



Original Article

Changes in dietary habits and prevalence of cardiovascular risk factors among school students in Macao, China



Vera Keung^{a,b}, Kenneth Lo^{a,c,d}, Calvin Cheung^{a,b}, Wilson Tam^{c,e,*}, Albert Lee^{a,b}

^a JC School of Public Health and Primary Care, Faculty of Medicine, Shatin, The Chinese University of Hong Kong, Hong Kong

^b Center for Health Education and Health Promotion, Shatin, The Chinese University of Hong Kong, Hong Kong

^c Department of Cardiology, Guangdong Cardiovascular Institute, Hypertension Research Laboratory, Guangdong Provincial People's Hospital, Guangdong Provincial Key Laboratory of Coronary Heart Disease Prevention, Guangdong Academy of Medical Sciences, South China University of Technology School of Medicine, Guangzhou, China

^d Centre for Global Cardiometabolic Health, Department of Epidemiology, Brown University, USA

^e Alice Lee Centre for Nursing Studies, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

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ABSTRACT

Objective: Given the increasing burden of childhood obesity, it is important to examine the changes in dietary habits and prevalence of cardiovascular risk factors among Macao students.

Methods: A cross-sectional study was conducted among primary and secondary school students in Macao, China in 2014–2015 with addition to data collected from 2008 to 2009 for comparison. The dietary behaviours, prevalence of obesity and dyslipidaemia were compared by study period.

Subjects: In 2014–2015, dietary assessment was conducted among 3635 students, physical assessment was conducted among 1427 school students. In 2008–2009, dietary assessment was conducted among 4271 students, physical assessment was conducted among 1700 school students.

Results: When compared with students in 2008, higher percentage of students from present study period consumed dairy products, crispy food and chocolate, while fewer students had fruits, vegetables and fried food at least once every day. Despite lower prevalence of elevated total cholesterol and low-density-lipoprotein cholesterol, the rate of general obesity, low high-density-lipoprotein cholesterol and hyperglycaemia has increased significantly in 2014–2015. Students aged 12–14 consumed less fruits and vegetables and suffered from higher rate of general and abdominal obesity, as well as low high-density-lipoprotein cholesterol and elevated serum triglycerides in 2014–15.

Conclusions: The students' diet had both favourable and unfavourable changes. The rate of obesity and dyslipidaemia rises, while the situation for students aged 12–14 is more concerning.

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Introduction

Obesity is a worldwide epidemic associated with coronary artery disease, hypertension, type 2 diabetes mellitus, respiratory disorders and dyslipidemia [1]. Although the obesity epidemic has been plateauing in many western countries including the United States and United Kingdom, a strong increasing trend is still being observed among Chinese children and adolescents [2]. During 1981 to 2010, the prevalence of overweight among Chinese children and

adolescents increases from 1.8% to 13.1%, while the prevalence of obesity increases from 0.4% to 7.5% [3].

Apart from obesity, other cardiovascular risk factors including childhood dyslipidemia and hyperglycemia are also attracting attention from researchers in recent years. In United States, 20.2% of children and adolescents had adverse concentration of total cholesterol, high-density-lipoprotein cholesterol (HDL-C) or non-HDL-C in 2011–2012 [4]. However, the pooled prevalence of dyslipidemia among Chinese children and adolescents from 1946 to 2014 was 25.3%, which was comparable to the situation in US [5]. As for hyperglycemia, its prevalence was 5.7% among children with obesity in Germany and Sweden [6] and 11.13% among US children [7]. Despite lower prevalence than obesity and dyslipidaemia, impaired fasting glucose during childhood is a significant predictor of type 2

* Corresponding author at: Alice Lee Centre for Nursing Studies, Yong Loo Lin School of Medicine, National University of Singapore, Singapore.

E-mail address: nurtwsw@nus.edu.sg (W. Tam).

diabetes (hazard ratio = 3.73) in early adulthood [8]. The impact of early life hyperglycaemia on future health cannot be overlooked.

With regard to the close relationship between diet, obesity and cardiovascular disease, a routine surveillance system is necessary for monitoring the early-life health risk behaviors in local, national and global level [9,10]. As advocated by the United Nations, a surveillance system of health risk behaviors identifies population with higher risk of chronic disease [11]. Stakeholders including policy makers, school principals and parents, can be well-informed and educate population with greater need of health information. For instance, the Youth Risk Behavior Surveillance System (YRBSS) in the United States tracks the health behaviors among a nationally representative sample of US high school students and representative samples of students in states and selected large urban school districts in a regular basis [12]. In 2013, 8.5% and 2.1% of high school students nationwide met fruit and vegetable recommendations respectively, while the percentages varied slightly among the states [13].

Macao, a highly urbanized region in China, has undergone rapid economic transition in recent years. However, it also faces a growing burden of chronic diseases. In 2008, a cross-sectional study was conducted in 40 schools in Macao. The rates of overweight or obesity were higher for male participants and students aged 9–12 [14]. When compared with other regions, Macao did not have an obesity rate as high as USA [15], but its prevalence of overweight was greater than that in Mainland China [3] and Hong Kong [16]. Given the increasing trend of childhood obesity in China, and the more severe situation in Macao, it is necessary to examine the changes of dietary habits and the prevalence of cardiovascular risk factors over the recent years.

Materials and methods

Subjects

During September 2008 to November 2008 (previous study) and December 2014 to June 2015 (present study), two repeated cross-sectional surveys were conducted among junior primary, (aged 6–8), senior primary (aged 9–11), junior secondary (aged 12–14) and senior secondary school students (aged 15–17) in Macao. Both study periods have used the same approaches in school sampling, subject recruitment and data collection. A total of 40 (previous study) and 35 (present study) schools out of 66 schools in Macao were randomly selected. Schools in Macao were categorized into three groups namely 'Government Schools', 'Subsidized Private Schools' and 'Private Schools' and further divided into nine groups according to the type of education the school was providing (primary, secondary, or both). In both study periods, half of the schools in each group were randomly selected. This sampling method covered a wide range of school systems in Macao, while the number of included schools were comparable with the previous study in 2008 (40 schools were selected). Students aged 18 or above were excluded from the analyses. In both study periods, consent for dietary, anthropometrics and physical assessments was obtained from students' parents prior to the tests.

Instruments for dietary assessment

A set of questionnaires was designed for students studying in primary 4 to secondary 6 (P4 to S6) and were available in Chinese or English. Surveys were not conducted to primary 1 to primary 3 students because of their limited ability to provide valid and reliable information on food consumption [17]. In each participating school, one class was randomly selected from each grade. All students in the selected class were invited to complete a questionnaire during a lesson. Written consents were obtained from their parents.

Dietary behaviours of students were also examined by items adapted from Youth Risk Behaviour Survey, which has been translated into Chinese and used for health surveillance among primary and secondary school students in Hong Kong [18]. The consumptions of thirteen food groups in the previous week were acquired by single-item questions. Responses ranged from 'none' to 'three times or more per day'. The food groups were dichotomized into whether consuming at least once every day. Healthy dietary habit: consumption frequency of (1 fruits, (2 vegetables, (3 dairy products and (4 breakfasts; unhealthy dietary habit: consumption frequency of (1 crispy food, (2 chocolate, (3 cake, (4 soft drinks, (5 juice drinks, (6 fried food, (7 processed food, (8 fried rice/noodle, (9 fatty food. Gender and ages of students were also acquired from the questionnaire.

Anthropometric assessments and blood drawing

Apart from dietary assessments, anthropometric measurement and blood drawing (physical assessments hereafter) was conducted among students in each participating school. Students were randomly selected to participate in physical assessments from the classes in proportion to gender, grade and age distribution of all Macao students [19]. Physical assessments recruited students from primary one to secondary six (generally aged 6 to 17). Physical assessments were carried out on location at the majority of participating schools and started from 8 am. Students were instructed to fast for at least 8 h prior to the tests and only allowed to drink water before blood sample collection.

Students were instructed to take off shoes and heavy clothing, then maintained standing position for anthropometrics measurements. Trained research staff from the research team conducted the measurements at the end of students' gentle expiration. Body height and weight was measured by portable stadiometer SECA 214 (SECA GmbH & Co. KG, Germany) and electronic scales Tanita TBF300 (Tanita Corporation of America Inc., USA). Waist circumference was measured with a measuring tape in the horizontal plane midway between lowest rib and the iliac crest. Average values of two readings for each anthropometric measure were calculated. Body height and waist circumference were recorded to the nearest 0.1 cm and body weight to the nearest 0.1 kg. Qualified phlebotomists from the Kiang Wu Hospital were responsible for drawing not more than 10 ml of blood from each participating student. Plasma and serum samples were tested immediately for lipoprotein levels. All samples were analysed in an accredited central laboratory in Macao (Health Care Centre, Kiang Wu Hospital) commissioned by the research team.

Body mass index (BMI) was calculated from measured body weight and height. The World Health Organization (WHO) growth reference and criteria set by International Obesity Task Force were used to identify participants with overweight/obesity. According to WHO, overweight/obesity was defined as more than +1 standard deviation of the median of BMI-for-age [20]. While for IOTF, overweight/obesity was defined by age- and sex-specific cut-off points using nationally representative cross-sectional surveys on growth from Brazil (N = 31,806), Great Britain (N = 32,222), Hong Kong (N = 23,965), the Netherlands (N = 41,766), Singapore (N = 33,972), and the United States (N = 28,996) [21]. The international criterion of abdominal obesity is yet established, so population-based cut-off values are considered acceptable for present study. To identify participants with abdominal obesity, age and gender specific cut-off values was adopted from the percentile charts for ethnic Chinese children's (N = 2,593) [22] and adolescents' (N = 2,102) [23] waist circumference. In addition, serum lipid profiles of participants, namely total cholesterol and triglycerides (TG), low high-density-lipoprotein (HDL) cholesterol, and elevated low-density lipoprotein (LDL) cholesterol were classified by cut-off points recommended

Table 1
Demographic characteristics of participants of dietary assessments in two study periods.

	2008–09 (N = 4271)	2014–15 (N = 3635)	p-Value
Gender			
• Male	2158 (50.5%)	1886 (51.9%)	0.23
• Female	2113 (49.5%)	1749 (48.1%)	
Age group			
• 9–11	1426 (33.4%)	1156 (31.8%)	0.01*
• 12–14	1367 (32.0%)	1289 (35.5%)	
• 15–17	1478 (34.6%)	1190 (32.7%)	
Healthy dietary habit			
• Fruits everyday	1745 (40.9%)	1399 (38.5%)	0.03*
• Vegetables everyday	2360 (55.3%)	1797 (49.4%)	<0.01*
• Dairy products everyday	808 (18.9%)	1050 (28.9%)	<0.01*
• Breakfast everyday	2493 (58.4%)	2241 (64.7%)	<0.01*
Unhealthy dietary habit			
• Crispy food	268 (6.3%)	297 (8.2%)	<0.01*
• Chocolate	468 (11.0%)	474 (13.0%)	<0.01*
• Cake	254 (5.9%)	214 (5.9%)	0.91
• Soft drinks	421 (9.9%)	355 (9.8%)	0.89
• Juice drinks	898 (21.0%)	728 (20.0%)	0.27
• Fried food	390 (9.1%)	275 (7.6%)	0.01*
• Processed food	398 (9.3%)	350 (9.6%)	0.64
• Fried rice/noodle	342 (8.0%)	306 (8.4%)	0.51
• Fatty food	618 (14.5%)	484 (13.3%)	0.14

^aPresented as mean ± standard deviation. *p < 0.05.

by Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents [24]. Outcomes were dichotomized into ‘normal or borderline’ versus ‘borderline’ (‘normal or borderline’ versus ‘low’ for HDL cholesterol).

Comparison with previous study data

To compare the prevalence in dietary habits and cardiovascular risk factors with previous study, the raw data from the study conducted in 2008–2009 was retrieved and re-analysed the prevalence using the cut-off points in the present study [25]. In addition, prevalence data was stratified into four age groups (6–8, 9–11, 12–14 and 15–17) to identify the population with higher cardiovascular risk. The stratification for the prevalence of dietary habits was the same except for having no students aged 6 to 8. It was because the questionnaires were only delivered to primary four students or above. This classification was in adherence to the school grades of students, e.g. aged 6–8 for junior primary students and 9–11 for senior primary students.

Statistical analysis

Descriptive statistics was used to describe and summarise the results. Prevalence data was stratified by age groups then tested for significant difference by study periods using chi-square test. In order to avoid false-positive findings due to multiple comparison, the p-values obtained from chi-square tests were adjusted using Bonferroni correction. In other words, p-values were multiplied by the number of comparisons (e.g. multiply by 4 for prevalence of cardiovascular risk factors because prevalence data was stratified into 4 age-groups). To account for the difference in demographics of subjects during two study periods, direct standardization method was adapted to calculate the adjusted prevalence of dietary habits and cardiovascular risk factors [26]. The reference population was the age distribution of students 2008–2009 as provided by the Education Bureau in Macao. (https://portal.dsej.gov.mo/webdsejspace/internet/Inter_main_page.jsp?id=8525) All analysis was conducted by SPSS version 23.0 (SPSS Inc., Chicago, IL, USA) with significance levels set at $\alpha = 0.05$.

Results

Students from both study periods have returned 4271 (2008–2009) and 3635 (2014–2015) questionnaires without missing data for analysis (Table 1). As tested from chi-square test and independent t-test, the gender distribution between two study periods was similar, but students from the present study were older in age. In the present study period, more students consumed dairy products, breakfast, crispy food, chocolate at least once every day, while fewer students consumed fruits, vegetables, fried food at least one time every day.

A total of 1427 students participated in the present physical assessments, while 1700 students with complete anthropometric and blood lipid data were retrieved from the previous study (Table 2). There was no significant difference in gender and age distribution between two studies. The prevalence for all outcomes except elevated waist circumference and elevated TG differed significantly between two studies. Students in 2014–2015 had higher rate of being overweight or obese (using WHO or IOTF standard), having low HDL or impaired fasting glucose, but lower rate of having high TC or LDL.

Table 3 compared the age-specific and age-standardized prevalence of healthy dietary habits in two studies. When compared with the previous study period, students aged 9–11 consumed more fruits, dairy products and breakfast. Students aged 12–14 consumed less fruits and vegetables, but more dairy products and breakfasts. Students aged 15–17 consumed less fruits and vegetables but more dairy products. Table 4 compared the age-specific and age-standardized prevalence of unhealthy dietary habits in two studies. Students aged 9–11 consumed more crispy food, while students aged ≥ 15 consumed more chocolate. The prevalence for consuming juice drinks decreased for students aged ≥ 12 .

Table 5 compared the age-specific and age-standardized prevalence of cardiovascular risk factors in two studies. In the present study period, students aged 6–8 had lower prevalence of elevated LDL, students aged 9–11 had lower prevalence of elevated waist circumference and LDL. Students aged 12–14 had higher prevalence of overweight/obesity identified by WHO and IOTF standard and higher prevalence of low HDL. Students aged ≥ 15 had higher

Table 2
Demographic characteristics of participants of physical assessments in two study periods.

	2008–09 (N = 1700)	2014–15 (N = 1427)	p-Value
Gender			
• Male	846 (49.8%)	740 (51.9%)	0.24
• Female	687 (48.1%)	687 (48.1%)	
Age group			
• 6–8	270 (15.9%)	241 (16.9%)	0.20
• 9–11	402 (23.6%)	371 (26.0%)	
• 12–14	488 (28.7%)	368 (25.8%)	
• 15–17	540 (31.8%)	447 (31.3%)	
Cardiovascular risk factors			
• IOTF-defined overweight or obese	292 (17.2%)	302 (21.2%)	<0.01*
• WHO-defined overweight or obese	359 (21.1%)	369 (25.9%)	<0.01*
• Elevated waist circumference	492 (28.9%)	405 (28.4%)	0.73
• Elevated TC	182 (10.7%)	102 (7.1%)	<0.01*
• Low HDL	88 (5.2%)	110 (7.7%)	<0.01*
• Elevated LDL	167 (9.8%)	61 (4.3%)	<0.01*
• Elevated TG	114 (6.7%)	110 (7.7%)	0.28
• Impaired fasting glucose	16 (0.9%)	31 (2.2%)	0.01*

Abbreviations: TC, total cholesterol; TG, triglycerides; HDL, high-density-lipoprotein cholesterol; LDL, low-density-lipoprotein cholesterol. *p < 0.05.

Table 3
Age-specific and standardized prevalence of healthy dietary habits in two cross-sectional studies.

Age	Fruits everyday		p-Value	Vegetables everyday		p-Value
	Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014	
9–11	45.1%	50.6%	<0.01*	50.7%	47.4%	0.01*
12–14	43.5%	37.7%	<0.01*	55.5%	50.0%	<0.01*
15–17	34.3%	27.6%	<0.01*	59.4%	50.8%	<0.01*
Standardized	40.5%	37.5%		55.6%	49.6%	
Age	Dairy products everyday		p-Value	Breakfast everyday		p-Value
	Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014	
9–11	22.8%	40.2%	<0.01*	75.0%	80.0%	<0.01*
12–14	18.4%	26.8%	<0.01*	52.5%	59.1%	1.00
15–17	15.7%	20.2%	<0.01*	47.8%	46.6%	1.00
Standardized	18.6%	28.1%		57.0%	60.3%	

* p < 0.05 in prevalence after Bonferroni correction using chi-square test.

Table 4
Age-specific and standardized prevalence of unhealthy dietary habits in two cross-sectional studies.

Age	Crispy food		p-Value	Chocolate		p-Value	Cake		p-Value
	Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014	
9–11	8.8%	10.6%	0.04*	11.2%	13.7%	1.00	7.6%	9.7%	1.00
12–14	6.7%	9.2%	0.30	13.0%	14.0%	0.10	5.9%	5.4%	0.08
15–17	3.5%	4.7%	1.00	8.9%	11.3%	0.02*	4.4%	2.8%	0.28
Standardized	6.1%	7.9%		11.0%	12.9%		5.8%	5.6%	
Age	Soft drinks		p-Value	Juice drinks		p-Value	Fried food		p-Value
	Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014	
9–11	10.3%	9.8%	1.00	17.7%	23.4%	0.12	10.9%	9.0%	0.38
12–14	10.4%	11.3%	1.00	24.9%	21.5%	<0.01*	10.6%	8.8%	0.43
15–17	8.9%	8.1%	0.49	20.6%	15.2%	<0.01*	6.1%	4.8%	0.57
Standardized	9.8%	9.7%		21.3%	19.7%		9.0%	7.4%	
Age	Processed food		p-Value	Fried rice/noodle		p-Value	Fatty food		p-Value
	Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014	
9–11	11.2%	12.7%	1.00	11.2%	11.2%	0.93	12.8%	10.6%	1.00
12–14	9.1%	9.5%	1.00	7.8%	8.9%	1.00	12.9%	13.9%	0.42
15–17	7.7%	6.8%	0.61	5.1%	5.1%	0.08	17.5%	15.4%	0.33
Standardized	9.2%	9.4%		7.8%	8.2%		14.6%	13.5%	

* p < 0.05 in prevalence after Bonferroni correction using chi-square test.

Table 5
Age-specific and standardized prevalence of cardiovascular risk factors in two cross-sectional studies.

Age	Overweight or Obese (IOTF)		p-Value	Overweight or Obese (WHO)		p-Value	Elevated waist circumference		p-Value
	Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014	
6–8	13.7%	14.9%	1.00	17.0%	18.3%	1.00	18.1%	13.3%	0.53
9–11	26.9%	22.1%	0.50	33.3%	29.1%	1.00	33.1%	24.0%	0.02*
12–14	17.2%	29.1%	<0.01*	22.5%	35.1%	<0.01*	29.1%	36.1%	0.11
15–17	11.7%	17.2%	<0.01*	12.8%	19.7%	0.01*	31.1%	33.8%	1.00
Standardized	17.1%	21.4%		21.1%	26.1%		28.8%	28.7%	

Age	Elevated TC		p-Value	Low HDL		p-Value	Elevated LDL		p-Value
	Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014	
6–8	12.2%	8.7%	0.79	3.7%	5.8%	1.00	10.7%	4.6%	0.04*
9–11	13.9%	9.4%	0.21	5.0%	5.1%	1.00	13.2%	6.7%	0.01*
12–14	10.5%	5.7%	0.05	5.1%	10.3%	0.02*	8.2%	4.1%	0.06
15–17	7.8%	5.6%	0.70	6.1%	8.7%	0.46	8.3%	2.2%	<0.01*
Standardized	10.7%	7.0%		5.1%	7.9%		9.8%	4.2%	

Age	Elevated TG		p-Value	Impaired fasting glucose		p-Value
	Rate in 2008	Rate in 2014		Rate in 2008	Rate in 2014	
6–8	8.9%	11.2%	1.00	0.7%	0.8%	1.00
9–11	10.4%	10.0%	1.00	0.5%	1.1%	1.00
12–14	5.30%	9.2%	0.11	1.8%	4.1%	0.20
15–17	4.1%	2.7%	1.00	0.6%	2.2%	0.08
Standardized	6.7%	7.7%		0.9%	2.3%	

Abbreviations: TC, total cholesterol; TG, triglycerides; HDL, high-density-lipoprotein cholesterol; LDL, low-density-lipoprotein cholesterol; *p < 0.05 in prevalence after Bonferroni correction using chi-square test.

prevalence of WHO-defined overweight/obesity and but lower prevalence of elevated LDL.

When compared with the unstandardized prevalence, the age-standardized value differed by less than 1% for most outcomes except for having breakfast every day and overweight/obesity identified by WHO standard (each 1.1% difference). The demographic difference between study periods only had small impact on the prevalence.

Discussion

The present study has revealed an increasing burden of cardiovascular risk factors among Macao school students, particularly for the group aged 12–14. Students' diet in two study periods were mixed with favourable (consuming more dairy products, less fried food) and unfavourable changes (less fruits and vegetables, more crispy food and chocolate), which indicated the specific needs for health promotions.

Despite lower prevalence of elevated TC and LDL, the rate of general obesity, the prevalence of low HDL (5.3% to 7.7%) and hyperglycaemia (0.9% to 2.2%) nearly or already doubled when compared with the previous study. High carbohydrate diet may associate with elevated fasting glucose [27] and low HDL levels as supported by a nationally representative study in Korea [28]. High carbohydrate diet, particularly white rice consumption, is prevalent among Asian population [29]. Reducing refined carbohydrate intake of Macao students is probably one of the strategies to reduce the prevalence of low HDL and impaired fasting glucose.

Interestingly, the prevalence of elevated TC and LDL reduced in the present study period despite the higher rate for low HDL and hyperglycaemia. The increased prevalence of consuming dairy products every day in the present study (18.9% to 28.9%) may help to explain the findings. The milk program implemented by Macao government since 2008 may help to increase the consumption of dairy products (<https://www.gov.mo/zh-hant/news/68527/>). The Macao government provided milk to school students for free, while students have the right to decline drinking them. According to a recent meta-analysis, dairy food consumption associated with a lower risk of metabolic syndrome and dyslipidemia [30]. Calcium is

abundantly found in dairy products, which may exert cholesterol-lowering effect by inhibiting the intestinal absorption of saturated fatty acids and increasing the faecal excretion of bile acids [31]. Although it is not compulsory for schools to provide low-fat milk, our study provided preliminary evidence to support the how dairy product provision may improve cardiometabolic health of students. Further studies should be conducted to evaluate the changes in dietary habits and serum lipids at individual level.

Age-specific analysis showed that the prevalence of overweight/obesity increased among students aged 12–14, while they had a lower consumption of fruits and vegetables. The changes in dietary habits of students when they enter secondary school may account for the sharp rise in cardiovascular risks. In general, students start attending secondary school in the age 12–14. Although over 75% of the schools in Macao provided lunch for their students, only 29.6%, 9.3% and 4.8% of senior primary (aged 9–11), junior secondary (aged 12–14) and senior secondary school students (aged 15–17) stayed in schools for lunch respectively [25]. The dietary environment outside schools may influence students' diet and body weight. As shown from the previous research, greater numbers of takeaways and grocers/convenience stores within 400 m of schools predicted lower dietary quality among 1382 adolescents in London [32]. A large-scale study in California (over 500,000 youths) found that students with fast-food restaurants within one half mile of their schools consumed fewer fruits and vegetables but more soda drinks, and had greater likelihood of being overweight or obese [33]. Although the prevalence of general and abdominal obesity gradually dropped in late adolescence, obesity prevention starting from early secondary school age is still warranted.

The strength of this study is to compare the individual data of two study periods, which enable comparison to identify specific groups of students with higher cardiovascular risk. However, our research is a repeated cross-sectional study instead of a cohort. Furthermore, the participants in study periods could not be matched because participants were sampled separately. The present findings only indicated the possibility instead of confirming the association between dietary habits and the change in cardiovascular risk across two study periods.

Conclusion

The present study has compared the changes in prevalence of dietary habits and cardiovascular risk factors among Macao students. Students aged 12–14 consumed less fruits and vegetables but consumed more dairy products, while their rates of general and abdominal obesity were comparable or even exceed the values in the previous study period. To facilitate resource allocation, obesity prevention should be targeted on students with the most needs.

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Ethics approval

Ethical approval for obtaining survey and physical assessments in each study period has been granted from the Joint CUHK-NTEC Clinical Research Ethics Committee. (Reference number: CRE-2007.510 and CRE-2014.175)

Authors' roles

All authors approved the publication of this version and agreed to be accountable for all aspects of its content.

Conflict of interest

All authors have disclosed no conflicts of interest.

CRediT authorship contribution statement

Vera Keung: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Project administration, Funding acquisition. **Kenneth Lo:** Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Project administration. **Calvin Cheung:** Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Project administration. **Wilson Tam:** Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Funding acquisition. **Albert Lee:** Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Funding acquisition.

Declaration of Competing Interest

The authors report no declarations of interest.

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