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The combined impact of adherence to five lifestyle factors on all-cause, cancer and cardiovascular mortality: a prospective cohort study among Danish men and women

Kristina E. N. Petersen[1]*, Nina F. Johnsen[1], Anja Olsen[1], Vanna Albieri[1], Lise K. H. Olsen[1], Lars O. Dragsted[2], Kim Overvad[3,4], Anne Tjønneland[1] and Rikke Egeberg[1]

[1]*Danish Cancer Society Research Center, Strandboulevarden 49, 2100 Copenhagen Ø, Denmark*
[2]*Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark*
[3]*Section of Epidemiology, Department of Public Health, Aarhus University, Aarhus, Denmark*
[4]*Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark*

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Abstract

Individual lifestyle factors have been associated with lifestyle diseases and premature mortality by an accumulating body of evidence. The impact of a combination of lifestyle factors on mortality has been investigated in several studies, but few have applied a simple index taking national guidelines into account. The objective of the present prospective cohort study was to investigate the combined impact of adherence to five lifestyle factors (smoking, alcohol intake, physical activity, waist circumference and diet) on all-cause, cancer and cardiovascular mortality based on international and national health recommendations. A Cox proportional hazards model was used to estimate hazard ratios (HR) with 95% CI. During a median follow-up of 14 years, 3941 men and 2827 women died. Among men, adherence to one additional health recommendation was associated with an adjusted HR of 0·73 (95% CI 0·71, 0·75) for all-cause mortality, 0·74 (95% CI 0·71, 0·78) for cancer mortality and 0·70 (95% CI 0·65, 0·75) for cardiovascular mortality. Among women, the corresponding HR was 0·72 (95% CI 0·70, 0·75) for all-cause mortality, 0·76 (95% CI 0·73, 0·80) for cancer mortality and 0·63 (95% CI 0·57, 0·70) for cardiovascular mortality. In the present study, adherence to merely one additional health recommendation had a protective effect on mortality risk, indicating a huge potential in enhancing healthy lifestyle behaviours of the population.

Key words: **Lifestyle factors: Mortality: Public health: Recommendations**

To improve public health and implement targeted efforts, it is necessary to acquire knowledge about health risk factors and quantify their influence on public health. The simplest and most objective measure of a population's health status is overall mortality. Tobacco smoking[1–3], alcohol consumption[4,5], physical inactivity[6–8], adiposity[9,10] and an unhealthy diet[11–17] are all modifiable lifestyle factors that by an accumulating body of evidence have been associated with a higher risk of developing lifestyle diseases and premature mortality. Among the leading causes of death worldwide are cancers and CVD[18]. Although these diseases are highly preventable, approximately 60% of all deaths are attributed to cancers and CVD in Denmark[19]. Multiple lifestyle behaviours coexist and may interact, and the underlying causes of death are probably multicausal of nature. Thus, studying the combined impact of lifestyle factors instead of their individual impact on health outcomes is highly relevant. Public health recommendations for the most important risk factors have been developed by many organisations and countries[20–22]. Applying a simple lifestyle index based on international and national lifestyle recommendations is useful for decision-makers and political governments and for counselling purposes, and may motivate subjects to change their lifestyle in a healthier direction – particularly if the message is simple.

Recently, the combined impact of healthy lifestyle behaviours on all-cause mortality has been examined in a meta-analysis of results from fifteen prospective cohort studies[23]. An inverse association was found between the number of healthy lifestyle factors adhered to and the risk of premature death. However, statistical heterogeneity in the meta-analysis was high[23], probably reflecting the variety of lifestyle indices applied as well as differences between study populations. Lifestyles differ across countries, even within the European populations[24,25]. For instance, the Nordic diet is characterised by its high content of whole grains compared with other

Abbreviation: HR, hazard ratio.

* **Corresponding author:** K. E. N. Petersen, fax +45 3527 1811, email kripet@cancer.dk

Western countries[26–29]. A higher whole grain intake has been associated with a lower risk of weight gain[30], type 2 diabetes[28,30], CVD[31] and colorectal cancer[32,33]. Studies examining the association between lifestyle factors and mortality risk were primarily conducted in the USA, the UK or the Asian region. To our knowledge, no study has investigated the association between a healthy lifestyle and mortality in a large population of exclusively Scandinavians.

The objective of the present study was to examine the association of a simple lifestyle index combining international and national health recommendations for smoking, alcohol consumption, physical activity, waist circumference and diet with all-cause, cancer and cardiovascular mortality in middle-aged men and women participating in the Danish Diet, Cancer and Health cohort study.

Methods

Study population

The Diet, Cancer and Health study is a prospective cohort study established with the primary aim of studying the aetiological role of diet in cancer development, but with the potential of studying other diseases as well[34]. From December 1993 to May 1997, all men and women living in the greater Copenhagen and Aarhus areas were invited to participate in the study if they were 50–64 years of age, born in Denmark, and not registered with a previous cancer diagnosis in the Danish Cancer Registry[35,36]. In total, 80 996 men and 79 729 women were identified by a unique ten-digit personal identification number that is assigned to every Danish citizen by the Central Population Registry[37]. Of the invited subjects, 27 178 men and 29 875 women were enrolled into the cohort corresponding to 35 % of those invited and 7 % of the entire Danish population aged 50–64 years. The cohort has been described in detail previously[34].

Data collection

Participants completed a semi-quantitative 192-item FFQ received by mail before the visit to one of the two study centres in Copenhagen and Aarhus. Development and validation of the FFQ have been described in previous studies[38–40]. Dietary intake was assessed in twelve predefined categories ranging from 'never' to 'eight times or more per d', and participants were asked to report their average intake over the past year. Daily intake of specific foods and nutrients was calculated by the software program FoodCalc[41] using specially developed sex-specific standardised recipes and portion sizes.

All participants completed a lifestyle questionnaire that provided information about health status, social factors, reproductive factors and lifestyle habits. Anthropometric measures were collected by trained personnel. The questionnaires were optically scanned and checked for missing values and nonsense. In the lifestyle questionnaire, a few missing values were accepted, whereas the FFQ was accepted only if all questions were answered[34].

Exposure assessment

Participants were divided into never, former and current smokers. Former smokers were asked about the age at which they stopped smoking in order to divide subjects according to years since quitting. The level of physical activity was assessed by questions covering the average number of hours per week spent in the past year on physical activity in leisure time during summer and winter, respectively, which then were averaged. Leisure-time physical activities included sports (e.g. jogging, exercising and swimming) and cycling, which is a common means of transportation in Denmark. The selected activities were presumed to be of moderate or high intensity, corresponding to the National recommendations, although it is recognised that this intensity might not always be achieved for cycling. Waist circumference was measured at the natural waist (smallest horizontal circumference between the ribs and the iliac crest) or, if the waist narrowing was indeterminable, halfway between the lower rib and the iliac crest. Participants were wearing light underwear and the circumference was measured to the nearest half centimetre. The 192-item FFQ was used to measure the intake of alcohol and dietary components. Alcohol intake was assessed by questions covering the frequency of consumption of specific beverages, and calculated by summing the products of the frequency by their ethanol content. Intake of red meat and processed meat was calculated based on questions concerning the intake of pork, veal, beef, and lamb eaten fresh, processed and in hot meals. The intake of fish was obtained by questions covering different varieties of fish eaten fresh, processed and in hot meals. Fruit and vegetable consumption was assessed by questions about different types of fruits and vegetables consumed fresh, as juices, as accompaniment, in hot meals, open sandwiches and in desserts. Whole grain intake was estimated based on the whole grain content of whole-grain products such as breakfast cereals, bread, crisp bread, rice, flour, biscuits and cakes. The definition of whole grain was in accordance with the definition of the American Association of Cereal Chemists[42]. Energy percentage from fat was calculated based on standardised recipes and portion sizes of foods containing fat as well as fat spread on bread. In the calculations of total energy percentage, alcohol consumption was included. Exposure to potential confounding factors was obtained by questions covered in the lifestyle questionnaire for length of education, use of non-steroid anti-inflammatory drugs, and, among women, use of hormone replacement therapy. For civil status, information was acquired by linkage to the Central Population Registry[37].

Construction of the lifestyle index

Factors included in the lifestyle index were chosen *a priori* based on knowledge about lifestyle factors affecting health and based on national and international recommendations. Lifestyle factors included smoking, alcohol consumption, physical activity, waist circumference and diet. Smoking was dichotomised in accordance with the recommendations

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from the WHO that emphasises the importance of not smoking and urges smoking cessation[43]. Former smokers were grouped with non-smokers if they quit smoking ≥15 years ago and with smokers if they had quit smoking <15 years ago. Based on suggestions from the World Health Organization[44] and in accordance with the Danish Health and Medicines Authority, a waist circumference of ≥88 cm for women and ≥102 cm for men was used to define abdominal fatness. The dichotomisation of alcohol consumption frequency was in accordance with the guidelines from the World Cancer Research Fund[20] and the Nordic Nutrition Recommendations[45] advising to consume no more than two drinks per d for men and no more than one drink per d for women. Likewise, being physical active for at least 30 min/d at moderate intensity was set as the cut-off following the guidelines from the World Cancer Research Fund[20] and the Nordic Nutrition Recommendations[45]. The measure of diet consisted of five dietary components reflecting dietary pattern and included energy percentage from fat, red and processed meat, fish, whole grain, and fruits and vegetables. These factors are quantifiable recommendations included in the Danish Dietary Recommendations. Energy percentage from fat was dichotomised based on a total fat intake of 25–30 % being recommended for the Scandinavian populations[45]. The intake of red and processed meat was dichotomised based on the guidelines of the World Cancer Research Fund recommending to consume <500 g/week of red meat and limiting the amount of processed meat[20], a recommendation recently adopted by Danish health authorities. The intakes of fish, whole grain, and fruits and vegetables were dichotomised based on the Danish Dietary Recommendations advising to consume 200–300 g/week of fish[46], at least 75 g whole grain/10 MJ per d[27], and 600 g/d of fruits and vegetables[47]. Of the 600 g/d intake of fruits and vegetables, 100 g are allowed to be consumed as fruit and vegetable juice[47]. Hence, subjects who consumed 500 g/d of fruits and vegetables and additionally 100 g of juice or more were defined as adhering to the recommendation.

Table 1 presents the recommended levels and score allocation of the lifestyle index. If subjects adhered to a recommendation at baseline, 1 point was assigned. No point was assigned for non-adherence. For the diet factor, 1 point was assigned for adherence to at least two out of the five dietary components considered. All the five lifestyle factors contributed equally to the score. The lifestyle index ranged from 0 to 5, where compliance with all recommendations resulted in 5 points.

Case ascertainment and follow-up

Information on vital status and emigration was obtained by linkage to the Central Population Registry[37]. Each cohort member was followed from the date of entry (first visit at the study centre) until the date of event or the date of censoring, whichever came first. Events were all-cause, cancer and cardiovascular mortality, and the end of the follow-up was 31 December 2010. During the follow-up, 384 subjects (0·7 %) were lost. For all-cause mortality, dates of censoring were the date of emigration or the end of the follow-up. For cancer mortality, dates of censoring were the date of death from other causes than cancer, the date of emigration or the end of the follow-up. Likewise, for cardiovascular mortality, dates of censoring were the date of death from other causes than CVD, the date of emigration or the end of the follow-up.

Table 1. Baseline characteristics of potential confounding factors, score allocation and adherence to the five lifestyle factors included in the lifestyle index and to the five dietary factors included in the diet factor for men and women participating in the Diet, Cancer and Health cohort study

(Number of participants and percentages; median values and 5th–95th percentiles)

	Men		Women	
	n	%	*n*	%
Population characteristics	24 265	47	27 256	53
Age (years)				
Median	55		56	
5th–95th percentile	50–64		50–64	
Education*				
No vocational	2287	9	5101	19
Short (<3 years)	3159	13	8418	31
Medium (3–4 years)	10 405	43	10 641	39
Long (>4 years)	8414	35	3096	11
Civil status				
Deceased spouse/partner	5259	2	2256	8
Divorced/annulment of civil partnership	306	14	5152	19
Married/civil partnership	18 815	78	18 006	66
Unmarried	1366	6	1686	6
Unknown	253	1	157	1
Lifestyle recommendations (index score)				
Smoking				
Smokers† (0)	13 557	56	11 852	43
Non-smokers‡ (1)	10 708	44	15 404	57
Alcohol consumption				
w/m: >7/14 units/week (0)	10 304	42	10 755	39
w/m: ≤7/14 units/week (1)	13 961	58	16 501	61
Physical activity§				
< 30 min/d (0)	14 977	62	16 052	59
≥ 30 min/d (1)	9288	38	11 204	41
Waist circumference				
w/m: >88/102 cm (0)	5323	22	6600	24
w/m: ≤88/102 cm (1)	18 942	78	20 656	76
Diet				
0–1 points (0)	18 470	76	15 557	57
≥ 2 points (1)	5795	24	11 699	43
Dietary components included in the diet factor				
Fat				
> 30 E% (0)	18 385	76	18 063	66
≤ 30 E% (1)	5880	24	9193	34
Red and processed meat				
> 500 g/week (0)	22 756	94	17 732	65
≤ 500 g/week (1)	1509	6	9524	35
Fish				
< 250 g/week (0)	9564	39	13 891	51
≥ 250 g/week (1)	14 701	61	13 365	49
Whole grain				
< 75 g/10 MJ/d (0)	22 851	94	24 803	91
≥ 75 g/10 MJ/d (1)	1414	6	2453	9
Fruits and vegetables‖				
< 600 g/d (0)	22 060	91	22 190	81
≥ 600 g/d (1)	2205	9	5066	19

w/m, Women/men; E%, percentage of energy.
* Higher education after primary school.
† Including former smokers who stopped smoking <15 years ago.
‡ Including former smokers who stopped smoking ≥15 years ago.
§ Moderate and high intensity.
‖ Including juices (maximum 100 g).

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Information about the underlying cause of death was obtained by linkage to the Register of Causes of Death[48] using the personal identification number. Cause of death was coded by personnel of the National Board of Health or by the physician, who verified the death, according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10)[48,49]. Deaths from cancer included ICD-10 codes C00 to 97 and D00 to D09. Deaths from CVD included ICD-10 codes I10 to I25, I27 to I52, I60 to I64, and I70 to I79.

Exclusions

Of the 57 053 subjects enrolled into the cohort, a total of 3173 men and women were excluded due to a diagnosis of cancer (*n* 572), CVD (*n* 1544) or diabetes (*n* 1057) before baseline. Information about these diseases was obtained using the personal identification number, and by cross-linking to the Danish Cancer Registry[35,36], the Danish National Patient Register[50] and the Danish National Diabetes Register[51]. In addition, 2359 subjects were excluded due to either missing data on exposure variables (*n* 905) or potential confounding factors (*n* 1454), leaving 51 521 participants (24 265 men and 27 256 women) for further analysis.

Statistical analyses

The associations between the lifestyle index and mortality rates were analysed based on the Cox proportional hazards model. Death from cancer and CVD, respectively, was entered into a competing risk model. Age was used as the underlying time scale to ensure that the estimation procedure was based on the comparison of individuals of the same age, thereby taking confounding by age into account. Time under study was included as a time-dependent variable and modelled by a linear spline with boundaries placed 1, 2 and 3 years after entry into the study cohort to allow different underlying hazards in the first years of follow-up. The assumption of proportional hazards was evaluated graphically; the assumption was not violated.

Exposure was entered into the model continuously and categorically with the least healthy group as the reference. Due to few participants meeting all the five recommendations, the groups with 4 and 5 points were pooled. Men and women were analysed separately. All models were analysed unadjusted and adjusted for potential confounding factors, which included civil status (deceased spouse/partner, divorced/annulment of civil partnership, married/civil partnership, unmarried and unknown) and length of education (education after primary school: no vocational, short (<3 years), medium (3–4 years) and long (>4 years)). Models were additionally evaluated after adjustment for use of non-steroid anti-inflammatory drugs (≥ 2 tablets per month, yes/no) and use of hormone replacement therapy among women (never, past and current); however, estimates were almost unaffected, and results are not shown. Linear trends reflect *P* values from the model with the continuous lifestyle index.

Two-sided 95 % CI for the hazard ratios (HR) were calculated based on Wald's test of the Cox regression parameter. Statistical analyses were performed with the SAS statistical software (version 9.2; SAS Institute, Inc.) on a Windows platform using the PHREG procedure.

Results

A total of 6768 eligible participants (3941 men and 2827 women) died during a median follow-up period of 14 years (range 10 d–16 years). Of these, 43 % (*n* 1962) of men and 51 % (*n* 1437) of women died due to cancer, and 20 % (*n* 793) of men and 12 % (*n* 1788) of women died due to CVD.

Table 1 summarises the baseline characteristics of potential confounding factors as well as the proportion of men and women who adhered to the recommendations included in the lifestyle index. Slightly more women (53 %) than men (47 %) participated in the study. The median age (5th–95th percentile) was 55 (50–64) years among men and 56 (50–64) years among women. The length of education was medium or long for 50 % of women and 78 % of men. The majority of men and women were married or registered as being in a partnership. Women were more likely than men to comply with the five individual recommendations except for the recommendation for waist circumference.

The baseline characteristics of the participants for lifestyle factors and potential confounding factors according to the lifestyle index score are presented in online Supplementary Tables S1 and S2. Among men, 3 % (*n* 802) scored 0 points, 18 % (*n* 4306) scored 1 point, 33 % (*n* 8026) scored 2 points, 29 % (*n* 6966) scored 3 points, and 17 % (*n* 4165) scored 4 or 5 points. Among women, 1 % (*n* 403) scored 0 points, 12 % (*n* 3250) scored 1 point, 28 % (*n* 7671) scored 2 points, 32 % (*n* 8629) scored 3 points, and 27 % (*n* 7303) scored 4 or 5 points. Men and women with the highest score were more likely to have a medium or long education. Men with the highest score were also more likely to be married or in a civil partnership compared with men with the lowest score.

Table 2 presents the all-cause and cause-specific HR associated with the lifestyle index score. In an adjusted linear model, a 1-point higher lifestyle index score was associated with a HR of 0·73 (95 % CI 0·71, 0·75) for all-cause mortality, 0·74 (95 % CI 0·71, 0·78) for cancer mortality and 0·70 (95 % CI 0·65, 0·75) for cardiovascular mortality among men. Among women, a 1-point higher lifestyle index score was associated with a HR of 0·72 (95 % CI 0·70, 0·75) for all-cause mortality, 0·76 (95 % CI 0·73, 0·80) for cancer mortality and 0·63 (95 % CI 0·57, 0·70) for cardiovascular mortality. When the lifestyle index was evaluated as a categorical variable, the risk of all-cause mortality was significantly lower across all the index categories compared with 0 scores among men and women, except for a score of 1 among women. The HR for all-cause mortality in individuals scoring 4–5 points in the index compared with individuals with a score of 0 was 0·29 (95 % CI 0·25, 0·34) among men and 0·32 (95 % CI 0·25, 0·41) among women. For men scoring 4–5 points in the index compared with men with a score of 0, HR were 0·33 (95 % CI 0·26, 0·42) for cancer mortality and 0·20 (95 % CI 0·14, 0·29) for cardiovascular mortality. Women scoring 4–5 points in the index had a HR of 0·41 (95 % CI 0·29, 0·58) for cancer mortality and 0·21 (95 % CI 0·11, 0·41) for cardiovascular

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Table 2. Associations between a healthy lifestyle index and all-cause, cancer and cardiovascular mortality among men and women participating in the Diet, Cancer and Health cohort study

(Hazard ratios (HR) and 95 % confidence intervals)

	Men (*n* 24 265)					Women (*n* 27 256)				
		Crude*		Adjusted†			Crude*		Adjusted†	
Index score	Deceased (*n*)	HR	95 % CI	HR	95 % CI	Deceased (*n*)	HR	95 % CI	HR	95 % CI
All-cause mortality										
Linear	3941	0·72	0·70, 0·74	0·73	0·71, 0·75	2827	0·72	0·69, 0·74	0·72	0·70, 0·75
Categories										
0	244	1·00	Reference	1·00	Reference	79	1·00	Reference	1·00	Reference
1	995	0·71	0·62, 0·81	0·72	0·62, 0·82	548	0·85	0·67, 1·07	0·84	0·67, 1·07
2	1438	0·54	0·47, 0·61	0·54	0·48, 0·62	989	0·63	0·50, 0·79	0·63	0·50, 0·80
3	871	0·36	0·31, 0·42	0·38	0·33, 0·43	727	0·41	0·32, 0·51	0·41	0·33, 0·52
4–5	393	0·27	0·23, 0·32	0·29	0·25, 0·34	484	0·32	0·25, 0·40	0·32	0·25, 0·41
P_{trend}			< 0·001		< 0·001			< 0·001		< 0·001
Cancer mortality										
Linear	1692	0·74	0·70, 0·77	0·74	0·71, 0·78	1437	0·76	0·72, 0·80	0·76	0·73, 0·80
Categories										
0	98	1·00	Reference	1·00	Reference	35	1·00	Reference	1·00	Reference
1	421	0·75	0·60, 0·93	0·75	0·60, 0·94	252	0·88	0·62, 1·25	0·88	0·62, 1·25
2	628	0·58	0·47, 0·72	0·59	0·48, 0·73	502	0·73	0·52, 1·02	0·73	0·52, 1·03
3	362	0·38	0·30, 0·47	0·39	0·31, 0·48	381	0·48	0·34, 0·68	0·49	0·35, 0·70
4–5	183	0·32	0·25, 0·41	0·33	0·26, 0·42	267	0·40	0·28, 0·56	0·41	0·29, 0·58
P_{trend}			< 0·001		< 0·001			< 0·001		< 0·001
Cardiovascular mortality										
Linear	793	0·69	0·64, 0·74	0·70	0·65, 0·75	351	0·62	0·56, 0·69	0·63	0·57, 0·70
Categories										
0	55	1·00	Reference	1·00	Reference	11	1·00	Reference	1·00	Reference
1	201	0·63	0·47, 0·85	0·64	0·48, 0·87	83	0·92	0·49, 1·73	0·92	0·49, 1·73
2	296	0·49	0·37, 0·65	0·50	0·38, 0·67	130	0·59	0·32, 1·10	0·60	0·32, 1·10
3	180	0·33	0·25, 0·45	0·35	0·26, 0·47	84	0·34	0·18, 0·64	0·35	0·19, 0·65
4–5	61	0·19	0·13, 0·27	0·20	0·14, 0·29	43	0·20	0·10, 0·39	0·21	0·11, 0·41
P_{trend}			< 0·001		< 0·001			< 0·001		< 0·001

* Including age as the underlying time scale and time under study as the time-dependent variable.
† Including age as the underlying time scale, time under study as the time-dependent variable, and adjusted for length of education and civil status.

mortality compared with women with a score of 0. Among men, cancer and cardiovascular mortality risk was significantly lower across all categories of the lifestyle index compared with a lifestyle index score of 0. Among women, a lifestyle index score of more than 2 compared with a score of 0 was associated with a significantly lower risk of cancer and cardiovascular mortality. Strong trends were found in all analyses ($P_{trend} < 0{\cdot}001$).

We also evaluated a lifestyle index in which waist circumference was excluded as a component of the index, because waist circumference may be considered a mediating factor in the causal pathway between lifestyle factors that affect energy intake and expenditure – including dietary factors, alcohol intake and physical activity – and disease and mortality. In adjusted analyses, effect estimates of the linear lifestyle index excluding the recommendation for waist circumference were similar to effect estimates of the corresponding analyses including the recommendation for waist circumference in the index for all endpoints. Among men, a 1-point higher score in this lifestyle index was associated with a HR of 0·73 (95 % CI 0·71, 0·75) for all-cause mortality, 0·72 (95 % CI 0·69, 0·76) for cancer mortality and 0·73 (95 % CI 0·68, 0·79) for cardiovascular mortality. Among women, a 1-point higher lifestyle index score was associated with a HR of 0·70 (95 % CI 0·68, 0·73) for all-cause mortality, 0·73 (95 % CI 0·70, 0·77) for cancer mortality and 0·65 (95 % CI 0·58, 0·73) for cardiovascular mortality. After adjustment for waist circumference in the model not including this factor in the index, effect estimates remained similar (data not shown). Compared with HR in the analyses of the categorical lifestyle index excluding waist circumference, HR were lower in the healthiest category of the lifestyle index including this recommendation for all endpoints. For men scoring 3–4 points (highest score) in the lifestyle index excluding waist circumference compared with men with a score of 0, HR were 0·41 (95 % CI 0·37, 0·46) for all-cause mortality, 0·41 (95 % CI 0·34, 0·48) for cancer mortality and 0·40 (95 % CI 0·31, 0·52) for cardiovascular mortality. For women scoring 3–4 points in this index compared with women with a score of 0, HR were 0·38 (95 % CI 0·33, 0·43) for all-cause mortality, 0·44 (95 % CI 0·37, 0·54) for cancer mortality and 0·28 (95 % CI 0·19, 0·42) for cardiovascular mortality.

Discussion

In the present prospective cohort study of Danish men and women, adherence to health recommendations for smoking, alcohol consumption, physical activity, waist circumference and diet combined was associated with a markedly lower risk of all-cause, cancer and cardiovascular mortality during a median follow-up period of 14 years. Adherence to merely one additional recommendation was associated with a significantly lower risk of all-cause, cancer and cardiovascular mortality among both sexes.

Strengths

Among the strengths of the present study are its prospective design, the almost complete follow-up (99·3 %), and the detailed baseline information on dietary and lifestyle exposures and potential confounding variables, which minimises the likelihood of selection bias and recall bias. Other strengths are the large sample size and the large number of cases providing a good statistical power to study overall mortality as well as cause-specific mortality with a relatively high precision. Individuals with prevalent cancer, CVD and diabetes were not included in the study population, thereby also making changes in lifestyle due to pre-existing disease less likely and minimising the risk of bias due to known illness. Because adverse health behaviours frequently coexist, studying lifestyle factors combined instead of isolated might better capture the impact of lifestyle behaviours on health outcomes, which is also a strength of the present study. By dichotomising variables, the dose–response relationship is lost. However, dichotomisation enabled the comparison of individuals who adhered and not adhered to the public health recommendations, thereby keeping the lifestyle index easily applicable and comprehensible for the public.

Limitations

The assessment of dietary and lifestyle habits was based on self-administrated questionnaires, making some misclassification unavoidable. However, this misclassification is most probably non-differential rather than differential, thereby affecting estimates towards unity.

Although the FFQ was validated[38–40], we cannot preclude that healthy lifestyle behaviours have been over-reported and unhealthy lifestyle behaviours have been under-reported. Misclassifications of this type would most probably affect estimates towards unity. Moreover, dietary and lifestyle factors were assessed at baseline only, and participants could have changed their exposure status during follow-up. There is a lack of studies investigating how lifestyle changes during middle age and how this affects mortality risk, making it difficult to predict what impact these changes may have had on the associations. It seems most probably that such misclassifications would be non-differential.

Of the invited participants, 35 % chose to participate. Participants of the Diet, Cancer and Health cohort study have a higher socio-economic status than non-participants[34], and are therefore possibly healthier than the general population (healthy cohort effect). Potentially, selection bias could have been introduced, however, only if non-participation is related to both the exposure and outcome under study. It is more likely that the selection into the cohort has resulted in a more homogeneous study population, thereby affecting generalisability rather than introducing selection bias. Homogeneity might have resulted in underestimated risk estimates due to few subjects in the outer index score categories.

Selection bias can also occur due to the loss of participants during follow-up; however, with a loss of only 0·7 % of participants in the present study, this should not be of concern.

Although it is biologically implausible that all lifestyle factors possess an equal influence on health, we decided to weight the lifestyle factors equally to ensure a simple and easily understandable index. Ascribing equal weights to all lifestyle factors means that the impact may have been overestimated for some factors and underestimated for others. However, if lifestyle factors should be weighted in a meaningful way, weights should be assigned based on judgements about the general health impact of each component. Such judgements are very complex and might not be possible to make[52].

Adjustment for potential confounding factors did not noticeably influence effect estimates, but residual confounding by unknown confounders or by inaccurate measurement of factors adjusted for cannot be precluded.

Generalisability

The magnitude of the associations found in the present study should be considered as specific to the population under study as participants had a higher socio-economic status and hence probably a healthier lifestyle than the general Danish population. Thus, the generalisability of our findings may be limited to 50- to 64-year-old individuals with a higher socio-economic status living in urban areas. However, the present results are in accordance with the findings from others[53–59], indicating a great preventive potential in lifestyle improvements on public health. It is very likely that the overall findings of the present study apply to the general population.

Comparison with other studies

Associations between lifestyle indices and all-cause mortality have been investigated in many prospective cohort studies, of which fifteen were included in a meta-analysis, concluding that individuals with the healthiest lifestyle had a markedly lower all-cause mortality compared with subjects in the least healthy category (relative risk 0·34, 95 % CI 0·27, 0·42)[23]. This is in accordance with the findings from the present study and novel studies not included in the mentioned meta-analysis[56,58–60]. Studies that examined the association between a lifestyle index and cause-specific mortality have also found a lower risk of cancer mortality and cardiovascular mortality with higher lifestyle index scores[53–57]. Yet, due to differences in the lifestyle factors included, cut-off values, and scores assigned in the indices, comparisons between studies are difficult. Our findings are in agreement with those of other studies reporting that a healthy lifestyle lowered the risk of cardiovascular mortality to a greater extent than the risk of cancer mortality[53–55,57]. This might be due to cancer being a more unspecific endpoint that encompasses various cancer types, with different lifestyle risk factors and differently affected by genetics.

Methodological considerations

Lifestyle factors included in our index are major health risk factors for which either international or national quantitative recommendations exist. For reasons of simplicity and future application, we decisively used pre-determined values and did not judge or adjust the cut-off values. However, regarding smoking, an exception was made: former smokers were classified as non-smokers if they had stopped smoking 15 years or more before baseline. This is considered reasonable because the mortality risk among former smokers seems to approach the risk of never smokers 10–20 years after cessation[61–64]. This grouping may have weakened the association between smoking and mortality as smoking cessation lowers mortality risk already few years after cessation[63,64]. Because mortality risk of former smokers is still higher than the risk of never smokers many years after cessation[62], this might, on the other hand, also have weakened the associations.

In the recommendation for fruit and vegetable intake, 100 g/d of fruit and vegetable juice were allowed to be included. In a recent meta-analysis[65], the association between the risk of incident type 2 diabetes and sugar-sweetened fruit juice as well as 100 % fruit juice intake was investigated. A higher intake of sugar-sweetened fruit juice was significantly associated with the risk of developing type 2 diabetes, while intake of 100 % fruit juice was not[65]. These findings indicate that consumption of fruit juice may have negative effects on health. In Denmark, there is no tradition for including sugar in fruit juices, and as vegetable juice is also encompassed in the recommendation for fruit and vegetable intake, the potentially harmful effects of fruit juice found should not be of concern in the present study.

We are only aware of one study[59] based on 51- to 71-year-old US men and women, assessing the association between all-cause mortality and healthy lifestyle behaviours, where waist circumference was included in a lifestyle index to reflect adiposity. Other studies have used BMI to define excess adiposity. Waist circumference may be a better predictor of adiposity in the middle-aged as excess fat is redistributed centrally with increasing age[44]. This is supported by a study based on the Diet, Cancer and Health cohort[66].

Waist circumference may be considered as an intermediate factor in the association between lifestyle and mortality, resulting from energy intake and expenditure. We excluded waist circumference from the lifestyle index in supplementary analyses. Effect estimates were similar between analyses of the lifestyle index including waist circumference and analyses of an index excluding this measure. Adjustment for waist circumference in the analyses of the lifestyle index excluding this recommendation likewise had a minor influence on effect estimates. Hence, the other lifestyle factors included in the index have an influence on mortality risk, and this is not mediated through waist circumference. In addition, a lower mortality was found in the healthiest category of the lifestyle index including waist circumference compared with the healthiest category of the index without this factor. In the present study, waist circumference within the recommended level thus contributed to lowering mortality risk further.

Potential biological mechanisms

Recommendations for the factors included in the lifestyle index have been established due to their association with lifestyle diseases and premature mortality. Tobacco smoking has been associated with an increased risk of a number of different cancers[2,20], CVD[1] and increased mortality[3]. Tobacco smoke contains more than eighty carcinogens, and promotes endothelial damage, oxidative stress and inflammation[1,2,20]. Contrarily, the effects of alcohol intake on health have been found to be more complex. Alcohol is classified as a human carcinogen, acts as a solvent for carcinogenic compounds such as tobacco smoke, and might mediate the generation of free radicals[2,20]. Light alcohol consumption has been found to reduce CHD, potentially by inhibiting the formation of atheroma and decreasing blood coagulation rate[4,67]. The association between alcohol intake and all-cause mortality has been found to be J-shaped[5], thus balancing both the beneficial and harmful effects of alcohol.

Being physically active is associated with a lower risk of lifestyle diseases probably by reducing chronic inflammation, enhancing insulin sensitivity and improving body composition[6]. Abdominal adiposity is associated with metabolic abnormalities including dyslipidaemia, decreased glucose tolerance, reduced insulin sensitivity and low-level chronic inflammation, thus increasing the risk of CVD, cancer and type 2 diabetes[20,68].

The adverse effects of a high intake of red meat on health might be mediated through its content of saturated fat, cholesterol, and haem-Fe or heterocyclic amines and polycyclic aromatic hydrocarbons formed during cooking and preparation[20]. Haem-Fe may promote the generation of free radicals, inflammatory mediators, and the formation of *N*-nitroso compounds, thereby possibly increasing the risk of developing both cancer[20] and CHD[12]. Heterocyclic amines and polycyclic aromatic hydrocarbons are potential carcinogens as are the by-products of nitrites and nitrates, which are added to preserve processed meat[20]. A high intake of saturated fat has been associated with obesity, insulin resistance and impaired glucose tolerance[44,69]. Fish contain the *n*-3 long-chain PUFA EPA and DHA that have been proposed to possess anti-arrhythmic effects, improve membrane function and reduce blood pressure[70], which reduces the risk of CVD. Whole grains, fruits and vegetables are high in dietary fibre and contain a variety of micronutrients. Foods containing dietary fibre seem to protect against CVD[71] and colorectal cancer[20]. Mechanisms responsible for the beneficial effects of whole grains, fruits and vegetables may include improvements in blood lipid profiles and insulin sensitivity as well as increased faecal bulk and decreased transit time that may prevent mutagens to interact with the intestinal epithelium[71,72]. Whole grains, fruits and vegetables are low in energy density and may therefore indirectly also lower the risk of lifestyle diseases by decreasing the risk of weight gain[20].

Conclusion

We found that a combination of publicly recommended lifestyle behaviours including non-smoking, alcohol consumption in moderation, regular physical activity, a restrained waist circumference and a healthy diet was associated with a lower risk of all-cause, cancer and cardiovascular mortality in a Danish population. Even adherence to one additional recommendation was associated with a significantly lower risk of all-cause, cancer and cardiovascular mortality among both men and women, indicating a huge potential in enhancing healthy lifestyle behaviours for public health and life expectancy. Public health efforts should be targeted at encouraging the public to adopt healthier lifestyles.

In applying targeted actions, it is necessary to understand the factors preventing individuals from having a healthy lifestyle. Future studies should attempt to investigate how to motivate the population to adopt a healthy lifestyle, which currently is a major challenge for public health authorities.

Supplementary material

To view supplementary material for this article, please visit http://dx.doi.org/10.1017/S0007114515000070

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The authors declare that there is no conflict of interest.

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