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Authors

Harrison, Krista L
Farrell, Ruth M
Brinich, Margaret A
et al.

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'Someone should oversee it': patient perspectives on the ethical issues arising with the regulation of probiotics

Krista L. Harrison BA,*† Ruth M. Farrell MD MA FACOG,‡ Margaret A. Brinich BA,§ Janelle Highland BA MA,§ MaryBeth Mercer BA MPH,¶ Jennifer B. McCormick PhD MPP,** Jon Tilburt MD MPH,†† Gail Geller ScD MHS,‡‡ Patricia Marshall PhD,§§¶¶ and Richard R. Sharp PhD,***¶¶

*Research Assistant, Berman Institute of Bioethics, Johns Hopkins University, Baltimore, MD, †Doctoral Candidate, Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, ‡Staff, Departments of Obstetrics/Gynecology and Bioethics, Cleveland Clinic, Cleveland, OH, §Research Assistant, Department of Bioethics, Cleveland Clinic, Cleveland, OH, ¶Research Coordinator, Department of Bioethics, Cleveland Clinic, Cleveland, OH, **Assistant Professor of Biomedical Ethics, Department of General Internal Medicine, Mayo Clinic, Rochester, MN, ††Assistant Professor of Biomedical Ethics, Associate Professor of Medicine, Department of General Internal Medicine, Mayo Clinic, Rochester, MN, ‡‡Professor, Department of Medicine and Berman Bioethics Institute, Johns Hopkins University, Baltimore, MD, §§Professor, Department of Bioethics, School of Medicine, Case Western Reserve University, Cleveland, OH, ¶¶Co-Director, Center for Genetic Research Ethics and Law, Case Western Reserve University, Cleveland, OH, and ***Staff, Department of Bioethics, Cleveland Clinic, Cleveland, OH, USA

Correspondence
Ruth M. Farrell MD MA FACOG
Assistant Professor of Surgery
Department of Bioethics and OB/GYN
9500 Euclid Avenue, JJ-60
Cleveland, OH 44195, USA
E-mail: farrelr@ccf.org

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Abstract

Background Although many probiotic products are currently available in yogurt or pill form in the United States (US), there is uncertainty surrounding the structure of regulation of these products. As more therapeutic probiotics are developed, changes to existing regulatory process in the United States may be required to meet the needs of patients and users in the population.

Objective This study examined how patients with chronic gastrointestinal (GI) diseases view the regulation of probiotics.

Design We conducted a multi-site qualitative study consisting of focus groups of patients with chronic gastrointestinal diseases at three tertiary hospitals: at [institutions removed for blinded review].

Results We conducted 22 focus groups with 136 patients with major gastrointestinal (GI) diseases between March and August 2009. Participants were not familiar with the existing regulation of probiotic products but wanted assurances of accurate labelling of strain as well as safety. Participants raised concerns that regulation of probiotics might be accompanied by greater costs, reduced access and increased involvement of pharmaceutical companies. Although participants voiced significant doubt of government regulators, they felt that products containing genetically modified probiotic strains should have oversight comparable to that of pharmaceutical drugs.

Discussion and conclusion If GI patient perspectives are indicative of public perceptions of therapeutic probiotics in the United States, consumers may expect more rigorous regulation in the future while simultaneously wanting low costs, easy access and low involvement of pharmaceutical companies. Manufacturers, translational scientists, clinicians and regulators should be sensitive to consumer attitudes when designing, testing and regulating new therapeutic probiotics.

Introduction

Research from the Human Microbiome Project (HMP) promises to produce important insights into the aetiology, diagnosis and treatment of various health problems, including gastrointestinal diseases, skin aliments and gynaecological problems.[1,2] This initiative by the National Institutes of Health in the United States (US) is supporting genomic studies of microbial communities at several body sites, with a focus on characterizing how symbiotic microorganisms impact human health.[1,2] There are several other comparable projects being conducted internationally as well, including in Canada,[3] France,[4] Australia and Korea.[5] While the basic concept of using bacteria and other microorganisms for therapeutic benefit is not novel, recent research has more clearly demonstrated the mechanistic role of microorganisms in the human microbiome and its impact on health and illness.[6,7] Probiotics are 'live microorganisms which when administered in adequate amounts confer a health benefit on the host',[8] and are the leading candidates for beneficially modifying an individual's microbiome.[9]

Despite growing familiarity with probiotics, these therapeutic options challenge fundamental paradigms of health and disease, historically based on the belief that microorganisms like bacteria and viruses are a source of illness.[10] This movement towards a beneficial conceptualization of bacteria is gaining legitimacy in the scientific community due in part to a growing body of literature on specific therapeutic purposes for probiotics in the gastrointestinal tract.[11–15] This direction may be embraced by patients with gastrointestinal disease in theory,[16] but may be potentially challenging for policymakers in practice.

Once in the clinical arena, regulations may challenge and reshape how patients can access key information about risks, benefits and efficacy about probiotics that would influence informed decisions about use. With advances in the science from the HMP, new applications and new probiotic types might challenge existing regulatory structures for probiotics in the United States. This development poses important and timely questions about the existing translational pathway and the practical role that regulation plays in the integration of resulting therapies into clinical care. As the fundamental notion of probiotics evolves from their current common status as food or supplement to a therapeutic agent, there will be the need for concurrent reevaluation of ethical, legal and social issues surrounding their development and use in the United States and elsewhere. The need to address these issues will increase with the introduction of probiotic agents tailored for an individual's genome, genetically modified probiotics and synthetic delivery platforms that enhance the collective action of bacteria.

To date, little is known about patient knowledge and attitudes towards the translation of innovative probiotic therapies, specifically the regulations that will guide their integration into research protocols and, eventually, clinical care. Individuals with gastrointestinal disorders are a key population to answer such formative questions because many probiotic products are marketed to ease gastrointestinal distress. In addition, GI patients are likely to be among the first line of recruits for clinical trials of

therapeutic and genetically modified probiotics as well as early adopters of those products that make it to market. As such, their opinions may provide important insight into the key issues surrounding the regulation of probiotics, adoption of probiotics in clinical research and patient care, and the specific informational needs of patient populations in the informed decision-making process. The objective of this study was to examine the attitudes of patients with gastrointestinal disease towards probiotic products in the United States, the evolution of clinical probiotic therapies in conjunction with the Human Microbiome Project and the role of regulation in access to and use uptake of new probiotic therapies.

Materials and methods

The results reported in this study are drawn from a larger qualitative research study exploring attitudes of patients with gastrointestinal disease towards probiotics and novel probiotic applications.[16]

Study design and sample

We conducted focus groups with adult patients with two main chronic gastrointestional diseases, inflammatory bowel disease (IBD) (including ulcerative colitis and Crohn's disease) and irritable bowel disease (IBS). Patients were recruited from tertiary care hospitals in the United States with large centres known for treating patients with digestive diseases: Cleveland Clinic Digestive Disease Institute, the Inflammatory Bowel Disease Clinic at Mayo Clinic and the Division of Gastroenterology at Johns Hopkins University. Eligibility was limited to patients with IBS or IBD, including those patients with pouchitis. Participants had to be at least 21 years of age, proficient in English and able to provide informed consent. Eligible patients were identified through a roster generated from the GI clinic databases and/or review of individual patient files. Multiple recruitment strategies were used, including direct mailings to a roster of patients of certain GI physicians as indicated on a hospital database, study fliers in patient-care areas and individual recruitment of eligible patients by a participating clinician.

Data collection

After the nature and possible consequences of the study were explained, participants provided written informed consent and then completed an anonymous demographic questionnaire prior to each focus group. A moderator facilitated focus group discussions using a structured list of open-ended questions (see Box 1). The moderator guide was designed to help focus the discussions on the broad content areas we wanted to explore. However, moderators were flexible with the guide when facilitating discussions, depending on where participants directed the conversation. Each moderator began by establishing baseline familiarity with probiotics, then providing a standard definition of probiotics to ensure patients without baseline familiarity were operating under a common understanding. In the course of this initial discussion, several topics relevant to this study either arose spontaneously or were probed by the moderator.

Box 1 Moderator Questions

- When you think of the word probiotics, what things come to mind?
- What are your thoughts about government's oversight of such products?
- Do you think that probiotics should be regulated like food? Or should they be regulated like pharmaceutical drugs?
- How would regulation affect your confidence in such products?
- Is there any downside to oversight?
- Scientists are working on changing the genetic make-up of microorganisms that live in our digestive tract to make genetically modified probiotics to treat digestive diseases; what are your thoughts about the genetic modification of these probiotics?

Moderators provided definitions of probiotics; genetically modified probiotics were introduced

as hypothetical entitites that might be created in the future and described using an example (Box 2). However, it was made clear that this was only one example of genetically modified probiotics that might be created in the future. Group discussions were digitally recorded. Content saturation was monitored throughout data collection; data collection continued at each site until we achieved content saturation.

Box 2 Moderator-provided definition of probiotics and example of GM probiotics

- Definition of Probiotics: '*Our digestive tracts are home to billions of living microorganisms. Some are considered friendly and some unfriendly. Our digestive tracts function best when there is the right balance of these microorganisms. Probiotics are foods or supplements that contain large amounts of friendly bacteria that are intended to improve digestive health by helping maintain this balance*'.
- Genetically modified probiotics example: '*Scientists might genetically modify probiotics to give people who cannot digest dairy products the ability to do so. This change might be permanent*'.

Data management and analysis

Focus group recordings were transcribed verbatim. All transcripts were independently reviewed and edited for accuracy by a research team member. Four analysts reviewed three transcripts, one from each study site, to identify themes that emerged from the data. Using an iterative process of independent review and consensus-building meetings, we used conceptual ordering to create a coding schema to categorize the text into major domains, subdomains and categories. Two data analysts applied this coding schema to a second set of three transcripts using QSR NVivo 8[17] and revised the coding schema based on this experience. All focus group transcripts were coded independently by two data analysts who met to review their respective codes and resolve any discrepencies. We then used an inductive approach with the coded transcripts[18] to identify major themes within core content areas and clarify participants' beliefs about probiotics and novel clinical applications of probiotics. We used SPSS 16.0[19] to calculate descriptive statistics on demographic items.

Human subjects protections

This research protocol and all study materials were approved by the institutional review boards at each of the three study sites. Written informed consent was obtained from all patients prior to focus group discussions. Participants received $50 for their participation in the study. Participants were not identified by name in focus group transcripts.

Results

Description of sample

We conducted twenty-two focus groups at the three study sites between March and August 2009; the mean number of participants was six with a range of 4–10 participants. Group composition by diagnosis was as follows: eight groups with mixed diagnoses; eight groups with IBD; three groups with IBS, two groups with Crohn's disease and one group of patients with ulcerative colitis. Three groups included all women, and one group included all men. Demographic characteristics of participants are summarized in Table 1. Themes that emerged from the focus group narratives are presented below, including participants' knowledge of current regulation of probiotics, attitudes towards regulation and perceived advantages and disadvantages of different regulatory mechanisms.

Regulatory structures around currently available probiotic products

Knowledge of the existing framework

Participants voiced a range of knowledge, beliefs and opinions regarding the current regulation of probiotics. In general, they were not familiar with the specific regulatory structures

Table 1 Characteristics of 136 patients participating in focus groups examining translational applications of human microbiome research

Age mean ± SD years (range)	48 ± 16 (21–88) *n* (%)
Gender	
Female	91 (67)
Male	45 (33)
Education	
Less than high school	3 (2)
High school/GED	23 (17)
Community college	34 (25)
Four-year college	43 (32)
Graduate school	28 (21)
Professional school	5 (4)
Income*	
Less than $15 000	11 (8)
$15 001–35 000	17 (13)
$35 001–55 000	27 (21)
$55 001–75 000	23 (18)
$75 001–100 000	25 (19)
Over $100 000	28 (21)
Ethnicity*	
Non-hispanic	127 (96)
Hispanic	5 (4)
Race*	
White or Caucasian	126 (93)
Black or African American	4 (3)
American Indian or Alaska Native	1 (1)
Asian	1 (1)
Multi-racial	3 (2)
Self-reported diagnosis*	
Crohn's disease	47 (35)
Ulcerative colitis	33 (24)
Pouchitis	6 (5)
Indeterminate IBD	3 (2)
Irritable bowel syndrome	38 (28)
Other/unknown diagnosis†	8 (6)
Health insurance*	
Yes	128 (96)
No	6 (4)
Previous participation in research*	
Yes	64 (47)
No	71 (53)

*Not all patients provided this information.
†Two patients reported a diagnosis of small intestinal bacterial overgrowth, and one reported a diagnosis of *Clostridium difficile*. Five patients reported no diagnosis to date.

governing probiotic products, but felt that some form of formal oversight would be appropriate,

> I do not know what the government oversees right now on health food. Like supplements and things that are sold there so I suppose it would be at least what they oversee there. But there may be no oversight. In which case, I think there should be some.

They were also unclear about when and why probiotic products fell into different regulatory categories,

> I just don't see why one thing is a supplement and one thing isn't.

Of concern to these GI patients was their own uncertainty about how federal agencies assess the safety of probiotics for general consumer use as compared to their use by patients with specific health conditions (e.g. digestive diseases), whom they viewed as potentially at greater risk of the adverse effects of probiotics. Existing regulatory standards and pathways were not reviewed with participants.

Despite their lack of familiarity with existing regulatory pathways, participants drew some conclusions about existing regulations based on their primary frame of reference for probiotics, that is, in the form of dietary supplements and food. A few individuals thought probiotics should be regulated similarly to over-the-counter vitamins or dietary supplements. Advantages to categorizing probiotics in this way included lower cost and fewer barriers to access:

> It should be like a vitamin too and over the counter.

However, other participants worried that probiotics regulated as supplements would be subject to less oversight and potentially be less safe than oversight as a pharmaceutical agent.

Participants did not expect these readily available probiotics to be proven effective at meeting a specific health claim in the way that drugs are:

> You can go to these natural food stores or these kinds of places and you just… just assume, 'this has not been FDA-approved,' so, you … you, basically there's no guarantee of the efficacy of the product.

In addition, participants assumed that probiotic products regulated as food would be safe

for most people, but wanted an additional level of scrutiny for themselves as a special population in terms of efficacy.

> I wouldn't be fearful of it [a currently available probiotic agent] not being safe, but I would not take it seriously as something that helped digestive disease….unless it's like my doctor, the FDA, or some other credible source agreed with that statement.

Impact on use

When questioned about how regulation would influence their actual usage of probiotics, they expressed a wide spectrum of opinions. Many participants indicated that for them, regulation in any form legitimizes a probiotic product but they did not ascribe this to a specific regulatory purpose. Even as they were undecided about whether regulation would have a significant effect on product quality or safety, one participant articulated this broad sense of reassurance that regulation would provide:

> It[regulation] wouldn't make me feel like [a probiotic product is] any safer, but, I don't know, it makes it seem official in some way. It would make me feel a little bit more confident.

When participants conceptualized probiotics as a pill or medicine, they tended to express a preference for more robust regulation in addition to truth-in-labelling assurances:

> If you want to use it as a therapeutic agent in Crohn's Disease, I feel that there's much more responsibility I would put it closer to conventional therapies in that case in terms of the stringency of oversight.

In contrast, another participant discounted the value of regulation entirely in their decision making about probiotic use, pointing out that the volatile and individualized nature of their diseases may make the intention of some regulations irrelevant to their specific cases.

> I think what works is what you use, so if you take something for a while and it works then you stick with it… I have spent a lot of time, like taking a stab here and there and trying to figure out what is good …I don't know that like a strict labelling policy would necessarily steer me one way or the other because if it doesn't work and it is labelled accurately, then that doesn't help you either.

Future regulation for novel probiotic applications

Participants also expressed a variety of preferences for the regulation of probiotic products in the future.

Participants discussed the notion that federal regulation may lend legitimacy to probiotics as an accepted therapeutic option among health-care providers. Specifically, they mentioned doctors might be more likely to suggest or prescribe probiotics as treatments if they had been developed, marketed and regulated as a pharmaceutical drug as opposed to a form of complementary or alternative medicine (CAM). Other participants mentioned additional benefits to the regulation of probiotics, such as the possibility of financial benefits if a medical prescription from a licensed health-care provider was required to obtain probiotics:

> I think … your prescription insurance [would cover the cost] if it was an FDA prescribed thing,

thus minimizing the financial burdens for individuals who wanted to utilize probiotics.

Lack of regulation as a potential barrier to access

Participants appreciated their existing freedom of access to probiotic products. In general, they voiced the concern that regulation might reduce access or create barriers to accessing probiotics, particularly if products were regulated as drugs to treat or mitigate specific illnesses. Examples they gave included the possibility of a need to visit a health-care provider to obtain a prescription or that currently available probiotics could be removed from the market during the regulatory transition process:

> But on the downside of regulating it, if they suddenly decide to regulate it, they'd probably pull all the drugs off the market and they wouldn't be available for ten years.

When participants thought about the prospect of increased future regulation, they discussed concerns about the potential for increased growth in involvement of pharmaceutical companies in the development of probiotic products. One participant commented that they liked that probiotics were natural but worried about the changes and consequences if pharmaceutical companies get involved:

> So, you know, the fact that it is natural and that people are doing these studies and trying to get it out there is fine but you know … If it is that great of an idea the drug companies are going to get their hands on it … and it is just whether you trust them or not …

The influence of pharmaceutical companies was highly suspected by participants:

> There is the possibility that pharmaceutical companies are in bed with the FDA. I know they are in bed with doctors.

These participants worried that,

> It's the drug company, it's somebody with their deep pockets with the FDA,

who shape regulatory requirements for pharmaceutical drugs, sometimes with negative consequences for the public. As one participant stated,

> I don't really think that whatever oversight there is [of pharmaceutical drugs] is really looking out for the best interest of citizens.

In addition, patients were concerned that the involvement of pharmaceutical companies might:

> make it as expensive as pharmaceutical drug;

a concern that was shared by many participants.

Genetically modified probiotics

Although these products are not currently available, we asked participants about their views of genetically modified probiotics. Participants generally agreed that, compared to existing forms of probiotics commonly available, genetically modified probiotics should require an additional level of regulatory oversight:

> Because it seems like it's taking it to a whole new level, it seems to me that it [genetically modified probiotics] should be tested for safety and regulated by the FDA.

Safety was most often cited as the reason a heightened level of regulation was preferred, both because regulation should ensure that genetically modified probiotics are safe and to give potential users more confidence about utilizing them as part of their health-care regime.

Views about appropriate and effective regulation

Themes of scepticism of the existing regulatory system in the United States arose several times in the focus groups. Participants expressed general uncertainty about government regulation and a preference for self-directed assessment of safety and efficacy:

> I wouldn't want it regulated because I do not think the government are the best people to make that decision…. I will search out quality brands … you have to do research on your own but I don't just want to turn it over to the government because I don't think turning anything over to the government is the best answer.

These comments were in reaction to probiotics in particular but may encompass a general preference about regulation.

Another theme pertained to doubt about whether existing regulations of any products were effectively being enforced:

> I am not sure how much, to what degree [regulation enforcement] takes place.

At least one participant attributed the lack of enforcement to the perception that regulatory agencies lacked the financial and organizational resources necessary for adequate oversight:

> They are so far understaffed now, they are not doing their job.

Participants who shared this belief did not anticipate benefit from the government regulation of probiotics.

Even those participants who were in favour of greater levels of regulation commented that

regulation itself does not guarantee the safety of products. Several participants cited recent recalls of food and drug products when making this point. Although these comments were general statements – not unique to probiotic products – participants pointed out that recalls undermined their confidence in government regulators:

> I have a huge sense of confidence in the FDA, but they have messed up royally several times in the past decade or so….

Alternatively, some participants looked to federal regulations in general as a way to build confidence in the use of probiotics:

> You always somehow feel a little better when you pick up something and it says FDA approved.

Discussion

Probiotics are typically marketed to promote general gastrointestinal health or to support well-being. Currently, probiotic products are consumed as dietary supplements, which is a category of food regulated by the US government's Food and Drug Administration (FDA). This category includes dietary ingredients, such as vitamins, minerals, herbs, botanicals, amino acids or other 'dietary substance[s] for use by man to supplement the diet' and intended for ingestion in pill, capsule, tablet or liquid form, and is not the sole item of a meal or diet (21 USC 231).

Probiotics straddle conventional and regulatory distinctions between foods and drugs. For example, some consider probiotics to be *functional foods*, or 'whole foods and fortified, enriched, or enhanced foods [that] have a potentially beneficial effect on health when consumed as part of a varied diet on a regular basis, at effective levels'.[20] This is not a legal or regulatory term, but a term frequently used by dieticians. In the future, as a result of genetic manipulation or research on disease-specific use, probiotics may be viewed as one of several examples of *medical foods* and thus subject to FDA regulations under the following legal definition: '[A] food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation' as defined in 21 USC 360ee(b)(3). Alternatively, some probiotics may be viewed as *pharmaceutical drugs* and regulated accordingly as defined in the US regulatory code.[21]

Based on the current US regulatory structure, food and dietary products are prohibited from making specific health claims such as those related to the treatment, prevention or mitigation of disease.[22] To make such claims, the product must fall under the categorization of 'drug', a designation that requires extensive clinical research to establish validated biomarkers and endpoints to measure human health benefits of probiotic products. This designation of a probiotic 'drug' would run contrary to current researcher[23]and patient[16] understandings of probiotics as complementary or alternative medicines.

Regulations help information about a new therapeutic from which users base their decisions about agents to preserve or promote health; however, our findings demonstrated that GI patients do not, as a group, understand product regulation in the United States generally or as it pertains to probiotic products. Participants expressed general agreement that some regulation of currently available probiotic products is desirable, but varied in their views about the aims of such regulation and the form that it might take. Participants exhibited a good grasp of, and strong opinions about, the benefits and burdens of regulating probiotics. Specifically, these uncertainties reflected how participants in our study population thought about the acceptable use of probiotics as part of their health care. Our findings suggest, at a minimum, some mechanism is in place to ensure evidence-based translation of these agents into clinical research and patient care.

Considerations of indications, risks and benefits are at the core of informed decision

making. In the United States, regulation plays an important role in how material information about probiotics is established and communicated downstream to users. Participants in our study expected regulators to ensure that probiotic products are safe and effective. Our findings suggest that patients will expect regulated probiotic products to be labelled accurately and provide them with information about content and safety to guide decision making about consumption. In addition, for those probiotics consumed to address specific medical conditions – for the prevention, treatment or mitigation of disease – issues of efficacy are equally important. Concerns about the adequacy of current regulations in the United States were raised within the context of a general lack of clarity about the categorization of probiotics as food or drugs. In addition, participants often did not understand what differentiated the regulation of food, supplements or drugs, and why. These concerns, in turn, gave rise to questions about structures to ensure safety and efficacy.

Regulations also play a central role in translating clinical research from the bed to the bedside. Patients and the general populations' beliefs and attitudes about the regulation of probiotics may help frame their interest, acceptance and willingness to use new probiotics therapies. These perceptions, in turn, will influence how patients make informed decisions about the use of these products as part of their health care. Thus, the translational process will hinge on the timing and shape of the regulatory process. These changes, in turn, will likely have an important impact on patient care as probiotics transition to a therapeutic agent with growing relevance and legitimacy in clinical medicine, engaging health-care providers in access and utilization. When and how the regulatory framework is adjusted for therapeutic probiotic products will be pivotal in the translational process of probiotics from bench to bedside use. Thus, the significance of regulation cannot be overlooked in the translational process as it has an unmistakable impact on clinical research, development and availability of probiotic products.[22]

One example of the probiotic products that may result from translational research was explored with patients in the form of genetically modified probiotics. The consideration of genetically modified probiotics also raises important questions about safety, efficacy and access to information. While concerns about regulation do not appear to interfere with participants' decisions to use probiotic products at the present, our results suggest that such concerns will play a more important role when genetically modified, and other novel forms of therapeutic probiotics are introduced into patient care in the future. Consistent with prior evidence, genetic modification increases public perceptions of risk of new technologies.[24] Participants in our study perceived genetic modification to inherently have more risks. This, in turn, might affect consumer's risk-benefit calculation when making informed decisions about the use of probiotics in the setting of clinical research or over-the-counter use. In addition, the development of genetically modified probiotics raises concerns about how such new technologies will be integrated into society and ethical challenges along the way.

Authenticity of information is another key aspect of the patients' decisions about whether or not to use novel therapeutics, GM or otherwise. Trust in product safety and in regulators will be crucial to the adoption of new probiotic therapeutics. Studies show that perceptions about risk associated with a new technology are primarily affected by how unfamiliar the technology is, whether it is perceived to have the potential to produce harm, and how trustworthy the stakeholders in its development are perceived to be.[25] Our findings suggest that current federal regulatory bodies and processes in the United States are viewed with deep scepticisms and that trust, transparency and the inclusion of stakeholders in the regulatory process will be key to the translational process of new probiotic therapies. An investigation into attitudes towards genetically modified food stakeholder organizations in the United States found an all-time low level of public trust in the federal government and industry.[26] Thus,

public engagement may be one avenue to improve overall trust in the regulatory system.[25] Another approach would be to promote further translational research that explores issues arising for patients during the development of these probiotic agents. Such methods will help regulators identify social and ethical concerns of the probiotic users and ultimately determine how best to address those concerns through education and regulation.

Our findings also speak to another emerging issue: access to new technology. Participants in our study raised dichotomous concerns about new forms of regulation becoming a barrier to access and use probiotics in the United States. On the one hand, regulation might legitimize probiotics as medical products, which, in turn, might lead more physicians to consider and use these agents in patient care. On the other hand, regulation might make it more difficult to use probiotics, in terms of both access to the products and information about them. The potential for increases in costs and barriers to access from regulation of probiotics as a therapeutic method raised the spectre of losing probiotics as a self-care option. The importance of this concern is underscored by our earlier work showing that patients with chronic gastrointestinal diseases value probiotics as a method to control their own on-going symptom prevention and management.[16] While regulation could both promote and reduce access to care, and thus our findings provide no clear policy response for US policymakers, they do indicate that this particular group of stakeholders are concerned about the outcome of regulation and have relevant comments.

Limitations

Participants were recruited from large US hospitals known for treating digestive diseases, and thus the views expressed by these participants may differ from other patients with chronic digestive diseases. Those who self-selected to participate in our focus groups may have greater awareness, knowledge or favour of probiotics and their regulatory status in comparison with patients who chose not to participate. The subpopulation of patients recruited for this study may not be representative of other non-patient stakeholder groups, in terms of their opinions towards probiotics or regulation. We do not know what the baseline level of knowledge of probiotic regulation was for each participant, nor did we establish a baseline understanding of the regulatory process. However, the participants do provide insight that GI patients are an important stakeholder group of the various perspectives for which regulations should account.

In addition, the focus group approach has inherent limitations: the potential to promote agreement and prevent the expression of dissention. Moderators did not communicate existing regulatory structures but merely recorded what participants reported. However, we triangulated data to establish converging themes using multiple study sites and focus groups comprising different GI disease diagnoses.

Conclusions

Our findings in the GI patient population provide important insight into guiding the process of updating or modifying the existing regulatory practices in the United States to accommodate emerging therapeutic probiotics, as gastrointestinal patients represent those individuals who are receptive to new approaches to chronic conditions. The data presented here capture the complexity surrounding the US regulation of existing probiotics, as our participants had a diversity of perspectives about regulation. If GI patient perspectives are indicative of public perceptions of therapeutic probiotics in the United States, consumers may expect more rigorous regulation, similar to current regulations for pharmaceutical drugs, while simultaneously wanting low costs, easy access and low involvement of pharmaceutical companies. Regulators in the United States should clarify and simplify the existing regulatory pathways for probiotics and their future therapeutic products, as well as engage in efforts to regain consumer trust. Ideally, these efforts should be made before

genetically modified probiotics emerge that blur the conceptual and regulatory line between functional foods and pharmaceutical drugs. Regulators in other countries may similarly wish to determine consumer attitudes towards both probiotic therapeutics and regulatory mechanisms.

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Conflicts of interest

None of the authors have any conflicts of interests to declare.

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