Chapter. V
Summary and Conclusion

With the rapid technological advances in the field of omics research, our insights into interindividual variability and its effect on disease risk are increasing. It is well established that the human genome and the microbial 'second genome' influences our response to the diet. In the recent years, several "consumer genomics" companies have started offering commercialised nutrigenetic and gut microbiome tests to design tailored dietary advice for promoting health and treating disease conditions.

Nutrigenetic testing focuses on understanding the specific genetic variations of the individual, whereas the gut microbiome testing provides information on the microbial composition, abundance and diversity to provide personalised nutrition advice that are designed to be genetically appropriate dietary and lifestyle recommendations. Thus offering a tailored dietary advice based on the individual's genetic susceptibility and gut microbiome could be a promising strategy for the prevention and treatment of obesity.

Research studies have examined the usefulness of nutrigenetic testing and gut microbiome testing in weight management in different populations. (Franzago*et al*.,2022) (Zeinalian*et al.,* 2022). There is a huge potential in improving the health outcomes of the individuals complying to the personalised dietary recommendations based on their genetics in treating and managing obesity. Few Indian genetic testing companies offer personalised, targeted nutrition recommendations for obesity-related polymorphisms based on the particular pattern of genetic variation and the gut microbiome composition. There is now a need for developing new tools that will allow us to utilise the potential of individual microbiome and genetic fingerprints for the benefit of precision nutrition approach in the prevention and management of obesity.

Recent evidence show that this concept of precision nutrition will provide new insights into the pathogenesis of obesity, elucidate the role of gene-host-microbiome-environment interactions in obesity thus contributing to a precision approach in prevention and management of obesity.

So far, the knowledge related to genetic contribution to obesity is only a small proportion and needs more validation through systematic research studies. Identification of

genetic predictors that are easy to measure and less expensive will improve the clinical validity and utility of these risk assessment predictors in the treatment and management of obesity. Lifestyle modifications that includes healthy diet and physically active lifestyle still remains the key to manage body weight irrespective of an individual's susceptibility to obesity.

The key findings of the study are:

- In survey conducted to know the consumer acceptance of genetic testing for personalized nutrition, almost 48% of the participants were males and 52% were females.
- The mean age of the participants was 38.3 ± 14.9 years. Majority of the participants were from the age group between 40- 49 years.
- Majority of the participants held a post graduate degree (n=181, 36.2%) and professional degree (n= 174, 34.8 %).
- Nearly 36% of the study participants had a university post- graduation degree and 34.8% had professional degree. Most of the participants had business as their occupation (33.4%) and 25.2% were working in private sectors.
- People were more inclined to follow a personalised diet based on their genetic makeup if they had diagnosed hypertension ($p = 0.02$), diagnosed type 2 diabetes ($p = 0.03$), and obesity ($p = 0.04$) and if they had diagnosed heart ailments ($p = 0.01$).
- More than 85% of participants who were diagnosed with type 2 diabetes reported to be willing to follow the dietary recommendations based on their genetic makeup.
- The participants who had any medical history or having any current medical condition were compared with those who did not have any medical history. Those who were willing to undergo a genetic test for a personalised diet were 1.34 times more likely to report obesity, 1.25 times more likely to report high blood pressure. Males were more likely to report their willingness to take the test done to follow a personalised diet.
- When asked about the perceived advantages of receiving DNA based dietary advice, ease of understanding and specificity of the diet advice was the most frequently reported theme (57.5%), followed by more personalised and enjoyable (22.4%) and reduced costs due to disease prevention (20.1%).
- Additionally, 23.5% of the study participants perceived no disadvantage to receiving DNA based dietary advice. And about the disadvantages, "adds cost by advising to

consume specific foods (45.7)% was the most frequently mentioned disadvantage followed by “personalised nutrition is much more time consuming” (34.3%) and non-feasibility and difficulty to prepare different foods for different family members (20%).

- Nearly, 31.2% of respondents feels confident that genetic test-based personalized nutrition helps them to have full control of their health and see it as an attractive option, while nearly 27.6% feels genetic based personalised nutrition has lot of risks. Nearly 28.2% of them believes that it could help them prevent diseases.
- Three statements were included in the survey to assess motivations to adopt personalised nutrition advice based on genetic testing in order to determine their perceptions of these statements to understand the underlying motivation factors. The most commonly selected response among the 500 participants was ‘personalised nutrition could help disease prevention’ (57%), followed by ‘can see more of benefits over drawbacks of genetic based personalised nutrition” (56.4%) and ‘personalised nutrition makes me able to live longer in good health’ (52%).
- The response options used in the questionnaire, ‘personalised nutrition makes me able to live longer in good health’ (Mean response ± SD, 4.17 ± 1.05), ‘personalised nutrition can help disease prevention’ (Mean response ± SD, 4.43 ± 0.79) and ‘If I weigh up the benefits and drawbacks of genetic based personalised nutrition, I can see more of benefits (Mean response ± SD, 3.98 ± 1.05).
- Almost, 80% strongly agreed that they were very capable of providing personalised nutrition advice.Participants assessed the service provider's knowledge and skills about personalized nutrition advice, with 0.4% strongly disagreeing, 0.6% disagreeing, 5% neither agreeing nor disagreeing, 30% agreeing, and 64.2% strongly agreeing.
- Participants indicated opinions on the availability of easily understandable information in the personalized nutrition report, with 0.6% strongly disagreeing, 2.4% disagreeing, 10.4% neither agreeing nor disagreeing, 16.6% agreeing, and 70% strongly agreeing.
- Concerning the health care provider's education and time, 0.2% strongly disagreed, 1% disagreed, 2% neither agreed nor disagreed, 40.2% agreed, and 56.6% strongly agreed that there was a lack of adequate education and time.
- Participants expressed opinions on the agreement and accountability of service

providers, resulting in 0.6% strongly disagreeing and 74.8% strongly agreeing.

- A substantial 82% of the respondents strongly agree that they benefit from personalized nutrition advice in daily life, showcasing a significant positive response. Similarly, 77.4% strongly agree that their families also benefit from personalized nutrition advice, indicating a high level of perceived utility among participants

- Notably, 86.4% of them strongly agree that gene-based dietary advice has helped them prevent diseases, highlighting the potential health impact of such personalized approaches.

- A noteworthy 77.2% strongly agree that they still follow their previous diet habits to the greatest possible degree, complementing it with personalized food and supplements, underscoring the integration of personalized recommendations into existing dietary practices.

- Regarding the emotional aspect, 56.4% strongly agree that knowing about their personalized nutrition test results caused some anxiety, emphasizing the need for thoughtful communication and support in delivering such information.

- Significantly, a vast majority (70.8%) strongly disagree that personalized nutrition puts restrictions on cultural dietary habits, indicating a general acceptance and adaptability to these recommendations within cultural contexts.

- Participants were asked to indicate which health care provider disseminated the information related to genetic test and personalised nutrition recommendations. The response options were ‘registered dietitian’, ‘physician’, ‘genetic counsellor’, ‘other’, and participants were asked to choose the source of information provider. The selected responses were ‘registered dietitian’ (56%), followed by ‘physician’ (27%), ‘genetic counsellor’ (14%) and ‘other’ (3%).
- More than a third of respondents, n=186 (37.2 %) had the intention to adopt personalised nutrition recommendations in their daily life. While 28.4 % (n = 142) of them responded that they will definitely adoptpersonalised nutrition recommendations.

- Nearly 20.8% (n= 104) of the respondents reported that they are benefited by personalised nutrition recommendations, whereas 13.6% (n= 68) considered adopting personalised nutrition recommendations in the near future.
- There were 52 participants in the standard diet group and 54 participants in the personalised nutrition group at the baseline. The participants were classified as obese (≥ 25 -30 kg/ m^2), with an average BMI of approximately 32 kg/m2 in both groups with no other co- morbidities.
- All the participants received nutrigenetic based advice in at least one of the recommendation categories, withthe majority (83%) receiving advice in 6 of the 10 recommendation categories.
- There were 50 participants in the precision nutrition group at the baseline. The participants were classified as obese (≥ 25 -30 kg/ m^2), with an average BMI of approximately 32 kg/m2 in all the three groups with no other co- morbidities.
- The study participants in precision nutrition group (n=50), personalised nutrition group (n= 52), standard diet group (n= 54) respectively, with a median age of 36. 3 years. In terms of sex, there were 22 females and 28 males in precision nutrition group and 23 females and 29 males and 20 females and 34 males in the personalised nutrition group
- Regarding the dietary intake, especially related to macronutrient intake, the mean percentage was 63.4% for carbohydrates, 15.3% for protein and 21.3 % for fats.
- In the majority of the study participants, obese individuals in the precision nutrition group (N =50), the firmicutes phyla constituted the highest proportion of the bacterial population, with the relative abundance of 55.7% firmicutes respectively.
- The phylogenetic characterization of all the samples of the study participants in the precision nutrition group uncovered four main bacterial phyla in the following proportions: Firmicutes (55.7%), Bacteriodetes (18.30%), actinobacteria (19.6%), proteobacteria (6.20%) and other less abundant bacterial phyla (<0.2%) were fusobacteria, verrucomicrobia were also present.
- Across all taxa, 115 genera and 9480 OTUs, with an average of 687 observed OTUs per sample were identified.
- The four major bacterial phyla namely firmicutes, bacteroidetes, actinobacteria and proteobacteria were included for this study. The female participants had significantly

lower firmicutes to bacteroidetes ratio (F/B) in comparison to the male participants of the study ($p = 0.040$) respectively.

- The relative abundance of the gut bacterial species present in the gut of the study participants of the precision nutrition group at the family and genus level and it showed the relative abundance of ≥1% among the study subjects.
- Five species namely Akkermansiamuciniphila, Bifidobacterium, Eubacterium, Roseburia and Faecalibacteriumprausnitzii were selected for the study of which bifidobacterium showed significant differences in their abundance across the population (≤ 0.05 Kruskal-Wallis H test).
- All the participants received gut microbiome-based advice in at least one of the recommendation categories, with the majority (76%) receiving advice in 3 of the 5 recommendation categories.
- Fifty participants completed the 90 days follow up in the precision nutrition group, 54 participants completed the three months in the personalised nutrition group and 52 in the standard diet group, corresponding to the number of participants excluded or lost to follow up, 5 participants in the precision nutrition group, 1 participant in the personalised nutrition group and 3 participants in the standard diet group.
- During the period from baseline to 90 days, the data in the records demonstrated that all the three groups were very similar. All the three groups showed a similar average weight loss and 85% of the study participants were able to maintain the weight loss (82% in the standard group, 86.5% in the personalised nutrition group and 87.5% in the precision nutrition group). The results were significantly better in the precision nutrition group ($p < 0.021$) than the other two groups.
- The study participants in the precision nutrition group were able to sustain the weight loss resulting in a gender adjusted odds ratio of 6.83 (95% CI 2.23- 24.5 $P< 0.003$).
- The difference in the weight loss was more apparent when it is calculated as percent of BMI weight gain/ weight loss in the precision nutrition group which had a 6.2% loss vs a 3.3 % gain in the non- tested group ($p < 0.001$)
- The difference in the body weight and BMI was more obvious in the precision nutrition group after 60 days. The study participants in the precision nutrition. The study participants in the personalized nutrition group had 7.5% loss vs 7.89 % in the precision nutrition group and 5.98% in the standard nutrition group ($P < 0.003$).
- The dietary intake and diet composition of the study participants were recorded at

different time points, at baseline, 30 days, 60 days and 90 days respectively. As evident from the data in the table, the total fat percentage among the study participants in the personalized nutrition significantly reduced from (34.3 ± 4.8 % Kcal to 28.2 ± 4.8% Kcal, P= 0.02). The amount of unsaturated fats consumed also reduced significantly among the precision nutrition group from baseline to 90 days (48.5 ± 17.24 g to 43.6 ± 17.2 g, P = 0.02).

- The protein intake of the study participants in the personalized nutrition group increased, (86.6±23.5 g to 88.6 ± 23.5g, P = 0.11), and the protein intake was more than the standard nutrition group participants.
- The calorie intake of the participants in the three study groups reduced approximately 100 – 120 kcal at the end of the study. The calorie intake of the participants in the personalized nutrition group reduced significantly, (1580.34±528.2% to 1452.1±680.8% kcal, P = 0.003) and the calorie intake of the participants in the precision nutrition group significantly reduced, (1510.9±528.2% to 1400.9±543.4 % Kcal, P= 0.002).
- The diet composition of the study participants in the three groups which were analysed showed that the addition of nutrigenetically tailored advice and adding gut microbiome-based information showed significant changes in the diet composition and dietary intake of the study participants in the three groups.

Conclusion

This study concludes that an individualized and personalized nutrition approach developed by understanding the human metabolic individual variability and taking into consideration the heterogeneity of the pathophysiology that exists among different obese individuals is more effective than a generic nutrition approach.

The rapidly burgeoning direct-to-consumer (DTC) genetic testing industry has made it easier to access individual's personal genetic data. This has enabled us to learn about different genetic variants and their response to diet on various health and disease outcomes and develop individualized gene- based dietary recommendations and in this study we were able to see the significant improvements in anthropometric measurements and dietary intakes when these gene based dietary recommendations were included in the diet of the obese individuals who participated in the study.

The gut microbiome, often referred to as our 'second genome' forms a large ecosystem that impacts human physiology, modulating our metabolism and disease risk. The gut microbiome plays various roles such as breakdown of nutrients, synthesis of essential vitamins and regulation of body weight. The inclusion of dietary recommendations based on the gut microbiome profile was more effective in reduction of body weight and improving dietary intake as well as improvements in dietary adherence of the study participants when compared to other study groups.

The incorporation of genetically-tailored, gut microbiome based nutrition advice can be used in clinical practice to motivate obese individuals to adhere to dietary recommendations in a long term.

Strengths & Limitations

This study was the first attempt to find the effect of individual responses to nutrigenetic diet and gut microbiome based personalized nutrition approach in managing and treatment of obesity among Indians. The present study contributes to the growing body of evidence of the feasibility of using precision nutrition approach in the treatment and management of obesity and also used of evidence-based approach in promoting healthier lifestyle and wellness. Although the current study results supports the use of nutrigenetic and gut microbiome profiling in dietary practice, further studies are required to validate by using larger sample sizes, more elaborate physical assessments of metabolic parameters are essential to validate and utilize the potential of these profiling in dietary assessment. Our study has some limitations. This study refers to only Indian obese individuals and hence the results need not necessarily be a representative of other population or ethnicity. The efficacy or the impact is seen with the lower sample size which needs further validation by large cohorts. The participants in the standard diet group were given a generic diet based on the RDA developed by the NIN, ICMR guidelines, whereas the personalized and the precision nutrition group received dietary advice based on the nutrigenetic and gut microbiome-based profiling. Although these analyses are predictive in nature that helps us to understand the human metabolic individuality and helps us to determine the type of diet that will lead to a healthy and greater weight loss for an individual, this has great potential to deliver more sustainable health outcomes, especially long-term weight loss sustenance, when validated and administered efficiently.

Recommendations

- More research studies evaluating the effectiveness of personalized nutrition interventions are needed.
- Efficacy of these interventions can be validated in a large-scale population with larger sample size.
- Education and awareness regarding the personalized nutrition approach and the tools such as nutrigenetic and gut microbiome profiling tests is needed.
- Development of Indian nutrigenome database is the need of the hour and can be served as a critical tool for various research and development activities in nutritional omics.
- Training of health professionals and academicians on nutritional omics will help progress the developments in the area of precision nutrition.