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CVD risk factors

Lifestyle interventions to change trajectories of obesity-related cardiovascular risk from childhood onset to manifestation in adulthood: a joint scientific statement of the task force for childhood health of the European Association of Preventive Cardiology and the European Childhood Obesity Group

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Abstract

There is an immediate need to optimize cardiovascular (CV) risk management and primary prevention of childhood obesity to timely and more effectively combat the health hazard and socioeconomic burden of CV disease from childhood development to adulthood manifestation. Optimizing screening programs and risk management strategies for obesity-related CV risk in childhood has high potential to change disease trajectories into adulthood. Building on a holistic view on the aetiology of childhood obesity, this document reviews current concepts in primary prevention and risk management strategies by lifestyle interventions. As an additional objective, this scientific statement addresses the high potential for reversibility of CV risk in childhood and comments on the use of modern surrogate markers beyond monitoring weight and body composition. This scientific statement also highlights the clinical

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importance of quantifying CV risk trajectories and discusses the remaining research gaps and challenges to better promote childhood health in a population-based approach. Finally, this document provides an overview on the lessons to be learned from the presented evidence and identifies key barriers to be targeted by researchers, clinicians, and policymakers to put into practice more effective primary prevention strategies for childhood obesity early in life to combat the burden of CV disease later in life.

Keywords Childhood obesity • Prevention • Cardiovascular risk trajectories • Lifestyle

Introduction

Obesity is currently one of the most serious global public health problems. There is robust evidence that metabolic and cardiovascular (CV) risk factors and psychosocial complications are already present in children with obesity and worsen in adulthood.[1–5] Childhood obesity is commonly defined as body mass index >95th percentile for age and sex in children older than 2 years of age.[6] Between 1980 and 2013, the worldwide prevalence of childhood obesity increased by 47%.[7] The WHO European Childhood Obesity Surveillance Program revealed that overweight and obesity rates among primary school children range from 15% to 52% in boys and from 13% to 43% in girls, with higher prevalence in southern European countries.[8] The lifetime costs of a child or adolescent with obesity have previously been estimated to be about €150 000 for both sexes.[9]

Obesity is associated with an increase in CV risk factors in children.[10,11] The rise in childhood obesity has subsequently been linked to an increase in non-communicable diseases such as type 2 diabetes mellitus (T2DM),[12] hypertension,[10] and atherosclerosis as target organ damage in young men.[13] A body of evidence exists on obesity-related CV risk in childhood, for example, higher systolic blood pressure (BP) in children with overweight (+4.5 mmHg) and obesity (+7.5 mmHg), with signs of adverse concentrations of blood lipids and higher left ventricular mass compared with normal weight children.[10] The number of risk factors increases with severity of childhood obesity.[11] The high prevalence of childhood obesity is worrying at the individual as well as public health level, as it has been linked with CV morbidity and mortality in adulthood.[3,14,15] Because of the persistent high prevalence rates and the risk trajectories into adulthood, it is important to reduce CV risk as early as childhood. As key determinants, childhood physical inactivity and unhealthy diet contribute to the development of obesity-related CV risk, and thus to the development of non-communicable diseases later in life.

In this document, we briefly review the aetiology of childhood obesity and current approaches for its management. The novel focus lies on the discussion of obesity-related risk trajectories from childhood to adulthood and on the need for childhood screening programs and consecutive preventive strategies. As a main aim, both physical activity (PA) and exercise as well as nutrition behaviour and diet are extensively reviewed as key risk managing strategies. This scientific statement does not intend to systematically review previous meta-analyses or international guidelines on the management of childhood obesity. Rather, it aims at giving expert insights on how obesity-related childhood CV risk may need to be approached in order to change risk trajectories as primary prevention strategies to reduce the high burden of CV disease.

Aetiology and management of obesity-related cardiovascular risk in childhood

Beyond caloric imbalance—the environment and biological factors

Obesity-related CV risk is caused by a complex interplay between genetic factors and the environment (*Figure 1*). Individual genetic predisposition, epigenetics, endocrine, metabolic, and immunologic responses interact with the child's nutrition, PA, sleep habits, and psychological factors.[16] Later in life, an association of genetic susceptibility and healthy lifestyle with incidence coronary artery disease and stroke has been shown in patients with hypertension.[17]

During early gestation, maternal diet and environmental factors can, for example, modify methylation status and thereby gene expression.[18] Even before conception, both maternal and paternal health and lifestyle behaviour affect the epigenetic phenotype of the offspring with potential consequences for the gestational development.[19,20] Moreover, psychological factors and the interaction between gut and brain hormones influence satiety mechanisms.[21] The gut microbiota and exposure to toxins and viruses contribute to the development of obesity. In addition, the so-called industrially produced endocrine-disrupting chemicals appear to be obesogenic.[22] Thus, the underlying mechanisms for the development of obesity in childhood are complex and need to be accounted for in future obesity prevention policies. Importantly, medical history needs to be considered and plays an important role in the detection of other causes of obesity, such as hormonal disturbances or specific antipsychotic medication.

Role of parents, socioeconomic status, and education

The role of family, caregivers, and peers in the development and maintenance of obesity in children is crucial. Several complex biological and social interactions between parent and child need to be considered. Maternal body mass index (BMI) at conception strongly predicts offspring BMI throughout childhood.[23] Prenatal maternal lifestyle, parenting style, feeding habits in early childhood, and family nutrition habits are important factors to help foster a healthy lifestyle and promote awareness of internal hunger and satiety cues.[24] Breast-feeding may also play a central role for obesity risk reduction, interacting with psychosocial and environmental factors.[25,26] Maintenance of a healthier diet was achieved in studies that specifically targeted parenting, modification of home environment, and behavioural constructs.[27]

Unhealthy food habits and low PA levels, as assessed by sedentary behaviours such as screen time, have been associated with low familial socioeconomic status and varying quality of child care.[28–30] Maternal, and not paternal, psychiatric symptoms have been shown to be associated with the severity of obesity in their offspring.[31] Implementing healthy lifestyle in the education of children is challenged by an irritable or reactive temper in children with overweight and obesity, which may be accompanied by anxious feelings, depressed mood, psychosomatic complaints or impulsive behaviour, aggression, and oppositional behaviour.[32]

Media (mis-)use, role models, psychological aspects

Unhealthy food marketing in media and social media is a powerful determinant of unhealthy diets and obesity among children and adolescents.[33] Foods embedded in entertainment media affect food choices and food intake in children. In addition to high caloric value, most of the embedded foods have low nutritional values. Most children are exposed to promotion and marketing of products such as fast food and sugar-sweetened beverages up to about 200 times per week on social

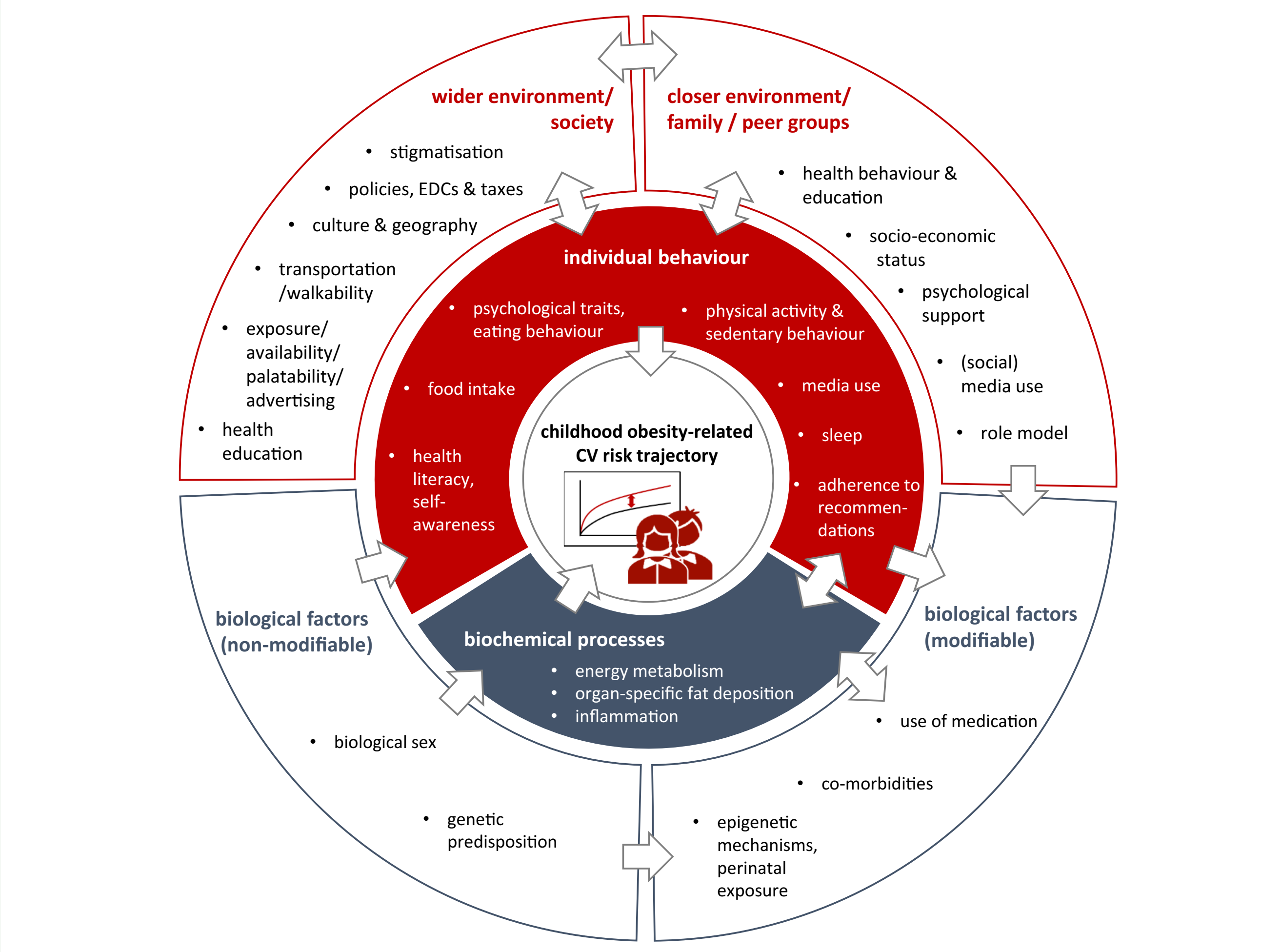

Figure 1 Aetiology of obesity-related cardiovascular risk highlighting the complex interplay between societal, psychological, environmental and biological factors. CV, cardiovascular; EDCs: industrially produced endocrine-disrupting chemicals.

media.[34] Of note, social media influencer marketing of unhealthy foods increased children's immediate food intake, whereas the equivalent marketing of healthy foods had no effect.[35] Therefore, promotion of healthy foods on social media may not be an effective means to improve healthy dietary behaviours in children. An association of fast-food consumption with adverse blood lipids and vascular impairments has been shown in adults but to a much lesser extent children, indicating the opportunity for primary prevention in childhood.[36]

Beyond PA and nutrition, psychological aspects are often associated with health status of children with obesity and should be addressed in prevention and lifestyle interventions. Individuals with obesity often experience social stigma in multiple settings, including the medical community.[37] Such stigmata may lead to serious physical and psychological consequences (for example, promoting obesity, eating disorders, stress and depression, and barriers to PA) and less frequent use of adequate medical care. Addressing weight stigma is therefore important to improve health and well-being in children with obesity.[38]

Management: what the guidelines say

Clinical guidelines recommend that lifestyle changes should be the initial step for the management of obesity and CV risk factors in children.[6] An overview of the classic cardiometabolic risk factors associated with childhood obesity and their definitions are shown in *Table 1*. Recommended targets for PA levels for school-age youth have been defined as ≥60 min/day of moderate to vigorous aerobic PA (MVPA). In addition, muscle strengthening and activities that increase bone strain are to be implemented at least three times per week. The time being sedentary, particularly the amount of screen time, should be limited.[39,40] With respect to diet, the guidelines recommended that children consume ≤25 g (100 kcal or ≈6 teaspoons) of added sugars per day.[41] Few children achieve such low levels, making this an important public health target. With respect to sodium intake, the WHO has recommended that children aged 2–15 years should reduce their intake to better control BP. Based on the estimated energy requirements of children compared with adults, the recommended adult sodium intake of a maximum level of 2 g sodium (5 g salt) per day should be adjusted downward.[42] According to the United Nations Children's Fund,[43] main other dietary advice are: eat an adequate breakfast, avoid eating between meals, eat three meals and no more than two snacks per day, limit portion sizes, avoid energy-dense and nutrient-poor foods (for example, fruit juices, or fast food), and increase intake of unprocessed fruit, vegetables, and fibre-rich cereals. Also, lowering fat and sugar intake should be main targets.[44,45]

Table 1 Definition and thresholds of childhood cardiometabolic risk factors

Cardiometabolic risk factors	Definition
Overweight and obesity	• Age- and gender-specific percentile curves based on national reference population *or* • Cut-off values for overweight and obesity according to International Obesity Task Force, World Health Organization, or Center for Disease Control
Hypertension	• 0–15 years: ≥95th percentile for SBP and DBP (according to sex-age-height-specific percentiles) • 16 years and older: ≥140/90 mm Hg (SBP and/or DBP values)
Dyslipidaemia	• Total Cholesterol ≥200 mg/dL • Low-density lipoprotein cholesterol ≥130 mg/dL • High-density lipoprotein cholesterol <40 mg/dL • TG ≥100 mg/dL <9 years • TG ≥130 mg/dL ≥10 years
Hyperglycaemia	• Fasting blood glucose ≥100 mg/dL *or* • Glycated hemoglobin ≥5.7%
Physical inactivity	• < 60 min/day moderate/vigorous physical activity • sedentary behaviour ≥2 h/day

SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride.

Early implementation of family-based multicomponent behavioural interventions with a minimum of 26 contact hours for children and adolescents with overweight and obesity aged 2–18 years is recommended.[46] However, there is insufficient evidence to recommend specific forms of interventions with respect to comparative effectiveness in patients and families with different socioeconomic backgrounds.[46] Recommendations for patient care and frequency of risk factor monitoring in children with established CV risk, such as hypertension, T2DM, and dyslipidaemia, have been expressed in previous international guidelines.[6,46–48]

The American Academy of Pediatrics has proposed different treatment strategies dependent upon the severity of obesity. This includes treatment for children or adolescent with overweight or obesity that can be delivered in primary care or a community-based setting, and intensive multicomponent interventions, pharmacotherapy and/or bariatric surgery delivered to adolescent with obesity or severe obesity in secondary or tertiary settings.[26,49] For severe obesity and T2DM in children over the age of 10, metformin has been shown to be beneficial for the treatment of insulin resistance and to support weight loss.[50] Orlistat (Food and Drug Administration approval) and liraglutide (European Medicines Agency approval) may also be considered as adjunct treatment in addition to lifestyle modifications in children with obesity older than 12 years.[6,51] For adolescents with a BMI greater than 35 kg/m^2, bariatric surgery in combination with lifestyle modifications may be considered,[6] but there are no data from randomized controlled clinical trials (RCTs) on the effectiveness of bariatric surgery in this age group.[52] An RCT comparing bariatric surgery to combined lifestyle interventions in adolescents is still ongoing.[53]

Risk trajectories from childhood to adulthood

The impact of CV risk factors such as obesity and hypertension on the development of CV disease and outcome are well understood in the adult population. These causal factors for an increased CV disease risk are already present in children and adolescents and are key determinants of adult health. A recent systematic review, which included more than 100 000 individuals, reported that children with excess weight had higher risk for T2DM, hypertension, and dyslipidaemia as an adult.[54] Decreasing PA and persistent inactivity have been shown to predict adult obesity and associated CV risk profiles.[55,56]

Children with obesity are five times more likely to suffer from obesity as adults compared with those without childhood obesity.[57] Childhood overweight and obesity are associated with a concomitant increased prevalence of elevated and high BP. The longitudinal Cardiovascular Risk in Young Finns Study showed that elevated BP in childhood tracks into adulthood.[58] Moreover, systolic BP in late adolescence was an independent predictor for coronary heart disease (CHD) in mid-adulthood.[2] In a study of 2.3 million adolescents, obesity during adolescence was associated with a substantially increased CV mortality in middle age.[3] A large cohort study in children demonstrated the association of a higher childhood BMI with an increased risk of CHD in adulthood.[15] A limitation of these studies is their retrospective design. Nonetheless, the increased obesity rate in adolescence is thought to lead to an estimated 5–16% increase in incidence CHD in 2035.[59] In a recent prospective cohort study from the International Childhood Cardiovascular Cohort (i3C) Consortium, childhood risk factors were shown to be associated with CV events in midlife.[1]

To reduce the obesity-induced accelerated CV disease risk in children, preventive interventions are essential. A meta-analysis, which assessed a total of 85 RCTs, reported that lifestyle interventions positively influenced BMI as well as systolic and diastolic BP.[60] Lifestyle interventions based on PA and nutrition in children[61,62] and adolescents[63] with overweight and obesity have previously been explored. Multicomponent behaviour-changing interventions seemed to have beneficial, albeit small effects on weight reduction in children of all age groups with low rates of adverse events.[64] Of note, mainly weight-related measures have previously been reported while information on overall health, cardiometabolic, and psychological factors are so far limited. Thus, PA and exercise as well as nutrition behaviour and diet are reviewed in this document with updated findings as potential risk managing strategies during childhood. Overall, weight loss treatment and reduction of associated overall CV risk for children and adolescents need to be better investigated, and long-term follow-up studies are necessary to better quantify and improve the health trajectory for the next generation. The principal concept and potential impact of a multi-modal screening program in childhood to reduce cumulative lifetime CV risk is visualized in *Figure 2*. The implementation of screening programs for obesity-related CV risk is discussed in the next chapter.

For children and adolescents, the consequences of the COVID-19 pandemic with lockdowns and closures of schools and sports clubs are threatening their long-term health. A review with more than 17 000 000 children, adolescents, and young adults concluded that lockdowns resulted in increased weight gain and adversely impacted food choices.[65] Physical inactivity, even before the COVID pandemic, has become a major attributable factor associated with development of childhood obesity and related CV risk factors.

Screening programs for obesity-related cardiovascular risk and surrogate markers

In childhood, the obesity-related predisposition for atherosclerosis can be non-invasively assessed by the use of structural and functional

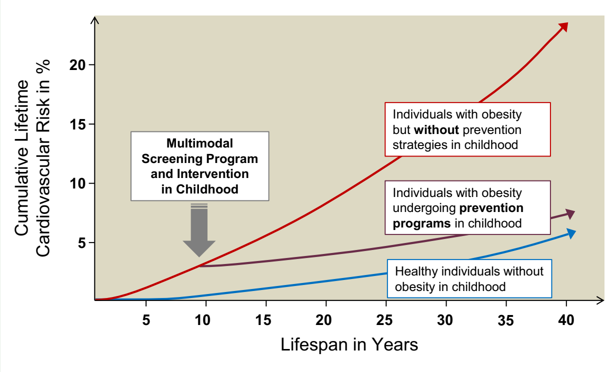

Figure 2 Call for action concept: implementation of childhood screening and prevention programs to change risk trajectories of obesity-related cardiovascular risk from childhood to adulthood.

vascular biomarkers that allow for diagnosis of subclinical atherosclerosis as cumulative surrogates for overall CV risk.[66] Childhood obesity is associated with endothelial dysfunction, irrespective of pubertal stage, even in the absence of comorbidities. Lifestyle interventions have the potential to reverse adverse vascular alterations. In children, a high reversibility of adverse CV risk was found after intensive lifestyle interventions including diet alone, exercise alone, or a combination of both.[67] Improvements were reported for body composition, metabolic parameters, brachial artery flow-mediated dilatation, and carotid intima-media thickness (cIMT).[67] Retinal arteriolar narrowing, an established microvascular biomarker of CV risk in adults, has recently been shown to predict development of high BP in 6–8 year old children after a 4 year follow-up.[68] Increases in cardiorespiratory fitness (CRF) were associated with reduction in BMI and consequently wider retinal arterioles at follow-up.[68] Use of time-efficient, affordable, non-invasive biomarkers of vascular health represents a promising perspective for the screening of cumulative CV risk in children once resilient normative data throughout childhood and adolescence have been established. In adolescent boys and girls, CRF with a maximum oxygen uptake of below 42 and 35 mL/kg/min, respectively, was associated with a 5.7 and 3.6 times greater likelihood of having CV disease risk later in life.[69] A reduced maximal oxygen uptake per lean body mass and reduced peak cycling power output are common in children and adolescents with obesity and underline the importance for the assessment of CRF in childhood screening programs and for the prescription of exercise-based prevention programs.[70]

Body mass index has been most commonly measured in previous decades as it is easily applied and most practical. Thus, a vast amount of data is available on childhood BMI percentiles and z-scores. The additional benefits of using other measures of body composition, such as waist circumference (WC), for routine paediatric care in addition to BMI for predicting metabolic risk have been shown to be small.[71] The use of waist-to-height ratio has not been shown to be superior to BMI or WC in predicting CV risk related to childhood obesity.[71] In large-scale cohort studies, BMI thus remains the most commonly used measure. Screening for clusters of CV risk factors is a challenging task in paediatric populations with difficulties in defining clear thresholds. Changing body size and weight, age-related variations in BP and lipids, as well as differences in sex and race have led to clustering of various CV risk factors as continuous variables rather than using strict cut-offs, which has been shown to be beneficial for childhood risk management.[72] Screening programs should focus on CV risk beyond BMI to avoid stigmatization. In addition, other variables such as family history, early life insults including maternal gestational diabetes exposure, as well as socio-economic status, media consumption, smoking, alcohol consumption, and drug abuse contribute to alterations in CV risk and should be accounted for in childhood and adolescence screening programs.

In adults, a nationwide screening program on obesity was associated only with small improvements in obesity and CV risk factors.[73] From a public health perspective, feasibility and long-term cost-effectiveness of childhood screening programs and interventions strategies at population level are to be established and remain challenging. A leadership role for school-based screening programs has been suggested and remains one of the most promising primary prevention strategies in a population-based approach. Nonetheless, measures of primordial prevention need to go beyond school-based screening programs and should address transport to schools and school sports as well as after-school programs and school-community linkages including participation of family and friends to promote the implementation of a healthy lifestyle. Support is warranted from paediatricians, family doctors, and healthcare workers as well as politicians and other stakeholders. However, the benefits and pitfalls, even potential harms (for example due to stigmatization) of screening programs for children with overweight and obesity, remain to be elucidated.[74] While the necessity for the prevention and treatment of obesity-related CV risk in children are not debatable, clear recommendations on how to implement cost-effective screening programs for obesity-related risk factors such as childhood hypertension and dyslipidaemia are still missing.[75,76]

Whether or not population-based screening programs have the potential to counteract the growing burden of obesity-related CV risk in childhood remains a matter of debate. Who, when, and how to screen in order to identify those at increased risk and greatest need for support remain critical questions. To this respect, cost-effectiveness will remain critical. Screening programs with a leadership role of schools, together with family- and community-based support, can be the backbone for effective prevention strategies for almost all children, independent of their socioeconomic background.

Physical activity and exercise as risk managing strategies

In this chapter, we give an overview on the evidence for exercise interventions to reduce obesity-related CV risk as a risk managing strategy including systematic reviews and meta-analyses as well as RCTs. While we appraised each endpoint individually, we used standardized mean differences (SMD) as a useful tool to summarize effect estimates (with SMD around 0.2 considered small, SMD around 0.5 medium, and SMD around or above 0.8 large).[77]

Supervised exercise interventions

A systematic review of meta-analyses on the effects of exercise-based interventions alone on health outcomes in children and adolescents with overweight or obesity showed consistent improvements in anthropometric and cardiometabolic outcomes.[78] Specifically, exercise interventions reduced body mass, BMI, fat mass, and central obesity, with overall small point estimates of effect for SMDs. These improvements were largely independent of duration of the sessions and exercise frequency, but programs cumulatively lasting a total of 1500 min or more were most effective in reducing BMI (either in absolute terms or as z-score), fat mass (%), visceral, and subcutaneous fat. The pooled SMDs were small for some cardiometabolic outcomes (CRF, and fasting concentrations of circulating triglycerides and insulin), and medium for fasting glucose concentrations, whereas there was no significant overall effect of exercise on concentrations of total cholesterol, low density lipoprotein cholesterol (LDL-C), or high density lipoprotein cholesterol (HDL-C).[78] In general, aerobic exercise training seemed to promote more beneficial changes in cardiometabolic parameters, and programs with higher intensities or volume yielded greater effects. Interventions of supervised exercise in children and/or adolescents (6–18 years old) with overweight and obesity induced significant reductions in cIMT, with a SMD of −0.31.[79]

A systematic review and network meta-analysis of randomized exercise interventions including aerobic exercise, combined aerobic and resistance exercise, as well as resistance exercise for 4 weeks or more showed that the combination of aerobic and resistance exercise was most effective in reducing BMI *z*-scores among children with overweight and obesity, with a 32% improvement.[80] Aerobic exercise alone led to a 29% improvement in BMI percentiles, with no significant effect of resistance training alone. Another meta-analysis on the effect of aerobic, resistance, and combined exercise training on insulin resistance markers showed that training in general did not induce significant reductions in fasting plasma glucose but that aerobic exercise interventions reduced fasting insulin concentrations.[81] Aerobic exercise at vigorous or moderate-to-vigorous intensities in sessions of at least 60 min showed a superior effect than lower doses of exercise. High intensity interval training (HIIT) seems to elicit even greater improvements in CRF and reductions in systolic BP compared with other forms of aerobic exercise, but with no superior effects on body composition, circulating lipids, and diastolic BP.[82] A later meta-analysis, which also included RCTs, however, concluded that there is insufficient evidence to determine if HIIT is more effective than traditional continuous endurance training with moderate intensity.[83] In the future, exergaming strategies may be used to guide children and adolescents to engage in more PA and exercise. A previous systematic review examined the potential role of exergames in improving weight status among overweight and obese children and adolescents.[84] There may be positive effects of active video games on weight-related outcomes in obese children and adolescents. However, available studies are limited in number and diversity. More research and high-quality studies are warranted to further explore the potential of exergaming in children and youth.

Exercise interventions combined with other lifestyle interventions

A meta-analysis on the efficacy of exercise interventions, alone or combined with other lifestyle interventions in adolescents (aged 10–19 years) with BMI ≥85th percentile, showed improvements in CRF, BMI, body mass, total lean mass, body fat percentage, systolic BP, insulin resistance, and glycaemic responses to an oral glucose tolerance test.[85] The SMD for these outcomes ranged from trivial (total lean mass: 0.10) to large (CRF: 1.27). There was inconclusive evidence for effects of exercise interventions on total cholesterol, LDL-C, HDL-C, fasting insulin, or fasting blood glucose concentrations. Interventions with exercise, or advice on PA and/or diet, reduced hepatic fat content among adolescents (aged 14–16 years) with obesity, with an absolute reduction of 2%, which corresponded to a relative reduction of more than 50% of existing hepatic fat.[86] Multicomponent lifestyle interventions that included supervised exercise training also reduced the prevalence of non-alcoholic fatty liver disease (NAFLD) after the intervention, with a pooled odds ratio of changes in NAFLD prevalence of 0.38.[87] Supervised exercise-only or combinations of exercise and diet interventions reduced visceral adipose tissue in youth (aged 7–19 years) with obesity.[88] Studies focusing on only exercise had the greatest effect (SMD = −0.85), while interventions combining exercise and diet showed a pooled SMD of −0.69. Yet, there were few high-quality RCTs on diet-only interventions, and the studies to date showed a small effect (SMD = −0.23).

An umbrella review of meta-analyses on prevention and treatment of childhood obesity suggested that lifestyle interventions demonstrated small and short-term effects or no effect on body mass, and that parental involvement and reducing television time provided the greatest benefits in reducing obesity-related CV risk.[89]

School-based interventions

School-based interventions hold promise as a universal context to access and influence all children. However, the evidence for effectiveness of school-based interventions on CV disease risk factors is inconclusive. A systematic review and meta-analysis of 33 health education interventions aiming to reduce BMI in adolescents reported statistically significant, albeit small effect of the interventions on BMI *z*-score (−0.06, 95% confidence interval [CI], −0.1 to −0.03, $P < 0.001$).[90] Similar effectiveness of school-based interventions on change in BMI and BMI *z*-score was reported among primary school children.[60] Studies that showed significant effect on BMI outcomes among adolescents typically included a face-to-face component for intervention delivery in the classroom and lasted more than 12 weeks.[90] Furthermore, parental involvement accentuated the beneficial effect of interventions.[60] School-based PA programs that involved additional PA time produced small, yet significant reductions in waist circumference, diastolic BP, and circulating insulin levels among children aged 3–12 years, but with no overall effect on circulating HDL-C, LDL-C, triglycerides, and total cholesterol concentrations, or systolic BP.[91] Reductions in both diastolic and systolic BP were, however, reported after school-based lifestyle interventions.[60] Finally, the evidence is equivocal for effectiveness of school-based interventions for increased PA and reduced sedentary behaviour, with some meta-analyses reporting small, but significant effects on MVPA but not on sedentary behaviour,[92] and others reporting no effect of interventions on MVPA[93] or sedentary behaviour.[94]

Nutrition behaviour and diet as risk managing strategies

Landmark publications and meta-analyses on prevention and treatment of children and adolescents with overweight and obesity indicate that weight control may be obtained by a multicomponent intervention focused on life-long changes in dietary and PA behaviour.[86,63,62] Healthy nutrition can, for example, act as a positive epigenetic factor during the critical developmental periods with impact on outcomes in adulthood. Therefore, nutritional interventions in children with overweight or obesity, standalone or in conjunction with exercise interventions, are first-line treatment options to reduce overall CV risk in young individuals.[95,96]

Supervised nutritional interventions

The diet effect on children with overweight and obesity has been evaluated using the BMI-standard deviation score (SDS): a reduction >0.5 in a growing child correlated with better body composition and decreased CHD risk later in life.[97] In the 6 year post-intervention follow-up of the Special Turku Coronary Risk Factor Intervention Project, beneficial effects of infancy onset dietary counselling on diet quality and cardiometabolic risk factors were found to be maintained into early adulthood.[98]

Prevention of adult CHD through interventions in childhood is supported by the fact that dietary habits and food preferences are formed early in life and that family-related lifestyle and eating habits tend to be maintained throughout the life span.[99] Several studies reported that the prescription of a low caloric diet is not effective in the medium- and long-term management of obesity among children, being associated to relapses and failures, increased risk of dropout, and progression of obesity.[100] Implementation of a more intensive lifestyle intervention program with low carbohydrate- and low fat-diets has previously resulted in limited improvements in body composition and metabolic health.[101] The evidence regarding the impact of dietary interventions on obesity-related risk factors such as dyslipidaemia, hypertension, fasting hyperglycaemia, and insulin resistance is inconclusive, according to a more recent systematic review of RCTs.[102] Also, a high protein diet did not improve anthropometric measures or other CV risk factors among children with overweight and obesity.[103,104] After a weight loss program including moderate energy-restricted diet and nutritional education, decreased oxidized LDL-C levels were found in children with the greatest weight loss (high-responders), and these levels were associated with improved BMI-SDS and cholesterol levels.[105] More research is needed to quantify achievable treatment targets by nutritional interventions to reduce CV risk in children with obesity.

Nutraceuticals

Alimentary fibres, such as psyllium, glucomannan, guar gum, and oats, have been shown to lower total cholesterol and LDL-C levels in children and adolescents.[106,107] For example, the use of phytosterol (1–2 g/day) can reduce total cholesterol levels in children with mild hypercholesterolaemia and in children with familial hyperlipaemia,[108] but the long-term efficacy has previously been questioned in adults.[109] Other nutraceuticals, combined with dietary approaches, including red yeast rice,[110] omega-3 and omega-6 long chain polyunsaturated fatty acids,[111] soy proteins,[112] and probiotics, have been tested in children with hypercholesterolaemia.[113] A 3 month treatment with alpha-lipoic acid showed improvement of endothelial function and metabolic risk factors in youth with overweight or obesity.[114] Red yeast rice can lower LDL-C levels by inhibiting hepatic cholesterol metabolism.[110] Omega-3 long chain polyunsaturated fatty acids, in particular docosahexaenoic acid, act by improving quantitative levels of HDL-C and reducing triglycerides levels.[111] Soy protein has been shown to have lipid lowering effects. Blockage of bile acid and/or cholesterol absorption are possible mechanism underlying this effect, as well as the stimulation of the LDL receptor.[112] Probiotics may reduce blood cholesterol levels by several mechanism, including production of short-chain fatty acids that can interfere with cholesterol biosynthesis and an increase in bile acids excretion.[113]

School-based interventions

Several school-based lifestyle interventions showed good results for improving dietary habits in children and adolescent.[60,115] However, some studies found low-certainty evidence that reduced availability of sugar-sweetened beverages in schools is associated with decreased sugar-sweetened beverages consumption.[116] They found very low-certainty evidence for improved availability of drinking water in schools and school fruit programs being associated with decreased consumption of high caloric beverages. Reported associations between improved availability of drinking water in schools and student body weight varied.[116] In a previous RCT including 12 secondary schools including more than 600 pupils, it was found that the intervention, with a focus on nutrition education and improvement of the food environment, significantly lowered sugar intake but had no effect on fibre intake and fruit and vegetable consumption unless the quality of school lunches was improved.[117] Marketing for unhealthy food and beverage should be minimized or altogether prohibited, especially in schools, since it has been shown to negatively influence dietary preference in children.[118] Educational programs in schools may help fight the potentially negative influence of commercials and media models oriented to attract children towards high caloric foods and sedentary lifestyle.

Research gaps and future needs

Despite significant research advances into the physical, social, and economic consequences of childhood obesity in the last decades, there remain major research gaps in the peer-reviewed literature, as well as major challenges in the practical implementation of prevention and treatment strategies. The challenges and 'lessons to be learned' can perhaps be summarized in these four key general areas: (i) a need for further longitudinal research and RCTs, including comprehensive individual-level pooled analyses of existing large, high quality longitudinal studies; (ii) pushing for adoption of targeted clinical and social interventions; (iii) emphasis on improved awareness among the healthcare sector, educational institutions, government, and general public; (iv) a need for changes in national and global policies to better mitigate the increasing risk trajectories of childhood obesity and their associated pressures on the healthcare system and society; and (v) consideration of novel pharmacotherapeutics as adjunct to lifestyle interventions in reducing CV risk trajectories.

An overview on key management strategies to lower childhood CV trajectories including the main challenges and key barriers are shown in *Table 2*. With respect to developing screening programs for primary prevention of obesity-related CV risk, it remains to be determined who, when, and how to screen in order to identify children at risk and most in need for early treatment interventions. From a public health perspective, no reliable data are available on how these prevention strategies in childhood may be cost effective. Although there has been an increase in the number of school-based childhood obesity interventions in recent years,[119] there is a need for longer follow-up in these studies to assess the sustainability and cost-effectiveness of any related reductions in BMI *z*-scores. Similarly, research into these interventions has not provided definitive results regarding whether there are improvements in BP, glucose, and lipid metabolism or markers of target organ damage such as vascular biomarkers, which should be adopted

Table 2 Overview on key management strategies to lower childhood cardiovascular risk trajectories

Prevention and screening strategies

✓ Focus on clustering of risk factors
✓ Screening for overall cardiovascular risk including psychological factors
✓ Screening programs from childhood into adulthood
✓ Include family and peers in addition to school-based education
✓ Governmental support for population-based education campaigns
✓ Promote awareness for role of parenting style for physical activity and nutrition behaviour
✓ Avoid stigmatization

Management strategies of multicomponent behavioural interventions

✓ Promotion of physical activity and exercise
✓ Raise awareness for the need to reduce physical inactivity
✓ Promotion of healthy eating habits
✓ Accessibility to diet counselling
✓ Reduce unhealthy food marketing in media and social media
✓ Psychological support for behaviour change
✓ Built environment: accessibility and affordable infrastructure for healthy foods and physical activity in urban settings
✓ Smoking cessation and alcohol avoidance
✓ Sleep hygiene

Key barriers

✓ Evidence-base for sustainability of interventions
✓ Evidence-base for cost-effectiveness
✓ Financing of prevention programs

into ongoing and future work in this area. Different types of lifestyle interventions also need further study, including direct comparison of types of aerobic exercise training programs—such as HIIT vs. moderate intensity continuous training[120]—and how they are delivered—such as in person, remotely, and/or via mobile apps.[121] To date, it is unclear at what time during childhood development specific lifestyle interventions may be most effective. As mentioned, exergaming may be a feasible way to attract children and adolescents to engage more in PA and exercise.[84] Several apps have been developed in recent years and are readily available to support implementation of PA programs. Most of these apps have been designed for adults, and more research is needed to investigate the potential for use in children and adolescents and to help guide healthy lifestyle early in life. The potential for school-based educational programs on the interrelation between PA and health and the potential use for exergaming strategies needs to be investigated in future research.

It will be of utmost importance to investigate how well any exercise-induced CV and metabolic benefits translate into longer term health improvements in adulthood. Similarly, how PA and dietary interventions impact on specifically lowering visceral adipose tissue remains to be more precisely determined. While pharmacological treatments such as semaglutide have shown to be effective for sustained body weight reduction in adult populations with obesity,[122] our understanding of the efficacy and safety in childhood and adolescent obesity is limited. Furthermore, how drugs such as semaglutide may benefit long-term CV physiology and metabolism is still an ongoing question even in adult populations.[123] Determining which drug therapies are needed for which individuals will be an important step for clinical implementation but will first require a better understanding of their potential efficacy and long-term benefits and risks. Furthermore, understanding whether pairing lifestyle interventions with pharmacological therapies improves efficacy needs to be incorporated into future work streams.

An area of immediate need is a push to increase awareness among the clinical community, parents, and society regarding the complexity of underlying causes of childhood obesity and associated CV risk. Part of this need is to reduce stigmatization that may impact on quality of life and be a driving stimulus for the development of eating disorders and physical inactivity. In line with this, there is a lack of consistent governmental support in school-based settings for health promotion and interventions,[124] including physical education curricula and availability of high-quality school meals. Further focus needs to be placed on executing policies for healthy nutrition standards and access to appropriate facilities and well-trained teachers to improve engagement with a healthy lifestyle. One of the main challenges in promotion of healthy behaviours remains local and national discrepancies in government support in limiting production and marketing of unhealthy, energy dense foods and increasing access to healthy foods at lower costs. It is thus of immediate public health importance that governments and policymakers adopt changes to these current societal limitations, with appropriate adoption of tools to measure their success in practice.

Conclusions

In summary, there is a severe need to invest in screening and treating obesity-related CV disease risk in children and adolescents to counteract the associated CV disease burden later in life. Considerable evidence suggests that multicomponent behavioural programs including exercise and diet have the potential to improve obesity-related CV risk and associated risk trajectories into adulthood. This scientific statement can be considered a 'global call for action' for implementation of such screening programs and consecutive multimodal lifestyle interventions in children at risk in order to reduce their cumulative lifetime risk. Before such programs can be routinely implemented on a population-level, further evidence for their long-term efficacy and relative cost effectiveness, for example in terms of quality-adjusted life years, is warranted. Despite the urgent need for more conclusive evidence on the benefits and pitfalls of long-term screening and sustainability of treatment effects, we believe research programs and prevention strategies of local, national, and international authorities should aim at facilitating the necessary infrastructure based on 'lessons learned' from the presented evidence. To facilitate primary prevention 'action plans' early in life should be favoured over a 'wait and see' approach, which is deemed to cause an ever-growing burden of CV disease and a socio-economic hazard on healthcare systems and society.

Conflict of interest: G.B.Z. has consulted for Cardionovum, Crannmedical, Innovheart, Guidotti, Meditrial, Opsens Medical, Replycare, Teleflex, and Terumo. D.W. has received consulting and lecturing fees from Novo Nordisk A/S. M.L.L. has received lecture fees from Bayer, Sanofi and BMS/Pfizer.

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