here Alto Charo and then Ellen, please.

Alta Charo: I know Ruth you know that I share your long-standing interest on the role of research ethics and the inclusion of pregnant women.

In this particular situation, though, and referencing both Renee and Alex as well, I find myself wondering how we can in fact do better than we did because if my instincts are right, the frequency of pregnancy, as well as all the other comorbidities and situational vulnerabilities, are going to be greatest in places in

the world like the less developed countries in the southern hemisphere. So those are the places where you really need the most to get pregnant women into trials and into vaccines and yet we have a long history of the perception or reality of exploitation, where the trials go on in those places precisely because you have a higher density of people who are eligible, and yet the therapies wind up going to the northern hemisphere and that would have happened here again because of vaccine availability.

So, I find myself struggling to figure out how when I follow through on the suggestion and avoid some of these traps we fallen into before on kind of research equity ethics in the construction of trials.

Ruth: Okay, so a couple of things Alta; actually, we had the prescription for how to prevent this already right, there I won't go through the details, but there was a very sort of aggressive effort, and I was grateful to be part of it, that came out with report, like just before COVID broke, with how we could avoid being in this situation again with respect to pregnant women and none of it was followed, basically. Almost none of it; and let me explain a little bit about what I mean. First of all, DART studies are done with non-human beings; they are the clinical studies will put aside for a moment the ethics of research with non-human animals but, for whatever reason, and there's debate about this in the value of it it's kind of a regulatory impasse globally. That unless DART studies are done in, and I will say in the drug spaces well regulators are hesitant to go forward and certainly public health policy makers in the backseat space hesitant to go forward, unless the DART studies are okay, the DART studies should have been done after the very first phase one studies you got enough success from phase one to come forward with a vaccine candidate, the DART studies should have started; they take a while, the animals have to reproduce multiple cycles, they were not done. Okay, they were not done then.

And, as a consequence that evidence base, limited though it was, was not available to the FDA, to the CDC, to the EMA, to the World Bank to all the countries of the world at the time that vaccine started to get you UEA approval. The next piece, and I hope don't come across this as saying that pregnant women should have been included in the very first trials. I don't think ethically we could have defended that; but what we could have done, and this was also a very clear recommendation and much discussed in the community is as the phase two three studies were going forward, and it was looking good on the general sort of reactive patterns right and we were getting more evidence that pregnant women globally were doing really badly from the infection, we could have started, we could add the community of people doing this work and, more importantly, the vaccine manufacturers and companies could have begun and could have ethically proceeded with sub-studies with pregnant women, you can't ever get enough pregnant women, to look at advocacy that you're going to have to infer from other adults. But just to look at safety that could have started; this was preventable right the evidence gap that leaving of pregnant women behind yet again globally was preventable.

On your bigger question, about also your bigger comment, about the conundrum with respect to do the trials and low-income countries, you know the canard the horrible global injustice that we've been dealing with and struggling with forever, this was a kind of flipped dynamic in the sense that the outbreaks were fast and furious, first, right China, the US Europe, right. The evidence base about consequences and pregnancy emerged first it's true, we have evidence stamped with respect to pregnant women in low- and middle-income countries, which is tragic. But it's a reasonable inference right that if it's bad for pregnant women in high-tech contexts, it's going to be worse for pregnant women that don't have in communities which have much less resources in the way of intensive medical

care just stands to reason. You don't need to kind of have evidence, and this is frank point you don't need to have evidence to go with that inference. this is a big issue at the country for low-income countries we're fighting for it to have trials in some cases with the understanding that with trials, they hoped would come access to product. And so, neither happen in most cases, right; there was neither trials done nor access available, so I think the picture is it's really bound up in the bigger questions why we in the wealthy countries that got to go shopping for a vaccine before other countries got to even go in the store to take that like metaphor is partly because we own the R& D and we conducted the R&D and our own populations.

Alex: To me, I see a reflection of part of the problem that I was identifying, which is that sometimes an ethical presumption actually has operated traditionally on a protective side when it is actually, less attractive. And joined with that is the fact of lack of accountability for statistical deaths, that is if women who are not vaccinated and with more complicated pregnancies, for which they die or they just died from the illness and the pregnancy goes with them, or they or they die in childbirth and they leave an orphan who's doesn't get the advantage that they would have had from circulating antibodies in the mother, if she got vaccinated. The people making those decisions are not accountable for those losses; what they're afraid of is being held accountable for women who have and their children who have bad results in the research and if there isn't a way of creating the accountability on the statistical deaths and having them take that into account, having everyone expect them to take that into account, then you don't have the impetus, you have quite the opposite and it's just like physicians thinking well I'm doing something I don't know if it'll work but I'm the least doing something I want to do good, so what I'm doing should be regarded as good because I want it to be beneficial rather than looking at the alternative of an adaptive clinical trial which embeds their clinical decisions into a study, which is going to give overall, on average, a better result for their patient.

Ellen: Well, mine's going to feel a little minor after this. You know 30 years ago, the Academy was addressing the issue of research involving women and had a hard time dealing with the issue of pregnant women back down, I will tell you that a workshop was just approved on research involving pregnant women and the last week or so and I, you know and you know whether this will actually lead us to be able to get some traction and move forward, I think it's hard to say, but I just but what we've heard here is why it is such a tragedy that pregnant women aren't getting this vaccine and why they and their children are dying.

Ruth: So true, I couldn't agree more, and just really quick hopeful note, I was part of another national academies panel on EUA, the FDA and heard for the first time I heard in a in a public setting someone from the biologics branch saying you know, we know we made a mistake on pregnant women and that's a separate set of issues, but that they know need to do differently. Going forward and that's just not here it's everywhere, I think there's finally, a recognition, because this has been was a disaster and Ebola but now what's it like a more in your face to faster.

Frank: The good answer is everyone now agrees and all the professional organizations are on board a strong recommendation to pregnant women to take the vaccine, finally, everyone is on board so there's hope here. Jeremy, any comments insights please you've been on the front line to any thoughts, you have.

Jeremy Sugarman: And I thought, these were three really great presentations that are sort of on that, on the cutting edge of some of the things we've been thinking about in the pandemic and I would love to for each of the speakers, think about what we need to do next, in terms of policy and conceptual work to reimagine what we do in sort of daily bioethics and human rights issues. What's a pandemic taught us about you know to force some rethinking in different ways, and I think each of you have touched on that briefly, but I think we may benefit from making that explicit in a way.

Frank: Renee what you want to take the first step is that.

Renee: I think one of the things that we really have to look at and I'm hoping that my talk talks about is that community engagement. Yes, there's a focus too much on autonomy, but there isn't much of a focus, at least in clinical practical ethics, on social justice and the voice of the Community. And I think this taught us, if anything, that bioethics needs to do in policy is to be more much more community-based. Even as I share all of our talks about talking about pregnant women, getting the vaccination, and certainly support all of the work that Frank and everyone has done that, I look at my communities that I'm in that have less access and wonder how we make that occur if we don't get their voice, if we don't get into their churches, if we don't dispel the myths, and if we don't stop thinking about that every time a community doesn't accept something it's because they don't trust us or it's about to Tuskegee and Willowbrook.

So, I'm hoping that, as we move forward, we go back into the community share some of the evidence and the data points that we talked about and get their honest reflection of what could have been.

Frank: Renee, excellent; Alex what would you like to add?

Alex: Well, I first say I entirely agree with Renee's emphasis I would say it's three things and they're interconnected. The first is, I think we learned, particularly when it came to issues of hesitancy around Public Health interventions, resistance to that, as well as vaccines, but also in understanding what was going on with clinical decision-making in those hospitals that had reached a breaking point and were making hard decisions. The importance of having the honest and frank conversations with patients. It isn't just the physician's problem it's our systems problem, we don't support that work, we don't create enough people who can do it, which is obviously not just physicians but nurses, nurse practitioners, and other people who were doing primary healthcare. With that communication, and I don't mean just

telling, but communicating, listening back and forth, concerns that people have can be address confusion.

As Ruth mentioned what is it the EUA mean; does that mean they applied a low standard, they just let anything happen or what does it actually mean, why is it different than a full license and so forth. All of those things are very important in physicians in where they exist are a major source of information.

To go to Renee's, point a second thing I would say is that there is a concern about the lack of healthcare coverage for so many people- that's rural populations, as our rural health systems fall apart and hospitals close, and obviously people in our inner cities where there is a low level of number of physicians per patient, many of those physicians are highly trusted, but they're also spread very thin. That's another thing that we obviously learn from this that is so important.

And finally, I think we need to make sure that frontline clinicians get information in the sources they read, not academic journals, but in the sources, they read that will help them and, of course, help all our medical students and future medical students right now to be fully conversant with the basic ideas of public health and how to talk about them, because it is a different mindset. And, and the whole notion that the Academy had all these reports on crisis standards of care, the average system wasn't ready, but certainly the average clinician had never really heard about this, was unfamiliar with it, and of course, I would hope that they would also get better information about how to evaluate things like these adaptive trials that would embed their clinical decisions and within that, they would find that the thing that they might want to try is actually being tested in a way which is quickly responsive, not waiting months and months and months for something. And that means we have to support those adaptive platforms and have them up and operating on contemporary problems, ready to be used for the pandemic or other healthcare crisis problem when we need them. Those are my lessons.

Frank: Alex, excellent. Ruth your turn.

Ruth: So, thank you, Jeremy that's like an easy question and I've been thinking a lot about it and none of these will be a surprise for people who know me well, first, I think that. We have had conversations in bioethics for a really long time about the fact that we have to spend more time thinking about justice and justice considerations and, of course, so much has happened in the past 21 months to make that clear. I think if we if we needed to punctuate that point, we have as the world experienced it, so I would say, the first thing is that we have to add bioethics going forward just make the recognition in reality of structural injustice, not just the sort of backdrop, yes, we know that it's there and it's terrible and then go work on a very small point.

Whatever issue it is that we are working on, we have to be thinking about it and embedded in the implications of the background structural injustices, national or global, that that issue is playing itself out on, and also the implications of whatever work we do for mitigating or exacerbating these pre-existing structural injustices. So, for me that's like a huge one. And, a second is another sort of thing we said, for a long time in in our field that I think again got punctuated and Alex and Renee's talks underscore this is whatever silos between the people who are interested in the ethics of science and the people who are

interested in R&D and the people who are interested in clinical ethics and the people who are interested in public health policy.

It does not work to separate these, at least in the context of responding to and planning for epidemic pandemic it just doesn't work. There the implications of one for the other, you can use the pregnant women example you could use a gazillion examples you can to show that decisions that are made, what you know, in the context is what makes sense in clinical practice what makes sense in the context of

R&D have profound implications, one for the other and they both have profound implications for public health policy and how people actually behave in the real world, so the need to step back and attack these problems from the broadest possible perspective. I am really tired of conversations about controlled trials, for example, without understanding sort of the wider context in which vaccine R&D occurs and the implications of that for clinical practice and for public health policy, so can take our fine points, and we need to push them back into this wider integrated perspective. And then, finally, I would say that in line, Renee, with what you were sort of extolling us to consider community engagement, it breaks my heart to say this, but I don't think I really understand right. For all the efforts that I've been engaged in trying to do a better job of transparency and accountability and community engagement what that actually means and how to make it happen. Certainly not, in the midst of a pandemic, but also, even in prospect for pandemic planning and preparedness and mindful, for example, of what the National Academy's wonderful committee on vaccine guidance- I forgotten it's official title but its report came out like in August and September - fabulous people, many of our colleagues on it and they held hearings and they took testimony and that was really great, and I know they responded to that testimony but who testifies who sends in comments to a national academies' draft report. And what does that mean, so I'm stuck. And I know there's been an awful lot of work, and I would hope that going forward to be an awful lot more work both trying to understand what we mean by engagement; it is in every report, it's in every paper each, it's in everything. And what moral forces it serves and how you actually do it in a way that serves those moral objectives.

Frank: Ruth wonderful. We have time for one last comment to Charles.

Charles Halpern: I am one of the longest serving Members of the Academy; I was elected to membership many years ago, and I just wanted what Ruth said triggered this thought for me is that the NAM could be doing a lot more about this problem.

We only have less than 25 people in this meeting, which I think is one of extraordinary importance, and I would like each of you 25 to think about ways that we can change that situation. The conversation about a more sophisticated discussion of public health and its ethical dimensions, particularly in the new globalized reality in which the COVID crisis has thrust us.

And, for example, I would encourage each of the members of this discussion to go back and take a look at the process for choosing members in the Academy. You will be shocked how few members there are, who are real public health people, it's startling; I've been working on the climate side in the area where that is the quote global crisis for the public health future, we have fewer than 1% of our members who have specialized expertise in that area- that's impossible. So those of us who are on this call, might think

about simply making it their business to figure out this arcane system for choosing members and to play it with sophistication and let's go for 10 new public health members and the list of 150 Members who are circulated next year; never happened before isn't it time for it now, thanks.

Frank: Charles, you're right; there are only 25 people here, but I think each one of us have benefited from the slides and how have learned a lot and gotten so much out of it. Michael, you're our most senior member, I thank you for being with us, and I thank each of you.