

Regulation of Microbiome-Based Diagnostic Tests:

Aim 2 – Tested and Untested Consumer Focus Group Findings



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1. Background

The overall goal of the *Regulation of Microbiome-Based Diagnostic Tests* project is to inform and support policy and regulatory approaches that will encourage innovation and scientific discovery of new microbiome-based products, while identifying and addressing regulatory concerns from researcher, physician, and consumer/patient perspectives. There are 3 Aims for this project:

- *Aim 1* – Review the federal and state laws and regulations that govern diagnostic testing and results to determine if they are appropriate for microbiome-based diagnostic tests.
- *Aim 2* – Understand stakeholder perceptions of microbiome-based diagnostic tests including test utility and value to health care decision-making and concerns with regard to privacy and data security. Conduct in-depth interviews and focus groups with three groups of stakeholders – microbiome researchers, providers, and consumers/patients.
- *Aim 3* – Develop and propose an appropriate and comprehensive regulatory framework for microbiome-based diagnostic tests. A multidisciplinary working group will review findings from Aims 1 and 2 to assess the current regulatory position for microbiome-based diagnostics and evaluate the appropriateness and effectiveness of that position.

The anticipated goal of this project is to develop a comprehensive review of the current legal and regulatory landscape, assessment of stakeholder perceptions of microbiome-based diagnostics and understanding of legal protections to inform an evaluation of the existing regulatory scheme and identification of a feasible, patient-centered approach to the regulation of microbiome-based diagnostics.

1.1 Purpose of Report

This report presents findings from Aim 2 focus groups conducted with consumers who have either used microbiome-based diagnostic tests (tested consumers) and those who have not (untested consumers). Findings from Aim 2 interviews with microbiome researchers, physicians, and focus groups with providers can be found in corresponding reports. Findings across all stakeholders for Aim 2 will:

- Identify the characteristics, motivations and perceptions of patients currently engaged with microbiome-based diagnostic tests;
- Determine under what circumstances potential consumers would or would not order such tests;
- Identify the education, demographic characteristics, practice variables and perceptions of providers ordering these tests for their patients or concerns they have about ordering such tests;
- Determine how well patients and providers understand the test results; and
- Elucidate potential legal or social implications of these diagnostics that should inform their regulation (e.g., potential for use by health insurance companies).

2. Methods

2.1 Participant Recruitment and Characteristics

Untested consumer participants were patients of the University of Maryland Medical System and have been diagnosed with various gastrointestinal conditions. Tested consumer participants were recruited from the American Gut Project. All recruitment materials were approved by the Institutional Review Board of the University of Maryland, Baltimore.

Table 1 describes participant characteristics by consumer type, as well as the number of focus groups and participants.

Table 1. Characteristics of Focus Group Participants (N=22)

Consumer Type	Number of Focus Groups	Number of Participants	Percentage of Total Participants
Tested	4	12	54.5
Untested	2	10	45.5
TOTAL	6	22	

2.2 Focus Group Data Collection

Focus group discussions were led by one of three trained facilitators who are members of the research team. A co-facilitator who also was a member of the research team was present during all groups to take notes and manage the logistics. All participants provided consent before the start of the session. Out of concern for attendees' health and safety during the COVID-19 pandemic, the workshop was conducted virtually using Zoom. Participants were asked to join the focus group from a computer or laptop, and use their device's video camera so all participants could see one another, similar to an in-person gathering. The discussion was recorded with permission of all focus group participants. Focus groups lasted approximately one hour.

Focus group moderator guides were developed based on the data collected in the individual interviews. Separate guides were developed for physician focus groups and patient/consumer focus groups. All guides included semi-structured questions that were used by the focus group moderator to facilitate the discussion. The untested and tested consumer focus group guides are located in Appendix A and B. Broad topics for the focus group guide included:

- Satisfaction with medical services/treatments;
- Attitudes toward alternative/complementary medicine;
- History of using or purchasing direct to consumer genetic tests;
- Experience with microbiome-based diagnostic tests;
- Interpretations of microbiome-based diagnostic test results; and

- Perceptions of the regulation of microbiome-based diagnostic tests.

2.3 Data Sources

Multiple data sources were analyzed for relevant information, as described in Table 2 below.

Table 2. Focus Group Data Sources

Source	Description	How used in analysis
Transcripts	Transcriptions based on focus group recordings	<ul style="list-style-type: none"> • Transcripts were imported into NVivo® 11 • Text was coded per the codebook (See Appendix B)
Summary notes	Notes taken by the co-facilitator during the interviews/focus groups	Notes provided additional context and insights to coded text
Focus group videos	Video recordings of the focus groups	Notes provided additional context and insights to coded text

2.4 Analytical Considerations

2.4.1 Data Management

The focus group Zoom recordings were professionally transcribed verbatim. A member of the research team reviewed the transcripts for accuracy and completeness. All transcripts were anonymous and any names of individuals, facilities, or other item that could compromise confidentiality were removed from the transcripts. Once validated, the facilitator posted the transcripts on a secured drive where members of the research team could access the data for analysis. Using standardized procedures, transcripts were formatted and imported into NVivo® 11 for analysis.

2.4.2 Data Analysis

Broad content areas and potential themes of interest based on discussions with the research team were explored. The initial broad content areas identified were:

- Satisfaction with medical services
- Experience with consumer tests
- Perceptions of microbiome tests
- Motivations for testing
- Attitude towards integrative medicine
- Understanding sample results
- Regulatory issues

The initial identification of content areas and themes was meant to be as expansive and inclusive as possible so that the analysis would capture the breadth and depth of issues discussed. In this manner, additional content areas and themes emerged during data analysis. Throughout the process, the

research team discussed prevalent concepts and themes that were mentioned in numerous focus groups. The research team developed a codebook (Appendix C) to document these concepts and themes. Throughout the coding process, the codebook was refined as codes were merged, expanded, deleted or divided. Previously coded text was recoded to reconcile variability.

The qualitative analyst utilized NVivo® 11 to code and analyze the transcripts. Passages of text relevant to the initial content areas were selected and codes were developed that reflected emergent themes. To provide in-depth perspectives of specific themes and to identify trends, coding reports were created to cross-reference coded text with physician type.

2.4.3 Coding Rules and Meetings

Prior to the start of analysis, the research team met to discuss and agree on the organization and use of the codebook. The research team met regularly to discuss the status of coding, analysis, interpretations, and modifications to the codebook. Additionally, the research team discussed the consumer focus group analysis in relation to the Aim 2 provider focus groups and researcher and provider interviews to assess any congruence or differences in the coding, analytic process or findings between the samples.

3. Results

The following sections detail the themes and subthemes that emerged from the focus group discussions. Descriptions of themes, as well as quotes are included; attributions to participant type are in parentheses after each quote.

3.1 Experience and Satisfaction with Medical Services and Treatments

Both consumers in the tested and untested groups were asked how satisfied they were about the healthcare services and treatments they have received. Participants also discussed their diagnoses, medical history and search for medical treatments and providers.

All participants in the untested consumer group were patients at the University of Maryland Medical Center (UMMC), seeking specialized treatments for gastroenterology conditions. Participants expressed that they have seen a series of doctors, both general gastroenterologists and specialists before transferring to UMMC. Several participants explained that they were referred to UMMC after their former provider was unable to address their health conditions. A number of participants reported that they traveled across Maryland or other states to receive specialized care. A few consumers also stated that they preferred their provider to be affiliated with a research university, as they considered the level of care received at these institutions to be advanced and state-of-the-art.

I've had very good care and I feel the doctor listened very well. And even with recommendations on the change of medicines, as well as just keeping up-to-date on the research studies which are really important to me, staying involved with the research front of medicine, not just the typical path, or what we think is correct. And so, yeah, I like the research scientist aspect of the care that I've received. (*Untested Consumer*)

While several participants primarily received care at UMMC, a few had providers at various institutions. For example, a participant preferred to have an alternative medicine provider working in conjunction with their traditional provider at UMMC. Another consumer who has multiple providers at various locations, stated that their use of incompatible electronic medical record systems made it difficult for his providers to coordinate his care. In general, after several years of researching treatments and seeking specialists, participants were satisfied with their current level of care.

In contrast to the untested consumers, the tested consumer group were recruited across the United States, and received healthcare services and treatments in a variety of settings and locations. Several participants noted that they were unsatisfied with their medical services, as they were interested in seeking more complementary and alternative treatment, but were unable to do so through their current medical system. Participants described their Western-centered care as “fragmented, that I feel that there's no way that I can get really proper care, because they're specialists in each area, and they don't really work together” (*Tested Consumer*). Tested participants also explained that they often had to conduct their own research, particularly to understand gastrointestinal, nutrition, metabolic and microbiome issues, as their primary care doctors were not well versed in these fields.

3.2 Experience with Direct-to-Consumer Tests

Participants in both untested and tested consumer groups were asked about their experience with direct-to-consumer (DTC) tests. Both consumer groups were asked about their experience with DTC consumer tests, such as Ancestry.com and 23andMe, as well as their awareness of DTC microbiome-based diagnostic tests. Tested consumers were specifically asked about their experience with microbiome-based diagnostic tests.

3.2.1 Experience with Consumer Genetic Tests

When asked if untested consumers have used consumer genetic tests, such as 23andMe and Ancestry.com, the majority of participants stated that they were aware of these tests, but have not used them. Many explained that they were hesitant to use these tests as they were concerned of the accuracy of these tests, how their data and DNA may be used by insurance companies or law enforcement, as well as privacy and security issues.

I'm not interested in it. But I'm also in a sensitive job position. And there's some security concerns with the data and who owns the rights to the data and other foreign entities, they may have access to that information. And then also I have heard that they're pretty inaccurate. The accuracy rate is not as good. So, there could be some information that may not be accurate. And I only want 100% accuracy, if that can be guaranteed. (*Untested Consumer*)

I have heard the same thing where your insurance company could get a hold of the results. I've even heard of your employers being able to get a hold of results. I'd primarily be concerned about possibly the authorities getting DNA results. (*Untested Consumer*)

When I did it, I got it for free and didn't really think too much about it. I don't regret doing it now, but that is something that has crossed my mind that no one's really holding the company accountable. Well, they put a bunch of privacy notifications on how they'll store your data. But again, I don't think anyone's truly holding that accountable. (*Untested Consumer*)

Several of the tested consumers purchased genetic tests for various reasons, such as learning about their ancestry or understanding their medical background. Compared to the untested consumers, the tested participants were less likely to express privacy concerns in regards to these tests. A few tested consumers stated that they were uninterested in these genetic tests, as they preferred to focus on prevention and a healthy lifestyle, regardless of their genetic markers.

I never purchased any of those testing kits. And I don't think I'm really interested in it because I still feel like you should just be taking preventive measures in your lifestyle. So, hopefully, no matter what I'm susceptible to, but with that holistic lifestyle or just healthy lifestyle, I just hope that reduce all the chances to a minimum. (*Tested Consumer*)

3.2.2 Awareness of and Interest in Microbiome-based Diagnostic Tests

Untested consumers were also asked if they were aware of DTC microbiome-based diagnostic tests. The majority of participants were not aware of these tests, citing that they have seen advertisements for DTC tests to detect cancer screenings, allergies, and food sensitivities, but not to assess the microbiome.

The only one I've heard of is the cancer one they have on TV, where they can screen your colon cancer. But as far as microbiomes or anything like that, no, I haven't heard of anything. *(Untested Consumer)*

I didn't know they had the direct-to-consumer microbiome tests if that's available or not, but I knew there was microbiome testing available and the research and clinical setting, but not the direct-to-consumer. *(Untested Consumer)*

Untested consumers stated that they were not interested in DTC microbiome-based diagnostic tests. This may be due to the fact that these consumers were previously unaware of these tests. A few participants stated that they may consider taking the test if their doctor suggested it, or if they continued to experience unspecified symptoms and exhausted all other options to identify the cause of these symptoms.

So, no, I would not do the direct-to-consumer tasks. I would do it if it was ordered by my doctor. However, only if it was necessary and needed, because I was not feeling well, and I've exhausted the options, then that would be the reason why I would do that. *(Untested Consumer)*

I'd consider it. I probably wouldn't go out and purchase it on my own. I'd probably rather have my doctor recommended it and recommend a specific test from a specific company. *(Untested Consumer)*

I'm in clinical remission with Crohn's, but I'm still symptomatic with my gut. And I'd be really curious to know what would be causing those symptoms, if it's not my Crohn's as well as unexplained health symptoms that I have. 'Cause trying to talk to some doctors about it, I kind of get dismissed and there's like, no real one answer. And if there was a test that can maybe find something that would be helpful. *(Untested Consumer)*

All tested consumers were recruited through the American Gut Project and have taken a microbiome-based diagnostic test at least once through the project. Several of these participants learned about the American Gut Project through their research to manage their gastrointestinal conditions or were generally interested about the microbiome. Participants also spoke of their interest in taking the microbiome-based diagnostic test through the American Gut Project as they believed it was more scientific or were interested in participating in citizen science and advancing the microbiome field, rather than purchasing a DTC test for consumer purposes.

When I saw that [American Gut] project, I was also excited like some of you. And then to me, if they need more samples, give more data to know more, and for our common good, why not? *(Tested Consumer)*

I think I was looking for ways to look at your microbiome. And then, when I came across it, I trusted American Gut because of the Citizen Science aspect, as opposed to uBiome or something that was fun. *(Tested Consumer)*

In addition to the microbiome test conducted through the American Gut project, a few have also taken DTC microbiome tests, such as Viome, although most have not.

3.3 General Perceptions of Microbiome-Based Diagnostic Tests

3.3.1 Modern Medicine vs Integrative Medicine

The majority of untested consumer participants reported that they have used various types of alternative or complementary medicine to control their symptoms. These types of therapies include acupuncture, dietary supplements, opium tincture and paregoric. Participants also noted the importance of researching alternative or complementary therapies before incorporating these therapies into their treatment plan.

But if it's something that's just a thought or the next hot trend that people are trying, then probably I would not feel comfortable going that path. Because I like to see the research that is associated with that and the evidence for it. (*Untested Consumer*)

Untested consumers who did not report using alternative or complementary medicine stated that they were open to using these in the future, but have not had any exposure or opportunities to integrate them into their treatment.

Almost all participants in the untested consumer focus groups stated that they viewed DTC microbiome tests as either an example of alternative/complementary medicine rather than traditional modern medicine. Several stated that while they categorize this type of testing as alternative/complementary medicine, they believed that as the microbiome field matures and more rigorous research is conducted, these tests will be considered a tool for traditional modern medicine.

I think the microbiome [field], it is evolving very rapidly. And I feel it's a research field that has grown. And I think as it grows and we learn more about it, it's going to transition more to that conventional type treatment...In my view on alternative medicines is that [they are] not based really on cause and effect per se. So, I'm looking to make hypotheses, they're proven, they're tested, and now you have scientific theory. And I don't know if that's been completely flushed out yet with microbiome research. (*Untested Consumer*)

The majority of tested consumers also reported using alternative or complementary medicine, such as acupuncture, dietary supplements, and yoga. Many participants stated that they preferred to utilize non-allopathic treatments or to focus on prevention versus treatment, which were not offered by their primary care physicians or specialists. Participants also spoke of the overuse of antibiotics in childhood, which contributed to health issues later in life; this led to their own research on the microbiome and probiotics.

Every time I talked to the doctor for advice on [cancer] prevention, so anybody who has had cancer, you just want to prevent it from reoccurring. Rather, they focus on how they could find it, find a new tumor. I don't ever want it to happen again, so I had to do a lot of research, a lot of reading. I teach at a community college of anatomy physiology, and then I picked up a nutrition. So basically, to me, it is true that a food is medicine. (*Tested Consumer*)

A few tested consumer participants, however, stated that they would need to see more research supporting alternative/complementary medicine in order to consider it for themselves.

3.3.2 Perceived Benefits of Microbiome-Based Diagnostic Tests

Baseline Assessment of Microbiome. Consumers reported several potential benefits to microbiome-based diagnostic tests. Both untested and tested consumers explained that test results could provide a baseline understanding of a patient’s microbiome, which can be assessed over time and correlated with any diet modifications or changes in symptoms.

This particular type of test could be good for a baseline, and then doing the test over again to see how those numbers high, low and normal have fluctuated over time. To see whether you're getting better and how that correlate to how you're feeling and your symptoms are manifesting and stuff. (*Untested Consumer*)

Inform Changes in Care and Treatment Regimen. Other participants cited that personalized information about the microbiome could optimize changes in care and treatment regimen. An untested consumer also stated that she would trust microbiome-based diagnostic test results as they are specific to her microbiome, and thus, the recommendations are more personalized and meaningful.

I've heard a range from the same doctor and the same conversation saying food makes no difference, but do this diet, and then having other doctors recommend completely different diets. So, I think if you're getting a “do list” and a “don’t list” that's based off of your [microbiome], that I trust that more than just saying, “Try this specific diet” and then you doing it and maybe not noticing any difference, because maybe one of your trigger foods is something that is included in that diet...If there was [a test] tied to my specific [microbiome] that someone can say, “Based on that you should eat this.” I would trust that a lot more than just saying, “Based off of this condition, you should or shouldn't eat this.” (*Untested Consumer*)

This sentiment about the direct usefulness of microbiome-based diagnostic tests was less apparent among the tested consumers. Several members of this group stated that they became involved in the American Gut Project to collect further personalized data about their health condition, and conducted their own research on how they may be able to alter their condition based on understanding their microbiome. As this group has had access to their personalized results, several stated that despite receiving these results, they were still unable to clearly understand the linkage between their microbiome and condition.

Yes, indeed, I got nothing meaningful, but I did hope that I would see something that stood out. And so, in that sense, I just chalked it up to almost as a donation [to the American Gut project]. But you see, I was curious, and wanted some information. So, I would say that that was disappoint, that aspect was disappointing. (*Tested Consumer*)

I had been dealing with [an illness] for about 10 plus years, but I just reached my breaking point where I decided to go all in, and go more on conventional routes, and figure it out once and for all. Ultimately, it led to a fecal transplant. Ultimately, that worked. And it's so nice to be able to say that, but, right, it was not easy arriving at that conclusion. So yeah, the American Gut Project, it was like just a stop on the journey. (*Tested Consumer*)

Contribute to the Scientific Understanding of the Microbiome Field. Other members of the tested consumer group mentioned that they participated in the American Gut project in order to contribute to the citizen science project, in hopes that their data are able to add to the knowledge of the microbiome field.

Since I was not having an issue that I wanted to resolve, I guess the benefit to me was in contributing to the knowledge. (*Tested Consumer*)

3.3.3 Willingness to Pay for Microbiome-Based Diagnostic Tests

Participants in the untested consumer group were asked how much they would be willing to pay for microbiome-based diagnostic tests. Many participants stated that they would pay less than \$100 for the test, while a few would pay between \$200-\$300. A few participants also stated that they would be willing to pay more for the test if these tests were regulated, as they would be more willing to trust the results.

3.3.4 Ability to Pay for Microbiome-Based Diagnostic Tests

All tested consumer participants reported that their insurance did not cover the cost of their tests. Participants stated that they paid \$99 for their microbiome test for the American Gut Project, and several explained that they viewed this cost as a donation to the citizen science project and believed this to be worthwhile. Others who also purchased DTC tests, such as Viome, reported that they paid from \$150-\$230.

3.4 Interpretation of Mock Microbiome-Based Diagnostic Test Results

Participants in the untested group were provided with a set of mock microbiome-based diagnostic test results to review during the focus group, and spoke about how well they understood the test results. Tested participants were asked if they shared their tests results with their health care provider and if they implemented any changes to their treatments or lifestyle based on the results.

3.4.1 Interpreting Microbiome-Based Diagnostic Test Results

Understanding Microbiome-Based Diagnostic Test Results. For those in the untested consumer group, several participants reported that in general, the test results were easy to comprehend. Some participants appreciated the details provided about specific bacteria or information about inflammatory markers, as well as the report format, which they have not seen in test results ordered by traditional doctors.

I thought I could follow it. Yeah, I didn't think it was too hard to get a grasp on. I liked how the first part had specific bacteria and stuff named which then if I'm curious I can Google what those bacteria are and find out more. So, I do like it that it was very specific that way. The other thing I liked was that general going as you go through the report, it has that inflammatory activity and intestinal barrier house and stuff like that. (*Untested Consumer*)

I found it pretty easy to follow, I mean, you can go through tells you the high, low, medium, everything. I like the middle section where it tells you as far as your inflammatory markers from having inflammation or anything...I've done the CRP, all the different blood works. And it never shows inflammation or anything like that. But I was structured to the point where it was almost completely clear. So, I've had inflammation over the years for a long time, but none of the tests are really picked up once. So, maybe this would be an alternative to [those tests]. (*Untested Consumer*)

Tested consumers spoke about their experiences when reviewing their results from the American Gut Project microbiome test. The American Gut Project test compared participants' microbiome to others in the project, but unlike DTC tests, did not provide recommendations based on results. Some tested consumers found this to be a disappointment, as they were unsure of what their results meant and how they should adjust their diet accordingly.

But the one thing that I was a little disappointed in, I got lots of information about my microbiome and what the different strains that I had. But it would say things like, you'd have a four rare strains that most people don't have. But then they don't tell me more. *(Tested Consumer)*

The first two sentences in the response was, in general, these data allow you to understand how similar or different you are to other people in terms of bacterial composition of the sample you sent. So, it doesn't say, we're going to tell you if your microbiome is good or bad. It just says, we're going to tell you how you compare with everybody else. *(Tested Consumer)*

Guidance from Providers to Interpret Microbiome-Based Diagnostic Test Results. Conversely, several untested participants were cautious about interpreting DTC microbiome-based diagnostic test results. For example, participants stated that although they believed that consumers should have the ability to purchase these tests and be empowered to research ways to improve their health, they were unsure of how to interpret the DTC results. Several stated that it was important to ask physicians to interpret these results and to seek their guidance.

The only thing that I hate though is, when you try to interpret the data yourself and you go to Google, and so, that's why I really think it's always important to have somebody that's been involved in medicine that has that experience. Not saying that we can't look up things, and we can try to understand it, but just in any professional field, or even any field, if you have more experience with it, you've seen more cases of things, and you can give the recommendations and the opinions. I think sometimes you when folks go to Google, they think they're becoming the experts in it. It's when we watch a YouTube video on fixing a car, yeah. I mean I think I know how to fix a car. But really, there're people with that experience that when you reach a problem that are going to be able to troubleshoot it better. And so, I put a lot of stock in the physicians and really walking me through just because they have that experience, and they do this on a daily basis. *(Untested Consumer)*

The suggestion to seek guidance from physicians when interpreting DTC microbiome-based diagnostic test results and recommendations was not as widely discussed among tested consumers. Several tested consumers reported that their physicians would not be able to interpret these tests results, as they are unfamiliar with the field, or there remains too many unknowns in the field of microbiome research.

Every physician that I've tried to approach the topic of that microbiome, and especially my neurologists say, "It's too new, I don't understand it. I don't know anything about it. I can't voice a judgment." So, at this point, not part of their world yet. *(Tested Consumer)*

I have a wonderful doctor, but he's clueless about this sort of thing. So, I think we're at the dawn of a new era, and a really new paradigm, and it's going to take a while for the medical system to catch up with this. *(Tested Consumer)*

3.4.2 Use of Microbiome-Based Diagnostic Test Results and Recommendations

Untested consumers were asked a hypothetical question, asking if they received test results, how they would implement changes to their diet and lifestyle based on the results and recommendations. Similar to comments regarding the difficulty of interpreting results, consumers found it difficult to implement these changes without the assistance of their physician.

There was so much information, I would want to go to my doctor and say, “What do I do with all this?” It's more than just about what to eat and not eat, I'm guessing...I don't know what I would need to do. I'm assuming I would need to do other things than just diet to fix this. (*Untested Consumer*)

Other untested consumers reported that the recommendations were too vague and wanted more information before making changes to their diet or lifestyle. Further explanation of recommendations and scientific references would increase consumers' trust.

I think the results provided isn't convincing enough to make me want to make me wanna actually make any change. What was touched on earlier about providing the details behind the recommendations that make like, “This specific food has shown to cause these symptoms. So, if you don't eat it that'll help work or whatever.” If there was more information with more detail, maybe more noted source science behind it, it would be more convincing. (*Untested Consumer*)

It kind of seems like all of the information is really good and then at the end it just says like, ‘Eat these foods and don't eat these foods.’ I would just want a little more information of because X, Y and Z is low or high or not in the range...being able to expand on that knowing that kale is going to be really good for this and increasing that. That information will be helpful for me, knowing the why behind it. (*Untested Consumer*)

Untested consumers also noted that the recommendations were very generic and simply suggested making health food and lifestyle choices.

And I do feel some of it did seem generic because I think everything with healthy lifestyle and good choices can change a variety of conditions. And then if you do have a specific food trigger by that time, you've pretty much have figured it out if you've already been diagnosed. And so, and then some of the other recommendations, I just felt healthy choices always make people feel better. (*Untested Consumer*)

Several tested consumers reported that they were interested in assessing changes in their microbiome, but despite making changes to their diet, such as adding fermented foods, fiber or probiotics, they did not see many alterations over time.

What I wanted was to see if I still have the gut of an obese person, even after losing the weight and I did. So, then I used that as a before and after by really changing my diet to include a lot more probiotics and whatever and see if I could change that. And I did six months of sauerkraut and a lot of sauerkraut too and then did it again. And unfortunately, my gut bacteria had not changed a lot, so it seems to be persistent. I've been thinking about doing it again to see if a

couple years down the road that's changed at all. But yeah, so it did answer the questions I had. And I did find it useful and depressing. (*Tested Consumer*)

Other tested consumers reported that they did not make large changes to their diet or lifestyle after reviewing their results, but either continued to follow their typical regimen, or ensured that they included more vegetables to their diet and meat raised without antibiotics.

3.5 Regulatory Concerns of Microbiome-Based Diagnostic Tests

3.5.1 Concerns Regarding Data Use, Privacy and Security

Less Concern for Data Use and Privacy Issues. There were a number of participants from both the tested and untested consumer groups that were not overly concerned about data use and privacy issues in relation to DTC microbiome-based diagnostic tests. A few of these participants explained that their lack of concern resulted from an assumption that as a society, our personal data is no longer private. Other participants stated that they were less concerned about a microbiome-based diagnostic tests compared to a genetic test, which involves DNA samples and testing.

I'm not really concerned. I just feel nowadays and probably in future, there is absolutely no privacy of any sort, and I'm fine. If they're interested, let's make some good out of it, and that's fine. I cannot think any adverse things come out and not at this point anyways. (*Tested Consumer*)

I just always feel like they know less about me, from my genetics or from my food than they do from my browsing history, which is what they're really mining for, to try to get stuff out of me. We're all open books at this point, even if we don't want to. (*Tested Consumer*)

For this specific test, I probably have less concerns, because it's not specifically your DNA. But for me, personally, concerns don't completely disappear. I'm just generally concerned about any access to information or whatnot. (*Untested Consumer*)

Need for Regulation of Data Privacy and Security. A few participants from both untested and tested consumer groups reported that they were concerned about privacy and how their data may be used by third parties, including affecting insurance policies.

I guess I'd be looking for something like the HIPAA, things that you sign for hospitals and that sort of thing. I'd be looking for what kind of protection do I have, who could have access to it. I wouldn't want people to have access to it then. (*Untested Consumer*)

I think we definitely should have some regulation, simply because if it's out there, and nobody's regulating it and nobody's keeping track of it, then the bad guys are going to get ahold of it. And we all know that there's bad guys out there....I have no doubt they would go after me personally. And use it to try to get my insurance rates really high or have been cancelled if you don't do this. So, I really think there should be some regulation on it, just for my protection. (*Tested Consumer*)

3.5.2 Availability of DTC Tests

Access to Personal Health Information. Tested and untested consumers were asked whether they believed microbiome-based diagnostic tests should be available DTC or only by a provider. The majority of all consumers believed that the public should be able to purchase the tests directly and have access to their own data, in order to be advocates for their own health.

I think when it comes to your own health, I think we should all be good stewards of our own health. And if that's something we want to do [purchase DTC microbiome-based diagnostic tests], then that's perfectly fine. That's your choice. *(Untested Consumer)*

And absolutely, I think so. We have to be able to be advocates for our own health. I'm happy that now we can all see the test results when we have a blood tests or something, which we didn't use to be able to when I was younger. That was not available to us, our test results. I think the more that we can know ourselves about our own health and get our own tests, the better. *(Tested Consumer)*

Personal Choice for Microbiome-based Diagnostic Tests. Tested consumers also reported that DTC microbiome-based diagnostic tests should be made available to the public, as many physicians would not recommend or order these tests for their patients. Tested consumers believe that this was due to physicians' lack of awareness of these tests, the microbiome, or lack of ability to interpret the results. This sentiment was not discussed in the untested consumer groups.

I think there are very few physicians that would recommend [these tests], even if the patient wanted it, because they simply don't know about it. *(Tested Consumer)*

The only reason I got to the point I got to [take the microbiome-based diagnostic test], was because I could circumvent a physician. *(Tested Consumer)*

3.5.3 Recommendation to Review Results and Recommendations with Providers

Several untested consumers reported that although these tests should be available DTC, companies should be required to recommend that consumers consult the results and recommendations with their provider. This was also reported in Section 3.4.1 - Interpreting Microbiome-Based Diagnostic Test Results and Section 3.4.2 - Use of Microbiome-Based Diagnostic Test Results and Recommendations. This was not found in the tested consumer group, which believed that the majority of physicians are not able to reliability interpret a microbiome-based diagnostic test or are knowledgeable of the microbiome.

3.5.4 Regulation of DTC Microbiome-Based Diagnostic Tests

Less Concern for Regulation of DTC Microbiome-Based Diagnostic Tests. Both tested and untested consumers were asked about their thoughts on regulating DTC microbiome-based diagnostic tests. A few participants in both tested and untested groups were not concerned about regulation of these tests, as they were not viewed as potentially harmful compared to drugs or treatments. Additionally, as scientists are continuing to understand the microbiome, it is unclear what aspects of testing are feasible or necessary to regulate.

I feel like there's a lot of things that should be regulated that aren't or things that don't have the regulations that they need...It doesn't turn me off if it's not FDA approved, I guess, I would say. Especially if it's [a] test and it's not a specific drug or something, so that doesn't really bother me that much. *(Untested Consumer)*

The FDA is still figuring out how to approach this topic at large. It's still the Wild West, as far as the microbiome goes. As far as adverse consequences of somebody buying a snake oil microbiome test, and what's the worst that could happen, they might alter their diet. So, I'd say the adverse consequences are benign enough that the FDA can just let it happen. *(Tested Consumer)*

A tested consumer also expressed that the regulation of microbiome-based diagnostic tests must not preclude innovation, particularly as the microbiome field is in the nascent stage.

Regulation can have a protective effect, and I applaud that. And it can also have an effect to sometimes eliminate innovation, or favor one branch of a discipline over, let's say, microbiome research and production of kits, and so on, over another, so we can skew things. So, the unintended consequences of regulation, I'm sure that regulators in the 21st century have been very made aware of and are really trying to respond. So, I think it's early, but I think that it's probably going to take several years. *(Tested Consumer)*

Several consumers in the untested and tested groups believed that these tests should be regulated by the FDA. These participants trusted the FDA and would have more confidence in the test if they were approved by the FDA. Specifically, consumers would feel assured of the accuracy of the test results, standardization across tests, and quality control. Despite some participants' concerns of government regulation in healthcare, several untested and tested consumers recommended this type of oversight.

I think the FDA gives a certain amount of credibility to things. And oftentimes when I get some of the alternative health products...in the drugstore, the comment that people often make, "Well, that's not FDA approved. We don't know the results of those. We don't know the side effects." ...I do think FDA approval is important. *(Untested Consumer)*

I fully actually agree with [name of participant] on a lot of that, where to say regulation by the government it's a little big and scary and you think, "I don't want the government involved in my health care." But I know if it is FDA, so you don't really have a choice. But definitely some sort of regulation to maintain quality and integrity and all that kind of stuff. And otherwise, any sort of startup company could create these things and it could vary differently. It could be the same test, but still vary so differently. *(Untested Consumer)*

I absolutely think it should be regulated by the FDA just because, I could, with the access to technology today, I can get a PCR instrument in my house and put a kit together and send that out and give people results that may be inaccurate or 50%. So, I like the idea of the FDA, because it's a way to keep the folks held accountable and making sure that the data that's delivered to the consumer is accurate. I mean, we're in this COVID era right now when a test was put out too soon, a diagnostic test, and you're getting these inaccuracies, and it's skewing results. And so, this to me is a diagnostic test, just diagnostic devices for any type of condition that we're trying to diagnose. So, I absolutely think it needs to be regulated, but that's my opinion. *(Untested Consumer)*

I agree with the others. I think that patients should definitely be empowered to do their own research and seek out their own solutions, their health. But I guess, my one thing, which would be if there was some regulation of information and the interpretations of the site, whether it's from a consumer board or FDA, just someone to verify that their interpretations are based on some medical facts. *(Untested Consumer)*

I did a test with one company, I got very scientific information. And then the other test was in more in layman's terms gave me more of a breakdown. I wish it was more consistent as far as maybe a template, you need to provide this, this, this, this, this to consumer and put it in a way that they can understand the information that you're providing to them. *(Tested Consumer)*

Appendix A – Microbiome Consumer Untested Focus Group Guide

MICROBIOME CONSUMER UNTESTED FOCUS GROUP MODERATOR'S GUIDE

[NOTE: The Moderator Guide consists of possible questions that researchers anticipate are relevant to ask. However, this does not mean that every question listed will definitely be asked. As per standard protocol for semi-structured interviews, researchers will allow the conversation to unfold naturally. Certain questions listed may not be asked because they may no longer be relevant to that particular discussion, or time constraints may not permit.]

Moderator: Welcome and thank you for agreeing to talk with us today. My name is [insert moderator name] and my colleague's name is [insert co-moderator/assistant's name]. As you know from the information sheet you were given, we are here to talk about your knowledge and attitudes toward testing for gut/vaginal microbiomes. This conversation should take about an hour.

Before we start, we ask that you silence your cell phones. We want to hear from each person, so if you are talking a lot, let others talk for a little while too. Our goal is not to get everyone to agree or disagree. It is about hearing each person's unique opinion.

Please just use a first name to refer to yourself (we will use a code in our study records instead of your name). We ask that you not disclose personal information with us that you are not comfortable sharing. Anything you tell us will be kept private. It will not be shared with anyone outside of the researchers performing this study. This includes your health care providers. We also ask that everyone who takes part in the discussion group keeps whatever we talk about completely private. We will use a code on the research records containing information you share today, so you won't be identified by name. We want to be sure you are comfortable in what you choose to discuss with us. Please let us know if you have any questions or concerns.

We appreciate your honest answers to questions, including letting us know if you don't know how to answer a question. In a focus group, it's important to express yourself openly. There are no right or wrong answers. We simply want to know what you think. I would like everyone to be a part of this conversation. You do not need to wait for me to call on you to talk, but only one person should speak at a time.

We will be recording this discussion for research purposes. Are there any questions before we begin? [If yes, answer questions, if no, proceed]

We will ask you to say your first name before speaking. If you would prefer not to identify yourself, you can use a different name. Since this discussion is being recorded, saying your name will help us identify who is speaking when we listen to the recording later on. The only people who will hear the tape or see the written record are the researchers working on this project.

[Moderator may elicit elaboration on questions below via prompts such as, "Tell me more about that," and "can you give me an example of what you mean?"]

Question 1: Generally, how satisfied have you been with your ability to get the medical services/treatments you need within our healthcare system?

Question 2: What is your view of alternative/complementary medicine (for example, acupuncture, homeopathy, and dietary supplements)? Have you ever used any of these? Why or why not?

Question 3: Have you used or purchased any direct to consumer genetic tests such as ancestry.com or 23andme? If yes, why? If not, would you consider doing so? Why or why not? (Follow up: Do you have any concerns about these companies having access to your genetic information?)

Question 4. Prior to this research study, had you heard about direct to consumer microbiome-based diagnostic tests? If so, where did you hear about them?

- a. If yes, are you interested in ordering one of these tests? Why or why not?
- b. If yes, have you ever requested or asked your health care provider to order one of these tests? If so, why? If not, why not?

Question 5. What benefits do you see for patients or consumers in getting one of these tests? (Additional Probe: For example, do you think these tests would predict future disease? Would they indicate risk for specific health conditions?)

Question 6: Do you see these direct to consumer microbiome tests as an example of traditional modern medicine or of alternative/complementary medicine?

Question 7: If you are interested in ordering one of these tests, how much would you be willing to pay out of pocket? Less than \$100? \$100 - \$200? \$200 –300,? \$300 - \$500?

Question 8: Now I'd like you to think about the test results we emailed to you for review. Did you find the results easy or difficult to understand? If difficult, what specifically did you find unclear?

Question 9: If you received these test results would you have any concerns about your health going forward? Would you make any changes to your diet or lifestyle?

Question 10: What concerns do you have, if any, about the use of these test results? (Additional Probe: For example, if you ordered one of these tests, would you have any worries about how your test results could be used? Or who gets access to your test results?)

Question 11: Do you think these tests should be available to patients without authorization from a physician? Why or why not?

Question 12: These tests are virtually unregulated by FDA or other government agencies. Do you think they should be more regulated than they are? Why or why not?

Moderator: That is all the questions we have for you. Do you have any questions for us or anything to add that we haven't already discussed? [If no, close, if yes, follow-up]

Thanks so much for taking the time to talk to us today. Feel free to contact us if you have any further questions.

Appendix B – Microbiome Consumer Tested Focus Group Guide

MICROBIOME CONSUMER TESTED FOCUS GROUP MODERATOR'S GUIDE

[NOTE: The Moderator Guide consists of possible questions that researchers anticipate are relevant to ask. However, this does not mean that every question listed will definitely be asked. As per standard protocol for semi-structured interviews, researchers will allow the conversation to unfold naturally. Certain questions listed may not be asked because they may no longer be relevant to that particular discussion, or time constraints may not permit.]

Moderator: Welcome and thank you for agreeing to talk with us today. My name is [insert moderator name] and my colleague's name is [insert co-moderator/assistant's name]. As you know from the information sheet you were given, we are here to talk about your knowledge and attitudes toward testing for gut/vaginal microbiomes. This conversation should take about an hour.

Before we start, we ask that you silence your cell phones. We want to hear from each person, so if you are talking a lot, let others talk for a little while too. Our goal is not to get everyone to agree or disagree. It is about hearing each person's unique opinion.

Please just use a first name to refer to yourself (we will use a code in our study records instead of your name). We ask that you not disclose personal information with us that you are not comfortable sharing. Anything you tell us will be kept private. It will not be shared with anyone outside of the researchers performing this study. This includes your health care providers. We also ask that everyone who takes part in the discussion group keeps whatever we talk about completely private. We will use a code on the research records containing information you share today, so you won't be identified by name. We want to be sure you are comfortable in what you choose to discuss with us. Please let us know if you have any questions or concerns.

We appreciate your honest answers to questions, including letting us know if you don't know how to answer a question. In a focus group, it's important to express yourself openly. There are no right or wrong answers. We simply want to know what you think. I would like everyone to be a part of this conversation. You do not need to wait for me to call on you to talk, but only one person should speak at a time.

We will be recording this discussion for research purposes. Are there any questions before we begin? [If yes, answer questions, if no, proceed]

We will ask you to say your first name before speaking. If you would prefer not to identify yourself, you can use a different name. Since this discussion is being recorded, saying your name will help us identify who is speaking when we listen to the recording later on. The only people who will hear the tape or see the written record are the researchers working on this project.

[Moderator may elicit elaboration on questions below via prompts such as, "Tell me more about that," and "can you give me an example of what you mean?"]

Question 1. Generally, how satisfied have you been with your ability to get the medical services/treatments that you need within our health care system?

Question 2. What is your view of alternative/complementary medicine (for example, acupuncture, homeopathy, and dietary supplements)? Have you ever used these? Why or why not?

Question 3. Have you used or purchased direct to consumer genetic tests such as ancestry.com or 23andme? If yes, why? If not, would you consider doing so? Why or why not?

Question 4. What led you to get/order a microbiome-based diagnostic test? Did you order this test on your own or did your health care provider order it?

Question 5. Where did you hear about this type of testing, in general? How did you find out about the specific test that you or your health care provider ordered?

Question 6. What benefits did you anticipate in getting this testing? What did you think about the results you received? Were the results helpful to you? If so, how? What questions, if any, did you have after receiving your results?

Question 7. Did insurance cover the cost of your test? How much did you pay out of pocket for the test? Do you think the cost to you of the test was worth it?

Question 8. What concerns do you have, if any, about the use of these tests?

Question 9. Do you think these tests should be available to patients without authorization from a physician? Why or why not?

Question 10. If you ordered the test on your own, did you share your test results with your health care provider? If a health care provider reviewed your test results, did they make any recommendations about changes to your medical treatments, diet, or lifestyle/behavior after seeing your test results?

Question 11. Did you make any changes to your medical treatments, diet, or lifestyle/behavior after getting your test results?

Question 12. These tests are virtually unregulated by FDA or other government agencies. Do you think they should be more regulated than they are? Why or why not?

Moderator: That is all the questions we have for you. Do you have any questions for us or anything to add that we haven't already discussed? [If no, close, if yes, follow-up]

Thanks so much for taking the time to talk to us today. Feel free to contact us if you have any further questions.

Appendix C – Regulation of Microbiome-Based Diagnostic Tests Codebook

Regulation of Microbiome-Based Diagnostic Tests
Aim 2 Codebook – Focus Group Analysis, Version 2
3/26/21

Parent/Child Code	Description	Notes
1. Experience with consumer tests	Experience with tests either as a provider ordering for patients, or as a consumer	
a. Awareness of microbiome tests	Comments re: provider or consumer awareness of microbiome tests, even if they have not previously used them	
b. Order/request microbiome tests	Comments from providers or consumers about ordering/requesting microbiome tests. Can be hypothetical responses to requests.	
c. Consumer genetic tests	Experience with genetic tests, such as ancestry.com and /or 23andme	
d. Other	Other comments that relate to experience with consumer tests	
2. Perceptions of microbiome tests	Perceptions of tests, including usefulness, validity, and medical disciplines, understandability of results, harms/benefits	Stratify by medical discipline
a. Clinical utility	Discussion re: if tests help with treatment decisions or lead to improved health outcomes	
b. Clinical validity	Discussion re: accuracy of test, ability to accurately identify or predict a disease or health condition	
c. Education tool	Comments from physicians who believe microbiome tests can be used as an educational tool for patients	

Parent/Child Code	Description	Notes
d. Modern medicine vs integrative medicine	Whether microbiome tests are examples of traditional modern medicine or alternative/complementary/integrative medicine	
e. Interpretation	Comments re: perception of ease or difficulty of interpreting test results	
i. Over specificity	Comments re: results focusing on specific species rather than the larger microbiome	
ii. Use in context	Discussion re: importance of viewing the tests results within the context of the patient's history and other tests	
iii. Lack of understanding to interpret data	Lack of understanding in the field of how interpret findings, meaning of findings for clinical use	
iv. Lack of belief in tests	General disbelief of microbiome tests and field of study (not only limited to questioning clinical validity)	
f. Benefits	Perceived benefits of microbiome tests	
g. Harms	Perceived harms of microbiome tests	
h. Costs	Costs consumers are willing to spend on microbiome tests	
i. Other	Other comments that relate to perceptions of test	
3. Motivations for testing	Providers and consumers' motivations to order tests	
a. Microbiome tests	Motivations specific to microbiome tests	Code may include discussion of consumers' past experience with similar tests, satisfaction/dissatisfaction with their diagnosis and treatments

Parent/Child Code	Description	Notes
		leading them to request tests. May need to create more grandchild codes once analysis begins
b. Genetic tests	Motivations specific to consumer genetic tests	
c. Other	Other comments that relate to motivations for ordering or requesting tests	
4. Attitude towards integrative medicine	Providers and consumers' attitudes towards alternative/complementary/integrative medicine	May need to create more child codes once analysis begins
5. Understanding sample results	Providers' and consumers' understanding of sample test results	
a. Interpretation	Comments re: how to interpret the test's clinical validity, reliability, utility and information needed for further interpretation	Code may include information re: content, range, relevant/irrelevant scientific information, which affects interpretation. May need to create more grandchild codes once analysis begins
b. Understandability	Discussion of whether results were easy or difficult to understand, what information needed to be clearer	May include discussion of format, volume of information that affects understandability. May need to create more grandchild codes once analysis begins
c. Other	Other comments that relate to understanding test results	
6. Regulatory issues		
a. Privacy	Discussion of privacy concerns, who has access to test results	

Parent/Child Code	Description	Notes
b. Data security	Discussion of data security concerns	
c. Use of data	Discussion of any concerns re: use of data, including possible insurance implications, discrimination, use for company's own research	
d. Availability of tests	Discussion whether tests should only be accessible to patients via physician order	
e. Thoughts on regulation	Comments re: benefits or concerns about regulation, including how regulation can lead to better tests	
f. Claims of tests	Comments re: quality or usefulness of tests, claims, truthfulness	
g. Recommendations	Any comments pertaining to recommendations including a disclaimer, or the need to regulate recommendations	
h. Validity	Comments re: need to regulate test results, determine validity	
i. Healthcare provider responsibility	Comments of how providers should be have formal responsibility for interpreting results, especially if ordering tests	
j. Balance innovation and regulation	Comments re: need to not let regulation hinder research and development	
k. Interpreting results with provider	Comments re: need for patients to review test results and recommendations with a provider, even if patient has ability to purchase test on their own	
l. Other	Other comments that relate to regulatory issues	
7. Satisfaction with medical services	Consumers' comments re: satisfaction with medical services/treatments that they have received	Determine if this relates to "motivation for testing" codes during analysis. May need to create

Parent/Child Code	Description	Notes
		more child codes once analysis begins.
8. Interesting Quotes	Any interesting, rich quotes that may be helpful for analysis or reporting	
9. To Discuss	Any quotes that need further deliberation, unsure of where to code	