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Welcome to Conversations on Health Care with Mark Masselli and Margaret Flinter. A show where we speak to the top thought leaders in health innovation, health policy, care delivery and the great minds who are shaping the health care of the future.

This week Mark and Margaret speak with former FDA Commissioner Dr. Scott Gottlieb. He's just released an in-depth analysis of the nation's failures in response to the pandemic, uncontrolled spread, why COVID-19 crushed us and how we can defeat the next pandemic. He examines the inherent weaknesses and the CDC's ability to respond to a crisis of this magnitude, the need for more widely deployed at-home testing, better surveillance diagnostics and the promising discoveries in vaccines and therapeutics coming down the pike.

Lori Robertson also checks in, Managing Editor of FactCheck.org looks at misstatements spoken about health policy in the public domain, separating the fake from the facts. We end with a bright idea that's improving health and wellbeing in everyday lives. If you have comments, please email us at cheradio@che1.com or find us on Facebook, Twitter, or wherever you listen to podcast. You can ask Alexa to play the program. Now, stay tuned for our interview with Dr. Scott Gottlieb here on Conversations on Health Care.

Mark Masselli:

We're speaking today with Dr. Scott Gottlieb, physician and 23rd, Commissioner of the US Food and Drug Administration from 2017 to 2019. Dr. Gottlieb is a senior fellow at the American Enterprise Institute. He also serves on the board of Pfizer, which produced the first approved vaccine for COVID 19.

Margaret Flinter:

Dr. Gottlieb is the author of Uncontrolled Spread: Why COVID-19 Crushed Us and How We Can Defeat the Next Pandemic, which just debut on the New York Times bestseller list. He's also a medical contributor to CNBC. Dr. Gottlieb, welcome to Conversations on Health Care.

Dr. Scott Gottlieb:

Thanks for having me here today.

Mark Masselli:

Dr. Gottlieb, your book, Uncontrolled Spread, congratulations debut a week ago. We're marking the same time 700,000 American deaths from COVID-19. We're still being crushed by this virus. But analysts are predicting the pandemic phase will end next year shifting from the pandemic to endemic. There was some promising news this last week on a New Oral Therapeutic produced by Merck that reduces illness and hospitalizations by 50% in infected people. You're calling this a new development, a game changer. Tell us more about the drug and your thoughts on why America might not be able to take full advantage of the drug, because we're simply not buying enough doses.

Dr. Scott Gottlieb:

Yeah, look, this is a orally available drug from Merck, it's probably the most profound treatment effect that I've seen from a pill in the treatment of any respiratory pathogen, 50% reduction in the risk of hospitalization and death. This was a population of patients that it was tested in who had risk factors for COVID. They had one or more risk factors for COVID, and they were also symptomatic at the time that the drug was administered, so they had to be within five days of the onset of symptoms. They had advanced disease, they had already progressed in the course of illness made to these patients, and so it was a high risk population, yet you still saw very profound treatment effect.

The problem is that we're just not going to have enough of it. Merck said that they will be able to make 10 million doses between now and the end of the year. But the US has procured so far only 1.7 million doses, and they have an option on some additional doses, but not a lot. We do know that some portion and maybe some good portion of that 10 million has been pledged outside the US. To give you a sort of a basis of comparison, 1.7 million doses might have been enough to cover us for a month, Delta wave. If this drug was sort of approved for the targeted population, it's approved more broadly than it wouldn't have even covered a month the Delta wave probably would have covered three weeks of the Delta wave.

To give you another basis of comparison, we've stockpiled somewhere between 50 to 80 million doses of flu medicines in preparation for a feared pandemic flu. We procured 1.7 million doses of this Coronavirus drug in the setting of a raging Coronavirus pandemic and we've stockpiled upwards of 80 million doses of a flu drug for a flu pandemic that we fear but it hasn't arrived yet. There's sort of a mismatch between what we what we need in the setting of this pandemic and what we ultimately procured. There's probably things we could have done much earlier to ramp up manufacturing of this drug to have more available now, but it's too late at this point. There's not much you're going to be able to do in the near term.

It just, it sort of underscores the lack of preparation. This is another point I'll get back to in the book, not having the reserve capacity to scale the production of some of the therapeutics and countermeasures that you're going to need in a setting of pandemic. We just don't have available capacity in this country that's ready to go that's being kept as sort of a hot base of preparedness.

Margaret Flinter:

Well, Dr. Gottlieb in your book, Uncontrolled Spread, you note that America was failed by not only some bad political decisions, but also an ill prepared public health infrastructure that you described as the fog of viral war. We know there were missteps along the pandemic trajectory, and particularly you call out some CDC, which we've all

long considered the gold standard for public health. But you point to issues in the inherent culture at CDC that contributed to this and that it just wasn't structurally designed for rapid response to a large scale crisis. Share some of that analysis with us.

Dr. Scott Gottlieb:

Look, the CDC is the gold standard for public health, there's no question about that. But there is a difference between the CDC's sort of normal function and being able to respond to a public health crisis of this magnitude having a logistical capacity and the ability to gather and do real time analytical work to inform policy decisions that need to be made in the moment. CDC is sort of a deeply analytical organization, high science organization, accustomed to doing very exquisite scientific analyses to try to be the definitive word on a public health question, not the first order on a public health question. In the setting of a crisis like this, when you need to have a capacity to mount a very large, coordinated logistical response, for example, being able to develop and deploy massive screening, massive testing that was required early on in the pandemic, or you need the ability to gather real time data and do very rapid analysis to inform decisions like what are the modes of transmission? What are the geographic and social compartments in society where the virus is spreading? How do we take steps to reduce transmission? Should we stand three feet apart or six feet apart or 10 feet apart? What's the right distancing? How effective are masks going to be? Answering those critical questions, w really didn't have an organization capable of doing that, in sort of the real time fashion that was required for this crisis.

CDC just didn't have the resources, the culture, the aptitude to do that. It's not an argument for sort of building a new organization, building a new agency. I think what we need to do going forward and thinking about this is how do we build those capabilities into CDC. I think there was a sort of a presumption that CDC had this ball and they were able to discharge this mission, it just was never going to be the case, and policymakers were slow to realize that.

Margaret Flinter:

Dr. Gottlieb, the subtitle for another book on this might be what we would have done and when we would have done it if we'd only known and really thought things through. You talk a bit about in your book, the CDC first attempted a COVID test failing and having to go back to square one with what that cost in terms of time and lives.

We recently had Harvard's Dr. Michael Mina on the show, and he says, if we'd simply focused on providing all Americans with simple athome rapid tests, we could have gotten out in front of the pandemic much earlier, and instead we focused on the more complex PCR tests. Is that your conclusion as well that --- and we say this is a organization that put enormous effort into doing mass testing clinics with PCR, should we really have been focused on the rapid test right from the

start, would that have made an appreciable difference?

Dr. Scott Gottlieb:

Yeah, we needed an all the above approach right from the outset. I talked a lot about the testing failures in the book and get into a lot of detail of why we didn't have tests that we could deploy more widely. But at some point in January, someone needed to recognize that this could become a global pandemic and we needed to get testing ramped up. Not just the diagnostic test kits that can run on a complex PCR machines that are inside labs, but also the point of care tests, because there's a long lead time to actually developing those tests. We didn't get started on that till much later, and that's why we don't - we didn't have those rapid point of care tests and at-home tests like the by next [inaudible 00:08:32] test until much later in the course of this pandemic.

Yeah, we didn't have a good strategy about how to scale and deploy testing in this country in the setting of a pandemic. If you go back and look at the pandemic plans that have been done, most of them had been focused on flu and the pandemic preparedness, that tabletop exercises that we did, and I was part of some of those when I was in the federal government. We never really envisioned diagnostic testing being an essential part of pandemic response because if you're dealing with a flu, first of all, the incubation period for flu is short, three days. Second of all, you're not contagious until you're symptomatic. Testing isn't as essential a component to try and to identify asymptomatic spread and asymptomatic carriers because number one, asymptomatic people aren't going to go on to spread the virus in an appreciable amount. Two, by the time you become contagious, it's a short incubation period, so you haven't been in contact with as many people so doing the testing and tracing isn't as essential of a component of actually preventing the pandemic, the progression of the pandemic.

Three, the installed base of flu tests that are available in every doctor's office would be sufficient, because if you had a pandemic with an influenza A or an influenza B, doctors in their offices have tests that could differentiate influenza A from influenza B and if that's the prevailing strain -- pandemic strain is influenza B and you can diagnose them with influenza B, you know they have a pandemic strain. We never really planned for being able to develop and mass deploy novel diagnostic tests in the setting of a pandemic, because we always plan for flu. In flue, we -- the testing wouldn't be as essential and we'd have an installed base of testing that we could use.

That was part of the real challenge early on is no one thought about this, no one thought of getting the diagnostic test kit makers in the game early enough, and we we've never had enough testing. Even now, we still don't have enough of these at-home test that could be highly effective at controlling the spread of the virus. The ones that are available are expensive and many people are priced out of it. We haven't adequately subsidized it for people who are priced out of this market.

Mark Masselli:

We're speaking today with Dr. Scott Gottlieb, former FDA Commissioner and author of Uncontrolled Spread: Why COVID-19 Crushed Us and How We Can Defeat the Next Pandemic. Dr. Gottlieb you say so eloquently in the book, the pandemic has shown that we need to reimagine the role at CDC. You suggest that we amp up the intelligence capacity of the agency more in line with what the NSA does. But that will require an act of Congress, President Biden's infrastructure bill allocated additional resources to improve the capacity of the CDC. But the question is, have they allocated enough? And how should that money be deployed if approved to make the CDC more responsive in a future crisis?

Dr. Scott Gottlieb:

The argument in the book is that we can't rely just on public health conventions to alert us to outbreaks in would be hotspots. We've long relied on the international health regulations, which is a binding set of commitments that countries make in the context of the work they do under the World Health Assembly as part of the World Health Organization. Countries sort of voluntarily agreed to surface information if they're host to an outbreak of a novel disease. That hasn't worked.

I mean, we've seen time and time again, countries haven't fulfilled their obligations under the IH --- the International Health Regulations, including the Chinese government haven't fulfilled their obligations, not just in the setting of SARS-cov-2 but also in the setting of SARS-1. We strengthen the IHR after SARS-1 on the hopes that if we strengthened it, it would be more binding. The Chinese government still flouted the commitments that they made under those regulations. They still haven't shared the source strains of the virus.

My argument is we can't rely on just public health institutions and public health conventions alone, we're going to have to get our intelligence services more engaged in monitoring these threats. It's actually been legislation introduced to do just that, by representative shift so it looks like we're moving in this direction of getting our national security tools more engaged in a global public health mission. As far as resources, there's a lot of resources right now being allocated and there's more being contemplated. The Biden administration put out a sort of template for what they think a future pandemic preparedness proposals should look like and it includes an enormous amount of money in it. I think the money is going to be there. The question is, how to program it, and also how to give very specific guidance to CDC in terms of how CDC needs to reform itself.

In the past, Congress has written legislation directing CDC to do certain things, and the agency has simply ignored the legislation. I mean, the most -- the one that's most apparent that I talk about in a book is Congress sort of obligated CDC to build out a new infrastructure for data collection in the country, and CDC never implemented it. The GAO did a report and came to the same conclusion that the CDC the agency just failed to act on Congress's mandate. Congress is going to need to come -- it's going to have to come in, and very specifically reprogram that organization to create these capacities. They did it with FDA.

When I was at FDA, you know, Congress was very specific and granular in directing the FDA to reform itself in certain ways. I think, ultimately had a very positive impact on the agency driving change in the agency. I think they're going to have to do with CDC the challenges. There's not that many people in Congress who really understand the CDC well. I mean, there was a lot of -- there was a group of Congress, people, senators, Congress, people who understood FDA well enough to write very specific legislation.

CDC has been a little bit more of a black box, and that's why Congress is sort of allocated money to CDC but left a lot of discretion to the agency, how it implemented reforms. I don't think we can afford that luxury anymore. I think we have to have sort of a -- put together a commission or some group that's going to write very specific legislation, prescribing a very specific set of reforms to get the agency to have the capacity to deal with a crisis like this in the future.

Margaret Flinter:

Well, Dr. Gottlieb thank you for that, and your early comments in your response about what we did and didn't know coming out of China back in the late fall, early winter at the beginning of the pandemic is certainly a case of if only we'd known. But here we are with vaccination is our best strategy to stop this relentless progression of infection and death. We have made progress but we still see resistance in different places around the country in the South and the Midwest, and then recently just really tragic news coming out of Alaska.

You've looked at the issue of federal vaccination mandates which the President is attempting in certain sectors and said, probably not the answer, probably further politicizes vaccine uptake. But it does seem like we're seeing some movement, maybe some positive impact from the mandates. Is that still your thought or are you swayed by some of the recent news showing some progress where there are mandates?

Dr. Scott Gottlieb:

Well, I think certain mandates make a lot of sense, and I've been very clear on this. I think mandating vaccination among health care workers makes a lot of sense. I think the federal government certainly within its -- the scope of its authority to mandate vaccination among

the federal workforce, it's a matter of readiness of the federal workforce, the Department of Defense. I think we should be prescribing greater mandates in the Medicare program using the star rating system, we could be requiring Medicare plans to have to vaccinate certain high percentage of their populations for COVID as well. We haven't done that yet. I think we should, because that's a very vulnerable population. But I think that the issue of mandating vaccination among private businesses and small businesses versus trying to use incentives to drive that, I think we need to look at that carefully.

What I haven't seen is the policymakers in the federal government step forward and say, this is what we need to achieve in terms of vaccination rates. These are the different policies that are going to get us there, and this is how much incremental vaccination we think we're going to achieve with these different policies so we can actually do a careful way from a policy standpoint of what we need to achieve, and what are the best ways to get there. Right now, it seems very open ended, it seems to be the policy is more, get more people vaccinated. We don't really know what the upper bound that is achievable, let alone sufficient from a public health standpoint in terms of providing a proper wall of immunity. Let's do everything and anything we can and not really understand which policies are going to achieve more vaccination versus which policies are going to be more divisive, create more acrimony, create more division around vaccination, not necessarily achieve a lot of vaccinations, so it doesn't feel very deliberate. To me, it doesn't feel like we have a very clear sense of where we want to get and what are the tools for getting there. That's, where I think we need to be much more careful in terms of policymaking, we ought to understand what the goal is, we ought to understand what the different measures are that could get us there and what the tradeoffs from those different approaches are. There's been no discussion of that.

At the end of the day, what is the limiting principle here? I mean, there's obviously an end to what you can do to try to drive more vaccination. But if you don't prescribe sort of a goal and a different set of measures and how you think that those different measures are going to achieve the outcome, it doesn't -- there's not a clear limiting principle to what you are able to or willing to do. We should -- policy should be much more deliberate than it feels right now.

Mark Masselli:

Yeah, and I think you say that data should drive some of that policy, we've got to line up that data to make sure that the policymakers are aligned with it. You talked earlier about the FDA thinking that it really didn't need a review, perhaps the CDC does. But I know there's been a lot of criticism of both the FDA and CDC around pediatric, the 5 to 11 year olds and sort of the time it's taken for us to get the vaccine

developed for young people. What's your sense about upcoming review that Pfizer has put their information in front of the FDA, the CDC, around young people, but the American Academy of Pediatrics has come out and criticized the length of delay here. What do you make of all of that and what's your sense about the timing for the 5 to 11 and then certainly the younger ones after that?

Dr. Scott Gottlieb:

Look, I don't think this has been significantly delayed. It's maybe a month past where we thought we might have been three or four months ago, because the agency, the FDA asked for some additional data, ask for the trials in the kids ages 5 to 11 to be a little bit longer, a little bit larger. But, so we're not talking about a significant amount of time. Now, obviously, in the setting of a pandemic, any amount of time is significant. But I think if the tradeoff of that is that you're going to have a bigger data set, a better data set on which to base a decision, try to give the public better information.

The public health can be benefited in the end, because you're going to be able to allow people have more confidence about using the vaccine and maybe get more uptake. This is where you have to engage in a careful balancing and you have to be very sort of prescriptive about what you're doing and why and what you think that the tradeoffs are. I think the FDA has been careful in doing that balancing. I think the FDA is oftentimes more deliberate and transparent about what it's doing, what it thinks the tradeoffs [inaudible 00:19:52] public health benefits are and it's kind of getting back to the last discussion about what are we trying to achieve in terms of vaccination rates and what are the policies to get us there? I think we've been fairly deliberate about it here.

Agency is going to be meeting on October 26 to discuss the Pfizer vaccine and company I'm on the border of and kids ages 5 to 11. Assuming that meeting has a positive outcome, the agency authorizes the vaccine based on the datasets that's available. CDC would be prepared to meet very soon after that, almost immediately after that as I've been doing and make a recommendation. This vaccine, I think is on course to be available by Halloween or thereabouts if everything goes well. Ultimately, these two agencies feel that the Pfizer data package supports its safe use.

Mark Masselli:

Tell me what your sense is on the horizon, you're very positive about the Merck drug. But what else do you see the public should be keeping its eyes on in terms of the development that's going on with antivirals or other improvements in the science that have happened because of the mRNA platform? What do you see out there that animates your thinking?

Dr. Scott Gottlieb:

Yeah, look, we have a much better toolbox now than we did when we started. Certainly, I mean, we have a safe and effective vaccines,

multiple vaccines, we have point of care test that can be used at home, FDA has undergone sort of a dramatic cultural shift in terms of making tests available in the home for the diagnosis of not just an infectious disease but a reportable pathogen. Maybe three years ago, two years ago, that would have been unheard of the agency allowing those kinds of authorization. Now the agency has undergone really a shift in its thinking around this.

We have orally available, the Merck drug, an orally available drug that looks very promising. There's two more in advanced development, one by Pfizer, come on the board of one by Roche, all three of those drugs could potentially be available by the end of this year, shortly thereafter. We have a much different toolbox. I mean, if we go into the future with effective vaccines, higher vaccination rates, we're chipping away at getting people vaccinated. We're at 70, almost 78% of adults over the age of 18 have now had at least one dose, most will complete the series. We're building that wall of immunity through vaccination.

Also, frankly, through infection, I mean, people are getting infected, and they do have a durable immunity, especially if Delta infection we're going to have orally available drugs that could treat people who have breakthrough infections or small number of people who unfortunately choose not to get vaccinated, we'll have drugs available, monoclonal antibody drugs are highly effective. Those are being formulated in subcutaneous delivery so you can you can deliver it in doctor's office just for the simple injection. In the advent of these point of care and home diagnostic test, it's going to make testing much more accessible.

Eventually supply will catch up to demand, it's getting there, and hopefully the costs come down. This is a much better toolbox. This will allow us to turn this into a more manageable pathogen as we sort of transitioned from the pandemic phase of this virus to a more endemic phase with this just becomes a persistent menace that we're going to have to learn how to grapple with.

Margaret Flinter:

Well, that is a positive note to end on. We've been speaking today with Dr. Scott Gottlieb, former FDA Commissioner and the author of Uncontrolled Spread: Why COVID-19 Crushed Us and How We Can Defeat the Next Pandemic. Learn more about his latest work and access his book by going to uncontrolled spread.com. Follow his policy work at the American Enterprise Institute, or follow him on Twitter @ScottGottliebMD.

Dr. Gottlieb, we want to thank you for your analysis on our pandemic response for illuminating ways that we can strengthen the nation's public health infrastructure to better meet the next challenge, and for joining us today on Conversations on Health Care.

Dr. Scott Gottlieb: Thanks a lot, thanks for having me.

Mark Masselli: Thanks so much.

Margaret Flinter: Thank you.

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Mark Masselli: At Conversations in Health Care, we want our audience to be truly in

the know when it comes to the facts about health care reform and policy. Lori Robertson is an award winning journalist and Managing Editor of FactCheck.org, a nonpartisan, nonprofit consumer advocate for voters that aim to reduce the level of deception in US politics. Lori,

what have you got for us this week?

Lori Robertson: Studies on whether Ivermectin is beneficial in treating COVID 19

patients haven't been conclusive, and health officials have warned people not to self-medicate. But multiple large trials are continuing to assess the antiparasitic drug. The Food and Drug Administration has not approved the use of Ivermectin to treat or prevent COVID-19. The drug is approved for human use only to treat some conditions caused

by parasites, including head lice.

Although the National Institutes of Health counts over 70 studies evaluating the safety and effectiveness of Ivermectin to treat or prevent COVID-19 In humans, the FDA says the currently available data don't show it's effective against the disease, and that using it for this purpose in humans or animals can be dangerous. In fact, the FDA said the agency has received multiple reports of people needing medical attention after ingesting Ivermectin intended for livestock, which comes in doses that can be toxic for humans.

Animal Ivermectin, which is different from the one intended for people helps prevent heartworm disease and other parasites in different animal species. One expert told us if people are interested in Ivermectin, and whether there is a benefit for COVID-19 treatment, they should participate in a clinical trial. Preliminary results from one trial in Brazil found no indication of a benefit in using Ivermectin among high risk non-hospitalized patients, but two large clinical trials are still being conducted in the United States.

One, a randomized controlled trial led by the University of Minnesota Medical School is recruiting volunteers. Researchers expect to have preliminary results by December. A second large study, funded by the National Institutes of Health and led by the Duke Clinical Research Institute is also enrolling participants. Both studies involve non-hospitalized patients, and they were also evaluating other medications. Researchers in the United Kingdom are also studying Ivermectin in a large trial that is analyzing possible COVID-19 treatments. The results of these trials will provide more definitive

data on the drug. That's my fat check for this week. I'm Lori Robertson, Managing Editor of FactCheck.org.

Margaret Flinter: FactCheck.org is committed to factual accuracy from the country's

major political players and is a project of the Annenberg Public Policy Center at the University of Pennsylvania. If you have a fact that you'd like checked, email us at chcradio.com, we'll have FactCheck.org's Lori Robertson check it out for you here on Conversations on Health Care.

Mark Masselli: Each week, Conversations highlights a bright idea about how to make

wellness a part of our communities and everyday lives. One in five Americans will suffer a diagnosable mental health condition in a given year, and most often don't seek treatment. For those with serious mental health conditions the consequences can be devastating, hospitalizations, loss of job or home or even early death. Seeing a rise in mobile apps aimed at behavioral health entering the marketplace, University of Washington Researcher Dror Ben-Zeev drawer thought a

comparative effective analysis study would be a good idea.

Dror Ben-Zeev: My team and I conducted a three year comparative effectiveness trial

with the objective of having a head to head comparison between a mobile health intervention for people with serious mental illness called Focus, and more traditional clinic based group intervention called WRAP or Wellness Recovery Action Planning. It's conducted at

a clinic setting, people with similar diagnoses.

The study really gets at some of the core differences between mobile health and clinic based care. Is there something about the mobile health approach that would make it more accessible or less

accessible? Would people find it less engaging over time?

Mark Masselli: more than 90% of the mobile app group engaged in the online

program, which was a series of text messages, offering coping strategies and self-monitoring of symptoms along with weekly call-ins

with a behavioral health clinician.

Dror Ben-Zeev: The second thing we want to see is after people complete care, what

are their subjective ratings of their experience and treatment? Are they satisfied with both interventions? Are there differences in their levels of satisfaction? Probably the most important piece of the study are the clinical outcomes. We measure to see whether involvement in both interventions for a 12 week period, would that create some sort

of difference in psychiatric symptom, severity and quality of life.

90% of the individuals who were randomized into the mobile health arm actually went on to meet a mobile health specialist to describe the app to them and train them how to use it, and use the

intervention app that's assigned to them at least once. Whereas in the

clinic based arm, we saw that only 58% of the participants assigned to

that clinic based intervention ever made it in for a single session.

Mark Masselli: Both groups of patients saw roughly equal results from their

completed treatment, but the mobile group was more likely to engage in therapy. Ben-Zeev says this suggests that mobile therapies may provide a useful tool for clinicians having trouble getting those

with serious mental health issues to engage with the clinical

interventions.

Dror Ben-Zeev: The group dynamics, the fact that there's a sense of shared

experience, and perhaps even normalization of some of the

experience, that on its own is quite potent for people, right? We know that the very existence of a group can be quite helpful. But for others, the interaction is anxiety provoking, just making it to the clinic to engage in that interaction is logistically complex. When it comes to the clinical outcomes, in both intervention arms, people improved both in terms of reduction in their symptoms of the distress associated with symptoms and improvements in their recovery.

Mark Masselli: The results of this study were published in the Journal of psychiatric

services, a targeted mobile app aimed at facilitating access to clinical care for those experiencing serious mental illness symptoms, proving equally effective and managing the condition, improving access to intervention for behavioral health needs. Now that's a bright idea.

[Music]

Mark Masselli: You've been listening to Conversations on Health Care. I'm Mark

Masselli.

Margaret Flinter: And I'm Margaret Flinter.

Mark Masselli: Peace and Health

[Music]

Female: Conversations on Health Care is recorded at WESU at Wesleyan

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