TATIANA BOGDANOVICH: Hi, good morning. Thank you for the introduction. Well, before I start, let me ask you a few questions. How many of you are treating, taking care of patients C. difficile infections? Quite a number. How many of you are aware or have heard about fecal microbiota transplantation? Probably the same number of patients. Excellent, so the most important for me question is, how many of you are aware of the FMT program here at UPMC? Just a handful. So thank you for this great opportunity, then, to give you some updates in general about FMT and about our FMT program. Wonderful.

I have now disclosures to present. And in the next 30, 40 minutes we're going to try to cover the following topics. The burden of C. difficile infection, the methodology, safety, and efficacy of FMT. FMT program here at UPMC and future research potential for FMT.

So, Clostridium difficile, gram positive, anti-aerobic spore-forming micro-organism. The name "difficile" comes from "difficult." It was very difficult to culture it, and it was only discovered very recently in 1935. And it took additional 40 years for us to establish a link between it and antibiotic or post-antibiotic diarrhea.

But with the new millennium, C. difficile has become a major global problem. In fact, it has surpassed MRSA as the most common cause of hospital-acquired infections here in the United States. In 2011, the CDC has estimated that almost 500,000 patients would develop C. diff, 83,000 will have recurrence after the first episode. Almost 30,000 would die from C. diff, and 90% of them are patients over the age of 65, and about 10% in the first 30 days after their C. difficile diagnosis.

Any patient, or any person, can be at risk potentially at C. diff, but there are some groups of patients who are at much higher risk for C. difficile. And those are solid organ and bone marrow transplant patients, patients with inflammatory bowel disease, patients on exogenous immunosuppressive medications. And these are data from our solid organ transplant program here at UPMC. When we reviewed our patients who had transplants done in 2011 and 2012 and found out post, in the year, 12 months, post-transplant, about 10% of them develop C. diff infections ranging from 5% in kidney transplant patients to astonishing 17%, one in six patients, to lung transplantation. And for them, C. diff infection in the first three months post-transplantations was associated with the increased mortality and [INAUDIBLE] loss.

But what's also unique about C. difficile is its potential to cause recurrent infection. So you can basically estimate that about 20, 25% of patients who had their first infection will have another infection or recurrence. Even after they had perfectly fine, successful clinical response to the anti-C. diff therapy. And of those who had their first recurrence, 50% or so will have a second recurrence or third episode. And once a patient has had four or more episodes, it's almost a guarantee that they're going to have another episode once you stop their anti-C. diff therapy.

Most of the recurrences happen in the first month, in the first four weeks after stopping anti-C. diff therapy. But they can happen as early as just days after stopping antibiotics, to up to three months after that. And most of those infections are either relapse. So caused by the same strain of C. difficile as the initial episode, or the previous episodes. But there are also new strains, so the infection that can happen in these patients.

What are the risk factors for recurring C. diff? So multiple studies have looked at it and by far, age, your elderly patients are at the highest risk. Patients who require antibiotics while systemic antibiotics, while they're being treated for C. diff, or soon after they have completed anti-C. diff treatment. Patients who spend a lot of time in the hospital, so multiple admissions or prolonged admissions. Patients on immunosuppressive medications. Patients with multiple previous occurrences. Patients on [INAUDIBLE] so your acid suppressive therapy is definitely a major risk factor for patients to have recurrent C. diff as well as patients with inflammatory bowel disease.

So physiologically speaking, it's this disruption of the normal gut microbiota, so dysbiosis in this patient is probably the most important risk factor for a current disease. There's also data that in appropriate even response, a human response to and toxin A and toxin B in these patients as well as other neurologic factors of C. difficile are important. So, in the '80s, it was shown that patients who did not develop good high titers of anti-toxin A or anti-toxin B antibodies are at higher risk for recurrence compared to those who mounted good antibody response.

And of course, exposure to C. difficile spores, either from those that survived in the intestinal tract or from exogenous C. difficile spores. During the period of dysbiosis of the microbiota, how do we treat recurrent C. diff? We give more antibiotics. It has been noted that if you give longer than two week courses of vancomycin, patients do better.

Now we use variety of taper and pulse courses, none of them really has been studied in randomized trials. Or in fact compared against one another, but overall it appears that patients who receive five, six, or longer weeks of vancomycin do better than patients who just get two weeks of vancomycin.

Fidaxomicin, a relatively new drug. Just has been around for about six or seven years. It was shown in the clinical trials to be superior to be associated with the decreased rate of recurrences compared to the standard of care. So you have vancomycin and metronidazole. But it comes with the expensive side of it. So it's very, it's up to $3,000 price tag for it. It hasn't been actually studied in a immunocompromised patients. It hasn't been studied in patients with multiple recurrences and in the clinical trials that were performed actually, the follow up period was only four weeks. And we know that many recurrences do happen beyond the four week periods.

We routinely recommend our patients to perform thorough home disinfection with bleach to decrease that what we call spore Veneer, or fecal veneer that they create around them in their environment after C. diff infection. So when people have symptoms, when they're symptomatic having diarrhea, they shed enormous numbers of spores in their stool. So 10 to the 7s, tend to the 8s per gram of stool matter. And studies have shown over and over again that both their skin as well as an environment that in unusual places, gets contaminated with spores. It's very hard to get rid of them, to decontaminate the environment.

But certainly if we try to do that, we could reduce the risk of re-infection, bringing back from the environment, those spores into the intestinal tract. Because this is one of the important steps needed for the infection to happen.

Perhaps the newest drug that we can use now, since November of last year for the treatment of C. difficile still is bezlotoxumab. That's the monoclonal antibody against toxin B. Now it is used as an adjunct therapy to the standard of care, so not alone but in addition to antibiotic therapy and was shown to reduce the risk of recurrences in the patients with the relative reduction rate of 40%. However, we only have a limited number of experience, about 2,000 or 3,000 patients, has not been extensively studied in immunocompromised patients and patients with multiple recurrences. It's expensive and again, we're still looking forward to see the real-world experience with it. So by far the most effective available currently therapy or approach for the treatment of recurrence C. difficile infection is fecal microbiotic transplantation that we're going to talk about now.

So I can guarantee you that we're all exposed to C. difficile spores very frequently. Probably especially those who practice in prolonged care settings or hospitals, nursing homes, probably on a daily basis. There are also studies that show that we have C. difficile spores in our homes, even those individuals who have no contact with health care settings. If you go in their households and swab their bathrooms, their kitchens, you will find that you will detect C. difficile spores. So we're all exposed but yet we're not developing the disease. And we have to thank our gut microbiota, that community of microorganisms that we're all carrying in our bodies for this colonization resistance against C. difficile.

So it's been shown that good bacteria in our intestines are competing with C. difficile for a niche, for a place, for room, for nutrients. But they also participate in the metabolism of primary bile acids that are very important for germination of the C. difficile spores. C. difficile is an anaerobic organism. It actually form spores to protect itself, and we pick it up as spores and deliver it into our intestinal tract. And it has to go through an important critical point of germination, transformation into a vegetative cell that then goes on to producing toxins and responsible for all the symptoms associated with the disease.

So primary bile acids are important for that. And on the other hand, secondary bile acids that are produced by good bacteria are toxic for C. difficile. So when we give our patients antibiotics, chemotherapy drugs, immunosuppressive medications, we disrupt that normal community and interfere with one or several of these protective mechanisms. And again, allowing for C. difficile to germinate, to become active, to produce infection, and all the devastating consequences of it.

So, basically speaking, kind of mechanically speaking, FMT is essentially a delivery of a specially-prepared stool sample from a healthy person to a person with the disease with the hope to normalize gut microbiota in the recipient and alleviate symptoms and protect that person future. And it's depicted in this picture, where, with the green arrow you see the results of the sequencing of the stool sample from a patient with recurrence C. diff. It looks very abnormal in that normal patients, normal individuals, have a lot of firmicutes and bacteroides, it's the most predominant phyla in colon.

Certain patients with C. diff, recurrent C. difficile infection, you see decreased in firmicutes, decrease and bacteroides and actually increase in the predominance of all protobacteria and actinobacteria.

Here's an example of a donor with the normal, healthy gut microbiota. And you see that it clearly looks very different. Again more, bacteroides and firmicutes. And when we transform our patients microbiota, when hopefully in engraftment of the bacteria from a donor happens within the recipient's gut, we see something in between. New microbiota that looks healthier, that has more of those good bacteria in it and can protect our recipients. Now it's been shown, by the way, that you don't need to have complete engraftment of the donors microbiota for a successful FMT, at least for a C. difficile infection.

While not many have heard of it, and it may seem like it's a very novel approach, it is not in fact. It's been used, actually, centuries ago for chronic diarrhea and wasting. And more recently, it was used in veterinary medicine, but as far as the modern era is concerned, the first report of the FMT for antibiotic associated diarrhea, that was by the way incorrectly, it was assumed incorrectly that was related to Staph. aureus, but it was done in 1958. And the first use of FMT for a confirmed C. difficile infection was done, was published in 1983. And now, there are more than 900 publications. If you going to PubMed and put FMT without it, and specifying C. diff, you will see more than 900 hits. With all but about 30 just in the last five years. And 30, 40% of them being reviewed. Every week I go and I look what's new published. And really end up with a pile of publications to read, to go through.

So the FMT, success of the FMT in C. difficile is paramount. It's on the range of 80, 90% and it really is now accepted as the treatment option in the guidelines. So both in here in America as well as in Europe and in Australia and Canada, it is recommended for patients with recurrent C. difficile infection.

So this is an example of the American College of Gastroenterology guidelines from 2013 recommending, suggesting FMT as the treatment option for patients with three or more occurrences. However, in 2013, the FDA came out with recommendations about the need to do, or to apply for investigational new drug protocol for FMT if it's used for anything but C. difficile. And this is done in order to provide some control and safety boundaries for providers and for patients because of this extremely enthusiastic acceptance of FMT. Really it has become so accepted that people are doing FMTs at home guided by the YouTube recommendations on how to do it at home, do it yourself. I'm not kidding you.

Again, for you to remember, is that it's absolutely mandatory that if you plan to use FMT for anything but recurrent C. difficile, an investigation on a new drug application should be obtained. And if it's used for the purpose of C. difficile treatment, you must obtain consent from the patient where it's stated that it's an experimental novel procedures and they understand all the associated possible risks of it.

And in terms of us as the medical society, really the interest was boosted perhaps by this most pivotal publication on the FMT that was published in the New England Journal of Medicine in 2013. The so-called van Nood publication where for the first time they presented results of their randomized controlled clinical trials of the FMT for recurrent C. diff. They divided patients in three groups. Those who were receiving an infusion of the stool matter into the through the nasoduodenal versus those who receive vancomycin, vancomycin and lavage. And clearly, you could see significantly higher efficacy of FMT. 81% was single installation. And even 94% with additional second FMT in two patients, compared to just 30% in vancomycin group. So the study was actually terminated early because it was felt to be unethical to continue to offer vancomycin, not to offer, to randomize into vancomycin group when FMT was so much more superior.

But what was also important about this publication is that it's also talked about the safety of FMT and presented the results information about the safety of FMT procedure. And as they could see from this table, it was very well-tolerated by the patients. It was very not severe, primarily GI-related adverse events following the FMT and very few adverse events post, in the fall out period, post FMT that were not thought to be related to it except for one procedural complication.

And, for me as an infectious disease doctor, it was great because they also talked a lot and described a lot about the donor selection process. And eliminated a lot of people as you can see just on the basis of a screening questionnaire because of their risk factors for carrying potential transmissible infectious agents. But also, through micro-biologic testing. And they detected a significant number of parasites as well as two donors, potential donors, with C. difficile colonization that could have transferred their C. difficile or other pathogens to the recipient. So it's important to provide very thorough donor selection for our recipients to prevent potential infectious complications.

Talking about C. diff carriage, it is estimated that anywhere between 5% to 15% of healthy individuals are carriers of asymptomatic carriers of toxigenic C. difficile. And actually here in Allegheny County, we did a very nice study, my colleagues did a very nice study and it was published in 2013. Where they looked at over 100 residents of Allegheny County and asked them to provide stool specimens and then cultured their specimens to detect C. diff. Culture is the best, the gold standard method to detect C. diff and we used enrichment as the part of that culture to increase the yield of the culture. We discovered 7% carriage rate, again asymptomatic toxigenic C. difficile carriage rate it in our own county. And for some of them, it was over prolonged period of time of several months. So there are quite a few of us here who are carrying C. difficile and I don't know about myself, for instance.

So important, again, important, important, important, important to provide the most thorough screening of your donors. So since van Nood, there have been additional trials, just a handful of randomized clinical trials. But these are just a few that looked at different aspects of FMT. they looked at the use of frozen still doses versus fresh doses. They looked to compare nasogastric, or nasoduodenal, so upper GI versus lower GI delivery. And at least in the early studies, they appeared to be similar. However, now with the growing number of patients treated, based on retrospective analysis, it does appear that perhaps colonoscopic or lower GI delivery is better than the upper GI.

People, have looked, Kelly has published the biggest trial of immunocompromised patients where they looked at eight individuals with underlying immunosuppression. 19 of them were sorted organ transplant recipients, HIV. There were also a bunch of IBD patients on biologics and showed FMT to be safe and also effective. And then, finally, people started looking into actually using stool banks versus receive directed donation to facilitate FMT and again showed it to be possible in the working approach to FMT.

So now since I started talking about, how do we screen our donors? Let's talk how again, and where we can get our donors for our recipients. So, historically, patients had to identify their own donors. And usually it was somebody from the immediate circle. Spouses, friends, children, grandchildren what not. So on the one hand, you can speculate that they potentially shared to some extent their microbiome because the co-habiting, and may have some common genetic background. On the other hand, for a lot of people it was a lengthy process. It's not something you can easily discuss. Right, hey can you be my donor, right, stool donor. There is no financial compensation for donor screening, so patients had to pay out of pocket for screening of the donors. And also, you can say that most of those donors are not the best donors, not the healthiest microbiota. Because they tend to be on the older side, they oftentimes have chronic conditions, receiving medications, et cetera, et cetera.

And to have a high risk of carrying C. diff because they share the same host household oftentimes with the recipients. So very rapidly, some commercial not for profits. Stool banks appeared, the most famous one and I'm sure some of you have heard is OpenBiome that offer FMT doses out of the box delivered to your doorstep. For a cost, it's quite significant, a few hundred dollars, so again, you have to ask a patient to cover that expense, and shipment actually cost almost as much as the dose itself. And of course they have no control over what type of donor you are receiving and you don't have full op information on the donor. And then finally they pay their donors and there is potential for some not complete disclosure of their sexual and medical and what not, travel history. So something that some people think is not quite acceptable.

So, finally, there have been some institutional and even national for smaller European countries stool banks opening up, including us here at UPMC. And again, the positive side is that we take that burden off identifying a donor away from our recipients who are suffering already. And providing them the safest, the healthiest, possibly if you think about it, donor, pre-screened and available for a patient pretty much on-demand. On the one hand, it also gives us as research as physicians practicing in academic settings, opportunity for research. So FMT-based research because we can change our protocols, we can adapt our requirements for donors, the recipients would not when we have access to our own stool bank.

In terms of safety and tolerability, again, usually by far, it's very well-tolerated with very few short-lived immediate, primarily GI-related adverse events. Has been used again that there's a growing number of reports on the safe use of FMT in immunocompromised patients as well as children. And some unusual reports are published for you just to be aware of. Primary [INAUDIBLE] colitis actually in a patient. And the person who did FMT at home by enema using stool sample from his wife and his child, and turned out it was not BT patient, developed primary [INAUDIBLE] colitis. Some gastroenterologist from norovirus, diverticulitis, fetal aspiration, pneumonia, so procedural complication post-FMT.

Peripheral neuropathy, didn't put it hear ITP. There was a report of ITP and a fairly highly, I think, publicized report of obesity developing in a donor to FMT was done for C. difficile infection. She used her own daughter's stool for treatment and they both developed, very rapidly, significant weight gain to a point where they shifted into the obesity range. But they have not done any microbiota studies to actually prove the causality between the FMT and the obesity. Although, again, with the growing information, with the growing knowledge about importance of microbiota not only in disease colonization resistance and disease protection, but also in immune metabolic processes, neuropsychiatric wellness. It's quite conceivable that something like that can happen and we have to be careful about it.

So shifting gears a little bit because I'm sure you want to see the actual pictures of how it's happening. And I can tell you how it's happening here at UPMC. So our program was started in 2013 and took almost two years to go through all this regulatory processes and steps and have the infrastructure established. We finally did our first colonoscopic FMT in December of 2014, followed by an FMT via nasoduodenal installation infusion. We wanted to scale up our program by opening up a volunteer stool bank because, again, the rate-limiting step was the lack of donors for our patients. For some of them, it was taking seven-plus months to find a suitable donor. And we had a couple of patients who, unfortunately, could not use their donors because they were either C. diff or did not match the recipients based on semilatent viruses that I'm going to talk to you about.

So we did our first FMT using a previously stored volunteer's stool dose in November of 2016. And in December of last year, we did our first FMT using freeze-dried capsules. So a very much more tolerable way of delivering FMT to our patients. Something that's done just in the office during the routine 30-minute clinic visit. So, there are really no standardized inclusion-exclusion criteria for FMT. Different places use different criteria, but overall they're more or less similar. There's not a significant variation in inclusion criteria. At this point, most places, and us, including us, are looking at patients with recurrence C. diff. So three or more episode that failed to respond to a prolonged course. So somebody comes and only has had three treatments, two weeks each, I have to show I have to see if the patient would respond to a longer course of vancomycin before we proceed to FMT.

And then we're also allowing patients who had severe infection that required admission. Now some asked me, so if I had a very bad C. diff, even if I ended up in the hospital, does that mean that if I have recurrence it's going to be as bad? No it doesn't, but it's certainly a risk. And we won't interfere at that early at that point. The exclusion criteria are not that many. So patients have to be willing to stop vancomycin, some people become really sort of vancomycin dependent, and feel very uncomfortable about stopping, and they have to stop it. So they have to be willing to say, yes, it's going to be done, it's going to be stopped.

Not listed here, but what we actually tried to listen during our conversation, we want to make sure that patients have no anticipated need for systemic antibiotic therapy in two to three months after FMT. So if somebody may need an elective procedure, we want to stop and wait and do it after they get their prophylactic dose of an antibiotic for that procedure. We have many more exclusion criteria for volunteers. Stool donors, so almost 30 of them, you don't really need to look down. But it does give you a sense that we're looking for elite, the healthiest cohort of patients, of individuals.

So, again, basically speaking, we're looking for patients who are not obese or aren't malnourished. Who are not on any chronic medications, they have no chronic conditions, have normal bowel habits, who did not have any risky sexual history or ongoing behavior. And no recent travel to endemic countries and no recent antibiotic use. So the process begins with the evaluation of a patient who has the history of recurrent C. diff and now a dedicated C. diff clinic, it's in the center of the care of infectious diseases in Folk Building. So we talk extensively. In fact, we're asking our patients to bring, if they can recall that, bring additional information about all of their testing, and medications used, and the duration, and the dose, and ask them to recall how they were responding to their therapies.

If somebody tells me they have three or four episodes and each time I get vancomycin, or fidaxomicin or whatnot. And it doesn't do anything for me, that's a major red flag for me. That indicates that there's something else going on, some additional underlying process responsible for the chronic diarrhea and these patients have to be evaluated and ruled out for something else. And some are down the line process before we would let them go into the FMT route.

Once we identify a suitable person, we talk about the route they'd like it to be done. And also the type of donor they would like to utilize. So we actually leave it to our patients to decide whether they want to go with somebody from their circle. Some people say, you know what I don't want somebody else's stuff, I want stuff from my spouse. Although most people I have, tell me 99%, say yes, just do it, do it. Do it, people are ready, really. By the way, a C. diff patient who comes for FMT, I know it may sound to you like, goodness FMT is so horrible, but a patient with a recurrent C. diff, 99.9% of them are ready to have it done. And think they can't wait for it to be done because of all the misery they've gone through for months.

And then we obtain extensive lab panel. We actually do extensive testing of our recipients in addition to the donors. Because what is perhaps somewhat unique about our program is that we're actually trying to avoid mismatches between our donors and recipients. Full-latent viruses like CMV, HSV, EBV, because again, our target population are elderly. Oftentimes immunocompromised, we don't want to run the risk of having a primary CMV infection in those patients. Or primary HSV infection. So if we see, for instance, by the way I think I mentioned that to you that, a donor is CMV positive and the receiver is CMV negative, we cannot use a stool sample from that donor. And we've had a couple of patients who had their own donors identified and paid out of pocket for their testing, who then ended up not going through the procedure with that donor because we could not allow this to happen. We don't want to run the risk of infection from it.

We ask our patients to stay on C. diff, anti-C. diff therapy for about three to five days prior to the procedure. We need that wash out period, so there is no antibiotic present in the colon, so there is no interference with engraftment of good bacteria, healthy bacteria. And just for your information, for those who choose to go through the freeze-dried capsules, we actually ask them to be fasting and expect to be fasting for a couple hours post-procedure. And also, we're using a PPI pre-procedure. Now, again, there also have been studies who have not used PPI, so acid suppression, and people have done well. So this is, again, sort of something that varies from place to place.

Graphic scenic pictures of how it is done. So everything is happening in the magic FMT Laboratory in the Presbyterian campus. So we have a dedicated space, bio-safety cabinet with laminar flow. We're wearing fully garbed wearing personal protective equipment. So we're trying to do everything to prevent introducing any new microbiota, any new micro-organisms into the stool sample. Everything that comes in contact with stool is actually sterile.

And, again, we're trying to prevent contamination of the environment also with the stool matter. So we're using a special collecting hat for our donors. We're making sure that they have our labels, we maintain chain of custody. We're using pharmaceutical-grade normal saline to homogenize stool samples. Essentially, we take a predefined amount of stool, homogenize it in a commercial-grade blender, filter it through a series of filters just to get rid of that ballast, undigested stuff, and end up with the bacterial slurring. So 60% of our stools are micro-organisms, so that's what we want to end up with and get rid of that undigested stuff. And we store this material at minus-80 degrees Celsius in a dedicated freezer until it needs to be used. And it can be delivered in our settings by three main ways.

It can be done either through enteroscopy or colonoscopy. So, during a same-day procedure in our GI suite. Or through a nasoduodenal infusion. So installations with nasoduodenal tubes. Again, in our RP, radiology procedure unit, same-day procedure, a few hours. And fully awake and have to live through the process of infusing it. And then the blue pills, the capsules that we just ask patients to take during and get a regular ID clinic appointment lasting for less than 30 minutes for most of the patients.

So we leave it to the patients to decide what route they prefer. But as you can see in this picture, most of the patients actually prefer capsules. So, again, these are just some of the posters that you might have seen around our Presbyterian campus. We're actively looking for donors with people who are willing to donate their good stuff for the benefit of poor, unhappy, unhealthy patients. So we go through the screening process. We have a short and a long questionnaire. Somewhat similar to a blood bank questionnaire that we ask our donors to complete. And if they pass all of these checks, then we go on to collecting their stool specimens. We need to process them within four hours of the production time. And two weeks after the last donation, and we need to have at least five or six doses per donor. We then go with the physical examination and laboratory testing of their blood, urine, and stool prior to clearance of those doses.

So I've collected over 45 doses. With the various virologic profile, again, remember we're trying to match our recipients and our donors. And we even have what I call my golden universal donor, who is only positive for HHV-6 but negative for CMV, BV, JC Virus, [INAUDIBLE] everything. So I'm keeping those doses as my most extensive stuff in my life.

We've done, treated 24 patients utilizing volunteer stool doses. And most of them, like I said, 19, were done via either the freeze-dried capsules, 4 by colonoscopy, and one by enteroscopy with a success rate of about, approaching 85%. So what do we do once we're done? So we don't just say hi, and bye and hope not to see you again. We are asking all of our patients, all of our recipients, as well as donors, to actually become part of our FMT registry where we collect prospective their information.

We collect pre and post FMT samples for our recipients. We counsel our patients about the need to avoid antibiotics, especially in the most crucial eight to 12 weeks after the FMT, and we're actually offering complimentary anti-microbial stewardship. We give our pager numbers, our phone numbers, email addresses so that if they need to talk, they have a provider wants to talk to us about the need to treat them for something, we're available there for them to call us and see if it's needed, if maybe we can avoid it. And if it's needed, then what would be the treatment. Although I always say, if you're sick enough, you need to go to the hospital. Get the treatment, then have your doctor call us. Because it's better to not delay the therapy but then stop it if it's not needed later on.

And then again, there's a potential for Irritable Bowel Syndrome post any infectious diarrhea, including C. diff. So some people may have every now and then some rounds of diarrhea, and we don't panic unless it is for two or three days or worsens rapidly. We don't routinely test for C. diff but you sort of have to be careful and especially with the PCR that detects the gene for the toxin but not necessarily identifies the person with the disease. You may want to consider a 2-step approach to diagnose C. diff and confirm a positive result by a toxin-detecting SA.

So with the amazing success story for FTM C. diff was the 95% plus efficacy of FMT was only natural for people to start looking what else, what other conditions that are related to these viruses FMT may be used in. This is just an incomplete list of some of those conditions that it has been tried. And there are ongoing clinical trials in pretty much all of these conditions.

We here at UPMC are very excited to be able to start our own number of protocols where we're going to look at maybe using FMT to de-colonize patients who are colonized by multi-drug resistant micro-organism, and also try to see if it's going to help with the chronic inflammation seen in some patients with HIV. So we want to follow even a couple of years.

Again, with a lot of knowledge available about FMT, we're still lacking a lot of important information listed here. So, again, people are trying to use it now for severe C. diff, for acute C. diff, and even for the early, for the first episode of C. difficile infection. No head to head again as I mentioned before, comparison in terms of different administrations about. We are very simple in how we define our FMT dose, we just go with the original amount of stool used to it. So there are some attempts at maybe defining the effective dose in sort of molecular biologic numbers and not in grammage, with not in weight.

We don't know what the success or the efficient, effective dose for non-C. difficile indications or the frequency of FMT for non-C. diff indications of FMT. And, of course, needless to say, that we need to always look and try to collect the data about the safety of FMT and especially the long-term data. And there's actually a big grant from YNH establishing a national FMT registry for our patients, for the benefit of our patients.

So, in summary, I hope I've convinced you that it's the most effective, I didn't tell you anything about the cost of it. I can only tell you that here at UPMC, we're only asking a patient to cover whatever expenses, the charges they may have associated with their visits or with their procedures, and a one time $100 out of pocket paid to help us cover the cost of donor for dose processing. It may be more expensive in some other places, but just to give an idea. So, in general, comparing to hundreds of thousands of dollars of other modalities, and with the efficacy of 80, at least, percent I think it's pretty cost effective.

But, again, remember this experimental procedure, it requires a consent. And if want to do it for something else but C. diff, you have to get an IND. There is, of course, a very real risk of transmitting infectious agents with the FMT. So you got to be sure that whatever source you are using for your stool material for your recipients is a safe source. There is all the necessary protocols and safety aspects in place.

And of course to work to bridge those knowledge gaps that exist. And, actually, maybe in five years if you call me I'll talk to you about different non-FMT related microbiota related therapeutics for C. diff and other conditions. So, finally, with 40 seconds to spare, I'd like to thank everybody in my ID division.

Dr. Muir, Scott Currey, he was the ID my colleague who actually started this process and really put everything in place and I could just carry over after he left. Lee Harrison, Dr. William Pascoe, he's the head of the microbiology lab in our hospital. So, again, it's important to have a good microbiology lab to have that back up to make sure that you're getting proper results.

GI Division, Dr. Venian, Mark Schwartz, again, they are absolutely important to keep us in check. And also to help us with those patients who do get their FMTs via endoscopic approach. And [INAUDIBLE] and Allison Morris, Barbara Methé from the Center for Medicine and Microbiome, who are helping us to know, to learn more about FMT, see what we're doing and to advance our knowledge in microbiota and FMT. Thank you.