The Human Microbiome and Public Health: Social and Ethical Considerations

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Rapid advances in human microbiome research point to an increasing range of health outcomes related to the composition of an individual's microbiome. To date, much research has focused on individual health, with a paucity of attention to public health implications. This is a critical oversight owing to the potentially shared nature of the human microbiome across communities and vertical and horizontal mechanisms for transferring microbiomes among humans. We explored some key ethical and social implications of human microbiome research for public health. We focused on (1) insights from microbiome research about damage to individual and shared microbiomes from prevalent societal practices, and (2) ethical and social implications of novel technologies developed on the basis of emerging microbiome science. (*Am J Public Health*. 2016;106:414–420. doi:10.2105/AJPH.2015.302989)

Human microbiome science is advancing rapidly and is showing promise of having important impacts on human health. Incorporating microbial information into the diagnosis and management of certain diseases is thought to provide important information regarding disease progression and treatment, particularly in the case of inflammatory, immune, and systemic disorders.[1] Knowledge of the human microbiome relating to several distinct body sites is leading to promising human health interventions. For example, studies of the oral metagenome reveal important differences in microbial environments in those who suffer from dental diseases such as periodontitis and dental cavities and those who do not. Such findings suggest that mechanisms of culturing and transferring protective bacteria, dominant in those without cavities or other dental disease, may help decrease cavities and improve oral health overall.[2]

Further studies are under way to help understand differences in geographically and socioeconomically diverse populations, contributing further to our understanding of the role of the human gut microbiome.[3] Such findings can help us first understand and subsequently develop strategies to modify or shape the gut microbiome via individualized diets or therapies,[4] potentially alleviating some of the disease burden caused by global trends in obesity and in other areas of gastrointestinal health, such as inflammatory bowel disease.[5–10] Furthermore, research suggests that the skin microbiome may play a role in protection against pathogens and physical agents as well as in heat regulation, sensation, and metabolic synthesis.[11]

Microbial communities in the nasal and oral cavities and in the respiratory tract may be implicated in allergies and asthma.[12] Microbes in the urogenital tract have been linked to vaginosis and other infections in women and may be implicated in aspects of fertility and pregnancy.[13–16] Research has demonstrated the longer term implications of microbial changes during pregnancy, delivery, and the newborn period on infant and childhood health.[17] In addition to physical health, autism and mental health conditions, such as depression, anxiety, stress, aggression, and other mood disorders, may also be linked to a microbial etiology.[1,18,19]

All these advances suggest that purposeful manipulation of the human microbiome is an increasingly promising avenue to effective therapies for a large range of conditions. There have already been important developments in this area, perhaps most notably in the dramatic success of fecal transplants for *Clostridium difficile*–mediated colitis,[20,21] the use of probiotics (we draw on the widely accepted definition of probiotics developed by a working group on behalf of the Food and Agriculture Organization of the United Nations and the World Health Organization: "live microorganisms which when administered in adequate amounts confer a health benefit on the host"[22(p506)]) to address the worldwide burden of enteric and diarrheal disease in children,[23] and the use of probiotic lozenges or mouthwash to decrease the risk of periodontal disease.[24] In addition to leading to new technologies, human microbiome research is helping us understand adverse health implications of existing medical interventions and other societal practices. For example, the role of antibiotic use in the development of autoimmune diseases has been documented,[25] and increasing evidence indicates a link between early childhood exposure to antibiotics and later development of asthma.[26]

Human microbiomes do not exist in isolation from each other but are constantly evolving and influenced by environmental factors such as antibiotic use, diet, and the microbiomes of family and other community members.

We explored some of the broader public health and ethical implications of microbiome research. Our analysis has 2 main points. First, we considered how knowledge generated

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from microbiome research allows us to better understand the implications of current societal practices and policies that have an impact on the microbiome, such as antibiotic use. Second, we considered possible implications of novel and potential technologies arising from microbiome research. In particular, we examined how microbiome technologies designed to have an effect on the individual level may have important and unanticipated consequences on family, community, and public health levels. We argue that future research needs to consider an obligation to our common microbial environment and the stewardship of the shared microbiome.

SOCIETAL PRACTICES, POLICIES, AND CULTURE

Recent studies have shown that the ecology of the microbiome changes and adapts to environmental and dietary conditions.[27–29] Many of these conditions are associated with broader societal practices, such as an industrialized diet, widespread use of antibiotics, and particular cultural practices. Some of these changes are associated with significant adverse health outcomes, and some of these changes to microbiomes may be long lasting or even permanent.

For example, studies suggest that the microbiota of individuals exposed to secondhand smoke are adversely affected, leading to reduced immunity.[30] Furthermore, studies of the human gastrointestinal tract suggest that of all environmental factors investigated to date, the gut microbiome is most influenced by diet.[31] The gut microbiome's adaptation to a modern diet, rich in simple carbohydrates and dairy products, may contribute to the current world obesity epidemic because intestinal microbes promote the recovery of energy from fermentation of dietary residue in obese individuals.[32,33] A recent study also illustrates that cultural preferences for certain spices (i.e., turmeric) can interact with the gut microbiome to influence important physiological processes (i.e., motility).[34,35] Other studies suggest that societal shifts to sedentary lifestyles have a negative effect on gut microbiota diversity, which has been linked to conditions such as autism, gastrointestinal disease, and decreased health among elderly populations.[36]

The mode of infant delivery is at least partially determined by cultural factors, rather than solely clinical considerations. For example, a Brazilian study shows that cesarean delivery rates are correlated to maternal education, and almost all wealthier Brazilian mothers deliver infants by cesarean delivery.[37] The authors of the study concluded that cesarean deliveries are scheduled in large part on the basis of convenience. Neonates are initially exposed to maternal and other bacteria during birth. Studies suggest that neonates delivered via cesarean delivery have bacterial communities from the mother's skin surface, whereas neonates born vaginally have communities reflecting their mother's vaginal microbiome.[38] Thus the mode of delivery determines the early construction of an infant's microbiota,[38] and individuals born via cesarean delivery have a higher chance of developing necrotizing enterocolitis and methicillin-resistant *Staphylococcus aureus* in the neonatal period as well as allergic disease later in life.[39] Another study found that obesity rates in later life are 58% higher among children born via cesarean delivery.[40] Hospitalization and contact with health care workers may also influence newborns' microbiomes.[41]

The infant microbiome may also have a role in the development of respiratory infections and wheezing early in life as well as allergies and asthma later.[42–44] Several studies have examined the effects of influencing the infant microbiome. For example, there have been trials randomizing infants to probiotic supplementation to determine whether daily exposure to *Lactobacillus GG* can prevent the development of early asthma markers.[45] Another study examined whether maternal supplementation with probiotics during pregnancy can affect the development of atopic eczema in childhood.[46] Formula feeding instead of breastfeeding has also been associated with changes to the infant microbiome, likely with adverse consequences.[38] Changing the maternal microbiome and environment during and after birth may, therefore, have a considerable impact on the development of an infant's microbiome, with consequences for various areas of health later in life, including oral health, infections, and gastrointestinal disorders.[17,47,48]

The widespread use of antibiotics has possibly the most significant effect on changes to human microbiomes. Evidence from different contexts suggests that overall antibiotic use in society is not governed only by clinical considerations but must to some extent be understood as a cultural or social practice. In particular, general practitioners' prescribing of antibiotics even in cases in which this is counterindicated relies on cultural assumptions about antibiotics and doctor–patient relationships[49]; antibiotic prescribing in hospitals is subject to cultural, contextual, and behavioral factors[50]; and prophylactic intrapartum antibiotics are administered to pregnant women who test positive for group B *Streptococcus* cultures in some countries but not in others.[51] Undoubtedly antibiotics have played a fundamental role in decreasing suffering and mortality from communicable diseases and infections and, in turn, increasing life expectancy. However, antibiotics also wipe out the "good" bacteria in our bodies, and the populations of these useful bacteria may never fully recover. The effects of this may be profound, with some researchers suggesting that overuse of antibiotics is responsible for the dramatic increase in obesity, allergies and asthma, type 1 diabetes, and inflammatory bowel disease.[52–54]

To complicate matters further, some bacteria seem to be both harmful and helpful, depending on context. The widely discussed example of *Helicobacter pylori* illustrates the point well. A decline in *H. pylori*, owing to improved hygiene and an increased use of antibiotics, has led to an associated decrease in the prevalence of peptic ulcers and stomach cancers. However, there has also been a concurrent increase in diseases of the esophagus, including the deadly esophageal adenocarcinoma, which has also been linked to the decline of *H. pylori*.[55] Additionally, individuals without *H. pylori* are more likely to develop hay fever, asthma, and skin allergies in childhood.[54]

Worldwide problems relating to antibiotic resistance are well documented.[56–58] Strategies to tackle antibiotic resistance include public education, controlling antibiotic use (particularly as one third of antibiotic use in hospitals is thought to be unnecessary[59]), developing new antibiotics, and using alternatives to antibiotics, such as more targeted approaches to eradicating specific microbes when possible.[57,60] These efforts fall under the category of antimicrobial stewardship programs, which, unfortunately, have been only marginally successful to date owing partly to the increasing prevalence of multidrug-resistant organisms. Such resistance leads to a vicious circle of broader antibiotic use followed by a further increase in antibiotic resistance.[61] Tosh and McDonald[62] suggest that antimicrobial stewardship programs need to be reframed in the context of human microbiome research.

The human microbiome has been subject to significant "collateral damage" because of the broadening spectrum and overuse of antimicrobials.[62] Thus microbiome research may be a key component to responding to and addressing antibiotic resistance. For example, recent research reveals that country-specific practices influence antibiotic resistance potential,[63] providing additional insights into results of antibiotic use policies. An increased understanding of the human microbiome may help to address some of the other concerns resulting from antibiotic resistance by allowing the development of techniques to preserve and reestablish an indigenous microbiome, developing and using antimicrobial therapies that spare the microbiome, and understanding and developing methods that mimic the protective effects of an intact microbiome.[62]

An increasing number of adverse health outcomes are associated with "damage" to the human microbiome. Evidence suggests that in many cases this damage is associated with contemporary societal practices. Advances in microbiome research have the potential to further shed light on what particular aspects of food consumption, antibiotic use, and other modern societal practices are problematic and, ideally, lead to appropriate changes being implemented. If this research indicates significant damage to the collective human microbiome or risk of such damage owing to societal practices, policies that safeguard our collective microbiomes (microbiome stewardship) are warranted.[64]

For example, inflammatory bowel disease is associated with perturbations of the gut microbiome.[5,65] If these perturbations are linked with modern dietary intake, then food production legislation may need to take into account the effect of particular ingredients or production processes on the human microbiome. Similarly, there should be risk calculations that weigh the benefits of prophylactic antibiotic use (e.g., in the case of preventing group B *Streptococcus* infection in newborns) against the risk of adverse consequences resulting from effects on the microbiome. Indeed, future research may even suggest the need for environmental risk assessments for certain pollutants to incorporate assessment of damage to microbiomes.

PUBLIC HEALTH AND ETHICAL IMPLICATIONS

As microbiome knowledge evolves, increasing numbers of products and strategies to modify and improve an individual's microbiome will become available. Social and ethical implications may arise from technologies whose primary purpose is to modify the state of individuals' microbiomes.

There is evidence that the microbial environment during critical periods in infancy can have a long-lasting influence on the development of an individual's microbiome.[44,66,67] There is also evidence that the composition of an individual's microbiome continues to be affected by the individuals with whom they come in contact, even in adulthood. Family members have similar microbiomes.[10,68,69] Although shared genetic information may shape the microbiome and offer some explanation for this similarity, family members who are not biologically related, such as spouses, also have similar microbiomes.[70,71] Studies also suggest that members of the same sports team have similar microbiome profiles.[72] The sharing of oral,[73,] seminovaginal,[74] and gut microbiota has been demonstrated.[75] Taken together, these findings suggest that (at least parts of) microbiomes from different body sites may be transmitted between individuals, even in adulthood.[76]

The fact that microbes are transmitted between individuals is self-evident. However, the notion that such transmission can permanently affect relatively stable microbiome profiles, and that such microbiome changes may be transmitted between individuals and shared among communities, raises important social and ethical questions. In particular, decisions by individuals to modify their own microbiome may under certain circumstances have implications for other individuals, particularly infants, family members, and others in regular close physical contact. Therefore, the prospect of microbiome technologies that allow permanent or long-lasting changes to be made to individual microbiomes has important implications for autonomy. We illustrate this consideration using a hypothetical example.

The connection between obesity and the gut microbiome has received considerable attention.[33,77] To our knowledge no applications with broad societal significance have emerged from this research to date, but the extent of scientific attention suggests that technologies may be developed that rely on the manipulation of the gut microbiome for achieving significant weight loss for obese individuals. We therefore propose the hypothetical example of a probiotic that helps to fight obesity resulting in an over-the-counter "slimming pill." Perhaps this probiotic targets the gastrointestinal microbiota and influences caloric uptake. As it is conceivable that manipulation of 1 person's microbiome may influence others' microbiomes, questions arise about the impact of an individual taking such a pill for other individuals, including sexual partners, family members, community members, and the broader population as a whole. We might further speculate on what might happen if there is widespread use of such a pill across the population.

Because of the extent of public perceptions regarding the "obesity epidemic," widespread use of such a technology certainly does not seem farfetched, and it raises the question of how such broad manipulation of individual microbiomes might affect the collective microbiome of the entire community. What then would be the wider public health impact for a community, cohort, or certain subsector of the population? Would such consequences be long or short term in their impact? What are the implications for underweight or malnourished individuals and communities if these microbes are transmitted? What are the implications for countries in which starvation is a major issue?

Another example is the possibility of a probiotic that stimulates and boosts the immune system. Although this might be beneficial for the individual who takes it, and possibly the majority of the population, it may have devastating consequences for those who have overactive immune systems (e.g., those with ulcerative colitis) or who have purposefully suppressed immune systems, such as transplant recipients.

Although hypothetical, these examples illustrate how 1 person's efforts to change his or her own microbiome might inadvertently affect the microbiomes of others in his or her immediate family or surrounding community. Such effects may be detrimental or beneficial, or there may be no effect at all. The important point here is that an individual's health may be directly affected by the health choices of others. From a bioethics perspective, there are implications for autonomy, in that individuals may have their microbiomes altered against their wishes (or even without their knowledge) in ways that are detrimental to them. From a public health perspective, there may be safety implications if large numbers of individuals changing their microbiomes leads to communitywide changes to the collective microbiome.

Because the evidence currently available is limited, it is not clear whether people's attempts to change their own microbiome would affect the microbiomes of those around them for any particular intervention, but the possibility certainly cannot be discounted. Although such speculations are exactly that, we raise these questions to promote further research and reflection in this area, particularly as initial microbiome research raises exciting and important implications that have great potential for individual and public health in resource-poor and resource-rich nations.

COMMUNITY AND PUBLIC HEALTH INTERVENTIONS

Currently, most actual and anticipated microbiome-based health interventions target the individual, such as the use of fecal transplants for *C. difficile* infections.[21] However, it stands to reason that microbiome interventions could be designed to target community and public health challenges. A familiar example of such a public health initiative is the fortification of milk with vitamin D to prevent bone disease. A microbial equivalent might involve purposeful microbiome manipulation for public health, for example, by fortifying the water supply or milk with probiotics to provide some beneficial or protective effects to the broad public.[78,79] Although the impact of such an initiative may be similar to that of the examples we have given, the issues with this are conceptually distinct. Public health initiatives generally bypass individual decision-making processes. Justification for overriding individual autonomy is determined by the premise that the improved public benefit outweighs the potential individual costs.[80]

Public health initiatives to reprogram microbiomes on a community level would likely be rationalized and implemented in a similar manner as existing public health campaigns are. For example, microbiome research has raised the potential for the development of probiotics or an organism that enables targeted eradication of *H. pylori*, a bacterium that may lead to stomach cancers.[81] If such a probiotic could be introduced into the food system as fortified flour, yogurt, and cereals, and iodized salt have been, it may be possible to reduce rates and suffering from stomach cancer, dental disease, or other illnesses on a broad population level.[79] Similarly, preliminary research suggests the utility of probiotics in decreasing upper respiratory tract infections,[82] raising the possibility of using probiotics on a public health scale to colonize the upper airways to make them resistant to such infections. Because of the link between the microbiome and mental health conditions,[83] it is theoretically possible to develop a probiotic targeted at those in the population at heightened risk of developing certain mental health conditions, such as depression or the conditions experienced by individuals from alcoholic or abusive homes.

Additionally, human microbiome technologies potentially could be developed to aid in public health disasters, such as the Walkerton tragedy, in which the water supply of the town of Walkerton, Ontario, became severely contaminated with fecal effluent from a nearby farm following heavy rainfall.[84] More than 2300 residents became ill and 7 people died because the water was contaminated with *Escherichia coli* O157:H7 and *Campylobacter fetus* subsp *jejuni*.[85] Longitudinal studies have revealed that residents who experienced bacterial gastroenteritis from the water contamination had a more than threefold increased risk of irritable bowel syndrome, with an absolute increase of 26.1%.[85,86] Prebiotics have been defined as

> nondigestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, thus improving host health.[87(p1505–1506)]

Research that suggests that probiotics and prebiotics may be helpful in treating those with irritable bowel syndrome[87,88] raises the possibility of using such technologies to interrupt the infectious process in response to future public health disasters.[89]

Although such initiatives do show promise, they also raise concerns about unanticipated and perhaps devastating consequences. For example, although destroying harmful strains of *H. pylori* may seem to be beneficial in terms of decreasing stomach cancers, by destroying such bacteria too early we may inadvertently increase the chance of developing asthma or allergies early in life.[52] Therefore, we have to proceed with caution in any such widespread public health initiative involving the introduction or removal of bacteria. A further concern that should be considered is what the impact of combinations of interacting microbiome interventions might be. Developing safety mechanisms in the implementation of such initiatives, including adequate oversight and regulation, and fostering trust will be essential.[90]

CONCLUSIONS

Research on the human microbiome is advancing rapidly and, although still in its early stages, is showing promise of having important effects on human health. Currently, most health interventions seem to be focused on the individual and clinical levels, although broader public health benefits from this research seem likely. We have argued that these advances, although on the whole positive, raise important social and ethical questions that should be considered simultaneously with scientific advances and the development of novel technologies. To summarize, we feel that particular attention needs to be given to the following:

1. *Damage to individual and shared microbiomes as a result of societal or medical practices*. Microbiome research is

allowing us to better understand the impact of certain practices—such as exposure of infants to antibiotics, mode of infant delivery, and modern patterns of food consumption—on the human microbiome and subsequent health outcomes. Evidence is accumulating that such practices, irrespective of their benefits, may have critical negative consequences. We, therefore, argue that we need to seriously consider the notion of microbial stewardship in evaluating interventions and practices that risk damage to the collective microbiome of communities.[64]

2. *Long-term consequences of microbiome manipulation*. Evidence is accumulating that suggests particular microbial exposures during critical periods of infancy and childhood have long-term or even permanent effects. Research efforts need to be directed at understanding such long-term effects in the form of cohort studies with sufficiently long time horizons. At the same time, interventions that affect the microbiomes of infants and children need to be precautionary by properly evaluating unintended long-term consequences of such manipulations.
3. *Shared nature of the microbiome*. Because of the potentially shared nature of the microbiome (or parts thereof) among families and communities, we may need to start conceiving of microbiome-related interventions targeting the individual as potentially having a broader effect on others. This is especially the case if we consider interventions that may be used by very large numbers of individuals (e.g., the hypothetical probiotic slimming pill). Empirical research is needed to assess whether such broader effects actually exist and, if so, to what extent.
4. *Public health interventions*. With advancing knowledge of ideal healthy microbiomes, there seems to be scope for developing broad community-based interventions for supporting or supplementing diets with probiotics or prebiotics. Such interventions may lead to important health benefits. However, such interventions should also be treated with extreme caution, because of the impossibility of controlling and predicting mutations of microbes outside the laboratory and because of the unknown long-term effects of changing the microbiomes of entire communities.

Human microbiome research is very young. Although such research has enormous and exciting potential for individual and public health, many clinical and ethical implications remain unknown. Studying an individual's microbiome to predict health, disease status, and longevity will be complex and require consideration and understanding of multiple interacting factors, many of which will be difficult, if not impossible, to measure and understand. Therefore, the utility of human microbiome research may be limited, at least at first, to certain sectors, and human microbiome research may capitalize on early successes, such as in fecal transplants, to influence the gastrointestinal microbiome.

Ultimately, the successful transition of human microbiome research from bench to bedside to pavement will rely not just on the science but also on public perception of proposed individual and public interventions. To benefit public health, human microbiome research needs to prove its utility on both the clinical and the community level. Lessons learned from public health campaigns, such as vaccination and screening programs, will help convince the public of the acceptability of programs derived from microbiome research. Public trust in the regulation and oversight of such products and campaigns is essential to their success.[91] AJPH

CONTRIBUTORS

K. C. O'Doherty conceptualized the study. K. C. O'Doherty and A. Virani drafted the article. A. Virani and E. S. Wilcox conducted background literature searches.

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No protocol approval was necessary because no human participants were involved in this study.

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