PERSPECTIVE

The human gut microbiome and health inequities

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Individuals who are minoritized as a result of race, sexual identity, gender, or socioeconomic status experience a higher prevalence of many diseases. Understanding the biological processes that cause and maintain these socially driven health inequities is essential for addressing them. The gut microbiome is strongly shaped by host environments and affects host metabolic, immune, and neuroendocrine functions, making it an important pathway by which differences in experiences caused by social, political, and economic forces could contribute to health inequities. Nevertheless, few studies have directly integrated the gut microbiome into investigations of health inequities. Here, we argue that accounting for host–gut microbe interactions will improve understanding and management of health inequities, and that health policy must begin to consider the microbiome as an important pathway linking environments to population health.

structural racism | health disparities | chronic disease | DOHad | policy

Inequities in morbidity and mortality are a persistent challenge among populations in the United States and globally. Some of these disparities are related to socioeconomic status (SES) (1). For example, in the United States, men in the highest and lowest percentile of income have an ∼15-y difference in life expectancy (2). In addition to SES, self-identified race, sexual identity, and gender status also powerfully predict many health outcomes (3–5). For instance, controlling for SES, Black adults have triple the odds of being diagnosed with diabetes compared to White adults (4), and LGBTQ adults are twice as likely to report multiple risks for cardiovascular disease than heterosexual individuals (3). Importantly, although racial health inequities are

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sometimes assumed to have biological underpinnings, race is a social construct created to control access to power and resources; it has no robust genetic or biological foundation (6–8). Therefore, traditional concepts of heritability or ancestry cannot account for intergenerational patterns in health inequities. Instead, biological patterns observed across minoritized populations are driven by the influences of social forces on physiology and health (9). Personal experiences of racism and discrimination create chronic stress that results in negative health outcomes (10). Similarly, discriminatory laws and policies hinder access to resources like health care, employment, and education, and foster the development of segregated neighborhoods with reduced access to fresh, unprocessed foods, limited space for safe exercise, and increased exposure to noise or chemical pollutants (5, 10–12).

In light of the importance of environmental and social inequities in health outcomes, clarifying the biological pathways that link lived experiences to disease is critical for devising strategies to ameliorate or reverse these effects. To date, much work in this area has focused on the impact of chronic stressors, such as discrimination, on systems like stress physiology or inflammation (10, 13). Structural disparities in experiences that influence nutrient intake, blood pressure, or carcinogenic exposure similarly contribute to health inequities in well-described ways (5, 10–12). This biological embodiment of structural inequity is increasingly recognized as manifesting across multiple timescales: Adults exhibit biological symptoms of their current environments, but adverse early life environments also can lead to persistent biological changes that increase adult risk for negative outcomes including heart disease, stroke, diabetes, and osteoporosis (14).

Adding to this established literature, the recent rise of work on the gut microbiome (GM)—the community of microbes that inhabits the human gastrointestinal tract—is revealing a novel set of pathways through which environmental exposures could contribute to health inequities. The composition and function of the GM is strongly shaped by host lifestyle and environment (15), including factors like diet (16), medication use (17), housing conditions (18), and social network characteristics (19). As these factors change, so does the GM, making it a plastic component of human biology. As a result, the adverse environmental effects of structural discrimination on the basis of SES, race, or gender/sexual identity are likely to be reflected in the GM of minoritized populations (Fig. 1).

In turn, the GM contributes to myriad aspects of host biology. It confers protection from pathogens through colonization resistance, influences host nutrition and metabolism, trains and modulates immune function, and contributes to patterns of brain development and behavior (20–24). As a result of these diverse effects, alterations to the GM during both early life and adulthood are recognized as leading to dysregulation of immune, metabolic, and neuroendocrine processes involved in a range of health disparities, including obesity, diabetes, atherosclerosis, asthma, allergies, depression, and anxiety (25–29). Although causality can be difficult to establish, evidence for a causal role of an altered GM in these conditions is growing (28, 29). In addition, because some of the pathological states that result from an altered GM (e.g., obesity, inflammation, diabetes) can have adverse effects on the gestational environment experienced by the next generation, and because microbes can be passed from parents to offspring (30, 31), the GM is increasingly recognized as influencing health in an intergenerational fashion. These relationships raise the possibility that differences in the GMs of minoritized populations reflect patterns of structural inequities and also amplify them by negatively impacting health outcomes (Fig. 1).

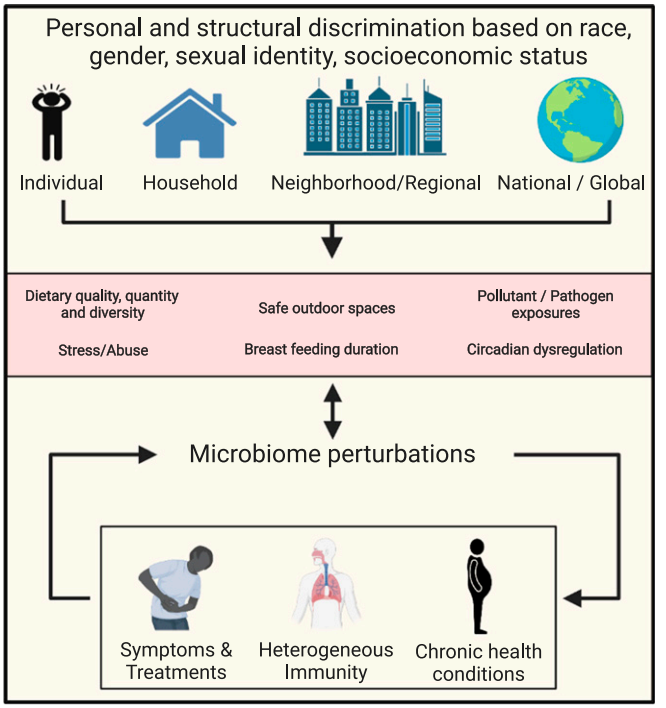

Fig. 1. Experiences of discrimination across multiple scales are likely to affect the structure and function of the microbiome through a variety of pathways across multiple life stages. Given links between the microbiome and metabolism, immunity, and nervous system function, microbiome perturbations incited by discrimination can result in negative health outcomes. These include acute symptoms, various chronic diseases, and heterogenous immunity to pathogens including respiratory viruses. Behaviors and treatments associated with these factors can feed back to further alter the microbiome, creating a positive-feedback cycle. (Created with BioRender.com.)

Despite growing calls for attention to these links (32, 33), few studies have directly investigated the role of the GM in health inequities. Here, we explore the potential that this work holds. After briefly summarizing concepts of GM health, we review evidence linking the GM to health inequities. We then outline the probable effects of environmental disparities on GM composition and function and discuss known contributions of the GM to nutrition and metabolic diseases, asthma, cognitive development, and mental illness. We also consider the potential role of the GM in COVID-19 outcomes. We conclude by explaining how the plasticity of the GM makes it a particularly useful lever for interventions and examine both the opportunities and challenges for using GM research to inform health policies aimed at reducing health inequities.

GM Ecology and Health

Identifying "healthy" and "unhealthy" GM states is difficult. Many microbial mechanisms of disease are still not fully understood, and the most influential GM impacts on host health are likely to be emergent community functions that result from the complex ecological interactions of multiple microbial taxa. As a result, a change in the relative abundance of a single microbial taxon may or may not affect community function depending on the composition of the rest of the community (34). Instead, the relative abundances of multiple interacting microbial taxa, as well as the stability and resilience of the overall community across time, more strongly shape GM function and, ultimately, host health (35). Because basic

ecological theory posits that more complex ecological communities are also more stable and resilient, GM diversity is often used as a proxy for health (36). However, as observed in the infant gut, reduced GM diversity does not always have adverse effects on the community or host health (31). Therefore, concepts such as modularity, or interconnectedness, of the GM are also useful for describing GM community structure and associated impacts on hosts (35). Additionally, identifying keystone microbial taxa or functions that promote modularity and/or disproportionately contribute to emergent community function can provide important insights into host health (34).

Evidence Linking GM to Health Inequities

To date, most studies of the human GM have a narrow biomedical focus or describe broad population-level trends in response to environmental variation. Few studies have assessed GM variation in relation to structural inequities, and fewer have attempted to link socially attributed variation in the GM to host health (37–41). Nevertheless, the existing literature provides growing evidence that the social and environmental gradients that contribute to health inequities also predict GM traits (Table 1). For example, across globally diverse populations, measures of SES have been associated with distinct GM traits in both adults (41–43) and children (44–48) (but see ref. 49). Similarly, the GM consistently varies with race (e.g., Asian, Black, Hispanic, White) and/or ethnicity/ancestry (Arapaho, Cheyenne, Dutch, Ghanaian, Moroccan) in adults (37, 38, 40, 50) and children (45, 46, 51, 52).

Three studies in particular have provided strong evidence linking structural inequities to GM variation in the context of SES. One demonstrated that after adjustment for demographic and lifestyle factors, neighborhood SES in Chicago explained 12–25% of the variation in adult GM composition and was positively correlated with GM diversity (42). A larger subsequent study in the United Kingdom similarly reported a positive association between neighborhood SES and GM diversity, including in a discordant-twin analysis, which minimizes the possibility of confounding by shared genetic or family influences (43). This paper also found that individual SES was positively correlated with GM diversity. Finally, a study of 14 districts in China showed that the relative abundances of taxa, accounting for 38.8% of the GM, varied in relation to personal yearly income and spending (41).

Despite the important contributions of these papers, however, most GM studies in minoritized populations do not operationalize structural inequities, and small sample sizes constrain multivariate approaches. Furthermore, race and ethnicity/ancestry are often incorrectly used interchangeably. As a result of these and other limitations, the relative importance of personal experiences of racism and discrimination versus structural impacts on environments for the GM remains largely unknown. Similarly, the scale (i.e., household, neighborhood, and beyond) at which structural inequities might affect the GM is unclear. Nonetheless, the existing literature demonstrates that the same social gradients that predict disparities in major classes of disease also predict variation in the GM. These relationships underscore the likely role of the GM in mediating socially driven health disparities.

Potential Pathways to Disparities in the GM

Population differences in GM communities are established in response to a combination of factors that include intergenerational transmission during infancy as well as ongoing effects of environment and lifestyle factors from infancy into adulthood. As a result, structurally imposed differences in lifestyle and environmental factors can preclude the establishment of an appropriate GM in minoritzed populations as early as birth. Infants are typically first exposed to microbes during labor and birth via contact with the maternal vaginal and fecal microbiome (31, 53, 54). Cesarean births are more frequent in low-SES and minoritized populations (55), and babies born via cesarean section exhibit altered GM developmental trajectories during the first year of life as a result of lower maternal microbial input compared to vaginal delivery, along with increased exposure to antibiotics (56).

Practices such as skin-to-skin contact and breastfeeding offer further opportunities for microbial exchange that may promote the establishment of keystone GM taxa and functions (56, 57). Breast milk is a source of probiotic bacteria, as well as of prebiotic oligosaccharides that help foster the establishment of beneficial microbes in the infant gastrointestinal tract (58). Mothers in low-SES or minoritized populations may engage in less skin-to-skin contact and shift from breast milk to formula earlier as a result of maternal work pressure or lack of relevant health information (59, 60). At 3 mo, breastfed babies have a distinct GM compared to formula-fed babies, including lower microbial diversity and increased relative abundances of beneficial microbes (61, 62). The combined loss of protective microbial factors in breast milk and increased exposure to waterborne pathogens and toxins [e.g., the Flint, Michigan water contamination crisis (63)] may place formula-fed children at higher risk for negative alterations in the GM.

As infants mature, GM composition stabilizes, and by approximately 3 y of age, the GM resembles that of an adult (61). Both before and after this age, a number of factors are known to influence the GM. Close physical proximity to other people and/or household animals leads to microbial transmission in both adults and infants (19, 64). Hygiene, sanitation, and medical practices can impact the GM, often by disrupting community composition and reducing diversity (65, 66). Finally, although environmental factors appear to play the strongest role in shaping the human GM (15), host genotype has been associated with variation in a subset of the GM (67, 68).

Diet has one of the largest known impacts on the GM, altering GM composition on timescales from hours to years (16, 69). Specifically, high-fat, low-fiber diets that tend to be more geographically and economically accessible to low-SES and minoritized families (70) have been shown to reduce GM diversity and negatively alter GM function (16, 69, 71). Increased time spent indoors and reduced exposure to outdoor environmental microbes is also believed to reduce GM diversity (72, 73), and low-SES and minoritized populations generally have less access to safe, outdoor green space compared to higher SES groups (74). Various forms of sleep disruption alter the GM (75, 76), which puts individuals with unusual sleep–wake cycles like shift workers, who are often disproportionately from minoritized populations (77), at risk for altered GM composition and associated diseases. Finally, low-SES and minoritized populations experience high levels of chronic stress (10, 11), which can result in altered GM composition (78–82).

Pathways through Which the GM Can Contribute to Health Outcomes

Determining the GM's contribution to health inequities in human populations, and harnessing this information to inform policy, will require strong evidence that variations in the GM exert a causal impact on specific health outcomes. Here, we explore the potential role of the GM in shaping health conditions with known

Table 1. Overview of published literature linking the microbiome to pathways of health inequities

Study	Location	Participant age	Sample size	Key findings
SES				
Miller et al. (42)	United States	Adult	44	Neighborhood SES explains 12–25% of GM variation; neighborhood SES and GM diversity positively correlated
He et al. (41)	China	Adult	6,896	Personal income and spending predicts relative abundance of taxa composing 38.8% of GM
Bowyer et al. (43)	United Kingdom	Adult	1,672	Neighborhood SES and GM diversity positively correlated (including in discordant twins); individual income, education, and SES positively correlated
Galley et al. (47)	United States	Children	77	Maternal obesity and infant GM only associated in high-SES dyads
Chong et al. (45)	Malaysia	Children	61	Household income and GM diversity negatively correlated
Levin et al. (46)	United States	Children	298	Maternal income and education explains 3–5% of GM variation
Gschwendtner et al. (49)	Germany	Children	166	No relationship
Flannery et al. (48)	United States	Children	40	SES, adverse life events, caregiver behavior explain 22.3% of GM variation
Amaruddin et al. (44)	Indonesia	Children	140	School district SES and GM diversity negatively correlated
Race/ethnicity				
Sankaranarayanan et al. (40)	United States	Adults	61	Cheyenne and Arapaho individuals have distinct GM from nonnative individuals in same location
Ross et al. (38)	United States	Adults	363	Mexican Americans have distinct GM from White Americans
Brooks et al. (50)	United States	Adults	1,163	Relative abundances of 12 GM taxa vary between White, Asian-Pacific Islander, Black, and Hispanic participants
Deschasaux et al. (37)	Netherlands	Adults	2,084	Diversity and composition of GM vary between Dutch, Ghanian, Moroccan, Turk, African Surinamese, South Asian Surinamese in same city
Chong et al. (45)	Malaysia	Children	61	Chinese, Malays, Indigenous participants have distinct GMs
Levin et al. (46)	United States	Children	298	Infants with Black mothers have more diverse GM (other covariates contribute to pattern)
Stearns et al. (51)	Canada	Children	355	South Asian participants have distinct GM from White participants
Sordillo et al. (52)	United States	Children	333	White infants have lower GM diversity distinct GM composition compared to Hispanic infants

disparities, including undernutrition, metabolic diseases, asthma, neurodevelopmental and mood disorders, and COVID-19.

Child Undernutrition. Child undernutrition affects more than 50 million individuals under 5 y of age, contributes to nearly half of all global child deaths (83), and is most common in low-SES and minoritized populations (84). Severe cases are surprisingly refractory to recommended nutritional-based therapies, with long-term sequelae that include stunting, decreased earning potential, impaired vaccine responses, and increased long-term risks of obesity, metabolic syndrome, and cognitive deficits (85).

Undernutrition is believed to have multiple biological causes, including both macro- and micronutrient deficiencies. In low resource settings, infection by enteropathogens that decrease nutrient absorption and assimilation while simultaneously increasing immune energy needs is a primary cause of undernutrition (86). As a result, inequities in undernutrition are commonly associated with structural variation in sanitation and availability of safe, treated water as well as maternal, prenatal, and perinatal factors affecting the function of the immune and endocrine systems (87). However, other mechanisms may also be at work. For example, the GM influences the establishment of enteropathogens by reducing their success via competitive exclusion or pathogen-defense functions (24). Therefore, variation in early life GM development as a result of the factors outlined above could dictate susceptibility to infection and its sequelae. The inflammation resulting from infection can further alter the GM, increasing risk of future infection and further impairing other aspects of physiology (88). Even in the absence of active infection at the time of sampling, undernourished children have GMs with reduced diversity and altered composition (89–91). These GMs can causally impair growth when introduced into germ-free mice (89, 90). Importantly, growth impairment can be ameliorated in both mice and piglets through the use of prebiotic foods (92) and probiotic administration of *Lactobacillus plantarum* (93).

Diseases Related to Overnutrition. More than half of the world's adult population is overweight or obese, and the related conditions of diabetes and cardiovascular disease are now the leading causes of death globally (94). The rise of these conditions has been particularly rapid in minoritized populations (95), and it is unclear why individuals and populations vary in susceptibility when faced with similar diets and environments (94). Factors such as stress and sleep disruption, cesarean births, and early life antibiotics have been implicated (96–99).

The GM is one potentially important pathway for understanding these relationships. In general, studies associate an altered, low-diversity GM with increased risk for obesity and diabetes (28, 100), and the GMs of obese human individuals can causally induce obesity in mice (28). These effects may operate via multiple mechanisms, including excess host-accessible energy production by microbes in the form of short-chain fatty acids (SCFAs), alteration of host metabolic programming via production of SCFAs and other metabolites, and promotion of host inflammation (28, 101, 102). Disparities in environmental factors that result in these GM traits could therefore contribute to disparities in metabolic disease. While many of the environmental factors described earlier could play important roles in affecting the GM in this context, high-fat, low-fiber diets that can be prevalent in minoritized populations in settings like the United States (70) consistently result in GM signatures that resemble those typical of obesity and metabolic disease (71).

Asthma. Asthma affects ~14% of children worldwide with incidence increasing by 50% every decade (103). Asthma disproportionately impacts low-SES, minoritized, and urban populations in middle- and high-income countries (104), with more than 80% of deaths occurring in these populations. In addition to its role in mortality, the impact of asthma includes wide-ranging factors like days lost from school and interference with physical exercise (105). Although genetic susceptibility contributes to asthma pathogenesis in some populations, it only explains a minority of cases (106). Instead, asthma prevalence and severity are linked to a range of environmental factors including reduced exposure to outdoor environments, animals, and helminthic infections, increased incidence of viral and bacterial infections, increased antibiotic exposure, cesarean birth, and formula feeding (106–110).

There is accumulating evidence for a role of the GM as mediator between these environmental factors and asthma morbidity. Microbial alterations have been observed in the airways of individuals with asthma (111, 112), and infant GM signatures can be used to predict asthma risk later in life (29, 113, 114). For example, *Faecalibacterium*, *Lachnospira*, *Veillonella,* and *Rothia* are negatively associated with future asthma development in 3-mo-old infants (29), and supplementation of these bacteria to germ-free mice colonized with asthma-associated stool samples ameliorates airway inflammation (29). While additional research is needed, research to date has linked asthma morbidity in children to GM-mediated impacts on immune function development and inflammatory responses (29, 108).

Preterm Birth and Neurodevelopmental Trajectories. Despite technology-enabled increases in the survival of extremely preterm (<28 wk) infants in the United States, cognitive outcomes in these individuals are often severely impaired (115, 116). Preterm babies born into low-SES families and/or minoritized populations often have poorer cognitive outcomes (117). While a number of factors, including access to early life education (118), likely contribute to these patterns, variation in inflammatory markers in infant serum is a key area of interest (119, 120).

The GM could play a key role in mediating the relationship between preterm neurodevelopmental outcomes and inflammation. Research in mice has demonstrated that the GM links key immune and neurological pathways in infancy (22), and the composition of the human GM has been associated with neurodevelopmental status at 1 y of age (121). Additionally, gnotobiotic mice colonized with the GM from human preterm infants experience systemic inflammation, as well as alterations in myelination, neuronal number, and neurotransmission pathways (122). No research to our knowledge has directly linked specific environmental disparities to preterm neurodevelopmental outcomes. However, if disparities in the environmental factors outlined above affect either the maternal or infant GM, it could alter infant inflammatory profiles, which in turn have well-established effects on cognitive development (123). Additionally, the parental ability to engage with infants in the neonatal intensive care unit via skin-to-skin contact and/or breastfeeding, as a result of professional or personal demands, or infant health status, may also result in disparities in infant microbial exposures.

Mental Health. Mental illness is recognized as one of the largest causes of morbidity globally (124). Depression is the leading cause of disability worldwide, and approximately half of those diagnosed with depression also suffer from anxiety (125). Individuals belonging to minoritized populations as well as individuals with reduced economic resources are disproportionately impacted by these conditions (1, 126), and experiential and behavioral factors such as stress and diet are considered among the strongest influences (127, 128).

The GM is emerging as a potentially important mediating pathway for mental illness. In both humans and rodents, individuals with symptoms of depression have distinct GM compositions compared with individuals without symptoms (129, 130), and a depressive phenotype can be induced in rats using a fecal transfer from depressed patients (131). Conversely, probiotics and prebiotics have been shown to ameliorate depressive symptoms in both animal models and humans (132, 133). These relationships are likely associated with the ability of the GM to influence the metabolism of host neurotransmitters and hormones including serotonin, dopamine, GABA, ACTH, and glucocorticoids (134, 135). There is also evidence from mice that the GM can directly influence nervous system functioning through interactions with sensory neurons, including the vagus nerve that connects the gut to the brain (136, 137). As a result, the roles of diet and stress in mental health are likely mediated, at least in part, through the GM (138), and disparities in mental illness likely reflect disparities in diet and stress that impact the GM.

The Role of the GM in Infectious Disease and the COVID-19 Pandemic. The COVID-19 global pandemic caused by coronavirus SARS-CoV-2 represents one of the most recent and acute examples of health inequities. Although all populations are susceptible, Black and Latino populations in the United States are exhibiting higher infection and mortality rates compared to their White and Asian counterparts (139–141). These disparities are likely due to a combination of factors including limited opportunities to engage in isolating behaviors to reduce exposure; increased probability of underlying comorbidities such as obesity, cardiovascular disease, and diabetes; and reduced access to health care (139–141).

Although there is still much to learn about this virus and its interactions with hosts, it is likely that the GM influences COVID-19 susceptibility and outcomes (142). To begin with, many of the underlying comorbidities that increase risk of morbidity and mortality from COVID-19 appear to be shaped by host–microbe interactions, as described previously. Additionally, since data from mice demonstrate that the GM trains the immune system and affects host responses to other respiratory viruses such as the influenza virus (143, 144), it is similarly likely to play a role in moderating host immune responses to SARS-CoV-2. For example, COVID-19 mortality rates appear to be strongly influenced by host susceptibility to out-of-control inflammatory responses, and the GM can directly influence these responses (145, 146). Similarly, COVID-19 can infect the gut as well as the respiratory tract (147), allowing for direct interactions between the GM and virus-infected cells.

Importance of Early Life and Intergenerational GM Dynamics on Health

The studies reviewed above show that a range of environmental and lifestyle factors can influence the GM in ways that influence risk for multiple disease end points. Although this work confirms that the GM exhibits responsiveness and plasticity to changing environments throughout life, GM community establishment during infancy is likely to be particularly important given emerging evidence that it is not only which microbial taxa and genes that are established, but when in the lifecycle, that matters to the long-term disposition of immune, metabolic, and neurological states (20, 148, 149). For example, mice that are not exposed to

key microbial strains during early life do not develop appropriate immune and nervous system function, even if they are exposed to those microbes later (149, 150). Likewise, mice exposed to low-dose antibiotics during early life exhibit altered metabolism and immune function even after their GM returns to its original state (151). Intergenerational GM dynamics also appear to be important. Mice fed a low-fiber diet lose fiber-dependent GM taxa cumulatively across generations (152). Some studies in mice also suggest that mothers may pass on inflammatory bowel disease, metabolic disease risk, or stress phenotypes to their infants via the GM (96, 153, 154). Therefore, to the extent that findings in mice apply to humans, the determinants of GM composition and its impact on health may not be limited to a single generation.

Leveraging the GM to Address Health Inequities

The growing evidence that the GM is a link between social environments and diseases characterized by marked disparities points to new levers that could be harnessed to help ameliorate their effects. However, key gaps remain to be addressed before the GM can be used to guide interventions. For example, current studies describe either the relationship between the social dynamics of SES/race/gender identity and the GM, or the relationship between the GM and health. We are aware of no study that simultaneously and empirically assesses SES/race/gender identity, the GM, and health outcomes to determine what facets of health inequities are mediated by the GM and the relative importance of the GM versus other potential mediating pathways. Additionally, no GM study has quantitatively examined the relative importance of inequities ranging from the personal to the global scale and the extent to which they interact with each other.

To begin to fill these gaps, future studies should engage a multidisciplinary approach that melds GM research with fields like epidemiology and the social sciences (32) to strengthen study design and quantitative assessment of inequities. For example, the social sciences can provide critical guidance in measuring variables such as SES and racism/discrimination consistently and robustly across studies. Additionally, the declining costs of GM sequencing will facilitate larger sample sizes and higher resolution microbial data for epidemiological approaches capable of teasing apart the independent effects of multiple environmental determinants. Quasi-experimental approaches (e.g., twin or adoption studies), interventions (e.g., randomized cash-transfer experiments), and controlled animal model experiments (e.g., social dominance challenges) currently used to study health inequities outside the microbiome context can also be used to further strengthen causal inference.

As evidence linking the GM to the embodiment of structural inequities in minoritized populations amasses, it will open up new opportunities for intervention to ameliorate or reverse health inequities. Although much basic research remains to be done, we imagine that future interventions will take multiple forms that could work in complementary ways to reduce the disproportionate societal burden of many common diseases. Specifically, we believe that the development of interventions should include a combination of research-based therapies and policy updates that use a biomedical approach to target known keystone GM traits as well as an ecological approach to support the development and maintenance of stable, resilient GM communities (Fig. 2).

Targeted Biomedical Interventions. Targeted GM interventions for specific diseases are receiving growing attention. For example, *Lactobacillus* and *Bifidobacterium* probiotics are being used in multiple clinical trials as a treatment for depression with mixed outcomes (155), and fecal transplants are an effective therapy for *Clostridium difficile* infections (156). Nevertheless, additional research will be necessary before these approaches can be routinely implemented. Even in the relatively simple case of probiotics, the microbial taxa of interest are only established in the gut in a subset of people, and it remains unclear whether there are durable health benefits (157, 158). Efforts may need to focus on keystone GM taxa that have large positive effects on their host, such as *Bifidobacterium longum* subsp. *infantis* in breast milk (159). Alternatively, researchers should look past microbial taxonomy to identify specific microbial genes, proteins, or metabolites that are associated with particular beneficial or detrimental effects (160).

While these personalized treatments could help treat many diseases, current practices surrounding their development and distribution limit their power to substantially alter patterns of health inequity. First, most GM biomedical research targets relatively homogenous populations that consist largely of adults of European descent living in high-income settings. Given the extent to which structural forces, acting through ecological, behavioral, and experiential factors, shape the GM, this narrow approach will result in therapies with untested utility in populations experiencing the highest burdens of GM-mediated disease, and that may not be easily translated across populations (161). Federal policies that prioritize funding for the development of targeted GM therapies for populations experiencing disproportionate burdens of disease will be necessary to reduce these biases. Additionally,

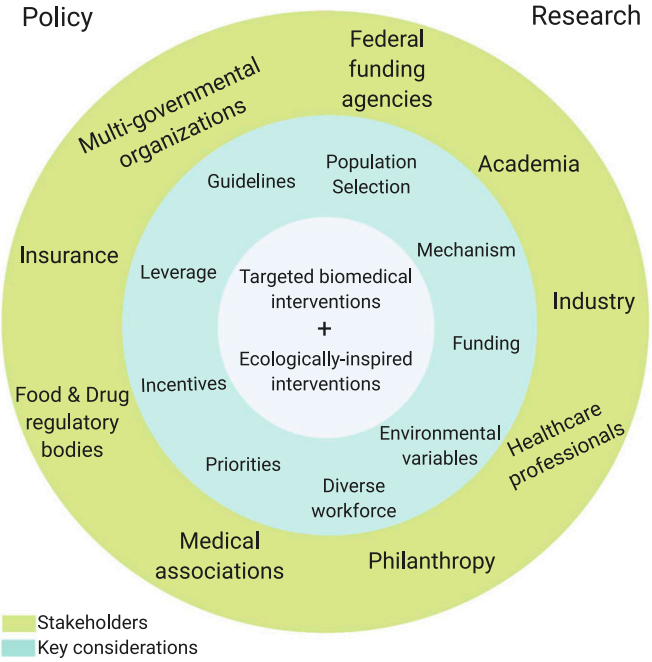

Fig. 2. The gut microbiome represents a lever for interrupting health inequities via complementary approaches that integrate both research and policy. These approaches include targeted biomedical interventions that aim to introduce key microbial taxa or functions and ecologically inspired interventions that support the development of a stable and resilient microbiome community. A variety of stakeholders and key considerations for addressing structural inequities operate within both the policy and research toolkits that contribute to these interventions. Although often considered separately, they are interrelated. We list some key examples here. (Created with BioRender.com.)

targeted GM therapies are likely to be distributed through channels constrained by unequal access, such as health care or prescription medications. Here, transformative policy interventions that strive for universal access to emerging health technologies, and to health care more generally, will be essential for ensuring that new GM developments reach the populations that would most benefit from them.

Ecologically Inspired Interventions. To complement targeted GM therapies, ecologically inspired interventions that support the development and maintenance of stable, resilient GM communities may be important tools to address health inequities. Specifically, policy interventions should be designed to counteract structurally induced disparities in environments that affect the development of robust GM communities in minoritized populations. While some policies, such as antibiotic stewardship programs and improvements to water and sewage infrastructure, already are informed by knowledge of microbial impacts on health (162, 163), most health policies are not.

Breastfeeding is an excellent example. In the United States, workplace efforts to facilitate breastfeeding often provide space for mothers to express milk. While this practice benefits infant GM development through the provision of breast milk, it also reduces mother–infant physical contact, which may alter microbial transmission patterns. It is also unclear whether freezing and reheating breast milk affects microbes and other bioactive milk components important for infant GM development (57). Recent movements in the United States to guarantee a minimum period of paid maternal leave, reflecting policies implemented in nearly all other high-income countries, could improve infant GM ecology and, ultimately, health.

Similarly, policies aimed at reducing health disparities by improving access to affordable, nonprocessed foods could be tailored to maximize beneficial impacts on the GM. Existing nutritional policies tend to emphasize the nutritive importance of lean protein sources and fresh produce and do not recognize the role of food in shaping GM ecology. However, as one example, high-fiber diets are strongly associated with diverse, interconnected GM communities (69, 164, 165). This information should be used to update policy and improve access to high-fiber, "microbe-friendly" foods through food banks and food supplement programs such as Special Supplemental Nutrition Program for Women, Infants, and Children in the United States. The feasibility of such efforts would be enhanced by the design of fresh food production and delivery systems that are more efficient, flexible, and resilient to disruption than those currently in use (166, 167).

Continued research is necessary to optimize these approaches by identifying keystone GM traits and determining the most effective pathways for promoting stable and resilient GM ecologies (168). Nevertheless, our current knowledge of the factors promoting diverse, interconnected GM ecologies, particularly during early life, provide an important foundation upon which new policy perspectives can be built as the field advances (Fig. 1).

Conclusion

Although there are many biological systems through which socially determined differences in environments lead to health inequities, the GM represents an important set of pathways that have yet to be fully explored. Given its sensitivity to myriad environmental factors as well as its role in shaping host physiology and health, the GM is likely to both respond to and perpetuate the structural inequities created by racism and other forms of discrimination. Because the environments that drive GM composition are modifiable, the GM represents an important tool for mitigating the impact of structural inequities and their downstream health consequences. In this context, biomedical approaches targeting individual GM taxa and functions, as well as ecological approaches promoting the maintenance of stable and resilient GM communities, should be combined with policy interventions aimed at equalizing access to resources and environmental exposures, and adopting an anti-racist stance in health care. Achieving this goal will require collaborations between GM researchers and fields specializing in the assessment of social environments and their impacts on health, including epidemiology and health-focused fields in the social sciences (169, 170), as well as medical doctors, nurses, and policymakers who can put key findings into practice.

Data Availability. There are no data underlying this work.

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