HEALTH CARE REFORM

Healthy Living Is the Best Revenge

Findings From the European Prospective Investigation Into Cancer and Nutrition–Potsdam Study

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Background: Our objective was to describe the reduction in relative risk of developing major chronic diseases such as cardiovascular disease, diabetes, and cancer associated with 4 healthy lifestyle factors among German adults.

Methods: We used data from 23 153 German participants aged 35 to 65 years from the European Prospective Investigation Into Cancer and Nutrition–Potsdam study. End points included confirmed incident type 2 diabetes mellitus, myocardial infarction, stroke, and cancer. The 4 factors were never smoking, having a body mass index lower than 30 (calculated as weight in kilograms divided by height in meters squared), performing 3.5 h/wk or more of physical activity, and adhering to healthy dietary principles (high intake of fruits, vegetables, and whole-grain bread and low meat consumption). The 4 factors (healthy, 1 point; unhealthy, 0 points) were summed to form an index that ranged from 0 to 4.

Results: During a mean follow-up of 7.8 years, 2006 participants developed new-onset diabetes (3.7%), myocardial infarction (0.9%), stroke (0.8%), or cancer (3.8%). Fewer than 4% of participants had zero healthy factors, most had 1 to 3 healthy factors, and approximately 9% had 4 factors. After adjusting for age, sex, educational status, and occupational status, the hazard ratio for developing a chronic disease decreased progressively as the number of healthy factors increased. Participants with all 4 factors at baseline had a 78% (95% confidence interval [CI], 72% to 83%) lower risk of developing a chronic disease (diabetes, 93% [95% CI, 88% to 95%]; myocardial infarction, 81% [95% CI, 47% to 93%]; stroke, 50% [95% CI, −18% to 79%]; and cancer, 36% [95% CI, 5% to 57%]) than participants without a healthy factor.

Conclusion: Adhering to 4 simple healthy lifestyle factors can have a strong impact on the prevention of chronic diseases.

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MANY OF THE MAJOR chronic diseases, such as cardiovascular disease (CVD), cancer, and diabetes, which together comprise the overwhelming burden of mortality, are in large part preventable. An impressive body of research has implicated modifiable lifestyle factors such as smoking,[1] physical activity,[2] diet,[3-5] and body weight[6] in the causes of these diseases.

See Invited Commentary at end of article

Previous studies have already demonstrated the potential that healthy lifestyle factors can have on reducing the risk of major chronic diseases.[7-13] However, the adverse effects of smoking, physical inactivity, unhealthy diet, and excess body weight echo across multiple outcomes. Thus, a study of the potential reduction in chronic disease morbidity by these lifestyle factors would be instructive and informative for those making health policy decisions and allocating resources to prevention, in particular if specific combinations of those factors are considered. Therefore, our objective was to examine the extent to which 4 major lifestyle factors and their combinations are associated with reduced risk of developing 4 leading causes of morbidity and mortality, ie, diabetes, coronary heart disease (CHD), stroke, and cancer.[14] Recognizing that other lifestyle choices can affect the risk of future chronic disease, we limited our analyses to not smoking, being physically active, adhering to healthy dietary principles, and avoiding excess body weight because these 4 healthy behaviors constitute a core set included in previous studies examining the effect of healthy lifestyles on morbidity and mortality. We did not include moderate use of alcohol as a potentially beneficial behavior given the adverse health impact of excessive use.

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METHODS

STUDY POPULATION

The European Prospective Investigation Into Cancer and Nutrition (EPIC)-Potsdam study is part of the multicenter prospective cohort EPIC study.[15,16] In Potsdam, Germany, men aged 40 to 65 years and women aged 35 to 65 years from the general population were invited to join the study. Between 1994 and 1998, 27 548 adults (16 644 women and 10 904 men) consented to participate.[15] The baseline examination included anthropometric measurements, a personal interview that included questions on prevalent diseases, a questionnaire on sociodemographic and lifestyle characteristics, and a food frequency questionnaire. Follow-up questionnaires to identify incident cases of CHD, stroke, diabetes mellitus, and cancer were administered every 2 to 3 years, with response rates of 95% on average. For this analysis, we considered the follow-up period until December 2006. Consent was obtained from all those participating in the study, and approval was given by the ethics committee of the State of Brandenburg, Germany.

After excluding participants who were younger than 35 years or older than 65 years at recruitment (n=263) and those who never completed a follow-up questionnaire (n=721), those who self-reported diabetes, CVD, or cancer at baseline (n=3130), those with unresolved prevalent or incident status of 1 of the 4 chronic conditions (n=287), and those who had missing information for a lifestyle factor (n=247) or missing covariates (n=18), 23 153 participants (8965 men and 14 188 women) were included in our analyses.

ASCERTAINING INCIDENT CHD, STROKE, DIABETES, AND CANCER

Potential incident diseases were identified primarily using self-reports of the respective conditions and, additionally, self-reported medication (for diabetes, CHD, or stroke), reasons for a reported change in diet (all conditions), specific symptoms (stroke),[17] or death information (all conditions). All potential incident diseases were verified through medical records from which the correct diagnosis, the date, and the means of confirmation of the diagnosis were abstracted to a standard inquiry form by the treating or study physician. Diseases were defined as incident when the date of diagnosis was later than the date of enrolment into the study. The diagnosis of CHD was based on the World Health Organization MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) criteria.[18] Additional cancer cases were identified using record linkage with a cancer registry that is approximately 80% complete. Diseases were coded based in the *International Statistical Classification of Diseases, 10th Revision (ICD-10)* codes I21 for CHD; E11 for diabetes; I160, I161, I163, and I164 for stroke; and C00 to C97 for cancer (except C44: nonmelanoma skin cancer).

HEALTHY LIFESTYLE FACTORS

The study investigated 4 lifestyle factors (smoking status, body mass index [BMI; calculated as weight in kilograms divided by height in meters squared], physical activity, and diet). Each factor was dichotomized into 2 categories, healthy (1 point) and unhealthy (0 points). Healthy lifestyle factors included never smoking, a BMI lower than 30, engaging in physical activity for 3.5 h/wk or more, and healthy dietary pattern, as evidenced by having a value above the median of the summed z scores. Anthropometric measurement procedures followed standard protocols under strict quality control.[19,20] Physical activity included the time spent doing sports and bicycle riding, which is a common mode of transportation in the Potsdam area. The consumption of fruits and vegetables, whole grain bread, and red meat reported on a food frequency questionnaire were used to construct a dietary score. For each of these variables that were expressed in grams of intake per day, we created a z score ([value − mean]/standard deviation) and then summed the 3 z scores. The z score for red meat consumption was set up in such a way that eating less red meat yielded higher positive z scores. The consumption of fish and fowl was not part of the dietary score. The food frequency questionnaire used in the EPIC-Potsdam study has been shown to have satisfactory reliability and validity.[21] The correlation coefficients (corrected for intraindividual variation in dietary recall data) between the food frequency questionnaire and twelve 24-hour dietary recalls for energy-adjusted intake were 0.67 for meat, 0.54 for fruits, 0.42 for vegetables, and 0.54 for bread. A correlation coefficient specific to whole grain bread was not calculated.

COVARIATES

We included the following covariates that were assessed with a self-administered questionnaire and a personal interview during the baseline data collection: age, sex, educational attainment (no vocational training completed, vocational training completed, technical school, or university), occupational status (unemployed, employed full time, employed part time, hourly worker, or retired), marital status, number of adults and children living in the household, and alcohol consumption. Although we elected not to include moderate intake of alcohol as one of the healthy lifestyle factors, we did include the use of alcohol as a potential confounder. Daily intake of alcohol consumption (grams per day) was measured with a food frequency questionnaire.

STATISTICAL ANALYSIS

Cox proportional hazards analysis was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Age was used as the primary time-dependent variable in all models, with entry time defined as the subject's age at recruitment and exit time as the age at diagnosis of the chronic disease of interest, death, or return of the last follow-up questionnaire, whichever came first. Analyses were stratified by age at baseline and adjusted for baseline information including sex, education, and occupational status. All analyses were performed with SAS statistical software (release 9.1; SAS Institute Inc, Cary, North Carolina).

RESULTS

The mean (SD) age of the sample was 49.3 (8.8) years (men, 51.2 [7.9] years; women, 48.2 [9.1] years) at baseline. Approximately 37.6% had basic training at school, 24.8% had completed vocational training or technical school, and 37.6% had completed technical college or a university education. Furthermore, 63.4% worked full time, 8.0% worked part time, 2.2% were hourly workers, 10.5% were unemployed, and 16.0% were receiving retirement payments.

The mean and median follow-up times were 7.8 and 8.2 years, respectively. In all, 2006 participants (1081 men and 925 women) were clinically diagnosed as having 1 of the 4 study outcomes: 1868 participants had 1 event, 134 had 2 events, and 4 had 3 events. Among the 2006 participants with an incident disease, 871 had diabetes (43.4%), 214 had a myocardial infarction (10.7%), 195 had a stroke (9.7%), and 868 had cancer (43.2%). Approximately 84% of participants had a BMI lower than 30, 48% had never smoked, 50% had a healthy score for diet, and 32% participated in physical activity for at least 3.5 h/wk (**Figure 1**). Approximately 4% of participants had zero healthy factors at baseline, most had 1 to 3 healthy factors, and approximately 9% had 4 factors.

Although the percentage of participants with zero healthy factors was limited, a substantial number of adverse events occurred in this category, thus providing a solid baseline rate (**Table 1**). After adjusting for age, sex, educational status, and occupational status, the risk decreased substantially as the number of healthy lifestyle factors increased. Thus, participants with 4 healthy factors had a 78% (95% CI, 72%-83%) reduction in risk compared with those with none (*P* value for linear trend, <.001). We also examined additional models in which we adjusted for marital status, the number of adults in the household, the number of children in the household, and alcohol consumption and alcohol consumption squared at baseline. These additional adjustments, however, had little effect on the adjusted HR (aHR) (0.22; 95% CI, 0.17-0.28) and were not included in the models for parsimonious reasons. Reductions in risk were similar for men (reduction of 84%; 95% CI, 73%-90%) (*P* value for linear trend, <.001) and women (reduction of 72%; 95% CI, 60%-81%) (*P* value for linear trend, <.001) (*P* value for interaction between sex and lifestyle factors, .26).

Each healthy lifestyle factor was associated with a reduction in risk of any chronic disease after taking age, sex, educational status, occupational status, and the other lifestyle factors into account (**Figure 2**). In this comparison, a BMI lower than 30 exerted the largest reduction in risk, followed by never smoking, physical activity for 3.5 h/wk or more, and adhering to good dietary principles. Judging by the magnitude of the HRs, never smoking exerted a stronger protective effect on incident myocardial infarction and diabetes than on stroke and cancer. A BMI lower than 30 was a particularly strong protective factor for incident diabetes. Physical activity for 3.5 h/wk or more was a stronger protective factor for incident diabetes and myocardial infarction than for cancer. Finally, adhering to good dietary principles provided a similar degree of protection for incident diabetes, stroke, and cancer.

The 4 dichotomized healthy factors yielded 16 combinations. The aHRs for these combinations were calculated using participants who had no healthy factors as the reference group (**Table 2**). The smallest aHR was observed for participants with all 4 healthy factors (aHR, 0.23; 95% CI, 0.18-0.29). However, participants who never smoked and had a BMI lower than 30 had an aHR of the same order of magnitude (aHR, 0.28; 95% CI, 0.23-0.34). Other combinations of 2 healthy factors that also resulted in marked reductions in risk included having a BMI lower than 30 and participating in physical activity for 3.5 h/wk or more (aHR, 0.36; 95% CI, 0.29-0.45) as well as participating in physical activity for 3.5 h/wk or more and practicing good dietary behavior (aHR, 0.34; 95% CI, 0.22-0.54). When comparing the observed with the expected HRs for the 16 combinations using the information of the individual factors given in Table 1, the expected HRs were similar to the observed HRs for all combinations but one. The combination of participating in physical activity for 3.5 h/wk or more and practicing good dietary behavior yielded an expected HR of 0.69 compared with an observed HR of 0.34.

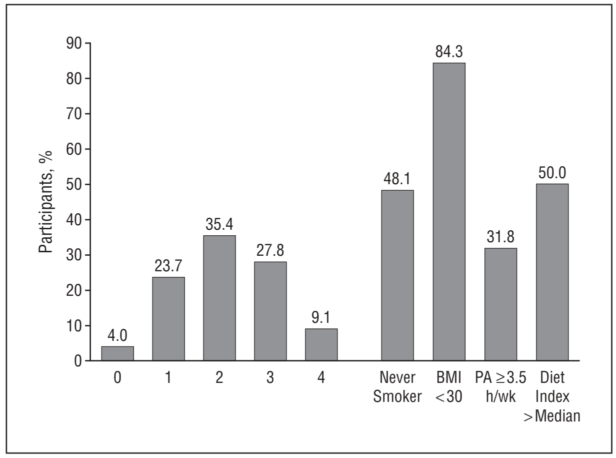

Figure 1. Distribution of healthy lifestyle factors among 23 153 participants aged 35 to 65 years (European Prospective Investigation Into Cancer and Nutrition–Potsdam study). BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); PA, physical activity.

The biggest impact of the 4 healthy lifestyle factors was on incident diabetes (**Figure 3**). Compared with participants with no healthy factors, those with all 4 healthy factors had reductions of 93% (95% CI, 88% to 95%) for diabetes (*P* value for linear trend, <.001), 81% (95% CI, 47% to 93%) for myocardial infarction (*P* value for linear trend, <.001), 50% (95% CI, −18% to 79%) for stroke (*P* value for linear trend, .054), and 36% (95% CI, 5% to 57%) for cancer (*P* value for linear trend, <.001). The prevented fractions were 75% for diabetes, 45% for myocardial infarction, 18% for stroke, and 19% for cancer.

We included smoking status as one of the healthy factors, but these results are only applicable to a population of people who had never smoked. Because current smokers can only revert to former smokers but not to never smokers, we decided to conduct a separate set of analyses that examined the 3 healthy factors (BMI <30, physical activity for ≥3.5 h/wk, and adhering to good dietary principles) among participants who were never smokers, former smokers, and current smokers (**Table 3**). Among the 3 subgroups, reductions in the risk of developing a chronic disease ranged from 47% to 53% for participants with 1 healthy factor, from 59% to 64% among participants with 2 such factors, and from 68% to 71% among participants with 3 such factors (*P* value for linear trend, <.001 for all 3 groups).

COMMENT

The message from our analysis of the data from the EPIC-Potsdam study is clear: adopting a few healthy behaviors can have a major impact on the risk of morbidity. The participants with all 4 healthy lifestyle factors had a

Table 1. Adjusted HRs for Incident Chronic Disease (Cancer, Diabetes, Myocardial Infarction, and Stroke) During Almost 8 Years of Follow-up Among 23 153 Participants Aged 35 to 65 Years From the European Prospective Investigation Into Cancer and Nutrition–Potsdam Study

	No. of Healthy Lifestyle Factors				
Variable	**0**	**1**	**2**	**3**	**4**
No. of participants	924	5491	8206	6432	2100
No. of events	209	640	667	394	96
PY of follow-up	6510	42 128	64 551	50 990	16 636
Unadjusted rate per 1000 PY	32.1	15.2	10.3	7.7	5.8
Adjusted HR (95% CI)[a]	1 [Reference]	0.51 (0.43-0.60)	0.37 (0.31-0.43)	0.28 (0.24-0.33)	0.22 (0.17-0.28)

Abbreviations: CI, confidence interval; HR, hazard ratio; PY, person-years.
[a] Stratified by age and adjusted for sex, educational status, and occupational status.

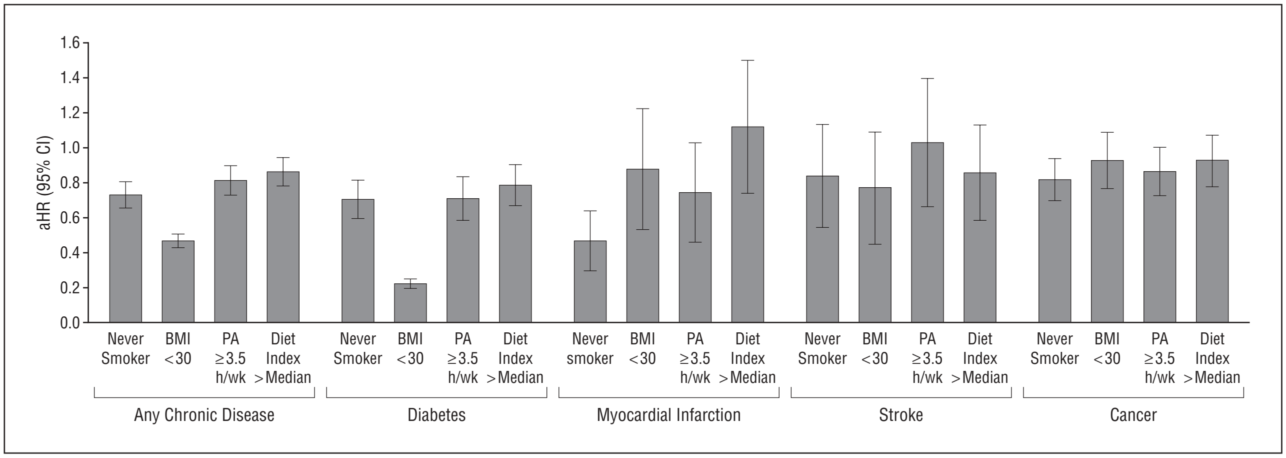

Figure 2. Adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for incident chronic disease (cancer, diabetes, myocardial infarction, and stroke) by individual healthy factors. Data for 23 153 participants aged 35 to 65 years from the European Prospective Investigation Into Cancer and Nutrition–Potsdam study were used. Results are stratified by age and adjusted for sex, education status, and occupational status. Individual healthy lifestyle factors are also adjusted for each other. BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); PA, physical activity.

reduced risk of major chronic diseases of almost 80% compared with those with none. These results applied equally to men and women.

Our results reinforce current public health recommendations to avoid smoking, to maintain a healthy weight, to engage in physical activity appropriately, and to eat adequate amounts of fruits and vegetables and foods containing whole grains and to partake of red meat prudently. By focusing our analyses on conditions that are among the leading causes of mortality in industrialized societies and that are on the rise in developing countries rather than on separate diseases, we have broadened the implications of our findings.

Although improvements in some behaviors have occurred, notably, the decline in the prevalence of smoking, substantial proportions of the population still engage in behaviors that are not conducive to achieving and maintaining health. Our data show that in this German cohort, approximately 9% of the participants met criteria for all 4 healthy lifestyle factors. Similarly, only a small fraction of the populations met recommendations for multiple lifestyle behaviors in US studies.[22] Thus, the opportunity to improve many of the lifestyle behaviors of people abounds. The public health community and clinicians can all contribute to helping people adopt and maintain healthy lifestyle behaviors.

The potential for preventing morbidity and mortality from CVD, diabetes, and cancer through healthy living is enormous. For example, it is estimated that each year 565 000 people have a first myocardial infarction and 500 000 have a first stroke,[23] 1.3 million adults develop diabetes,[24] and 1.4 million develop cancer[25] in the United States. In addition, 221 000 deaths were attributable to myocardial infarction and 273 000 to stroke in 2002,[23] 69 301 deaths to diabetes in 2000,[24] and almost 560 000 deaths to cancer.[25]

IN THE CONTEXT OF THE PREVIOUS STUDIES

Our findings build and expand on those from other prospective studies that have examined the relationships between the number of healthy lifestyle factors and various end points. Of the 84 129 participants of the Nurses' Health Study,[7] 1128 of whom developed a coronary event during 14 years of follow-up, those who were at low risk had a relative risk of developing CHD of 0.17 (95% CI, 0.07-0.41). The lifestyle factors considered were not currently smoking, a BMI lower than 25, alcohol consumption of at least 0.5 drinks per day, at least 0.5 hours of moderate to vigorous physical activity per day, and adhering to several dietary elements (increased intake of cereal fiber, marine omega-3

Table 2. Adjusted[a] HRs for Incident Chronic Disease (Cancer, Diabetes, Myocardial Infarction, Stroke) by Combination of Individual Healthy Factors Among 23 153 Participants Aged 35 to 65 Years From the European Prospective Investigation Into Cancer and Nutrition–Potsdam Study

Combination	Never Smoker	BMI <30	PA ≥3.5 h/wk	Diet Index >Median	No.	No. of Events	PY of Follow-up	Unadjusted Rate per 1000 PY	Adjusted HR (95% CI)
1	0	0	0	0	924	209	6510	32.1	1 [Reference]
2	1	0	0	0	517	84	3854	21.8	0.67 (0.52-0.87)
3	0	1	0	0	4154	411	32 270	12.7	0.43 (0.36-0.51)
4	0	0	1	0	296	53	2173	24.4	0.76 (0.56-1.03)
5	0	0	0	1	524	92	3830	24.0	0.79 (0.61-1.01)
6	1	1	0	0	2915	175	23 753	7.4	0.28 (0.23-0.34)
7	1	0	1	0	166	25	1172	21.3	0.71 (0.47-1.09)
8	1	0	0	1	665	103	4889	21.1	0.64 (0.50-0.82)
9	0	1	0	1	2726	219	21 317	10.3	0.39 (0.32-0.48)
10	0	1	1	0	1466	124	11 350	10.9	0.36 (0.29-0.45)
11	0	0	1	1	268	21	2070	10.1	0.34 (0.22-0.54)
12	1	1	1	0	1135	76	9018	8.4	0.30 (0.23-0.39)
13	1	1	0	1	3364	196	27 058	7.2	0.27 (0.22-0.33)
14	1	0	1	1	273	27	2032	13.3	0.42 (0.28-0.63)
15	0	1	1	1	1660	95	12 881	7.4	0.30 (0.23-0.38)
16	1	1	1	1	2100	96	16 636	5.8	0.23 (0.18-0.29)
Total					**23 153**	**2006**	**180 815**		

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; HR, hazard ratio; PA, physical activity; PY, person-years.

[a] Stratified by age and adjusted for sex, educational status, and occupational status.

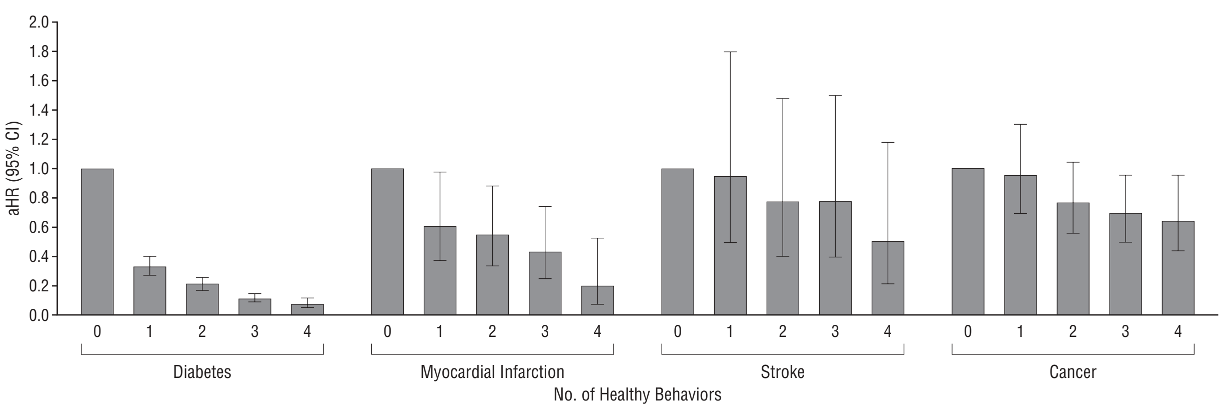

Figure 3. Adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for incident diabetes, myocardial infarction, stroke, and cancer by number of healthy factors. Data for 23 153 participants aged 35 to 65 years from the European Prospective Investigation Into Cancer and Nutrition–Potsdam study were used. Results are stratified by age and adjusted for sex, educational status, and occupational status.

fatty acids, and folate; increased ratio of polyunsaturated fats to saturated fats; and low *trans* fat intake and glycemic load). Another analysis[8] of this same cohort showed that women who were at low risk as evidenced by practicing a healthy lifestyle had a substantially reduced risk of developing diabetes (3300 events during 16 years of follow-up) (relative risk, 0.09; 95% CI, 0.05-0.17). The behaviors of interest were similarly specified, but the dietary variable was modified.

Among 2539 participants of the Healthy Aging: a Longitudinal Study in Europe,[26] the aHR was 0.35 (95% CI, 0.28-0.44) for those with all 4 factors of interest (Mediterranean diet, moderate alcohol use, physical activity, and not smoking) compared with those not engaging in any of these factors.

In an analysis of data from 37 636 participants aged 45 years or older from the Women's Health Study,[10] 450 of whom developed a stroke during a mean 10 years of follow-up, the aHRs for participants who scored higher on an index of lifestyle factors than those who scored lower were 0.45 (95% CI, 0.24-0.83) for total stroke, 0.29 (95% CI, 0.14-0.63) for ischemic stroke, and 1.27 (95% CI, 0.37-4.29) for hemorrhagic stroke. Lifestyle factors considered in this study were smoking, alcohol use, exercise, BMI, and diet.

In the Health Professionals Follow-up Study,[9] 42 847 men aged 40 to 75 years were followed up over 16 years, and 2183 developed a coronary event. Compared with men with no healthy lifestyle factors, those with all 5 factors had a large reduction in the risk of developing CHD

Table 3. Adjusted HRs (95% CIs) for Incident Chronic Disease (Cancer, Diabetes, Myocardial Infarction, and Stroke) by Smoking Status During Almost 8 Years of Follow-up Among 23 153 Participants Aged 35 to 65 Years From the European Prospective Investigation into Cancer and Nutrition–Potsdam Study

Smoking Status	No. of Healthy Lifestyle Factors			
	0	1	2	3
Never smokers (n=11 135)				
No. of participants	517	3746	4772	2100
No. of events	84	303	299	96
PY of follow-up	3854	29 814	38 108	16 636
Unadjusted rate per 1000 PY	21.8	10.2	7.8	5.8
Adjusted HR (95% CI)[a]	1 [Reference]	0.53 (0.42-0.68)	0.41 (0.32-0.52)	0.32 (0.24-0.44)
Former smokers (n=7273)				
No. of participants	603	2780	2768	1122
No. of events	143	307	223	68
PY of follow-up	4257	21629	21736	8771
Unadjusted rate per 1000 PY	33.6	14.2	10.3	7.8
Adjusted HR (95% CI)[a]	1 [Reference]	0.47 (0.38-0.57)	0.36 (0.29-0.45)	0.31 (0.23-0.41)
Current smokers (n=4745)				
No. of participants	321	2194	1692	538
No. of events	66	249	141	27
PY of follow-up	2253	16645	13001	4110
Unadjusted rate per 1000 PY	29.3	15.0	10.8	6.6
Adjusted HR (95% CI)[a]	1 [Reference]	0.50 (0.38-0.66)	0.40 (0.29-0.53)	0.29 (0.18-0.46)

Abbreviations: CI, confidence interval; HR, hazard ratio; PY, person-years.
[a]Stratified by age and adjusted for sex, educational status, and occupational status.

(HR, 0.13; 95% CI, 0.09-0.19). The lifestyle factors in this study were characterized in much the same way as in the previous studies.

In an analysis of 15 708 participants in the Atherosclerosis Risk in Communities Study,[11] those who adopted a healthy lifestyle experienced a lower risk of all-cause mortality (odds ratio, 0.60; 95% CI, 0.39-0.92) and CVD (odds ratio, 0.65; 95% CI, 0.39-0.92) during 4 years of follow-up. The 4 healthy lifestyles considered were eating 5 or more fruits and vegetables per day, exercising 2.5 h/wk or more, having a BMI between 18.5 and 30.0, and not smoking.

Among 20 244 participants in the EPIC-Norfolk study,[12] sizeable reductions in all-cause mortality were demonstrated with increasing numbers of health factors. Participants with all 4 factors (current not smoking, not physically inactive, moderate alcohol use, and plasma vitamin C level greater than 0.88 mg/dL [to convert to micromoles per liter, multiply by 56.78] as a surrogate for fruit and vegetable consumption) had an advantage of approximately 14 years in chronological age over those without 1 of the 4 factors.

Finally, analyses of data from 43 685 participants in the Health Professionals Follow-up Study (994 strokes) and 71 243 participants in the Nurses' Health Study (1559 strokes) showed substantial reductions in the risk of developing an incident stroke among men (relative risk, 0.31; 95% CI, 0.19-0.53) and women (relative risk, 0.21; 95% CI, 0.12-0.36) who practiced a low-risk lifestyle compared with those who did not.[13] Men were followed up from 1984 to 2004, and women were followed up from 1986 to 2004. The lifestyle factors considered were not currently smoking, at least 30 minutes of moderate to vigorous physical activity per day, a diet score in the top 40%, alcohol consumption of 5 to 15 g/d for women and 5 to 30 g/d for men, and a BMI lower than 25.

We showed that each lifestyle factor was associated with a reduction in risk and that the reduction in risk from combinations of factors followed the multiplicative model. This finding implies that each factor contributes to risk reduction independently of the other factors in the estimated magnitude. The only exception was the combination of diet index above the median and physical exercise, which showed a larger risk reduction as estimated from the relative risk of the single factors. The favorable effect on the risk of developing chronic disease of these 2 factors was likely partially mediated through BMI. The previous prospective studies that examined the effect of healthy factors on adverse outcomes did not examine the effects of different combinations of lifestyle factors on outcomes. Because our findings may have occurred by chance, the results of other studies investigating the effects of healthy lifestyle on incident chronic disease will be valuable in gauging the significance of this result.

In contrast to some of these studies, we elected not to include moderate use of alcohol as a potentially beneficial behavior. Because of the well-documented harms caused by alcohol abuse,[27] a great deal of reluctance exists in the public health community to recommend drinking moderately for fear that the message will be misinterpreted and viewed as endorsing unfettered alcohol use. Although moderate alcohol consumption may add to the risk reduction generated by the other 4 behaviors, any recommendations regarding moderate use of alcohol will require a thoughtful evaluation of whether potential benefits outweigh the clear harms of alcohol abuse.

STUDY LIMITATIONS

Our results should be considered in the light of several limitations. The assessment of end points was based on self-reported information with physician confirmation. Thus, some proportion of incident end points remained undetected. If the association between the exposures and the end points was similar for detected and undetected end points, our HRs should be unbiased.[28] Second, information about the lifestyle factors except BMI was self-reported and thus is subject to information bias and misclassification. If the misclassification were random, our HRs would have been attenuated. Third, we used a few simple concepts to define adherence to good dietary principles. However, other approaches to characterizing good dietary practices exist and could generate different results. Finally, the results of this study are generalizable to the German population where the study was conducted. Additional studies in other populations will be needed to evaluate how much of chronic disease morbidity and mortality is potentially preventable in other populations.

CONCLUSIONS

The data from the EPIC-Potsdam study show the unfulfilled potential of preventing chronic diseases. Adhering to recommendations for the 4 lifestyle factors considered in our analyses can potentially yield enormous reductions in the onset of major chronic diseases such as CVD, diabetes, and cancer. For those with none of the factors, achieving even 1 promises to increase the time free of the 4 chronic conditions, and further gains accrue as the number of such factors increases. However, our findings also illustrate the heterogeneity in potential risk reduction that exists among the various combinations of healthy factors, a finding that expands on the previous literature concerning the relationships between healthy lifestyle factors and the incidence of chronic disease. Our results and those of others emphasize the importance and urgency of continuing vigorous efforts to convince people to adopt healthy lifestyles. Because the roots of these factors often originate during the formative stages of life, it is especially important to start early in teaching the important lessons concerning healthy living.[29]

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INVITED COMMENTARY

HEALTH CARE REFORM

Life and Death, Knowledge and Power: Why Knowing What Matters Is Not What's the Matter

For a span of decades prior to 1993, when asked what is the leading cause of death in the United States, there was only one reasonable answer—heart disease. The answers for the second, third, and fourth leading causes were similarly circumscribed: cancer, stroke, and diabetes. But in that year, McGinnis and Foege[1] refashioned our understanding and forever changed these answers with the publication of their seminal article, "Actual Causes of Death in the United States." As of 1993, the leading cause of death in the United States became tobacco use.

McGinnis and Foege[1] looked beyond the diseases that are proximal causes of death to the causes of those diseases, the root causes of death. They concluded that half of the annual mortality toll in this country—roughly a million deaths—was premature. These deaths could be prevented, or more accurately, deferred, with the modification of just 10 behaviors subject to our will: tobacco use, dietary pattern, physical activity level, alcohol consumption, exposure to microbial agents, exposure to toxic agents, use of firearms, sexual behavior, motor vehicle crashes, and illicit use of drugs. That list of 10 was, in turn, much dominated by the top 3—tobacco use, dietary pattern, and physical activity level—which alone accounted for nearly 800 000 premature deaths in 1990.

In 2004, Mokdad and colleagues[2] at the Centers for Disease Control and Prevention, again publishing in *JAMA*, refreshed this perspective. Despite a decade of awareness, the same 10 modifiable behaviors, dominated by the same 3, persisted as leading causes of both premature death and chronic disease. If ever a matter of public importance belied the notion that knowledge is power, this decade of underutilized knowledge was it. And if we are once again to be updated in 2013, there is little cause to think, based on our progress to date, that we will have fared much better across an informed expanse of 2 decades, although progress in tobacco control warrants honorable mention.

It is in this context that the findings of Ford et al should be considered. In a cohort of over 23 000 German adults enrolled into the expansive EPIC study, a mere 4 behaviors accounted for a 78% variance in the apparent risk of a serious chronic disease. Since 1 of the 4 (maintenance of a BMI <30) is not a behavior per se, but rather largely a by-product of 2 other behaviors already on the list (eating well and being active) the difference between life and death and health and illness is substantially dictated by just 3 behaviors. Those 3 (smoking, diet, and physical activity) are the familiar levers of destiny McGinnis and Foege[1] handed us 16 years ago.

In the study by Ford et al, for those with all 4 "healthy behaviors" compared with those with none, the hazard ratio for diabetes, myocardial infarction, stroke, or cancer was a mere 0.22, with an impressively narrow 95% confidence interval from 0.17 to 0.28. On average, the presence of just 1 healthy behavior as compared with none cut the chronic disease risk fully in half (aHR, 0.51; 95% CI, 0.43-0.60).

The authors cite a number of studies that have associated healthful living with longevity, reduced risk of various chronic diseases, and less risk of premature mortality; still more have been published since their article went to press.[3,4] The point estimates, confidence intervals, and measured components of a "health-promoting" lifestyle