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Physical activity in relation to metabolic health and obesity: The Feel4Diabetes study

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Abstract

Aim: To examine physical activity levels in association with metabolic health and estimate the stability of metabolically healthy obese (MHO) phenotypes over a 2-year period.

Methods: In total, 2848 men and women from families at risk of the development of diabetes were recruited. Participants were classified as obese or non-obese and metabolic health was defined using five existing definitions. Physical activity was estimated with the International Physical Activity Questionnaire and pedometers.

Results: Prevalence of the MHO phenotype varied among definitions (0% to 20.2%). Overall, the MHO were more active than the metabolically unhealthy obese (MUO). Daily sitting hours (odds ratio [OR] = 1.055, 95% confidence interval [CI]: 1.009-1.104) and daily steps (per 500; OR = 0.934, 95% CI: 0.896-0.973) were remarkable predictors of metabolic health in individuals with obesity; and likewise, in individuals without obesity. After 2 years, 44.1% of baseline MHO adults transitioned to MUO, while 84.0% of the MUO at baseline remained at the same phenotype. Although physical activity was not a major determinant in phenotype transitioning, daily steps were associated with the maintenance of metabolic health over time in the non-obese group.

Conclusion: A universally accepted definition for MHO is needed. Being physically active can contribute to a metabolically healthy profile even in the presence of obesity; still, MHO is a transient condition and physical activity alone may not be an adequate factor for its maintenance.

KEYWORDS

IPAQ, MHO phenotype, MHO prevalence, pedometers, phenotype stability

1 | INTRODUCTION

In recent decades, obesity has become one of the greatest public health concerns as its prevalence has increased rapidly worldwide.[1,2] The obesity phenotype is usually linked to multiple metabolic abnormalities in human health, which increase the risk of cardiovascular disease and total mortality.[1,3,4] Nonetheless, a subset of individuals with obesity described as metabolically healthy obese (MHO) appear to exhibit no adverse metabolic abnormalities and thus face fewer cardiometabolic risk factors than the typical obese phenotype.[5,6]

A recent meta-analysis of 40 population-based studies indicates that the prevalence of the MHO phenotype is approximately 35% of the population with obesity,[7] while an earlier systematic review by Rey-López et al. proposed that the prevalence ranged from 6% to 75%.[8] To date, there is no universally established definition for the concept of metabolic health in obesity, leading to inconsistent evidence on the prevalence and clinical outcomes among studies.[6,9] More than 30 definitions have been proposed to identify MHO[8] and most of these are mainly focused on the absence of metabolic syndrome (M.S.) components, insulin resistance (IR), hypertension and dyslipidemia, but not all of them simultaneously and with different cut-off values.[5,8,10,11] However, a number of longitudinal studies point out that metabolic health in obesity is an unstable condition leading to various health risks. In fact, the stability of the metabolically healthy phenotype is debated, as approximately 30%-50% of the MHO will probably convert to the unhealthy status in a follow-up period of 5-10 years.[12–15]

Even although the MHO seem to have significant differences from at-risk individuals with obesity in terms of body composition and metabolic profile, it is currently unclear if energy expenditure and physical activity (PA) levels are key determinants of metabolic health.[16] Most studies examining the MHO ignore the potential role and crucial impact of physical fitness in the prognosis of the phenotype and, consequently, the existing evidence is limited and inconsistent.[17] Both positive and no associations of activity levels and the MHO phenotype have been identified when compared with the unhealthy obesity phenotype.[18] According to recent reviews, the MHO tend to be more physically active and less sedentary, especially when the activity was objectively quantified.[18,19] A higher level of cardiorespiratory fitness (CRF) has also been observed in MHO individuals, which may explain to a degree the differences observed between the two obese phenotypes.[18,19] The need for harmonization the definitions of MHO is urgent in order to make equal comparisons. Reinforcing the available literature, we aimed, in the current study, to estimate the presence of the MHO phenotype in a large multiethnic sample of early middle-aged adults (mean age of 42 years), according to five different existing definitions for metabolic health. Our second objective was to investigate the association between phenotypes and PA levels, as well as the impact of PA in the presence of metabolic health in the population with and without obesity. Furthermore, we conducted a prospective analysis to examine the stability of the phenotypes during 2 years of follow-up and their association with PA as well, to predict metabolic health based on different levels of PA.

2 | METHODS

2.1 | Study design and study population

We used data from the Feel4Diabetes study, which aimed to develop, implement and evaluate a school- and community-based intervention programme for the prevention of type 2 diabetes, primarily focusing on families from vulnerable groups across Europe. The Feel4Diabetes study, which had a cluster-randomized design, was conducted in six European countries representing low-income countries (Bulgaria and Hungary), high-income countries (Belgium and Finland) and countries under austerity measures (Greece and Spain). The 'high-risk families' were identified based on type 2 diabetes risk estimation using the Finnish Diabetes Risk Score (FINDRISC) questionnaire. A family was regarded as 'high risk' if at least one parent fulfilled the country-specific cut-off point for FINDRISC that indicated increased type 2 diabetes risk. Recruitment took place via primary schools of the randomly selected areas. Individuals entering the 2-year intervention (2016-2018) were adults from the 'high-risk families' and 'all families' components, including individuals with normal fasting plasma glucose levels, undiagnosed prediabetes and those who were not under any treatment for prediabetes or diabetes. More details on the Feel4Diabetes study, its design, recruitment and intervention, can be found elsewhere.[20] For the needs of the current analysis, we used baseline data from all individuals, as well as prospective data from the control group of the intervention of the study. Overall, 2848 recruited adults were used for cross-sectional analyses and 681 participants for the longitudinal analyses. Baseline biochemical and anthropometric data, as well as data from PA questionnaires and pedometers, were used for the purposes of the study. Those diagnosed with diabetes were excluded from our analyses. Out of all the study participants, 1027 provided us with the necessary data from the pedometers. The Feel4-Diabetes-study adhered to the Declaration of Helsinki and the conventions of the Council of Europe on human rights and biomedicine. All necessary approvals and ethical clearance were obtained from the relevant ethical committees and local authorities. Potential participants had to sign a consent form before their enrolment in the study.

2.2 | Definition of metabolic health

To define metabolic health, we applied five different definitions based on the most commonly used criteria for MHO.[9] M.S. components, according to International Diabetes Federation thresholds,[21] and low IR, according to Homeostatic Model Assessment (HOMA),[22] were used for the identification of metabolically healthy individuals. In detail, we used the following criteria for each definition:

1. 'Metabolic Syndrome Definition': fulfilment of a maximum of two of the five components of the M.S.
2. 'Strict Metabolic Syndrome Definition': no fulfilment of any component of the M.S.
3. 'Low IR-Q3 Definition': HOMA values equal to or less than the 75th percentile in the specific population.
4. 'Low IR-Q2 Definition': HOMA values equal to or less than the 50th percentile in the specific population.
5. 'Zero M.S. Components + Low IR Definition': no fulfilment of any component of the M.S. plus HOMA values equal to or less than the 50th percentile in the specific population.

Individuals with a body mass index (BMI) of 30 kg/m^2 or higher were considered obese, according to the World Health Organization classification,[2] and individuals with a BMI of less than 30 kg/m^2 were registered in the non-obese group. For the purposes of our study, status of metabolic health and obesity categories were combined to create the four phenotypes that were examined: metabolically healthy obese (MHO), metabolically unhealthy obese (MUO), metabolically healthy non-obese (MHNO) and metabolically unhealthy non-obese (MUNO).

2.3 | Questionnaire-assessed physical activity

Total PA was first assessed by the International Physical Activity Questionnaire (IPAQ)—short form.[23,24] Participants were required to take into account their activity pattern over the last 7 days and answer seven questions that covered the frequency and the amount of time spent involved in vigorous or moderate PA and walking, as well as the amount of time spent sitting. They were instructed to record only those physical activities that lasted at least 10 minutes or a maximum of 180 minutes. Activities with a duration of less than 10 minutes or more than 180 minutes were truncated as 0 or 180 minutes, respectively. Time spent in vigorous activities, moderate activities and walking were converted to metabolic equicalents of each task (MET) by multiplying the time spent in each activity (in minutes per week) by 9.0, 4.0 and 3.3, respectively. A total PA score was generated as the sum of each activity category, expressed in MET.min.wk^{-1}. Sedentary activities were calculated as daily total minutes of time spent sitting.

2.4 | Accelerometer-assessed physical activity

PA was objectively assessed in 1027 participants who voluntarily wore a pedometer for at least 3 consecutive days. The following pedometers were used among countries: Omron Walking Style Pro Step Counter (Omron), Trax Activity Tracker (Trax Fitness) and Triaxial Actigraph Accelerometer (Actigraph). A mean stepping score per day was calculated for each individual.

2.5 | Statistical analyses

Descriptive data on participants' characteristics are presented as means ± standard deviation for continuous variables and as proportions (%) for categorical values. Comparisons among groups were performed with a one-way analysis of variance (ANOVA), using Bonferroni post hoc tests for between-group comparisons.

Multiple logistic regression models were applied to examine the association between PA levels and metabolic health. In our model, the presence or absence of metabolic health was defined as a dependent variable (binary variable, where 1 = absence of metabolic health/0 = presence of metabolic health) and PA indices were used as the independent variables. In those models, metabolic health was assessed based on the fourth definition, requiring a low IR index value (HOMA ≤ 50th percentile). We opted to use this definition because the criteria were neither too restrictive nor too flexible compared with the other definitions and, consequently, a satisfactory number of MHO people were detected. Age, sex, education level and smoking status were used as potential confounders, as they have been found to be associated with PA levels and health in general.

In longitudinal analyses, we examined the time effect on the stability of the metabolically healthy phenotypes over the 2-year follow-up period, and differences in PA levels were also examined and compared between stable and unstable groups using ANOVA. Bonferroni post hoc tests for between-group comparisons were performed when a statistically significant main effect was detected. Similar to our cross-sectional multiple logistic regression models, we examined prospectively the effect of PA variables on metabolic health using generalized linear models, taking into consideration the same potential confounders. Significance was set at .05 for all analyses.

3 | RESULTS

3.1 | Sample characteristics

Participants had a mean age of 42.0 years and 65% were females (Table 1). As expected, obese individuals had a worse metabolic profile and lower walking score, compared with the non-obese group. Out of all participants, 26% were reported to be current smokers, while the vast majority of the study sample (74%) had a comparatively high (>12 years) educational background.

3.2 | Prevalence of metabolically healthy and unhealthy phenotypes according to BMI categories

The proportion of metabolically healthy and unhealthy phenotypes, according to BMI categories, varied considerably across the five definitions. The prevalence of MHO and MUNO phenotypes ranged from 0.0% to 20.2%, and from 8.2% to 51.2%, respectively (Figure 1).

3.3 | Physical activity levels across metabolic health and weight status

Differences in PA levels were tested among the MHO and non-obese phenotypes based on the fourth definition of metabolic health (Low IR-Q2). Analysis of variance revealed an overall group effect for vigorous activity ($p = .005$), total activity ($p = .011$), walking ($p < .001$) and daily steps ($p < .001$), but not for moderate activity ($p = .504$) and sitting time ($p = .082$) (Figure S1). MHNO individuals had statistically significant higher levels of total activity and recalled walking and total steps per day compared with MUNO. MHO individuals performed more steps compared with MUO or MUNO individuals. Similar results were derived from the phenotype comparisons according to the rest of the metabolic health definitions.

3.4 | Associations between metabolic health and physical activity levels

Regarding cross-sectional data, multiple logistic regression was conducted to investigate the relationship between different levels of PA and the presence of metabolic health in the obese and non-obese groups, as well as in the total population (Figure 2). Vigorous PA was positively associated with metabolic health, leading to an approximately 1% odds reduction of being unhealthy for every extra 100 MET.min of vigorous exercise (equivalent to 12.5 minutes of vigorous activity) per week, in both individuals with obesity (odds ratio [OR] = 0.989, 95% confidence interval [CI]: 0.982-0.995) and without (odds ratio [OR] = 0.990, 95% confidence interval [CI]: 0.983-0.996). No significant associations were found for moderate activity in both groups. Walking appeared to be a strong predictor of metabolic health

TABLE 1 Baseline characteristics of the study sample.

	All (N = 2848)	Non-obese (N = 1787)	Obese (N = 1061)	*P* value
Age (y)	42.0 ± 7.4	41.7 ± 7.2	42.4 ± 7.8	.020
Sex (female) (%)	65.0	70.1	56.4	< .001
BMI (kg/m^2)	28.7 ± 5.5	25.3 ± 2.9	34.4 ± 3.9	< .001
Education (%)				< .001
≤ 6 y	2.8	2.0	4.0	
7-12 y	22.9	20.5	27.0	
>12 y	74.3	77.5	69.0	
Waist circumference (cm)	95.1 ± 14.4	87.4 ± 10.3	108.0 ± 10.5	< .001
Glucose (mg/dL)	95.7 ± 20.8	93.2 ± 18.6	99.9 ± 23.4	< .001
Triglycerides (mg/dL)	111.0 ± 81.6	97.0 ± 66.9	134.6 ± 97.1	< .001
HDL cholesterol (mg/dL)	53.1 ± 14.2	56.0 ± 14.6	48.3 ± 12.2	< .001
Systolic blood pressure (mmHg)	119.1 ± 17.0	115.3 ± 15.7	125.6 ± 17.1	< .001
Diastolic blood pressure (mmHg)	78.9 ± 11.5	76.3 ± 10.6	83.4 ± 11.6	< .001
Physical activity				
Vigorous (MET.min.wk^{-1})	867.9 ± 34.7	817.6 ± 41.2	952.8 ± 62.2	.06
Moderate (MET.min.wk^{-1})	526.3 ± 19.6	513.6 ± 24.2	547.7 ± 33.5	.402
Walking (MET.min.wk^{-1})	896.8 ± 21.6	951.1 ± 27.9	805.4 ± 34.0	.001
Sitting (min.day^{-1})	245.4 ± 4.1	246.5 ± 5.1	243.4 ± 6.8	.721
Total (MET.min.wk^{-1})	2291.0 ± 56.1	2282.3 ± 67.6	2305.8 ± 98.7	.839
Steps per day	6051.7 ± 91.0	6131.9 ± 115.8	5929.5 ± 147.1	.277

Abbreviations: BMI, body mass index; MET, metabolic equivalent of task.

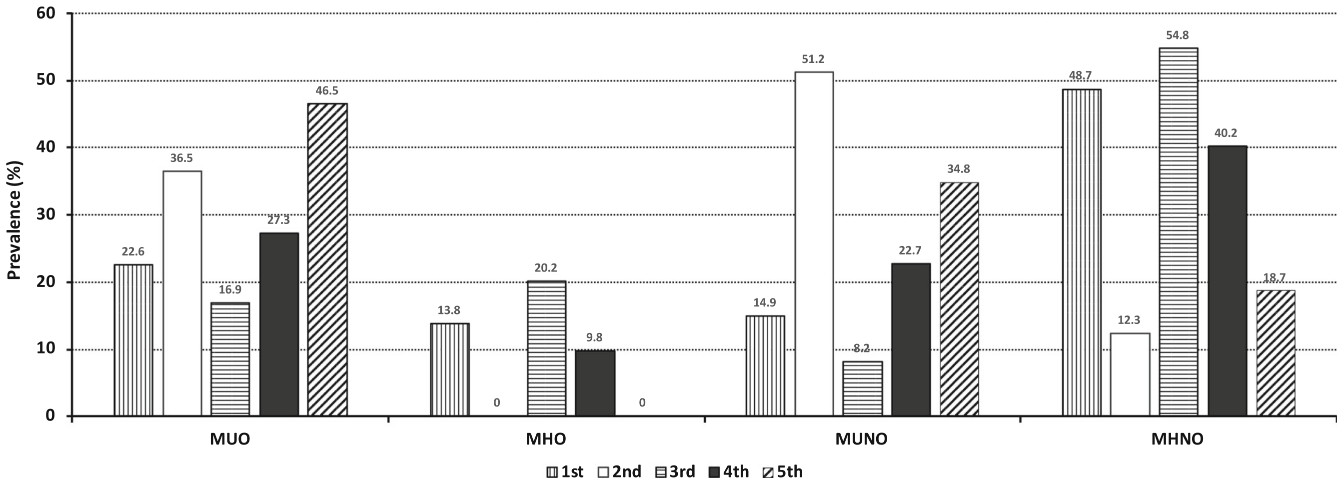

FIGURE 1 Prevalence of metabolically healthy and unhealthy obese and non-obese phenotypes, according to the five definitions used for metabolic health. Values are percentages within each definition. First: Metabolic Syndrome Definition; second: Strict Metabolic Syndrome Definition; third: Low IR-Q3 Definition; fourth: Low IR-Q2 Definition; fifth: Zero M.S. Components + Low IR Definition. IR, insulin resistance; MHNO, metabolically healthy non-obese; MHO, metabolically healthy obese; MUNO, metabolically unhealthy non-obese; MUO, metabolically unhealthy obese.

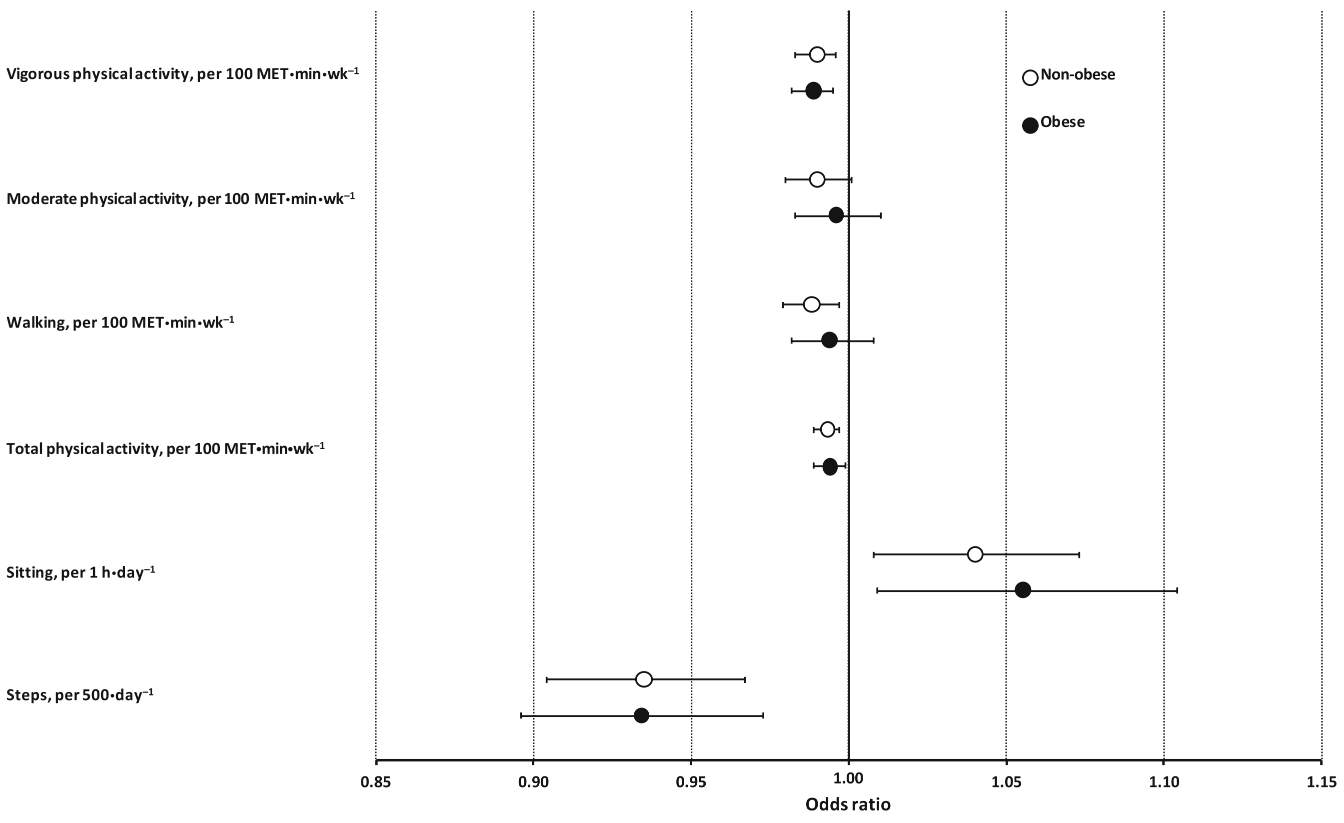

FIGURE 2 Multiple logistic regression predicting metabolically healthy status, according to the Low IR-Q2 definition of metabolic health, by PA in individuals with or without obesity. Values are odds ratios and 95% confidence intervals. Models were adjusted for age, sex, education level and smoking status. IR, insulin resistance; MHNO, metabolically healthy non-obese; MHO, metabolically healthy obese; MUNO, metabolically unhealthy non-obese; MUO, metabolically unhealthy obese.

(OR = 0.988, 95% CI: 0.979-0.997), because for every 100 MET.min increase in walking per week (equivalent to 30 minutes of walking), there was a 1.2% reduction in the odds of being metabolically unhealthy in the non-obese group. Daily sitting time was associated with the deterioration of metabolic health, increasing the odds for the absence of metabolic health by 5.5% (OR = 1.055, 95% CI: 1.009-

1.104) and 4.0% (OR = 1.040, 95% CI: 1.008-1.073) in obese and non-obese individuals, respectively. On the other hand, the number of total daily steps, assessed by pedometry, was reported as the most important positive predictor of metabolic health status. Increasing daily stepping by 500 steps was associated with 6.6% and 6.5% reductions in the odds of being MUO (OR = 0.934, 95% CI: 0.896-0.973) and MUNO (OR = 0.935, 95% CI: 0.904-0.967), respectively.

3.5 | Stability of phenotypes of metabolic health and weight status over time

Using prospective data, we examined the stability of the four phenotypes over a 2-year follow-up period. Data selected from the follow-up in the control group of the Feel4Diabetes intervention indicated that 44.1% of baseline MHO adults (26 out of 59 individuals) transitioned to the MUO state (Figure 3). Conversely, of the MUO group at baseline, 84.0% of individuals remained as MUO (142 out of 169 individuals). Regarding the non-obese groups, almost one-half of the MUNO did not change phenotype and 37.7% (58 out of 154 individuals) transitioned to the MHNO state. Of the MHNO group, the vast majority (77.3%; 231 out of 299 individuals) preserved the metabolically healthy phenotype and 20.1% (60 out of 299 individuals) shifted towards the MUNO group.

3.6 | Physical activity levels in relation to phenotypes of metabolic health and weight status after 2 years of follow-up

We further examined engagement in physical activities as a contributing factor in the stability of the metabolic phenotypes. Our aim was to assess the impact of PA, in terms of intensity and duration, in the transitioning from one phenotype to another, during the 2 years of follow-up (Figure S2).

Participants with MHO who remained 'healthy' had similar PA levels (in terms of total activity and total daily steps), as well as a similar daily sedentary time, when compared with their unstable counterparts. In addition, although the majority of MUO individuals at baseline remained stable during follow-up, a few individuals transitioned to the metabolically healthy phenotype; however, no important differences were observed in any type of examined PA compared with the stable group. Likewise, similar overall results with no significant differences were observed for the groups of non-obese individuals (Figure S2). Regarding the other variables, comparable trends were also observed for walking, vigorous and moderate physical activities.

3.7 | Longitudinal logistic regression

A second multiple analysis was conducted using longitudinal data. Interaction between PA levels and time during the 2-year follow-up was tested as a predictor of metabolic health in the obese and non-obese groups (Figure 4). Total daily steps was positively associated with metabolically healthy status only in non-obese group (OR = 0.924, 95% CI: 0.871-0.979). All the other associations between physical activities and the presence of metabolic health did not reach statistical significance in any of the two study groups.

4 | DISCUSSION

In the current study, we explored the impact of PA, assessed both subjectively and objectively, on metabolic health in a large multiethnic group of adults from families at risk of developing type 2 diabetes. Our overall findings suggest that metabolic health is positively associated with PA levels; however, high levels of PA may not be a significant predictor for maintaining metabolic health over time, at least in the obese population. Therefore, it may be assumed that PA levels may not counteract the detrimental effects of obesity per se on

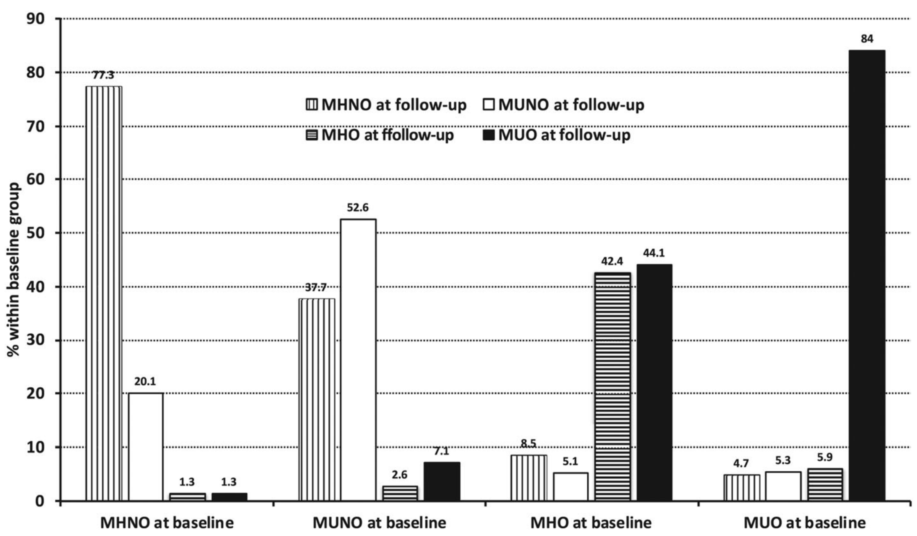

FIGURE 3 Stability of phenotypes of metabolic health and weight status over 2 years of follow-up, according to the Low IR-Q2 definition of metabolic health. IR, insulin resistance; MET, metabolic equivalent of each task.

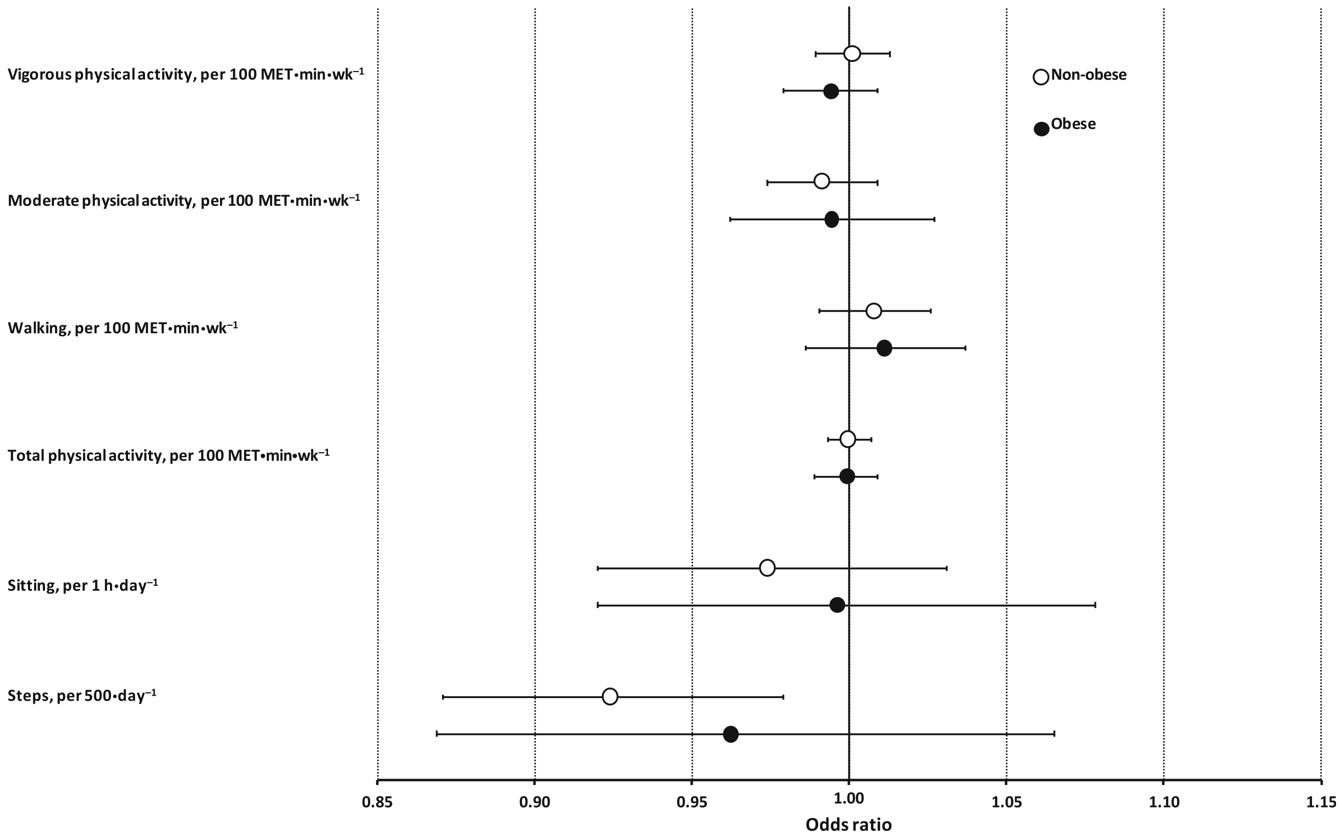

FIGURE 4 Generalized linear models predicting metabolically healthy status, according to the Low IR-Q2 definition of metabolic health, by PA levels during 2 years of follow-up, in individuals with or without obesity. Values are odds ratios and 95% confidence intervals. Models were adjusted for age, sex, education level and smoking status. IR, insulin resistance; MET, metabolic equivalent of each task.

metabolic health in the MHO phenotype over time and thus may not be an adequate factor to preserve metabolic health.

Describing metabolic health by five different definitions in obese and non-obese participants resulted in identifying 0% to 20.2% as MHO, while the MUNO phenotype ranged from 8.2% to 51.2%. In a cross-sectional study with a sample size of approximately 2000 adults aged 45-74 years, the prevalence of MHO varied considerably between definitions (from 2.2% to 11.9%).[25] The comparisons in all cases lead to poor agreement between metabolic phenotype classifications. In the study conducted by Ingle et al.,[26] metabolic health was estimated in 9000 men using M.S. components, leading to a prevalence of 17.9% as MHO. Other studies, which defined metabolic health as having zero M.S. components excluding waist circumference, resulted in approximately 13% and even 4.1% of MHO phenotype.[27,28] As a matter of fact, the prevalence of MHO depends each time on the definition used to operationalize the phenotypes, and even when the same criteria are applied, the outcome is not in accordance among studies.

Outcomes from a systematic review and meta-analysis of Ortega et al. support that MHO groups are related to significantly higher levels of PA and less sedentary behaviours in contrast to MUO.[19] These outcomes align with our strong cross-sectional findings; however, it is worth mentioning that they do not reflect a causal relationship. The MHNO participants reported greater levels of total PA and walking, while their obese counterparts spent more time engaged in vigorous activities. Taken together, these results assume that, in the absence of obesity, total activity may be the key factor for metabolic health, while in the obese population, vigorous activity may be necessary to ensure metabolic health. However, in our longitudinal analysis, even vigorous activity was not associated with preserving metabolic health over time in individuals with obesity. Pedometer data revealed that MHO and MHNO individuals achieved a greater total number of steps per day in comparison with both of their metabolically unhealthy counterparts, a finding that was only confirmed for the non-obese participants in the questionnaire's data. In most studies, differences in PA patterns between metabolically healthy and unhealthy individuals are only confirmed when objective measures are employed.[18] According to the Maastricht Study, the MHO took more steps in comparison with their unhealthy counterparts, as was confirmed from our results with pedometers,[29] indicating that walking may also be a significant contributor to metabolic health, irrespective of obesity.

In our study, a longer sitting time was indicated as an aggravating factor and an even greater impact factor for metabolic health than the different PA levels. This could be justified by the increased daily sedentary behaviours, especially in the at-risk groups, which overtopped the daily active time and thus formed a less active profile. On the other hand, inactivity per se may be a considerable independent factor for determining metabolic health. Research shows that increasing the duration and time spent in sedentary behaviours elevates the metabolic risk in adults, while the opposite has a protective effect.[30] Interestingly, patterns of moderate to vigorous PA did not retain the positive association with MHO when taking into consideration the sedentary behaviour of the participants in any of the age groups studied.[27]

Numerous longitudinal studies, especially those with a long follow-up period, have suggested that metabolic health in obesity is a transient condition leading to various health implications.[7,12–15] In our prospective analysis, out of all the MHO adults at baseline, 44% transitioned to MUO, and among the MHNO, 20% transitioned to the MUNO phenotype. In a study using multiple definitions to describe metabolic health, a proportion of 30.1%-47.8% of previously MHO participants became metabolically unhealthy depending on the criteria during the 6-year follow-up period.[13] Likewise, large sample-size studies with follow-up periods of 10 years[31] or longer[12] confirmed that metabolic health in overweight and obese groups is unstable, because almost one-half of MHO participants converted to the unhealthy group as a result of changes in clinical observations and lifestyle behaviours. A systematic review and meta-analysis also indicated that the pooled incidence of becoming metabolically unhealthy was 0.49 in the MHO compared with 0.27 in the metabolically healthy normal weight (MHNW) during a 10-year period, which agrees with the results from our prospective analysis regarding the stability of the two phenotypes.[7]

Our longitudinal analyses only revealed a positive association between total daily steps and metabolic health in the non-obese individuals and total population groups. A large prospective cohort study found that PA lowered the risk of becoming unhealthy, but only in the two non-obese population groups and not among the MHO, during a mean follow-up of 6 years.[28] Only a few prospective studies have investigated the role of PA in metabolic health over the long term, but the results remain inconsistent.[18] When no differences were detected in PA between healthy and unhealthy obese, energy expenditure did not appear to be a major determinant in phenotype transitioning.[32] Consequently, to be metabolically healthy over time, PA alone may not be as important factor in obese individuals as it is in those who are non-obese; additional metabolic and behavioural factors should be explored further.

Our study has several strengths. The Feel4Diabetes study is a large European study including volunteers from six European countries. Our findings are considered strong and reliable and can contribute meaningfully to existing literature regarding the prevalence of the MHO phenotype and its determinants. Five definitions of metabolic health were examined, providing useful information for comparisons with previous studies. PA was assessed with both subjective and objective assessment tools, providing evidence of better quality. Additionally, the study design allowed us to examine the impact of PA both cross-sectionally and longitudinally.

Regarding the limitations of the current study, PA levels were assessed with a self-reported questionnaire, a method inherent to potential bias and thus including a risk of overestimation or underestimation by the volunteers. Other PA factors, such as step intensity and the CRF of participants, were not assessed, restricting our ability to address fitness as a determinant and confounder of MHO. In addition, we did not assess PA over time, only baseline data. Changes in PA over time could provide more in-depth information on transitions over phenotypes examined and certainly more valid results.

In conclusion, defining metabolic health in obesity is a matter of much debate and the need for a harmonizing definition is vital. The MHO tend to be more active than the unhealthy groups: they reported less sedentary time and a greater number of steps per day. Reducing sedentary time, as well as increasing PA (vigorous PA, walking, total PA) and the daily number of steps, appear to play key roles in the presence of metabolic health in both obese and non-obese individuals. Although PA was not a determinant factor of phenotype transitioning, increasing the total number of daily steps could protect metabolic health in the non-obese population. Based on our findings, MHO is a transient condition and encouraging more PA may not be enough to prevent the metabolic shift to the unhealthy state. Our findings indicate that only focusing on PA, and not taking into consideration other modifiable factors, may not be adequate to ensure metabolic health over time in people with obesity. Lifestyle factors such as a healthy diet, preventing weight gain and/or smoking cessation may counterbalance the adverse effects of excessive fat deposition in the long term.[9]

AUTHOR CONTRIBUTIONS

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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