

# Exploiting interrelated genomic, biochemical, nutritional and pathophysiological data to optimize athletic performance (Review)

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**Abstract.** The present review describes a multidimensional approach for enhancing athletic performance through the integration of innovative and interrelated methodologies. In this respect, telomere dynamics, genotyping/phenotype analysis, metabolomics, biochemical tests, essential elements quantitation, echocardiography and burnout testing are jointly employed to provide a comprehensive assessment of athlete health wellness and longevity. Telomere analysis as a biomarker of effect provides novel insight into cellular dynamics, aging and adaptability, elucidating the impact of training on cellular well-being. Genotype/phenotype analysis reveals genetic variances related to athletic performance (i.e., strength, flexibility, endurance, power, VO<sub>2</sub> max), injury predisposition and recovery needs, facilitating the customization of training programs and interventions. Metabolomics provides a detailed overview of low-molecular weight metabolites, revealing pivotal metabolic pathways and responses to exercise. Biochemical tests critically evaluate markers associated with energy metabolism, inflammation and recovery, providing crucial information for tailored performance optimization. Essential elements quantitation assesses micronutrient status, a vital factor for sustained peak performance. Echocardiography enables the assessment of cardiac structure and function, fine-tuning cardiovascular performance for superior athletic output and for early detection of underlying abnormalities. Burnout testing evaluates psychological stress,

fatigue levels and readiness for optimal performance, ensuring holistic well-being. By integrating these advanced scientific methodologies, this approach yields a comprehensive understanding of athlete health. This, in turn, informs personalized interventions in training, nutrition, supplementation, injury prevention and mental wellness. Through evidence-based, personalized strategies, this rigorous scientific framework holds significant promise in advancing athletic performance and longevity, propelling the field of sports performance optimization, and unlocking athletic excellence.

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## 1. Introduction

Athletes continuously strive to improve their results and achieve an optimal level of performance. Regardless of their level or athletic category, whether they are involved in professional sports or are amateur athletes, they typically aim to ensure that their goals are clear and focused (1,2). For example, rather than simply seeking to improve overall performance, they may set specific objectives, such as increasing shooting accuracy. Moreover, they need to track their progress, such as aiming to run a distance (i.e., a mile) in under a specified amount of time and set goals that are sufficiently challenging to motivate them, but are also within reach of their abilities. Lastly, athletes need to establish deadlines to create urgency

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and maintain focus on their performance goals. A commonly applied rule, which simplifies this extensive and often complex information in a comprehensible and memorable manner, is ensuring that athletic goals are specific, measurable, achievable, relevant, and time-bound (SMART). SMART heuristics are widely recognized as feasible and practical to be followed by professionals and health organizations. However, recently, a debate regarding their applicability has emerged, questioning the need to reassess best practices in goal setting for physical activity promotion (3-5).

Nevertheless, in addition to the SMART goals, athletes should consider several other factors to maximize their potential and success (6-8). Adaptability is crucial, allowing athletes to adjust to changing circumstances and overcome obstacles effectively. Developing a sport-specific strategic edge involves understanding the intricacies of their sport, refining tactics and exploiting strengths to gain a competitive advantage. Skill mastery is paramount, as athletes need to continually improve their techniques and abilities to excel in their selected sport. These factors are strongly related to the natural talent of athletes and their ability to perceive the requirements of their sport. Furthermore, attaining the optimal physical condition for their sport is essential, requiring a dedicated focus on fitness, strength, speed and endurance. Mental toughness and resilience are equally vital, enabling athletes to navigate pressure, setbacks and adversity with composure and determination. Balancing training with rest is key to preventing burnout and injury, ensuring that athletes can maintain peak performance over the long term. Consistency is another critical factor, as steady progress and effort lead to sustainable improvement and success. These attributes are mostly related to the determination and willingness of the athletes to work hard and practice to further develop their natural talent. By integrating adaptability, sport-specific strategic planning, skill mastery, optimal physical condition, mental toughness, resilience, balanced training and rest, as well as consistency into their approach, athletes can position themselves for success (9). With these elements in place, and if luck and momentum are on their side, athletes can set and achieve ambitious goals, performing at their best in competitions. Combining all the above into their selected sport can lead them to a successful career, leaving behind a legacy while making a meaningful impact on their community and beyond.

It is noteworthy that aside from factors related to natural talent and luck, all other factors are within the control of an individual willing to work hard to succeed in their chosen sport. The present aimed to expand upon well-established approaches, discussing how they can be combined with innovative methods to optimize athletic performance.

## **2. Ergophysiology, biomechanics and biochemical monitoring**

Systematic measurement and analysis of various physiological parameters and biochemical data are necessary to assess the performance and track the progress of an athlete, and prevent overtraining or injuries. Ergophysiology and biomechanics focus on understanding how the physiological processes of the body relate to performance in a specific sport or physical activity. This multidisciplinary field considers factors, such as cardiovascular function, respiratory capacity, neuromuscular

coordination and biomechanics to optimize athletic performance (10,11). For example, monitoring heart rate and blood pressure provides information about cardiovascular fitness and effort exerted during training or competition, as well as how the heart responds to exercise. Measurements of respiratory function, such as ventilation rate and  $\text{VO}_2$  max, provide insight into respiratory efficiency and stamina, critical indicators of cardiovascular fitness. Neuromuscular function tests provide insight into coordination, balance and responses to stimuli, while the analysis of muscle function and endurance yields information about movement, force, strength effort, stamina or fatigue. Moreover, the analysis of movement patterns, joint kinetics and muscular activation patterns for biomechanical analysis assist in the identification of potential biomechanical inefficiencies and risk factors for injury (12-14).

Complementing the ergophysiology measurements, biochemical tests provide valuable insight into various aspects of the physiology and metabolism of an athlete by analyzing biomarkers in the body, such as blood, urine, or tissue samples, to assess different parameters related to health, performance and recovery (15-18). For example, the analysis of blood biomarkers, such as lactate levels can provide insight into the anaerobic threshold and metabolic efficiency of an athlete during high-intensity exercise. Similarly, measuring glucose levels provides information on glycogen utilization, helping athletes tailor their nutritional strategies to optimize fuel availability for training and competition. Assessing creatine kinase levels can indicate muscle damage and recovery status, guiding adjustments in training intensity and recovery protocols. Monitoring cortisol levels provides insight into stress responses and adrenal function, aiding athletes in managing training loads and avoiding overtraining syndrome (19).

In addition to biochemical tests, athletes also undergo evaluations of organ function, particularly focusing on the heart. Echocardiography is a typical method used for this purpose, providing a detailed assessment of heart function. It visualizes cardiac structures, including chambers, valves and blood flow patterns, providing valuable insight into cardiac anatomy and function (20-22). This technique assesses parameters, such as chamber dimensions, ejection fraction and valve function, aiding in the detection of abnormalities, such as hypertrophic cardiomyopathy or congenital heart defects. Echocardiography ensures the cardiac health and safety of athletes during exercise, guiding appropriate management strategies.

While ergophysiology and biochemical tests provide a comprehensive understanding of the physiological state of an athlete, enabling targeted interventions to enhance performance, recovery and health, equally important is understanding recovery needs and mental function. For example, measurements of resting heart rate indicate readiness for training and competition, while evaluating sleep quality provides necessary information of the rested status of an athlete (23,24). This is strongly associated with psychological profiling or stress assessments regarding mental burnout, which may compromise athletic performance.

## **3. Exposome analysis and athletic wellness**

In systems biology, unravelling the complexities underlying the comprehensive health status and athletic performance of

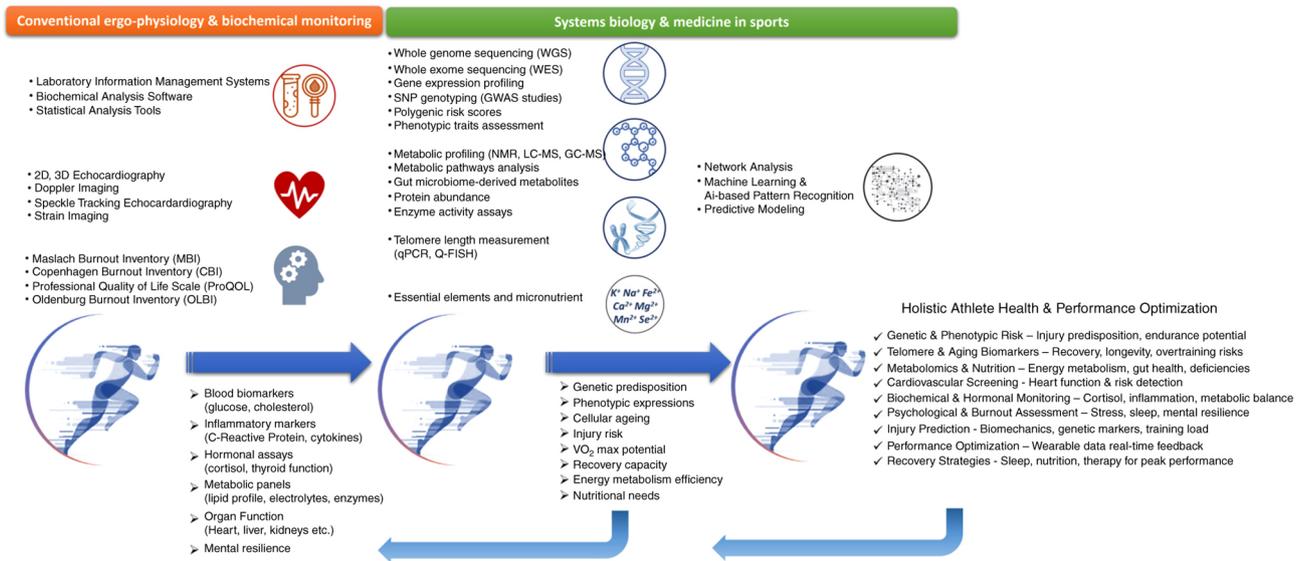


Figure 1. Integration of interrelated techniques for athletic wellness evaluation.

an individual necessitates a thorough exploration extending beyond genetic determinants. This analysis refers to the exposome, which encompasses the integration of environmental exposures encountered throughout the lifespan of an individual, including dietary habits, physical activity, psychosocial stressors, chemical pollutants and all related xenobiotic compounds (25-27). Encompassing all these effects, the exposome summarizes a vast array of factors intricately shaping a the overall health, wellness and longevity of an individual. For athletes, exposome analysis provides critical information on the physiological background, psychological resilience and overall athletic prowess or illegal actions of an athlete (28). Through rigorous exposome analyses, researchers in sports medicine can potentially gain a detailed understanding of the multifaceted interplay between environmental determinants and the health trajectory and performance dynamics of an athlete. For instance, the thorough analysis of the exposure of an athlete to environmental pollutants or dietary components elucidates potential determinants of injury susceptibility or fluctuations in performance metrics (29). Likewise, exposing the impact of stress physiology and sleep patterns on the adaptive responses of an athlete provides crucial insight for refining training paradigms and formulating tailored recovery schedules (30).

The integration of exposome analytics into athletic wellness frameworks not only empowers stakeholders, including coaches, trainers and athletes, to execute evidence-informed interventions, but also adopts a proactive stance towards environmental stressors that may compromise performance or precipitate injuries towards optimum athletic wellness. By optimizing training protocols, dietary interventions and lifestyle modifications informed by exposome elucidations, athletes stand poised to fortify their physiological resilience, prolong their athletic longevity, and amplify their competitive prowess. Fundamentally, exposome inquiry emerges as an important tool in research to interpret and enhance athletic performance, exceeding genetic predispositions to uncover the different environmental determinants modulating an athlete's

physiological equilibrium and potential for sustained peak performance.

#### 4. A multidimensional approach for the assessment of athletic wellness

Over the previous years, state-of-the-art approaches have emerged as tools to support the ergophysiology and the biochemical monitoring of athletes and assist them in attaining their goals. For example, advancements in technology have facilitated the development of wearable sensors, portable analyzers and digital health platforms, enabling the real-time monitoring of ergophysiological parameters and biochemical markers in field settings (31,32). These tools empower coaches, trainers and athletes to make data-driven decisions, optimize performance outcomes and maximize athletic potential, while minimizing the risk of overtraining, injury and fatigue. Going beyond the state-of-the-art, the utilization of systems medicine approaches in sports, and notably the integration of data with conventional methods and novel technological tools, represents an advanced paradigm in sports medicine (33). Systems medicine employs a holistic perspective, considering the interconnectedness of various biological systems and their influence on the health, performance and recovery status of an athlete. By leveraging omics technologies, such as genomics, proteomics, metabolomics and relevant approaches alongside advanced computational modeling and data analytics, sports medicine practitioners gain unprecedented insights into the complex interactions underlying athletic performance and adaptation (Fig. 1). The optimization of the health of an athlete begins with an initial evaluation of their medical history, lifestyle and a physical examination to establish a baseline health profile. In addition, biological matrices (blood, saliva, urine and hair samples) are analyzed to assess various physiological and metabolic aspects. Biochemical tests play a crucial role in evaluating the overall health, metabolic efficiency and recovery capacity of an athlete by analyzing key biomarkers related to energy

production, inflammation, oxidative stress and physiological strain. Cardiovascular assessments, such as echocardiography, provide valuable insight into heart structure and function, linking metabolic adaptations with cardiovascular performance and identifying potential underlying health risks. Furthermore, mental resilience and burnout assessments add another layer to athlete monitoring by evaluating psychological stress, emotional well-being and motivation, which directly affect performance and recovery. These conventional approaches are currently expanded with advanced systems biology and medicine in sports science, integrating multi-omics technologies and computational modeling for a more holistic and data-driven analysis. All data are enriching each other providing an holistic understanding of athlete mental and physical health and wellness.

Genotype/phenotype analysis, including whole genome sequencing (WGS), whole exome sequencing, gene expression profiling, SNP genotyping (GWAS studies), polygenic risk scores, and phenotypic traits assessment, provides valuable genetic insight into athletic potential, injury susceptibility, metabolic adaptations, and recovery patterns (34-37). Genetic, epigenetic and phenotypic analyses can be utilized to investigate genetic variants and their potential effects on athletic performance, injury risk and recovery needs (38-40). Key athletic performance traits, typically evaluated through traditional ergophysiology analysis, can be highlighted by examining potential polymorphisms for endurance, strength, power generation ability,  $VO_2$  max, flexibility, neuromuscular coordination, psychological responses, injury susceptibility, post-workout stress recovery needs and other variables (41). This information can also be evaluated under the prism of potential effects on performance and longevity, along with the epigenetic regulation expressed as phenotype, which is revealed through biochemical tests and other conventional methods. For example, epigenetic regulation is influenced by lifestyle, nutrition and environmental factors, manifesting as phenotypic expression (42). This expression not only reflects an athlete's cellular health but also provides insights into their adaptive responses to training stimuli and external stressors. This aspect can be further explored through related biomarkers such as telomeres, which can serve as an indicator of athletic wellness and longevity.

Telomeres play a key role in preserving genetic information, maintaining chromosome integrity and safeguarding against degradation, recombination, or fusion serving as a biological clock for cellular aging (43-45). Telomere analysis contributes to this comprehensive assessment by providing insight into cellular aging, its association with metabolomic markers, genotype-phenotype interactions and biochemical indicators of inflammation, while also reflecting the environmental impact of nutrition and lifestyle factors (46-49). Moreover, it is well-established that the analysis of telomere dynamics not only unveils the cellular aging process, but also serves as a biomarker of effect, revealing molecular mechanisms underlying specific traits or susceptibility to age-related health conditions (45,50-58). Available evidence suggests that regular exercise and endurance training may help preserve telomere length and attenuate the aging process at the cellular level. Athletes tend to sustain their telomeres compared with

people with limited physical activity. Conversely, overtraining, excessive stress and inadequate recovery may accelerate telomere shortening, potentially increasing the risk of age-related diseases and injuries (47,49,59).

Metabolic profiling, incorporating metabolic pathway analysis, gut microbiome-derived metabolites, protein abundance and enzyme activity assays, enhances the understanding of energy metabolism, training-induced biochemical shifts and fatigue indicators (60-63). Metabolomics enhances biomarker data from traditional biochemical tests, providing a comprehensive insight into metabolic adaptations, energy production, and potential indicators of fatigue or overtraining (64). By analyzing targeted metabolites involved in the metabolism of fatty acids and ketones, amino acids, and the influence of nutrition and microbial metabolites, metabolomics provides crucial insight into athletic performance and overall wellness. Fatty acids and ketones are essential energy sources for athletes, particularly during prolonged exercise or periods of low carbohydrate availability, revealing the metabolic flexibility, substrate utilization and endurance capacity of athletes (65,66). This knowledge guides the tailoring of nutrition and training strategies to optimize fat oxidation and enhance endurance performance. The metabolomic profiling of amino acids and protein metabolism allows for the assessment of amino acid levels and metabolic pathways, providing insight into the protein turnover rates, muscle adaptation processes and recovery kinetics of athletes, valuable information for targeted dietary interventions to support muscle growth, repair and adaptation (67,68).

In addition to metabolomics, essential elements and micronutrient analysis uncover nutrient deficiencies or imbalances that can greatly affect metabolism, organ function and cellular aging, ultimately influencing performance, endurance and recovery efficiency (69,70). By analyzing the impact of dietary components such as macronutrients, micronutrients and phytochemicals on metabolic pathways, researchers can identify dietary patterns associated with enhanced performance, improved recovery and reduced inflammation (71). For example, the determination of essential elements enriches the overall metabolic profile of an athlete, uncovering additional nutrient requirements or imbalances that may affect metabolic status and organ function (e.g., heart, liver and kidneys) (69,72). This knowledge updates nutrition plans tailored to the specific energy needs, training goals and physiological demands of athletes. Furthermore, although there is no direct association, the exploitation of these innovative tools can further enrich the current knowledge and understanding of burnout symptoms or mental fatigue in athletes.

To fully harness these diverse datasets, network analysis, machine learning and artificial intelligence (AI)-based pattern recognition are integrated into predictive modeling frameworks (73,74). AI-driven injury prediction models leverage biomechanics, genetic markers and training load analysis, while real-time performance optimization utilizes wearable data and feedback systems. Overall, by integrating genetic, biochemical, metabolic, cardiovascular and psychological insights with AI-driven analytics, sports medicine advances toward a more precise, data-driven approach that enhances performance, minimizes injury risks, and supports athlete longevity.



health. The genotypic background suggests that the athlete may need to focus more on endurance training to overcome the possible predisposition to a low endurance phenotype. This notion is supported by biochemical tests revealing slightly lower-than-expected values for hemoglobin (HGB) and hematocrit (HCT). Although these values appear typical for any other individual, for an athlete, enhancing oxygen-carrying capacity is crucial for improving endurance. As regards other metabolomic traits, the athlete should consider readjusting vitamin D levels, as it significantly affects muscle strength, power and endurance, all of which the athlete aims to improve (76). Concerning the environment, given the need for training in favorable conditions, the athlete is not exposed to dangerous heavy metal elements. However, nutritional interventions are necessary, considering several essential elements are at risk of deficiency, particularly iron, which is related to HCT through HGB and thus affects endurance (77). Finally, in terms of overall wellness, the athlete appears to adhere to a proper lifestyle, as evidenced by telomere analysis, which indicates the maintenance of longer telomeres, resulting in a calculated biological age lower than the chronological age.

The hypothetical example of the athlete presented in Fig. 2 highlights the intricate interplay between genetic predispositions, physiological markers, environmental factors and lifestyle choices in optimizing athletic performance and overall wellness. Despite the genetic predisposition of an athlete towards strength, power and motivation, there exists a potential limitation in endurance, as indicated by certain genetic markers and biochemical tests. However, by strategically focusing on endurance training and addressing nutritional deficiencies, particularly in vitamin D and iron, the athlete can work towards enhancing their performance in running sports. Moreover, the commitment of an athlete to a healthy lifestyle, evidenced by telomere analysis reflecting a biologically younger age, underscores the importance of holistic wellness practices in athletic endeavors. By leveraging insights from genetics, biochemistry and environmental considerations, tailored training regimens and nutritional interventions can be devised to optimize performance and mitigate injury risks. Overall, this example underscores the significance of personalized approaches in sports training and highlights the potential of integrating multidisciplinary insights to unlock the full potential of an athlete and promote long-term health and performance excellence.

## 6. Synopsis and future perspectives

Athletic performance and overall wellness are influenced by a complex interplay of physiological, biochemical, biomechanical, genetic and environmental factors. Ergophysiology, biomechanics and biochemical monitoring provide critical insight into the physical condition, performance capabilities and injury risks of an athlete. The integration of these disciplines into sports science allows for a more comprehensive assessment of athletic health, enabling targeted interventions that optimize training, recovery, and injury prevention (40,78,79). A key aspect of performance monitoring is cardiovascular, as well as in respiratory function assessment, which provides valuable data on the endurance and metabolic efficiency of an athlete. Parameters such as heart rate, blood pressure,

ventilation rate and  $\text{VO}_2$  max allow for personalized training strategies that enhance aerobic and anaerobic capacity (80,81). Similarly, the biomechanical analysis of movement patterns, joint kinetics and neuromuscular coordination helps identify inefficiencies that could increase the risk of injury, providing opportunities for corrective training techniques.

Biochemical markers further enrich these assessments by providing insight into the metabolic state, recovery efficiency and physiological stress levels of an athlete (82). Blood biomarkers, including lactate, glucose, creatine kinase and cortisol levels, reflect metabolic adaptations to training, muscle damage and stress responses. Analyzing these biomarkers aids in adjusting training loads to prevent overtraining and optimize recovery (16,17,79). Additionally, echocardiography serves as a valuable tool for cardiac function evaluation, ensuring that athletes maintain cardiovascular health while undergoing intense physical exertion (22). Beyond physiological and biochemical monitoring, exposome analysis plays a crucial role in understanding how environmental factors shape athletic wellness (28). The exposome encompasses dietary habits, pollutant exposure, psychosocial stressors and other external influences that can affect the performance and recovery of an athlete. By integrating exposome data with conventional assessments, researchers and practitioners can develop evidence-based strategies that enhance training effectiveness and long-term athletic health (83).

As regards personalized medical interventions, they also play a crucial role in managing injuries and diseases in athletes (84,85). A precision medicine approach tailors treatment plans to the specific physiological, genetic and biomechanical characteristics of an athlete, ensuring optimal recovery and minimizing long-term consequences (38,80). Individualized rehabilitation programs incorporating neuromuscular re-education, biomechanical correction and sport-specific conditioning help athletes return to peak performance with reduced reinjury risk (86,87). In addition to personalized medical intervention, sport-pharmacy plays a pivotal role in the personalized medical management of athletes by ensuring the safe, legal and effective use of medications and supplements (88). Sport pharmacists provide evidence-based guidance on drug use, doping regulations and personalized supplementation strategies that align with the unique metabolic profile and sport-specific demands of an athlete. By integrating sport-pharmacy into the multidisciplinary approach of sports medicine, athletes receive tailored pharmacological support that enhances performance, promotes recovery, and ensures compliance with anti-doping standards (88,89). In cases of chronic conditions, such as exercise-induced asthma, cardiovascular anomalies, or metabolic disorders, personalized interventions involve pharmacogenomic testing to determine the most effective and least disruptive treatments (90). Monitoring biomarkers for inflammation, oxidative stress and immune function helps in adjusting therapeutic protocols and dietary plans to enhance resilience and recovery (70,91-94). Additionally, AI-driven predictive models support the early detection of potential health risks, allowing for proactive management strategies tailored to the needs of each athlete (95,96).

Advancements in technology have introduced new tools, such as wearable sensors, portable analyzers, and AI-driven data analytics, which facilitate real-time performance

monitoring and injury risk assessment (12,13,73). These innovations contribute to precision sports medicine by leveraging systems biology approaches, including genomics, proteomics, and metabolomics, to tailor interventions based on an athlete's unique genetic and phenotypic profile (41,74). For example, genotype/phenotype analysis using WGS and polygenic risk scores helps identify traits related to endurance, muscle performance and injury susceptibility, allowing for customized training programs (34,35,41,97-99).

In conclusion, the integration of network analysis, machine learning and AI-based pattern recognition further enhances predictive modeling in sports science. AI-driven injury prediction models utilize biomechanics, genetic markers, and training load data to minimize risks, while real-time feedback from wearable devices informs adjustments in training intensity and recovery strategies (100-102). By embracing a multidimensional approach that synthesizes physiological, biochemical, genetic and environmental data, sports science continues to advance towards a more personalized, data-driven framework. This approach not only improves performance outcomes, but also promotes longevity and resilience in athletes, ensuring that they can sustain peak performance while minimizing health risks.

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AT conceptualized and designed the study. MS, PF, ER, SB, IF, EV, NT, AEN and ET engaged in the acquisition, analysis and interpretation of data from the literature, and were also involved in the drafting and finalization of the manuscript. All authors were involved in critical revisions of the intellectual content. All authors have read and approved the final manuscript. Data authentication is not applicable.

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