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## Prevention of T2DM in Pediatric Population

## Gilles Plourde<sup>1,2\*</sup>

<sup>1\*</sup>Associate Professor at the Faculty of Health Sciences, University of Ottawa, Ontario, Canada <sup>2</sup>Faculty of Medicine, University of Montreal, Montreal, Quebec Canada

\*Correspondence to: Gilles Plourde, Drug Safety Unit – Director's Office, Health Canada, Ontario, Canada; E-mail: gilles.plourde@hc-sc.gc.ca; drgplourde@mail.com

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## Introduction

The large numbers of children and adolescent with obesity suggests that we have the potential for greater numbers of youth developing T2DM in the near future. Prevention of T2DM in the pediatric population requires prevention of obesity, particularly in at risk groups such as children and adolescent from ethnic minorities, children and adolescent with a family history of T2DM and others as discussed in the previous article. Prevention of T2DM involves reversing inadequate eating and sedentary habits in homes, schools and communities that lead to excess calorie intake and decreased energy expenditure. Chapter 2 of the book from Dr Plourde as well as his learning module provide very useful information on the prevention of pediatric obesity that can also be applied to pediatric patients with T2DM [1-2].

As explained in these documents, most lifestyle interventions (LSI) to prevent pediatric T2DM at the individual or family level should target changes in dietary and physical activity habits [1-3]. In a recent study the participants were able to reverse obesity-related markers of inflammation after 3 months of participation in LSI despite negligible changes in body weight (4). There were significant decreases in body fat mass and insulin resistance confirming that LSI approaches are very useful tools to prevent T2DM in pediatric patients [1-4].

A multicomponent family-based randomised controlled trial (RCT) with severely obese children has shown improvements in cardiometabolic factors that persisted into follow-up even though differences in weight between the intervention group and the usual care participants did not persist [5]. In this RCT, LSI has focused more exclusively on manipulating the macronutrient composition of the diet without the inclusion of an exercise component [6]. Again this study confirm that LSI is very helpful at preventing T2DM and supports the concepts discuss in the book and articles by Plourde that involving the family in the treatment of obese children and adolescent further increases the chance for success [1-3]. In a study conducted in obese adolescents, it was found that a low glycemic index diet through home provision of water and diet beverages to displace consumption of sugar-sweetened beverages (SSBs) was superior to a more traditional low-fat diet for weight loss and improving insulin resistance [7] which goes in the sense of the recommendation of no added sugar and no SSBs to promote weight loss in overweight or obese youth [1-3]. There is no doubt that this recommendation is also applicable to T2DM pediatric patients since the majority of them are overweight or obese.

The PREMA study (Prediction of Metabolic Syndrome in Adolescence) has identified other risk factors that could be associated with a higher risk of developing T2DM in youth that are important to consider in the medical history of a pediatric patient presenting with T2DM. These risk factors include low birth weight, small head circumference, and parental history of overweight and obesity [8]. Therefore, prenatal interventions with prospective parents may be useful to reduce future risk of T2DM in children and adolescent. Unfortunately, it may be difficult to create changes at the individual level since our current environment or societal influence is so unfavorable. Even with targeted early prevention programs, overcoming these larger societal issues is difficult [9].

As stated earlier, before the development of T2DM in youth, atrisk children and adolescent progress through a period of IGT due to insulin resistance accompanied by  $\beta$ -cells dysfunction [10-11]. Establishing adequate lifestyle routines and decreasing sedentary behaviours time before puberty may be especially important to help prevent T2DM, given that T2DM in youth generally develops during the adolescent years and especially at the time of mid-puberty as explained earlier.

Furthermore, physical inactivity has an additive impact upon the patient who may already show signs of insulin resistance before puberty [12-14]. In the other hand, increased isometric muscle strength and cardiorespiratory fitness in children and adolescent with insulin resistance and  $\beta$ -cells dysfunction has been associated with reductions in fasting insulin level, HOMA-IR and HOMA-B in young adulthood [15]. Considering that the prevention and even the reversal of inadequate glycemic control is possible with LSI [16-17] it is essential that our public health efforts should be oriented on the prevention of T2DM throughout LSI. To be successful in this prevention effort, we need the collaboration of the entire community. In the following sections of this article, I am presenting the role of various groups in the prevention of T2DM and its associated complications. Since the prevention of T2DM in this population is tightly linked to the prevention of pediatric obesity in the following paragraphs I also include pediatric obesity in the discussion.

## Parents

While it is apparent that the involvement and support of parents in behavior change programs is critical for the success in the prevention and treatment of children and adolescent at risk for T2DM and CVD, the long-term impact of family-based LSI efforts toward prevention of risk factors for T2DM and eventually CVD deserves our attention [18]. Some experts in the obesity field would argue that efforts to prevent the devastating health effects of obesity should begin in early childhood and it is the same with T2DM in pediatric patients. As for the treatment of pediatric obesity, children are not the only individuals targeted by LSI since parental weight loss has been shown to predict weight loss in overweight children when parents have been encouraged to lose weight along with their children. In fact, it was found that for every 1 BMI unit reductions in parents, their children experienced a 0.255 reduction in BMI units [19]. Therefore, encouraging weight loss in parents who are overweight should be included in any family- or home-based obesity prevention program for children. Since pediatric obesity is highly linked to pediatric T2DM, this approach is suitable for the latter.

Improving the health of prospective parents may be an important focus in T2DM prevention efforts. Family-based interventions are important, as the analysis of the community-based pediatric obesity prevention program, "Be Active Eat Well," (http://www.healthinfonet. ecu.edu.au/key-resources/programs-projects?pid=50) suggests [20]. This analysis demonstrates that the home environment has more influence on zBMI than the school environment, but other studies have shown that community-based programs to prevent obesity in children benefit from the inclusion of dietary and physical activity components that are implemented within the schools as well [21-22].

#### Peer and Social Support

As adolescents with T2DM often report feeling isolated from peers, marginalized and that support for behaviour change is essential in changing lifestyle, we can argue that peer-led approaches may be necessary for behaviour change in children and especially adolescent with T2DM. It was found that young children receiving curriculum that supported healthy living behaviours from older peers experienced significantly greater reductions in measures of adiposity and noted improvements in healthy living knowledge. Children and adolescent living with and at risk for T2DM often require programmes more relevant to their immediate needs and often their immediate needs is to be accepted by the groups, not being isolated from peers and other primary needs even more immediate than losing weight [1-3].

#### School-/Community-Based Interventions

A multicomponent lifestyle intervention delivered to inner city was also tested in a minority of children and adolescent at risk for T2DM within the school [23]. In this study the authors investigated the addition of coping skills training (CST) and health coaching to see if these would improve outcomes by addressing participants' barriers to incorporating lifestyle changes. Schools were randomized to either the CST intervention (four schools) or the general education (GE) intervention (two schools). All seventh graders in the schools received the same nutrition and activity educational component (eight classes), but the CST schools received an additional five classes in CST and the youth identified as at-risk for T2DM received 9 months of telephone health coaching. Interestingly, the participants from the schools randomized to the CST intervention evidenced improvements in some key markers of metabolic risk such as decreased BMI of T2DM patients at the end of the intervention. Recent reviews suggest that school-based obesity prevention interventions can be effective in reducing BMI among children [24-25], particularly for those programs with more comprehensive content, involving parental support, and duration longer than 1 year. It was concluded that there is strong evidence that school-based studies of physical activity, that include a home component, improve obesity outcomes [26] and even though not studied in children and adolescent with T2DM indirectly we can conclude that these approach would have a similar impact. Two of the three studies reviewed by Wang et al [27] focused on reducing sedentary activity, which may have contributed to the positive results. In addition, combined interventions of diet and physical activity interventions in schools that included home and community involvement should be more effective [1-3].

#### **Public Health Initiatives and Interventions**

Savoye and colleagues [16] evaluated the effects of the Bright Bodies (BB) Healthy Lifestyle Program (http://www.brightbodies.org/ program.html) on 2-h OGTT results in comparison with adolescents receiving standard of care. The intervention group attended exercise and nutrition/behavior modification classes over the course of 6 months. The BB program significantly decreased 2-h glucose in children at high risk for T2DM after 6 months. In addition, the intervention group lowered BMI z scores by maintaining weight close to baseline values, while the control group continued to gain weight. The BB group also had greater improvements in systolic blood pressure, fasting triglycerides, reduced total body fat, improvements in insulin sensitivity, and statistically and clinically significant improvements in glucose tolerance.

Several public health initiatives have been created at the national and international levels in an effort to reduce children's CVD risk factors [28]. The World Heart Federation has created a program for children and adolescent called the Youth for Health (Y4H) campaign (http:// hriday-shan.org/?page\_id=439) in which children and adolescent are encouraged to mentor and educate their peers on the importance of preventing CVD risk factors in their lives. The American Heart Association, the Clinton Foundation and the Alliance for a Healthier Generation work across several sociocultural levels, families, schools, corporations, and HCPs, to prevent childhood overweight and obesity which indirectly would have an impact on the prevention of T2DM in pediatric patients (https://www.healthiergeneration.org/). The First Lady's signature program, "Let's Move!," seeks to improve children's health and decrease CVD risk factors by increasing children's physical activity, improving the nutritional quality of their school lunches, and increasing families' access to healthy food and activity (http://www. letsmove.gov/) which would also have an impact on the prevention of T2DM in pediatric patients.

The Creating Opportunities for Personal Empowerment (COPE) (https://www.cope2thriveonline.com/) intervention provides promising evidence that the inclusion of educational materials that promote self-efficacy, problem solving, stress management, coping and communication can positively influence both mental and biological health outcomes in overweight adolescents. Compared to standard intervention that promoted simple healthy living messages, the

COPE-enhanced programme led to significant short and long-term reductions in adiposity, improvement in social skills and lower substance use in overweight adolescents. Among children and adolescents, the promotion of structured physical activity, particularly within schools, is an effective approach for reducing depression. The effects were particularly robust among adolescents older than 13 years and those that are overweight or obese. Although no data are published for children and adolescent with T2DM, there is no doubt that such program is also beneficial for them.

The Centers for Disease Control and Prevention's Steps program (also known as the Steps to a Healthier US program) (http://www. cdc.gov/nccdphp/dch/programs/healthycommunitiesprogram/ evaluation-innovation/pdf/stepsinaction.pdf) is another initiative targeting the prevention of chronic diseases such as T2DM and CVD in children and adolescent [29]. The biomedical results from a state-level study, the Carolina Abecedarian Project (ABC), have recently been analyzed. This early intervention initiative targeted disadvantaged children and adolescent between ages 0 and 5 years resulted in significantly lower prevalence of risk factors for CVD and metabolic diseases when the participants were assessed in their mid-30s [29]. This is an example of initiative that can be used by other states or other countries with the chances of resulting on positive preventive impact on their at risk population.

The ABC project has demonstrated the persistence of early intervention benefits into adulthood, and more such longitudinal studies are needed to determine whether lifestyle-induced changes targeting cardiometabolic risk factors in childhood persist over the long term [29]. Although LSI aimed at reducing the risk of T2DM and CVD have traditionally focused on dietary and physical activity behaviors, there is strong evidence identifying other modifiable risk behaviors that should be included as targets in LSI to prevent non communicable diseases such as T2DM and CVD.

Smoking, sleep, and mental health such as depression are a few examples of the concerns that warrant attention in the design of future risk reduction efforts. While smoking has long been associated with CVD risk, it has been implicated as a risk factor for T2DM as well [30-31]. Smoking initiated at an early age (age 16) has been found to be associated with increased risk for T2DM in men [32]. Therefore, CVD and T2DM prevention efforts with children and adolescent would benefit from including smoking cessation treatment components in their LSI efforts [33-34]. There is evidence in adults that there is a relationship between sleep duration and T2DM risk since both long and short sleep durations have been found to be associated with increased risk for T2DM [35-37]. Additional research into the role of sleep disturbance and risk for T2DM and CVD in children and adolescent is warranted since Matthews et al. [38] found a relationship between short sleep duration and insulin resistance in youth but not for long sleep duration.

#### Social Networks and Social Media

Social media is largely present in the lives of adolescents and significantly influence their behaviour. The American Heart Association recently released a statement regarding the efficacy of social networks in the prevention and management of childhood obesity [39] and indirectly T2DM. There is significant evidence that behaviours related to weight are associated with individuals within social networks, in some cases in a dose-response manner [40-41]. As overweight and obese children and adolescent are more likely to be socially isolated [42], the use of social media may be an attractive approach to support behaviour modification, particularly using a peer-based approach [40-44].

Systematic reviews of web-based approaches to behaviour modification in children and adolescent revealed mixed results [45]. In most cases, internet-based approaches lead to changes in lifestyle behaviours and in some cases reductions in adiposity. The effects of the interventions are often modest; however, these approaches are often used in clinical practice with very good succes. Future studies aimed at behaviour modification for lifestyle management in youth with T2DM may want to consider these approaches.

#### For the Health Care Providers and Policy Makers

The ADA (in 2000) and ISPAD (in 2011) have formulated recommendations for screening asymptomatic children with T2DM predominantly based on BMI and family history. Screening should be initiated from 10 y of age or at onset of puberty; if puberty occurs earlier, and repeated every 2 y. Screening is done by measuring HbA1C, FPG, or performing OGTT. The OGTT is a more sensitive test than FPG, because OGTT detects patients with diabetes early in the development of their disease when the FPG may not be elevated. It is recommended to use fasting glucose and HbA1C for screening routinely and to use OGTT when results are discrepant, with intermediate (FPG 5.5-7.0 mmol/L or HbA1C 5.7–6.4%) values or clinical suspicion for T2DM is strong. In children with blood glucose in pre-diabetic range, repeat testing should be done annually and LSI initiated to induce weight loss.

HCPs can use the following simple slogan to promote a healthy lifestyle among youth and their families: "5, 3, 2, 1, 0", designating five [5] portions and more of fruits and vegetables per day, three [3] structured meals per day (including breakfast), two (2) hours or less of television or video games per day an (1) hour or more of moderate to vigorous physical activity daily and no (0) sugary drink or added sugar. It is a great message of prevention to leave to pediatric patients and their parents. His promotion to the general public, through the media, is also recommended [1-3]. Policy makers and Governments should work at different levels in order to create an environment facilitating the acquisition of better eating and physical activity habits among young people and promote their implementation at the school, family and community levels, i.e. by changing the environment so that the choices presented to children are favourable to a healthy lifestyle. They should opt for a strategy named 'create default options' by which a pre-selected choice is created with the purpose of producing the desired behaviour change. However, the patient and his/her parents remain free to choose a different option to the proposed one but it becomes more difficult to obtain. In the field of the treatment of obesity or T2DM, «create default options» means changing the food environment and physical activity of the population, so that the default options are not favourable to obesity or T2DM, but favourable to a healthy lifestyle [1-3].

### Conclusion

There is some evidence from the National Health and Nutrition Examination Survey (NHANES) that indicates that childhood obesity rates in the US may have stabilized in the past several years, with some decreases in preschool-age groups, although the results should be interpreted with caution. In Canada, currently almost 1 in 7 children and youth are obese. But overall; the rates of excess weight have been relatively stable over the past decade [47]. Consequently, there may be small, but hopeful changes in the overall prevalence of childhood obesity as a result of current obesity intervention and prevention efforts. Since T2DM is highly linked to obesity in the pediatric population, it may not be too speculative to hypothesis that we will also observe a decrease in the prevalence of T2DM in this population in a near future.

Intensive public health efforts are needed and should involve a variety of different stakeholders to target changes at personal, environmental, and socioeconomic levels. Such efforts need to be sustainable, economically feasible, and culturally acceptable so the policies can be effectively implemented across multiple domains. Prevention of T2DM may be classified as primary and include the prevention of overweight or obesity. Prevention of T2DM can also be classified as secondary and include the prevention of weight regain following weight loss, or limiting weight gain in obese people who have not been successful at losing weight. In order to prevent obesity in children and the possibility of developing obesity-associated T2DM, it has been suggested that LSI should focus on those children at high risk for obesity: children with BMIs in the 85th–95th percentiles, who have a family history of obesity in one or both parents or those coming from specific minorities.

Prevention of childhood overweight and obesity may be an even more appropriate target for preventing T2DM, particularly since obesity is very challenging to treat once it is established. For these reasons, organizations such as the National Institute for Health and Care Excellence guidelines (https://www.nice.org.uk/guidance/ng28) recommend a focus on all people achieving and maintaining a healthy weight in order to have the most substantial impact on the prevalence and financial costs of T2DM. The National Heart, Lung, and Blood Institute's (NHLBI) Expert Panel's Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents also notes the importance of maintaining a healthy weight in childhood to prevent the development of CVD in adulthood (48). LSI have primarily focused on changing dietary and physical activity behaviors, but interventions designed to prevent T2DM may improve prevention outcomes by targeting additional health behaviors such as sleep habits, stress management or mental health treatment, and smoking [48].

Our prevention efforts have lagged way behind in embracing technology to help effective targeting of this population. Much of our research investigating LSI for young people and their families have relied upon traditional education and behavior change methodology such as paper and pencil self-monitoring of eating and exercise behaviors, hard or soft-bound educational materials and handouts, in-person coaching, and teaching in clinics or other community settings. However, the children and adolescent today are familiar with and more comfortable using web based applications, even available on their cell-phone, to learn new information and to track weight and behavior changes. More research is needed to determine in what ways these web-based applications and computing devices as well as social media can be used to impact health behaviors to reduce the risk of T2DM in youth. Therefore, it is hoped that early screening and intervention to address the unhealthy lifestyle behaviors may help prevent the development of T2DM in later years.

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