

Informatics for your Gut: at the Interface of Nutrition, the Microbiome, and Technology

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Summary

Background: A significant portion of individuals in the United States and worldwide experience diseases related to or driven by diet. As research surrounding user-centered design and the microbiome grows, movement of the spectrum of translational science from bench to bedside for improvement of human health through nutrition becomes more accessible. In this literature survey, we examined recent literature examining informatics research at the interface of nutrition and the microbiome.

Objectives: The objective of this survey was to synthesize recent literature describing how technology is being applied to understand health at the interface of nutrition and the microbiome focusing on the perspective of the consumer.

Methods: A survey of the literature published between January 1, 2021 and October 10, 2022 was performed using the PubMed database and resulting literature was evaluated against inclusion and exclusion criteria.

Results: A total of 139 papers were retrieved and evaluated against inclusion and exclusion criteria. After evaluation, 45 papers were reviewed in depth revealing four major themes: (1) microbiome and diet, (2) usability, (3) reproducibility and rigor, and (4) precision medicine and precision nutrition.

Conclusions: A review of the relationships between current literature on technology, nutrition and the microbiome, and self-management of dietary patterns was performed. Major themes that emerged from this survey revealed exciting new horizons for consumer management of diet and disease, as well as progress towards elucidating the relationship between diet, the microbiome, and health outcomes. The survey revealed continuing interest in the study of diet-related disease and the microbiome and acknowledgement of needs for data re-use, sharing, and unbiased and rigorous measurement of the microbiome. The literature also showed trends toward enhancing the usability of digital interventions to support consumer health and home management, and consensus building around how precision medicine and precision nutrition may be applied in the future to improve human health outcomes and prevent diet-related disease.

Keywords

Consumer health informatics, microbiota, user-centered design, telemedicine, information systems

Yearb Med Inform 2023;89-98

<http://dx.doi.org/10.1055/s-0043-1768723>

1 Introduction

The relationship between dietary patterns and the microbiome has surfaced as a critical factor in management of human health, including prevention and treatment of diseases including obesity [1-3], type 2 diabetes (T2D) [2, 4], Inflammatory Bowel Disease (IBD) [5, 6], and more. As research moves towards precision nutrition as a means to mitigate increasing rates of diet-driven disease, many challenges have come into view.

Diet is not the only factor influencing rising rates of obesity and T2D. Recent literature suggests that factors such as sleep patterns [7], access to food [8], and time available for food preparation in the home [9] also play a role, for example.

Consumers in the United States face challenges when providing a nutritious diet for themselves and their households, including, but not limited to, low nutrition literacy, food costs, food waste, supply chain shortages, lack of time to prepare meals, and food ac-

cess. These challenges translate to increased risk for personal health problems as well as increased burden on the healthcare system over time, with diet-driven disease accounting for an estimated 20% of healthcare costs in the United States [10].

Consumers are largely responsible for the management of nutrition and dietary choices in their own lives and households. Even when access to health care providers is available, most primary care physicians have limited time to discuss nutrition with their patients in depth [11]. Existing nutrition research has reinforced the importance of consumer understanding of food composition, preparation, access, and dietary behaviors for prevention, management, and treatment of diet-driven diseases [12-20]. To this end, there are several digital health applications designed to support the consumer in making nutritious food choices and preparing nutritious meals for themselves and their households. The effectiveness of a digital application is tied not only to its accuracy and quality, but also the application's ability to engage a consumer in a consistent manner [21, 22]. Therefore, the impacts of digital health interventions aimed at behavioral modifications in diet, physical activity, sleep, or wellness are directly tied to consumer adoption and consistent use [23, 24]. The research described in this brief year-in-review survey focuses on the design and development of tools for self-management in an outpatient or community setting. The research highlighted recognizes both the challenges of and needs for self-management tools that support consumer use and engagement, as

well as enhanced rigor when understanding mechanisms that influence our diet, such as the microbiome. This survey aims to provide a means for acknowledgement and understanding of the breadth of relationships and knowledge needed to address diet-related disease from an interdisciplinary informatics perspective.

The diet, the microbiome, and consumer behavior are intrinsically linked. The aim of this survey was to synthesize recent literature describing how technology is being applied to understand health at the interface of nutrition and the microbiome, with a special focus on the perspective of the consumer, as shown in Figure 1.

2 Methods

A survey of the literature published between January 1, 2021, and October 10, 2022 was performed using the PubMed database. The search was performed exactly as written below using the exact query provided:

("nutrition" AND "microbiome" AND "informatics") OR ("consumer health informatics" AND "nutrition") OR ("consumer health" AND "informatics" AND "nutrition") OR ("user experience" AND "nutrition") OR ("accessibility" AND "nutrition" AND "microbiome") OR ("health informatics" AND "microbiome") OR ("consumer health" AND "microbiome")

All results from the search above were downloaded as a comma-separated values (csv) file; after checking for duplicate articles, a total of 139 total papers were found. Inclusion and exclusion criteria (Table 1) were formed around identifying recent literature that focused on the intersection of diet and the microbiome from the perspective of a consumer or a patient managing diet-driven disease at home. For

example, diet-driven interventions that were self-managed applied in a patient population would be included, but diet-driven interventions applied to a patient population requiring majority clinical involvement or surgical interventions were excluded. Only studies describing human data in whole or in part (i.e., studies including data from mouse and human) were included.

Articles were screened against these inclusion and exclusion criteria. A total of 45 papers were included in the final survey. A total of 39 of the 45 papers (86.7%) included in the final survey were available freely on PubMed Central and the remaining papers were access through institutional access or interlibrary loan. This survey does not reflect a comprehensive review of the literature but aims to identify emerging themes and trends published in PubMed over the past year on this topic. The citations for the 45 papers and their major theme classifications are listed in Table 2, below. Table 2 reports major themes found in the survey, composition, and references for papers examined for each theme.

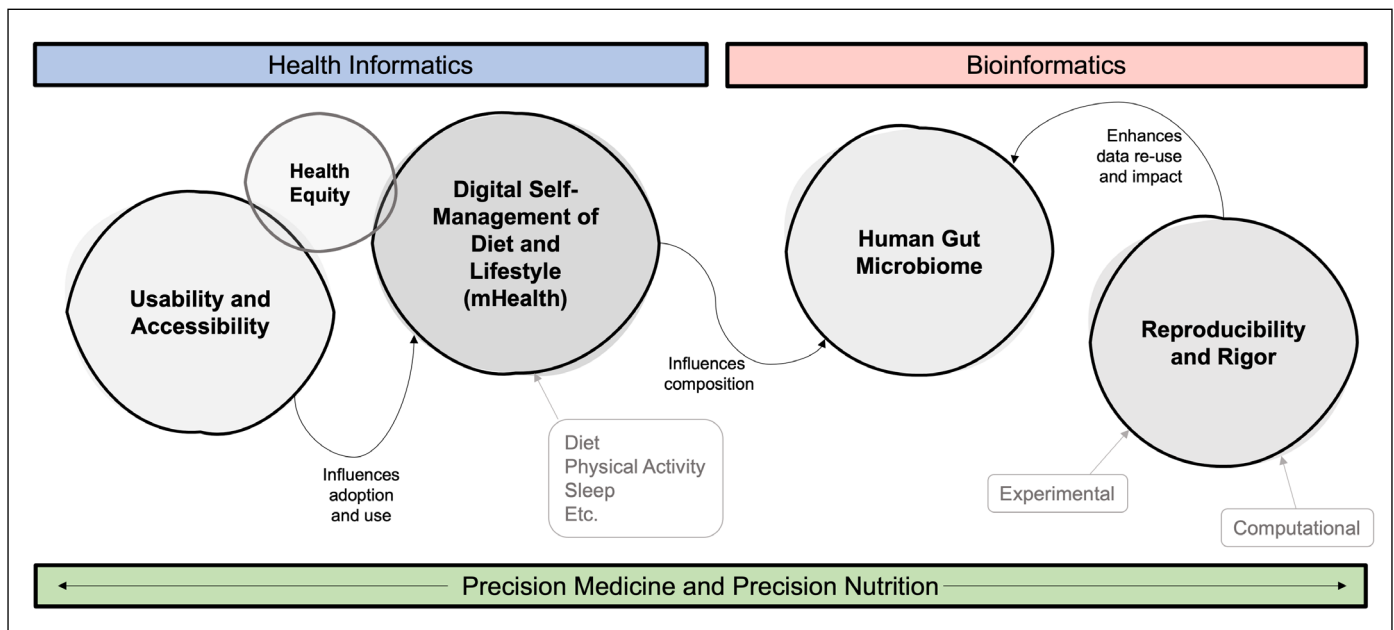


Fig. 1 A high-level overview of themes and topics covered in this survey. The concept of dietary patterns, impact on the gut microbiome, and impact of literature reviewed on precision medicine and nutrition is inclusive of multiple disciplines, including health informatics and bioinformatics.

Table 1 Inclusion and exclusion criteria used. A table describing the inclusion (top) and exclusion (bottom) criteria used when examining the literature included in this manuscript. Table 1. Inclusion and exclusion criteria used. A table describing the inclusion (top) and exclusion (bottom) criteria used when examining the literature included in this manuscript.

Inclusion Criteria	
Date	Published between January 1, 2021, and October 10, 2022
Database	PubMed database searched
Organism	Only include articles focusing on or including human studies/data
Article Type	Peer Reviewed Original Research, Review Articles only included Review papers were included to capture consensus on future trends and current challenges
Focus	Microbiome, disease, diet OR Usability and feasibility of digital diet self-management OR Computational rigor of microbiome analyses OR Consumer-based digital health/diet interventions
Location	Studies from any location were included
Data Type	Studies using 16s rRNA or metagenomic shotgun sequencing of fecal microbiome data included
Exclusion Criteria	
Focus	Excluded research with a majority focus on singular dietary intervention of commercial supplements OR focus on non-self-managed interventions (i.e., surgical or clinical interventions)
Transparency	Excluded research with unclear conflict of interest statements OR lack of clarity in performance of peer review OR concerns regarding quality of experimental design

Table 2 Survey Themes.

Major Theme	Papers (#)	Papers (%)	References
Microbiome and Diet	21	46.67%	[25-45]
Usability	14	31.11%	[23,24,46-57]
Reproducibility and Rigor	6	13.33%	[58-63]
Precision Medicine and Precision Nutrition	4	8.89%	[64-67]
TOTAL	45	100%	

In this context, “usability” refers to the ability of a product to be used by a consumer. A more thorough explanation on usability is well defined by the International Organization for Standardization (ISO) [68].

3 Results

A total of four major themes were identified in the literature and synthesized by KC, each with its own emerging subthemes: (1) Microbiome and Diet-driven Disease, (2) Usability

and Accessibility of Consumer Health Tools, (3) Reproducibility and Rigor of Computational Analysis in the Microbiome, and (4) Precision Medicine and Precision Nutrition.

3.1 Microbiome and Diet-driven Disease

Microbiome. With decreasing costs of microbiome sequencing as well as increased interest in the impact of the microbiome on health, the literature and data availability on this topic is expected to grow. The literature

in this review circled around diet-driven disease with major public health implications: obesity/overweight, T2D, COVID-19, Irritable Bowel Syndrome (IBS), Irritable Bowel Disease (IBD), and food allergies/intolerance, among others. The literature on the microbiome and diet also focused on pre-natal health (gestational diabetes) and infant health. Notable subthemes observed in this research include (1) continued interest in the impact of singular, short-term interventions on microbiome composition, (2) proliferation of smaller studies on the microbiome in diet-related disease, and (3) implicit need for reliable aggregation and analysis of microbiome data to ensure replicability and rigor when applied in a larger human population.

Diet-driven Disease. Most studies described in this survey capture data in a post-COVID world. It is expected that the COVID-19 pandemic has influenced the gut microbiome due to rapid changes in physical activity, diet, access to food, and exposure to one's community [39] via mechanisms such as lockdowns, social distancing, isolation protocols, and quarantines. One retrospective study of 3,055 16s rRNA microbiome datasets across 12 countries aimed to find any population level changes associated with the COVID-19 pandemic [27]. Authors separated microbiome data into two groups: countries with higher COVID-19 hospitalization rates and countries with lower COVID-19 hospitalization rates [27]. Diversity in bacterial abundance (measured by Shannon's alpha) was higher in countries with “high” COVID-19 hospitalizations; this difference was statistically significant [27]. It is possible to speculate on reasons why a relationship between microbiome diversity and COVID-19 hospitalization might be found. Research outside this survey found evidence that hospitalization rates vary due to differences in diet, physical activity, alcohol and tobacco use, and other behaviors [69-71], although this evidence may be conflicting.

Irritable Bowel Syndrome (IBS). The potential impact of supporting patients living with gastrointestinal disease is large – for example, an expected 25-45 million individuals suffer from Irritable Bowel Syndrome (IBS) in the United States [72]. Four studies

examined means to reduce symptoms for individuals living with IBS through dietary management. In one study an oral probiotic was trialed ($n=15$ adults) with IBS over a period of 4 or 8 weeks [30]. The probiotic, called VSL#3®, contains bacteria from the genus *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* [73]. Microbiome composition studies from before and after the study period detected bacteria from all three genera in the group treated with the probiotic, but found no difference in abundance before and after treatment [30]. Despite this, participants in the probiotic group reported reduction in pain and symptoms [30]. Another study of the gut microbiome collected from $n=34$ individuals diagnosed with IBS and receiving Cognitive Behavioral Therapy (CBT) as treatment was performed [32]. Interestingly, significant differences in microbiome composition were found between individuals who responded to CBT treatment versus treatment non-responders [32]. This apparent conflict in early results, along with relatively small cohort size, suggest that this is an area that will benefit from efforts to store, share, and re-use microbiome data, as well as efforts to aggregate data for comparison in an unbiased and rigorous way. This concept is supported by a fourth study reviewed in the survey: one study reviewed of women with IBS concluded that there was evidence for further investigation of the relationship between bile acid levels, the microbiome, and its mechanism or role in IBS [45]. These studies demonstrate a changing microbiome in individuals with IBS, but highlight the need for evidence to understand the role of the microbiome in IBS and potential means for treatment.

Type 2 Diabetes. Type 2 diabetes (T2D) in the United States has a similarly sized impact on public health: according to the CDC, 33-35 million Americans are estimated to have T2D as of December 2021 [74]. The gut microbiome has also emerged as a focus within the research community to understand T2D and identify treatments and prevention methods [4, 75-77]. Although T2D is a highly researched disease, only one study found passed the inclusion and exclusion criteria. In this study, 405 individuals with T2D found

significant differences in taxa present in the fecal microbiome at the genus level according to disease severity [42]. A cursory search of the query “T2D AND microbiome” alone on PubMed for 2021-2023 revealed 1,051 resulting papers, although inclusion of the terms “diet” or “nutrition” on the query vastly reduced the search results. One study from management of lifestyle factors for T2D using digital health applications or mHealth [55] indicates that our search terms used may have excluded some relevant papers in this area.

Amyotrophic Lateral Sclerosis (ALS).

The microbiome is also being investigated in diseases not traditionally thought to be “diet-driven”. For examples, a study of 66 individuals with Amyotrophic Lateral Sclerosis (ALS) and 73 controls found a significant difference in abundance of certain taxa in the fecal microbiota of individuals with ALS [44]. Outside of this survey, there is some research on diet and development of ALS, but diet is not currently considered a causal factor [78, 79]. It is important then to recognize that although there is evidence of the impact of diet on the microbiome, that the microbiome may also be a potential tool for prevention, diagnosis, and treatment of diseases not traditionally considered “diet-driven”. Rather, the microbiome should be considered an important factor in human health that can be modified by dietary behaviors.

Pregnancy. Three studies focused on microbiome during pregnancy and during the postpartum period. A study of $n=115$ pregnant individuals with and without gestational diabetes found no significant difference in microbiome composition or alpha diversity, although some significant changes in bacteria at the genus level were found in the third trimester [26]. The authors of this study state that their work adds to existing studies [76, 80-83] on microbiome changes in pregnancy, noting a knowledge gap and need for further studies of the microbiome during gestation [26]. A 2022 study of 90 infant-mother pairs examined the relationship between maternal weight (overweight or obese) on infant microbiome, also finding no significant associations between the microbiomes of infants born to individuals who had developed gestational diabetes versus

not [31]. Outside of gestational diabetes, a study of $n=48$ pregnant individuals found evidence for an association between diet and decreased alpha diversity in the fecal microbiome, speculating that pre-term birth may have links to the microbiome [41]. This implicates diet as a modifiable factor through which maternal and infant health can potentially be addressed [41]. These studies again demonstrate a changing microbiome in pregnant individuals but highlight the need for evidence to understand the role of the microbiome before, during, and after pregnancy. The literature reviewed also suggests the importance of postnatal support for caregivers of infants and children in managing household tasks. This trend is continued in the *Infant Diet* themed literature, below.

Infant Diet. Food allergies and intolerance in infancy emerged as a trend in microbiome studies examined. One study on 30 infants examined microbiome composition between infants fed a typical cow’s milk-based formula versus a hydrolyzed formula (often used for infants with dairy intolerances), observing significant differences in microbial composition after 4 months, as well as observing *Ruminococcus gnavus* as a taxa on that significantly differentiates between the two groups [29]. Another study of 148 infants with a cow’s milk protein allergy found a significant decrease in symptoms, caregiver burden and healthcare resources when a symbiotic was prescribed alongside specialized formulas versus no symbiotic [38]. Considering the rapid growth and establishment of the infant gut microbiome as well as its impact on health, it is unsurprising that these studies on infant diet and microbiome have begun to emerge. A study of 28 preterm infants found a significant difference between microbiome composition and growth in head circumference, especially in the phyla *Bacteroidota* and family *Lachnospiraceae* [33]. This literature also implicitly suggests the importance of postnatal support for caregivers of infants and children in managing household tasks such as feeding, grocery purchasing, and food preparation especially in infants with specialized feeding needs. These needs may be addressed using digital health interventions or informatics approaches.

Microbiome and Diet. Five studies focused on understanding diet and the microbiome, continuing an existing trend in the literature. A 2022 review described the current knowledge about the role of the gut microbiome in lipid metabolism and short chain fatty acid modulation [28]. The authors acknowledge the impact of diet on the microbiome, including how quickly the microbiome reacts to changes in dietary composition, timing of meals, fiber intake, and impact of micronutrients [28]). One study performed a week-long at-home immersion experience for 74 participants focusing on improving behaviors in physical activity and diet [35]. The authors report that anti-inflammatory taxa increased in the microbiome of participants after the intervention [35]. Another study examining long term dietary intake effects on the microbiome ($n=128$ adults) found an association between self-reported carbohydrate intake and gut microbiome composition [44]. A study of 59 individuals aged 40-85 found no significant changes in fecal microbiome composition's alpha diversity by age. However, authors did report age-related differences in microbiome composition from samples taken from salivary and gastrointestinal sites [37]. The results of these four studies highlight a need for larger microbiome studies, how the microbiome is captured, and the diversity of evidence that is building our understanding of the gut microbiome. Lastly, a larger cohort study of diet and microbiome in $n=3,308$ participants reported taxa that was able to differentiate between individuals consuming high levels of animal protein versus low levels of animal protein [34].

3.2 Usability and Accessibility of Digital Health Applications

This literature survey focused on digital interventions that could be self-managed: this includes improving, tracking, or monitoring modifiable behaviors for patients or consumers who are managing their health at home. The subthemes that emerged from this literature were consistent despite a broad array of research topics and foci: Applications intended to support or enhance lifestyle factors impacting health need to be

easy to use, easy to learn, fast, accessible, and perceived as useful. Noncompliance was when users experienced technical issues, or when an application or intervention was not convenient to use.

There is a wealth of diet-driven applications already online: food trackers, meal planners, label scanning applications, weight loss programs, and fasting trackers are all examples. Demand for consumer support in pursuit of health and wellness is high. Similarly, a focus on usability and feasibility of prototype applications and interventions emerged in the literature.

Applications Examining Diet or Physical Activity Exclusively. Four studies focusing on exclusively diet or physical activity applications were reviewed. A web-based application for management of dietary patterns, eNutri, was evaluated for usability using the System Usability Scale using $n=106$ participants in Germany [24]. Participant feedback demonstrated above average usability but stated concerns about the amount of time required by the application to complete its purpose (26.7 minutes, mean) [24]. Another approach aimed to design a "user-centered" dietary management tool for type 2 diabetics, surveying 21 individuals over 4 project phases to understand user needs [50]. The study revealed participant's desire for ease of access to information, ease of communication, provision of information/content that is easy to understand to accommodate a busy lifestyle [50]. Physical activity-only interventions were also reviewed. A 2022 mHealth study of a smartphone application designed to encourage physical activity was performed to compare usability and enjoyment [46]. A total of 20 participants gave feedback on the system, and results indicated that technical issues when using the application negatively affect use [46]. A separate study of a Bluetooth-enabled resistance band for enhancing strength reported positive feedback on usability in terms of ease of use, ease of learning, and user satisfaction [56]. These studies highlight the importance of user-centered design in lifestyle management applications designed to support behaviors that improve positive health outcomes.

Diet, Sleep, and Physical Activity. Four studies examined applications or interventions designed to support multiple lifestyle factors versus one single factor (i.e., diet, exercise, sleep), especially in vulnerable patient populations. Authors of a 2022 study ($n=17$) on user experience with a web-based weight management application found important factors to enhance use for self-management of diet and physical activity in kidney transplant recipients [47]. An mHealth application supporting healthy diet, physical activity, and sleep habits for wheelchair users ($n=14$) also concluded that successful user engagement relied on ease of use, usefulness, and ease of learning [23]. For this study, users also demonstrated interest in personalization of the application, ability to access user history, and access to personalized insights based on their input data and behaviors [23]. A prototype application designed to support improved health behaviors in $n=50$ prediabetic participants shared results supporting a focus on applications that are easy to use and perceived as useful [55]. A much larger study of over 16,000 users of a phone-based app for self-management of T2D reported that app engagement was associated with improved patient outcomes (as measured by blood A1C) [49].

Applications for Parents and Caregivers. As described previously, food allergies and intolerance in infancy emerged as a trend in microbiome studies examined. Mirroring this trend, four studies were reviewed that reflect the use of technology to support parents and caregivers. A 2022 study of $n=126$ postpartum individuals evaluated subject use of applications meant to track infant feeding patterns, including feeding times, duration, volume of feed, and more [48]. Most of the subjects ($n=72$) who used the infant feeding application used it for logging or tracking; factors describing their support for use of a tracking app included ease of use and ability to use with a co-parent or co-caregiver [48]. A 3-phase study to evaluate design needs for a social and emotional well-being application in Aboriginal and Torres Strait Islander women concluded that app design for this approach requires extensive end-user consultation and investment in user-centered design [53]. A study of $n=45$ parents of newborn infants was performed to discern end-user needs for a

chatbot application supporting parental sleep habits and infant feeding in the first 6 months of life [54]. Some of the findings of this study included a desire for short interactions within the application, willingness to share their data, and noncompliance due to technical issues, lack of sleep, and physical discomfort [54]. A web-based app designed for menu planning was studied for usability by 64 childcare services employees in Australia; feedback noted by the authors described a need for improvements in speed and ease of use [57]. Feedback also demonstrated majority enthusiasm and usefulness of a menu planning application for use in their daycare center [57].

Virtual Health Assistants. A 2021 review of the literature on virtual health assistants ($n=48$) examined the user experience of interactive information sharing resources (virtual health assistants or chatbots) based on their visual design and conversational style, recommending focus on empathetic interaction, humanistic visual and conversational designs would fare best [52].

3.3 Reproducibility and Rigor of Computational Analysis in the Microbiome

The literature on microbiome sample collection, sample processing, nucleotide extraction, sequencing, and data freely acknowledges concerns around data quality, reproducibility, and the need for quality assessment and control. As microbiome data gathering becomes cheaper and calls for improved biomedical data management standards increase [84], the need for these methods will continue to grow. Tools, methods, or calls for enhanced data management infrastructure, re-use, and code sharing were described.

Removal of Bias in Microbiome Analysis. Many microbiome datasets have small sample sizes, and there is interest in means to compare, combine, or otherwise aggregate results to see which findings can be generalized. Methods, applications, and recommendations for this type of broad scale comparison and quality assessment in microbiome data were proposed in the literature to correct for environmental batch effects [58],

for population-level data stratification [36], filtering of rare taxa for reproducibility and generalizability [63], among others. Reproducibility continues to be present as a topic of interest, including a method (RESCRIPT) for enhancing reproducibility of reference databases commonly used for taxonomic identification in microbiome analysis [60].

A review performed in response to challenges in defining a microbial association network in an environment that is not biased by experimental or computational artifacts, calling for focus on benchmarking and validation [62]. Development of minimum information standards, called the STORMS checklist, for microbiome research that recognizes the interdisciplinary nature of microbiome research, and the data management processes that must be in place to enhance reproducibility and replicability [59]. There is a need and enthusiasm for training materials on microbiome composition analysis as demonstrated by sessions provided for the microbiome analysis software QIIME2, with requests for additional trainings on reproducibility and workflow documentation [61].

The Future of Artificial Intelligence in Microbiome Research. A review on machine learning in the microbiome space proposed recommendations for reliable application of artificial intelligence for precision medicine, including creation of standards, increase in quantity and quality of microbiome data, application of appropriate data management solutions such as the Findable, Accessible, Interoperable, and Reusable (FAIR) data principles, and support for interdisciplinary team science [66]. A similar review examining machine learning challenges in human microbiome data echoes a need for larger studies of a certain quality, experimental and computational bias, and need for interpretability of machine learning model outputs [67].

3.4 Precision Medicine and Precision Nutrition

Precision medicine and precision nutrition were emerging topics that encompassed multiple disciplines within the computational health and biology space. There is massive interest in the role of the microbiome in

precision medicine [85-87], both generally and for specific applications such as the treatment of cancer [88] and to enhance pharmacologic intervention [89]. This interest extends to the relationship between nutrition and the microbiome. In May 2020, the National Institutes of Health described the role of nutrition informatics in its 2020-2030 Strategic Plan for NIH Nutrition Research, which details four questions as a part of its strategic approach: “*What do we eat and how does it affect us?*”, “*What and when should we eat?*”, “*How does what we eat promote health across our lifespan?*”, and “*How can we improve the use of food as medicine?*” [90]. Answering these high-level questions requires interdisciplinary, team-science based approaches that span the translational science spectrum, from bench to bedside. As methods for capturing dietary behavioral data, food composition, provenance, and preparation data improve, and our understanding of the impact of dietary patterns on the microbiome improves, it is possible to imagine a future where the interface of bioinformatics and health informatics is more clearly realized.

Future Trends. Trends discussed through research studies and reviews examined clearly outline diet-driven diseases as a target for precision medicine and nutrition. Obesity is one a high-impact target for the development and application of precision nutrition approaches. A 2021 review predicts that future applications of microbiome research to benefit precision nutrition will include manipulation of the gut microbiome through diet, pre- and probiotic supplementation to alter microbiome composition, as well as fecal microbiota transplantation for treatment of disease [25]. A perspective article in PNAS notes the relationship between the microbiome and health inequities [65]. Therefore, it can be recognized as a tool for researchers to examine as a modifiable factor to improve human health in those populations experiencing health inequity [65]. One study, upon finding differences in fecal microbiome taxa between obese and non-obese African American children ($n=30$) aged 6-10 years old, speculated on a need for personalized approaches that are inclusive of ethnicity and other factors

such as socioeconomic status [40]. A 2022 review on racial disparities and cardiovascular health notes the role of dietary behaviors and environmental factors on the microbiome, stating that they will likely factor into “precision medicine” to improve outcomes [51]. Other angles include the examination of dietary trends over longer periods of time. For example, another review described the “nutribiography”, a collection of behavior over the lifetime is proposed as a potential future means for examining the impact of long-term diet on inflammation and aging [64]. Research in this space appears to be trending towards the understanding of food environment and socioeconomic factors in supporting consumer purchasing and dietary choices leading to positive health outcomes. This work recognizes the need for improved nutrition literacy and improved food access, as well as accessible and clear product labeling.

4 Discussion

Technology is allowing for the scientific community to bridge the gap between health informatics and bioinformatics for the understanding of nutrition and the microbiome. This work identified major themes in (1) Microbiome and Diet-driven Disease, (2) Usability and Accessibility of Consumer Health Tools, (3) Reproducibility and Rigor of Computational Analysis in the Microbiome, and (4) Precision Medicine and Precision Nutrition. While each of the individual themes on usability and accessibility, microbiome and diet, and reproducibility has a clearly defined limit to its scope, these limits have potential for overlap through the application of technology and informatics. The possibility of digital dietary applications for supporting modification of the gut microbiome has great potential for improving health outcomes, for example. However, researchers pursuing these pathways must also be aware of the need for user-centered design in their applications, the reality of food access challenges, and the need for rigorous research supporting recommendations based on existing microbiome data.

Approximately 60% of the United States population experiences diet-related chronic disease such as overweight/obesity, heart disease, stroke, or T2D [91, 92]. Approximately 56 million adults aged 65 and older currently live in the United States, and up to 60% of those individuals are estimated to experience malnutrition [93,94]. Another 10% of the United States population experiences physician-diagnosed food allergies and/or intolerances [95, 96]. There is great potential to enhance disease prevention via technology and precision nutrition, but research in this area must address the factors of health equity that play into making dietary choices that fuel positive outcomes. This includes developing technology to support those choices that is easy to use, easy to learn, fast, personalized, and addresses gaps in health literacy found in vulnerable populations [97-99]. This also includes acknowledgement of research demonstrating that purchase and preparation of nutritious food in the home requires time, effort, and support [20, 100, 101].

From a bioinformatics perspective, there is great potential for continued microbiome research and its relationship to dietary patterns to enhance human health. The literature reviewed on microbiome research in this survey demonstrates a need for methods to compare and aggregate data, a need for reporting standards, workforce training, and needs for understanding challenges in both experimental and computational reproducibility and generalizability in microbiome analysis. This requires engagement of the informatics community and resources to build data sharing and re-use infrastructure, as well as communication of biases and challenges in data analysis. This charge is supported by existing work in the literature [102-105].

5 Conclusions

A survey of recent literature exploring the relationships between technology, nutrition and the microbiome, and self-management of dietary patterns was performed. A total of 45 papers relevant to the inclusion and exclusion criteria were examined for major and minor themes, including:

1. **Microbiome and Diet-driven Disease**, with subthemes focusing on the impact of diet on the microbiome, diet-driven or related diseases including but not limited to IBS, T2D, overweight/obesity, pregnancy, and infancy;
2. **Usability and Accessibility of Consumer Health Tools**, with subthemes focusing on digital health applications to support subset populations in diet, physical activity, sleep, or combinations of all three and other lifestyle factors. Subthemes highlighted user needs of caregivers and parents in their caregiving roles;
3. **Methods, Reproducibility, and Rigor**, with subthemes including removal of bias in microbiome analysis and the potential for artificial intelligence in microbiome research;
4. **Precision Medicine and Precision Nutrition**, with a focus on how these will be applied in the future to improve human health.

Acknowledgements

Research reported in this publication was supported by the Office Of The Director, National Institutes Of Health of the National Institutes of Health under Award Number K01OD030514 and the National Institute Of General Medical Sciences of the National Institutes of Health under Award Number R25GM141506. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The general conceptualization of this work was performed by KC, JC, and MC over the course of multiple discussions on emerging research since 2020. KC was responsible for primary development of methodology, formal analysis, drafting, review, editing, and project administration. JC and MC performed draft review, critique, and editing.

References

1. Ley RE. Obesity and the human microbiome. *Curr Opin Gastroenterol* 2010 Jan;26(1):5-11. doi: 10.1097/MOG.0b013e328333d751.
2. Devaraj S, Hemarajata P, Versalovic J. The human gut microbiome and body metabolism: implications for obesity and diabetes. *Clin Chem* 2013 Apr;59(4):617-28. doi: 10.1373/

- clinchem.2012.187617.
3. Lee CJ, Sears CL, Maruthur N. Gut microbiome and its role in obesity and insulin resistance. *Ann NY Acad Sci* 2020 Feb;1461(1):37-52. doi: 10.1111/nyas.14107.
4. Sharma S, Tripathi P. Gut microbiome and type 2 diabetes: where we are and where to go *J Nutr Biochem* 2019 Jan;63:101-108. doi: 10.1016/j.jnutbio.2018.10.003.
5. Glassner KL, Abraham BP, Quigley EM. The microbiome and inflammatory bowel disease. *J Allergy Clin Immunol* 2020 Jan;145(1):16-27. doi: 10.1016/j.jaci.2019.11.003.
6. Kostic AD, Xavier RJ, Gevers D. The microbiome in inflammatory bowel disease: current status and the future ahead. *Gastroenterology* 2014 May;146(6):1489-99. doi: 10.1053/j.gastro.2014.02.009.
7. Ogilvie RP, Patel SR. The epidemiology of sleep and obesity. *Sleep Health* 2019 Feb;5(1):84-90. doi: 10.1016/j.sleh.2018.10.010.
8. Chen S, Florax RJ, Snyder S, Miller CC. Obesity and access to chain grocers. *Econ Geogr* 2010;86(4):431-52. doi: 10.1111/j.1944-8287.2010.01090.x.
9. Kolodinsky JM, Goldstein AB. Time use and food pattern influences on obesity. *Obesity (Silver Spring)* 2011 Dec;19(12):2327-35. doi: 10.1038/oby.2011.130.
10. Jardim TV, Mozaffarian D, Abrahams-Gessel S, Sy S, Lee Y, Liu J, et al. Cardiometabolic disease costs associated with suboptimal diet in the United States: A cost analysis based on a microsimulation model. *PLoS Med* 2019 Dec 17;16(12):e1002981. doi: 10.1371/journal.pmed.1002981.
11. Adamski M, Gibson S, Leech M, Truby H. Are doctors nutritionists? What is the role of doctors in providing nutrition advice? *Nutrition Bulletin* 2018 May 18; 43(2):146-52. doi: 10.1111/nbu.12320.
12. Fitzgerald N, Damio G, Segura-Pérez S, Pérez-Escamilla R. Nutrition knowledge, food label use, and food intake patterns among Latinas with and without type 2 diabetes. *J Am Diet Assoc* 2008 Jun;108(6):960-7. doi: 10.1016/j.jada.2008.03.016.
13. Kretzer A, Murphy D, Starke-Reed P. A partnership for public health: USDA branded food products database. *J Food Compos Anal* 2017 Dec 1;64:10-2. doi: 10.1016/j.jfca.2017.07.019.
14. Boland M, Bronlund J. eNutrition-The next dimension for eHealth? *Trends in Food Science & Technology* 2019 Sep 1;91:634-9. doi: 10.1016/j.tifs.2019.08.001.
15. Anastasiou K, Miller M, Dickinson K. The relationship between food label use and dietary intake in adults: A systematic review. *Appetite* 2019 Jul 1;138:280-91. doi: 10.1016/j.appet.2019.03.025.
16. Slavin JL. The challenges of nutrition policy-making. *Nutr J* 2015 Feb 7;14:15. doi: 10.1186/s12937-015-0001-8.
17. Spronk I, Kullen C, Burdon C, O'Connor H. Relationship between nutrition knowledge and dietary intake. *Br J Nutr* 2014 May 28;111(10):1713-26. doi: 10.1017/S0007114514000087.
18. Kessler DA. The evolution of national nutrition policy. *Annu Rev Nutr* 1995;15:xiii-xxvi. doi: 10.1146/annurev.nu.15.070195.005033.
19. Malloy-Weir L, Cooper M. Health literacy, literacy, numeracy and nutrition label understanding and use: a scoping review of the literature. *J Hum Nutr Diet* 2017 Jun;30(3):309-25. doi: 10.1111/jhn.12428.
20. Williams P. Consumer understanding and use of health claims for foods. *Nutr Rev* 2005 Jul;63(7):256-64. doi: 10.1111/j.1753-4887.2005.tb00382.x.
21. McCurdie T, Taneva S, Casselman M, Yeung M, McDaniel C, Ho W, et al. mHealth consumer apps: the case for user-centered design. *Biomed Instrum Technol* 2012 Fall;Suppl:49-56. doi: 10.2345/0899-8205-46.s2.49.
22. World Health Organization. mHealth: new horizons for health through mobile technologies. 2011 [Available from: <https://www.afro.who.int/publications/mhealth-new-horizons-health-through-mobile-technologie>].
23. Hoevenaars D, Holla JF, Te Loo L, Koedijker JM, Dankers S, Houdijk H, et al; WHEELS Study Group. Mobile app (WHEELS) to promote a healthy lifestyle in wheelchair users with spinal cord injury or lower limb amputation: usability and feasibility study. *JMIR Form Res* 2021 Aug 9;5(8):e24909. doi: 10.2196/24909.
24. Kaiser B, Stelzl T, Finglas P, Gedrich K. The Assessment of a Personalized Nutrition Tool (eNutri) in Germany: Pilot Study on Usability Metrics and Users' Experiences. *JMIR Form Res* 2022 Aug 4;6(8):e34497. doi: 10.2196/34497.
25. Cifuentes L, Eckel-Passow J, Acosta A. Precision medicine for obesity. *Dig Dis Interv* 2021 Sep;5(3):239-48. doi: 10.1055/s-0041-1729945.
26. Dualib PM, Taddei CR, Fernandes G, Carvalho CR, Sparvoli LG, Silva IT, et al. Gut microbiota across normal gestation and gestational diabetes mellitus: A cohort analysis. *Metabolites* 2022 Aug 26;12(9):796. doi: 10.3390/metabo12090796.
27. Lymberopoulos E, Gentili GI, Budhdeo S, Sharma N. COVID-19 severity is associated with population-level gut microbiome variations. *Front Cell Infect Microbiol* 2022 Aug 23;12:963338. doi: 10.3389/fcimb.2022.963338.
28. Jian Z, Zeng L, Xu T, Sun S, Yan S, Zhao S, et al. The intestinal microbiome associated with lipid metabolism and obesity in humans and animals. *J Appl Microbiol* 2022 Nov;133(5):2915-30. doi: 10.1111/jam.15740.
29. Mennella JA, Li Y, Bittinger K, Friedman ES, Zhao C, Li H, et al. The macronutrient composition of infant formula produces differences in gut microbiota maturation that associate with weight gain velocity and weight status. *Nutrients* 2022 Mar 15;14(6):1241. doi: 10.3390/nu14061241.
30. Boonma P, Shapiro JM, Hollister EB, Badu S, Wu Q, Weidler EM, et al. Probiotic VSL#3 treatment reduces colonic permeability and abdominal pain symptoms in patients with irritable bowel syndrome. *Front Pain Res (Lausanne)* 2021 Sep 22;2:691689. doi: 10.3389/fpain.2021.691689.
31. Guzzardi MA, Ederveen TH, Rizzo F, Weisz A, Collado MC, Muratori F, et al. Maternal pre-pregnancy overweight and neonatal gut bacterial colonization are associated with cognitive development and gut microbiota composition in pre-school-age offspring. *Brain Behav Immun* 2022 Feb;100:311-20. doi: 10.1016/j.bbi.2021.12.009.
32. Jacobs JP, Gupta A, Bhatt RR, Brawer J, Gao K, Tillisch K, et al. Cognitive behavioral therapy for irritable bowel syndrome induces bidirectional alterations in the brain-gut-microbiome axis associated with gastrointestinal symptom improvement. *Microbiome* 2021 Nov 30;9(1):236. doi: 10.1186/s40168-021-01188-6.
33. Oliphant K, Ali M, D'Souza M, Hughes PD, Sulakhe D, Wang AZ, et al. Bacteroidota and Lachnospiraceae integration into the gut microbiome at key time points in early life are linked to infant neurodevelopment. *Gut Microbes* 2021 Jan-Dec;13(1):1997560. doi: 10.1080/19490976.2021.1997560.
34. Bel Lassen P, Attaye I, Adriouch S, Nicolaou M, Aron-Wisniewsky J, Nielsen T, et al. Protein intake, metabolic status and the gut microbiota in different ethnicities: Results from two independent cohorts. *Nutrients* 2021 Sep 10;13(9):3159. doi: 10.3390/nu13093159.
35. Ahrens AP, Culpepper T, Saldivar B, Anton S, Stoll S, Handberg EM, et al. A six-day, lifestyle-based immersion program mitigates cardiovascular risk factors and induces shifts in gut microbiota, specifically lachnospiraceae, rumenococcaceae, faecalibacterium prausnitzii: a pilot study. *Nutrients* 2021 Sep 29;13(10):3459. doi: 10.3390/nu13103459.
36. Lymberopoulos E, Gentili GI, Alomari M, Sharma N. Topological data analysis highlights novel geographical signatures of the human gut microbiome. *Front Artif Intell* 2021 Aug 18;4:680564. doi: 10.3389/frai.2021.680564.
37. Schütte K, Schulz C, Vilchez-Vargas R, Vasapolli R, Palm F, Simon B, et al. Impact of healthy aging on active bacterial assemblages throughout the gastrointestinal tract. *Gut Microbes* 2021 Jan-Dec;13(1):1966261. doi: 10.1080/19490976.2021.1966261.
38. Sorensen K, Cawood AL, Gibson GR, Cooke LH, Stratton RJ. Amino acid formula containing synbiotics in infants with cow's milk protein allergy: A systematic review and meta-analysis. *Nutrients* 2021 Mar 14;13(3):935. doi: 10.3390/nu13030935.
39. Burchill E, Lymberopoulos E, Menozzi E, Budhdeo S, McIlroy JR, Macnaughtan J, et al. The unique impact of COVID-19 on human gut microbiome research. *Front Med (Lausanne)* 2021 Mar 16;8:652464. doi: 10.3389/fmed.2021.652464.
40. Balakrishnan B, Selvaraju V, Chen J, Ayine P, Yang L, Ramesh Babu J, et al. Ethnic variability associating gut and oral microbiome with obesity in children. *Gut Microbes* 2021 Jan-Dec;13(1):1-15. doi: 10.1080/19490976.2021.1882926.
41. Gershuni V, Li Y, Elovitz M, Li H, Wu GD, Compher CW. Maternal gut microbiota reflecting poor diet quality is associated with spontaneous preterm birth in a prospective cohort study. *Am J Clin Nutr* 2021 Mar 11;113(3):602-11. doi: 10.1093/ajcn/nqaa361.
42. Diener C, Reyes-Escogido MD, Jimenez-Ceja LM, Matus M, Gomez-Navarro CM, Chu ND,

- et al. Progressive shifts in the gut microbiome reflect prediabetes and diabetes development in a treatment-naïve Mexican cohort. *Front Endocrinol (Lausanne)* 2021 Jan 8;11:602326. doi: 10.3389/fendo.2020.602326.
43. Oluwagbemigun K, O'Donovan AN, Berding K, Lyons K, Alexy U, Schmid M, et al. Long-term dietary intake from infancy to late adolescence is associated with gut microbiota composition in young adulthood. *Am J Clin Nutr* 2021 Mar 11;113(3):647-56. doi: 10.1093/ajcn/nqaa340.
 44. Nicholson K, Bjornevik K, Abu-Ali G, Chan J, Cortese M, Dedi B, et al. The human gut microbiota in people with amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Frontotemporal Degener* 2021 May;22(3-4):186-94. doi: 10.1080/21678421.2020.1828475.
 45. Kamp KJ, Cain KC, Utleg A, Burr RL, Raftery D, Lun, RA, et al. Bile acids and microbiome among individuals with irritable bowel syndrome and healthy volunteers. *Biol Res Nurs* 2021 Jan;23(1):65-74. doi: 10.1177/1099800420941255.
 46. Spörrel K, Wang S, Ettema DD, Nibbeling N, Kroese BJ, Deutekom M, et al. Just-in-Time Prompts for Running, Walking, and Performing Strength Exercises in the Built Environment: 4-Week Randomized Feasibility Study. *JMIR Form Res* 2022 Aug 1;6(8):e35268. doi: 10.2196/35268.
 47. Castle EM, Dijk G, Asgari E, Shah S, Phillips R, Greenwood J, et al. The Feasibility and User-Experience of a Digital Health Intervention Designed to Prevent Weight Gain in New Kidney Transplant Recipients—The ExERTion2 Trial. *Front Nutr* 2022 May 23;9:887580. doi: 10.3389/fnut.2022.887580.
 48. Dinour LM. Infant Feeding Tracker Applications: Cross-Sectional Analysis of Use. *J Nutr Educ Behav* 2022 Sep;54(9):835-43. doi: 10.1016/j.jneb.2022.03.012.
 49. Kamath S, Kappaganthu K, Painter S, Madan A. Improving Outcomes Through Personalized Recommendations in a Remote Diabetes Monitoring Program: Observational Study. *JMIR Form Res* 2022 Mar 21;6(3):e33329. doi: 10.2196/33329.
 50. Dening J, George ES, Ball K, Islam SM. User-centered development of a digitally-delivered dietary intervention for adults with type 2 diabetes: The T2Diet study. *Internet Interv* 2022 Feb 12;28:100505. doi: 10.1016/j.invent.2022.100505.
 51. Akam EY, Nuako AA, Daniel AK, Stanford FC. Racial disparities and cardiometabolic risk: new horizons of intervention and prevention. *Curr Diab Rep* 2022 Mar;22(3):129-36. doi: 10.1007/s11892-022-01451-6.
 52. Curtis RG, Bartel B, Ferguson T, Blake HT, Northcott C, Virgara R, et al. Improving user experience of virtual health assistants: scoping review. *J Med Internet Res* 2021 Dec 21;23(12):e31737. doi: 10.2196/31737.
 53. Kennedy M, Kumar R, Ryan NM, Bennett J, Fuentes GL, Gould GS. Codeveloping a multi-behavioural mobile phone app to enhance social and emotional well-being and reduce health risks among Aboriginal and Torres Strait Islander women during preconception and pregnancy: a three-phased mixed-methods study. *BMJ Open* 2021 Nov 24;11(11):e052545. doi: 10.1136/bmjopen-2021-052545.
 54. Wong J, Foussat AC, Ting S, Acerbi E, van Elburg RM, Chien CM. A chatbot to engage parents of preterm and term infants on parental stress, parental sleep, and infant feeding: usability and feasibility study. *JMIR Pediatr Parent* 2021 Oct 26;4(4):e30169. doi: 10.2196/30169.
 55. Subramaniam S, Dhillon JS, Wan Ahmad WF. Behavioral Theory-Based Framework for Prediabetes Self-Care System—Design Perspectives and Validation Results. *Int J Environ Res Public Health* 2021 Aug 31;18(17):9160. doi: 10.3390/ijerph18179160.
 56. Seo LM, Petersen CL, Halter RJ, Kotz DF, Fortuna KL, Batsis JA. Usability Assessment of a Bluetooth-Enabled Resistance Exercise Band Among Young Adults. *Health Technol (Berl)* 2021 Apr;5(1):4. doi: 10.21037/ht-20-22.
 57. Kempler JV, Love P, Bolton KA, Rozman M, Spence AC. Exploring the Use of a Web-Based Menu Planning Tool in Childcare Services: Qualitative Cross-sectional Survey Study. *JMIR Form Res* 2022 Jul 18;6(7):e35553. doi: 10.2196/35553.
 58. Liu Z, Liu L, Weng S, Guo C, Dang Q, Xu H, et al. Machine learning-based integration develops an immune-derived lncRNA signature for improving outcomes in colorectal cancer. *Nat Commun* 2022 Feb 10;13(1):816. doi: 10.1038/s41467-022-28421-6.
 59. Mirzayi C, Renson A; Genomic Standards Consortium; Massive Analysis and Quality Control Society; Zohra F, Elsafoury S, Geistlinger L, Kasselmann LJ, Eckenrode K, van de Wijgert J, et al. Reporting guidelines for human microbiome research: the STORMS checklist. *Nat Med* 2021 Nov;27(11):1885-92. doi: 10.1038/s41591-021-01552-x.
 60. Robeson MS, O'Rourke DR, Kaehler BD, Ziemski M, Dillon MR, Foster JT, et al. RESCRIPT: Reproducible sequence taxonomy reference database management. *PLoS Comput Biol* 2021 Nov 8;17(11):e1009581. doi: 10.1371/journal.pcbi.1009581.
 61. Dillon MR, Bolyen E, Adamov A, Belk A, Borsom E, Burcham Z, et al. Experiences and lessons learned from two virtual, hands-on microbiome bioinformatics workshops. *PLoS Comput Biol* 2021 Jun 24;17(6):e1009056. doi: 10.1371/journal.pcbi.1009056.
 62. Matchado MS, Lauber M, Reitmeier S, Kacprowski T, Baumbach J, Haller D, et al. Network analysis methods for studying microbial communities: A mini review. *Comput Struct Biotechnol J* 2021 May 4;19:2687-98. doi: 10.1016/j.csbj.2021.05.001.
 63. Cao Q, Sun X, Rajesh K, Chalasani N, Gelow K, Katz B, et al. Effects of rare microbiome taxa filtering on statistical analysis. *Front Microbiol* 2021 Jan 12;11:607325. doi: 10.3389/fmicb.2020.607325.
 64. Secchi R, Hartmann A, Walter M, Grabe HJ, Van der Auwera-Palitschka S, Kowald A, et al. Biomarkers of geroprotection and cardiovascular health: An overview of omics studies and established clinical biomarkers in the context of diet. *Crit Rev Food Sci Nutr* 2021 Oct 14;1-21. doi: 10.1080/10408398.2021.1975638.
 65. Amato KR, Arrieta MC, Azad MB, Bailey MT, Broussard JL, Bruggeling CE, et al. The human gut microbiome and health inequities. *Proc Natl Acad Sci U S A* 2021 Jun 22;118(25):e2017947118. doi: 10.1073/pnas.2017947118.
 66. Marcos-Zambrano LJ, Karaduzovic-Hadziabdic K, Loncar Turukalo T, Przymus P, Trajkovic V, Aasmets O, et al. Applications of machine learning in human microbiome studies: a review on feature selection, biomarker identification, disease prediction and treatment. *Front Microbiol* 2021 Feb 19;12:634511. doi: 10.3389/fmicb.2021.634511.
 67. Moreno-Indias I, Lahti L, Nedyalkova M, Elbere I, Roshchupkin G, Adilovic M, et al. Statistical and machine learning techniques in human microbiome studies: contemporary challenges and solutions. *Front Microbiol* 2021 Feb 22;12:635781. doi: 10.3389/fmicb.2021.635781.
 68. Usability of consumer products and products for public use — Part 2: Summative test method. [Available at: <https://www.iso.org/obp/ui/#iso:std:iso:ts:20282:-2:ed-2:v1:en>. Accessed March 13, 2023].
 69. Lange KW, Nakamura Y. Lifestyle factors in the prevention of COVID-19. *Glob Health J* 2020 Dec;4(4):146-52. doi: 10.1016/j.glojh.2020.11.002.
 70. Tavakol Z, Ghannadi S, Tabesh MR, Halabchi F, Noormohammadpour P, Akbarpour S, et al. Relationship between physical activity, healthy lifestyle and COVID-19 disease severity: a cross-sectional study. *Z Gesundh Wiss* 2023;31(2):267-75. doi: 10.1007/s10389-020-01468-9.
 71. De Frel DL, Atsma DE, Pijl H, Seidell JC, Leenen PJ, Dik WA, et al. The impact of obesity and lifestyle on the immune system and susceptibility to infections such as COVID-19. *Front Nutr* 2020 Nov 19;7:597600. doi: 10.3389/fnut.2020.597600.
 72. International Foundation for Gastrointestinal Disorders. IBS Facts and Statistics. [Available at: <https://aboutibs.org/what-is-ibs/facts-about-ibs/>. Accessed 11/29/, 2022].
 73. Cheng FS, Pan D, Chang B, Jiang M, Sang LX. Probiotic mixture VSL# 3: An overview of basic and clinical studies in chronic diseases. *World J Clin Cases* 2020 Apr 26;8(8):1361-84. doi: 10.12998/wjcc.v8.i8.1361. Erratum in: *World J Clin Cases* 2021 Jul 16;9(20):5752-3.
 74. Centers for Disease Control. Type 2 Diabetes. 2021. [Available at: <https://www.cdc.gov/diabetes/basics/type2.html>. Accessed 11/28/, 2022].
 75. Hartstra AV, Bouter KE, Bäckhed F, Nieuwdorp M. Insights into the role of the microbiome in obesity and type 2 diabetes. *Diabetes Care* 2015 Jan;38(1):159-65. doi: 10.2337/dc14-0769.
 76. Mokkela K, Houttu N, Vahlberg T, Munukka E, Rönnemaa T, Laitinen K. Gut microbiota aberrations precede diagnosis of gestational diabetes mellitus. *Acta Diabetol* 2017 Dec;54(12):1147-9. doi: 10.1007/s00592-017-1056-0.
 77. Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes:

- perspectives on the past, present, and future. *Lancet* 2014 Mar 22;383(9922):1068-83. doi: 10.1016/S0140-6736(13)62154-6.
78. Morozova N, Weisskopf MG, McCullough ML, Munger KL, Calle EE, Thun MJ, et al. Diet and amyotrophic lateral sclerosis. *Epidemiology* 2008 Mar;19(2):324-37. doi: 10.1097/EDE.0b013e3181632c5d.
 79. Ngo ST, Steyn FJ, McCombe PA. Body mass index and dietary intervention: implications for prognosis of amyotrophic lateral sclerosis. *J Neurol Sci* 2014 May 15;340(1-2):5-12. doi: 10.1016/j.jns.2014.02.035.
 80. Koren O, Goodrich JK, Cullender TC, Spor A, Laitinen K, Bäckhed HK, et al. Host remodeling of the gut microbiome and metabolic changes during pregnancy. *Cell* 2012 Aug 3;150(3):470-80. doi: 10.1016/j.cell.2012.07.008.
 81. Cortez RV, Taddei CR, Sparvoli LG, Angelo AG, Padilha M, Mattar R, et al. Microbiome and its relation to gestational diabetes. *Endocrine* 2019 May;64(2):254-64. doi: 10.1007/s12020-018-1813-z.
 82. Crusell MK, Hansen TH, Nielsen T, Allin KH, Rühlemann MC, Damm P, et al. Gestational diabetes is associated with change in the gut microbiota composition in third trimester of pregnancy and postpartum. *Microbiome* 2018 May 15;6(1):89. doi: 10.1186/s40168-018-0472-x.
 83. Ye G, Zhang L, Wang M, Chen Y, Gu S, Wang K, et al. The gut microbiota in women suffering from gestational diabetes mellitus with the failure of glycemic control by lifestyle modification. *J Diabetes Res* 2019 Oct 23;2019:6081248. doi: 10.1155/2019/6081248.
 84. Lauer M, Jorgenson L. Implementation Updates for the New NIH Data Management and Sharing Policy. 2022; [Available at: <https://nexus.od.nih.gov/all/2022/08/05/implementation-updates-for-the-new-nih-data-management-and-sharing-policy/>. Accessed 11/28, 2022].
 85. Chuong KH, Mack DR, Stintzi A, O'Doherty KC. Human microbiome and learning healthcare systems: integrating research and precision medicine for inflammatory bowel disease. *OMICS* 2018 Feb;22(2):119-26. doi: 10.1089/omi.2016.0185.
 86. Kuntz TM, Gilbert JA. Introducing the microbiome into precision medicine. *Trends Pharmacol Sci* 2017 Jan;38(1):81-91. doi: 10.1016/j.tips.2016.10.001.
 87. Petrosino JF. The microbiome in precision medicine: the way forward. *Genome Med* 2018 Feb 22;10(1):12. doi: 10.1186/s13073-018-0525-6.
 88. Cammarota G, Ianiro G, Ahern A, Carbone C, Temko A, Claesson MJ, et al. Gut microbiome, big data and machine learning to promote precision medicine for cancer. *Nat Rev Gastroenterol Hepatol* 2020 Oct;17(10):635-48. doi: 10.1038/s41575-020-0327-3.
 89. Lam KN, Alexander M, Turnbaugh PJ. Precision medicine goes microscopic: engineering the microbiome to improve drug outcomes. *Cell Host Microbe* 2019 Jul 10;26(1):22-34. doi: 10.1016/j.chom.2019.06.011.
 90. NIH Nutrition Research Task Force (NRTF). 2020-2030 Strategic Plan for NIH Nutrition Research. NIH NIDDK 2020; [Available at: <https://dpcpsi.nih.gov/onr/strategic-plan/>].
 91. Heart Disease and Stroke. 2020; [Available at: <https://www.cdc.gov/chronicdisease/resources/publications/factsheets/heart-disease-stroke.htm>. Accessed 05/19, 2021].
 92. Centers for Disease Control. Chronic Diseases in America. 2022; [Available at: <https://www.cdc.gov/chronicdisease/resources/infographic/chronic-diseases.htm>. Accessed 11/8, 2022].
 93. Fraser AM. Malnutrition in older adults in the united states. In: Preedy V, Patel VB, editors. *Handbook of Famine, Starvation, and Nutrient Deprivation*; 2017. p. 1-20.
 94. Streicher M, van Zwiene Pot J, Bardon L, Nage, G, The R, Meisinger C, et al. Determinants of incident malnutrition in community dwelling older adults: a MaNuEL multicohort meta analysis. *J Am Geriatr Soc* 2018 Dec;66(12):2335-43. doi: 10.1111/jgs.15553.
 95. Gupta RS, Warren CM, Smith BM, Jiang J, Blumenstock JA, Davis MM, et al. Prevalence and severity of food allergies among US adults. *JAMA Netw Open* 2019 Aug 2;2(8):e199144. doi: 10.1001/jamanetworkopen.2019.9144.
 96. Vierk KA, Koehler KM, Fein SB, Street DA. Prevalence of self-reported food allergy in American adults and use of food labels. *J Allergy Clin Immunol* 2007 Jun;119(6):1504-10. doi: 10.1016/j.jaci.2007.03.011.
 97. Cha E, Kim KH, Lerner HM, Dawkins CR, Bello MK, Umpierrez, et al. Health literacy, self-efficacy, food label use, and diet in young adults. *Am J Health Behav* 2014 May;38(3):331-9. doi: 10.5993/AJHB.38.3.2.
 98. Berkman ND, Sheridan SL, Donahue KE, Halpern DJ, Crotty K. Low health literacy and health outcomes: an updated systematic review. *Ann Intern Med* 2011 Jul 19;155(2):97-107. doi: 10.7326/0003-4819-155-2-201107190-00005.
 99. Silk KJ, Sherry J, Winn B, Keesecker N, Horodyski MA, Sayir A. Increasing nutrition literacy: testing the effectiveness of print, web site, and game modalities. *J Nutr Educ Behav* 2008 Jan-Feb;40(1):3-10. doi: 10.1016/j.jneb.2007.08.012.
 100. Monsivais P, Aggarwal A, Drewnowski A. Time spent on home food preparation and indicators of healthy eating. *Am J Prev Med* 2014 Dec;47(6):796-802. doi: 10.1016/j.amepre.2014.07.033.
 101. Drichoutis AC, Lazaridis P, Nayga Jr RM. Nutrition knowledge and consumer use of nutritional food labels. *Eur Rev Agric Econ* 2005 Mar 1;32(1):93-118. doi: 10.1093/erae/jbi003.
 102. Poussin C, Sierro N, Boué S, Battay J, Scotti E, Belcastro V, Peitsch, et al. Interrogating the microbiome: experimental and computational considerations in support of study reproducibility. *Drug Discov Today* 2018 Sep;23(9):1644-57. doi: 10.1016/j.drudis.2018.06.005.
 103. Schloss PD. Identifying and overcoming threats to reproducibility, replicability, robustness, and generalizability in microbiome research. *mBio* 2018 Jun 5;9(3):e00525-18. doi: 10.1128/mBio.00525-18.
 104. Babaei P, Shoaie S, Ji B, Nielsen J. Challenges in modeling the human gut microbiome. *Nat Biotechnol* 2018 Aug 6;36(8):682-6. doi: 10.1038/nbt.4213.
 105. Wilkinson MD, Dumontier M, Aalbersberg IJ, Appleton G, Axton M, Baak A, et al. The FAIR Guiding Principles for scientific data management and stewardship. *Sci Data* 2016 Mar 15;3:160018. doi: 10.1038/sdata.2016.18. Erratum in: *Sci Data* 2019 Mar 19;6(1):6.

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