European Journal of Preventive Cardiology (2024) **31**, 205–213
https://doi.org/10.1093/eurjpc/zwad316

FULL RESEARCH PAPER
CVD risk factors

Long-term lifestyle change and risk of mortality and Type 2 diabetes in patients with cardiovascular disease

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Received 31 May 2023; revised 18 August 2023; accepted 22 September 2023; online publish-ahead-of-print 29 September 2023

See the editorial comment for this article 'Lifestyle change in patients with cardiovascular disease: never too late to adopt a healthy lifestyle', by Y. Gao and I.X.Y. Wu, https://doi.org/10.1093/eurjpc/zwad320.

Aims To quantify the relationship between self-reported, long-term lifestyle changes (smoking, waist circumference, physical activity, and alcohol consumption) and clinical outcomes in patients with established cardiovascular disease (CVD).

Methods and results Data were used from 2011 participants (78% male, age 57 ± 9 years) from the Utrecht Cardiovascular Cohort—Second Manifestations of ARTerial disease cohort who returned for a re-assessment visit (SMART2) after ∼10 years. Self-reported lifestyle change was classified as persistently healthy, improved, worsened, or persistently unhealthy. Cox proportional hazard models were used to quantify the relationship between lifestyle changes and the risk of (cardiovascular) mortality and incident Type 2 diabetes (T2D). Fifty-seven per cent of participants was persistently healthy, 17% improved their lifestyle, 8% worsened, and 17% was persistently unhealthy. During a median follow-up time of 6.1 (inter-quartile range 3.6–9.6) years after the SMART2 visit, 285 deaths occurred, and 99 new T2D diagnoses were made. Compared with a persistently unhealthy lifestyle, individuals who maintained a healthy lifestyle had a lower risk of all-cause mortality [hazard ratio (HR) 0.48, 95% confidence interval (CI) 0.36–0.63], cardiovascular mortality (HR 0.57, 95% CI 0.38–0.87), and incident T2D (HR 0.46, 95% CI 0.28–0.73). Similarly, those who improved their lifestyle had a lower risk of all-cause mortality (HR 0.52, 95% CI 0.37–0.74), cardiovascular mortality (HR 0.46, 95% CI 0.26–0.81), and incident T2D (HR 0.50, 95% CI 0.27–0.92).

Conclusion These findings suggest that maintaining or adopting a healthy lifestyle can significantly lower mortality and incident T2D risk in CVD patients. This study emphasizes the importance of ongoing lifestyle optimization in CVD patients, highlighting the potential for positive change regardless of previous lifestyle habits.

Lay summary In this study, we investigated whether lifestyle changes were related to improved health outcomes in individuals with cardiovascular disease (CVD). We assessed self-reported lifestyle behaviours (smoking, waist circumference, alcohol consumption, and physical activity), at inclusion in the cohort and again ∼10 years later. The results emphasize the importance of making healthy lifestyle choices, even for individuals already diagnosed with CVD, and suggest that it is never too late to improve one's lifestyle.

Keywords Established cardiovascular disease • Healthy lifestyle • Lifestyle changes • Mortality • Diabetes

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Key findings

- Cardiovascular disease (CVD) patients who maintained or improved to a healthy lifestyle had an almost 50% lower risk of death from any cause, cardiovascular-related death, and developing Type 2 diabetes compared with CVD patients who maintained an unhealthy lifestyle.
- Not smoking and compliance with physical activity recommendations were associated with the lowest risk for all-cause and cardiovascular mortality in patients with established CVD.

Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality, posing a significant worldwide health burden.[1,2] Patients with established CVD are not only at a high risk of recurrent cardiovascular events but also at a high risk of other diseases, including Type 2 diabetes (T2D), due to common risk factors such as unhealthy lifestyle habits.[3,4]

Healthy lifestyle factors, including regular physical activity, healthy body composition, non-smoking, and limited alcohol intake, have been associated with the improvement of traditional cardiovascular risk factors such as systolic blood pressure and LDL cholesterol levels.[5–9] A healthy lifestyle also exerts beneficial effects on insulin sensitivity, cardiorespiratory fitness, and inflammation.[10–12] Furthermore, a healthy lifestyle is strongly related to reductions in risk of cardiovascular events, mortality, and incident T2D in apparently healthy individuals.[13] Therefore, optimizing lifestyle habits is a cornerstone in CVD and T2D prevention and a first-line recommendation in the clinical management of established CVD.[14–21]

While extensive research has explored the relationship between lifestyle factors and health outcomes in healthy populations, it is important to investigate their applicability and impact specifically within the context of CVD populations. The few available studies in CVD populations indicate potentially large benefits from lifestyle improvement, which may even exceed those observed in apparently healthy populations.[22] Lifestyle improvement in patients with CVD has been associated with the attenuation of cardiovascular risk factors such as systemic inflammation and kidney function.[23,24] However, the relationship between overall lifestyle change and risk of (cardiovascular) mortality and incident T2D has not been studied in patients with established CVD.

Predominantly, evidence on lifestyle-related health gains emerges from observational studies that primarily address individual lifestyle components. However, these components interconnect and jointly affect health, necessitating research that investigates multiple lifestyle components simultaneously.[25] Moreover, most epidemiological studies assess lifestyle behaviours only at baseline, and using such single measurements does not provide insights into the effects of changing lifestyle habits on long-term health outcomes.

The aim of the current study was to investigate the association between long-term changes in self-reported lifestyle behaviours (smoking, waist circumference, physical activity, and alcohol consumption) and risk of all-cause mortality, cardiovascular mortality, and incident T2D in patients with established CVD. Through these analyses, we aimed to enhance the knowledge about the potential benefits of changing lifestyle behaviours in this high-risk population.

Methods

Study population

The Utrecht Cardiovascular Cohort—Second Manifestations of ARTerial disease (UCC-SMART) study is an ongoing, single-centre, prospective, cohort study in the Netherlands. From 1996 onwards, patients referred to our centre for cardiovascular risk management were asked to participate in the cohort. The study was approved by the local Medical Ethics Committee, and all participants gave written informed consent. Details on the study design have been published previously.[26] From 2006 onwards, a random sample of UCC-SMART participants with either established CVD or T2D and at least 4 years of follow-up after the baseline visit has been invited for a re-assessment visit (i.e. the SMART2 visit, *Figure 1*).

For the current study, data were used from 2011 participants of the SMART2 re-assessment visit with established CVD at inclusion in the UCC-SMART cohort. The established CVD was defined as coronary artery disease, cerebrovascular disease, peripheral arterial disease, or abdominal aortic aneurysm (AAA), in accordance with the previously published definitions.[26,27] Information on cardiovascular history was based on assessments by the treating physician and self-reported medical history. For the T2D endpoint, the study population was limited to patients with CVD without prevalent diabetes (Type 1 or 2) at the SMART2 visit as these were not at risk of developing diabetes ($n = 1567$, *Figure 1*). Participants in the current study were included in the UCC-SMART study between 1996 and 2012, and the SMART2 visits took place between 2006 and 2019.

Assessment of lifestyle behaviours and other covariates

At inclusion in the UCC-SMART study and at the SMART2 visit, participants completed health questionnaires, anthropometric measurements, and laboratory testing. The health questionnaire included questions on medical history, family history, medication use, and lifestyle behaviour. Data on smoking and alcohol consumption were self-reported. Smoking status was classified as current, former, or never. Alcohol consumption was collected categorically (no alcohol, <1, 1–10, 11–20, 21–30, or >30 units/week). Leisure-time physical activity was quantified using a modified version of a validated ranking physical activity questionnaire with an additional question on sport activities.[28] Metabolic equivalent of task (MET) values were obtained from the Compendium of Physical activity[29] and used to calculate a total physical activity level per week (in METh/week) by multiplying the MET value with hours spent on physical activity per week. Waist circumference was measured twice, halfway between the lowest rib and the iliac crest while patients were wearing light clothing, and the two measurements were averaged.

Definition of healthy lifestyle and lifestyle change

To assess lifestyle change, self-reported lifestyle behaviours at the SMART2 visit were compared with those reported at the inclusion visit. The lifestyle components included in this analysis were smoking status, body composition (measured as waist circumference), leisure time physical activity, and alcohol consumption. Data on dietary habits, psychological stress, and sleep were not available.

Healthy lifestyle targets were obtained from the current guidelines for CVD management (*Table 1*). One point was awarded for each target that participants achieved; when a patient did not reach the target, no points were given. A score of 3 or 4 (i.e. 3 or 4 healthy behaviours) was defined as a healthy lifestyle. A lower score (0, 1, or 2 healthy behaviours) was deemed to be indicative of an unhealthy lifestyle. Overall lifestyle was assessed at both visits and used to classify an individual's lifestyle trajectory. Lifestyle trajectories were classified as:

(1) *Persistently healthy*: healthy lifestyle at both visits.
(2) *Improved*: unhealthy at baseline but healthy at the SMART2 visit.
(3) *Worsened:* healthy at baseline but unhealthy at the SMART2 visit.
(4) *Persistently unhealthy:* unhealthy lifestyle at both visits.

Overall lifestyle trajectory served as the main determinant in this study, and the persistently unhealthy trajectory was used as reference category. Secondary analyses with changes in the four individual lifestyle components as determinants were performed.

Outcome ascertainment

The endpoints in this study were all-cause mortality, cardiovascular death, and incident T2D. All-cause mortality comprised all deaths during follow-up.

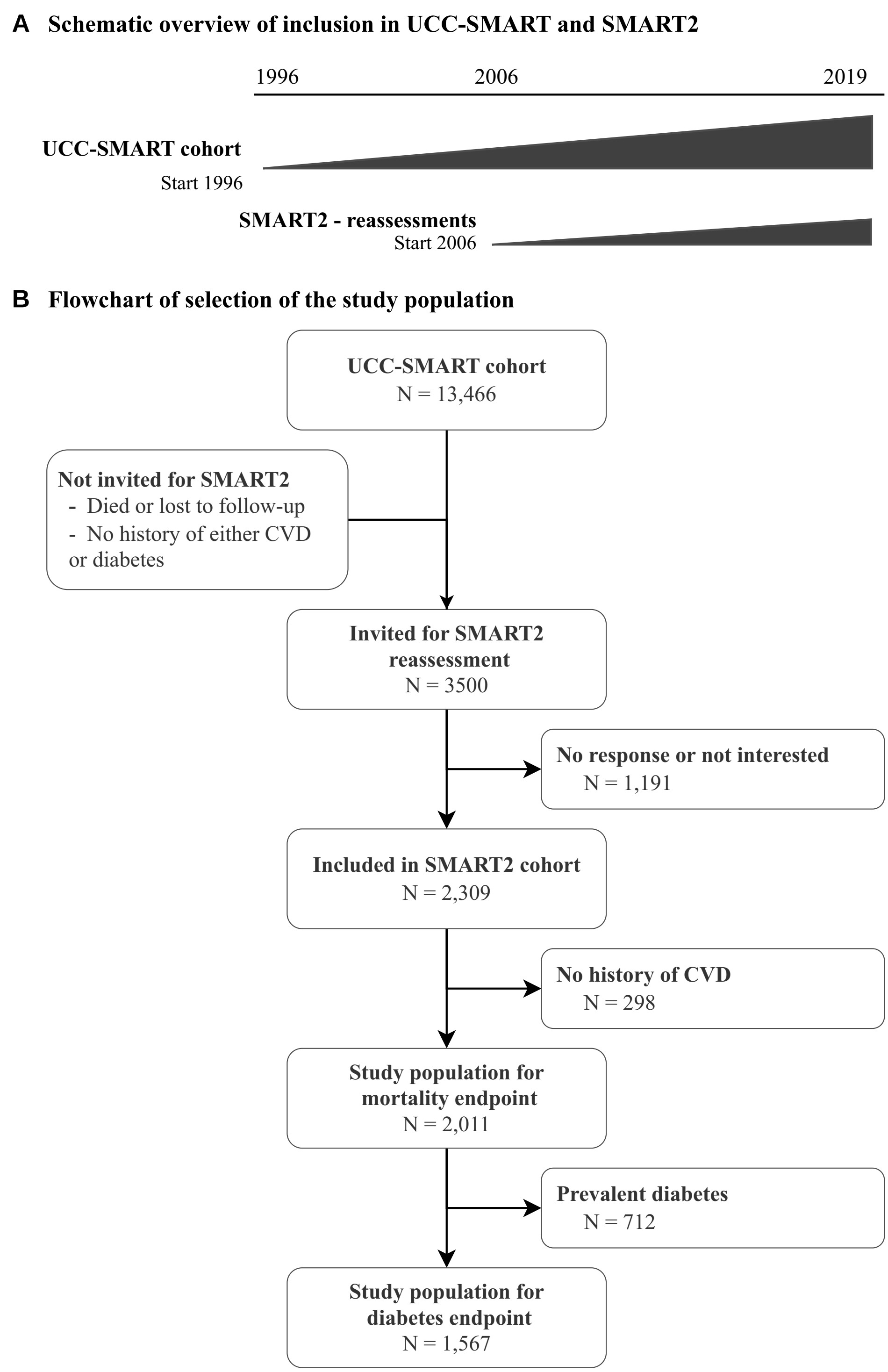

Figure 1 Schematic representation of inclusion in the UCC-SMART study and SMART2 substudy. UCC-SMART (Panel A). Flowchart of selection of the study population for the current analysis (Panel B). UCC-SMART, Utrecht Cardiovascular Cohort-Secondary Manifestations of Arterial disease; CVD, cardiovascular disease.

Cardiovascular death was defined as sudden death and death from myocardial infarction, stroke, congestive heart failure, rupture of AAA, or secondary causes after a cardiovascular event or intervention, e.g. sepsis after bypass surgery. Type 2 diabetes was defined as a new and physician-confirmed diabetes diagnosis in patients aged 35–40 years with body mass index (BMI) >33 kg/m^2 or in patients aged >40 years with BMI >27 kg/m^2.

All participants were asked to complete an annual follow-up questionnaire on vital status and occurrence of cardiovascular events. When an event was reported, the relevant medical information was obtained from the treating physician. The final categorization of the type of event was made independently by three physicians from the UCC-SMART endpoint committee.[27]

Table 1 Lifestyle goals for patients with established cardiovascular disease

Lifestyle component	Healthy behaviour	Unhealthy behaviour
Smoking	Never or former smoker	Current smoker
Body composition (*measured as waist circumference*)	Female: <88 cm Male: <102 cm	Female: ≥88 cm Male: ≥102 cm
Leisure-time physical activity	≥15 METh/week	<15 METh/week
Alcohol consumption	No alcohol or ≤10 units/week	>10 units/week

Lifestyle target levels were obtained from international guidelines for the prevention and management of cardiovascular disease.[14,15]

Data analyses

The characteristics of patients at baseline and at the SMART2 visit were described: categorical variables as absolute number (percentage) and continuous variables as mean and standard deviation or median and inter-quartile range (IQR), as appropriate. To assess comparability, the characteristics of SMART2 characteristics were compared with those of UCC-SMART participants who were not included in SMART2.

The relationships between lifestyle trajectories and (cardiovascular) death and incident T2D were quantified using the Kaplan–Meier method and Cox proportional hazard models. Time-to-event was defined as the time after an individual's final visit (i.e. the SMART2 visit) until the outcome of interest or until censoring, whichever came first. The time between the initial visit and SMART2 visit was not taken into account in the survival analyses. Person time was calculated separately for each outcome as the sum of time-to-event for all study participants.

Stepwise adjustments were made for confounders. The first model was adjusted for age and sex. The second, main model was additionally adjusted for education level. Education level was included as a measure of social-economic position, which is an important confounder in the relationship between lifestyle behaviours and health outcomes. No adjustments were made for cardiovascular risk factors such as hypertension, lipid levels, and insulin resistance because these were hypothesized to be mediators in the relationships of interest. The proportional hazard assumption was assessed using a visual inspection of Schoenfeld residuals.

All analyses were repeated for trajectories of the individual lifestyle components. These models were adjusted for change in the other lifestyle components. The relationship between the absolute change in physical activity and waist circumference and the endpoints was assessed using Cox models with restricted cubic splines (three knots). These models were adjusted for age, sex, education, change in the other three lifestyle components and baseline level of the lifestyle component of interest.

Missing data were imputed with single imputation using predictive mean matching. The main sources of missingness were education level ($n = 381$, 19%), waist circumference ($n = 255$, 13%), and LDL cholesterol ($n = 33$, 2%). For all other covariates, missingness did not exceed 1%. Physical activity measurements taken before January 2002 ($n = 662$) were replaced with imputed values, as a new questionnaire was used from this date onwards. Information from the repeated measurements was incorporated in the imputation.

All statistical analyses were performed using R statistical software, version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided P-value <0.05 was considered statistically significant.

Sensitivity analyses

Sensitivity analyses were performed to assess the impact of potential sources of bias. Reverse causation in the relation between lifestyle trajectory and (cardiovascular) death was assessed by running the Cox models after the exclusion of 1, 3, and 5 years of follow-up after the SMART2 visit and by adjusting for the occurrence of cardiovascular events between the two study visits. The impact of time between the study visits was assessed by introducing an interaction term in the models and assessing the relation between lifestyle trajectory and mortality in subgroups with an interval of less or more than 10 years between the two assessments. A sensitivity using BMI instead of waist circumference as a measure of body composition was performed with a BMI <25 kg/m^2 considered as healthy. A *minimally required change* analysis was performed where a change in the continuous lifestyle components (physical activity and waist circumference) was defined as at least 5% increase or decrease from the baseline visit. The definition of change in smoking and alcohol consumption remained the same in this analysis. Finally, a sensitivity analysis was performed where all four lifestyle behaviours were needed to classify as healthy to constitute an overall healthy lifestyle.

To explore the potential impact of healthy survivor bias on the study results, expected smoking behaviour, waist circumference, physical activity, and alcohol consumption at the second visit were imputed using multiple imputation for all participants who did not partake in SMART2. The date for the imputed SMART2 visit was set at 4 years after the inclusion visit (i.e. the minimum follow-up before patients would be eligible for participation in SMART2), and survival analyses with Cox proportional hazard models were repeated in these imputed datasets comprising 7191 patients with established CVD and 5328 participants with CVD but without diabetes and pooled according to Rubin's rules.

Results

Lifestyle trajectories

A total of 2011 patients with established CVD underwent two consecutive vascular screening visits. The majority of participants was men ($N = 1567$, 78%), and the mean age at inclusion was 57 ± 9 years. The median time between the first and the second visit was 10.0 (IQR 6.5–10.8) years. Patient characteristics at the first and second assessments are shown in Supplementary material online, *Table S1*.

The majority of patients had a healthy lifestyle (i.e. 3 or 4 healthy behaviours) at the baseline visit ($n = 1327$, 66%), and 169 participants (8% of the total population) worsened over time. The remaining 34% of participants ($n = 684$) had an unhealthy lifestyle at baseline, and of these, 336 (17%) had improved to a healthy lifestyle at the SMART2 visit (*Table 2*). Peripheral arterial disease and metabolic syndrome were relatively prevalent among patients with an unhealthy lifestyle at baseline. These patients also had higher C-reactive protein and LDL-cholesterol levels (*Table 2*).

Table 3 shows the change in individual lifestyle components and overall lifestyle between the first and the second visits. Almost half of all smokers at baseline had ceased smoking at the second visit, and very few participants had initiated smoking. On average, waist circumference increased between the two visits (women: 86 ± 11 to 91 ± 13 cm, men: 97 ± 10 to 101 ± 11 cm). Physical activity levels and alcohol consumption remained stable over time.

Lifestyle changes and risk of cardiovascular mortality, all-cause mortality, and incident Type 2 diabetes

The median follow-up time after SMART2 was 6.1 (IQR 3.6–9.6) years and ranged from 0 to 14 years. During this time, 285 deaths occurred, of which 150 were due to cardiovascular causes (*Figure 2*, see Supplementary material online, *Figure S1*). Compared with a persistently unhealthy lifestyle, patients with a persistently healthy lifestyle were at the lowest risk of all-cause mortality, cardiovascular mortality, and incident T2D (*Figure 2*). Improving lifestyle from an unhealthy to a healthy lifestyle was related to ∼50% relative risk reductions for all-cause mortality, cardiovascular mortality, and incident T2D. Patients

Table 2 Baseline characteristics stratified for lifestyle trajectories

Characteristic	Persistently healthy	Worsened	Improved	Persistently unhealthy
N	1158 (58)	169 (8)	336 (17)	348 (17)
Female sex	255 (22)	50 (30)	71 (21)	68 (20)
Age, years	58 ± 9	57 ± 9	56 ± 9	55 ± 8
Education				
Low	397 (34)	70 (41)	126 (38)	136 (39)
Middle	652 (56)	85 (50)	182 (54)	185 (53)
High	109 (9)	14 (8)	28 (8)	27 (8)
Coronary artery disease	814 (70)	112 (66)	181 (54)	184 (53)
Cerebrovascular disease	278 (24)	41 (24)	92 (27)	97 (28)
Peripheral arterial disease	128 (11)	32 (19)	76 (23)	94 (27)
Abdominal aortic aneurysm	52 (5)	8 (5)	22 (7)	26 (8)
Diabetes	142 (12)	28 (17)	40 (12)	47 (14)
Metabolic syndrome	439 (38)	85 (50)	217 (65)	235 (68)
Smoking				
Never	357 (31)	24 (14)	23 (7)	18 (5)
Former	669 (58)	109 (65)	116 (35)	97 (28)
Current	132 (11)	36 (21)	197 (59)	233 (67)
Alcohol intake, units/week				
0	187 (16)	20 (14)	47 (11)	23 (7)
<1	130 (11)	13 (7)	22 (8)	23 (7)
1–10	654 (56)	84 (25)	85 (50)	58 (17)
>10	187 (16)	52 (54)	182 (31)	244 (70)
BMI, kg/m^2	26 ± 3.1	26.8 ± 3.2	27.6 ± 4.2	28.5 ± 4.1
Waist circumference, cm	F: 83 ± 10	F: 86 ± 8	F: 91 ± 13	F: 94 ± 12
	M: 94 ± 8	M: 99 ± 8	M: 100 ± 10	M: 103 ± 11
Systolic BP, mmHg	139 ± 20	140 ± 22	139 ± 20	140 ± 19
Diastolic BP, mmHg	82 ± 11	81 ± 12	81 ± 11	83 ± 10
Total cholesterol, mmol/L	4.6 (4.0–5.5)	4.9 (4.1–5.6)	5.1 (4.4–5.9)	5.2 (4.4–5.9)
LDL-cholesterol, mmol/L	2.6 (2.1–3.4)	2.8 (2.3–3.4)	3.1 (2.5–3.8)	3.1 (2.4–3.8)
HDL-cholesterol, mmol/L	1.2 (1.0–1.5)	1.2 (1.0–1.4)	1.1 (0.9–1.4)	1.1 (0.9–1.4)
eGFR, mL/min	78 ± 15	77 ± 17	80 ± 16	82 ± 15
CRP, mg/L	1.4 (0.7–3.0)	2.1 (1.0–4.7)	2.4 (1.2–4.8)	2.6 (1.3–5.2)
Physical activity, METh/week	43 (25–69)	35 (19–55)	12 (5–34)	18 (7–41)

CAD, coronary artery disease; CeVD, cerebrovascular disease; PAD, peripheral arterial disease; AAA, abdominal aortic aneurysm; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein.

Table 3 Change in lifestyle components between baseline and SMART2 visits

	Persistently healthy	Worsened	Improved	Persistently unhealthy
Smoking	1358 (68)	55 (3)	301 (15)	297 (15)
Waist circumference	1054 (52)	385 (19)	88 (4)	484 (24)
Physical activity	1374 (68)	154 (8)	375 (18)	108 (5)
Alcohol consumption	1231 (61)	115 (6)	239 (12)	426 (21)
Overall lifestyle score	599 (29)	728 (36)	559 (28)	125 (6)

Number of patients who were persistently healthy, improved, worsened, or persistently unhealthy per lifestyle component and overall lifestyle.

with a worsened lifestyle had a lower risk of all-cause and cardiovascular mortality, but not of incident T2D.

Of the four lifestyle components, smoking (non-smoking or smoking cessation) and physical activity (persistently healthy or improved levels) were most strongly associated with risk reductions for all-cause mortality and cardiovascular mortality (*Figure 3*). Changes in waist circumference were not related to all-cause mortality and cardiovascular mortality risk. For incident T2D, the strongest association was found for a

Lifestyle trajectory	Events/N	Follow−up (pers.yr)	Hazard ratio (95%CI)
All−cause mortality			
Persistently healthy	171/1,155	7,222	0.48 (0.36−0.63)
Worsened	32/169	1,114	0.67 (0.44−1.01)
Improved	54/336	2,524	0.52 (0.37−0.74)
Persistently unhealthy	82/348	7,223	*Reference*
Cardiovascular mortality			
Persistently healthy	84/1,155	7,222	0.57 (0.38−0.87)
Worsened	14/169	1,114	0.74 (0.39−1.40)
Improved	19/336	2,524	0.46 (0.26−0.81)
Persistently unhealthy	33/348	7,223	*Reference*
Incident type 2 diabetes			
Persistently healthy	44/933	5,334	0.46 (0.28−0.73)
Worsened	10/124	749	0.75 (0.37−1.55)
Improved	16/254	1,733	0.50 (0.27−0.92)
Persistently unhealthy	29/252	1,563	*Reference*

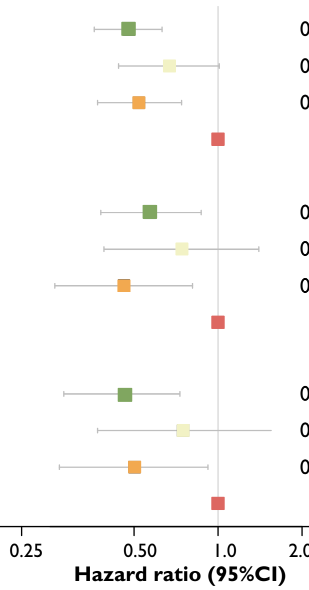

Figure 2 Risk of all-cause mortality, cardiovascular mortality, and incident Type 2 diabetes for a different lifestyle trajectory. Hazard ratio for all-cause mortality and cardiovascular mortality compared with a persistently unhealthy lifestyle. Hazard ratios were adjusted for age, sex, and education level. Follow-up time in person years after the SMART2 study visit. HR, hazard ratio; 95% CI, 95% confidence interval.

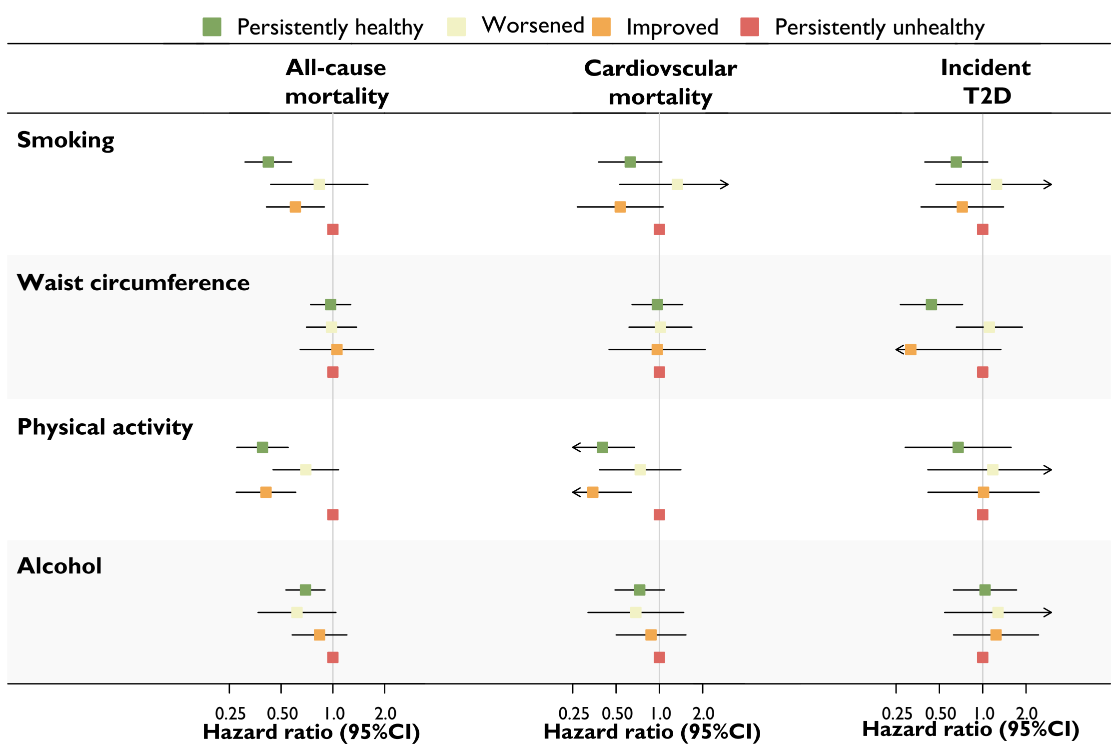

Figure 3 Risk of all-cause mortality, cardiovascular mortality, and incident Type 2 diabetes in relation to changes in individual lifestyle component. Hazard ratio for changes in the four individual lifestyles compared with a persistently unhealthy behaviour. Hazard ratios were adjusted for age, sex, and education level. Follow-up time in person years after the SMART2 study visit. HR, hazard ratio; 95% CI, 95% confidence interval.

persistently healthy and improved waist circumference (*Figure 3*). No statistically significant relationship with the three other lifestyle components was observed. These findings were supported by an analysis using changes in physical activity level and waist circumference as continuous variables (see Supplementary material online, *Figure S2*).

Sensitivity analyses

Characteristics and lifestyle behaviour at baseline were comparable between participants who did and did not partake in the SMART2 visit, although SMART2 participants were younger (mean age 57 vs. 61 years) and had lower education levels compared with non-participants. When an overall healthy lifestyle was defined as the presence of four of four healthy behaviours instead of three of four, the results for a persistently healthy lifestyle were somewhat attenuated compared with the main analysis (see Supplementary material online, *Figure S3*). The analyses in datasets with imputed values for lifestyle change in non-SMART2 participants yielded similar results for a persistently healthy lifestyle compared with the main analysis but resulted in a stronger beneficial relation for a reduced lifestyle trajectory (see Supplementary material online, *Figure S4*). In this sensitivity analysis, no protective relationship was observed for an improved lifestyle (see Supplementary material online, *Figure S4*).

In a sensitivity analysis requiring a minimal 5% change from baseline, the size and direction of the effect estimates were similar to the main analysis (see Supplementary material online, *Figure S5*). In analyses exploring potential reverse causation by excluding the first 1, 3, and 5 years of follow-up, the associations between lifestyle trajectory and all-cause and cardiovascular mortality were similar in size and direction compared with the main analysis (see Supplementary material online, *Figure S6*). However, for incident T2D, the association was attenuated or even reversed (see Supplementary material online, *Figure S6*). Additional adjustment for the occurrence of cardiovascular events between the first and the second assessments as a source of reverse causation yielded near identical effect estimates to the main analysis, as well as additional adjustment for the time between inclusion and the SMART2 visit. Using BMI as a measure of body composition yielded the same results as when waist circumference was used.

Discussion

In a cohort of patients with established CVD and repeated lifestyle assessments, maintaining a persistently healthy lifestyle or transitioning from an unhealthy to a healthy lifestyle over time was linked to a nearly 50% decrease in all-cause mortality, cardiovascular mortality, and incident T2D, compared with those with a persistently unhealthy lifestyle. The findings suggest that even after CVD manifestation, maintaining or adopting a healthy lifestyle can reduce residual cardiovascular risk.

These study findings align with previous research. Similar reductions in the risk of coronary calcification, cardiovascular events, and (cardiovascular) mortality were observed in primary CVD prevention cohorts evaluating multiple lifestyle behaviours.[13,21,30–32] An analysis of the UK Biobank demonstrated that maintaining an unhealthy lifestyle over time correlated with almost twice the risk of ischaemic heart disease, while lifestyle improvements were protective, regardless of baseline lifestyle behaviours.[13] In the current study, these relationships with CVD outcomes appear to hold true in a secondary CVD prevention population, despite differences in baseline risk, concomitant medications, and morbidity. This conclusion continues upon a previous European-wide survey that showed that CVD patients with poor compliance with lifestyle recommendations had higher CVD risk factor levels.[33,34] Furthermore, increasing physical activity levels has been associated with 50% relative risk reductions in coronary artery patients.[35] To our knowledge, the relationship between combined lifestyle changes and incident T2D has never been assessed in an established CVD population, but findings in the present study are in line with previous observations that a healthy lifestyle has the potential to significantly improve cardio-metabolic risk factors.[33]

Patients with initially healthy lifestyles that declined over time still showed survival benefits compared with persistently unhealthy patients. Similar patterns were noted in earlier studies evaluating lifestyle changes over time. In the UK Biobank, people with declining lifestyle habits had similar cardiovascular event rates compared with those who were able to maintain a healthy lifestyle.[13] This suggests that the benefits of a healthy lifestyle endure over time. This hypothesis is reinforced by findings from multiple imputed analyses in the current study, which indicated a protective relationship with all outcomes for a worsened lifestyle trajectory, potentially explained by the after-effects of the initial healthy lifestyle. However, this does not mean that patients with a healthy lifestyle should not be motivated to maintain that lifestyle, because the largest protective relationships are found for people with a persistent healthy lifestyle. Patients with declining lifestyle habits should be counselled to resume their healthy lifestyle habits, especially sufficient physical activity and not smoking.

Most CVD patients in this study reported being compliant with guideline-recommended lifestyle behaviours and were able to maintain their healthy lifestyle over a period of ∼10 years. This high adherence rate is consistent with, or even exceeds, adherence rates reported in previous research about compliance with guideline recommendations in secondary prevention of CVD.[33,36–38]

This study is among the first to jointly assess the relation of changes in multiple lifestyle components with clinical outcomes because previous studies primarily focused on change in individual components.[35,38–40] This approach allows for direct comparison between components and aids in prioritization of specific lifestyle changes. Not smoking and high physical activity showed the strongest links to all-cause and cardiovascular mortality, while a healthy waist circumference was more closely tied to lower incident T2D risk.

Strengths and limitations

The strengths of the current study include the large cohort size, the repeated assessment of lifestyle behaviours, and the long follow-up duration. Study limitations need to be considered. Data on alcohol consumption were collected categorically and could therefore not be analysed continuously. In the current analysis, lifestyle was limited to smoking, waist circumference, physical activity, and alcohol consumption and did not include other lifestyle factors such as diet, sleep, and stress, potentially resulting in an under-estimation of the relationship between lifestyle changes and clinical outcomes. To assess overall lifestyle, a healthy lifestyle was defined as having a score of 3 of 4 for healthy behaviours. However, this approach led to a counterintuitive finding wherein 132 participants categorized as having a 'healthy' lifestyle were identified as current smokers. Relatively few outcomes occurred in the worsened and improved groups due to the smaller size of these groups, which resulted in wide confidence intervals. Although lifestyle was assessed at two separate time points, there was no information available on changes between the two measurements. Further limitations include that lifestyle behaviours were self-reported, meaning that they are subject to misclassification and social desirability bias. However, as lifestyle behaviours were compared within individuals, the impact of these potential biases will likely be small. Residual confounding may bias the results, e.g. from social-economic position, which was only evaluated based on education in the UCC-SMART study. Evaluating lifestyle changes over time inherently introduces healthy survivor bias, because only patients who survive until the second assessment can be included. Sensitivity analyses showed that the size and direction of the observed relations were not modified by the interval between the first and second visits, which implies that the effects of healthy survivor bias are small. For the T2D endpoint, associations with lifestyle change attenuated or even reversed when the first 1, 3, or 5 years of follow-up were excluded. This may be due to limited power for these analyses or reverse causation could have biased these findings. Therefore, some caution should be taken in extending the association with T2D to a longer follow-up time.

This study illustrates that in CVD patients, a persistently healthy and improved lifestyle were associated with a lower risk of (cardiovascular) mortality and incident T2D compared with persistently unhealthy patients. The largest benefit was observed for patients who were able to maintain a healthy lifestyle over time. However, the study also reveals encouraging findings for individuals with an unhealthy lifestyle that change to a healthy lifestyle, indicating that it is never too late to improve their prognosis after CVD has manifested. A non-smoking status and healthy level of physical activity were the main drivers of lifestyle-related mortality risk reductions, while a low waist circumference was most important to prevent T2D. Conversely, patients with an unhealthy lifestyle over time faced a relatively high risk of cardiovascular mortality and incident T2D, underscoring the importance of addressing lifestyle habits in CVD management.

Conclusions

This study assessed the relationship between self-reported changes in lifestyle behaviour and (cardiovascular) mortality and T2D. The findings emphasize the pressing need for ongoing attention for maintaining or adopting a healthy lifestyle within the clinical management of CVD patients. By incorporating lifestyle interventions into their treatment plans, healthcare providers can potentially mitigate the risk of cardiovascular mortality and T2D for their patients. Ultimately, these findings underscore the profound impact that lifestyle choices can have on the outcomes and overall well-being of CVD patients.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

Acknowledgements

We gratefully acknowledge the contribution of the participants, the research nurses, R.B. van Petersen (data manager), Angela Vandersteen (study manager), and the members of the UCC-SMART Study Group: M.J. Cramer, H.M. Nathoe, and M.G. van de Meer (co-PI), Department of Cardiology; G.J. de Borst and M.Teraa (co-PI), Department of Vascular Surgery; M.L. Bots and M. van Smeden, Julius Center for Health Sciences and Primary Care; M.H. Emmelot-Vonk, Department of Geriatrics; P.A. de Jong, Department of Radiology; A.T. Lely, Department of Gynaecology and Obstetrics; N.P. van der Kaaij, Department of Cardiothoracic Surgery; L.J. Kappelle and Y.M. Ruigrok, Department of Neurology; M.C. Verhaar, Department of Nephrology and Hypertension; and J.A.N. Dorresteijn (co-PI) and F.L.J. Visseren (PI), Department of Vascular Medicine, UMC Utrecht.

Author contributions

N.E.B.: conceptualization, formal analysis, writing—original draft. F.L.J.V.: conceptualization, supervision, funding acquisition, writing—review and editing. M.J.C., J.A.N.D., M.G.v.d.M., Y.M.R., T.T.v.S., and M.T.: writing—review and editing. J.M.G.: supervision, funding acquisition, writing—review and editing. C.K.: conceptualization, supervision, writing—review and editing.

Funding

The research presented in this paper was supported by a grant from the Regio Deal Foodvalley (162135). The funding sources had no role in the study design and conduct, data analysis, or manuscript preparation.

Conflict of interest: none declared.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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