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# Modifiable lifestyle factors and their relationships with metabolic disorders among adults in Burkina Faso: findings from the first national survey

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Modifiable lifestyle factors should primarily be targeted for the cardiovascular diseases' prevention. This study aimed to report the magnitude of modifiable lifestyle factors, their relationships with metabolic disorders in Burkinabè adults using nationally representative data. This cross-sectional study included 4100 adults selected through multistage cluster sampling performed during the first national survey conducted in Burkina Faso. The modifiable factors considered were tooth cleaning, fruit and/or vegetable (FV) intake, substances' use, physical activity and overweight/obesity, while metabolic syndrome abnormal components defined metabolic disorders. We performed logistic regressions. 31.1% cleaned the teeth at least twice a day, 4.9% consumed five or more FV, 39.7% used alcohol and/or tobacco, the prevalence of physical inactivity and overweight/obesity was, respectively 6.6 and 17.7%. About 41.0% had at least two metabolic disorders and 9.5% had at least three. Lifestyle factors associated with having at least two metabolic disorders were overweight/obesity, more FV intake (when five or more aOR=1.7, p<0.001), physical inactivity (aOR=1.3, p<0.05), and tooth cleaning (aOR=0.8, p<0.01). The same trend of relationships was observed with having at least three metabolic disorders. Excluding overweight/obesity and physical inactivity, unhealthy modifiable lifestyle factors were common and tooth cleaning was found as a protective practice for metabolic disorders.

Key words: Modifiable lifestyle factors, metabolic disorders, prevalence, relationships, Burkina Faso.

## INTRODUCTION

Non-communicable diseases (NCDs) are emerging as significant contributors to disease burden in the low- and middle-income countries (LMICs) (Gheorghe et al., 2018;

Gouda et al., 2019).

Modifiable risk factors such as unhealthy lifestyle behaviour contribute to the shifting disease burden and

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Author(s) agree that this article remain permanently open access under the terms of the <u>Creative Commons Attribution</u> <u>License 4.0 International License</u> so should primarily be targeted (O'Donnell et al., 2016), particularly for cardiovascular diseases' prevention (Yusuf et al., 2015; Owolabi et al., 2018). Systematic reviews and meta-analyses have assessed the relationships between the modifiable lifestyle factors such as the alcohol consumption (Sun et al., 2014), tobacco use (Slagter et al., 2013; Oh et al., 2020), oral hygiene practices (Santoso et al., 2021), fruit and/or vegetable (FV) consumption (Lee et al., 2019; Picasso et al., 2019), physical inactivity (Amirfaiz and Shahril, 2019) excess weight and the metabolic disorders (Opio et al., 2020).

The World Health Organization (WHO) recommends the implementation of a national surveillance system for the risk factors for the NCDs (stepwise approach to surveillance [STEPS]) including those for cardiovascular diseases (Alwan et al., 2010) and while the US Centre for Disease Control and Prevention recommends the Behavioural Risk Factor Surveillance System (Mokdad et al., 2003). The WHO STEPS surveys use a standardized tool for data collection which include specific sections on behavioural risk factors (the alcohol and tobacco use, oral hygiene practices, fruit and vegetable intake, physical activity), anthropometry (measurement of the body mass index [BMI]) and the measurement of some biological parameters (World Health Organization, 2005) which may help identify metabolic disorders.

Observational studies (Panayiotou et al., 2013; La Carrubba et al., 2016) including cohort studies (McNeill et al., 2005) and meta-analyses (Gami et al., 2007) have supported that the presence of only two metabolic syndrome (MetS) abnormal components increased the risk for subclinical/clinical cardiovascular dysfunctions or events, alongside having the MetS (that is, having at least three abnormal components). Thus, highlighting the associated factors with the presence of at least two or at least three abnormal components may lead to the relevant awareness with regard to those who may receive particular benefit from healthy lifestyle practices. Moreover, among the modifiable lifestyle factors, the most easily achievable at lower intervention costs should be known and prioritised in policies in LMICs.

The survey using the STEPS method in Burkina Faso provided the first national lifestyle variables which have not yet been analysed and especially in relation to metabolic disorders. This study aimed to examine the modifiable lifestyle factors and their relationships with metabolic disorders among adults in Burkina Faso, by using the first nationally representative data.

#### METHODOLOGY

#### Description of the Burkina STEPS survey

The cross-sectional study covered all the 13 administrative regions of Burkina Faso and involved all three components (behavioural or lifestyle factors, anthropometric and biological measurements) (World Health Organization, 2005). The survey enrolled 4800 adults aged 25 to 64 years, based on a calculated sample size considered to achieve sufficient accuracy by weighting the numbers of age groups for each sex. It was also weighted to ensure representativeness with regard to the living environment (rural or urban areas).

Data were collected from 3 September to 24 October 2013 through face-to-face interviews in the language spoken by the participant. The data were collected using personal digital assistants with standardized WHO STEPS questionnaires loaded with eSTEPS software. Blood samples were collected for biological measurements.

The protocol of the STEPS survey was approved by the Ethics Committee for Health Research of the Ministry of Health of Burkina Faso (deliberation No: 2012-12092; December 05, 2012).

Written informed consent was systematically obtained from each participant in the STEPS survey.

#### Study variables

Sociodemographic data collected included living environment, sex, age, marital status, education level and occupation. Self-reported data on the modifiable lifestyle factors were also collected: alcohol and/or tobacco use, oral hygiene practices, FV consumption, and physical inactivity. The anthropometric measurements of weight, height, waist circumference (WC) were taken together with blood pressure (BP). These physical measurements and the biological measurements of fasting blood glucose (FBG) and high-density lipoprotein cholesterol (HDL-C) were used to determine the presence of metabolic disorders.

Alcohol consumption was defined as alcohol intake in the past one month while current tobacco use was defined as use of smoked or smokeless tobacco in the past 12 months.

The oral hygiene practices were categorized based on the frequency of cleaning teeth per day, with, at least, twice daily cleaning being recommended (Chapple et al., 2015). Typical daily FV intake was derived from the number of servings of FV consumed per day during a typical week. Five or more daily FV servings were recommended (World Health Organization & Food and Agriculture Organization, 2003). Data on self-reported physical activity were collected using the validated Global Physical Activity Questionnaire (Bull et al., 2009). Physical activity was determined from the amount of time being physically active in three domains; transport, at work and during leisure time. Participants were asked about the frequency, intensity and duration of their work-, traveland leisure-related physical activity (vigorous or moderate), in a typical week. BMI, calculated as a subject's weight divided by height<sup>2</sup>, in kg/m<sup>2</sup>, was characterized as underweight (BMI<18.5 kg/m<sup>2</sup>), normal (BMI=18.5 - 24.9 kg/m<sup>2</sup>), overweight (BMI=25 - 29.9 kg/m<sup>2</sup>), and obesity (BMI ≥30 kg/m<sup>2</sup>) states (World Health Organization, 2000).

Each MetS abnormal component counts as one metabolic disorder and using the International Diabetes Federation criteria (Alberti et al., 2006), the metabolic disorders were: (i) elevated BP with systolic BP  $\geq$  130 or diastolic BP  $\geq$  85 mmHg, or currently taking anti-hypertensive medication; (ii) raised FBG  $\geq$  5.6 mmol/l or previously diagnosed type 2 diabetes; (iii) reduced HDL-C of < 1.03 mmol/l in men and <1.29 mmol/l in women; (iv) and central obesity defined a WC  $\geq$  94 in men and 80 cm  $\geq$  in women (Alberti et al., 2006). Since consistent data supported that the increased number of MetS abnormal components showed a significant increased value in predicting cardiovascular impairment or events (Gami et al., 2007), the outcome variables we considered were having at least two on the one hand; and at least three metabolic disorders on the other hand.

WC was measured, to the nearest 0.1 cm, using a flexible

measuring tape placed at midpoint between the last rib and the iliac crest, with the subjects in light clothing, standing upright and breathing normally (Després et al., 2001). BP (in mmHg) was measured three times using an electronic BP device, and the mean value used in the analysis. The biochemical tests were done on fasting capillary blood samples.

Of the sample of 4800 individuals surveyed, 105 were not eligible; 10, 493 and 92 subjects had missing or invalid data on sociodemographic variables, lifestyle factors and MetS components, respectively. The number of missing or invalid lifestyle factors was as follows: 1 for tobacco, 6 for oral hygiene practice, 279 for FV intake, 2 for physical activity and 205 for BMI. Thus, we included 4100 participants who had complete data in our secondary data analyses.

#### Statistical analyses

StataCorp Stata Statistical Software for Windows (Version 14.0, College Station, Texas, US) was used to analyze the data. The continuous variables were expressed as the means ± standard deviations, and categorical variables expressed as percentages. In the stepwise logistic regression models, we dichotomized the outcome variable as the presence of at least two (yes/no), or at least three metabolic disorders (yes/no), while the lifestyle factors were the explanatory variables, with adjustment on sociodemographic factors (sex, age, urban-rural residence, marital status, education and occupation). For all analyses, a p-value below 0.05 was considered significant.

## RESULTS

The sample was made up of 2087 (50.9%) females and the mean age was 38.6 ± 11.1 years. The participants were predominantly aged 25-29 years (44.2%), rural residents (79.7%), illiterates (77.3%), currently married or cohabiting (86.7%) or engaged in an occupation without formal and regular income (94.3%) (Table 1). Of the sample studied, 31.1% cleaned the teeth at least twice a day, only 4.9% consumed five or more FV servings, 39.7% were current alcohol and/or tobacco users, 6.6% physically inactive and 17.7% were were overweight/obese. About 40.7 and 9.5% of participants had at least (any) two or three metabolic disorders, respectively.

Table 2 summarizes results from stepwise logistic regressions and sociodemographic factors associated with having at least two metabolic disorders were living in urban area (aOR=1.4, p<0.001), being female (aOR=1.9, p<0.001) and older age (aOR = 1.2 to 2.3; p<0.01). Concerning modifiable lifestyle factors, consuming more FV (when the number was three to four servings, aOR=1.3, p<0.0001; for five or more servings aOR=1.7, p<0.001) and physical inactivity (aOR=1,3; p<0.05) and increased BMI (for overweight aOR=3.7, p<0.001 and for obesity aOR=9.6, p<0.001) were unfavourable factors for having at least two metabolic disorders, while cleaning the teeth at least twice a day was a protective factor (aOR=0.8, p<0.01). Furthermore, when the binary variable "having at least three metabolic disorders" was considered as the outcome in the logistic regression model, the significant factors remained identical, except

only for the variable professions earning formal and regular income (aOR=1.4; p=0.02).

## DISCUSSION

Only 4.9% consumed five or more FV. The low rainfall in the wide area of Burkina Faso (the Sahelian and Sudano-Sahelian areas) may explain the low availability of FV. Despite. These products are not sustainable over all seasons because of the issue of their storage and processing remains a major challenge for the country. Moreover, the value of the FV consumption is not be well known by the general population and thus, the nutrition education should be undertaken (Wagner et al., 2016). There was an insufficient prevention for the licit psychoactive substance use such as alcohol and tobacco in Burkina Faso (respective prevalence of the use was 28.1 and 20.4%). The WHO reported in 2014 as in 2018, the absence of a national monitoring system regarding alcohol consumption, alcohol-related health disorders, and alcohol policy response in Burkina Faso. There were no restrictions for on- or off-premise sales concerning the hours, days, density, specific events and intoxicated persons (WHO, 2014, 2018). At the time of this study, the WHO also noticed the low level of achievement with regards to the tobacco control policy, that is, the "MPOWER" guidelines: Monitoring (epidemiological data collecting on tobacco use), Protect (smoke-free policies), Offer (cessation programs), Warnings (health warnings, mass media), Enforce (advertising bans) and Raise (taxation). As was observed in a STEPS survey in Indian adults STEPS survey in Indian adults (prevalence of 29%) (Sreenivasan et al., 2016), less than a third of Burkinabè adults cleaned the teeth at least twice a day (31.1%).

The prevalence of overweight/obesity (17.7%) was among the low levels in sub-Saharan Africa (Bosu, 2015) but it should be read in conjunction with the higher rate of underweight (Yaya et al., 2018), especially in rural areas (Diendéré et al., 2020) with the lower food availability. The prevalence of the physical inactivity (6.6%) was also low and identical to the previous rate (6.7%) described in the study including sub-Saharan African countries (Guthold et al., 2008) or to the level found in a Kenyan STEPS survey (7.7%) (Gichu et al., 2018). Evidence from the literature suggests that triglycerides may be normal among West Africans with MetS (Sumner et al., 2010) and the absence of this parameter in our study would at least affect our results. The prevalence of MetS may be perceived as low (9.5% had at least three abnormal components). However, a significant part of Burkinabè adults (about 41% who had at least two abnormal components). The presence of multiple components are associated with significant risk of cardiovascular events (McNeill et al., 2005; Gami et al., 2007). Such authors recommended that these individuals should be considered as being in an early stage of the arteriosclerosis

Table 1. Description of the socio-demographic characteristic, lifestyle factors and metabolic disorders.

Socio-demographic characteristic	n (%)
Age ranges (years)	
25 - 29	1814 (44.2)
30 - 44	1036 (25.3)
45 - 54	757 (18.5)
55 - 64	493 (12.0)
Sex	
Men	2013 (49.1)
Women	2087 (50.9)
Residence area	
Rural	3267 (79.7)
Urban	833 (20.3)
Education level	
No formal/No education	3171 (77.3)
Primary achieved	634 (15.5)
Secondary or more	295 (7.2)
Occupation	
Professions providing formal and regular income	234 (5.7)
Professions without formal and regular income	3866 (94.3)
Marital status	
Never or previously married	547 (13.3)
Currently married/cohabiting	3553 (86.7)
Lifestyle factors	
Oral hygiene practices	
Tooth cleaning frequencies	
Never cleaned the teeth	233 (5.7)
Less than once a day	512 (11.5)
Cleaning the teeth once a day	2079 (50.7)
Cleaning the teeth at least twice a day	1276 (31.1)
Use of alcohol or tobacco	
Current alcohol consumption	
Not consumers	2948 (71.9)
Consumers	1152 (28.1)
Current tobacco use:	
Not users	3262 (79.6)
Users	838 (20.4)
Current alcohol and/or tobacco use:	
Non-user of alcohol or tobacco	2472 (60.3)
User of alcohol and/or tobacco	1628 (39.7)
Physical lifestyle (number of the practice of physical activities per week):	
Physically inactive	271 (6.6)
Physically active	3829 (93.4)

Table 1. Cont'd

Consumption of fruits and vegetables (number of servings consumed per day	):
0	2187 (53.3)
1 - 2	975 (23.8)
3 - 4	739 (18.0)
≥5	199 (4.9)
Body mass index status:	
Underweight	456 (11.1)
Normal weight	2919 (71.2)
Overweight	547 (13.4)
Obese	178 (4.3)
Metabolic disorders	
Presence of abnormal metabolic components	
Raised waist circumference: yes	889 (21.7)
Raised blood pressure: yes	1381 (33.7)
Raised fasting blood sugar: yes	359 (8.8)
Reduced high-density lipoprotein cholesterol (HDL-C): yes	3162 (77.1)
Metabolic disorders' accumulation	
No abnormal metabolic component	402 (9.8)
With one abnormal metabolic component	2030 (49.5)
With two abnormal metabolic components	1278 (31.2)
With three abnormal metabolic components	355 (8.7)
With four abnormal metabolic components	35 (0.8)

Source: Authors 2022

#### process (Chen et al., 2015; Zhu et al., 2018).

Associations with increased number of metabolic disorders: consuming more FV was an unfavourable factor for having at least two abnormal components. This findings contrary the results from the meta-analysis including international studies (Tian et al., 2018) highlighting that FV intake was inversely associated with risk of MetS. It is possible that individuals who consume FV may be those who already have cardiovascular disease or diabetes and may want want to prevent any complications. Similar pattern (concerning vegetable servings and overweight/obesity) was observed among adolescents whom the parents were highly aware of their weight status and also advised to change their children's health behaviours (Tovar et al., 2012), suggesting actually the therapeutic lifestyle change process (Wagner et al., 2016).

The increased metabolic risk in physically inactive individuals we reported was consistent with the literature (Houti et al., 2016; Díaz-Martínez et al., 2018; Gallardo-Alfaro et al., 2020). The number of abnormal components usually increases in tobacco or alcohol users (Vancampfort et al., 2016) but this analysis did not find a significant relationship. Tobacco and alcohol are the psychoactive substances and their contents (nicotine and ethanol from tobacco and alcoholic beverages,

respectively) can decrease the appetite (Edge and Gold, 2011) via the ghrelin hormone pathway (these substances have an acute inhibitory effect on human ghrelin secretion (Deschaine et al., 2021), lower the hunger rate (Levin et al., 2006) with anorectic effects (Koopmann et al., 2015, 2018), that may result into insufficient food intake (Jo et al., 2002), particularly in the context of low food availability (Yeomans, 2010). Burkina Faso usually has a low food availability (particularly in rural area with 77.3% of the population), and subjects may adjust to hunger through tobacco consumption. Such behaviour was noted in a supplemental qualitative study (interview) in three Ethiopian pastoral communities with a long tradition of tobacco use (Etu et al., 2017). Thus, the decrease of anthropometric (including WC) values was plausible (Edge and Gold, 2011) and combined to the diastolic BP decreasing due to the potential effect of nicotine included in tobacco (Diendéré et al., 2020), the number of abnormal components could be lowered. The similar observations may be reported in alcohol users (Deschaine et al., 2021; Levin et al., 2006). Overweight or obesity increased the risk for having at least two abnormal components or having at least three abnormal components as the finding of Omuse et al. (2017) concerning relationships with MetS in Kenya aOR=5.01, p<0.001 and 5.23, p<0.001) for overweight

Table 2. Factors associated with the presence of "at least two metabolic disorders" and "at least two metabolic disorders" in the multivariable analyses.

Parameter	Relationships with having at least two abnormal components						Relationships with having at least three abnormal components					
	Univariable analysis			Multivariable analysis			Univariable analysis			Multivariable analysis		
	cOR	95% CI	p-value	aOR	95% CI	p-value	cOR	95% CI	p-value	aOR	95% CI	p-value
Residence: Urban vs rural (Ref)	2.1	1.8-2.4	0.0001	1.4	1.2-1.7	0.0001	3.1	2.5-3.8	0.0001	1.6	1.2-2.1	0.001
Sex: Female vs male (Ref)	1.8	1.6-2.0	0.0001	1.9	1.6-2.1	0.0001	3.2	2.5-4.1	0.0001	3.1	2.3-4.1	0.001
Age range (years)												
25 – 34 (Ref)	1			1						1		
35 - 44	1.3	1.1-1.5	0.001	1.2	1.1-1.5	0.015	1.6	1.2-2.1	0.001	1.5	1.1-2.1	0.007
45 – 54	1.6	1.4-1.9	0.0001	1.7	1.4-2.0	0.0001	2.2	1.6-2.9	0.0001	2.3	1.7-3.2	0.0001
55 - 64	2.0	1.7-2.5	0.0001	2.3	1.9-2.9	0.0001	2.6	1.9-3.5	0.0001	3.6	2.6-5.2	0.0001
Marital status: Married/cohabiting vs no (Ref)	0.9	0.7-1.1	0.084	>0.9	0.8-1.2	0.73	0.7	0.6->0.9	0.03	0.9	0.6-1.2	0.44
Education levels												
No formal/no education (Ref)	1			1			1			1		
Primary achieved	1.2	0.9-1.4	0.073	1.1	0.9-1.4	0.31	1.2	0.9-1.6	0.24	>0.9	0.7-1.4	0.81
Secondary or more	1.5	1.2-1.9	0.001	>1.0	0.7-1.3	0.89	2.3	1.6-3.1	0.0001	1.4	0.9-2.1	0.17
Professions providing formal and regular income Yes vs No (Ref)	1.6	1.4-1.8	0.0001	1.1	0.9-1.3	0.18	2.3	1.8-2.8	0.0001	1.4	1.1-1.8	0.02
Physical activity: Yes vs No (ref)	1.8	1.4-2.3	0.0001	1.3	1.1-1.8	0.04	2.3	1.6-3.1	0.0001	1.5	1.1-2.2	0.038
Current use of alcohol and/or tobacco: Yes vs no (Ref)	0.8	0.7-0.9	0.002	0.9	0.8-1.1	0.14	0.8	0.6-0.9	0.013	>0.9	0.7-1.2	0.75
Cleaning the teeth at least twice a day: Yes vs no (Ref)	0.9	0.8-1.1	0.15	0.8	0.7-0.9	0.005	0.9	0.7-1.2	0.61	0.7	0.5-0.9	0.017
Number of fruits/vegetables consumed												
0	1			1			1			1		
1 - 2	1.2	1.1-1.4	0.027	1.2	1.1-1.5	0.012	1.3	>0.9-1.6	0.07	1.2	0.9-1.6	0.20
3 - 4	1.4	1.2-1.7	0.0001	1.3	1.1-1.6	0.007	1.3	1.1-1.7	0.049	1.2	1.9-1.7	0.17
≥5	1.4	1.2-1.8	0.001	1.7	1.2-2.3	0.001	1.5	>0.9-2.4	0.054	1.9	1.1-3.1	0.015
BMI categories												
Normal BMI	1			1			1			1		
Underweight	0.9	0.8-1.2	0.54	0.8	0.6-0.9	0.03	0.6	0.4-1.01	0.07	0.4	0.3-0.8	0.003
Overweight	3.9	3.2-4.8	0.0001	3.7	3.0-4.5	0.0001	5.9	4.5-7.5	0.0001	5.4	4.1-7.1	0.0001
Obese	13.0	8.3-20.3	0.0001	9.6	6.1-15.1	0.0001	16.3	11.7-22.8	0.0001	11.2	7.7-16.2	0.0001

Source: Authors 2022

and obesity, respectively (Omuse et al., 2017) and this is (consistent with international data (Brazil

(Ramires et al., 2018), China (Li et al., 2018), and Iran (Jahangiry et al., 2019)).

Cleaning the teeth at least twice a day was a protective factor (aOR=0.8, p<0.01). Indeed,

having demonstrated that more frequent toothbrushing was related to a lower prevalence and incidence of MetS and its components, Kobayashi et al. (2012) suggested that more frequent toothbrushing may contribute to the prevention of MetS due to the inflammation/triglyceride pathway (Kobayashi et al., 2012). Moreover, the finding of the link between the poor oral hygiene and the high levels of inflammatory cytokines with the risk of excess of weight resulted in authors concluding that the early proper dental prophylaxis and treatment could lead to the better prevention of metabolic disorders (Nijakowski et al., 2020). The 5-year follow-up retrospective study (of 3722 participants aged 35-64 years) reported that participants with more frequent daily toothbrushing tend to have significantly lower odds of developing the increased number of components or MetS (p for trend = 0.01) (Tanaka et al., 2018). It also specified that the risk of development of MetS was significantly lower in participants brushing teeth  $\geq 3$  times/day than in those brushing teeth  $\leq 1$  time/day (aOR=0.64, CI: 0.45-0.92). The efficiency of the healthy oral hygiene practice in the secondary prevention of cardiovascular events was also described. It was reported that patients with coronary heart disease who reported practicing interdental cleaning reduced tobacco exposure and had a significant decreased adjusted risk for new cardiovascular events (HR=0.2, CI:0.06-0.6) than those who did not report practicing interdental cleaning (Reichert et al., 2015). Other researchers noted the significant relationship between oral health behaviour and stroke (odds for stroke even was of 2.15, CI: 1.01-4.58 for those who daily did not clean the teeth) (Cho et al., 2021). Although, consistent data reported benefits (with regards to the MetS prevention) from the adequate/healthy oral practice, this fundamental public health issue is still neglected by the healthcare workers (Chen, 2018).

Findings suggested that (except for overweight/obesity and physical inactivity) unhealthy lifestyle practices were common among adults in Burkina Faso and the adequate oral hygiene practice should be included among the protective behaviours of metabolic disorders.

### Limitations

We did not assess some important potentially-modifiable variables such as psychological stress (Kuo et al. 2019) and sleep quality (Lian et al. 2019). Triglycerides were not measured and so our estimate of the prevalence of MetS may be underestimated. However, we based our definition of MetS, on the most common components. Evidence from the literature suggests that triglycerides may be normal among West Africans with MetS (Sumner et al., 2010). While these first nationally-representative data from 2013 may no longer reflect the current situation, they provide a baseline that can be compared with future WHO STEPS survey data.

## Conclusion

Except for overweight/obesity and physical inactivity, unhealthy modifiable lifestyle factors were common in Burkinabè adults. Similarly, the prevalence of multiple metabolic disorder components was significant. The unfavourable and unexpected effect of more FV intake with increased number of abnormal components may be understood as the therapeutic lifestyle change effect. Tooth cleaning at least twice a day was revealed as a protective practice and should be promoted in the general population and included in the therapeutic lifestyle change policy for the potentially at risk individuals.

## **CONFLICT OF INTERESTS**

The authors have not declared any conflict of interests.

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