

OBESSE AND DISEASE FREE (ODF) POPULATION IN MALAYSIA: FINDINGS FROM NATIONAL HEALTH AND MORBIDITY SURVEY (NHMS) MALAYSIA 2015

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ABSTRACT

Background: Obesity does not always lead to non-communicable diseases. The objective of this paper is to estimate the prevalence of obese and disease-free population among Malaysian adult aged 18 years and above and to determine the lifestyle and dietary factors on this population.

Materials and Methods: Data from the Malaysia National Health and Morbidity Survey (NHMS) 2015, a cross sectional design, applied two stage stratified cluster sampling. Obese and disease-free population was defined as population of obese adults with no known diagnosis of diabetes, hypertension, and high cholesterol. Descriptive analysis of the background characteristics was performed and complex sampling was used to determine the prevalence of obese and disease-free population. Multiple logistic regression was used to determine factors associated with obese and disease free. Data was analysed using SPSS version 25. A *p*-value of <0.05 was considered significant.

Result: 23.7% of Malaysian adults were obese and disease free. Multivariate analysis showed there were no association between lifestyle determinants (physical activity, smoking and alcohol) and dietary factors (fruits and vegetables intake) on these population. Significant associations were revealed among adults aged 18-24 [aOR: 5.00 (95% CI 3.22-7.73)] and 25-44 years old [aOR: 2.45 (95% CI 1.65-3.64)]. The Nagelkerke R Square analysis predicted that with each passing year, the probability of these population becoming unhealthy obesity increases by 4.4%.

Conclusion: Obese and disease-free population is present among obese population. No significant association was reported for lifestyle determinants and dietary factors on these population. A focus shift on parameters of metabolic health should be considered.

Keywords: Obese, disease-free, obesity, non-communicable diseases

1.0 Introduction

Obesity prevalence is set to increase drastically by 2030 to around one billion people worldwide [1]. Malaysia as a developing country is also plagued with high obesity prevalence with an increasing trend every year. National Health Morbidity Survey (NHMS) 2015 showed that the national prevalence of overweight, obesity, and abdominal obesity has increased by 0.6%, 2.6% and 2.0% respectively as compared to the previous findings of NHMS 2011 [2]. Obesity is known to cause major non communicable diseases (NCD) such as type 2 diabetes mellitus, cardiovascular disease, and hypertension [3].

However, recent evidence indicates that obesity or adiposity does not generally lead to insulin resistance, hypertension, and cardiovascular disease [4]. Currently, there is a group of population known as metabolically healthy obese (MHO) that seems to be disease free from metabolic syndrome [5]. To date, not much is known about the determinants of MHO, the factors that delay the onset or protect obese individuals from developing metabolic disturbances. This group of phenotype seems to be having an absence of metabolic syndrome components (e.g. normal blood pressure, normal lipid values, normal fasting glucose concentrations, and in some studies normal C-reactive protein concentrations); and absence of insulin resistance [6].

Despite the prevalence and existence of MHO, there are no standardized criteria to classify or define MHO. This resulted in a wide prevalence of estimation (6.0-35.0%) depending on criteria which is used [7]. In addition, other factors such as sex, lifestyle, ethnicity, or age can influence the prevalence of MHO [8]. Currently, intervention programmes available and established do not distinguish treatment between metabolically unhealthy obesity (MUO) and MHO [8]. Identifying this group of population will be important in determining the appropriate therapeutic strategy [9].

Table 1: Criteria used to define metabolic health status:

Risk Factor	Defining level
Central Obesity <ul style="list-style-type: none"> • Men • Women 	Waist circumference >102 cm (40 in) >88 cm (35 in)
Triglycerides	≥150 mg/dL (1.7 mmol/L)
HDL <ul style="list-style-type: none"> • Men • Women 	<40 mg/dL (1.03 mmol/L) <50 mg/dL (1.29 mmol/L)
Blood Pressure	≥110 / ≥ 85 mmHg
Fasting glucose	≥110 mg/dL (6.1 mmol/L)

Reference: The Adult Treatment Panel Guidelines (ATP III).

Potential mechanisms contributing to MHO, target for future research (Current Hypertension Report 2020) are genetic variants, loss of functions Reduced chronic inflammation, changes in adipose tissue composition, variants of adipose function, protection from NAFLD gastrointestinal microbiota variation and less sedentary lifestyle (“fat” and “fit”)

Metabolically healthy obesity could not be used to classify NHMS 2015 respondents as it lacks the data for triglycerides and high-density lipoprotein (Table 1). Therefore, we could not use MHO terminology but to continue investigating the prevalence of these (disease free) population in our survey. We decided to use the term of obese and disease free (ODF) for this study. The results obtained will be discussed with evidence-based MHO literature reviews since MHO is the closest source for ODF.

The objectives of this paper is to investigate the prevalence of obese respondents that were not having any non-communicable diseases (diabetes, high blood pressure and high cholesterol) or also known as ODF and to find the association of lifestyle (physical activity, alcohol intake and smoking) and dietary factors (fruits and vegetables intake) in terms of impact among these population.

2.0 Materials and Methods

The sampling frame was updated in 2014 prior to sampling process. Based on the frame, areas in Malaysia were divided into Enumeration Blocks (EB). The sampling design used two staged stratified random sampling. Primary stratum made up of states of Malaysia while second stratum made up of urban and rural strata. Sampling involve 2 stages; the Primary Sampling Unit (PSU), which was Enumeration Block (EBs) and the second sampling Unit (SSU) which was Living Quarters (LQs) within the selected EBs. A total of 10,428 LQs were selected from the total EBs in Malaysia. Twelve LQs were randomly selected from each selected EBs. Pregnant women, post-natal (less than 60 days at time of visit), bed ridden due to chronic / prolonged illness, injury/ accident, having physical disability that can affect the normal standing including on wheel chair, body deformities such as no hand and leg, spondylolysis except deaf, blind and mute were excluded from this study. Data collection was from Mac 2015 till June 2015. After considering exclusion of duplicates, a total of 15757 respondents were analysed

Mobile data collection was used to collect data in the field. Data collection was done using e-NHMS 2015 application. The application contained all the modules that were required in the face-to-face interview. After data collection, all the data entered will be sent to main server.

Clinical assessment was done by nurses. For the assessment of weight, Tanita personal Scale HD 319 was used. Tool was validated and calibrated. For field implementation, a standard weight was supplied for each team for standardisation. For measurement of height, Seca Stadiometer 213 was used. Tool was validated and calibrated. BMI was defined as weight in kilograms divided by square of the heights (kg/m^2). Reference from WHO 2004 was used for BMI Individuals with a BMI $\geq 30 \text{kg/m}^2$ were defined as obese. Omron Japan Model HEM-907 which has been validated and calibrated was used for blood pressure assessment, while PA CardioChek which has been validated was used to assess fasting blood glucose and cholesterol.

Descriptive analyses were performed to estimate the prevalence and 95%CI of ODF and characteristics associated. Univariate analysis using binary logistic regression was then applied for each variable to get the crude OR and p-value. Variables having a p-value less than 0.25 from the univariate analysis were included in the initial multivariate logistic regression model.

Enter method was applied to arrive at the final model. Multicollinearity and interaction terms were checked, and the Hosmer Lemeshow test, classification table and ROC curve were applied to check the model fitness. The strength of association for each risk factor was assessed using crude and adjusted odds ratios (AOR).

3.0 Result

Table 2: Prevalence of ODF among Adults in Malaysia

Variable	Estimated population	n	%	95%CI	
				Lower	Upper
Overall	761965	741	23.7	21.8	25.8
Socio-demographic					
Sex					
Male	345550	299	24.4	21.6	27.5
Female	416415	442	23.2	20.7	25.9
Age group (years)					
	34.58				
Mean (SE)	(0.57)				
18 - 24	184165	140	44.6	37.9	51.6
25 - 44	425965	403	26.8	23.9	29.8
45 - 64	127846	165	12.4	10.2	14.9
65+	23989	33	14.0	9.5	20.3
Ethnicity					
Malay	427465	497	22.7	20.7	25.0
Chinese	97079	62	20.6	15.8	26.3
Indian	83936	76	24.9	19.3	31.6
Other Bumis	101989	74	27.4	22.4	33.1
Others	51496	32	34.7	23.4	48.0
Locality					
Urban	585548	447	24.1	21.8	26.5
Rural	176417	294	22.7	19.4	26.4
Household income group (RM)					
Less than RM1000	81022	90	20.6	16.3	25.6
RM1000 - 1999	99644	115	19.8	15.8	24.4
RM2000 - 2999	121566	118	23.9	19.3	29.2
RM3000 - 3999	99612	99	23.4	18.6	28.9
RM4000 - 4999	71268	69	21.6	16.3	28.0
RM5000 - 5999	62406	55	25.0	18.2	33.4
RM6000 - 6999	48763	37	27.8	19.1	38.6
RM7000 - 7999	33324	35	21.9	14.0	32.6
RM8000 - 8999	37318	32	29.1	21.1	38.8
RM9000 - 9999	16855	13	22.8	10.8	42.0
RM10000 and above	90186	78	33.7	26.9	41.2
Life Style					
Physical activity					

	Active	509446	504	23.3	21.1	25.6
	Inactive	248281	232	24.8	21.4	28.6
Alcohol intake						
	Non drinker	685235	688	24.1	22.0	26.2
	Ex-drinker	10399	8	26.9	10.8	52.8
	Current drinker	47246	33	21.0	14.4	29.5
	Unclassified	17585	11	18.8	9.8	33.0
Smoking						
	Current non-smoker	622943	618	23.6	21.4	25.8
	Current tobacco smoker	139023	123	24.6	20.3	29.5
Fruit and vegetable intake						
	Adequate	57645	54	26.6	19.6	35.1
	Not Adequate	702226	686	23.5	21.5	25.6

The results showed about 741 respondents (23.7%) or 1 in 4 of the obese respondents were obese and disease free. There were 299 (10.8%) male respondents and 442 (13.0%) female respondents. In terms of age group, the largest population were from 25-44 age group which consists of 403(13.3%) respondents. In terms of ethnicity, Malays has the highest respondents of 497 (13.3%), followed by other Bumiputra 74(3.2%), Chinese 62 (3.0%). Urban dwellers had higher respondents 447(18.2%) compared to rural 294(5.5%).

In terms of monthly income, those who were earning RM 2000-2999 had the largest respondents of 48 (3.8%). About 505 (16.0%) respondents were physically active while 232 (7.8%) inactive. Those who do not consume alcohol were 688 (21.4%) while current drinker was 33 (1.5%) only. Non-smokers were 628 (19.4%) while current smokers were 123 (4.3%) respondents. Fruits and vegetables intake were inadequate among these population. Only 54(1.8%) consume adequate fruits and vegetables while 686 (21.9%) intake was inadequate.

Table 2: Univariate and multivariate analyses of factors associated to obese and disease-free adults in Malaysia.

Variable	Crude OR	95%CI		p-value	AOR	95%CI		p-value
		Lower	Upper			Lower	Upper	
Socio-demographic								
Sex								
Male	1.16	0.98	1.36	0.087	1.06	0.86	1.30	0.578
Female	1.00				1.00			
Age group (years)								
Original (numerical)	0.96	0.95	0.96	<0.001				
18 - 24	4.86	3.18	7.44	<0.001	5.00	3.23	7.73	<0.001
25 - 44	2.38	1.62	3.49	<0.001	2.45	1.65	3.64	<0.001
45 - 64	0.87	0.59	1.30	0.511	0.88	0.59	1.33	0.547
65+	1.00				1.00			
Ethnicity								
Malay	1.00							

Chinese	0.96	0.71	1.29	0.777				
Indian	1.21	0.92	1.59	0.179				
Other Bumis	1.29	0.98	1.71	0.071				
Others	1.58	1.03	2.40	0.034				
Locality								
Urban	1.26	1.07	1.48	0.006	1.08	0.91	1.29	0.386
Rural	1.00				1.00			
Household income group (RM)								
Less than RM1000	0.51	0.36	0.73	<0.001	0.59	0.40	0.85	0.005
RM1000 - 1999	0.52	0.37	0.72	<0.001	0.51	0.36	0.73	<0.001
RM2000 - 2999	0.54	0.38	0.75	<0.001	0.50	0.35	0.71	<0.001
RM3000 - 3999	0.58	0.41	0.82	0.002	0.55	0.38	0.79	0.001
RM4000 - 4999	0.60	0.41	0.87	0.007	0.55	0.37	0.81	0.003
RM5000 - 5999	0.60	0.40	0.89	0.011	0.58	0.38	0.88	0.011
RM6000 - 6999	0.64	0.41	1.01	0.056	0.61	0.38	0.97	0.037
RM7000 - 7999	0.63	0.40	1.00	0.048	0.54	0.33	0.87	0.011
RM8000 - 8999	0.78	0.48	1.26	0.314	0.77	0.47	1.26	0.298
RM9000 - 9999	0.71	0.36	1.40	0.325	0.63	0.31	1.27	0.197
RM10000 and above	1.00				1.00			
Life Style								
Physical activity								
Active	0.91	0.77	1.09	0.307	0.88	0.73	1.06	0.183
Inactive	1.00				1.00			
Alcohol intake								
Current drinker	1.00							
Non drinker	0.95	0.64	1.41	0.803				
Ex-drinker	1.14	0.47	2.77	0.765				
Unclassified	0.59	0.28	1.24	0.161				
Smoking								
Current non-smoker	0.86	0.69	1.07	0.179	1.10	0.84	1.44	0.505
Current tobacco smoker	1.00				1.00			
Fruit and vegetable intake								
Adequate	1.06	0.78	1.45	0.706				
Not adequate	1.00							

Use Enter method, Nagelkerke R Square (0.095), Hosmer and Lemeshow Test (p-value=0.969), Classification Table (79.1%). Multicollinearity and Interaction were checked.

Multivariate analysis showed there were statistically significant and positive association for respondents aged 18-44 years old and those with income less than RM1000 to RM7999. There were no significant association for physical activity and non-smoker. This study also revealed that with each passing year, the probability of these population becoming unhealthy obesity increases by 4.4%.

4.0 Discussion

1 in 4 or 23.7% of obese Malaysian adults were obese and disease free. No significant associated was reported in this study between role of lifestyle and dietary factors on obesity and disease-free respondents. The sociodemographic data suggest that many populations are physically active, non-smokers and non-alcoholic drinkers. These coincides with the evidence that these population are not sedentary and are fat but fit. Dietary and lifestyle factors play an important role in the development of insulin resistance, obesity, metabolic syndrome and T2DM [10,11]. Increased consumption of high-energy, high fat diets and deterioration in dietary quality coupled with increased sedentary behaviour, result in increased accumulation of adipose tissue and progression to overt obesity, which is associated with insulin resistance, low-grade inflammation, and increased risk of associated cardio metabolic abnormalities [12].

In general, the risks of diabetes, cardiovascular disease, and all-cause mortality are higher in people with metabolically unhealthy obesity than in those with metabolically healthy obesity and greater in those with metabolically healthy obesity than in those who are metabolically healthy and lean (MHL) (13). Moreover, the risks of these adverse outcomes are directly related to the number and severity of metabolic abnormalities (14). For this paper, we did not investigate the differences between these two populations.

According to literature review, 25-30% of metabolically unhealthy obesity subjects convert to metabolically healthy phenotype after a modest weight loss, even if obesity is not solved (15-17). There are also a lot of evidence suggesting multiple health benefits of non-weight-loss-centred paradigm for obesity treatment. The data from longitudinal studies suggest that approximately 30% to 50% of people with MHO convert to MUO after 4 to 20 years of follow-up (18-20). The major factors associated with the conversion of MHO to MUO are a decline in insulin sensitivity and an increase in fasting blood glucose (21). The risk of transitioning from MHO to MUO is greater in those with a high BMI, older age, evidence of more severe metabolic dysfunction (i.e., number of abnormal metabolic criteria and values that are closer to the upper limit of the normal range, and the presence of hepatic steatosis) (22-24), a poor lifestyle index (a composite of diet composition, leisure time physical activity, and cigarette smoking) (25), and weight gain during the observation period (26-27).

The Finnish Type 2 Diabetes (FIN D2D) survey examined fruit and vegetable intake and did not identify differences between individuals with or without the metabolic syndrome according to BMI category [28]. Our study did not show any associated of fruits and vegetables intake with ODF. This was further supported with prevalence of adequate intake which is only 1.8% among the population.

Previous studies have produced conflicting results regards metabolic health and smoking [29] and alcohol consumption [30]. The beneficial effects of moderate alcohol consumption on HDL-C are well known, but detrimental effects of alcohol include raised triglyceride concentrations, insulin resistance and abdominal obesity, which may partly account for the lack of a relationship between alcohol and MHO(30). The present study showed that even though ODF population were mostly non-smokers (19.4%) and non-alcohol drinkers (21.4%), there were no association with ODF with these two factors.

Moderate weight loss has long been considered the cornerstone of obesity treatment, with most scientific organizations and expert panel committees recommending 5–8% weight loss in order to reduce risk of cardio metabolic disease and obesity-related comorbidities (31). A recent study in subjects with metabolically healthy obesity who lost <10% or >10% of their baseline body weight after a 12-mo lifestyle intervention found changes in the plasma metabolome that are consistent with a dose-dependent weight-loss-induced improvement in the cardio metabolic risk profile (32), suggesting that greater weight loss can improve metabolic function in people with obesity irrespective of baseline metabolic status. Clearly, this is an area of investigation in which more research is required.

A variety of eating patterns can have beneficial effects on metabolic parameters independent of changes in body weight (33), but whether they can help in the conversion of metabolically unhealthy obesity to the metabolically healthy phenotype is not known.

Physical activity has received little attention in studies evaluating morbidity and mortality in metabolically healthy and unhealthy obese and lean individuals. In our study, there were no association between physical activity and ODF but the percentage of respondents who were active (16.0%) was higher than non-active (7.8%). A recent meta-analysis of cross-sectional studies concluded that subjects with metabolically healthy obesity are more physically active, spend less time in sedentary activities, and have ~30% greater cardiorespiratory fitness (an objective measure of aerobic/endurance capacity)—but not different muscle strength—compared with subjects with metabolically unhealthy obesity (34). Cardio respiratory fitness is an important physiological trait of metabolic health independent of BMI status (35), and adjusting for physical activity or fitness attenuates or abolishes the increase in cardiovascular disease morbidity and mortality associated with metabolically healthy obesity compared with the metabolically healthy normal-weight status (36).

Limitation of these research is that the dietary intake component was not available. We also could not use metabolically healthy obesity classification due to the unavailability of certain data such as low-density lipoprotein and high-density lipoprotein. Total calories and nutrients consumed by respondents could not be measured as diet recall was not obtained from respondents. Therefore, types of food or diet that are “protecting” the population could be investigated.

The biggest strength of this study is that this is the first study in Malaysia to look at obese people who are disease free. This study also has a large sample size and is a population-based study.

5.0 Conclusion and recommendation

Focusing on weight loss as the main treatment outcome can have negative effects on long-term adherence because the gradual slowing of the rate of weight loss with time and the subsequent weight regain can make patients feel disappointed and helpless, and thereby more likely to relapse to pre-treatment patterns of eating and physical activity (37). It has been shown repeatedly that adherence to the diet—whichever diet that may be—is a key factor for long-term weight-loss treatment success (38). As a result, ~25–30% of metabolically unhealthy

subjects with obesity convert to a metabolically healthy phenotype after a modest ~10% weight loss, even if obesity is not resolved (39).

Perhaps it's time that we start focusing and assess the problem of obesity from a different perspective all together. Focussing on improving metabolic parameters in obesity should be a primary focus as well as weight loss in the coming future.

Acknowledgement

The authors wish to thank the Director General of Health Malaysia for his permission to publish this study.

Funding

The research was fully supported by the Ministry of Health Malaysia research grant. There is no conflict of interest with the funder; no influence in the design, data collection, data analysis or the manuscript writing.

Declaration

These authors declare that there is no conflict of interest in any form

Authors contribution

Author 1: Proposal planning and introduction .

Author 2: Analysis and Methodology

Author 3: Analysis and results

Author 4: Discussion writing and

Author 5: Referencing and editorial

References

1. World Health Organisation: Obesity. Preventing and Managing the Global Epidemic. Report of a WHO Consultation on Obesity, Geneva 3–5 June 1997.
2. National Health and Morbidity Survey Malaysia, 2015.
3. Clinical Practice Guidelines Malaysia for Obesity, 2004.
4. Sims, E. Are there persons who are obese, but metabolically healthy? *Metabolism* 2001, 50, 1499–1504.
5. Roberson, L.; Aneni, E.; Maziak, W.; Agatston, A.; Feldman, T.; Rouseff, M.; Tran, T.; Blaha, M.J.; Santos, R.D.; Sposito, A.; et al. Beyond BMI: The “Metabolically healthy obese” phenotype & its association with clinical/subclinical cardiovascular disease and all-cause mortality—A systematic review. *BMC Public Health* 2014, 14, 1–12
6. Pajunen, P.; Kotronen, A.; Korpi-Hyövälti, E.; Keinänen Kiukaanniemi, S.; Oksa, H.; Niskanen, L.; Saaristo, T.; Saltevo, J.T.; Sundvall, T.; Vanhala, M.; et al. Metabolically healthy and unhealthy obesity phenotypes in the general population: The FIN-D2D survey. *BMC Public Health* 2011, 11, 754–762.
7. Van Vliet-Ostaptchouk, J.; Nuotio, M.; Slagter, S.; Doiron, D.; Fischer, K.; Foco, L.; Gaye, A.; Gögele, M.; Heier, M.; Hiekkalinna, T.; et al. The prevalence of metabolic syndrome and metabolically healthy obesity in Europe: A collaborative analysis of ten large cohort studies. *BMC Endocr. Disord.* 2014, 14, 9–22.
8. Karelis AD (2008) Metabolically healthy but obese individuals. *Lancet* 372: 1281–1283.
9. Lynch LA, O’Connell JM, Kwasnik AK, Cawood TJ, O’Farrelly C et al. (2009) Are Natural Killer Cells Protecting the Metabolically Healthy Obese Patient? *Obesity* 17: 601–605. doi:10.1038/oby.2008.565. PubMed: 19238145.
10. Phillips CM (2013) Nutrigenetics and metabolic disease: current status and implications for personalised nutrition. *Nutrients* 5: 32–57. doi: 10.3390/nu5010032. PubMed: 23306188.
11. Harrington J, Phillips CM (2013) Nutrigenetics: Bridging two worlds to understand type 2 diabetes. *Curr Diab Rep.*
12. Hotamisligil GS (2006) Inflammation and metabolic disorders. *Nature* 444: 860–867. doi:10.1038/nature05485. PubMed: 17167474.
13. Mongraw-Chaffin M, et al. Metabolically healthy obesity, transition to metabolic syndrome, and cardiovascular risk. *J Am Coll Cardiol.* 2018;71(17):1857–1865.

14. Caleyachetty R, et al. Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women. *J Am Coll Cardiol.* 2017;70(12):1429–1437.
15. Echouffo-Tcheugui JB, et al. Natural history of obesity subphenotypes: dynamic changes over two decades and prognosis in the Framingham Heart Study. *J Clin Endocrinol Metab.* 2019;104(3):738–752.
16. Mongraw-Chaffin M, et al. Metabolically healthy obesity, transition to metabolic syndrome, and cardiovascular risk. *J Am Coll Cardiol.* 2018;71(17):1857–1865. 28. Mongraw-Chaffin M, et al. Metabolically healthy obesity, transition to metabolic syndrome, and cardiovascular risk. *J Am Coll Cardiol.* 2018;71(17):1857–1865.
17. Bell JA, Hamer M, Sabia S, Singh-Manoux A, Batty GD, Kivimäki M. The natural course of healthy obesity over 20 years. *J Am Coll Cardiol.* 2015;65(1):101–102.
18. Achilike I, Hazuda HP, Fowler SP, Aung K, Lorenzo C. Predicting the development of the metabolically healthy obese phenotype. *Int J Obes (Lond).* 2015;39(2):228–234.
19. Soriguer F, et al. Metabolically healthy but obese, a matter of time? Findings from the prospective Pizarra study. *J Clin Endocrinol Metab.* 2013;98(6):2318–2325.
20. Appleton SL, et al. Diabetes and cardiovascular disease outcomes in the metabolically healthy obese phenotype: a cohort study. *Diabetes Care.* 2013;36(8):2388–2394.
21. Bell JA, Hamer M, Batty GD, Singh-Manoux A, Sabia S, Kivimäki M. Incidence of metabolic risk factors among healthy obese adults: 20-year follow-up. *J Am Coll Cardiol.* 2015;66(7):871–873.
22. Guo F, Garvey WT. Cardiometabolic disease risk in metabolically healthy and unhealthy obesity: stability of metabolic health status in adults. *Obesity (Silver Spring).* 2016;24(2):516–525.
23. Hashimoto Y, Hamaguchi M, Fukuda T, Ohbora A, Kojima T, Fukui M. Fatty liver as a risk factor for progression from metabolically healthy to metabolically abnormal in non-overweight individuals. *Endocrine.* 2017;57(1):89–97.
24. 2Moussa O, et al. Fate of the metabolically healthy obese-is this term a misnomer? A study from the Clinical Practice Research Datalink. *Int J Obes (Lond).* 2019;43(5):1093–1101.
25. Schröder H, et al. Determinants of the transition from a cardiometabolic normal to abnormal overweight/obese phenotype in a Spanish population. *Eur J Nutr.* 2014;53(6):1345–1353.
26. Cui Z, Truesdale KP, Bradshaw PT, Cai J, Stevens J. Three-year weight change and cardiometabolic risk factors in obese and normal weight adults who are metabolically healthy: the atherosclerosis risk in communities study. *Int J Obes (Lond).* 2015;39(8):1203–1208.

27. Espinosa De Ycaza AE, Donegan D, Jensen MD. Long-term metabolic risk for the metabolically healthy overweight/obese phenotype. *Int J Obes (Lond)*. 2018;42(3):302–309.
28. Pajunen P, Kotronen A, Korpi-Hyövälti E, Keinänen-Kiukaanniemi S, Oksa H et al. (2011) Metabolically healthy and unhealthy obesity phenotypes in the general population: the FIN-D2D Survey. *BMC Public Health* 11: 754. doi:10.1186/1471-2458-11-754. PubMed: 21962038.
29. Cena H, Fonte ML, Turconi G (2011) Relationship between smoking and metabolic syndrome. *Nutr Rev* 69: 745-753. doi:10.1111/j. 1753-4887.2011.00446.x. PubMed: 22133198.
30. Wildman RP, Muntner P, Reynolds K, McGinn AP, Rajpathak S et al. (2008) The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: prevalence and correlates of 2 phenotypes among the US population (NHANES 1999-2004). *Arch Intern Med* 168: 1617-1624. doi:10.1001/archinte. 168.15.1617. PubMed: 18695075.
31. American College of Cardiology/American Heart Association Task Force on Practice Guidelines Obesity Expert Panel. Executive summary: guidelines (2013) for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Obesity Society published by the Obesity Society and American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Based on a systematic review from the The Obesity Expert Panel, 2013. *Obesity (Silver Spring)* 2014;22(Suppl 2):S5–39
32. Palau-Rodriguez M, Garcia-Aloy M, Minarro A, Bernal-Lopez MR, Brunius C, Gómez-Huelgas R, Landberg R, Tinahones FJ, Andres-Lacueva C. Effects of a long-term lifestyle intervention on metabolically healthy women with obesity: metabolite profiles according to weight loss response. *Clin Nutr* 2019
33. Katz DL, Meller S. Can we say what diet is best for health? *Annu Rev Public Health* 2014;35:83–103.
34. Lavie CJ, Ortega FB, Kokkinos P. Impact of physical activity and fitness in metabolically healthy obesity. *J Am Coll Cardiol* 2018;71: 812–13.
35. Stefan N, Schick F, Haring HU. Causes, characteristics, and consequences of metabolically unhealthy normal weight in humans. *Cell Metab* 2017;26:292–300.
36. Ortega FB, Cadenas-Sanchez C, Migueles JH, Labayen I, Ruiz JR, Sui X, Blair SN, Martínez-Vizcaino V, Lavie CJ. Role of physical activity and fitness in the characterization and prognosis of the metabolically healthy obesity phenotype: a systematic review and meta-analysis. *Prog Cardiovasc Dis* 2018;61:190–205.

37. Middleton KR, Anton SD, Perri MG. Long-term adherence to health behavior change. *Am J Lifestyle Med* 2013;7: 395–404.
38. Dansinger ML, Gleason JA, Griffith JL, Selker HP, Schaefer EJ. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA* 2005;293:43–53.
39. Stefan N, Haring HU, Schulze MB. Metabolically healthy obesity: the low-hanging fruit in obesity treatment? *Lancet Diabetes Endocrinol* 2018;6:249–58.