



An assessment of Body Mass Index and sensitive period for overweight development in Macao students at primary school age

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ABSTRACT: The concomitant risk of physical inactivity and sedentary lifestyle development causing various non-communicable diseases is recognized worldwide. Therefore, development of strategies to form a concrete public health policy overcoming this problem is most important. This study observed the distribution and changes of Body Mass Index (BMI) over six years among boys and girls. Data on children height and weight and their BMI were collected. A total of 5369 (3368 male and 2001 female) children were recruited from 10 schools in Macao. The children were 6 years old in 2008 and turned 11 in 2013. Statistical analyses involved descriptive statistics, t-test, and a Chi-squared test. The findings indicated greater BMI among males than females across all age at the 0.05 level of significance, and the ages of 8 and 9 seemed to be a sensitive period for an increase in overweight and obesity. The results indicate the need to have focused strategies and structured interventions for males at the critical ages from 8 to 9 years.

KEY WORDS: body mass index, weight status, school-age children

Introduction

Lack of physical activity, the development of sedentary lifestyle and an increasing rate of obesity among children are be-

coming a health issue in both developed and developing countries. The problem emerged and arose as a global concern due to the increasing number of obese and overweight people. The use of Body

Mass Index (BMI) became a common method to track the problem of obesity, overweight, standard weight or underweight due to its low cost in operation, simplicity and proven convenience when applied to analysis with large number of samples. The index was also adopted as a popular measuring tool in observing the rate of obesity, lifestyle development, health habits (Zayed et al. 2018; Ahmed et al. 2017) in people with an obesity problem and active living over the last thirty years due to its easy application and inexpensive nature (CDC 2015; Romero-Corral et al. 2008). The World Health Organization (WHO 2006) and the National Institutes of Health (NIH) suggested that in adults overweight be defined as a BMI between 25.0 and 29.9 kg/m² and obesity be defined as a BMI greater than 30.0 kg/m² (Nguyen and El-Serag 2010). In 2007, there were already an estimated number of 22 million overweight children under the age of 5 throughout the world. This figure rose in 2013 to an estimate of over 42 million overweight children (UNICEF–WHO–World Bank Group 2015). In terms of regional breakdowns, the number of overweight children under the age of 5 years in 2013 was estimated at 18 million in Asia, 11 million in Africa and 4 million in Latin America and the Caribbean (UNICEF–WHO–World Bank Group 2015). An estimated 31 million of these children lived in developing countries (UNO, World Population Prospects 2015 Revision). In North America, almost 32.6 percent of children were overweight and 18.0% were obese (Overweight and Obesity Statistics 2008). In Canada, 26% of children and youth between the ages of 2 and 17 years were overweight or obese (Nutrition: findings from the Canadian Community Health Survey 2005).

Nevertheless, the reliability of BMI was challenged due to the limitation in providing information to assess the body fat distribution (Chan et al. 2003). The Centers for Disease Control and Prevention (CDC) (2015) supplied information on the clinical limitation of BMI to indicate the surrogate problem of measuring the excess weight rather than excess body fat. The debate on the use of BMI seemed to reach a consensus that when someone was classified as obese according to BMI, the person was also most likely to be obese according to body fat percentage. The Romero-Corral et al. (2008) study on the accuracy of BMI in diagnosing obesity in the USA adults indicated that over 95% of men and 99% of women identified as obese by BMI were also obese by body fat percentage measures. The CDC (2015) further suggested that BMI was a reasonable indicator of body fat for both adults and children. However, because BMI does not measure body fat directly, it should be used not as a diagnostic tool but rather as a measure to track weight status in populations or serve as a screening tool to identify potential weight problems among individuals. Although there is a debate on the understanding of obesity accumulation and its significant impact on both physical and psychological health, obesity has also been related to various other difficulties in health, the development of community disease, lifestyle and food preferences, socio-economic and family problems (Kim 2004; Dehghan et al. 2005; Ramachandran et al. 2012; Żądzińska et al. 2012). Research such as Lamon-Fava, Wilson and Schaefer's (1996) study of BMI and coronary heart disease, Wils-gaard and colleagues' (2005) correlational study on BMI and lifestyle development and recently Sohlberg et al.'s study

(2012) of BMI, height, and risks of pre-eclampsia are examples of research that addresses the problem of obesity. This research indicated that the impact of low physical activity and excessive intake of energy was highly associated with obesity (Dehghan et al. 2005; Ho et al. 2017; Ahmed et al. 2016; Sánchez et al. 2016; Sánchez et al. 2017) and various health risk (Miles 2007, Rosset et al. 2016). The concern with the increase of obese and overweight has motivated government and non-government organizations to respond with strategies to observe, monitor and achieve improvement. Lee (2003) engaged with the research of Trim and Fit, which was launched in 1992 to assist Singapore to become healthy, active and fit. BMI was adopted as the observational tool to track the health conditions of the general public.

The present study focused on child growth data, namely height, weight and BMI classification, which were obtained over 6 years from the 2008/2009 to 2013/2014 school academic years. The present study hypothesized that there were significant differences in the level of BMI between sexes and also hypothesized that boys have a greater mean level of weight and BMI than girls. These hypotheses were postulated through the research project completed by Gortmaker et al. (1999). It is a school-based Interdisciplinary intervention study conducted over 2 academic year. The study observed 1295 children garnered from ethnically diverse communities of Massachusetts, between the ages of 6 to 8 years. The project aimed at decreasing TV time and increasing vegetable intake and activities by participants. When compared with the control group, the prevalence of obesity among girls decreased but remained unchanged in boys. The comment implies a

consolidated pattern of excessive weight gain in boys compared to girls. Because overweight and obesity are not sudden events, questions such as “when did it happen?” and “were there any sensitive periods for overweight to develop?” were asked to understand Gortmaker et al.’s (1999) work. If there was such a sensitive period for overweight to develop, it would be important to determine whether effects in this period were a temporary phenomenon or persisted into the age of adolescence. Plachta-Danielzik and colleagues (2007) study indicated this concern because their conclusion on overweight and obese children was that after nearly 4 years of school-based intervention program, no positive effect on the incidence of overweight and obesity was found. There is a small trend in the intervention schools that more overweight and obese children reach normal weight, but this result was not significant. There is reason to believe that once overweight and obesity have developed in childhood, it will be difficult to reverse the situation. If this is the case, the application of suitable intervention activities at the beginning of such a sensitive period will be important (Graf 2011; Kriemler et al. 2011).

Material and Methods

Ethical Concern

Upon receiving official approval from the Research and Development Office of the University of Macau, the Principal Investigator and his team approached the school principals for final consideration to continue with the data collection. Written consent was received from the participating schools as well as from parents. In order to seek parents’ per-

mission, participating schools contact all parents and informed them about the project's aims and significance. Further, parents were requested to submit their written consent to the schools authorities whether their child/children would participate in the project, once the participating schools garnered parents' permission they disseminated the details to the principal investigator about the participant's interest to be involved in the project. Succinctly, participate to take part in the study was totally a voluntary decision whereby children's successful participation in this project was associated with their greater interest and understanding involved in the entire process (Shaw et al. 2011). Additionally, health education has been considered as a compulsory educational policy in Macau. According to the government health education policy, the research team was supposed to provide a simple report card to students to indicate their health status (DSEJ 2018). As a result, such productive manifestation profusely encouraged parents to participate in the research project. Further, a detail briefing of every child was conducted, and the parents were informed and provided with a handbook and information brochure to assist in their understanding of the data collection. The schools were provided with the necessary apparatus to conduct height and weight measures and calculate the BMI status of every child.

Participants

For the present study, data were collected over 6 years starting from 2008 to 2013 on a total sample of 5369 school children. The sample included 3368 male and 2001 female school children from 10 schools in Macao. Their ages ranged from 6 years in 2008 to 11 years in 2013.

During this period, all of the children in the same class were observed, but because some children left and others joined, the number of children in each year of observation differed according to the following figures representing the mean and standard deviation of male and female participants in Table 1 in the Result section.

Tool used in the study

BMI was calculated as the primary variable in this study and was defined as the weight in kilograms divided by the height in metres squared (kg/m^2). To determine the body mass in relation to height and weight, BMI values were further categorized into one of four groups, namely underweight, standard weight, overweight and obese, according to the norms and indicators used in Taiwan from 2008 to 2011 (Ministry of Education 2016).

Statistical analysis

Descriptive statistics such as the mean and standard deviation were used to analyse the basic features. Furthermore, to determine the difference between sexes in the variables, an independent t-test was used. Finally, Chi-squared was implemented to explore prevalence of the BMI categories among cohorts (age and year-wise).

Results

The sex and year-wise descriptions of the measured variables are presented in Table 1.

The results show a steady increase in the BMI with age for both boys and girls, with the BMI of boys slightly greater than that of girls. The standard deviation also

increases with age, suggesting that there is more variance in the BMI as children get older. At a younger age, the BMI of individuals is thus fairly similar, but as children grow older, there is a trend towards bigger differences among them in relation to their BMI, regardless of their sex. These differences between sex and age groups were further analysed to determine whether these differences were significant, and the results are presented in Table 2.

Independent-samples t-tests were conducted to determine the sex group differences for the height, weight and BMI of the school children in each age group. The results are presented in Table 2. When the heights of boys and girls were compared, a significant difference was found only for the 7-year-old males (Mean=128.24 cm, SD=6.12 cm) and females (Mean=126.59 cm, SD=6.67 cm; $t(895)=3.77, p=0.001$), and 8-year-old males (Mean= 133.47 cm, SD=7.12 cm) and females (Mean=131.90 cm, SD=7.38 cm; $t(922)=3.15, p=0.002$).

The magnitude of the difference for the 7- and 8-year-old groups was small (Eta Squared = 0.015 and 0.010, respectively). No significant sex differences were found for the height of 6-year-old and 9- to 11-year-old children. When the weight of boys and girls was compared, a significant difference was found for sex in all of the age groups. The relevant means and standard deviations are presented in Table 1, and the significant differences in the weight between boys and girls are presented in Table 2. Overall, the weight of boys in all of the age categories was significantly heavier than the weight of girls in each age group. The magnitude of the differences was small for all of the age groups, with an Eta squared of 0.01 (Table 2). When the BMI of boys and girls was compared, a significant difference was also found by sex in all of the age groups. The relevant means and standard deviation are presented in Table 1, and the significant differences in the BMI between boys and girls are presented in Table 2. Overall,

Table 1. Sex and year-wise descriptive statistics of all the parameters examined in the study

Year of the study	Age group (n)	Age (years) Mean±SD	Characteristics		
			Height (cm) Mean±SD	Weight (kg) Mean±SD	BMI (kg/m ²) Mean±SD
Males					
2008	6 (556)	6.47±0.55	122.77±6.14	23.82±5.23	15.70±2.75
2009	7 (569)	7.50±0.57	128.24±6.12	27.14±6.61	16.37±3.01
2010	8 (594)	8.56±0.62	133.47±7.12	30.07±8.28	16.72±3.49
2011	9 (612)	9.62±0.73	139.04±7.50	36.04±9.96	18.54±3.98
2012	10 (525)	10.69±0.77	145.98±8.77	41.85±12.35	19.38±4.32
2013	11 (512)	11.72±0.81	152.57±9.38	47.19±13.63	20.02±4.37
Females					
2008	6 (338)	6.50±0.58	121.96±6.42	22.61±4.62	15.13±2.33
2009	7 (328)	7.55±0.64	126.59±6.67	25.37±5.56	15.71±2.40
2010	8 (330)	8.56±0.64	131.90±7.38	28.58±7.31	16.23±2.90
2011	9 (338)	9.55±0.67	139.05±7.74	33.63±8.27	17.21±3.12
2012	10 (333)	10.58±0.65	147.03±7.63	38.66±9.51	17.73±3.36
2013	11 (334)	11.66±0.77	152.54±7.24	44.63±10.02	19.03±3.39

Table 2. The independent samples t-test to see the difference between the sexes for height, weight and BMI from the year 2008 to 2013

Characteristics Year of examination	t-test for Equality of Means					
	t-value	df	Sig. (2-tailed)	Mean Δ	Std. Error Δ	Effect size
Height (cm)						
6 years – 2008	1.88	892	0.060	0.81	0.431	0.053
7 years – 2009	3.77*	895	0.000	1.65	0.439	0.015
8 years – 2010	3.15*	922	0.002	1.56	0.496	0.010
9 years – 2011	1.32	948	0.186	-1.13	0.854	0.098
10 years – 2012	1.79	856	0.073	-1.05	0.585	0.015
11 years – 2013	0.05	844	0.963	0.03	0.605	0.075
Weight (kg)						
6 years – 2008	3.51*	892	0.000	1.21	0.346	0.010
7 years – 2009	4.08*	895	0.000	1.76	0.433	0.018
8 years – 2010	2.69*	921	0.007	1.46	0.545	0.007
9 years – 2011	3.80*	948	0.000	2.42	0.637	0.015
10 years – 2012	4.01*	856	0.000	3.18	0.794	0.018
11 years – 2013	2.94*	844	0.003	2.55	0.868	0.010
BMI (kg/m ²)						
6 years – 2008	3.20*	892	0.001	0.57	0.179	0.011
7 years – 2009	3.38*	895	0.001	0.66	0.194	0.012
8 years – 2010	2.16*	922	0.031	0.49	0.226	0.005
9 years – 2011	5.32*	948	0.000	1.33	0.251	0.030
10 years – 2012	5.93*	856	0.000	1.65	0.279	0.041
11 years – 2013	3.51*	844	0.000	0.99	0.282	0.014

*statistically significant at $p < 0.05$; values of the t-distribution at $t_{0.05}$ (two-tailed) for $\alpha = 1.960$.

Table 3. Distribution of body weight status stratified by sex, age group and year of the study

Year of the study	Age group (n)	Category of weight status based on BMI (kg/m ²)			
		Underweight n (%)	Standard n (%)	Overweight n (%)	Obesity n (%)
Males					
2008	6 (556)	143 (25.7)	326 (58.6)	49 (8.8)	38 (6.8)
2009	7 (569)	219 (38.5)	251 (44.1)	55 (9.7)	44 (7.7)
2010	8 (594)	246 (41.4)	240 (40.4)	59 (9.9)	49 (8.2)
2011	9 (612)	143 (23.4)	293 (47.9)	82 (13.4)	94 (15.4)
2012	10 (525)	103 (19.6)	247 (47.0)	79 (15.0)	96 (18.3)
2013	11 (512)	91 (17.8)	251 (49.0)	83 (16.2)	87 (17.0)
Females					
2008	6 (338)	113 (33.4)	182 (53.8)	29 (8.6)	14 (4.1)
2009	7 (328)	116 (35.4)	160 (48.8)	39 (11.9)	13 (4.0)
2010	8 (330)	96 (29.1)	188 (57.0)	23 (7.0)	23 (7.0)
2011	9 (338)	85 (25.1)	191 (56.5)	38 (11.2)	24 (7.1)
2012	10 (333)	94 (28.2)	173 (52.0)	40 (12.0)	26 (7.8)
2013	11 (334)	55 (16.5)	206 (61.7)	39 (11.7)	34 (10.1)

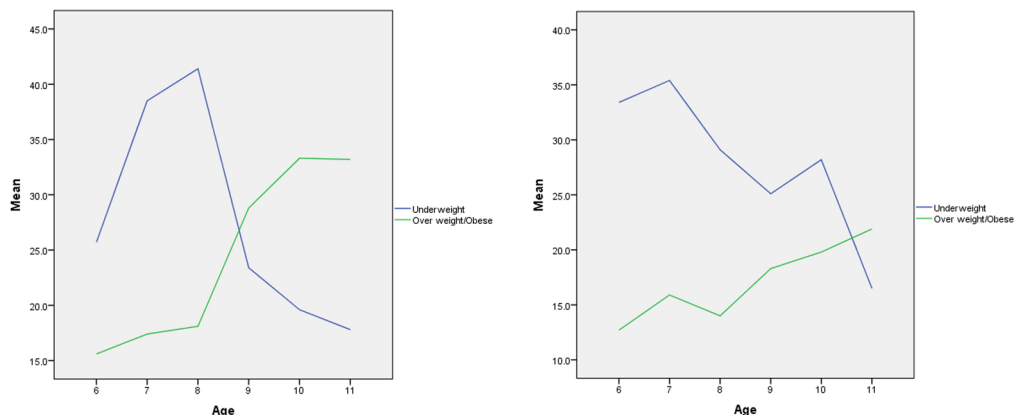


Fig. 1. Year-wise sex-based graphical representation of Body Mass Index for males (left) and females (right)

the BMI of boys in all of the age categories was significantly greater than the BMI of girls in each age group. The magnitudes of the differences were small, with Eta squared ranging from .005 to .041 for all of the age groups (Table 2). Further analysis to determine the number of children in each BMI category for each age group was conducted and is presented in Table 3.

The table shows that overweight and obesity is prevalent when boys and reached to 10 years (overweight – 15% and obesity – 18.3% in boys and overweight – 12% and obesity – 7.8% in girls) and 11 years (overweight – 16.2% and obesity – 17.0% in boys and overweight – 11.7% and obesity – 10.2% in girls).

Figures show the mean level of body mass index (underweight and overweight) of male and female. Male shows a greater mean level (overweight) in comparison to female children. Further, in both the cohorts, the trend of obesity appears when they reached to 10 and 11 years.

Discussion

One of the purposes of the study was to observe the BMI level in different categories such as Underweight, Standard, Overweight and Obese among boys and girls aged 6 to 11 years from 10 schools in Macao over a six year period from 2008 to 2013. The findings indicated that 24.2% (overweight 12.1% and obesity 12.1%) of boys were categorized as either overweight or obese, compared to 17.1% (overweight 10.4% and obesity 6.7%) of girls. The overall rate showed that 20.7% (overweight 11.3% and obesity 9.4%) of the children over the six-year period of observation were either overweight or obese. When these figures of overweight and obesity were compared with figures from Japan (23.0% overweight and 3.0% obese) (Prentice 2006), China (25.0% overweight and 4.0% obese) (Deurenberg et. al. 2001), Hong Kong (25.1% overweight and 3.8% obese) (Ko et. al. 2001), South Korea (27.4% overweight and 3.2% obese) (Kim et. al. 2005) and Malaysia (12.5% overweight and 5.0% obese) (Ismail et. al. 2002), it seems that less children are

categorized as overweight or obese in Macao. Nevertheless, this observation could be misleading because it does not take the diverse range of BMI classifications of overweight and obesity between countries into consideration. Various countries have different norms for the categorization of overweight and obesity, especially for children. For example, the WHO (2006) recommended the range of 18.5 to 25 kg/m² as normal adult mass, 25 to 30 kg/m² as overweight and over 30 kg/m² as obese, whereas the Hospital Authority of Hong Kong recommended the normal range at 18.5 to 23 kg/m², 23 to 25 kg/m² as overweight at risk and 25 to 30 kg/m² as moderately obese (2013). The Singapore Heart Foundation (2016) adopted the range of below 18.5 kg/m² as at risk of nutritional deficiency disease and osteoporosis, 18.5 to 23 kg/m² as normal, 23 to 27.5 kg/m² as moderate risk and above 27.5 kg/m² as high risk for obesity.

The information may indicate the difficulty in having BMI as the source to predict the number of children as overweight or obese in Asia. Nevertheless, the difficulty also highlights the debate of the establishment of single categorization criterion for BMI to be used in Asia. Regarding this agenda, WHO consulted experts on BMI for adults in Asian populations and suggested the range of 18.5 to 27.5 kg/m² as low to moderate risk, 23 to 33 kg/m² as moderate to high risk and 27.5 to 37.5 kg/m² as high to very high risk. Ramachandran and colleagues' (2012) study indicated the need to have a lower BMI range for Asian populations due to the high total and central adiposity for a given body weight when compared with matched populations of European origin, which made them more susceptible to metabolic diseases, which were common among

Asians. The recommendation from WHO and the mentioned study (Ramachandran et al. 2012) may indicate the possibility of undertaking cross continent study on the problem in overweight/obesity with one single categorization. Nevertheless, the use of a single standard in measuring the overweight/obesity problem has implication as it may have tremendous impact on the public health spending on children with special health needs.

The findings on the schoolchildren indicated that there was not much difference between the two sexes. At ages 6–8 and 11, the boys are slightly taller than the girls, whereas the girls are slightly taller than the boys at age 9 and 10. However, there was only a statistically significant difference in the height of the sexes at age 8 and 9 years. The effect size, however, was very small, indicating that the difference does not have much practical value. When the weight of children is considered, the boys were significantly heavier than girls of the same age over the six years of observation. Further, the male students from 6 to 11 years (2008 to 2013) had significantly heavier BMI levels than their female counterparts of the same age.

A similar pattern of observations was found in other studies; for example, Qiu and colleagues (2013) carried out a study on BMI for children aged 6 to 18 years in Beijing, China. The results indicated that BMI curves differed for boys and girls. The BMI curves for urban children were also higher than rural children at the upper percentile. The results from this study showed furthermore that Beijing BMI curves were higher than that of the Chinese national level. Beijing boys had a higher BMI in medium (6.5–14 years) and upper percentiles and a lower BMI in lower percentiles than WHO and other refer-

ences, whereas Beijing girls were lower in medium and lower percentiles but higher compared to a WHO reference before age 15.5 years in the upper percentiles. Hao and colleagues (2015) investigated sex differences in physical fitness indices with regard to BMI levels among Inner Mongolia medical students in China. The study showed that male students may be likely to spend more time using computers than female students, cutting down their time of participating in physical activities. Similarly, Santaliestra-Pasías and colleagues (2015) identified that dietary patterns, physical activity and sedentary behaviours are some of the main behavioural determinants of obesity. It is often understood that sexual maturation could be a reason for the high level of BMI among male students. However, Wang (2002) found to the contrary that early sexual maturation was positively associated with overweight and obesity in girls, whereas the association was reverse for boys. Many correlates identified here are consistent with previous work. A study conducted by LeBlanc and colleagues (2015) on a sample including 5,844 boys with mean age of 10.4 years from Australia, Brazil, Canada, China, Colombia, Finland, India, Kenya, Portugal, South Africa, the United Kingdom, and the United States of America aimed to investigate correlates of total sedentary time (SED) and screen time (ST) in children around the world. The results of the study showed that children averaged 8.6 hours of daily SED, and 54.2% of children failed to meet ST guidelines. In all of the study sites, boys reported longer ST, were less likely to meet ST guidelines, and had higher BMI z-scores than girls. In 9 of the 12 sites, girls engaged in significantly more SED than boys. Common correlates of longer SED and ST included poor weight status, not meeting physical

activity guidelines, and having a TV or a computer in the bedroom. The decrease in physical activity lead to an increase in sedentary activities: watching television, playing video games, and using the computer (Morales-Suárez-Varela et al. 2015). It is clear that globally, the “energy out” side of the energy balance equation is tilting towards weight gain. Therefore, it could be a reason why weight and BMI levels are higher among male students than female students. Al-Hazzaa et. al. (2014) conducted a study from 2009 to 2010 in three major cities in Saudi Arabia, Al-Khobar, Jeddah, and Riyadh on 2,908 students in secondary schools (1,401 males and 1,507 females) aged 14 to 19 years. The sample was randomly selected, using a multistage stratified cluster-sampling technique with an overarching objective of examining the prevalence of overweight, obesity, and abdominal obesity among Saudi adolescents. The result of the study showed that across all ages, overweight and obesity ranged from 39.9% to 45.6% in males and from 30.4% to 38.7% in females. Finally, it is important to note that although our findings are supported by previous work, with the emergence of sedentary behaviour research, the age of 9 to 10 years for male boys seemed to be a sensitive or critical period for boys to become overweight or develop obesity. It is probable that once this overweight and obesity problem has developed, such a life pattern might persist into the adolescent period, where it would be difficult to reverse the situation. If this is a pattern for the overweight problem to develop, suitable intervention activities at the sensitive period (of 9 years) seem to be an important strategy in helping students to adopt a healthy lifestyle.

The present study has generated some information that has value as a ref-

erence and can be used as a basis from which policy can be developed in Macao and other Asian countries. Changing the behaviours of individuals, diet and exercise are pressing issues and have been placed on researcher agendas worldwide. Nevertheless, these initiatives and strategies need to be implemented with suitable format and delivered at the right time to create the necessary impact on groups with different needs. The need of different activities levels for boys and girls seemed to be a message in Sarkin and colleagues (1997) and Jandric (2010)'s study. For example, in the first mentioned study (Sarkin et al. 1997) study observed the different activity levels for boys and girls during physical education lessons and recess periods. Boys were significantly more active than girls during recess periods while girls were significantly more active during physical education lesson than recess period. Jandric (2010)'s study indicated the differences of boys and girls in the activity level. The idea to find out the different contributors in arriving at this pattern seems to be the issue of further discussion. In fact, to maintain the obesity rate at a reasonable level in boys and girls and establishing effective measures to prevent excessive increases in BMI seem to be an important agenda as once overweight has happened, it becomes difficult to reverse the situation. This effect has no sex differences.

Recommendation

The childhood period is the crucial stage to predict a better adolescent period to adulthood and so on. Thus, children should be considered the priority cohort for intervention strategies. Prevention may be achieved through a variety

of interventions targeting built environments, physical activity, and diet. Therefore, almost all researchers agree that prevention could be the key strategy for controlling the current epidemic of obesity so that children can gain a healthier entry into adolescence and adulthood. Attention is required when students reach the age of 9 to 10 years because this is a sensitive period for children to easily develop overweight and obesity problems. Raising levels of activity and participation in sport will not only reduce economic costs but can also result in a range of social and community benefits, including reducing anti-social behaviour, improving educational attainment and building community cohesion (CSJ Sport Working Group 2011). Nevertheless, it is important for the planner to match the right activities at the suitable time. Almost all researchers agree that prevention could be the key strategy for controlling the current epidemic of obesity. Therefore, it is highly recommended that BMI-for-age should be used to routinely screen for overweight in adolescents and other age groups as well (Himes and Dietz 1994). Alongside this action, special attention must be given to boys' activity levels in physical education and sport activities.

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Authors' contributions

WH was Principal Investigator and wrote the paper; MdDA wrote the paper, performed statistical analysis and literature search, ChIL was Project Co-coordinator;

PCh and PI were Strategic Partners; RL-VanN wrote the paper and served as statistical expert; FH, JCh, NCh and JS were responsible for data entry.

Conflict of interest

The authors declare that they have no conflicts of interest.

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