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Pediatric Sarcopenia: What do We Know?

Sarcopenia Pediátrica: O que Sabemos?

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ABSTRACT

Pediatric sarcopenia is an emerging health issue that affects muscle development, strength, and overall well-being in children and adolescents. While it was initially linked to aging, recent studies highlight its presence in younger populations, particularly among those with chronic conditions. This condition affects growth and neurodevelopment in the short term and is associated with an increased risk of long-term complications, namely metabolic and cardiovascular diseases. Several factors contribute to pediatric sarcopenia, including inadequate prenatal nutrition, low birth weight, genetic susceptibility, insufficient dietary protein intake, sedentary behaviors, obesity, metabolic imbalances, and chronic illnesses. Reduced muscle mass impairs bone health, delays growth spurts, and affects physical performance, which may result in a lower quality of life. In children with chronic diseases, sarcopenia exacerbates clinical outcomes, prolongs hospital stays, and increases the likelihood of complications. Diagnosing sarcopenia in children is complex due to differing growth patterns. Existing assessment methods, such as imaging techniques and body composition analysis, lack standardized reference values tailored to pediatric populations, which makes early detection challenging. Preventive strategies emphasize physical activity, especially resistance exercises (muscle strengthening), reduced screen time, improved dietary habits, and sleep hygiene. Innovative treatments are being explored, including targeted drug delivery to the muscle to minimize side effects, regenerative approaches utilizing nanoparticles, and myostatin inhibitors for stimulating muscle growth. Stem cell therapy and biomaterial-based muscle reconstruction are also under investigation; however, pediatric-specific therapeutic guidelines remain undefined. Early intervention is crucial for reducing its negative effects and fostering healthier developmental paths.
Keywords: Child; Sarcopenia/diagnosis; Sarcopenia/etiology; Sarcopenia/prevention and control

RESUMO

A sarcopenia pediátrica é um problema de saúde emergente que afeta o desenvolvimento muscular, a força e o bem-estar geral em crianças e adolescentes. Embora inicialmente associada ao envelhecimento, estudos recentes destacam a sua presença em populações mais jovens, especialmente entre aqueles com doença crónica. Esta condição afeta o crescimento e o neurodesenvolvimento a curto prazo, estando associada a um maior risco de complicações a longo prazo, nomeadamente doenças metabólicas e cardiovasculares. Diversos fatores contribuem para a sarcopenia pediátrica, incluindo uma nutrição pré-natal inadequada, baixo peso ao nascimento, suscetibilidade genética, ingestão insuficiente de proteínas na dieta, estilo de vida sedentário, obesidade, desequilíbrios metabólicos e doenças crónicas. A redução da massa muscular compromete a saúde óssea, atrasa o pico de crescimento e afeta o desempenho físico, o que pode levar a uma redução da qualidade de vida. Em crianças com doenças crónicas, a sarcopenia agrava o prognóstico, prolongando o internamento hospitalar e aumentando a probabilidade de complicações. O diagnóstico da sarcopenia em crianças continua a ser complexo devido aos padrões de crescimento variáveis. Os métodos de avaliação disponíveis, como as técnicas de imagem e a análise da composição corporal, carecem de valores de referência padronizados adaptados às populações pediátricas, o que dificulta a deteção precoce. As estratégias preventivas enfatizam a atividade física, especialmente os exercícios de resistência (fortalecimento muscular), juntamente com a redução do tempo de ecrã, a melhoria dos hábitos alimentares e a higiene de sono. Tratamentos inovadores estão a ser desenvolvidos, incluindo medicação dirigida ao músculo para minimizar os efeitos secundários, abordagens regenerativas utilizando nanopartículas e inibidores de miostatina para estimular o crescimento muscular. O uso da terapia com células estaminais e com biomateriais para reconstrução muscular também está a ser estudado, mas as normas de orientação clínica específicas para pediatria ainda não estão definidas. A intervenção precoce é crucial para mitigar os seus efeitos adversos e promover trajetórias de desenvolvimento mais saudáveis.
Palavras-chave: Criança; Sarcopenia/diagnóstico; Sarcopenia/etiologia; Sarcopenia/prevenção e controlo

INTRODUCTION

Skeletal muscle is the most abundant tissue in the human body and plays vital physiological roles, including maintaining posture, facilitating locomotion, and supporting metabolic homeostasis. It serves as a reservoir for amino acids and triglycerides, with approximately 25% of ingested glucose mobilized when needed for energy.[1] Additionally, skeletal muscle at rest accounts for a significant portion of energy expenditure.[2] This tissue is fundamental to metabolic processes and is closely linked to childhood development, making it a valuable tool for assessing growth and age- and sex-specific psychomotor milestones.[3]

Lean mass acquisition from birth has been linked to enhanced neurodevelopment in hospitalized low-birth-weight infants, improved brain growth in preterm infants[4] quicker neuronal processing and superior speech development by two years of age,[5] independently of prenatal, postnatal, or parental influences.[6]

Optimal muscle mass and strength development during childhood and adolescence is also critical for bone growth and the prevention of conditions such as sarcopenia and osteoporosis in adulthood.[7]

Myokines secreted by skeletal muscle can cross the blood-brain barrier, promoting neurogenesis and synaptic plasticity.[8] They also mediate communication between muscle and

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other organs (e.g., the liver and adipose tissue). Consequently, impaired muscle function can significantly impact lipid and carbohydrate metabolism, leading to increased adipose tissue, elevated inflammatory adipokines, intramuscular lipid accumulation, free radical production, and reduced mitochondrial oxidative activity.[9,10]

The detrimental effects of reduced muscle mass in children have been documented across neurological, metabolic, and skeletal domains.[11–14]

Pediatric sarcopenia is characterized by inadequate muscle development, whether in strength or function, compared to the normal physiological requirements for age, sex, and maturation stage. This condition can adversely affect growth, psychomotor development, metabolic health, and mental well-being in children and adolescents, both in the short and long term.[12,15,16]

The European Working Group on Sarcopenia in Older People, in 2019, established the diagnosis and severity of sarcopenia with the presence of low muscle strength, low muscle quantity and low physical performance (handgrip strength by dynamometry and/or chair test).[17]

Although initially focused on the elderly, sarcopenia has emerged as a growing concern among pediatric populations, particularly in children with chronic diseases. Recently, some studies have suggested that it may also be present in asymptomatic children.[17]

Accurately assessing body composition in children and adolescents is essential for a thorough evaluation of their health, especially as it must account for growth-related changes. This approach can help identify and address potential future health issues. The aim of this review is to compile current knowledge and offer a structured overview of the existing literature on this subject.

RISK FACTORS FOR PEDIATRIC SARCOPENIA

Risk factors for pediatric sarcopenia encompass a broad range of prenatal and postnatal influences, as well as underlying medical conditions. Prenatal factors include maternal nutrition during pregnancy and genetic predisposition. Postnatal contributors include inadequate protein intake, physical inactivity, sedentary behavior, and hormonal imbalances and insufficient sleep.[17] In addition, chronic diseases, metabolic disorders (such as obesity and insulin resistance), and neuroendocrine or neuromuscular conditions may also play a significant role in the development of pediatric sarcopenia (Fig. 1).

Barker's hypothesis posits that fetal growth and development are programmed by the intrauterine environment and maternal lifestyle.[18] Maternal malnutrition during pregnancy reduces the size and density of muscle fibers in mammals.[18] This effect extends beyond fetal life, as studies show that individuals born with low birth weight exhibit impaired muscle growth[19] and reduced handgrip strength, persisting into their 30s.[20] A meta-analysis of 13 longitudinal studies with over 20 000 participants also found a link between birth weight and future muscle strength, where each kilogram of birth weight corresponded to an additional 0.86 kg of muscle strength from ages 9.3 to 67.5 years.[21]

Physical inactivity is a critical factor in muscle loss postnatally. For example, one week of bed rest can result in a 3% loss of thigh muscle mass, while three months of inactivity can reduce quadriceps and gastrocnemius and soleus muscle volume by 30%.[22] A sedentary behavior combined with an unhealthy diet is also an independent risk factor for sarcopenia in youth.[23]

Metabolic syndrome (characterized by obesity, hypertension, hyperglycemia, and dyslipidemia) has been

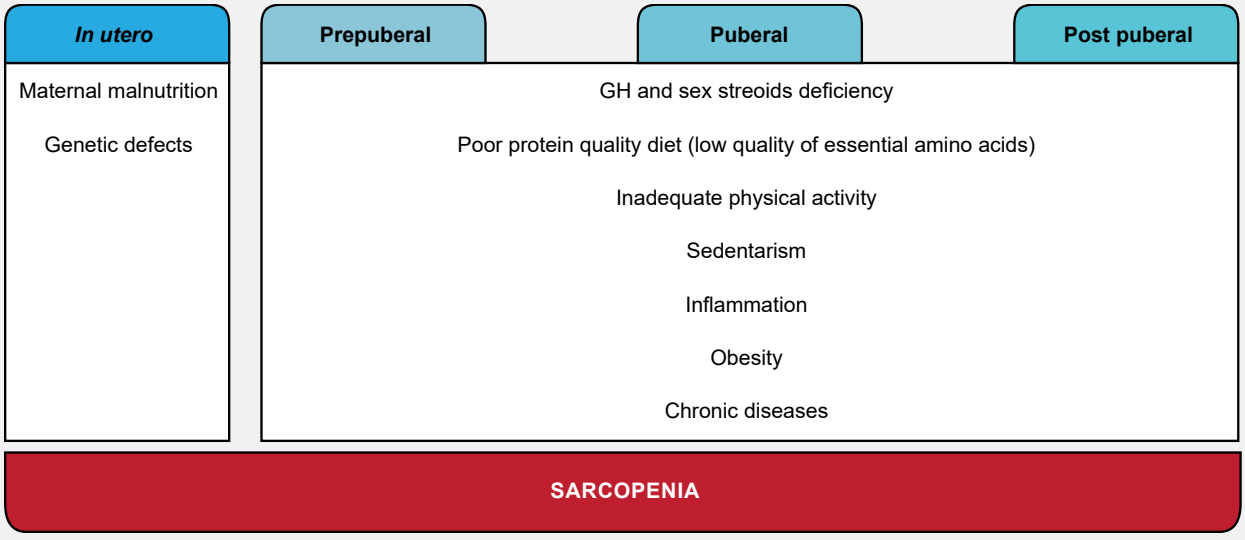

Figure 1 – Factors promoting sarcopenia during childhood and adolescence

identified as a risk factor for sarcopenia in children and adolescents.[24,25] Hyperinsulinemia associated with metabolic syndrome promotes protein degradation and inhibits protein synthesis.[26] Insulin resistance further increases myostatin production, a growth differentiation factor (GDF-8) that negatively regulates muscle growth by reducing muscle mass and suppressing growth hormone (GH) production.[27]

Obesity contributes to muscle mass reduction by promoting fat accumulation within and around muscles, impairing satellite cell function and myoblast proliferation[28] and adipocytes exacerbate muscle loss by inducing systemic inflammation.

Chronic diseases are a major risk factor for pediatric sarcopenia, acting through mechanisms such as reduced protein synthesis, accelerated catabolism, inflammatory cytokine production, nutritional deficits, corticosteroid therapy, and physical inactivity.[29,30]

Genetic factors, including hereditary conditions affecting muscle metabolism (e.g., neurodegenerative diseases) or endocrine function (e.g., congenital hypothyroidism, type 1 diabetes, hypogonadism, hypopituitarism), are also significant contributors.[31]

Inadequate sleep (quality or quantity) is another risk factor, as sleep is essential for growth and muscle recovery. Sleep deprivation can impair muscle function, increase injury risk, and contribute to chronic inflammation, insulin resistance, and reduced physical activity, all promoting muscle loss.[32]

The gut microbiome plays a crucial role in muscle health by influencing nutrient absorption, inflammation, and energy metabolism. A balanced microbiome improves insulin sensitivity, enhances muscle glucose uptake, and reduces inflammation. Conversely, dysbiosis can lead to systemic inflammation and insulin resistance, which in turn contribute to muscle loss. Promoting a healthy microbiome through a fiber-rich diets and probiotics may help prevent pediatric sarcopenia.[33]

The ongoing pandemic of sedentary behavior in childhood exacerbates sarcopenia, obesity, and sarcopenic obesity (which is more severe than either condition individually).

THE IMPACT OF SARCOPENIA IN CHILDREN AND ADOLESCENTS

Growth

Normal growth depends on multiple factors (genetic, hormonal, nutritional, and environmental) and reflects the health and well-being of children or adolescents.[34]

Growth and maturation depend on available energy levels and the regulation of energy homeostasis, with muscle and adipose tissue playing a crucial role in this process.[35] Most researchers focus on linear growth (height change over time), but changes in body composition and regional fat distribution are key for growth and sexual maturation.[36] Assessing cardiovascular risk in adults strongly depends on regional fat distribution (especially abdominal). The precursors of adult fat distribution patterns are present in adolescents and, in some cases, even in younger children.

Adipose tissue and body mass index (BMI) are inversely related to sexual maturation (onset of secondary sexual characteristics, due to the activation of the hypothalamic-pituitary-gonadal axis) and somatic maturation (pubertal growth spurt).[37,38] In other words, a higher BMI in a prepubertal child is associated with an earlier onset of the growth spurt but a reduced overall magnitude of the pubertal growth spurt.[38] If a child has a body composition with a deficit in muscle mass (risk of sarcopenia), the peak growth velocity in height will be lower and occur later than in obese children for both sexes.[37] In sarcopenic individuals, insufficient musculature may compromise the child's or adolescent's growth and final adult height.[39]

Bone development

During childhood and adolescence, muscle development occurs alongside bone tissue differentiation, and several observational studies have shown a positive correlation between muscle mass, strength, and bone parameters: bone mineral density (BMD), bone mineral content (BMC), and bone area.[40-42] This association can be explained by the mechanostat theory, which posits that bone mass and geometry adapt to the mechanical loads imposed by muscle force.[40] Muscles generate mechanical loads on bones during contraction, promoting bone formation (osteoblasts) and preventing bone loss (osteoclasts). In sarcopenia, this mechanical traction is reduced, decreasing the stimulus for bone remodeling and resulting in lower BMD.[43]

Lean mass significantly influences bone development and co-determines the peak bone mass maintained throughout adulthood,[44] potentially contributing to osteosarcopenia. The effect of muscle mass and strength variation (mechanical load) on bone mass is well known. Several studies have demonstrated that 40% of postnatal bone development is determined by muscle development.[45] Ensuring the maintenance of excellent muscle mass during childhood and adolescence contributes to peak muscle and bone strength and has beneficial effects on the cardiovascular system and overall health in adulthood.[12]

Physical development

Evidence shows that suboptimal muscle development, known as the sarcopenic-like phenotype, affects children's physical development.

Sarcopenia increases the risk of injury and contributes to sedentary behavior. It reduces physical activity levels,

impacting musculoskeletal health and development. Children with sarcopenia often face difficulties in daily activities like running, jumping, or playing, which are vital for physical and social development. Physical inactivity worsens muscle strength and mass loss, creating a vicious cycle.

Consequences for physical activity, quality of life and general health

Sarcopenia significantly affects quality of life, leading to social difficulties, exclusion, and frustration due to physical limitations. This can result in isolation, low self-esteem, and poorer academic and social performance. Reduced participation in physical activities is linked to higher anxiety and depression symptoms.[46] Severe sarcopenia can cause difficulties in basic motor activities, leading to reduced cardiopulmonary performance and increased sedentary behavior, which exacerbates the condition.[47]

Sedentary behavior, even with low physical activity, is associated with adverse health outcomes: reduction of insulin sensitivity that contributes to fat accumulation in the liver, proxy of metabolic syndrome and type 2 diabetes.[48] Sarcopenia is associated with an unfavorable metabolic profile (measured by high-density lipoprotein, low-density lipoprotein cholesterol, and/or triglycerides) and hypertension, increasing the risk of premature cardiovascular disease.[14]

Patients with chronic disease

Sarcopenia worsens the prognosis of patients with chronic diseases, leading to more comorbidities, prolonged hospitalization, higher risk of complications (e.g., nosocomial infections), and increased mortality.[49]

In oncology**,** patients with acute lymphoblastic leukemia manifest a significant decrease in lean muscle mass early in

Table 1 – Summary of commonly used techniques for sarcopenia assessment in pediatrics

Methods	Components measured	Strengths	Limitations
Skinfold	Subcutaneous fat surrogate measure of muscle mass	Inexpensive. Noninvasive. Simple to perform.	Intraobserver and interobserver variability. Prone to errors in obese children and children with edema.
BIA	Fat mass, fat-free mass	Inexpensive. Quick and simple to perform. Noninvasive.	Potential errors due to altered hydration. Underestimates total body fat in leaner children and overestimates in obese.
DXA	Fat mass, lean mass, tissue mass, bone mineral content and density	Precise. Validated against MRI and with equation to determine skeletal muscle mass (SMM).	Trained technician required. Potential errors due to altered hydration (less than BIA). With anthropometric limitations (200 kg and 197 cm). Low dose of radiation.
MRI		Gold standard. No radiation. Precise.	High cost. Trained technician required. Lack of normative data (especially for healthy subjects).
CT	Total, subcutaneous, intramuscular, visceral and adipose tissue, SMM	Gold standard. Very precise. Normative data.	High cost. Trained technician required. Radiation.
Ultrasound		Quick. Portable. No radiation. Inexpensive.	Lack of normative data for pediatric population.
Total body potassium	Total body water	Gold standard to estimate fat-free mass. Easy to carry out. Suitable for infants and toddlers.	Expensive equipment. Labor intensive for analysis.
D3-creatine dilution(63)	Total body muscle mass	Noninvasive. Can be used in premature infant	Risk of overestimation. Lack of normative data.

treatment.[50] Adverse events are more common in sarcopenic cancer patients, and this condition significantly reduces the patient's quality of life[51] and the prognosis of the disease.

Sarcopenia is more harmful when combined with obesity than obesity alone.[52] Sarcopenic obesity is becoming increasingly important in the pediatric population due to rising childhood obesity rates linked to sedentary behaviors.[53] Obesity is often underdiagnosed in children because they may appear to have a normal weight while having reduced muscle mass.

Increased adipose tissue exacerbates sarcopenia through lipotoxicity to muscle cells.[54] This condition maintains a moderate pro-inflammatory state, with cytokine secretion and activation that affects muscle cell proliferation and differentiation.[55] Muscle neural activation also seems impaired in obese children compared to non-obese children.

In patients with severe chronic diseases, detecting sarcopenia helps monitor disease progression and improve prognosis by reducing complications.

DIAGNOSTIC METHODS AND THEIR LIMITATION

Currently, there is no standardized method for diagnosing sarcopenia. In children, muscle mass has been assessed using various methods, including anthropometry,[56] ultrasound,[57] bioelectrical impedance analysis (BIA),[58] DXA,[3] computed tomography (CT),[59] magnetic resonance imaging (MRI),[60] plethysmography,[61] creatinine excretion,[62] total body potassium,[63] and neutron activation (Table 1).[64] Despite this variety, there is no consensus on diagnostic criteria for sarcopenia.

Diagnosing sarcopenia in children is particularly challenging due to the varying rates of muscle growth and development, influenced by age, pubertal growth spurts, and biological maturation, which differ significantly even among peers of the same age group. These factors make it difficult to establish accurate cutoff values for identifying sarcopenia in children and adolescents.

Signs of sarcopenia in children are often subtle and may not become apparent until significant muscle mass and function are lost. More sensitive methods are needed to detect early-stage pediatric sarcopenia.

PREVENTION OF SARCOPENIA IN CHILDREN AND FUTURE DIRECTIONS

The incidence of pediatric sarcopenia is rising due to sedentary behavior, particularly from excessive screen time. Without early intervention, it may progress to sarcopenic obesity, increasing the risk of metabolic and cardiovascular diseases. Early intervention prevents both short- and long-term complications (reduces the risk of sarcopenia in adulthood, promoting healthier aging).

The consequences of sarcopenia affect physical growth, development, and health. Prevention and early detection are the best approaches for effective treatment and reducing public health costs. Nutritional interventions and exercise programs are most effective when starting early (Table 2).

Educating parents and healthcare professionals is essential to prevent, detect, and manage sarcopenia in children and adolescents. Informed parents and professionals can recognize early signs of sarcopenia, such as muscle weakness, fatigue, and loss of muscle mass, and risk

Table 2 – Preventive measures to reduce the risk of sarcopenia in children and adolescents

Preventive measure	Recommendation
Regular physical activity	At least 60 minutes/day of moderate to vigorous physical activity. Include resistance exercises (e.g., jumping rope, squats, push-ups) 2 - 3 times per week. Bone-strengthening activities (e.g., running, jumping, sports) at least 3 times per week.
Limiting sedentary behaviors	Reduce screen time to less than 1 hour per day. Encourage frequent active breaks (e.g., walking, stretching) and outdoor play.
Balanced diet	Ensure adequate high-quality protein intake (e.g., meat, fish, eggs, beans, dairy) and essential nutrients (vitamins D, B complex, calcium, iron, antioxidants) to support muscle growth and repair.
Education on healthy habits	Promote awareness of physical activity and nutrition among children, parents, and caregivers to establish lifelong health behaviors.
Active play & sports	Encourage participation in structured and unstructured physical activities to stimulate musculoskeletal development and improve coordination and motor skills.
Adequate sleep	Ensure 9 - 11 hours of sleep per night (ages 5 - 13) and 8 - 10 hours (ages 14 - 17) for optimal muscle recovery, growth, and hormone regulation.

factors like sedentary behaviors or poor diets.

Parents should implement healthy practices at home, such as balanced diets and regular physical activity. Healthcare professionals must be well-informed to provide specific guidance to parents during routine check-ups and in cases of hospitalization. This knowledge enables early detection and referral to specialized services, such as physiotherapy, exercise physiology, and nutritional support, ensuring targeted interventions that improve the quality of life for affected children.

With informed parents and healthcare professionals, the number of cases advancing to critical stages is reduced, lowering the need for complex interventions and reducing healthcare system costs.

Further research on age-appropriate muscle mass and reference values for body composition at each stage of development is necessary for accurate health assessments in children and adolescents.

FUTURE PERSPECTIVES

Due to the multifactorial nature of sarcopenia, there is an urgent need to develop validated biomarker panels for clinical use in both children and adults. Currently, inflammatory markers like TNF-alpha and IL-6 and others like testosterone, GH, creatinine, and carnitine are used.[65]

Genomic studies have identified certain sequences linked to an increased risk of sarcopenia, such as the *rs34415150* variant of *HLA-DQA1*, *rs143384* of *GDF5*, and *rs62102286* of DYM.[66] Additionally, in sarcopenic patients, genes like *MT1X* and ARHGAP36 have shown higher diagnostic precision compared to *FAM171A1, GPCPD1, ZNF415*, and *RXRG*, indicating their potential as predictive markers for early screening.[67] Circulating microRNAs (e.g., microRNA-1, microRNA-29a, microRNA-29b) have also been observed in patients with reduced physical performance.[68]

Regarding treatment, there are new developments like delivering medication directly to the muscle, minimizing metabolization in other organs and reducing side effects. For example, we have the generation 5 polyamidoamine dendrimer (G5-PAMAM), a peptide for cell and gene therapy in sarcopenia.[69] Other research groups are developing nanoparticles for muscle regeneration,[70] myostatin inhibition via iontophoresis,[71] transdermal testosterone,[72] mitochondrial antioxidants (MitoQ 90), and exosome-based systems.[73]

Mesenchymal stem cell therapies derived from various tissues (e.g., umbilical cord, bone marrow, adipose tissue) are being explored to improve stem cell proliferation, angiogenesis, and differentiation via paracrine signaling and/or immune modulation.[74] Transplanting these cells into sarcopenic individuals may enhance musculoskeletal health by restoring cellular function and reducing inflammation.[75]

With advances in regenerative medicine, research is also being conducted into replacing muscle with natural polymers, synthetic polymers or hybrid materials that mimic the mechanical and morphological characteristics of muscle tissues.

There is still a lack of consistent studies regarding the most appropriate treatment for pediatric sarcopenia, including dosage, treatment duration, and expected side effects. The mechanisms and risk factors for sarcopenia in children, as well as its long-term impact on children, adolescents, and young adults, are not fully understood.

CONCLUSION

It is critical to establish universal criteria for assessing body composition in children and adolescents, including reference values for muscle mass and strength.

Integrating body composition assessments into routine pediatric consultations, combined with early intervention, is essential to mitigate the long-term impact of sarcopenia. Longitudinal studies and the inclusion of diverse populations are crucial for defining more effective diagnostic and treatment strategies.

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AUTHOR CONTRIBUTIONS

MM: Writing of the manuscript.

FB: Critical review of the manuscript.

All authors approved the final version to be published.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

ETHICS

Ethical approval is not required for this review as it is a secondary study based on public and published data.

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