Commentary

Consequences of Childhood Obesity

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Abstract

Introduction: The incidence of childhood obesity is rising across the globe, and obesity related co-morbidities are increasing concomitantly in the paediatric population. Materials and Methods: PubMed search for research and review papers on complications of childhood obesity was performed. Results: The consequences of childhood obesity can be broadly classified into medical and psychosocial consequences. Medical consequences include metabolic complications such as diabetes mellitus, hypertension, dyslipidaemia and non-alcoholic fatty liver disease, and mechanical problems such as obstructive sleep apnoea syndrome and orthopaedic disorders. Psychological and social consequences are prevalent but often overlooked. Local data on these complications were also discussed. Conclusion: Childhood obesity is associated with significant morbidities, which not only have immediate impact on the health of the obese children, but also significantly increase the risk of morbidities in adulthood.

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Key words: Medical consequence, Psychosocial consequence

Introduction

The global escalation of childhood obesity is a major concern, as excessive adiposity is the root cause of leading metabolic and cardiovascular diseases, and related mortality. Widely prevalent in obese adults, these metabolic co-morbidities are beginning to surface in obese children, and it will not be unreasonable to expect a dramatic increase in young adults afflicted with glucose intolerance, hypertension, dyslipidaemia, non-alcoholic fatty liver disease (NAFLD) and ischaemic heart disease in the near future. Substantial consequences to the physical and mental health must be anticipated when caring for these young obese patients, as many of these chronic diseases are now appearing in childhood rather than adulthood. Paediatricians now have to handle chronic illnesses that were once regarded as adult diseases. The epidemic of childhood obesity and its attendant risks is a relatively recent phenomenon, and there is limited experience in the management of childhood onset obesity-related complications, with a paucity of evidence-based data and management guidelines.

Definition of Childhood Obesity

As the body mass index (BMI) changes with age during childhood and adolescence, the BMI cut offs used for defining overweight and obesity in adults cannot be applied directly to the paediatric population. Surrogate measures of childhood adiposity are skinfolds, percentage of ideal weight for height, and BMI standard deviation scores specific for the population. Although these measures reflect slightly different aspects of body composition or body size, they are moderately well correlated with body fat, even in growing children.[1] Unfortunately, there is no uniform consensus on the definition of childhood obesity, and the lack of a standard definition and consistent anthropometric measure has resulted in varying epidemiological reports of childhood obesity and its complications. For countries with gender specific BMI charts of their paediatric population, obesity is generally defined as the 95th percentile or greater of BMI for age, and those with BMI between the 85th and 94th percentiles are considered overweight.[2] The percentage of ideal weight for height is also a valid tool for populations without local BMI charts,[3] and childhood obesity is commonly defined as weight being >120%, and severe obesity >140% to 150%, of ideal weight for height. An obvious problem with these definitions is that these are arbitrary statistical measures and not based on biological data related to the risk of morbidity later in life. Moreover, as the population gets heavier through the years, the threshold for defining obesity also changes.

Using growth data of 97,876 males and 94,851 females

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aged 0 to 25 years from 6 large representative cross-sectional surveys from Brazil, Great Britain, Hong Kong, the Netherlands, Singapore and the US, Cole et al[4] developed age and gender specific BMI cut off curves for definition of overweight and obesity in childhood, such that at 18 years of age, these 2 lines each coincided with the BMI 25 kg/m^2 and 30 kg/m^2 respectively, which are the accepted definition of overweight and obesity in adults. The proposed cut off lines are thought to be less arbitrary as they attempt to extrapolate risk from the adult experience to children, and are more internationally based. While the International Obesity Task Force has recommended this approach for epidemiological studies to ensure uniformity and comparable childhood obesity rates between countries,[5] the proposed curves may underestimate the prevalence of obesity in some populations, and these charts are also not useful for longitudinal follow-up of individual patients as they lack precise percentiles.

Consequences of Childhood Obesity

The complications of childhood obesity can be classified as medical and psychosocial consequences as depicted in Figure 1.

Medical Consequences

Medical consequences can be broadly classified into mechanical or metabolic complications. The 2 main mechanical complications are obstructive sleep apnoea syndrome and orthopaedic problems such as genu varus and valgus deformity of the knees, Blount's disease and slipped capitate femoral epiphysis. Metabolic consequences of obesity have been extensively studied in obese adults, and in recent years the problem is increasingly recognised in obese children. While the complications may not become apparent until years later, these metabolic derangements may be in progress and continue to stress the body, and may even be evident already in some obese children. This review will focus primarily on the metabolic complications.

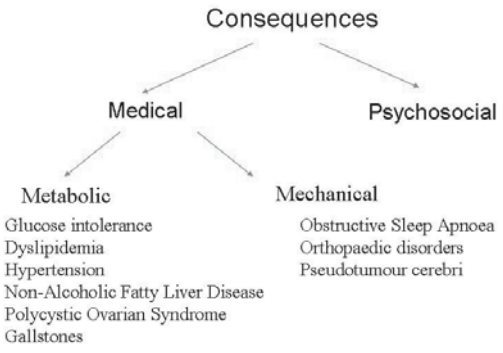

Fig. 1. Classification of medical and psychosocial consequences of childhood obesity.

Insulin Resistance and Glucose Intolerance

Childhood obesity is associated with insulin resistance, which in turn leads to glucose intolerance (impaired fasting glucose, impaired glucose tolerance and diabetes mellitus), dyslipidaemia and hypertension, and also implicated in the pathogenesis of polycystic ovarian syndrome and non-alcoholic steatohepatitis.

It is clear that the increasing prevalence of type 2 diabetes mellitus (T2DM) in children and adolescents observed in many parts of the world, is attributed to the parallel increase of childhood obesity prevalence, as a result of the increasingly affluent environment we now live in. Ten years ago, less than 10% of childhood diabetes in Singapore is T2DM, but currently T2DM accounts for up to 1/3 of all childhood diabetes here, as well as approximately half of all new adolescent diabetics, as the risk of T2DM increases during puberty (unpublished data). It has been estimated that 10% to 25% of obese children may have impaired glucose tolerance (IGT) and 4% may have silent diabetes.

We have recently published the results of a local study which examined the metabolic complications of our children with severe obesity,[7,8] where 201 Singaporean children with early onset severe obesity were recruited from the School Health Service, a primary healthcare service and facility which routinely screens schoolchildren. Consecutive patients who met the inclusion criteria of severe obesity with body weight at least 140% of the ideal weight for height (WFH) based on local weight for height chart were invited to participate in the study. Anthropometric measurements, body fat assessment, estimation of physical activity and fasting blood samples and oral glucose tolerance test (OGTT) were performed. Of the 201 obese subjects, 128 were boys (63.7%). The ethnic distribution was as follows: Chinese, 105 (52.2%); Malay, 69 (34.3%); Indian, 21 (10.4%) and Others, 6 (3%). The mean (SD) age was 11.1 (3.0) years (age range 5.7 to 17.5 years), WFH 170.5 (22.7)%, BMI 31.9 (5.5) kg/m^2 and percentage body fat 40.7 (5.2)% by DEXA or 45.7 (9.1)% by bipedal bioimpedance. The ethnic and gender distribution of the study sample was fairly representative of the local obese paediatric population (Chinese, 61.7%; Malay 25.9%; Indian 10.4%; Others 2.0%) (unpublished data). Glucose intolerance was present in 35 (17.4%) of the subjects, of which 26 (12.9%) had IGT (n = 25) or impaired fasting glucose (n = 1), and 9 (4.5%) had T2DM. Only 3 of the diabetics were symptomatic. This is slightly more severe than a study of comparably obese Caucasian children (mean age 11.2 yeas, mean BMI 33 kg/m^2) by Sabin et al[7] who reported 10.3% had IGT. None had T2DM, and acanthosis nigricans was only present in 12.7%. The frequency of IGT in our study is higher than that reported by other European studies,[9-11] but lower compared to reports

of about 25% in multi-racial clinics from the USA.[12,13]

Of the 9 T2DM subjects in our study, 3 with diabetes had normal fasting glucose (<6 mmol/L), and all 25 IGT subjects had normal fasting glucose (<6 mmol/L). The diagnosis was made based on abnormal glucose level 2 hours post-oral glucose tolerance test (OGTT), and reconfirmed with repeat OGTT. This underscores the importance of the standard OGTT in detecting children with early T2DM and especially IGT, where intervention may prevent the relentless slide down the glucose intolerance spectrum to frank diabetes. The American Diabetes Association recommends screening for type 2 diabetes in obese children after 10 years of age or pubertal onset (amongst other criteria), and fasting plasma glucose was preferred because of its lower cost and convenience.[14] However, in our cohort of severely obese Asian children,[7,8] 3 of the 9 T2DM subjects and all 25 IGT subjects had normal fasting glucose, and we would have failed to make an early diagnosis if OGTT was not the method of testing. Our youngest IGT subject was 7.1 years of age, and 7 IGT subjects were less than 10 years old and pre-pubertal. Diabetes screening of severely obese Asian children with OGTT, even for pre-pubertal children younger than 10 years old, can help to identify early cases of glucose intolerance.

How likely are obese children with IGT to progress to frank diabetes? We were given a glimpse of the progress of these children by Weiss et al[15] who followed up the changes in glucose tolerance status in 117 obese children and adolescents with 2 OGTTs, at a mean interval of 20.4 ± 10.3 months. Of the 33 subjects who were IGT at baseline, 8 (24.2%) developed diabetes, 10 (30%) remained IGT and 15 (45%) reverted to NGT. Of the 84 subjects (of comparable BMI) with normal OGTT, 76 subjects remained so on follow-up, while 8 subjects (9.5%) deteriorated to IGT.

Hypertension

Primary hypertension in children was previously considered rare, but in recent years it has become increasingly common in association with obesity. Obese children are at approximately a 3-fold higher risk for hypertension than non-obese children.[16] In addition, the risk of hypertension in children increases across the entire range of BMI values and is not defined by a simple threshold effect. About 20% to 30% of obese children (weight >120% ideal) between 5 to 11 years old have elevated systolic or diastolic blood pressure.[17] Overweight adolescents (BMI >75th percentile) have more than an 8-fold increased risk of developing hypertension as adults.[18] As in adults, a combination of factors including insulin resistance, overactivity of the sympathetic nervous system, activation of the renin-angiotensin system leading to increased renal sodium re-absorption and reduced natriuresis, and abnormalities in vascular structure and function may contribute to obesity-related hypertension in children. Therefore blood pressure in obese adolescents seemed to be sensitive to sodium intake.[19] The benefit of weight loss for blood pressure reduction in children have been demonstrated in both observational and interventional studies.

Dyslipidaemia

Insulin resistance is associated with higher levels of total cholesterol, low density lipoprotein (LDL) cholesterol and triglycerides in obese children.[20,21] However, in our local cohort of obese children,[7,8] LDL was not correlated with markers of insulin resistance (homeostasis model assessment or HOMA,[22] fasting insulin and c-peptide levels), severity of obesity (ideal weight for height, and percentage body fat) or age. Though HDL-cholesterol did not correlate with severity of obesity, it was negatively correlated with fasting C-peptide (Pearson correlation -0.223, $P = 0.002$), leptin levels (Pearson correlation -0.174, $P = 0.023$), and age (Pearson correlation -0.161, $P = 0.023$). There was also significant association between triglyceride (TG) levels and insulin resistance, which demonstrated positive correlation with insulin resistance indices HOMA (Pearson correlation 0.246, $P < 0.001$), fasting C-peptide (Pearson correlation 0.258, $P < 0.001$) and fasting insulin (Spearman's correlation coefficient 0.249, $P < 0.001$). TG also showed strong positive correlation with age (Spearman's correlation coefficient 0.167, $P = 0.018$). These correlations remained significant even after correcting for gender and race (using linear regression).

Thus it appeared that LDL-cholesterol, HDL and TG were not correlated with the severity of obesity, while LDL also did not correlate with insulin resistance. While adiposity and insulin resistance may not be directly involved in the pathogenesis of these metabolic derangements, their roles should not be disregarded yet, as they may still contribute indirectly. Obesity may have a threshold effect on dyslipidaemia, in which increased adiposity results in abnormal lipid levels. However, the severity of the dyslipidaemia may be determined by other factors.

Metabolic Syndrome

Metabolic syndrome refers to a constellation of metabolic disorders comprising of hyperglycaemia, hypertension, dyslipidaemia and visceral obesity. Central obesity and Insulin resistance are believed to be the chief abnormalities. Visceral fat depot enters the portal system and the free fatty acids induce significant insulin resistance at the liver and muscles, and abnormal insulin secretion by the islet cells. There is no consensus in the definition of metabolic

syndrome for children, and its value in predicting future cardiovascular risk can only be inferred from adult studies. It is important to address these metabolic complications because they lead to early cardiovascular disease and premature death, and aggressive intervention can reduce the risk of life-threatening events.

We used a modified criterion for the definition of metabolic syndrome for our local childhood obesity study[7,8] adapted from the NCEP ATP III[23] and another paediatric study,[24] which is the presence of at least 3 of the following abnormalities: obesity, high triglycerides, low HDL-cholesterol, glucose intolerance and significant or severe hypertension. In our cohort, 24.4% satisfied the criteria for metabolic syndrome (with mean HOMA of 6.96). Subjects with metabolic syndrome were more obese with higher percentage weight for height, percentage body fat and higher insulin resistance. This is comparable to the 30% reported by a US study on Hispanic youths who had less severe obesity (mean age 10.9 years, mean BMI 28.1 kg/m^2),[25] but more than the 15.9% reported by a French study of predominantly Caucasian children, albeit less obese (mean age 11 years, mean BMI 28.0 kg/m^2).[26] However, a multi-ethnic US study of similarly obese and insulin resistant Black, White and Hispanic children (n = 244, mean age 12.8 years, mean BMI 33.4 kg/m^2, mean HOMA 7.05) reported higher incidence of metabolic syndrome in 38.7%.[24]

Non-alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease (NAFLD) is a spectrum ranging from simple steatosis to steatohepatitis to frank cirrhosis.[27] It is characterised by elevated hepatic enzymes and hyperechoic liver on ultrasonography and diagnosis is made by exclusion of other causes. Histological examination of the liver will reveal variable degrees of microvesicular and macrovesicular steatosis, and even periportal fibrosis in severe cases. The pathogenic mechanism is hypothesised to result from a combination of insulin resistance, hyperlipidemia, and increased oxidative stress.[28] Briefly, insulin resistance results in increased insulin level which stimulates fatty acid synthesis in hepatocytes, and also increased lipolysis which leads to hypertriglyceridemia and increased fatty acid uptake by liver cells. The net result is accumulation of triglycerides in the hepatocytes, which induced cytochrome P450 2E1 activity and generation of free oxygen radicals, causing lipid peroxidation and cytokines and Fas ligand induction, which leads to cell death and fibrosis. While the majority of patients with elevated hepatic transaminases have simple hepatic steatosis without inflammation or fibrosis, a significant number may have steatohepatitis and can progress to cirrhosis.[29] NAFLD is a metabolic consequence of obesity and a common cause of chronic liver disease in obese adults, and it is increasingly recognised as a common cause of chronic liver disease in obese children. Our local obese cohort study[7,8] found that 26.4% of the obese children had raised liver enzymes ALT/AST, similar to a report of similarly obese Chinese children from Hong Kong (mean age 12 years, mean BMI 30.3 kg/m^2) which reported 24%.[30] However, this is considerably higher than the 12.4% reported by a study of severely obese children (BMI SDS >2.29) in the US based on raised ALT,[31] and we hypothesise it may be related to genetic and geographic differences. Our obese subjects also demonstrated increasing mean levels of GGT (P <0.001), ALT (P = 0.023), and AST (P = 0.006) with an increasing severity of metabolic syndrome, as defined by the number of criteria present (one-way ANOVA linear trend analysis) (Fig. 2), further supporting the relationship between the severity of the metabolic syndrome, insulin resistance and NAFLD.

Using stepwise logistic regression analysis, our study also found that Chinese ethnicity (odds ratio 5.889, 95% CI 1.164-29.791, P = 0.032; Indian ethnicity as reference), waist hip ratio (Exp[B] 1643.663, 95% CI 10.333-261444.17, P = 0.004), reduced physical activity (odds ratio 2.368, 95% CI 1.100-5.100, P = 0.028), and HOMA (Exp[B] 3.742, 95% CI 1.101-12.724, P = 0.035) were significant predictors of raised liver enzymes in our obese children. Insulin resistance, truncal adiposity and physical inactivity are identified as major determinants which are potentially modifiable to reduce the risk of NAFLD, and hopefully will provide further impetus to convince patients and caregivers of the value of regular exercises in the management of this condition.

Hence it appears that obese Asian children may be more prone to glucose intolerance, NAFLD and metabolic syndrome than European Caucasians, but less so than children

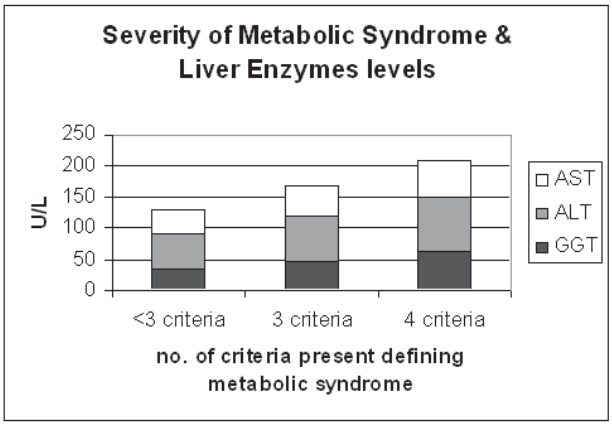

Fig. 2. Increasing mean levels of GGT (P <0.001*, P <0.001†), ALT (P = 0.026*, P = 0.023†), and AST (P = 0.009*, P = 0.006†) in subjects with increasing number of features of metabolic syndrome (using one-way ANOVA combined* and linear trend analysis†).

in the US. However, the variability in the definitions of metabolic syndrome and its components has made it difficult to perform accurate comparisons across populations.

Recommended treatment for NAFLD therefore include weight reduction, regular exercise, and some would propose low-glycaemic index diet that reduces postprandial hyperglycaemia and low in harmful fats. There was also significant improvement in trials using insulin sensitisers such as metformin.[32]

Menstrual Abnormalities

Menstrual abnormalities in obese children are also common. Obese girls are observed to experience earlier menarche,[33] usually before 10 years old, in keeping with the hypothesis that body weight and fatness are critical physiologic triggers of menarche.[34] Conversely, oligomenorrhoea or amenorrhoea is also associated with obesity, as obese adolescent girls frequently develop polycystic ovarian syndrome (PCOS) and hyperandrogenism, driven again by insulin resistance resulting from visceral adiposity.

Gallstones

In obesity, the biliary excretion of cholesterol is increased relative to bile acid and phospholipids secretion, increasing the likelihood of gallstone formation. Though gallstones in children are often associated with underlying conditions such as haemolytic disease, childhood obesity accounts for the majority of gallstones in children without underlying conditions. Obesity is associated with 8% to 33% of cholelithiasis seen in children.[35,36] The relative risk of developing gallstones in overweight teenage girls (percentage weight for height >110%) was estimated to be 4.2, and other risk factors also include metabolic syndrome and insulin resistance.[37]

Obstructive Sleep Apnoea (OSA)

An estimated 33% to 94% of children with severe obesity suffer from sleep apnoea.[38-40] The wide range of this estimate is due to different definitions of severe obesity and recruitment strategies. A local study estimated that 0.7% of our obese children had OSA, but the prevalence was about 13.3% among those with severe obesity (≥180% ideal weight for height).[41] 3671 obese children from the School Health Nutritional Clinic were screened using questionnaires for OSA. The obese children suspected to have OSA based on these questionnaires, and all those with body weight equal to and greater than 180% of ideal weight for height, were reviewed and subjected to polysomnography where clinically indicated. 146 were selected to undergo polysomnography, and 26 had abnormal sleep studies with apnoea/hypoxia indices (AHIs) >5/hr. Thus the prevalence of OSA was 0.7% (26/3,671) among obese schoolchildren in Singapore based on this strategy of identification. Among the severely obese (≥180% ideal weight for height), the prevalence rate is higher at 13.3% (8/60).

OSA is a big concern because it is associated with daytime somnolence and neurocognitive deficits such as concentration and memory lapses, as well as decrements in learning function resulting from poor quality sleep.[42,43] The children can present with just hyperactivity and attention deficit disorders. Fat deposition result in anatomical distortion and narrowing of upper airway, and thus will be more prone to obstruction during sleep when pharyngeal muscles relax in REM sleep. The classic description of Pickwickian syndrome refers to severe obesity associated with hypoventilation, somnolence, polycythemia and right ventricular hypertrophy and failure. A large amount of abdominal fat leads to rapid, shallow breathing with subsequent increase in dead space ventilation and carbon dioxide accumulation. When assessing obese children in the clinic, the index of suspicion must be high, and confirmation of diagnosis using polysomnography should be offered. Weight loss will help the condition but this is usually difficult to achieve; a more definitive therapy will be tonsillectomy and adenoidectomy (T&A). Repeat polysomnography should be performed after T&A, and continuous positive airway pressure (CPAP) therapy should be offered if T&A fails to alleviate the problem.

Neurological

Idiopathic increased intracranial hypertension or pseudotumor cerebri often occurs in females in the third decade, but a review found that about 15% presented before 20 years, and about 90% were obese.[44] The prevalence of pseudotumor cerebri increased 14-fold in patients with weights >10% above ideal and 20-fold in patients with weights above 20% above ideal.[45] It was estimated that 30% to 80% of children with pseudotumor cerebri are obese, and probably accounts for the majority of cases not associated with infection or medication.[46] The postulated mechanism is increased intra-abdominal pressure due to obesity causing increased pleural pressure and cardiac filling pressure, which results in increased resistance to venous return from the brain.[47]

Persistence of Obesity, Cardiovascular Risk and Other Long-term Morbidities

The overweight child is likely to become an overweight adult. A study reported that 43 % of obese children persisted to be obese adults, and another 29% were overweight as adults.[48] The severity of obesity in childhood increases this likelihood, and childhood BMI and insulin resistance are significant predictors of subsequent development of metabolic syndrome.[49] Early onset obesity is a risk factor

for significant morbidity and mortality later in life, where rates of diabetes mellitus, coronary artery disease, atherosclerosis and gout are increased in those overweight as adolescents, which underscores the importance of weight control early in life. Most worryingly, higher BMI during childhood is associated with an increased risk of coronary heart disease (CHD) in adulthood. In a remarkable study of 5,063,622 person-years of follow-up, a cohort of 276,835 Danish schoolchildren for whom BMI in childhood (7 to 13 years of age) were available revealed that the risk of CHD event later in adulthood was positively associated with BMI at 7 to 13 years of age for boys and 10 to 13 years of age for girls.[50] The associations were linear for each age, and are stronger in boys than in girls. The risk increased across the entire BMI distribution, and with the age of the child in both sexes. As children are becoming heavier across the globe, we have to be prepared for a drastic increase in CHD in the very near future, even in relatively young adults.

Psychosocial Consequences

Psychological and social consequences are probably more prevalent than medical complications. Childhood obesity has significant impact on the emotional development of the child or adolescent, who suffers discrimination and stigmatisation, as the obese individual is often associated with negative characteristics, and commonly regarded as a glutton and greedy, weak-minded and ill-disciplined. Obese children were unfortunately uniformly ranked by other children as least desired friends,[51] and may be more prone to being bullied.[52]

Overweight children and adolescents frequently reported reduced health-related quality of life in physical, emotional and social aspects.[53-56] Individuals who were obese in childhood are more likely to have poor body image, and low self-esteem and confidence, even more so than those with adult onset obesity, as mid-childhood is the critical period of development of body image and self esteem.[57,58] This is supported by observations that overweight young children were able to maintain a positive self image and self-esteem,[59-61] but overweight adolescents, particularly girls, tend to develop negative self image that persists into adulthood.[58]

These negative factors work against the child with a weight problem, and those with childhood obesity may have fewer opportunities in school, and smaller social circle. A vicious circle ensues, and some obese individuals may consequently have less education, lower incomes and higher poverty rates.[62,63]

Conclusion

Obesity in childhood should really be considered a chronic medical condition with medical and psychosocial consequences, associated with a multitude of medical and psychosocial complications, which not only have an immediate impact on the well-being of our children, but also significant bearing on their health in adulthood. Given the unrelenting rise in childhood obesity rates in many countries, we have to brace ourselves for the onslaught of metabolic disorders and cardiovascular diseases in the young adult population in the very near future, if we fail to do enough to curb this epidemic.

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