Pediatric Diabetes 2007: 8: 299–306

Pediatric Diabetes

Review Article

The metabolic syndrome in children and adolescents – an IDF consensus report

Zimmet P, Alberti K George MM, Kaufman F, Tajima N, Silink M, Arslanian S, Wong G, Bennett P, Shaw J, Caprio S; IDF Consensus Group. The metabolic syndrome in children and adolescents – an IDF consensus report.
Pediatric Diabetes 2007: 8: 299–306.

Paul Zimmet[a], K George MM Alberti[b], Francine Kaufman[c], Naoko Tajima[d], Martin Silink[e], Silva Arslanian[f], Gary Wong[g], Peter Bennett[h], Jonathan Shaw[a] and Sonia Caprio[i]; IDF Consensus Group

[a]International Diabetes Institute, Melbourne, Victoria, Australia; [b]Department of Endocrinology and Metabolic Medicine, St Mary's Hospital, London, UK; [c]Center for Diabetes, Endocrinology and Metabolism, Children's Hospital, Los Angeles, CA, USA; [d]Division of Diabetes, Metabolism and Endocrinology, Jikei University School of Medicine, Tokyo, Japan; [e]Institute of Endocrinology and Diabetes, The Children's Hospital at Westmead, Sydney, New South Wales, Australia; [f]Division of Endocrinology, Children's Hospital of Pittsburgh, Pittsburgh, PA, USA; [g]Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong; [h]Phoenix Epidemiology and Clinical Research Branch, NIDDK, National Institutes of Health, Phoenix, AZ, USA; and [i]Department of Pediatrics, Yale University School of Medicine, New Haven, CT, USA

Key words: cardiovascular risk – children – diabetes – metabolic syndrome – obesity

Corresponding author:
Prof. Paul Zimmet
International Diabetes Institute
250 Kooyong Road
Caulfield, Vic. 3162
Australia.
Tel: +613 9258 5047;
fax: +613 9258 5098;
e-mail: pzimmet@idi.org.au

Submitted 16 April 2007. Accepted for publication 8 June 2007

The urgency for global criteria

The growing worldwide prevalence of type 2 diabetes mellitus in the young, as underlined by an earlier International Diabetes Federation (IDF) Consensus Statement (1), has highlighted a significant shortfall of data on the epidemiology of the disorder and the identification and treatment of children and adolescents at risk of progression to this disease.

Urbanization, unhealthy diets, and increasingly sedentary lifestyles have contributed to increase the prevalence of childhood obesity, particularly in developing countries (2). Current treatment initiatives include school-based programs addressing physical activity and diet, which have been conducted with mixed success in reducing adiposity. There are limited safety data supporting the use of drugs for the treatment of obesity and related conditions such as type 2 diabetes in children and adolescents, and noncompliance in this population suggests that pharmacotherapy is unlikely to be effective long term (1). Although criteria have now been developed for bariatric surgery in teenagers (3), there are few evidence-based data available to support the increasing use of this modality in adolescents. Governments and society in general must be made more aware of the problems associated with obesity and the likelihood of progression to the metabolic syndrome in children and adolescents.

Obesity, particularly in the central (abdominal) region, has been determined as a key factor in the etiology of type 2 diabetes (2). The prediction of health risks associated with obesity in youth is improved by the additional inclusion of waist circumference (WC) measure to the body mass index (BMI) percentile (4, 5). Such observations reinforce the importance of including WC in the assessment of childhood obesity to identify those at increased metabolic risk as a result of excess abdominal fat (5). The role of obesity can clearly be demonstrated in Japan, where a parallel increase in type 2 diabetes and obesity in children has occurred over the past few decades (6). Central (abdominal) obesity is also a key component in the IDF definition of metabolic syndrome in adults (2).

The link between obesity, metabolic syndrome, and type 2 diabetes has already been characterized in adult populations (2). At present, 50–80% of almost 250 million adults worldwide with diabetes (7) are at risk of death from cardiovascular disease. Those with the metabolic syndrome are also at increased risk being twice as likely to die from, and three times as likely to have, cardiovascular complications as compared with those without the syndrome (8, 9). In addition, adults with the metabolic syndrome have a fivefold greater risk of developing type 2 diabetes (10). Already, one-quarter of the world's adult population have metabolic syndrome (11, 12), and this condition is appearing with increasing frequency in children and adolescents, driven by the growing obesity epidemic in this young population (13–15).

In 2004, the World Health Organization (WHO) reported that an estimated 22 million children younger than 5 yr of age and 10% of school-aged children, between 5 and 17 yr, were overweight or obese (16). WHO predicts that the prevalence of childhood obesity in developed and developing countries will continue to increase as has been seen in recent years. For example, from 1985 to 1997, in young Australians, the prevalence of overweight and obesity combined doubled and that of obesity trebled (17). In Thailand, the prevalence of obesity in those aged 5–12 yr increased from 12.2 to 15.6% in just 2 yr (18). In 2003–2004, 17.1% of children aged 2–19 yr in the USA were obese (19).

Obesity is associated with an increase in cardiovascular risk factors (also indicators of metabolic syndrome) (20), and the persistence of these indicators from childhood and adolescence to young adulthood has been shown in several studies, including the Quebec Family Study (21, 22).

Recently, the IDF released its guidelines for defining and diagnosing the metabolic syndrome in adults (2). The intention was to rationalize the existing multiple definitions of the syndrome and to avoid the confusion that arose as a result of conflicting opinions on the value of each set of criteria. The use of a single unified definition makes it possible to estimate the global prevalence of metabolic syndrome and make valid comparisons between nations. However, to date, there has not been a unified definition that can be used to assess risk in children and adolescents, and existing adult-based definitions of the metabolic syndrome may not be appropriate to address the problem in this age group.

Prevalence studies

A study of adolescents using modified National Cholesterol Education Program (NCEP) [Adult Treatment Panel III (ATP III)] criteria (23) identified that 12% of the study group had the metabolic syndrome (24). When the $\geq$95th percentile of BMI was used as a cutoff point in the same study group, 31.3% were identified as having the syndrome, more than double of those previously found to be at risk. Duncan et al. (25) studied 991 adolescents (aged 12–19 yr) from National Health and Nutrition Examination Study (NHANES) 1999–2000 and used the ATP III definition modified for age. The overall prevalence of a metabolic syndrome phenotype among US adolescents increased from 4.2% in NHANES III (1988–1992) to 6.4% in NHANES 1999–2000. Based on population-weighted estimates, they estimated that

more than 2 million US adolescents currently have a metabolic syndrome phenotype.

In a population-based study of a Canadian Qji-Cree community involving 236 children aged 10–19 yr, Retnakaran et al. reported that 18.6% of the children met the criteria for the metabolic syndrome based on a pediatric metabolic syndrome definition based on the ATP III definition, and they used the ATP III definition modified for age and gender (26). Goodman et al. reported on a school-based, cross-sectional study of 1513 black, white, and Hispanic teenagers (27). Overall, the prevalence of ATP III-defined metabolic syndrome was 4.2% and that of the WHO-defined metabolic syndrome was 8.4%. The metabolic syndrome was found almost exclusively among obese teenagers in whom prevalence of the ATP III-defined metabolic syndrome was 19.5% and prevalence of WHO-defined metabolic syndrome (28) was 38.9%. No race or sex differences were present for ATP III definition. However, non-white teenagers were more likely to have metabolic syndrome by WHO criteria, and it was more common among girls if the WHO definition was used.

Chi et al. have recently undertaken a literature review on definitions of the metabolic syndrome in children and adolescents published in the past decade (29). They noted that the prevalence of metabolic syndrome in pre-adolescent girls varies widely because of disagreement among proposed definitions of metabolic syndrome in pediatrics. They called for a consensus definition for the metabolic syndrome in children, which would allow researchers to make better temporal, biological, environmental, and social comparisons between data sets.

The American College of Endocrinology definition (30) is not ideal in pediatric subjects as WC is rarely measured in children, and nomograms have only recently become available (31) for some ethnic groups but are not available for all. A recent paper has suggested yet another set of criteria with age- and gender-specific cutoff points (32). The variety of cutoff points used for the different components in this paper underlines the need for a single consistent definition with easily measurable components. Therefore, to date, no formal definition for the diagnosis of the metabolic syndrome in children and adolescents has been developed. The rapid increase in obesity highlights the urgency for a definition that could be used to further understand who is at high risk and to distinguish them from those with 'simple' uncomplicated obesity.

Problems in definition of the metabolic syndrome in children and adolescents

The metabolic syndrome in adults is defined as a cluster of cardiovascular and diabetes risk factors including abdominal obesity, dyslipidemia, glucose intolerance, and hypertension (2). While the danger associated with clustering of components of the metabolic syndrome has been demonstrated in adults, where the presence of three or more components significantly increases the risk for coronary heart disease death/non-fatal myocardial infarction and the onset of new diabetes (33), few, if any, outcome data in children exist.

While one definition, although with gender- and ethnicity-specific cutoff points, is suitable for use in the at-risk adult population (2), transposing a single definition to children and adolescents is problematic. Blood pressure, lipid levels, and anthropometric variables change with age and pubertal development. Puberty impacts on fat distribution and is known to cause a decrease both in insulin sensitivity, of approximately 30% with a complementary increase in insulin secretion (34), and in adiponectin levels (35). Therefore, single cutoff points cannot be used to define abnormalities in children. Instead, values above the 90th, 95th, or 97th percentile for gender and age are used. However, there has not been universal agreement as to which level to use for the criteria for the metabolic syndrome.

Risk factors for the metabolic syndrome

The importance of the early identification of children at risk of developing the metabolic syndrome and subsequently progressing to type 2 diabetes and cardiovascular disease in later life must not be underestimated. From birth and before, circumstances can predispose a child to conditions such as obesity or dysglycemia. The presence of maternal gestational diabetes (36), low birth weight (37), infant feeding practices (38), early adiposity rebound (39), and genetic factors may all contribute to a child's future level of risk. Being raised in an 'obesogenic' environment can also have a strong impact, as can the influence of socioeconomic factors (40), with weight gain often being observed as a positive correlate to affluence in developing countries.

Longitudinal outcome studies and further research on the progression and etiology of the metabolic syndrome are urgently required to ascertain the long-term outcomes of abdominal obesity and clustering of the components of metabolic syndrome in at-risk children and to help improve future definitions of the syndrome.

Outline of the components of the new IDF definition

This new IDF definition of metabolic syndrome in children and adolescents was developed during

a consensus workshop that brought together experts in the field of the metabolic syndrome and pediatrics. The purpose of the new definition of metabolic syndrome in children and adolescents is to expand on the IDF recommendations for managing type 2 diabetes in the young (1) and to provide a useful and unified tool for identifying those at risk. A clinically accessible diagnostic tool, avoiding measurements that may only be available in research settings, is needed to identify the metabolic syndrome in children and adolescents globally. This need has prompted the IDF to develop a definition that has used the limited data available from existing studies in youth. As with the adult criteria, we look on these new criteria as a starting point. As new information emerges, they can be modified.

Inspired, in part, by the IDF worldwide definition of metabolic syndrome in adults (2), this new definition builds on previous studies investigating the prevalence of metabolic syndrome in children and adolescents, which have used modified adult criteria with varying cutoff points (12–14, 41, 42) (Table 1). The wide variety of cutoff points used has emphasized the need for a single consistent set of criteria, which is easily measurable and can be used as the basis for future work (29).

Because of the developmental challenges presented by the age-related differences in children and adolescents, the new IDF definition of metabolic syndrome has been divided according to the following age groups: 6 to <10, 10 to <16, and ≥16 yr (Table 2). In all the three age groups, abdominal obesity is the '*sine qua non*'. We suggest that below the age of 10 yr, the metabolic syndrome as an entity is not diagnosed, although a strong message for weight reduction will be made for these children. At the age of 10 yr and more, a diagnosis of metabolic syndrome can be made. It requires the presence of abdominal obesity plus the presence of two or more of the other components (elevated triglycerides, low high-density lipoprotein (HDL)-cholesterol, high blood pressure, and elevated plasma glucose). The IDF adult criteria (2) can be used for adolescents aged ≥16 yr, while a modified version of these criteria will be applied to those aged 10 to <16 yr (use 90th percentile cutoff point for waist and <40 mg/dL of HDL for both sexes). On the basis of emerging new data, these criteria may change in the future.

The informed evidence base for the use of WC as the '*sine qua non*' and the given cutoff points

In adults, insulin resistance and abdominal obesity are considered to be significant causative factors in the development of the metabolic syndrome (9, 43, 44). The link between obesity, insulin resistance, and the risk of developing the metabolic syndrome has also been described in children (22, 27). With measurement of insulin resistance considered to be impractical for clinical use, abdominal adiposity was positioned as the '*sine qua non*' in the IDF definition of metabolic syndrome in adults (2) and is recognized to be an independent risk factor for the development of cardiovascular disease in adults (45).

Abdominal obesity can be easily assessed using the simple measure of WC, which is known to correlate more strongly with visceral adipose tissue (VAT) than BMI in adults (46) and is a strong predictor of cardiovascular disease risk factors in children (47). The correlation between WC and VAT has also been more recently demonstrated in children (48), further strengthening the existing evidence that WC is an effective measure of abdominal obesity (49) in the youth population.

In children and adolescents, a number of studies have demonstrated a similar link between childhood obesity and elevated cardiovascular risk in later life. The Bogalusa Heart study showed that childhood overweight is related to the development of adverse risk factors (BMI, lipids, insulin, diabetes mellitus, and blood pressure) in adulthood and is attributable to the strong persistence of weight status from childhood to adulthood (50). Of the overweight children in the Bogalusa Heart study (BMI ≥95th percentile), 77% remained obese in adulthood. Furthermore, the Muscatine study demonstrated that in young adults, excess weight was the earliest predictor of coronary artery calcification (51). The ATP III definition, applied to a cohort of individuals aged 12–19 yr (NHANES III), identified that 4% of those studied were found to have the metabolic syndrome, with 80% of those meeting the criteria of being overweight (13). Using a modified version of the ATP III definition, metabolic syndrome in adolescents has also been linked to high levels of C-reactive protein, a pro-inflammatory marker. Of the five components of metabolic syndrome, C-reactive protein was higher only among those with abdominal obesity (41).

Waist circumference in children is an independent predictor of insulin resistance, lipid levels, and blood pressure (4, 52–54) – all components of metabolic syndrome. Moreover, in obese youth with similar BMI, insulin sensitivity is lower in those with high VAT and high waist/hip ratio (53, 54). Furthermore, insulin sensitivity decreases and insulin levels increase with increasing WC percentiles (3). These data, combined with the unequivocal evidence of the dangers of abdominal obesity in adulthood, support the use of abdominal obesity as the '*sine qua non*' for the diagnosis of metabolic syndrome in children and adolescents.

Table 1. A range of the published metabolic syndrome definitions in pediatrics

Cook et al. (14)	de Ferranti et al. (42)	Cruz et al. (15)	Weiss et al. (13)	Ford et al. (41)
Three or more of the following				
Fasting glucose ≥110 mg/dL	Fasting glucose ≥6.1 mmol/L (≥110 mg/dL)	Impaired glucose tolerance (ADA criterion)	Impaired glucose tolerance (ADA criterion)	Fasting glucose ≥110 mg/dL (additional analysis with ≥100 mg/dL)
WC ≥90th percentile (age and sex specific, NHANES III)	WC >75th percentile	WC ≥90th percentile (age, sex and race specific, NHANES III)	BMI – Z score ≥2.0 (age and sex specific)	WC ≥90th percentile (sex specific, NHANES III)
Triglycerides ≥110 mg/dL (age specific, NCEP)	Triglycerides ≥1.1 mmol/L (≥100 mg/dL)	Triglycerides ≥90th percentile (age and sex specific, NHANES III)	Triglycerides >95th percentile (age, sex and race specific, NGHS)	Triglycerides ≥110 mg/dL (age specific, NCEP)
HDL-C ≤40 mg/dL (all ages/sexes, NCEP)	HDL-C <1.3 mmol/L (<50 mg/dL)	HDL-C ≤10th percentile (age and sex specific, NHANES III)	HDL-C <5th percentile (age, sex and race specific, NGHS)	HDL-C ≤40 mg/dL (all ages/sexes, NCEP)
Blood pressure ≥90th percentile (age, sex and height specific, NHBPEP)	Blood pressure >90th percentile	Blood pressure >90th percentile (age, sex and height specific, NHBPEP)	Blood pressure >95th percentile (age, sex and height specific, NHBPEP)	Blood pressure ≥90th percentile (age, sex and height specific, NHBPEP)

ADA, American Diabetes Association; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; NCEP, National Cholesterol Education Program; NGHS, National Growth and Health Study; NHBPEP, National High Blood Pressure Education Program; WC, waist circumference.

Percentiles rather than absolute values of WC have been used in the new criteria to compensate for varying degrees of development and ethnicity in the youth population. WC percentile data are becoming increasingly available worldwide (31, 55–58). Children with a WC >90th percentile are more likely to have multiple risk factors than those with a WC below this level (59). Several studies attempting to estimate the prevalence of metabolic syndrome in children and adolescents have already used the 90th percentile as a cutoff point for WC (13, 14, 41). We have also chosen to use the 90th percentile as a cutoff point for WC based on this existing evidence and aim to reassess criteria and cutoff points in 5 yr and modify the guidelines, if necessary, based on the new outcome data.

Criteria for the other components of the new IDF definition

Previous studies investigating the metabolic syndrome in children and adolescents have used a range of cutoff points primarily based on ATP III criteria for categorizing additional components of the syndrome, i.e., triglycerides, HDL-cholesterol, blood pressure, and fasting glucose (Table 1) (12–14, 41, 42). Other definitive sources include the National High Blood Pressure Education Program, which recommends blood pressure cutoff points of >90th or >95th percentile adjusted for height, age, and gender to identify 'high normal' blood pressure or prehypertension and high blood pressure or hypertension in children and adolescents (60). Cutoff points for impaired fasting glucose have previously followed recommendations by the American Diabetes Association (ADA) [100–125 mg/dL (≥5.6–6.9 mmol/L)] (61) and the NCEP/ATP III in adults [≥110 mg/dL (6.1 mmol/L)] (23), although the latter has recently changed to the lower ADA recommended levels (62). Criteria for defining lipid (triglyceride and HDL-cholesterol) imbalances are even less consistent in the youth population, with recommendations by the NCEP/ATP III (age specific), NHANES III (age and gender specific), and the National Growth and Health Study (age, gender, and ethnic specific), employing either absolute value or percentile cutoff points. In view of this lack of consistency, we believe that use of the adult levels for the present is wise until further information is available.

Recommendations for future research

We recommend the following topics as priorities for future research:

(i) Develop a better understanding of the relationship between body fat and its distribution in children and adolescents, e.g., dual energy X-ray absorptiometry (DEXA), WC, BMI, and height and weight percentiles;

Table 2. The IDF definition of the at risk group and metabolic syndrome in children and adolescents

Age group (years)	Obesity (WC)	Triglycerides	HDL-C	Blood pressure	Glucose
6–<10†	≥90th percentile				
10–<16	≥90th percentile or adult cut-off if lower	≥1.7 mmol/L (≥150 mg/dL)	<1.03 mmol/L (<40 mg/dL)	Systolic BP ≥130 or diastolic BP ≥85 mm Hg	FPG ≥5.6 mmol/L (100 mg/dL)** or known T2DM
16+(Adult criteria)	WC ≥ 94cm for Europid males and ≥ 80cm for Europid females, with ethnic-specific values for other groups*)	≥1.7 mmol/L (≥150 mg/dL) or specific treatment for high triglycerides	<1.03mmol/L (<40 mg/dL) in males and <1.29mmol/L (<50 mg/dL) in females, or specific treatment for low HDL	Systolic BP ≥130 or diastolic BP ≥85 mm Hg or treatment of previously diagnosed hypertension	FPG ≥5.6 mmol/L (100 mg/dL)** or known T2DM

BP: blood pressure; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; IDF, International Diabetes Federation; T2DM, type 2 diabetes mellitus; WC, waist circumference.
*For those of South and South-East Asian, Japanese, and ethnic South and Central American origin, the cutoffs should be ≥90 cm for men, and ≥80 cm for women. The IDF Consensus group recognise that there are ethnic, gender and age differences but research is still needed on outcomes to establish risk.
†Metabolic syndrome cannot be diagnosed, but further measurements should be made if there is a family history of metabolic syndrome, T2DM, dyslipidemia, cardiovascular disease, hypertension and/or obesity.
**For clinical purposes, but not for diagnosing the MetS, if FPG 5.6-6.9 mmol/L (100-125 mg/dl) and not known to have diabetes, an oral glucose tolerance test should be performed.
Diagnosing the metabolic syndrome requires the presence of central obesity plus any two of the other four factors.

(ii) a) Explore whether early growth patterns predict future adiposity and features of the metabolic syndrome, diabetes, and cardiovascular disease and b) explore whether low birth weight predicts future metabolic syndrome, diabetes, and cardiovascular disease;
(iii) Perform factor analysis in children and adolescents to establish grouping of metabolic characteristics – adiposity, dyslipidemia, hyperinsulinemia, hypoadiponectinemia, and insulin resistance;
(iv) Investigate how should obesity in children could be better defined, e.g., weight/height, WC etc.;
(v) Develop ethnic-specific normal ranges for WC, ideally based on healthy values;
(vi) Perform ethnic-specific studies of WC etc. vs. abdominal (truncal) fat based on magnetic resonance imaging and DEXA;
(vii) Support studies of adiponectin, leptin, etc. in children and adolescents to determine if they may be predictors of metabolic syndrome in adulthood;
(viii) Initiate long-term studies of multi-ethnic cohorts followed into adulthood to determine the natural history and effectiveness of intervention strategies, particularly lifestyle.

In conclusion, to combat any conflict that could arise from these multiple interpretations of the metabolic syndrome in children and adolescents, the IDF consensus group has aimed primarily at developing a simple, easy-to-apply definition to begin using in the clinical setting. In the absence of definitive research findings at this time, the proposed IDF definition of the metabolic syndrome in children and adolescents (Table 2) adheres to the absolute values presented in the adult definition (2), with the exception of WC. As described previously, until such time that outcome data from studies in children and adolescents indicate otherwise, WC percentiles are recommended for use.

Early detection, followed by treatment in the form of lifestyle intervention and possibly pharmacotherapy, if its safety has been clearly demonstrated, is vital in halting the progression of this syndrome pathway in the adolescent population. It is likely that this will reduce morbidity and mortality in adulthood, as well as minimize the global socioeconomic burden of cardiovascular disease and type 2 diabetes.

Acknowledgements

The workshop was sponsored by an unrestricted educational grant to the IDF Task Force on Epidemiology and Prevention from sanofi-aventis.

References

1. Alberti G, Zimmet P, Shaw J, Bloomgarden Z, Kaufman F, Silink M. Type 2 diabetes in the young: the evolving epidemic: the International Diabetes Federation Consensus Workshop. Diabetes Care 2004: 27: 1798–1811.
2. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome – a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med 2006: 23: 469–480.
3. Inge TH, Garcia V, Daniels S et al. A multidisciplinary approach to the adolescent bariatric surgical patient. J Pediatr Surg 2004: 39: 442–447.
4. Lee S, Bacha F, Gungor N, Arslanian SA. Waist circumference is an independent predictor of insulin resistance in black and white youths. J Pediatr 2006: 148: 188–194.
5. Lee S, Bacha F, Arslanian SA. Waist circumference, blood pressure, and lipid components of the metabolic syndrome. J Pediatr 2006: 149: 809–816.
6. Urakami T, Kubota S, Nitadori Y, Harada K, Owada M, Kitagawa T. Annual incidence and clinical characteristics of type 2 diabetes in children as detected by urine glucose screening in the Tokyo metropolitan area. Diabetes Care 2005: 28: 1876–1881.
7. Sicree R, Shaw J, Zimmet P. The Global Burden. Diabetes and Impaired Glucose Tolerance. Prevalence and Projections. In: Gan D, ed. Diabetes Atlas, 3rd edn. Brussels: International Diabetes Federation, 2006: 16–103.
8. Isomaa B, Almgren P, Tuomi T et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001: 24: 683–689.
9. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005: 365: 1415–1428.
10. Stern MP, Williams K, Gonzalez-Villalpando C, Hunt KJ, Haffner SM. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? Diabetes Care 2004: 27: 2676–2681.
11. Cameron AJ, Shaw JE, Zimmet PZ. The metabolic syndrome: prevalence in worldwide populations. Endocrinol Metab Clin North Am 2004: 33: 351–376.
12. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002: 287: 356–359.
13. Weiss R, Dziura J, Burgert TS et al. Obesity and the metabolic syndrome in children and adolescents. N Engl J Med 2004: 350: 2362–2374.
14. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. Arch Pediatr Adolesc Med 2003: 157: 821–827.
15. Cruz ML, Weigensberg MJ, Huang TT, Ball G, Shaibi GQ, Goran MI. The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. J Clin Endocrinol Metab 2004: 89: 108–113.
16. World Health Organization. Global strategy on diet, physical activity and health: obesity and overweight. 2004 (available from http://www.int.dietphysicalactivity/publications/facts/obesity/en). Accessed February 2007.
17. Booth ML, Chey T, Wake M et al. Change in the prevalence of overweight and obesity among young Australians, 1969–1997. Am J Clin Nutr 2003: 77: 29–36.
18. Mo-suwan L, Junjana C, Puetpaiboon A. Increasing obesity in school children in a transitional society and the effect of the weight control program. Southeast Asian J Trop Med Public Health 1993: 24: 590–594.
19. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. JAMA 2006: 295: 1549–1555.
20. Burke V, Beilin LJ, Simmer K et al. Predictors of body mass index and associations with cardiovascular risk factors in Australian children: a prospective cohort study. Int J Obes (Lond) 2005: 29: 15–23.
21. Katzmarzyk PT, Perusse L, Malina RM, Bergeron J, Despres JP, Bouchard C. Stability of indicators of the metabolic syndrome from childhood and adolescence to young adulthood: the Quebec Family Study. J Clin Epidemiol 2001: 54: 190–195.
22. Rosenberg B, Moran A, Sinaiko AR. Insulin resistance (metabolic) syndrome in children. Panminerva Med 2005: 47: 229–244.
23. NCEP/ATPIII. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001: 285: 2486–2497.
24. Gungor N, Bacha F, Saad R, Janosky J, Arslanian SA. The metabolic syndrome in healthy children using in-vivo insulin sensitivity measurement (abstract). Pediatr Res 2004: 55: 145A.
25. Duncan GE, Sierra ML, Zhou X-H. Prevalence and trends of a metabolic syndrome phenotype among U.S. adolescents, 1999–2000. Diabetes Care 2004: 27: 2438–2443.
26. Retnakaran R, Zinman B, Connelly PW, Harris SB, Hanley AJG. Nontraditional cardiovascular risk factors in pediatric metabolic syndrome. J Pediatr 2006: 148: 176–182.
27. Goodman E, Daniels SR, Morrison JA, Huang B, Dolan LM. Contrasting prevalence of and demographic disparities in the World Health Organization and National Cholesterol Education Program Adult Treatment Panel III definitions of metabolic syndrome among adolescents. J Pediatr 2004: 145: 445–451.
28. World Health Organization. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications; Part 1: Diagnosis and Classification of Diabetes Mellitus. Geneva: Department of Noncommunicable Disease Surveillance, 1999: 31–33.
29. Chi CH, Wang Y, Wilson DM, Robinson TN. Definition of metabolic syndrome in preadolescent girls. J Pediatr 2006: 148: 788–792.
30. American College of Endocrinology Task Force on the Insulin Resistance Syndrome. American College of Endocrinology position statement on the insulin resistance syndrome. Endocr Pract 2003: 9: 236–252.
31. Fernandez JR, Redden DT, Pietrobelli A, Allison DB. Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. J Pediatr 2004: 145: 439–444.
32. Joliffe CJ, Janssen I. Development of age-specific metabolic syndrome criteria that are linked to the Adult Treatment Panel III and International Diabetes Federation Criteria. J Am Coll Cardiol 2007: 49: 891–898.
33. Sattar N, Gaw A, Scherbakova O et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. Circulation 2003: 108: 414–419.
34. Bloch CA, Clemons P, Sperling MA. Puberty decreases insulin sensitivity. J Pediatr 1987: 110: 481–487.
35. Reinehr T, Roth C, Menke T, Andler W. Adiponectin before and after weight loss in obese children. J Clin Endocrinol Metab 2004: 89: 3790–3794.

36. Pettitt DJ, Nelson RG, Saad MF, Bennett PH, Knowler WC. Diabetes and obesity in the offspring of Pima Indian women with diabetes during pregnancy. Diabetes Care 1993: 16 (Suppl. 1): 310–314.
37. Wei JN, Sung FC, Li CY et al. Low birth weight and high birth weight infants are both at an increased risk to have type 2 diabetes among schoolchildren in Taiwan. Diabetes Care 2003: 26: 343–348.
38. Pettitt D, Forman M, Hanson R, Knowler W, Bennett P. Breast feeding in infancy is associated with lower rates of non-insulin-dependent diabetes mellitus. Lancet 1997: 350: 166–168.
39. Eriksson JG, Forsen T, Tuomilehto J, Osmond C, Barker DJ. Early adiposity rebound in childhood and risk of type 2 diabetes in adult life. Diabetologia 2003: 46: 190–194.
40. Abu Sayeed M, Ali L, Hussain MZ, Rumi MA, Banu A, Azad Khan AK. Effect of socioeconomic risk factors on the difference in prevalence of diabetes between rural and urban populations in Bangladesh. Diabetes Care 1997: 20: 551–555.
41. Ford ES, Ajani UA, Mokdad AH. The metabolic syndrome and concentrations of C-reactive protein among U.S. youth. Diabetes Care 2005: 28: 878–881.
42. de Ferranti SD, Gauvreau K, Ludwig DS, Newfeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the third national health and nutrition examination survey. Circulation 2004: 110: 2494–2497.
43. Saad M, Lillioja S, Nyomba B et al. Racial differences in the relation between blood pressure and insulin resistance. N Engl J Med 1991: 324: 733–739.
44. Anderson PJ, Critchley JA, Chan JC et al. Factor analysis of the metabolic syndrome: obesity vs insulin resistance as the central abnormality. Int J Obes Relat Metab Disord 2001: 25: 1782–1788.
45. Yusuf S, Hawken S, Ounpuu S et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004: 364: 937–952.
46. Pouliot M-C, Després J-P, Lemieux S et al. Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. Am J Cardiol 1994: 73: 460–468.
47. Savva SC, Tornaritis M, Savva ME et al. Waist circumference and waist-to-height ratio are better predictors of cardiovascular disease risk factors in children than body mass index. Int J Obes Relat Metab Disord 2000: 24: 1453–1458.
48. Brambilla P, Bedogni G, Moreno LA et al. Cross-validation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children. Int J Obes (Lond) 2006: 30: 23–30.
49. Taylor RW, Jones IE, Williams SM, Goulding A. Evaluation of waist circumference, waist-to-hip ratio, and the conicity index as screening tools for high trunk fat mass, as measured by dual-energy X-ray absorptiometry, in children aged 3-19 y. Am J Clin Nutr 2000: 72: 490–495.
50. Freedman DS, Khan LK, Dietz WH, Srinivasan SR, Berenson GS. Relationship of childhood obesity to coronary heart disease risk factors in adulthood: the Bogalusa Heart Study. Pediatrics 2001: 108: 712–718.
51. Mahoney LT, Burns TL, Stanford W et al. Usefulness of the Framingham risk score and body mass index to predict early coronary artery calcium in young adults (Muscatine Study). Am J Cardiol 2001: 88: 509–515.
52. Flodmark CE, Sveger T, Nilsson-Ehle P. Waist measurement correlates to a potentially atherogenic lipoprotein profile in obese 12–14-year-old children. Acta Paediatr 1994: 83: 941–945.
53. Hirschler V, Aranda C, Calcagno Mde L, Maccalini G, Jadzinsky M. Can waist circumference identify children with the metabolic syndrome? Arch Pediatr Adolesc Med 2005: 159: 740–744.
54. Bacha F, Saad R, Gungor N, Arslanian SA. Are obesity-related metabolic risk factors modulated by the degree of insulin resistance in adolescents? Diabetes Care 2006: 29: 1599–1604.
55. Katzmarzyk PT. Waist circumference percentiles for Canadian youth 11–18y of age. Eur J Clin Nutr 2004: 58: 1011–1015.
56. McCarthy HD, Jarrett KV, Crawley HF. The development of waist circumference percentiles in British children aged 5.0–16.9 y. Eur J Clin Nutr 2001: 55: 902–907.
57. Eisenmann JC. Waist circumference percentiles for 7- to 15-year-old Australian children. Acta Paediatr 2005: 94: 1182–1185.
58. Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference, and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. Pediatrics 2004: 114: e198–e205.
59. Maffeis C, Pietrobelli A, Grezzani A, Provera S, Tato L. Waist circumference and cardiovascular risk factors in prepubertal children. Obes Res 2001: 9: 179–187.
60. NHBPEP. Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: a working group report from the National High Blood Pressure Education Program. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Pediatrics 1996: 98: 649–658.
61. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997: 20: 1183–1197.
62. Grundy SM, Cleeman JI, Daniels SR et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation 2005: 112: 2735–2752.