

Physical Activity and Lifetime Risk of Cardiovascular Disease and Cancer

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ABSTRACT

KUBOTA, Y., K. R. EVENSON, R. F. MACLEHOSE, N. S. ROETKER, C. E. JOSHU, and A. R. FOLSOM. Physical Activity and Lifetime Risk of Cardiovascular Disease and Cancer. *Med. Sci. Sports Exerc.*, Vol. 49, No. 8, pp. 1599–1605, 2017. **Purpose:** Although the World Health Organization has recommended moderate- to vigorous-intensity physical activity (MVPA) to prevent cardiovascular disease (CVD) and some cancers, there are no estimates of lifetime risk of these noncommunicable diseases according to PA levels. We aimed to estimate the lifetime risk of CVD and cancers according to PA levels. **Methods:** We followed 5807 men and 7252 women in the United States, 45–64 yr old, initially free of CVD and cancer from 1987 through 2012, and used a life table approach to estimate lifetime risks of CVD (coronary heart disease, heart failure, and stroke) and total cancer according to PA levels: poor (0 min-wk⁻¹ of MVPA), intermediate (1–74 min-wk⁻¹ of VPA or 1–149 min-wk⁻¹ of MVPA), or recommended (≥ 75 min-wk⁻¹ of VPA or ≥ 150 min-wk⁻¹ of MVPA). **Results:** During the 246,886 person-years of follow-up, we documented 4065 CVD and 3509 cancer events and 2062 non-CVD and 2326 noncancer deaths. In men, the lifetime risks of CVD from 45 through 85 yr were 52.7% (95% confidence interval = 49.4–55.5) for poor PA and 45.7% (42.7–48.3) for recommended PA. In women, the respective lifetime risks of CVD were 42.4% (39.5–44.9) and 30.5% (27.5–33.1). Lifetime risks of total cancer were 40.1% (36.9–42.7) for poor PA and 42.6% (39.7–45.2) for recommended activity in men and 31.4% (28.7–33.8) and 30.4% (27.7–32.9), respectively, in women. **Conclusions:** Compared with a poor PA level, the PA recommended by the World Health Organization was associated with lower lifetime risk of CVD, but not total cancer, in both men and women. **Key Words:** ARIC STUDY, WHO, RISK FACTOR, NONCOMMUNICABLE DISEASE

Noncommunicable diseases (NCD) are responsible for 38 million global deaths, and 16 million NCD deaths are premature (39). Most NCD deaths (68%) are from cardiovascular disease (CVD) and cancer (39), and thus it is essential to prevent these two diseases for the prevention of premature deaths.

Physical inactivity is considered to be one of the most important modifiable risk factors for NCD (39). Abundant reports have suggested that physical inactivity is associated with increased risks of coronary heart disease (37), stroke (8),

heart failure (7), and cancer (20). Physical activity may reduce the risk of CVD or cancer by preventing obesity, hypertension, dyslipidemia, and glucose intolerance (20,22,29). In addition, several previous studies suggested direct effects of physical activity, such as improved endothelial function or immune function, and reduced systemic inflammation, platelet aggregation, estrone/estradiol levels, or oxidative stress (10,12,20).

A World Health Organization (WHO) guideline on physical activity recommends at least 150 min of moderate-intensity aerobic physical activity, at least 75 min of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity throughout the week (40). To encourage people to achieve this level, it is important to cultivate an understanding of its potential effect on major NCD risk. One way for that may be to provide information on the lifetime risk of major NCD according to physical activity levels. Lifetime risk estimates, which are absolute risks to a certain age, are often more easily understood than relative risks (15–17). However, to our knowledge, there has been no study estimating lifetime NCD risks according to physical activity levels.

Therefore, the purpose of this study was to estimate the lifetime risk of incident CVD and cancer in a U.S. cohort,

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according to physical activity levels based on the WHO recommendation, separately for men and women.

METHODS

Study design, setting, and population. The Atherosclerosis Risk in Communities (ARIC) study is an ongoing population-based prospective study of CVD (14,38). In 1987–1989, the ARIC Study recruited and examined 15,792 mostly Caucasian or African American men and women 45–64 yr of age from four U.S. communities (Washington County, MD; Forsyth County, NC; Jackson, MI [African Americans only]; and suburbs of Minneapolis, MN). The baseline home interview and clinic examination measured various chronic disease risk factors, health behaviors, and cardiovascular conditions. Participants were followed through 2012 for this report. The institutional review boards of the collaborating institutions approved the study protocol, and each participant provided written informed consent.

Risk factor measurements. The main exposure of interest was baseline physical activity. We assessed sports physical activity via an interviewer-administered Baecke questionnaire (3). The reliability and the validity of the Baecke questionnaire were evaluated in several populations and summarized elsewhere (11,30,38). The Baecke questionnaire asked participants to report the frequency and the number of hours of participation in as many as four sports or leisure activities in the previous year. As in previous ARIC studies (5,35), each activity was converted into METs of task using the compendium of physical activities (1). Moderate activities were defined as those involving intensities of 3–6 METs and vigorous activities were those involving intensities of >6 METs (1). Information from the questionnaires was subsequently converted into minutes per week of moderate or vigorous physical activity, and participants were categorized into three groups: “recommended” (based on the WHO recommendation [40] of $\geq 75 \text{ min}\cdot\text{wk}^{-1}$ of vigorous intensity or $\geq 150 \text{ min}\cdot\text{wk}^{-1}$ of any combination of moderate + vigorous intensity), “intermediate” ($1\text{--}74 \text{ min}\cdot\text{wk}^{-1}$ of vigorous intensity or $1\text{--}149 \text{ min}\cdot\text{wk}^{-1}$ of any combination of moderate + vigorous intensity), or “poor” ($0 \text{ min}\cdot\text{wk}^{-1}$ of moderate or vigorous intensity).

We also assessed potential confounding factors, including race, smoking status, and a healthy diet score, and lung diseases (chronic obstructive pulmonary disease and restrictive lung disease). Diet was assessed by a slightly modified 66-item Harvard food frequency questionnaire (31), and a healthy diet score was calculated by adding each point (0 or 1) of the following five healthy dietary metrics: ≥ 4.5 cups per day of fruits and vegetables (approximately ≥ 4.5 servings per day in the ARIC study), 2 or more ≥ 3.5 -oz servings per week of fish (approximately 3- to 5-oz servings per week), 3 or more 1-oz servings per day of whole grains (approximately ≥ 3 servings per day), sodium ($<1500 \text{ mg}\cdot\text{d}^{-1}$), and $\leq 36 \text{ oz}\cdot\text{wk}^{-1}$ of sugar-sweetened beverages (approximately ≤ 4 glasses per week). We defined individuals with lung diseases as those with forced expiratory volume in 1 s (FEV1)/forced vital

capacity (FVC) < lower limit of normal (LLN) (chronic obstructive lung disease), those with $\text{FEV1}/\text{FVC} \geq \text{LLN}$ and $\text{FVC} < \text{LLN}$ (restrictive lung disease), or those who self-reported chronic bronchitis, emphysema, or asthma (13).

Confirmation of CVD and total cancer. We defined incident CVD events as coronary heart disease, heart failure, and stroke. ARIC staff contacted participants or their proxies annually by telephone to capture all hospitalizations and deaths related to possible CVD (9). They also surveyed lists of discharges from local hospitals and death certificates from state vital statistics offices for potential CVD events. Abstractors reviewed medical records and recorded information to validate CVD outcomes. Incident coronary heart disease was validated by physician review and was defined as a definite or probable myocardial infarction, definite coronary death, or coronary revascularization procedure. Incident heart failure was defined as the first occurrence of either a hospitalization that included an *International Classification of Diseases, Ninth Revision* (ICD-9) discharge code of 428 (428.0 to 428.9) among the primary or secondary diagnoses or else a death certificate with an ICD-9 code of 428 or an ICD-10 code of I50 among the listed or underlying causes of death (18). ARIC has shown the validity of ICD-9 code 428 to be moderately high, with a sensitivity of 93% for identifying acute decompensated heart failure (32). For patients hospitalized for potential strokes, the abstractors recorded signs and symptoms and photocopied neuroimaging (computed tomography or magnetic resonance imaging) and other diagnostic reports. Using criteria adopted from the National Survey of Stroke, definite or probable strokes were classified by computer algorithm and separately reviewed by a physician, with disagreements resolved by a second physician (24).

Incident cancer cases were obtained by linking to cancer registries (28). ARIC hospital surveillance was used to identify additional cancer cases. For participants who had hospital ICD codes for cancer but were not in cancer registries, including those who may have moved, records of hospitalized events were obtained. Primary site and date of cancer diagnosis were obtained. If a participant had more than one type of incident cancer during follow-up, the earliest date of cancer incidence was chosen for analysis of the combined, total cancer end point.

Statistical analysis. SAS version 9.3 software (SAS Institute Inc., Cary, NC) was used for statistical analyses. We excluded participants who reported or had electrocardiographic evidence of prebaseline CVD or cancer ($n = 2342$) and participants whose data on physical activity or outcome status were missing ($n = 391$). After exclusions, 13,059 participants initially free of CVD and cancer were followed from 1987 through 2012 or until death and included in the analyses.

We estimated sex-specific remaining lifetime risks of incident CVD or total cancer through age 85 yr according to physical activity levels, using a modified version of survival analysis (4) as previous studies described (15–17). We separately estimated cumulative risks for CVD and for total cancer.

TABLE 1. Remaining lifetime risk of CVD and total cancer from selected index ages to 85 yr according to physical activity levels, ARIC, 1987–2012.

Index Age, yr	Men			Women		
	Lifetime Risk (%) to 85 yr (95% Confidence Interval)			Lifetime Risk (%) to 85 yr (95% Confidence Interval)		
	Poor	Intermediate	Recommended	Poor	Intermediate	Recommended
CVD						
45	52.7 (49.4–55.5)	49.4 (45.3–52.9)	45.7 (42.7–48.3)	42.4 (39.5–44.9)	38.6 (34.8–42.1)	30.5 (27.5–33.1)
55	49.6 (46.1–52.4)	46.4 (42.2–50.0)	42.7 (39.6–45.3)	40.7 (37.7–43.2)	37.2 (33.5–40.5)	29.4 (26.4–32.1)
65	42.5 (38.3–45.8)	39.2 (34.4–43.3)	36.6 (33.2–39.4)	35.3 (32.2–38.1)	33.4 (29.5–36.8)	26.6 (23.5–29.3)
Total cancer						
45	40.1 (36.9–42.7)	39.6 (35.6–43.0)	42.6 (39.7–45.2)	31.4 (28.7–33.8)	27.6 (24.6–30.3)	30.4 (27.7–32.9)
55	40.2 (37.0–42.8)	38.5 (34.5–41.8)	41.3 (38.3–43.8)	28.2 (25.7–30.3)	24.5 (21.7–27.0)	26.6 (24.2–28.9)
65	34.9 (31.3–37.7)	31.3 (27.0–35.0)	35.5 (32.3–38.2)	21.9 (19.3–24.1)	19.0 (16.2–21.5)	21.0 (18.5–23.2)

This method uses survival age as the time scale, combines information on participants entering the observation periods at different ages, and accounts for varying durations of follow-up of individuals (4). In addition, it takes into account the occurrence of competing risks of death from other causes through adjustment to yield estimates of age-specific hazards and incidence rates as well as cumulative incidences and survival probabilities. By contrast, traditional Kaplan–Meier estimates do not properly account for competing risks, often resulting in overestimates of the remaining lifetime risk (15–17).

Because the lifetime risk model cannot adjust for confounding variables, we stratified participants by potential confounding factors—race (African American vs White), smoking status (current vs noncurrent), healthy diet score (≤ 1 vs ≥ 2 points), and presence versus absence of lung diseases—and examined lifetime risks of CVD and total cancer within strata. Risk factors that could be a consequence of physical inactivity and potentially mediate its effects, such as obesity, hypertension, and dyslipidemia, were not considered confounders and, thus, not evaluated.

RESULTS

During 1987–2012 (mean \pm SD = 18.9 \pm 7.2 yr), 13,059 participants (5807 men and 7252 women) provided 246,886 person-years of observation. During the follow-up, we documented 4065 incident CVD (coronary heart disease, heart failure, or stroke) and 3509 cancer events, and 2062 non-CVD and 2326 noncancer deaths. The overall lifetime risks to age 85 yr of total CVD, coronary heart disease, heart failure, stroke, and total cancer were 49.1%, 34.2%, 25.3%, 11.2%,

and 41.1% for men and 37.5%, 18.1%, 23.6%, 10.5%, and 30.0% for women, respectively.

The remaining lifetime risks of incident CVD and total cancer at ages 45, 55, and 65 yr are shown according to physical activity levels in Table 1. The lifetime risks were generally higher among men than among women. Physical activity displayed an inverse dose–response relation with lifetime risks of CVD, such that CVD was 2%–8% lower in men and women at any index age for each higher physical activity category (i.e., poor to intermediate or intermediate to recommended). Similar trends for physical activity and lifetime risks of CVD were observed in all strata of race, smoking status, healthy diet score, and with or without lung diseases (Table 2). On the other hand, the lifetime risks of total cancer did not appreciably differ across physical activity levels in both men and women. The remaining lifetime risks of CVD and total cancer at age 45 yr are illustrated in Figure 1. In men, the lifetime risks of CVD from 45 to 85 yr were 52.7% for poor physical activity and 45.7% for recommended physical activity. In women, the respective lifetime risks of CVD were 42.4% and 30.5%. Lifetime risks of total cancer at age 45 yr were 40.1% for poor physical activity and 42.6% for recommended activity in men and 31.4% and 30.4%, respectively, in women (Table 1 and Fig. 1).

We also estimated the lifetime risks from age 45 to 85 yr of CVD subtypes—coronary heart disease, heart failure, and stroke—according to physical activity levels (Fig. 2). In men, the lifetime risks of coronary heart disease were 36.2% for poor physical activity and 31.6% for recommended physical activity, those of heart failure were 29.8% for poor physical activity and 21.9% for recommended activity, and

TABLE 2. Remaining lifetime risk of CVD from selected index ages to 85 yr according to physical activity levels, stratified by race, smoking status, or healthy diet score, ARIC, 1987–2012.

	Men			Women		
	Lifetime Risk (%) to 85 yr (95% Confidence Interval)			Lifetime Risk (%) to 85 yr (95% Confidence Interval)		
	Poor	Intermediate	Recommended	Poor	Intermediate	Recommended
African American	55.0 (49.6–59.7)	47.4 (37.2–55.3)	45.4 (37.0–52.3)	45.7 (41.6–49.4)	45.6 (37.4–52.6)	37.6 (29.1–44.7)
White	51.6 (47.3–55.1)	50.2 (45.8–54.2)	45.6 (42.4–48.4)	39.5 (35.5–42.9)	36.5 (32.2–40.6)	29.0 (25.8–31.8)
Current smokers	54.7 (50.8–57.9)	51.3 (46.5–55.5)	48.1 (44.4–51.3)	48.9 (44.5–52.5)	45.9 (39.9–52.0)	33.7 (28.8–37.8)
Noncurrent smokers	46.5 (40.0–52.0)	44.7 (37.2–51.3)	39.9 (34.9–44.4)	36.4 (32.6–39.7)	32.9 (28.1–37.0)	27.9 (24.1–31.4)
Diet score ≤ 1	54.5 (49.7–58.5)	50.8 (43.9–56.4)	46.7 (41.1–43.6)	44.2 (38.6–48.9)	39.5 (32.1–46.1)	33.3 (25.3–40.3)
Diet score ≥ 2	51.0 (46.2–55.1)	48.6 (43.4–53.2)	45.2 (41.6–48.4)	41.3 (37.8–44.2)	38.8 (34.3–43.1)	29.8 (26.5–32.7)
With lung diseases	54.9 (49.3–59.6)	53.2 (45.6–59.4)	48.3 (43.0–52.9)	46.2 (41.1–50.5)	48.5 (41.0–55.9)	35.0 (29.3–39.9)
Without lung diseases	51.5 (47.4–55.0)	47.9 (42.9–52.2)	44.7 (41.1–47.8)	40.6 (37.1–43.7)	34.8 (30.5–38.6)	28.6 (25.1–31.7)

Lung diseases were defined as FEV1/FVC < LLN (chronic obstructive lung disease), FEV1/FVC \geq LLN and FVC < LLN (restrictive lung disease), or self-reported chronic bronchitis, emphysema, or asthma.

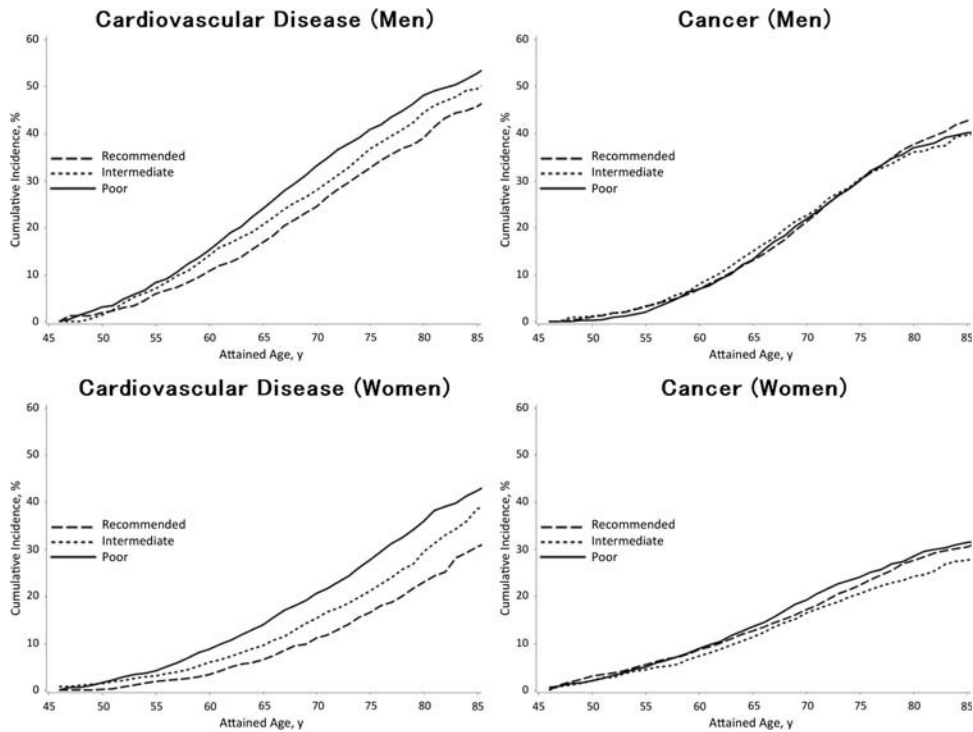


FIGURE 1—Sex-specific lifetime risk estimates of CVD and total cancer at age 45 to 85 yr according to physical activity levels based on the WHO recommendation, ARIC, 1987–2012.

those of stroke were 11.9% for poor physical activity and 10.5% for recommended activity. In women, the lifetime risks of coronary heart disease were 20.8% for poor physical activity and 12.8% for recommended physical activity, those

of heart failure were 27.3% for poor physical activity and 19.2% for recommended activity, and those of stroke were 11.5% for poor physical activity and 8.6% for recommended activity.

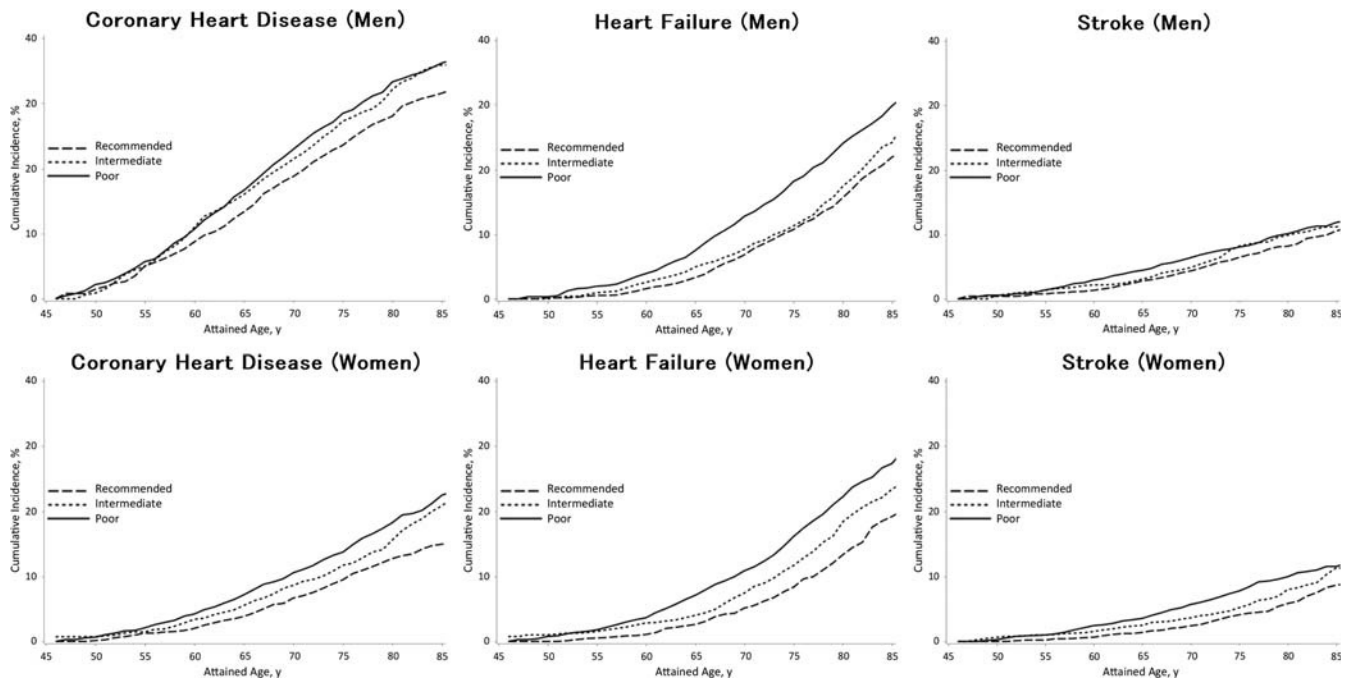


FIGURE 2—Sex-specific lifetime risk estimates of coronary heart disease, heart failure, and stroke at age 45 to 85 yr according to physical activity levels based on the WHO recommendation, ARIC, 1987–2012.

We also ran models after combining men and women and obtained similar results (see Table, Supplemental Digital Content 1, Lifetime risk of cardiovascular disease and total cancer according to physical activity levels among men and women, <http://links.lww.com/MSS/A894>; Figure, Supplemental Digital Content 2, Lifetime risk estimates of cardiovascular disease and total cancer according to physical activity levels based on the WHO recommendation among men and women, <http://links.lww.com/MSS/A895>; Table, Supplemental Digital Content 3, Lifetime risk of cardiovascular disease according to physical activity levels, stratified by several factors among men and women, <http://links.lww.com/MSS/A896>; Figure, Supplemental Digital Content 4, Lifetime risk estimates of coronary heart disease, heart failure and stroke according to physical activity levels based on the WHO recommendation among men and women, <http://links.lww.com/MSS/A897>).

DISCUSSION

In this population-based prospective study in the United States, we estimated the remaining lifetime risk of incident CVD and total cancer according to baseline physical activity levels based on WHO recommendation. Compared with people who were inactive, men meeting the WHO-recommended physical activity level had 7% lower lifetime risk of CVD from age 45 to age 85 yr (46% vs 53%) and women had 11% lower risk (31% vs 42%). The lifetime risks of total cancer were approximately 41% for men and 30% for women regardless of physical activity levels. To the best of our knowledge, this is the first study to investigate the lifetime risk of incident CVD and total cancer in both men and women according to physical activity levels.

Lifetime risk reductions were similar when projected from index ages of 45, 55, or 65 yr, and the pattern was similar after stratifying by race, smoking status, healthy diet score, and with or without lung diseases. A previous study, which examined lifetime risk of CVD in relation to cardiovascular fitness, but not physical activity, showed a comparable reduction in the lifetime risk of CVD (approximately 9%) among men with a high level of cardiovascular fitness compared with those with a low level (6). The WHO-recommended level of physical activity was associated with a reduced lifetime risk of CVD, but those who met WHO recommendation still had a substantial lifetime risk of CVD. Thus, people must avoid additional risk factors such as smoking and unhealthy diet to further reduce their lifetime risk of CVD.

The Framingham Study, which started in 1948, reported lifetime risks of coronary heart disease, which were approximately 50% for men and 30% for women (15); lifetime risks of heart failure in absence of antecedent myocardial infarction, which were approximately 20% for both men and women (16); and lifetime risks of stroke, which were approximately 15% for men and 20% for women (34). In the ARIC cohort of 45–64 yr olds at baseline starting in 1987, we found that overall lifetime risks of coronary heart disease and stroke were

lower compared with the Framingham cohort. ARIC estimates of lifetime risk of heart failure were higher than Framingham, but our estimate did not exclude heart failure with antecedent coronary heart disease. Lower lifetime risks of CVD in a younger cohort are expected given the decline in CVD in the United States for the past three decades.

The National Cancer Institute has reported that lifetime risks of invasive cancer at age 40 yr through death in the United States are approximately 42% for men and 37% for women (23). We observed a similar lifetime risk at age 45 to 85 yr for men (approximately 41%). We observed a slightly lower lifetime risk at age 45 to 85 yr for women (approximately 30%); this could be due, in part, to the relatively higher proportion of African American participants in ARIC as compared with the United States. Although lifetime risk of invasive cancer is comparable for men by race, it is slightly lower among African American women than White women. In contrast to CVD, cancer showed no clear difference in lifetime risks across physical activity levels, although a previous study have reported higher relative risks of certain cancers for physically inactive compared with active adults (20). In addition, physical activity is also associated with reduced risk of cancer mortality (26) and greater gains in life expectancy among cancer survivors (21). Generally, the association between physical activity and the most common cancers in ARIC has been weak. For example, in ARIC, physical activity was not associated with breast cancer during early follow-up (19), although other studies have reported a relatively strong inverse association regardless of menopausal status (25). Among ARIC men, the most common cancers are prostate and lung, neither of which are strongly associated with physical activity. Thus, although the present study did not show an inverse association between physical activity and lifetime cancer risk, there may be beneficial effects of physical activity on certain cancers.

Generally speaking, it is difficult to achieve the recommended level of physical activity for health benefits during work alone. Leisure-time physical activities, sports, and exercise have consistently been reported to be associated with health benefits (2,27,33). In addition, even individuals performing all their exercise in one or two sessions per week like “weekend warriors” appear to have decreased risk of mortality (27). By contrast, whether domestic physical activities convey health benefits appears controversial (33,36). This discrepancy may be partially because sports and exercises offer more aerobic activity. Thus, it may be most practical to recommend leisure-time physical activities to achieve health benefits.

Some limitations of our study need to be addressed. First, estimates of lifetime risks of CVD and total cancer should be carefully interpreted, as they may be to some degree confounded by other risk factors, such as smoking and diet, although we showed similar patterns within strata of smoking and healthy diet score. Nonetheless, these estimates of lifetime risk may be helpful from a policy perspective to determine where public health resources should be allocated. Second, physical activity levels were measured via a questionnaire and are subject to measurement error. Misclassification of physical

activity would tend to attenuate the estimated difference in lifetime risks between active and inactive adults. Third, as pointed out earlier, estimates of lifetime risk are subject to birth cohort effects and therefore can change over time. Fourth, the estimates of lifetime risk that we present are conditional on survival to the baseline ARIC survey without the event of interest and are computed to age 85 yr. Fifth, we used data on physical activity only at baseline. Thus, we cannot negate the possibility that changes of physical activity during follow-up might have affected our results. Finally, we estimated the lifetime risk of total cancer but not site-specific cancers because site-specific cancer data are not available yet in ARIC. Physical activity may be associated with a lower lifetime risk of certain cancers, such as colorectal and breast cancer. Thus, further studies will be needed for the association between physical activity and lifetime risks of site-specific cancers.

CONCLUSION

In conclusion, in the prospective population-based ARIC cohort, the WHO-recommended level of physical activity was

associated with lower lifetime risk of CVD, but not total cancer, compared with intermediate or poor levels of activity.

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The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

The authors have no conflicts of interest relevant to this article to disclose. The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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