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Review article

The social microbiome of older people

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ABSTRACT

The human gut microbiome (GM) is increasingly recognized as one of the main systems influencing the aging trajectory. Age-related dysbiosis, with imbalance between symbionts and pathobionts, can in fact fuel chronic inflammation (inflammaging) and promote frailty. In older individuals, GM composition is characterized by marked inter-individual variability and consistently influenced by environmental exposures. Studies conducted in animals and closed human communities suggest that social contacts are associated with horizontal transmission of commensal bacteria, enhancing biodiversity and preventing dysbiosis. Recent studies also suggest transmission of intestinal commensal bacteria from animals to humans sharing the same household. Bacterial populations residing on environmental surfaces may also have an influence on GM composition. In this framework, impoverishment of social relationships in older individuals may not be only associated with cognitive and emotional disengagement, but also with unfavorable changes in GM composition, driven by isolation and top-down neuromodulation of intestinal function. In fact, studies conducted during forced social distancing in the COVID-19 pandemic suggest GM changes pointing towards dysbiosis. Therefore, the detrimental consequences of social isolation for health outcomes of older individuals, including frailty progression towards disability, could be at least partly mediated by GM dysbiosis. Conversely, interventions aimed at restoring sociality, including animal-assisted activities, could expose older individuals to a range of novel bacterial species helping to counteract GM dysbiosis. This perspective article critically discusses the concept of social microbiome, its possible relevance for maintenance of good health in human beings, and its implications for the care of older patients.

1. Introduction: gut microbiome in aging

Gut microbiome (GM) is a term referring to the extremely complex and diverse community of microorganisms, mainly bacteria but including also viruses, fungi and protozoa, living in symbiosis with the host in the gastrointestinal lumen, and their corresponding genomes (Berg et al., 2020). Each mammal, and even non-mammalian animals, harbor their own GM, with consistent inter-species differences. GM can influence several aspects of host physiology and can be involved in the pathophysiology of several illnesses and conditions, not limited to the gastrointestinal system (Haran and McCormick, 2021; Fan and Pedersen, 2021). Increasing evidence from both animal models and human beings indicates that the GM can be involved in the pathophysiology of neurocognitive disorders (gut-brain axis) (Cryan et al., 2019; Cryan et al., 2020) and age-related sarcopenia (gut-muscle axis) (Ticinesi et al., 2017; Liu et al., 2021), through multiple mechanisms including also modulation of the chronic subclinical activation of the inflammatory response associated with aging (i.e., inflammaging) (Sayed et al., 2021; Olivieri et al., 2023). Indirect evidence also suggests that the GM is involved in modulation of the aging trajectory and prediction of health status and survival (Gupta et al., 2020; Salosensaari et al., 2021; Wilmanski et al., 2021). Thus, GM represents one of the emerging systems studied in geroscience, contributing to the elevated heterogeneity of aging patterns among human beings (Kroemer et al., 2025).

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In comparison with other species, human GM is characterized by marked inter-individual variability, that depends on a complex interaction between life-long environmental exposures and intrinsic factors such as host genetics, influencing local intestinal immune development and responses (Rothschild et al., 2018; Gacesa et al., 2022; Kurilshikov et al., 2021). The inter-individual differences are particularly pronounced when comparing individuals belonging to different populations living in different geographical areas but are present also when comparing the GM of subjects with the same culture living in the same place (Mancabelli et al., 2024; Kachroo et al., 2021). The main environmental factors explaining this variability include diet, eating habits, exercise, drugs, pollution and type of living setting (i.e., urban vs rural) (Asnicar et al., 2021; Mailing et al., 2019, Bowyer et al., 2022).

A healthy GM, able to establish cooperative interactions with the host, generally shows resilience after stressors potentially able to disrupt microbial communities, such as, for example, a course of antibiotic treatment for acute infection (Berg et al., 2020). Unhealthy lifestyle, exposure to unhealthy environments and prolonged stress can overcome the GM capacity of resilience (Sommer et al., 2017; Bhattarai et al., 2024) and lead to dysbiosis, a state of imbalance between beneficial and potentially harmful bacteria, causing pathophysiological alterations for the host (Shanahan et al., 2021; Van Hul et al., 2024; Carías Domínguez et al., 2025). Dybiosis is generally considered a contributor to the pathophysiology of many diseases, but clear thresholds of normality of GM composition cannot be established at the current state of knowledge (Shanahan et al., 2021; Van Hul et al., 2024; Carías Domínguez et al., 2025).

Aging emphasizes inter-individual variability in GM, and the aging GM is characterized by reconfiguration of microbial communities towards dysbiosis (Ling et al., 2022; Bradely and Haran, 2024). This phenomenon partly depends on the accumulation of life-long environmental exposures. However, it also represents the consequence of the unavoidable senescence of the gastrointestinal system, particularly of the local immune cells that have a pivotal role in maintaining the balance between gut microbial communities and the host (Jang et al., 2024; Kawamoto and Hara, 2024). The pace and the extent of these biological processes could show correlation with the aging phenotype and thus have great clinical relevance (Ferrucci and Fabbri, 2018). Frailty, a geriatric syndrome characterized by increased vulnerability to stressors resulting from a decline in reserve and function of multiple physiologic systems and increasing the risk of unfavorable health outcomes, is associated with a higher level of GM dysbiosis than healthy aging (D'Amico et al., 2023; Wang et al., 2024). Longevity, on the other side, is associated with distinctive traits in GM. Centenarians usually show a representation of beneficial bacterial taxa, such as Bifidobacteria, higher than expected for their chronological age (Biagi et al., 2017).

Understanding the determinants of GM dysbiosis in aging could therefore be extremely important to issue effective GM-centered strategies against frailty. Recent data suggest that, even in the older age, GM composition is consistently shaped by environmental exposures dating back to several years, and that the GM ages under the influence of the environmental background (Si et al., 2022). Other studies have recently underlined the fundamental roles of social networks and relationships for determining a healthy GM in adult life (Valles-Colomer et al., 2023). Frailty, which is basically a multidimensional concept not only regarding the biological aspects of aging, is frequently associated with impoverishment of social relationships, reduction of non-domestic activities and feelings of loneliness that may contribute to cognitive and emotional disengagement and, ultimately, to unfavorable prognostic trajectory in a sort of vicious cycle (Gale et al., 2018; Mehrabi and Béland, 2020; Kojima et al., 2022). Therefore, it can be hypothesized that GM represents one of the mediators of the association between frailty, particularly in its social aspects, and unfavorable health outcomes.

The aim of this review article was to critically summarize the current state of knowledge on social factors directly and indirectly influencing GM composition, with a particular focus on aging, and to identify areas of future development of research in this field. The literature search strategies employed to identify relevant articles are detailed in Supplementary Material.

2. The social microbiome hypothesis

2.1. Evidence of horizontal transmission of commensal microorganisms in animals

GM, in both animals and human beings, should not be considered an isolated system establishing relationships only with the host. It is constantly influenced by the communities of microorganisms residing in the environment nearby. Surfaces of natural and built environment, foods and water harbor communities of microorganisms, mainly bacteria, that have the potential of influencing the composition of the individual's GM (Browne et al., 2017). The composition of this environmental microbiome is significantly influenced by other individuals that had contact with it before. Therefore, there is a continuous bidirectional interplay between GM and environmental microbiomes, even in contexts where hygienic standards are high and there is a low level of environmental fecalization (Sarkar et al., 2024). The environment each individual lives in can basically be considered as a reservoir of microorganisms, and the interplay with GM is more intense if the contact is more prolonged (Browne et al., 2017; Sarkar et al., 2024). Therefore, the same pathways of microbial transmission that are well known for pathogenic microorganisms are valid also for commensal microorganisms.

This phenomenon is well known and studied in animals (Sarkar et al., 2020). In general, the closer, more intense and prolonged are inter-individual contacts within an established social network, the more similar are the intestinal microbiomes among individuals. This principle is valid for a wide range of animal species, from *Drosophila melanogaster* to spiders, birds, bats, mice, horses, up to non-human primates (Leech et al., 2021; Busck et al., 2022; Rose et al., 2023; Maraci et al., 2022; Yarlagadda et al., 2021; Raulo et al., 2021; Antwis et al., 2018; Tung et al., 2015; Moeller et al., 2016; Murillo et al., 2022). In all the existing studies, the presence of shared and unique bacterial taxa in the microbiomes of individuals belonging to the same social networks supports the existence of inter-individual transmission during close social contacts.

The dynamics of microbial transmission, however, are influenced by behavioral aspects and social structure of each species. Those species where members of the same community engage in sexually promiscuous behaviors or social grooming, implying very close contact, show marked inter-individual similarity in the intestinal microbiome (Tung et al., 2015; Li et al., 2021; Prüter et al., 2023). Conversely, species with less intense social contacts show reduced inter-individual transmission of microbial communities, with maintenance of individual traits (Pinacho-Guendulain et al., 2022; Orkin et al., 2023; Gogarten et al., 2018). These characteristics are particularly evident in non-human primates, exhibiting intestinal microbiome structure and function very close to human beings (Pinacho-Guendulain et al., 2022; Orkin et al., 2023; Gogarten et al., 2018). In a recent study conducted in wild marmots, the bacterial biodiversity of the fecal microbiome was negatively associated with the number of social contacts of each community member, with those engaging in less social activity exhibiting a higher number of unique traits in their fecal bacterial communities (Pfau et al., 2023). Changes of social groups can be also associated with increased GM biodiversity, as demonstrated by a study conducted in feral free-living horses (Vaziri et al., 2023).

On the other side, honeybees, exhibiting a very complex social structure and very close social interactions but a relatively simple microbiome structure, have evidence of poor inter-individual transmission of commensal bacteria, although the representation of certain microbial species is important for influencing behavior and maintaining

social status (Anderson et al., 2023; Liberti et al., 2022). The relationship between social environment and intestinal microbiome may in fact be bidirectional. A recent study conducted in wild mice suggests that loss of social status in the community is associated with GM perturbations, probably a consequence of reduced interaction with other members of the community (Yang et al., 2025).

Horizontal transmission of commensal bacteria has been demonstrated also in animals living in captivity, particularly in goats and pigs, where cohousing in the same pen is associated with a substantial standardization of intestinal microbiome structure with high sharing of bacterial taxa (Zhang et al., 2022). From a "one-health" perspective, this phenomenon can lead to negative consequences, because reduced microbiome biodiversity implies higher vulnerability to infections, low quality of milk and meat, and increased susceptibility to acquire antibiotic resistance (Dallas and Warne, 2023). Therefore, modern breeding techniques should adopt strategies to counteract the loss of microbiome biodiversity, for example increasing dietary diversity, including probiotic supplementation in foods and assuring adequate periodic exposure to wild environments (Dallas and Warne, 2023).

The significance of horizontal transmission of GM in animals may change according to the setting (Sarkar et al., 2020; Pinacho-Guendulain et al., 2022) and to the metabolic characteristics of bacteria (Raulo et al., 2024). In wild animals, social contacts may represent an occasion of increasing biodiversity of the intestinal microbiome, which is generally associated with good health (Baniel and Charpentier, 2024). Very close social contacts with a limited number of individuals, however, may paradoxically be associated with inter-individual uniformity of the intestinal microbiome, and thus with reduced biodiversity. This phenomenon is particularly evident in animals living in captivity and is generally associated with negative health consequences. Therefore, the functional significance of horizontal transmission of commensal microorganisms in animals is far from understood, although well

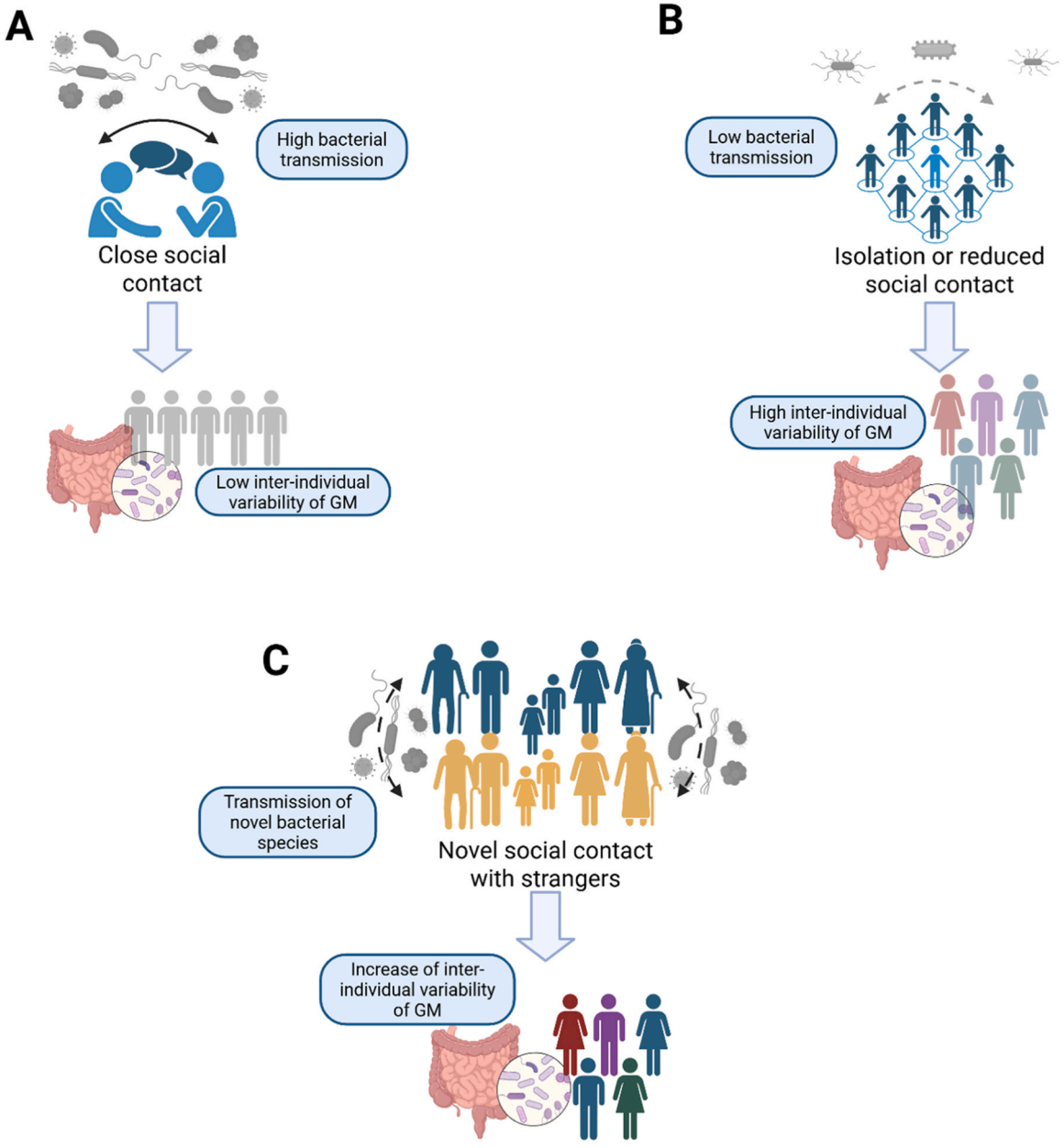

Fig. 1. Dynamics of transmission of bacteria of the gut microbiome (GM) that can be hypothesized according to the available evidence from animals and human beings. Panel A shows a scenario of close contact among individuals living in a closed community. Panel B shows a scenario of individuals with reduced social contact living in relative isolation. Panel C shows a scenario where members of two stranger communities undergo a novel social contact.

demonstrated from a mechanistic perspective (Sarkar et al., 2020; Pinacho-Guendulain et al., 2022; Baniel and Charpentier, 2024).

2.2. Evidence of horizontal transmission of commensal microorganisms in humans

The dynamics of horizontal transmission of commensal bacteria that have been observed in animals can be at least in part valid also for human beings (Browne et al., 2017; Heidrich et al., 2025). Fig. 1 provides a depiction of the hypothesized dynamics of GM transmission among individuals with close contact (panel A), individuals with reduced social contacts living in isolation (panel B) and individuals engaging in novel contacts with strangers (panel C).

Subjects who have close contact with a specific environment, particularly indoor spaces such as households, contaminate the surfaces with vegetative bacterial cells or spores. The surfaces can thus act as reservoirs of commensal bacteria, that can be inapparently ingested by other individuals experiencing close contact with the same environment and, if the intestinal ecosystem is permissive to colonization, can become part of the intestinal microbiome (Browne et al., 2017; Heidrich et al., 2025). Donor health status can also influence transmission dynamics: subjects with disease-related dysbiosis have less probability of horizontally transmitting commensal bacteria but can transmit pathobionts and pathogens (Browne et al., 2017; Heidrich et al., 2025).

This theoretical framework has been clearly demonstrated by only a few studies, because the horizontal transmission dynamics of human commensal bacteria are extremely difficult to assess, considering the complexity of social contacts in modern societies and the elevated inter-individual variability of human GM. Investigating these issues is perhaps easier in rural communities living in relative isolation from outer social contacts, or in relatively close family groups. An overview of the existing studies is provided in Table 1.

Overall, sharing the same household or engaging in social activities with significantly enduring contacts implied a higher level of gut and oral microbiome composition similarity than looser social contacts (Brito et al., 2019; Beghini et al., 2025; Musciotto et al., 2023; Dill-McFarland et al., 2019; Valles-Colomer et al., 2022; Valles-Colomer et al., 2023). The stronger similarities were seen in spouses and between mothers and their siblings, and the closeness of social relationships was proportional to GM similarities (Brito et al., 2019; Beghini et al., 2025). This association, however, was mitigated in older individuals, indicating probably a higher level of colonization resistance with aging (Valles-Colomer et al., 2023). In comparison with family life, the condition of living alone was associated with reduced GM diversity (Dill-McFarland et al., 2019). However, data also suggest that subjects living alone exhibit higher sensitivity to colonization by novel species in

Table 1
Overview of the studies that have investigated horizontal transmission of commensal members of the gut microbiome (GM) or oral microbiome (OM) in human beings, in relation to social contacts, kinship and cohabitation status.

Author, year	Country	Setting	Population	Key results and patterns of transmission
Brito et al. (2019)	Fiji	Rural (5 agrarian villages)	287 adult subjects	– High level of species and strain sharing in GM between spouses and among individuals sharing the same household – Looser level of species and strain sharing among individuals with less durable contacts – No common transmission patterns identifiable across members of different households
Beghini et al. (2025)	Honduras	Rural (18 isolated villages)	1787 adult subjects (301 re-sampled after 2 years)	– High level of strain sharing in GM for couples of individuals with close social contact, proportional to the amount of time spent together and number of meals shared – Clusters of GM composition mirror clusters of social contacts – Changes of social contacts are associated with changes in GM
Musciotto et al. (2023)	Philippines	Rural (nomadic tribe)	138 hunter gatherers of Agta ethnicity	– Species and strain sharing in OM is directly proportional to closeness of social relationships and number of social contacts – Species shared in OM are mainly pathogenic
Dill-McFarland et al. (2019)	United States	Urban	408 individuals (60-year-old Wisconsin Longitudinal Study graduates, their spouses and siblings)	– Cohabiting individuals had overall more similar GM composition than individuals living alone – Social interactions with friends were stronger predictors of GM diversity in individuals living alone than in cohabiting individuals – GM similarity increases in closer relationships, especially in spouses
Valles-Colomer et al. (2022)	Belgium	Urban	102 healthy individuals from 24 multigenerational families	– Family membership explains the 14.7 % of genus-level compositional variation of GM – Kinship and cohabitation explain most of strain sharing in GM across individuals – *Bacteroidales* species display the highest potential of transmission between family members
Valles-Colomer et al. (2023)	Africa (Guinea-Bissau, Tanzania, Ghana); America (USA, Argentina, Colombia); Asia (China); Europe (Italy, United Kingdom)	Rural and urban	7647 stool and 2069 saliva samples from public datasets	– High GM and OM bacterial strain sharing among cohabiting individuals (from 11 % to 71 %), irrespective of geographic provenience – Strain sharing is lower in older individuals, indicating reduced bacterial transmission and colonization resistance – Close social contacts between individuals not living in the same household are associated with lower sharing of GM members than cohabiting individuals – Non-cohabiting monozygotic twins show low degree of GM strain sharing

GM=Gut Microbiome; OM=Oral Microbiome.

their GMs when engaging in social contacts with members of other households (Dill-McFarland et al., 2019).

2.3. Evidence of horizontal transmission of commensal bacteria from animals to humans

The number of human beings undertaking regular close contact with animals is significant, either for professional reasons (for example, farmers), or for leisure (pet owners). Cohabitation with animals can be considered in the same way as social contact, providing exposure to a wide range of diverse microorganisms (Sarkar et al., 2024). The differences of GM are in fact more pronounced between different species (animal vs human) than between individuals belonging to the same species (i.e., human vs human), and animals harbor unique bacteria in their GMs that are unusually found in human beings. Many studies, recently reviewed by Abdolghanizadeh et al. (2024), have investigated the possible transmission of bacteria from animals to human beings in these contexts. Although most of the studies were focused on transmission of pathogenic bacteria and not on commensals, the evidence suggests that close and prolonged contact with animals can be mildly associated with shared microbial taxa and strains in the respective fecal microbiomes (Abdolghanizadeh et al., 2024).

In particular, similarities between animal and human fecal microbiomes were more pronounced in dog owners (Arenas-Montes et al., 2021; Jiang et al., 2022), where Actinobacteria abundance was increased, and in those subjects owning both a dog and a cat (Nermes et al., 2013; Kates et al., 2020; Tun et al., 2017; Du et al., 2021; Azad et al., 2014), where Proteobacteria abundance was increased. The effect of cat ownership on the fecal microbiome was instead less established. The similarities were more pronounced in males and in normal-weight individuals, in comparison with females and overweight subjects (Jiang et al., 2022; Du et al., 2021). A recent study also showed that the oral microbiome composition of dog-owning adolescents was significantly different than that of peers not exposed to pets, with a possible influence on GM composition and social behavior (Miyauchi et al., 2026).

Despite evidence suggesting that pet ownership may not be one of the major determinants of GM inter-individual variability in humans (Song et al., 2013), cohabitation with a pet, especially a dog, was proven as significantly able to decrease the incidence of diseases well known for their association with dysbiosis, such as *Clostridium difficile* enterocolitis (Pomba et al., 2017; Stoesser et al., 2017). Even more interestingly, in the only study to date focused on pet ownership by older individuals, cohabitation with a dog was associated with increased GM abundance of bacteria, such as *Bifidobacteria* and *Ruminococcaceae*, known for their properties of maintenance of gastrointestinal barrier function, suppression of inflammatory response and promotion of insulin sensitivity (Jiang et al., 2022).

The coexistence of microbial taxa in both GM of pets and their owners may not be sufficient to prove horizontal transmission, because pets usually share the domestic environment, diet and lifestyle of their owners (Hernandez et al., 2022). However, recent studies conducted with different metagenomics techniques have highlighted that the sharing of bacterial species and strains between pets' and their owners' GM is evident also at the molecular level (Derakhshandeh et al., 2018; Yang et al., 2023; Ito et al., 2024). The presence of the same sequence variants in the genomes of bacteria isolated from pet's and owner's feces suggests horizontal transmission, and not simple exposure to the same diet or environment promoting the growth of specific bacterial species or strains. Interestingly, the sharing of genes between cohabiting human beings and pets was also demonstrated for antibiotic-resistance genes, suggesting a very close mutual relationship between pets and their owners (Yang et al., 2023).

This sharing was also recently demonstrated in two large independent studies, investigating the relationship between livestock and farmer's microbiomes (Maciel-Guerra et al., 2023; Mahmud et al., 2024), and in one study conducted in a low-income setting where livestock are kept in close contact with humans in an urban environment (Muloi et al., 2022). These findings suggest that human GM is influenced by exposure to animals also when the contact is motivated by professional reasons and not just for leisure.

2.4. Possible transmission of bacteria from built environments' surfaces to human beings

The surfaces of indoor environments harbor many microbial species, mainly bacteria, either as spores or vegetative forms (Gilbert and Stephens, 2018). These microbial communities are influenced by several environmental elements, including building layout, ventilation, sunlight, airflow, temperature, moisture and material of the surface, cleaning and disinfection (Kembel et al., 2014; Li et al., 2021). However, the perhaps most important determinant of the indoor built environment microbiome is occupancy from human beings, its duration and the specific activities held (Leung and Lee, 2016). Evidence suggests that the frequency a surface is touched by human occupants of the built environment is directly associated with the number and the load of human bacteria harbored on it (Hoisington et al., 2023). In a study from China, the bacterial communities of classrooms in schools were strongly influenced by rate of student occupancy and specific activities held (Feng et al., 2021). In a large environmental sampling from restrooms of a Brazilian university, Dobbler and colleagues were able to detect significant variations in bacterial communities according to floors and gender of occupants (Dobbler et al., 2018). Sharma and colleagues demonstrated that, in United State Air Force cadet dormitories, occupancy of beds was associated with homogenization among bacterial communities of surfaces and skin microbiome of occupants, while GM was relatively unaffected (Sharma et al., 2019).

Microbial communities are present also on surfaces that do not have direct contact with human beings (Davies et al., 2023). Their complexity is usually related to architectural elements of the building, including the epoch of construction, ventilation, cleaning and the porosity of walls, and less dependent on the rate of human occupancy (Cao et al., 2021). Seasonality and climate variations seem also to play an important role in shaping these microbial communities (Zhou et al., 2021).

In this framework, the transmission of bacterial taxa from indoor environmental surfaces to human GM of occupants is still uncertain, and research in this field is still at the beginning. However, growing evidence suggests that the built environment microbiome can potentially influence human health (Bosch et al., 2024). In particular, several studies suggest that unhealthy microbial communities in classrooms can be associated with sick building syndrome – a collection of nonspecific symptoms including mucosal symptoms in eye, nose and throat, cutaneous manifestations, headache and tiredness occurring after prolonged occupancy of indoor environments – in children (Fu et al., 2021a; Fu et al., 2021b; Zhang et al., 2025), although with significant regional differences (Adams et al., 2021). The bacterial microbiome of indoor environments can also influence respiratory infections in children (Fu et al., 2020). The presence of a farm-like indoor microbiome in urban houses was associated with a reduced incidence of asthma (Kirjavainen et al., 2019). House dust can represent a relevant reservoir of bacteria able to influence human immune system response and the onset of respiratory diseases (Shan et al., 2019). However, the influence of these bacterial communities on human GM is still uncertain.

Finally, recent studies also emphasize the role of indoor fungal species as novel determinants of human health (Weikl et al., 2016; Coombs et al., 2018; Hickman et al., 2022). The environmental mycobiome seems strongly influenced by the presence of vegetation nearby and by house occupants, including pets (Weikl et al., 2016; Coombs et al., 2018; Hickman et al., 2022). The relationship of environmental mycobiome with human GM, however, remains only hypothetical at the current state of knowledge.

3. Effects of social isolation on the intestinal microbiome

3.1. Evidence from animal models

The effects of social isolation on GM composition were first studied in mouse models, under controlled experimental conditions. A 4-week isolation in a single cage immediately after weaning resulted in deep modulation of the GM composition, with an increase in Actinobacteria and decrease in Clostridia, in comparison with group-housed controls (Dunpy-Doherty et al., 2018). Interestingly, socially isolated mice exhibited impaired associative learning and memory functions in comparison with controls, suggesting the existence of a socially modulated gut-brain axis (Dunpy-Doherty et al., 2018). According to another study focused on adolescent mice, the GM changes induced by social isolation were more pronounced in females than males (Lopizzo et al., 2021). The dysbiotic traits of GM associated with social isolation could also be transmitted to offspring, probably through mediation of the house environment (Siddi et al., 2024).

Besides GM composition, social isolation also induced disruption of the intestinal barrier, with reduced tight junction protein, colonic goblet cell and mucin expression, and increased mucosal permeability (Wang et al., 2024; Tanabe et al., 2024). Such effects may both be the consequence of GM dysbiosis and regulation of gastrointestinal function by the central nervous system. In any case, these changes can stimulate inflammation, both locally and in the brain, particularly at the hippocampal level, as witnessed by increased levels of pro-inflammatory cytokines (Dunpy-Doherty et al., 2018; Lopizzo et al., 2021; Wang et al., 2024).

The influence of GM traits associated with isolation on brain function was also confirmed by recent animal studies. The presence of decreased mobility during forced motor tasks, an occurrence comparable to depressive behavior, was observed in association with reduced GM abundance of bacterial taxa with purported beneficial actions, such as Ruminococcaceae and Akkermansiaceae, in chronically socially isolated mice (Ding et al., 2024). Propionic acid, a well-known short-chain fatty acid produced by GM and involved in regulation of multiple physiological functions, was also identified as a potential effector of this gut-brain connection (Huang et al., 2021), while ingestion of soy peptide determined attenuation of behavioral and cognitive symptoms associated with isolation (Tamura et al., 2024).

3.2. Evidence from human studies and lessons learnt from the COVID-19 pandemic

Few studies have explored the effects of social isolation on GM composition and function of human beings at the current state of the art. However, the detrimental health consequences of the impoverishment of social networks, and particularly of romantic relationship dissolution, are well known in clinical and epidemiological terms. These consequences probably depend on affective and neurohormonal changes influencing physiology and behavior, but a contributing role of GM dysbiosis cannot be excluded (Chuang, 2021). In a group of 184 healthy community-dwellers aged 28–97 years old, Nguyen et al. identified an inverse correlation between feelings of loneliness and GM alpha diversity (Nguyen et al., 2021). Loneliness is a subjective feeling of sadness due to a perception of insufficient social support, which does not automatically imply that the individual is socially isolated. For example, nursing home residents are daily exposed to a high number of social contacts, including other residents and care personnel, but feelings of loneliness are reported with a very high frequency in this setting (Gardiner et al., 2020). Conversely, isolated subjects with poor social networks may not experience loneliness about their situation. Therefore, the two conditions do not always overlap, but the association between loneliness and dysbiosis suggests that social networks play a role in determining microbiome diversity (Nguyen et al., 2021).

Subjects experiencing social exclusion from a group they previously were part of exhibited signatures of dysbiosis in their GM, including reduced Firmicutes/Bacteroidetes ratio, increased abundance of *Prevotella* and reduced representation of *Faecalibacterium prausnitzii*, a well-known microorganism with anti-inflammatory and pro-anabolic actions (Kim et al., 2022). The evidence, however, comes from a case-control study, where it is not possible to determine the direction of the causality nexus, if any. In fact, the gut-brain axis implies bidirectional communication, with significant modulation of intestinal motility and function by the central nervous system by autonomic mediation (Cryan et al., 2019). The GM changes experienced by socially isolated individuals may be also the result of anxiety, depression and psychological distress, determining significant changes in lifestyle with impact on GM.

The experience of social distancing imposed for public health reasons during the early waves of the coronavirus disease-19 (COVID-19) pandemic has represented an unprecedented experimental model useful to assess the effects on fecal microbiome of forced reduction of social contacts in human beings (Domingues et al., 2020). The severity and duration of social distancing precautions significantly differed among countries, due to different health care policies, lifestyles of populations, patterns of urbanization and spread of the SARS-CoV-2 infection. However, the reduction of social contact was experienced by everyone on a global scale, especially during the first wave of the pandemic in 2020.

The results of the studies that have sampled the fecal microbiome composition of different groups of individuals before and after the initiation of COVID-19 related social distancing policies are summarized in Table 2. Briefly, all studies showed changes in GM composition and, in some cases, function (Rashidi et al., 2021; Larcher Longo et al., 2022; Aguilera et al., 2022; Viciani et al., 2022; Novak et al., 2022; Korpela et al., 2024). The tendency was towards a decline in GM biodiversity, with reduced representation of microorganisms usually transmitted by contact with other individuals, some of which have purported health-promoting activity (Table 2). However, the overall methodological quality of studies was low, mostly due to objective constraints in the conduction of research during the COVID-19 pandemic. The studies also regarded small samples of healthy individuals already enrolled in other research projects. Furthermore, covariates such as physical exercise and diet, that presumably changed during social distancing and influenced fecal microbiome composition, were not properly assessed. The microbial markers of social isolation detected across these studies were also various, making it difficult to define the effects of reduced social contacts on the intestinal microbiome (Table 2). In any case, the COVID-19 lockdown was associated with shifts in GM composition of healthy individuals, with presumably negative consequences for human physiology, even if the clinical relevance of these changes remains uncertain.

4. The burden of social isolation in older people

According to systematic reviews and meta-analyses, social isolation is associated with worse health outcomes in older individuals, from increased odds of non-communicable diseases to frailty and reduced survival (Sherman et al., 2024; Hanlon et al., 2024; Kojima et al., 2022). In particular, the pace of frailty progression towards disability is higher in subjects experiencing social vulnerability, a construct not including merely a scarce social network, but also implying the lack of adequate support in daily activities (Hanlon et al., 2024).

In robust individuals, high levels of social isolation were associated with increased odds of becoming pre-frail and frail (Jarach et al., 2021; Davies et al., 2021). In frail individuals, social isolation was associated with worsening severity of frailty itself (Davies et al., 2021). Therefore, older individuals with poor social networks have an increased risk of disability, cognitive impairment and all-cause mortality, according to longitudinal studies (Makizako et al., 2015; Yamada and Arai, 2018; Hoogendijk et al., 2020; Lee et al., 2024). The relationship between social isolation and cognitive decline was mediated by depressive symptoms (Bai et al., 2024). A recent study also identified social

Table 2
Summary of the studies investigating the changes in fecal microbiome composition before and after the implementation of social distancing policies during the COVID-19 pandemic in human beings.

Author, year	Country	Population	Study design	Type of restrictions	Main changes observed in GM during the pandemic	Issues concerning interpretation of results
Rashidi et al. (2021)	US	263 patients with AML undergoing chemotherapy (196 before and 67 during COVID-19)	Comparison of patients admitted before and during the first pandemic wave	Social distancing, masking	Increased representation of bacteria associated with mucosal barrier function, reduced representation of pathobionts	The use of antibiotics for treatment or prophylaxis of infections was different between the two study periods, and much lower during the pandemic due to effective pracautions.
Larcher Longo et al. (2022)	Brazil	15 older women (age 66 ± 2 years)	Two-time point analysis in March and September 2020	Social distancing, compulsory social isolation (quarantine)	Different GM configuration, with significantly higher representation of *Blautia.*	Physical activity and diet quality decreased during the quarantine period, with possible effects on GM composition. Serum inflammatory markers increased after the quarantine. Cessation of social distancing was associated with return to GM baseline state.
Aguilera et al. (2022)	Argentina	23 healthy subjects (39 ± 8 years)	Two-time point analysis in July-August 2016 and July-September 2020	Compulsory social isolation (quarantine)	Maintenance of a core microbiome structure, with reduced representation of some taxa belonging to the Verrucomorbia phylum.	Beta diversity was significantly different between the 2016 and the 2020 analysis, but no lifestyle covariates were considered. The long time before first and second evaluation does not allow us to attribute changes in GM composition only to social distancing measures.
Viciani et al. (2022)	Italy	34 elite soccer players	Repeated sampling during the 2019–2020 competitive season	Forced interruption of competitive season and training, social distancing	Reduction in the representation of SCFA-producing bacteria.	The effects of social distancing on microbiome composition cannot be distinguished from the effects of training interruption and dietary changes.
Novak et al. (2022)	Slovenia	38 healthy subjects aged 20–60 years old	Two-time point analysis in February and June 2020	Social distancing, home working	Reduced species richness with increased representation of Proteobacteria and decreased abundance of SCFA-producing bacteria.	The changes in fecal microbiota composition were correlated with psychological stress, but exercise and diet were not considered as covariates
Korpela et al. (2024)	Ireland	343 infants born during the lockdown period	Two-time point analysis at 6 and 12 months of age	Social distancing during the early months of life	Reduced representation of bacteria associated with horizontal transmission, predominance of vertically transmitted bacteria (in particular Bifidobacteria)	The delay in acquisition of horizontally transmitted bacteria was more pronounced in those infants not attending nursery, but was not associated with immunological consequences (risk of allergy).

US=United States; AML=Acute Myeloid Leukemia; SCFA=Short-Chain Fatty Acid.

isolation as an independent indicator of 1-year mortality in older individuals hospitalized with heart failure (Saito et al., 2024). Finally, cross-sectional studies also indicated an association between social isolation and falls, which are generally associated with functional decline and mortality in geriatric patients (Hayashi et al., 2020; Risbridger et al., 2022).

Social isolation, however, is a multidimensional concept with several nuances. Data from the English Longitudinal Study on Ageing suggested that isolation from wider social networks, including friends and colleagues, is more associated with frailty worsening than isolation from children or other family members (Maltby et al., 2020). Moreover, the association between isolation and frailty was stronger in males than in females (Gale et al., 2018). Different patterns of social support were also associated with frailty trajectories in The Chinese Longitudinal Healthy Longevity Survey (Pan and Cao, 2023a). Among the UK Biobank participants, frailty paradoxically attenuated the relationship between social isolation and adverse outcomes, particularly unplanned hospitalizations (Politis et al., 2024). Studies from the Netherlands and Singapore even denied the existence of an independent association between social isolation and frailty, focusing instead on loneliness as a major predictor of frailty (Ge et al., 2022; Mehrabi et al., 2024).

What is generally accepted in the literature is the bidirectionality of the relationship between social isolation and frailty (Mehrabi and Béland, 2020). Being frail increases the risk of reduced social support and isolation (Pan and Cao, 2023b). During the COVID-19 pandemic, social distancing measures were associated with a generalized deterioration of cognitive status of older individuals with previous cognitive complaints, but the presence of frailty increased impoverishment of social networks and social isolation (Terziotti et al., 2023). Multimorbidity (Bevilacqua et al., 2022) and falls (Sawa et al., 2024) also increased the risk of subsequent social isolation.

The complexity and individuality of aging patterns do not allow to disentangle the complex epidemiological association between frailty, frailty-related outcomes, and social isolation. In fact, social isolation may simply represent a moderator or mediator of the relationship between frailty and adverse health outcomes (Fig. 2) (Mehrabi and Béland, 2020). From a pathophysiological perspective, however, different studies conducted in adult community-dwellers suggest that social isolation is associated with increased chronic inflammation, that represents one of the major pathophysiological drivers of frailty (Matthews et al., 2024; Smith et al., 2020).

5. The social microbiome in older people and its relevance for geriatric medicine

At the current state of knowledge, it is not possible to prove a link between social isolation, GM dysbiosis and worsening of the aging trajectory. However, the evidence discussed in the previous sections allows us to hypothesize that impoverishment of social networks, social isolation and feelings of loneliness, that frequently occur in the older age, can have a negative impact on the GM composition and function, reinforcing the pathophysiological mechanisms of frailty. The interplay between

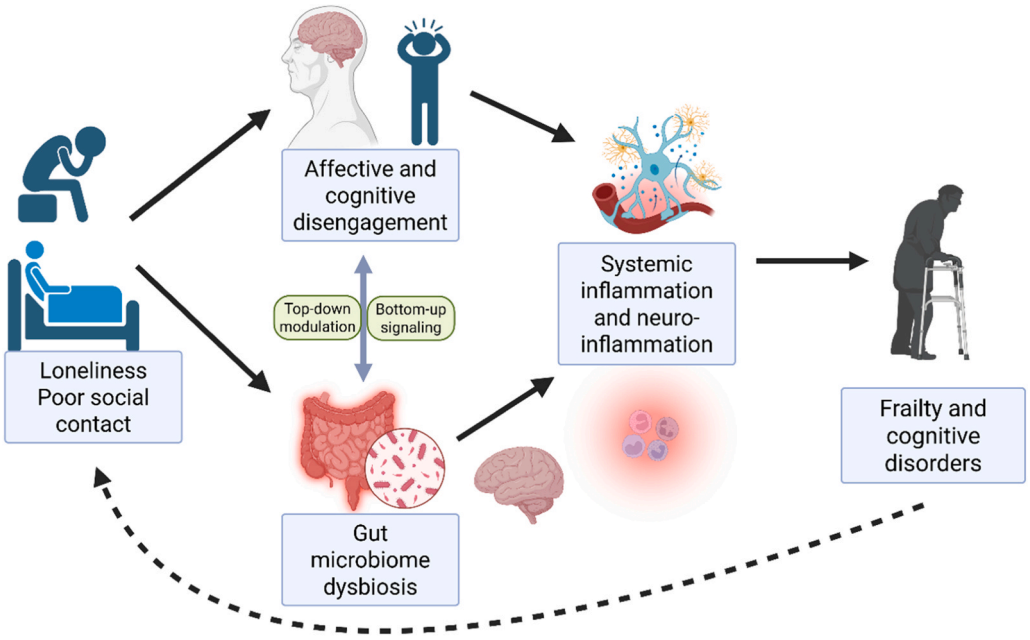

Fig. 2. Representation of the relationships between social isolation, loneliness, frailty and adverse health outcomes, and the possible role of gut microbiome dysbiosis as mediator.

GM, intestinal function and central nervous system is in any case extremely complex and should be considered as a "tripartite conversation", with each component influencing the others through pleiotropic mechanisms (Gershon and Margolis, 2021). The neuropsychological aspects of social isolation with the experience of loneliness during aging may both represent a cause and a consequence of GM alterations. Age-related dysbiosis, in fact, can influence mood, behavior and cognition by bottom-up signaling to the brain (Margolis et al., 2021). Conversely, top-down modulation of intestinal function by the central nervous system, particularly through GABA signaling, can contribute to changes in GM composition (Belelli et al., 2025), as suggested by data showing that cognitive behavioral therapy can modulate gastrointestinal symptoms and GM composition in patients with irritable bowel syndrome (Jacobs et al., 2021).

From a clinical point of view, these possible associations underscore the importance of a thorough assessment of social aspects when dealing with older patients. Loss of social relationships and social isolation, in fact, may imply a tendency towards dysbiosis, a possible contributor to

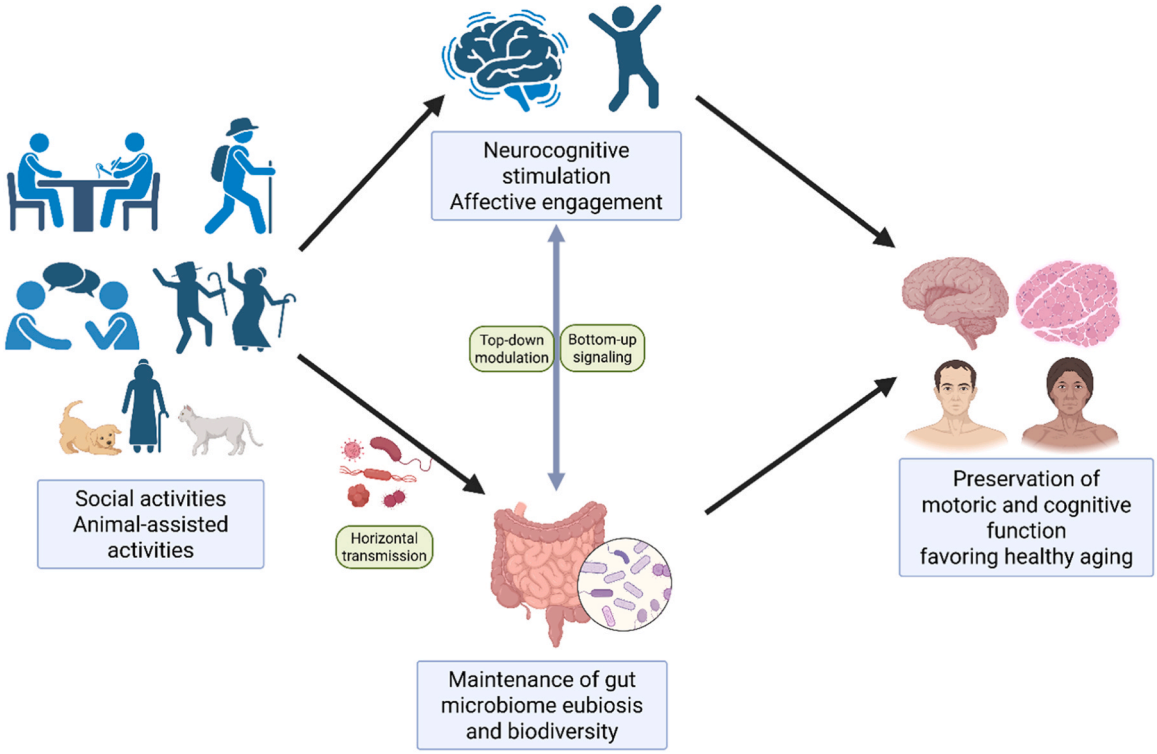

Fig. 3. Schematic overview of the effects of engagement in social and animal-assisted activities in the older age, and the role of gut microbiome in this process.

the pathophysiology of frailty, either by reducing the occasions of contact with diverse gut microbial species, or by altering gastrointestinal function with a top-down regulation. Living alone with reduced exposure to greenspace, a condition frequently occurring in older individuals in Western societies, may also represent a driver towards dysbiosis.

Therefore, promoting engagement in social activities and establishing novel social networks could represent an effective strategy to counteract loss of function and promote healthy aging at multiple levels, ranging from the psychoneural to, unexpectedly, the microbiological one. Collective interaction with other individuals obviously promotes communication and affectivity, with positive modulation of cognition and mood, but may also enable transmission of commensal bacteria, improving GM biodiversity and counteracting the mechanisms of inflammaging, that ultimately represent the biological substrate of cognitive and physical frailty (Fig. 3).

Prolonged contact with the same individuals without real social engagement may however be detrimental. Living in nursing homes, from a GM perspective, may imply an ongoing exchange of gut bacteria among a limited number of subjects – a situation comparable to the one depicted in Fig. 1 panel A. Interestingly, studies from Haran and colleagues provided evidence that nursing home residents living in the same ward have a high level of similarity in their GM composition, and have peculiar traits of GM in comparison with residents from other wards, irrespective of their clinical conditions and functional performance (Haran et al., 2018; Haran et al., 2021). This circumstance could be associated with reduced capacity of microbiome resilience to stressors. In fact, the presence of unique traits in the GM of older individuals is generally associated with reduced hospitalization risk and mortality (Wilmanski et al., 2021). Therefore, nutritional and nutraceutical interventions to maintain GM diversity in nursing home residents should be encouraged, in conjunction with interventions aimed at promoting sociality.

Moreover, promoting regular exposure of frail older individuals to pets could provide benefits to health not only through promotion of affective engagement (Orr et al., 2023), but also improving GM composition (Fig. 3). The beneficial effects of cohabitation with pets, that have been demonstrated in small case series of older individuals with cognitive complaints, depression or physical disability (Santaniello et al., 2020; Rodrigo-Claverol et al., 2020; Kamioka et al., 2014; Mossello et al., 2011; Thodberg et al., 2016; Berry et al., 2012), could be at least partly explained by the effects of pet exposure on GM. At the current state of knowledge, no studies investigating the effects of animal-assisted treatments, the so-called “pet therapy”, in older individuals has considered GM as an endpoint variable, although evidence from other scientific fields strongly supports transmission of gut bacteria between animals and humans.

Overall, the current state of knowledge on the relationship between social isolation and GM composition in aging leaves many questions open and suggests several research questions that should be addressed in future research. An overview of the main ones is discussed in Box 1.

6. Conclusions

The GM of human beings seems to be significantly modulated by number, type and duration of social contacts with other humans and animals, even if horizontal transmission of bacteria has been demonstrated in only few cases. Social isolation seems to be associated with reduced biodiversity of GM and tendency towards dysbiosis, which is an important promoter of inflammation. The detrimental consequences of social isolation in older individuals, including increased frailty incidence, accelerated frailty progression, disability and mortality, could thus be mediated by unfavorable changes in GM composition, among other mechanisms.

Interventions aimed at reducing social isolation and promoting sociality and social engagement, including animal-assisted activities, should be encouraged also for their possible beneficial effects on GM composition, in addition to their well-known psychoneurological effects on mood, cognition and affectivity. Further studies, either observational or interventional, should investigate whether social isolation does affect GM and, in turn, frailty status and the functional trajectory of geriatric

Box 1
Open questions and research perspectives on the social microbiome in older patients.

The existing population-based studies investigating the influence of social networks on GM composition, such as those summarized in Table 1, do not include older individuals and are not focused on comprehensive geriatric assessment. The importance of assessing social isolation and loneliness in older individuals is well known in clinical terms, to identify features of social frailty. Future population-based GM studies should therefore include a significant proportion of older individuals, including frail ones, and consider feelings of loneliness, depression and richness of social networks as covariates when analyzing GM composition. Such studies could also include clusters of individuals belonging to the same family, to improve the understanding of horizontal transmission dynamics across individuals belonging to different generations. The inclusion of older subjects cohabiting with pets could also enable profiling of pet GM, to elucidate the dynamics of animal-human transmission of microbial species. Environmental profiling of microbial communities harbored on domestic surfaces could also help to understand whether the features of buildings, where older subjects are living in, may be associated with distinctive features in their GM. These kinds of observational studies should be also performed in the nursing home setting, where older individuals with the highest burden of frailty and disability usually live, experiencing limited social contacts. Seminal data suggesting that the GM of nursing home residents is characterized by homogenization towards dysbiosis should be confirmed by larger multicenter studies, with a specific focus on tracking social contacts of each participant. This setting would be ideal to verify the hypothesis that marked feelings of loneliness are associated with distinctive unfavorable features in GM composition. The main questions on the social microbiome hypothesis, however, concern whether microbiome-centered treatments could influence social behavior of older individuals with feelings of loneliness and, in turn, interventions aimed at improving sociality could beneficially modulate GM composition. Intervention studies testing the health effects of pre-, pro-, postbiotics and synbiotics or microbiome-centered dietary strategies in older individuals should thus consider also loneliness and social behavior among their outcomes. On the other side, innovative studies investigating the effects of social activities, such as dance or theater, or animal-assisted therapies should consider GM composition and function among their outcomes. The beneficial effects of such interventions on cognition and mood could be at least partly mediated by the GM through the gut-brain axis. Nursing home residents or older individuals living alone in the community with poor social networks could represent the ideal participants to such innovative intervention studies.

patients. The beneficial role of non-pharmacological interventions, such as animal-assisted therapy and engagement in social activities, in frail older patients and in patients with cognitive decline or dementia should be also assessed in future studies considering GM composition and function as a possible clinical and biological endpoint.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.arr.2025.103008.

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