Review article

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Polygenic risk scores and personalized approaches to cardiometabolic disease prevention and treatment: A short review

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ABSTRACT

Accounting for the role of genetic variants in disease is increasingly gaining ground as a major contributing factor to the maximization of successful precision medicine and personalized nutrition approaches. An aggregated technique to quantifying genetic effect refers to the development and use of disease-specific Polygenic Risk Scores (PRSs) deriving from the sum of the weighted effects of multiple disease-related Single Nucleotide Polymorphisms (SNPs), mainly from Genome-Wide association studies (GWAS). Integration of PRS use in medical and nutritional practice is largely discussed in current literature, with special attention to: i) disease prediction accuracy after PRS consideration and their potential utility; ii) the role of current methodological approaches used to derive reliable results and the effect of limitations such as ancestry or population size; iii) the familiarization of healthcare professionals with the meaning of genetic information; and iv) the context-based interpretations of PRS results in the formation of personalized advice. In this context, the present short review aims to summarize current findings on PRS use and utility in cardiometabolic, weight-related disorders and discuss future directions for their potential integration in the practice of personalized nutrition.

KEY WORDS: *Polygenic risk scores, cardiometabolic disease, weight management, personalized nutrition*

INTRODUCTION

Deciphering disease etiology by quantifying the impact of genetic predisposition constitutes the focal point in the conduct of research surrounding genetics during the last years. Identifying and investigating the effect of disease-associated single nucleotide polymorphisms (SNPs), as well as using them to create aggravated genetic scores, provided encouraging results in the field of cardiovascular (CVD) and cardiometabolic disease[1,2]. Those findings shed a quantifiable light on the role of genetic makeup while expanding the horizons for the potential creation of new and personalized treatment approaches. The construction of polygenic risk scores (PRSs) thus quickly expanded to the notion of potentially contributing to determining

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disease risk and subsequently contributing to effective disease prevention, diagnosis and even treatment[1-3]. The need for more extensive research resulted in the gradual evolution of continuously enhanced methodological approaches for PRS extraction[4]. As the latter examine the effect of multiple variants on the outcome of interest based on a large SNP pool in populations of increased size, their creation and use were extensively investigated through genome-wide association studies (GWAS) in large consortia. The increasing presence of PRSs for multiple phenotypes in the current literature ultimately led to the creation of PGS catalog, an inclusive database comprising of all PRS entries created to date[5].

Discussion and research around PRS use as a prediction and treatment tool has recently yielded encouraging results, with studies reporting beneficial effects in cardiovascular and cardiometabolic disease[1,2]. Provision of lifestyle recommendations appeared to significantly contribute to obesity treatment[2] and coronary artery disease (CAD) prediction and greatly benefit individuals with high PRS across the spectrum of CVD, with PRSs constructed even for stroke and hypertension[1,3]. In like manner, the American Heart Association recently focused on the potential utility of PRS in CVD and other cardiometabolic disorders such as type 2 diabetes (T2D), underlining the need for the conduct of additional research to strengthen PRS inclusion in current practice[2]. Subsequently, discussion around the integration capacity of PRSs as a way to promote precision medicine and personalized nutrition is ongoing, with special attention on ameliorating relevant challenges, namely the differentiational influencing capacity following interaction with environmental stimuli, the diverse methodological approaches in PRS extraction and the understanding of the true meaning of genetic information both from professionals and patients alike.

PRS and weight-related parameters

Evaluation of genetic risk in the form of summed risk scores primarily treated CVD danger but quickly expanded to other disorders of cardiometabolic profile[2]. The conduct of extensive GWAS was accompanied by the development and expansion of the Genetic Investigation of Anthropometric Traits (GIANT) consortium[6]. This led to the identification of multiple Body Mass Index (BMI)-associated loci with the milestone discovery of the first 97 loci accounting for about 2.8% of the marker's variation[7]. Nowadays, approximately 6% of BMI variance is explained by 785 near-independent genome-wide significant SNPs[8,9]. Thus, the beginning approaches of quantifying genetic predisposition mainly involved the literature-based, a priori selection of disease-related variants and the subsequent investigation of the impact of their added effects. Therefore, various genetic risk scores of tens of SNPs were created and used in the examination of associations between increased genetic risk and disease manifestation or severity. In like manner, research on personalized approaches for combatting cardiometabolic and weight-related disorders primarily focused on examining the combined effect of target SNPs with different dietary regimens. In this context, the first large initiatives such as the FOOD4ME project and the POUNDS lost clinical trial[10,11], attempted to unveil the interactive role of genetic makeup and nutritional habits in overweight and obesity. Focusing on target SNPs and macronutrient content, the projects provided limited, but encouraging, evidence on the effect of gene-diet interactions on anthropometric traits.

Based on GIANT-derived information or the conduct of independent GWAS, different teams proceeded to the development of PRSs for BMI in populations of various sizes. To date, PRSs associated to anthropometric traits and body measurements account for 154 of the database entries[5]. Indeed, nowadays, attempting to decipher the multifactorial obesity etiology using genetic information has become central in research surrounding BMI, with efforts made to explain the polygenic prediction of weight formation throughout the life course[12,13] Khera et al. highlighted the role of including a multi-variant PRS in explaining weight variance in populations ranging from birth cohorts to middle-aged individuals[12]. Correspondingly, Shi et al recently constructed a different BMI PRS to investigate potential associations with overall cardiometabolic health from early age to adulthood. The study revealed significant associations between the score and other indices of cardiometabolic profile, namely fasting glucose and systolic blood pressure[13]. Building on the data and the role of genetic makeup in overweight or obesity presence, current research also focuses on the potential influence of genetic markers on weight loss. A study by de Toro-Martín investigating the extent of the genetic effect on the success of bariatric surgery, showed an increase in the prediction model accuracy when including PRSs, as well as significant interactions between the scores and the reduction in post-surgery recovery and surgery type[14]. In the same context, Katsareli et al showed that adults with increased genetic risk score for obesity noted a decrease in post-bariatric surgery loss of excess weight, with each unit of the score being associated with a 4.618% decrease in the 12-month observed weight loss[15].

In the same spectrum and building on the findings of previous key projects, emphasis should also be given on studies looking into the potential interactions between genetic scores and macronutrient content[16]. Moreover,

studies focusing on the genetic influence on the observed weight loss after lifestyle interventions to combat overweight and obesity even outside of a clinical environment are also needed. Research on this field could unravel the gene-diet interactions surrounding weight management and loss and ultimately maximize the impact of individualized recommendations using genetic data to determine optimal treatment strategies. As a result, effectively unravelling the genetic proportion of body weight variance could progressively allow for the formation of more inclusive strategies to its management.

PRS Interactions with Lifestyle Determinants

In addition to accounting for the risk attributed to genetic makeup, the impact of PRS interactions with lifestyle factors such as diet, ultimately influencing weight management have also been studied. In a 2021 study by Wang et al, a 60-SNP PRS was constructed using variants found to be associated with birth weight and later-life disease. The interactions between the genetic score and dietary parameters showed that healthy habits during early life, such as breastfeeding, were beneficial in reducing the risk for worse lipidemic profile in adult life in participants with higher genetic risk[17]. The significant modifying effect of diet was also demonstrated by Tan et al, who showed that individuals with higher PRS for obesity indeed presented higher levels of C-reactive protein but those levels appeared reduced in the presence of high dietary protein intake[18]. Similarly, middle-aged individuals with a higher genetic risk score for thinness presented lower body weight; an association aggravated with high protein and low carbohydrate intake, among others[19]. The multidisciplinary character of genetic risk-associated interactions is evident throughout the reciprocal interplay between the formation of anthropometric characteristics' levels and the formation of the lifestyle choices surrounding them. In adult populations, Dashti et al. showed that adults with higher genetic risk for obesity were less likely to make healthier food choices at workplace and more likely to purchase more food and adhere to unhealthy dietary habits such as delaying or skipping breakfast and homemade meals[20]. However, Lee et al showed that BMI PRSs were related to body weight in Korean adults, but not to their respective caloric or macronutrient intake[21]. Similarly, Konttinen et al highlighted that elevated genetic risk was more correlated with increased weight gain during a 7-year period in individuals not demonstrating restrained eating than those who adhered to it. However, the study attributed the effect to the role of previous processes entailing weight gain and nutritional habits, rather than a separate factor which will influence future weight gain[22]. Extended associations have also been explored, with Park et al showing that individuals with a high genetic risk for BMI, early menarche and attrition to an unhealthy diet (i.e. high consumption of fried foods and low consumption of fruits and vegetables) presented an increased obesity risk compared to those with late menarche and attrition to a healthier diet[23]. A different study focusing on European children and adolescents, underlined the modifying effect of diet, where genetic influence was attenuated by fiber intake in participants presenting higher genetic risk for obesity[24].

To boot, PRS-lifestyle interactions constitute a focal point across the spectrum of understanding more weight-related diseases. The emphatic effect of nutrition is underlined in studies of approximately 70000 participants of the UK Biobank, where adherence to a healthier diet was associated with reduced risk for cardiovascular disease, even in individuals with a high genetic risk score. Similarly, adoption of a healthier lifestyle was linked to lower CVD risk and overall mortality, again irrespective of genetic danger[25,26]. Moreover a different large study with data for almost 340000 UK Biobank participants showed that increased genetic risk for type 2 diabetes (T2D) was associated with higher chances for CVD manifestation; an effect reduced in individuals with better quality of lifestyle[27]. With regards to T2D alone, increased values of a PRS for the disease and attrition to the Western dietary pattern were associated with higher levels of fasting glucose[28]. Likewise, López-Portillo et al demonstrated that fasting glucose levels were higher in non-diabetic individuals with increased genetic risk for T2D and higher consumption of sugary beverages, compared to those with lower genetic risk scores and reduced intakes of the latter[29]. Biochemical interactions have also been studied, where PRS for T2D have been found to significantly interact with triglyceride and cholesterol levels in the subsequent formation of fasting glucose levels[30]. Merino et al showed the dominating effect of unhealthy diet in increasing T2D risk even by 30%, again irrespective of genetic risk[31]. Additionally, although Zhang et al did not show significant interactions between genetic risk and adherence to the plant-forward EAT-Lancet diet for T2D onset, their study did note that individuals with increased genetic risk and lower attrition to the dietary pattern did present the highest risk for T2D presence during a 24-year follow-up period[32]. Correspondingly, PRS-diet interactions have been evident in more disorders, such as cancer and dementia, where an increased diet quality lower the

chances for disease onset, even in individuals of high genetic risk[33-35]. In a similar context, lifestyle can also indirectly affect the gravity of genetic risk on actual disease manifestation via increase in weight-related anthropometric measurements alone. Esteve-Luque et al showed that higher values of BMI significantly interacted with genetic risk in increasing triglyceride levels and the subsequent risk for hypertriglyceridemia[36]. A different study underlined that obesity presence led to higher risk for T2D, even in individuals with lower genetic risk and better lifestyle quality[37].

PRS Utility in Personalized Recommendations

Research around the potential role of PRS use in clinical practice has shown that inclusion of PRSs in models for cardiometabolic disorders such as cardiovascular disease (CVD) can account for risk prediction in a manner similar to established contributing factors such as cholesterol levels[38-40]. The Task Force of the International Common Disease Alliance has further underlined the importance of PRS inclusion in increasing the accuracy of predicting CVD disease risk and severity, throughout one's lifetime[41], and the weighted contribution of PRS to maximizing patient outcomes[41]. Given the potential increase in accuracy observed in prediction models after the addition of PRS, testing their potential utility has also expanded to the field of anthropometrics. Choe et al showed that a BMI PRS was associated not only with longitudinal BMI change, but also other cardiometabolic phenotypes, such as fatty liver[42]. A similar attempt was made by Padilla-Martinez et al., who displayed significant associations between PRSs for T2D and obesity and manifestations of prediabetes and other disrupted cardiometabolic parameters[43].

In this context, PRS use could be seen as a useful tool to increase disease prevention through successful prediction and/or early detection. This notion carries both favorable effects for public health and financial parameters of healthcare systems, as well as optimizing individual understanding and ability to choose and decide optimal combatting strategies[44]. Although the inclusion of PRSs and relevant interactions can explain cardiometabolic disease risk[45], the conversation around its clinical validity underlines the importance of real-time context on PRS information evaluation and decision-making in order to avoid confusion with genetic determinism[40,41]. This sheds a light on the vital role of both development of valid methodologies to increase PRS reliability, transferability and accuracy, as well as the professionals' familiarization with the interpretation of its information. This is also why the education of healthcare professionals is put in the center of integrating genetic information into daily practice.

Furthermore, taking PRS information into account can prove beneficial on its own accord in patients with extremely high genetic risk[41] and, thus, PRS utility is also discussed at personal level[38]. PRS information can be differentially valuable to each individual, according to both their personal interest and understanding of the information, as well as relevant genetic risk in outcomes of interest. The latter might not always correlate to matters of clinical importance, but do account for increasing awareness on genetic predisposition for various matters significant to the individual. It is therefore why, a reliable approach to PRS calculation for various traits, with easily understandable and interpretable results is central in future research surrounding PRS use[38]. Especially in cases regarding cardiometabolic disorders such as overweight, obesity and type 2 diabetes, finding ways to efficiently include PRS prediction in easily applicable risk tools is considered a priority for the maximization of PRS efficacy.

Challenges in PRS Construction and Interpretation

Although inclusion of PRSs in disease prognosis can be beneficial, several considerations arise when discussing the methodological aspect of PRS construction, the efficacy of the various PRS development methodologies presented in current literature and the real-time interpretation capacity in clinical and non-clinical settings. Firstly, the fundamental limitation of PRS' universal application concerns the underrepresentation of data used from populations of different genetic ancestry[44]. To date, although several attempts for PRS construction using data from various populations have been made, PRSs presented in literature mainly focus on European ancestry. The lack of existent PRSs deriving from large cohorts of global populations affects their translational capacity in less frequently examined populations where contextually phenotype-associated variants, SNP linkage disequilibrium (LD) or allele frequency may vary. Therefore, a preceding necessity of developing more PRSs using data from populations around the globe is formed before discussing their maximum use, in order to ensure universal application capacity.

Another pillar of PRS development refers to the biases of the different methodological approaches undertaken in calculating the scores[44]. Diverse current practices consist of: i) the replication of simple aggravations of the risk-alleles for phenotype-associated variants using their respective effect sizes from current literature (i.e. consortia such as the GIANT one or data from large studies such as

the UKBiobank[46] of the Twins Early Development Study -TEDS[47]) ; and ii) the conduct of novel GWAS in populations of sufficiently large sample sizes, extraction of summary statistics, subsequent identification of phenotype-associated variants and their risk alleles' aggravation in a holistic score. As PRS development and phenotype examinations are ongoing, research may simultaneously focus on the identification of novel phenotype-associated variants and the replication of previously identified ones. As a result, the statistical design and assessment may significantly differ across studies and the final choice for the optimal model to be used may lie in the discretion of the researcher according to the needs of the research question at hand. Additionally, differences in samples sizes significantly matter in effective PRS validation. Although the effect of using target-SNPs outside of reference populations can be limited, current discussion around the role of population size has shown that cohorts with a few thousands of participants can be of use in replicating results and using SNPs from PRSs deriving from even larger populations[48]. Moreover, the additional variety in statistical methods (i.e. p-value thresholds, clumping, Bayesian or lasso-based penalization), packages (eg PRScs, LDpred2) and assessment applied can largely affect the end product which may be ultimately differentiated across studies. It is therefore highlighted that standardization of the PRS extraction process[49] is central to facilitating their validation and sequentially increasing their predictive ability. Additionally, in this context, attempts to practically compare PRS results and methodology[4,50-52] can provide useful data for the next steps in the need for a unified, applicable approach to allow for PRSs capable of yielding rapid but reliable results and effective comparisons of findings between populations of different characteristics.

Moreover, familiarization with the true meaning deriving from the information of the PRS is vital in its correct interpretation. Understanding the potentially indirect effects of SNPs included in the models and weighing the environmental factor in are key considerations in constructing future PRSs as reliable disease prediction risk tools. Apart from the technical aspects, a different cornerstone of practical PRS use appertains to the familiarization of healthcare professionals with the field. Proper assuefaction with the practical meaning of PRS information is critical for professionals to address disease risk and convey the appropriate message to patients. The delicate understanding of individual risk and its practical meaning in ultimate disease manifestation can be challenging in cases where the risk is small or the patient is not properly acquainted with the details of their genetic profile. Both professional and patient education and perceptions around PRS utility are integral in its successful use as a disease screening and treatment tool[40,44].

PRS and Nutrigenetics/Nutrigenomics in Future Healthcare Practice

Although there is a limited number of studies investigating and discussing the extent of PRS effective translation to date, future directions can be encouraging on the incorporation of PRS methodologies in the daily practice[1-3]. PRS inclusion in disease screening and the formation of personalized recommendations could potentially offer a solution to the growing pressure applied to healthcare systems for more inclusive strategies and efficient use of financial resources[49]. In the field of nutrigenetics (i.e. the impact of SNPs on certain nutrient interaction or role in metabolic pathways) and nutrigenomics (i.e. the impact of nutrients on gene expression), PRS use can be considered as a promising tool in the advancement of personalized nutrition.

Understanding the connective links between research conduct and translation is substantial in order to be able to reinforce PRS practical use. An integral part to such an effort would be the effective translational communication between bioinformatics and healthcare sectors in order to enhance proper PRS use and interpretation[49]. Especially when referring to the use of PRSs in cardiometabolic and weight-related disorders, understanding, quantifying and translating the contribution of genetic predisposition is vital in interpreting genetic impact. Incorporating genetic information in medical and nutritional advice can maximize the success of the proposed strategies, while informing the individuals in main aspects of their genetic profile. In this spectrum, PRS interpretation in weight-related disorders can only be effective when conducted and evaluated alongside the effect of other lifestyle determinants (Figure 1). This can allow for increased motivation on behavioral change and lifestyle adaptations[41] to the proposed measures, which can subsequently strengthen the disorders' effective management.

In an attempt to dissect the steps of including genetic details in current practice and promote personalized nutrition, in 2022 the Academy of Nutrition and Dietetics published the creation of a *Nutrigenomics Care Map* specifying the timeline of nutrigenetic information integration in nutritional assessment[53]. The map puts professional formation on the forefront of the practice, by inserting the sufficient nutrigenomics training prerequisite as the first out of the four steps of the process. Patient screening, genetic testing and communication of genetic profiling results as part of the nutritional assessment and the setting

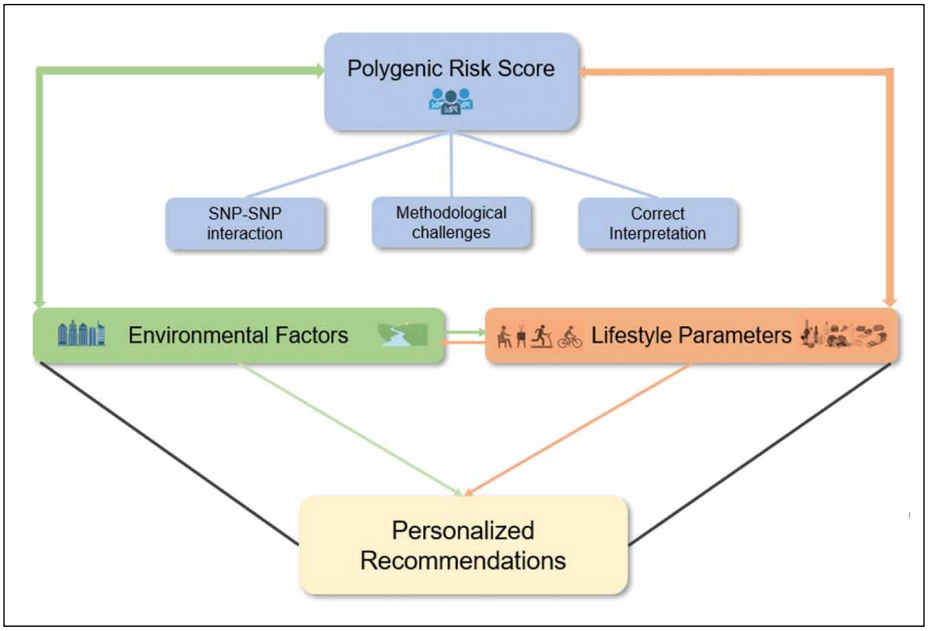

FIGURE 1. Polygenic Risk Score (PRS) in Personalized Recommendations (created with BioRender.com).

of SMART (specific, measurable, attainable, relevant and time-based) goals complete the suggested procedure[53]. Such an approach aims to maximize nutritional consulting by actively involving the patient in the formation of goals and dietary regimens optimally corresponding to their genetic profile. Integration of PRSs in this effort could allow the practice to move forward from personalized advice provided only based on specific genotypes of key genes associated to body weight or obesity[54,55]. As a result, more research in the form of Randomized Clinical Trials (RCTs) is needed, regarding the interactions between BMI PRSs and dietary regimens in order to establish the evidence-based approaches required for the nodes of individualized advice. Such efforts would subsequently enhance our understanding and forming of optimal recommendations, each-time targeting the outcome of interest and adopting the literature-based, corresponding strategy (eg advice on adherence to a dietary regimen of specific macronutrient content for the achievement of weight loss in individuals with specific PRS for obesity). Due to the current increase observed in the offer of nutrigenetic services, establishment of scientific, quality guidelines for directing healthcare professionals is vital[56].

Furthermore, on principle, the meaning of PRS information differentiates itself according to the nature of the disorder in reference. For example, a PRS will be differently interpreted in cases of monogenic rather than polygenic diseases, such as the cardiometabolic and weight-related ones. The multidisciplinary character of those disorders therefore reciprocally affects the creation of the appropriate framework in which it will be communicated. This interplay between genetic information communication and healthcare setting factors centrally affects both the formation and the influencing capacity of public health policies in precision medicine and nutrition[38-40]. The latter, thus, re-enforces the need for sectors simultaneously operating on unravelling the relations between the creation, interpretation and communication of genetic information across healthcare professionals. These could, in turn, be incorporated into screening tools for multiple traits and contribute to the creation of individualized disease prevention or treatment strategies.

CONCLUSIONS

Future incorporation of PRS information in the daily healthcare practice could present considerable advantages to advancing precision medicine and personalized nutrition. Creation of sound methodologies, accounting for the extent of the impact for environmental stimuli and simultaneously able to allow for the effective inclusion of PRS results in disease prediction, diagnosis and prognosis is deemed vital in bringing PRS research and application forward. PRS information on cardiometabolic and weight-related disorders can increase the prognostic validity of already existent tools and the fruitful formation and implementation of individualized recommendations. However, sufficient familiarization of healthcare professionals with the meaning and contextual translation of PRS results plays a major part in its proper communication where attention must be given in the role of the interac-

tions between SNPs, environment and lifestyle determinants in ultimate disease manifestation. Future initiatives should aim at uniformly enhancing both methodology development and educational formation in attempting to firmly establish, integrate and distribute PRS use as a daily practicum.

Conflict of Interest

The authors declare no conflict of interest

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ΠΕΡΙΛΗΨΗ

Πολυγονιδιακοί Δείκτες Κινδύνου και προσωποποιημένες προσεγγίσεις στην πρόληψη και την αντιμετώπιση καρδιομεταβολικών ασθενειών: Σύντομη Ανασκόπηση

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Η διερεύνηση του ρόλου των γενετικών παραλλαγών στην εμφάνιση ασθενειών χρησιμοποιείται ολοένα και περισσότερο με στόχο τη βελτιστοποίηση των επιτυχών προσεγγίσεων στα πεδία της ιατρικής ακριβείας και της προσωποποιημένης διατροφής. Μια συγκεντρωτική τεχνική για την ποσοτικοποίηση της γενετικής επίδρασης αφορά στην ανάπτυξη και τη χρήση ειδικών-για-κάθε-ασθένεια Πολυγονιδιακών Δεικτών Κινδύνου (ΠΔΚ), μέσω τους αθροίσματος της επίδρασης συσχετιζόμενων μονονουκλεοτιδικών πολυμορφισμών (ΜΝΠ) προερχόμενων από μελέτες σάρωσης του γονιδιώματος. Η σύγχρονη βιβλιογραφία πραγματεύεται εκτενώς την ενσωμάτωση της χρήσης των ΠΔΚ στην ιατρική και διαιτολογική πρακτική, με ιδιαίτερη έμφαση: i) στην προβλεπτική ακρίβεια εμφάνισης ασθενειών έπειτα από την ενσωμάτωση της πληροφορίας των ΠΔΚ σε αντίστοιχα μοντέλα, ii) στο ρόλο των σύγχρονων μεθοδολογικών προσεγγίσεων για την εξαγωγή αξιόπιστων αποτελεσμάτων και την αντίστοιχη επίδραση περιορισμών όπως η γενεαλογική καταγωγή και το μέγεθος του πληθυσμού αναφοράς, iii) στην εξοικείωση των επαγγλματιών υγείας με τη σημασία της γενετικής πληροφορίας και iv) στην κάθε φορά προσαρμοσμένη στα υπάρχοντα πλαίσια ερμηνεία των αποτελεσμάτων των ΠΔΚ στη δημιουργία προσωποποιημένων συστάσεων. Σε αυτό το πλαίσιο, η παρούσα σύντομη ανασκόπηση συνοψίζει τα σύγχρονα ευρύματα της βιβλιογραφίας σχετικά με τη χρήση και τη χρησιμότητα των ΠΔΚ σε καρδιομεταβολικές νόσους και νόσους που σχετίζονται με το σωματικό βάρος, καθώς και πραγματεύεται τις μελλοντικές κατευθύνσεις για την πιθανή ενσωμάτων των ΠΔΚ στην πρακτική της προσωποποιημένης διατροφής.

ΛΕΞΕΙΣ ΚΛΕΙΔΙΑ: *Πολυγονιδιακοί δείκτες κινδύνου, καρδιομεταβολικές ασθένειες, διαχείριση βάρους, προσωποποιημένη διατροφή*

REFERENCES

1. O'Sullivan JW, Raghavan S, Marquez-Luna C, Luzum J.A., Damrauer S.M., Ashley E.A., et al. Polygenic Risk Scores for Cardiovascular Disease: A Scientific Statement From the American Heart Association. Circulation [Internet]. 2022 Jul [cited 2023 Feb 16];146(8):e93-e118. Available from: https://www.ahajournals.org/doi/10.1161/CIR.0000000000001077. Doi:10.1161/CIR.0000000000001077.
2. O'Sullivan JW, Ashley EA, Elliott PM. Polygenic risk scores for the prediction of cardiometabolic disease. Eur Heart J. 2023 Jan;44(2):89-99. Doi:10.1093/eurheartj/ehac648.
3. Patel AP, Khera AV. Advances and Applications of Polygenic Scores for Coronary Artery Disease. Annu Rev Med. 2023 Jan;74:141-54. Doi:10.1146/annurev-med-042921-112629.
4. Pain O, Glanville KP, Hagenaars SP, Selzam S, Fürtjes AE, Gaspar HA, et al. Evaluation of polygenic prediction methodology within a reference-standardized framework. PLoS Genet [Internet]. 2021 May [cited 2023 Feb 16];17(5):e1009021. Available from: https://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1009021. Doi:10.1371/journal.pgen.1009021.
5. PGS Catalog [Internet] [accessed 2023 Feb 17]. Available from: https://www.pgscatalog.org/

6. GIANT consortium [Internet] [accessed 2023 Feb 17]. Available from: https://portals.broadinstitute.org/collaboration/giant/index.php/GIANT_consortium
7. Locke AE, Kahali B, Berndt SI, Justice AE, Pers TH, Day FR, et al. Genetic studies of body mass index yield new insights for obesity biology. Nature. 2015 Feb;518(7538):197-206. Doi:10.1038/nature14177.
8. Yengo L, Sidorenko J, Kemper KE, Zheng Z, Wood AR, Weedon MN, et al. Meta-analysis of genome-wide association studies for height and body mass index in ~700000 individuals of European ancestry. Hum Mol Genet. 2018;27(20):3641-9. Doi:10.1093/hmg/ddy271.
9. D'Silva S, Chakraborty S, Kahali B. Concurrent outcomes from multiple approaches of epistasis analysis for human body mass index associated loci provide insights into obesity biology. Sci Rep. 2022 May;12(1):7306. Doi:10.1038/s41598-022-11270-0.
10. Livingstone KM, Brayner B, Celis-Morales C, Moschonis G, Manios Y, Traczyk I, et al. Associations between dietary patterns, FTO genotype and obesity in adults from seven European countries. Eur J Nutr. 2022 Sep;61(6):2953-65. Doi:10.1007/s00394-022-02858-3.
11. Li X, Zhou T, Ma H, Heianza Y, Champagne CM, Williamson DA, et al. Genetic variation in lean body mass, changes of appetite and weight loss in response to diet interventions: The POUNDS Lost trial. Diabetes Obes Metab. 2020 Dec;22(12):2305-15. Doi:10.1111/dom.14155.
12. Khera AV, Chaffin M, Wade KH, Zahid S, Brancale J, Xia R, et al. Polygenic Prediction of Weight and Obesity Trajectories from Birth to Adulthood. Cell. 2019 Apr;177(3):587-96.e9. Doi:10.1016/j.cell.2019.03.028.
13. Shi M, Chen W, Sun X, Bazzano LA, He J, Razavi AC, et al. Association of Genome-Wide polygenic risk score for body mass index with cardiometabolic health from childhood through midlife. Circ Genom Precis Med [Internet]. 2022 Aug;15(4):e003375. Available from: https://www.ahajournals.org/doi/10.1161/CIRCGEN.121.003375. Doi:10.1161/CIRCGEN.121.003375.
14. de Toro-Martín J, Guénard F, Tchernof A, Pérusse L, Marceau S, Vohl MC. Polygenic risk score for predicting weight loss after bariatric surgery. JCI Insight. 2018 Sep;3(17):e122011. Doi:10.1172/jci.insight.122011.
15. Katsareli EA, Amerikanou C, Rouskas K, Dimopoulos A, Diamantis T, Alexandrou A, et al. A Genetic risk score for the estimation of weight loss after bariatric surgery. Obes Surg. 2020 Apr;30(4):1482-90. Doi:10.1007/s11695-019-04320-6.
16. Kafyra M, Kalafati IP, Katsareli EA, Lambrinou S, Varlamis I, Kaliora AC, et al. The iMPROVE Study; Design, dietary patterns, and development of a lifestyle index in overweight and obese Greek adults. Nutrients. 2021 Oct;13(10):3495. Doi:10.3390/nu13103495.
17. Wang CA, Attia JR, Lye SJ, Oddy WH, Beilin L, Mori TA, et al. The interactions between genetics and early childhood nutrition influence adult cardiometabolic risk factors. Sci Rep. 2021 Jul;11(1):14826. Doi:10.1038/s41598-021-94206-4.
18. Tan PY, Amini F, Mitra SR. Dietary protein interacts with polygenic risk scores and modulates serum concentrations of C-reactive protein in overweight and obese Malaysian adults. Nutr Res. 2022 Nov;107:75-85. Doi:10.1016/j.nutres.2022.09.002.
19. Zhou JY, Liu M, Park S. Interaction of environmental factors with the polygenic risk scores of thinness-related genes in preventing obesity risk in middle-aged adults: The KoGES. J Hum Nutr Diet. 2023 Jan; [published online ahead of print]. Available from: https://pubmed.ncbi.nlm.nih.gov/36632775/ Doi:10.1111/jhn.13132.
20. Dashti HS, Levy DE, Hivert MF, Alimenti K, McCurley JL, Saxena R, et al. Genetic risk for obesity and the effectiveness of the ChooseWell 365 workplace intervention to prevent weight gain and improve dietary choices. Am J Clin Nutr. 2022 Jan;115(1):180-8. Doi:10.1093/ajcn/nqab303.
21. Lee WJ, Lim JE, Jung HU, Kang J-O, Park T, Won S, et al. Analysis of the Interaction between polygenic risk score and calorie intake in obesity in the Korean population. Lifestyle Genom. 2021;14(1):20-29. Doi:10.1159/000511333.
22. Konttinen H, Llewellyn C, Silventoinen K, Joensuu A, Männistö S, Salomaa V, et al. Genetic predisposition to obesity, restrained eating and changes in body weight: a population-based prospective study. Int J Obes (Lond). 2018 Nov;42(4):858-65. Doi:10.1038/ijo.2017.278.
23. Park S, Yang HJ, Kim MJ, Hur HJ, Kim SH, Kim MS. Interactions between polygenic risk scores, dietary pattern, and menarche age with the obesity risk in a large hospital-based cohort. Nutrients. 2021 Oct;13(11):3772. Doi:10.3390/nu13113772.
24. Hüls A, Wright MN, Bogl LH, Kaprio J, Lissner L, Molnár D, et al. Polygenic risk for obesity and its interaction with lifestyle and sociodemographic factors in European children and adolescents. Int J Obes (Lond). 2021;45(6):1321-30. Doi:10.1038/s41366-021-00795-5.
25. Livingstone KM, Abbott G, Bowe SJ, Ward J, Milte C, McNaughton SA. Diet quality indices, genetic risk and risk of cardiovascular disease and mortality: A longitudinal analysis of 77 004 UK Biobank participants. BMJ Open [Internet]. 2021 Apr;11(4):e045362. Doi:10.1136/bmjopen-2020-045362.
26. Livingstone KM, Abbott G, Ward J, Bowe SJ. Unhealthy Lifestyle, Genetics and Risk of Cardiovascular Disease and Mortality in 76,958 Individuals from the UK Biobank Cohort Study. Nutrients. 2021 Nov;13(12):4283. Doi:10.3390/nu13124283.
27. Yun JS, Jung SH, Shivakumar M, Xiao B, Khera AV, Won H-H, et al. Polygenic risk for type 2 diabetes, lifestyle, metabolic health, and cardiovascular disease: a prospective UK Biobank study. Cardiovasc Diabetol. 2022 Jul;21(1):131. Doi:10.1186/s12933-022-01560-2.
28. Hur HJ, Yang HJ, Kim MJ, Lee KH, Kim MS, Park S. Association of polygenic variants with type 2 diabetes risk and their interaction with lifestyles in Asians. Nutrients. 2022 Aug;14(15):3222. Doi:10.3390/nu14153222.
29. López-Portillo ML, Huidobro A, Tobar-Calfucoy E, Yáñez C, Retamales-Ortega R, Garrido-Tapia M, et al. The association between fasting glucose and sugar sweetened beverages intake is greater in Latin Americans with a high polygenic risk score for type 2 diabetes mellitus. Nutrients. 2021 Dec;14(1):69. Doi:10.3390/nu14010069.
30. Lim JE, Kang JO, Ha TW, Jung H-U, Kim DJ, Baek EJ, et al. Gene-environment interaction in type 2 diabetes in Korean cohorts: Interaction of a type 2 diabetes polygenic

risk score with triglyceride and cholesterol on fasting glucose levels. Genet Epidemiol. 2022 Jul;46(5-6):285-302. Doi:10.1002/gepi.22454.
31. Merino J, Guasch-Ferré M, Li J, Chung W, Hu Y, Ma B, et al. Polygenic scores, diet quality, and type 2 diabetes risk: An observational study among 35,759 adults from 3 US cohorts. PLoS Med [Internet]. 2022 Apr;19(4):e1003972. Available from: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003972. Doi:10.1371/journal.pmed.1003972.
32. Zhang S, Stubbendorff A, Olsson K, Ericson U, Niu K, Qi L, et al. Adherence to the EAT-Lancet diet, genetic susceptibility, and risk of type 2 diabetes in Swedish adults. Metabolism. 2023 Apr;141:155401. Doi:10.1016/j.metabol.2023.155401.
33. Francis ER, Cadar D, Steptoe A, Ajnakina O. Interplay between polygenic propensity for ageing-related traits and the consumption of fruits and vegetables on future dementia diagnosis. BMC Psychiatry. 2022 Jan;22(1):75. Doi:10.1186/s12888-022-03717-5.
34. Byrne S, Boyle T, Ahmed M, Lee SH, Benyamin B, Hyppönen E. Lifestyle, genetic risk and incidence of cancer: A prospective cohort study of 13 cancer types. Int J Epidemiol. 2023 Jan. [published online ahead of print]. Doi:10.1093/ije/dyac238.
35. Park S, Liu M, Huang S. Association of Polygenic Variants Involved in Immunity and Inflammation with Duodenal Ulcer Risk and Their Interaction with Irregular Eating Habits. Nutrients. 2023 Jan;15(2):296. Doi:10.3390/nu15020296.
36. Esteve-Luque V, Fanlo-Maresma M, Padró-Miquel A, Corbella E, Rivas-Regaira M, Pintó X, et al. Polygenic risk of hypertriglyceridemia is modified by BMI. Int J Mol Sci. 2022 Aug;23(17):9837. Doi:10.3390/ijms23179837.
37. Schnurr TM, Jakupović H, Carrasquilla GD, Ängquist L, Grarup N, Sørensen TIA, et al. Obesity, unfavourable lifestyle and genetic risk of type 2 diabetes: a case-cohort study. Diabetologia. 2020 Jul;63(7):1324-32. Doi:10.1007/s00125-020-05140-5.
38. Moorthie S, Hall A, Janus J, Brigden T, Babb de Villiers C, Blackburn L, et al. Polygenic scores and clinical utility. PHG Foundation. 2021 Jan [accessed 2023 Jan 24]. Available from: https://www.phgfoundation.org/media/35/download/polygenic-scores-and-clinical-utility.pdf?v=1.
39. Kumuthini J, Zick B, Balasopoulou A, Chalikiopoulou C, Dandara C, El-Kamah G, et al. The clinical utility of polygenic risk scores in genomic medicine practices: a systematic review. Hum Genet. 2022 Nov;141(11):1697-1704. Doi:10.1007/s00439-022-02452-x.
40. Lewis CM, Vassos E. Polygenic risk scores: From research tools to clinical instruments. Genome Med. 2020 May;12(1):44. Doi:10.1186/s13073-020-00742-5.
41. Polygenic risk score task force of the international common disease alliance. Responsible use of polygenic risk scores in the clinic: potential benefits, risks and gaps. Nat Med, 2021 Nov. 27(11):1876-84. Doi: 10.1038/s41591-021-01549-6.
42. Choe EK, Shivakumar M, Lee SM, Verma A, Kim D. Dissecting the clinical relevance of polygenic risk score for obesity-a cross-sectional, longitudinal analysis. Int J Obes (Lond). 2022 Sep;46(9):1686-93. Doi:10.1038/s41366-022-01168-2.
43. Padilla-Martinez F, Szczerbiński Ł, Citko A, Czajkowski M, Konopka P, Paszko A, et al. Testing the Utility of Polygenic Risk Scores for Type 2 Diabetes and Obesity in Predicting Metabolic Changes in a Prediabetic Population: An Observational Study. Int J Mol Sci. 2022 Dec;23(24):16081. Doi:10.3390/ijms232416081.
44. Slunecka JL, van der Zee MD, Beck JJ, Johnson BN, Finnicum CT, Pool R, et al. Implementation and implications for polygenic risk scores in healthcare. Hum Genomics. 2021 Jul;15(1):46. Doi:10.1186/s40246-021-00339-y.
45. Ye Y, Chen X, Han J, Jiang W, Natarajan P, Zhao H. Interactions Between Enhanced Polygenic Risk Scores and Lifestyle for Cardiovascular Disease, Diabetes, and Lipid Levels. Circ Genom Precis Med. 2021 Feb;14(1):e003128. Doi:10.1161/CIRCGEN.120.003128.
46. UKBiobank [Internet] [accessed 2023 Feb 19]. Available from: https://www.ukbiobank.ac.uk/
47. Twins Early Development Study [Internet] [accessed 2023 Feb 19]. Available from: https://www.teds.ac.uk/
48. Janssens ACJW. Validity of polygenic risk scores: Are we measuring what we think we are?. Hum Mol Genet. 2019 Nov;28(R2):R143-50. Doi:10.1093/hmg/ddz205.
49. Cross B, Turner R, Pirmohamed M. Polygenic risk scores: An overview from bench to bedside for personalised medicine. Front Genet. 2022 Nov;13:1000667. Doi:10.3389/fgene.2022.1000667.
50. Zhang C, Ye Y, Zhao H. Comparison of methods utilizing Sex-Specific PRSs derived from GWAS summary statistics. Front Genet. 2022 Jul;13:892950. Doi:10.3389/fgene.2022.892950.
51. Zhao Z, Fritsche LG, Smith JA, Mukherjee B, Lee S. The construction of cross-population polygenic risk scores using transfer learning. Am J Hum Genet. 2022 Nov;109(11):1998-2008. Doi:10.1016/j.ajhg.2022.09.010.
52. Kafyra M, Kalafati IP, Dimitriou M, Grigoriou E, Kokkinos A, Rallidis L, et al. Robust bioinformatics approaches result in the first Polygenic Risk Score for BMI in Greek adults. J Pers Med. 2023 Feb;13(2):327. Doi.org/10.3390/jpm13020327.
53. Horne JR, Nielsen DE, Madill J, Robitaille J, Vohl MC, Mutch DM. Guiding global best practice in personalized nutrition based on genetics: The development of a Nutrigenomics Care Map. J Acad Nutr Diet. 2022 Feb;122(2):259-69. Doi:10.1016/j.jand.2021.02.008.
54. Peña-Romero AC, Navas-Carrillo D, Marín F, Orenes-Piñero E. The future of nutrition: Nutrigenomics and nutrigenetics in obesity and cardiovascular diseases. Crit Rev Food Sci Nutr. 2018;58(17):3030-41. Doi:10.1080/10408398.2017.1349731.
55. Vyas S. Advances in nutrigenomics and applications in public health: A Recent Update. Curr Res Nutr Food Sci. 2022 Dec;10(3). Doi: http://dx.doi.org/10.12944/CRNFSJ.10.3.23.
56. Floris M, Cano A, Porru L, Addis R, Cambedda A, Idda ML, et al. Direct-to-Consumer Nutrigenetics Testing: An Overview. Nutrients. 2020 Feb;12(2):566. Doi:10.3390/nu12020566.