

Impact of walking on life expectancy and lifetime medical expenditure: the Ohsaki Cohort Study

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ABSTRACT

Objective: People who spend a longer time walking have lower demands for medical care. However, in view of their longer life expectancy, it is unclear whether their lifetime medical expenditure increases or decreases. The present study examined the association between time spent walking, life expectancy and lifetime medical expenditure.

Method: The authors followed up 27 738 participants aged 40–79 years and prospectively collected data on their medical expenditure and survival covering a 13-year-period. Participants were classified into those walking <1 and ≥1 h per day. The authors constructed life tables and estimated the life expectancy and lifetime medical expenditure from 40 years of age using estimate of multiaadjusted mortality and medical expenditure using a Poisson regression model and linear regression model, respectively.

Results: Participants who walked ≥1 h per day have a longer life expectancy from 40 years of age than participants who walked <1 h per day. The multiaadjusted life expectancy for those who walked ≥1 h per day was 44.81 years, significantly lower by 1.38 years in men ($p=0.0073$) and 57.78 years in women, non-significantly lower by 1.16 years in women ($p=0.2351$). In addition to their longer life expectancy, participants who walked ≥1 h per day required a lower lifetime medical expenditure from 40 years of age than participants who walked <1 h per day. The multiaadjusted lifetime medical expenditure for those who walked ≥1 h per day was £99 423.6, significantly lower by 7.6% in men ($p=0.0048$) and £128 161.2, non-significantly lower by 2.7% in women ($p=0.2559$).

Discussion: Increased longevity resulting from a healthier lifestyle does not necessarily translate into an increased amount of medical expenditure throughout life. Encouraging people to walk may extend life expectancy and decrease lifetime medical expenditure, especially for men.

INTRODUCTION

Previous studies have agreed that a higher level of physical activity extends life expect-

ARTICLE SUMMARY

Article focus

- Medical expenditure per month was reduced when the amount of time spent walking was increased.
- Walking is associated with a decreased risk of mortality.
- In view of the increased life expectancy of those who walk longer, it is unclear whether lifetime medical expenditure increases or decreases as a result.

Key messages

- Lifetime medical expenditure from the age of 40 years for men and women who walked ≥1 h per day was reduced by 7.6% and 2.7%, respectively, in comparison with those who walked <1 h per day.
- Years of life added as a result of a healthy lifestyle did not necessarily translate into an increased amount of lifetime medical expenditure.

Strengths and limitations of this study

- This is the first study to investigate the association between walking, life expectancy and lifetime medical expenditure.
- We assessed walking using a simple questionnaire, in which we asked the participants to report only the time spent walking, and did not ask about walking pace, distance walked or any distinction between walking for exercise and other reasons.

ancy.^{1–4} Walking is part of a physically active lifestyle. Previous studies have indicated that a longer time spent walking,^{5–13} walking pace^{8 14–16} and a longer distance walked^{17 18} are significantly associated with a decreased risk of mortality.

We previously reported that medical expenditure per month was significantly reduced among those who spent a longer time walking, based on the same cohort dataset as that used here.¹⁹ Similar findings have been reported worldwide.^{20 21} However,

in view of the increased life expectancy of those who walk for a longer time, it is unclear whether lifetime medical expenditure increases or decreases as a result. In other words, the question to be answered here is whether a lifelong healthy lifestyle eventually increases lifetime medical expenditure because of extended life expectancy.

So far, only one study has examined the association between physical activity and lifetime costs.⁴ This revealed that people with a high physical activity level tended to live longer than people with a lower physical activity level, and that the former had lower lifetime medical costs than the latter. However, that study was only a simulation analysis based on assumed variations in the health and economic effects of active and sedentary lifestyles.

The objective of the present study was to examine the association between walking, life expectancy and lifetime medical expenditure using actual individual data derived from a population-based 13-year prospective observation period. The population comprised 27 738 Japanese adults aged 40–79 years living in the community who were free of any functional limitations or chronic conditions interfering with physical activity, with an accrued total of 285 342 person-years. This cohort study has been monitoring survival and medical care utilisation, and its costs, for all participants.^{19–22} Using this dataset, we constructed a life table to estimate life expectancy and lifetime medical expenditure according to the time spent walking.^{24–25}

MATERIALS AND METHODS

Study cohort

The present data were derived from the Ohsaki National Health Insurance (NHI) Cohort Study.^{19–22–25} We conducted a self-administered questionnaire survey of various lifestyle habits between October and December 1994 for all NHI beneficiaries aged 40–79 years who lived in the catchment area of Ohsaki Public Health Center, Miyagi Prefecture, northeastern Japan. Out of 54 996 eligible individuals, 52 029 (95%) responded.

We excluded 776 participants who had withdrawn from the NHI before 1 January 1995 because their cost data were not available. Thus, the remaining 51 253 participants formed the study cohort. The study protocol was approved by the Ethics Committee of Tohoku University School of Medicine. Participants who had returned the self-administered questionnaires and signed them were considered to have consented to participate.

For the present analysis, we excluded participants who had functional limitation or chronic conditions interfering with physical activity. Physical function status was assessed using the six-item measure of the Medical Outcomes Study Short-form General Health Survey.²⁶ Participants were excluded if they stated on the Medical Outcomes Study questionnaire that they were unable to perform moderate or vigorous activities (n=15 916). We

excluded participants who reported severe bodily pain (n=949), or any history of stroke (n=474), myocardial infarction (n=585) or arthritis (n=2176). We also excluded those who died within the first year (n=174) or did not provide complete responses in the walking status questionnaire (n=3241). Thus, a total of 27 738 participants (15 521 men and 12 217 women) remained. These participants were apparently healthy enough to walk for as long as they wished.

Time spent walking

The self-administered questionnaire included items on time spent walking. Time spent walking was assessed through the subject's response to the question, 'About how much time do you walk per day on average?' The participants were asked to choose one of three answers: '1 h or more,' '30 min—1 h' or '30 min or less.' In Japan, the Ministry of Health, Labour and Welfare recommended to walk ≥ 1 h per day in Exercise and Physical Activity Reference for Health Promotion 2006. Then, we divided the participants into two groups according to the time spent walking daily: < 1 h and ≥ 1 h. We had previously evaluated and reported the validity of self-reported time spent walking.^{5–19–27} This validation study had indicated that self-reported walking time was reasonably reproducible and sufficiently valid for studying the health effects of walking.

Health-insurance system in Japan

Details of the Japanese NHI system have been described previously.^{22–28–29} Briefly, everyone living in Japan is required to enrol in a health-insurance system. The NHI covers 35% of the Japanese population, mainly farmers, self employed or retired people. The NHI covers almost all medical treatment, including diagnostic tests, medication, surgery, supplies and materials, physicians and other personnel costs, inpatient care and most dental treatment. It covers treatment by physicians and nurses but not that by other professionals such as home health aides. Payment to medical providers is made on a fee-for-service basis, where the price of each service is determined by a uniform national fee schedule.

When a participant withdraws from the NHI system because of death, emigration or employment, the withdrawal date and its reason are coded in the NHI withdrawal history files. We recorded any mortality or migration by reviewing the NHI withdrawal history files and collected data on the death of participants by reviewing the death certificates filed at Ohsaki Public Health Center. We thus followed up the participants and prospectively collected data on medical care utilisation and its costs for all individuals in the cohort from 1 January 1995 to 31 December 2007. Study participants (16.3%) were lost to follow-up, so their vital status was unknown.

Statistical analysis

Using the Ohsaki NHI cohort database, we estimated mortality and medical expenditure for individual age

groups, and for the categories of time spent walking, for both men and women. We divided age into the following groups: 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84 and ≥ 85 years. The multiadjusted mortalities for each age category were estimated from a Poisson regression model based on person-years and the number of deaths from 1996 until 2007. The dependent variable was mortality, and the independent variables were age groups, categories of time spent walking and the following covariates: smoking status (current and past smoker, or never smoker), alcohol consumption (current drinker consuming 1–499 g/week, current drinker consuming ≥ 450 g/week, or never and past drinker), body mass index (BMI: < 21 kg/m², 21–24.9 kg/m² or ≥ 25 kg/m²), self-rated health (good or not good), sports and physical activity (≥ 3 h/week or < 3 h/week), history of hypertension disease (presence or absence), history of diabetes mellitus (presence or absence), history of cancer (presence or absence), history of liver disease (presence or absence) and history of kidney disease (presence or absence).¹⁹ The data on all covariates were obtained from a self-administered questionnaire. We estimated the mortality of participants aged ≥ 85 years by multiplying the estimated mortality for the 85–89-year age group by the ratio of mortality for the same age group relative to the mortality for ≥ 85 years from complete life tables for the year 2000, as there were few person-years for participants aged over 90 years in our dataset.³⁰

Because medical expenditure increases before death, we separately calculated medical expenditure for participants who survived through the index year and for those who died. The multiadjusted medical expenditure per year for survivors and decedents, respectively, was estimated for each of the age groups and the categories of time spent walking using a linear regression model adjusted for the above covariates.

The estimates of multiadjusted mortality and medical expenditure for each age group were used for estimating life expectancy and lifetime medical expenditure from 40 years of age. Life expectancy was calculated using Chiang's analytical method on the basis of the latest published complete life tables of Japan for the year 2000.^{23–30} Lifetime medical expenditure was estimated from the sum obtained by multiplying the static population in life table by the medical expenditure for survivors and the number of deaths in the life table by the increased medical expenditure owing to death, which was calculated by subtracting the medical expenditure in year of survivors from that in the period of 1 year before death. That is, the life expectancy (e_x) and lifetime medical expenditure (M_e) for each age group (x) were estimated using the numbers of survivors (l_x), deaths (d_x), static population (L_x), multiadjusted medical expenditure for survivors (a_y) and multiadjusted medical expenditure for the deceased (b_y) as follows:

\sum is the sum of $y \geq x$

$$e_x = \frac{\sum L_y}{l_x}$$

$$M_x = \frac{\sum (L_y a_y + d_y b_y)}{l_x}$$

The 95% CIs were estimated using a Monte Carlo simulation with 100 000 replicates based on a Poisson regression model and linear regression model. All analyses were used the SAS V.9.1 statistical software package.

We used a purchasing-power parity rate (British pounds to Japanese yen) of $\text{£}1.00 = \text{¥}140$.

RESULTS

After 13 years of follow-up, we observed 2936 deaths (2193 men and 743 women) among the 27 738 participants (15 521 men and 12 217 women). The mean medical expenditure per year for survivors who walked ≥ 1 h per day was $\text{£}1714.2$ in men and $\text{£}1621.4$ in women, significantly lower than for those who walked < 1 h per day (men: $\text{£}2064.3$, $p < 0.0001$; women: $\text{£}1878.6$, $p < 0.0001$). Also, the mean medical expenditure in the year of death for participants who walked ≥ 1 h per day was $\text{£}16 878.6$ in men and $\text{£}17 464.3$ in women, which was not significantly different from those who walked < 1 h per day (men: $\text{£}16 650.0$, $p = 0.7315$; women: $\text{£}17 742.9$, $p = 0.8330$).

Baseline characteristics in terms of categories for time spent walking

Table 1 shows the baseline characteristics of the study participants according to the categories of time spent walking for men and women, respectively.

As compared with those who walked < 1 h per day, participants who walked ≥ 1 h per day were less likely to be smokers and obese. Self-reported histories of hypertension, diabetes mellitus and liver disease were all significantly less prevalent in those who walked ≥ 1 h per day.

Mortality in terms of categories for time spent walking

Figure 1A (for men) and Figure 1B (for women) show the multiadjusted mortality (per 1000) in each of the age groups according to the categories of time spent walking.

In men in each age group, the multiadjusted mortality was lower in participants who walked ≥ 1 h per day than in those who walked < 1 h per day. In women in all age groups except for the aged 40–44 and 45–49 year groups, the multiadjusted mortality was lower in participants who walked ≥ 1 h per day than in those who walked < 1 h per day.

Table 1 Baseline characteristics by time-spent-walking categories in 27 738 participants

	Men			Women		
	Time spent walking		p Value*	Time spent walking		p Value*
	<1 h	≥1 h		<1 h	≥1 h	
No of subjects	7363	8158	0.2784	6303	5914	0.0714
Mean (SD) age	57.4 (10.6)	57.2 (10.2)		57.9 (10.1)	57.6 (9.7)	
Smoking status (%)						
Current and past smoker	81.9	79.8	0.0011	12.6	9.9	<0.0001
Never smoker	18.1	20.2		87.5	90.1	
Alcohol drinking (%)						
Never and past drinker	26.5	25.1	0.1117	74.7	75.4	0.1380
Current drinker, 1–449 g/week	61.3	62.2		24.3	23.9	
Current drinker, ≥450 g/week	12.2	12.8		1.1	0.7	
Body mass index (%)						
<21 kg/m ²	18.5	20.5	<0.0001	18.6	19.4	0.0019
21–24.9 kg/m ²	53.3	55.8		50.7	52.9	
≥25 kg/m ²	28.3	23.7		30.7	27.7	
Self-rated health (%)						
Good	73.1	79.3	<0.0001	72.5	78.2	<0.0001
Not good	26.9	20.7		27.5	21.8	
Sports and physical activity (%)						
≥3 h/week	13.2	18.7	<0.0001	10.7	16.6	<0.0001
<3 h/week	86.8	81.3		89.3	83.4	
History of hypertension (%)						
Presence	21.5	18.6	<0.0001	24.2	20.1	<0.0001
Absence	78.5	81.4		75.8	79.9	
History of diabetes mellitus (%)						
Presence	7.4	4.8	<0.0001	5.1	3.2	<0.0001
Absence	92.6	95.2		94.9	96.8	
History of cancer (%)						
Presence	2.1	1.8	0.2563	2.8	2.8	0.9032
Absence	97.9	98.2		97.2	97.2	
History of liver disease (%)						
Presence	6.9	5.7	0.0013	3.7	2.9	0.0223
Absence	93.1	94.4		96.3	97.1	
History of kidney disease (%)						
Presence	2.9	2.7	0.3493	3.6	2.7	0.0049
Absence	97.1	97.3		96.4	97.3	

*p Values were calculated using the χ^2 test.

Table 2 shows the mortality ratio with 95% CIs according to the categories of time spent walking. In men, the multiaadjusted mortality ratio for participants who walked ≥1 h per day was significantly lower than that for participants who walked <1 h per day (0.90, 95% CI 0.82 to 0.98, $p=0.0153$). In women, the multiaadjusted mortality ratio for participants who walked ≥1 h per day was non-significantly lower than that for participants who walked <1 h per day (0.95, 95% CI 0.82 to 1.10, $p=0.4693$).

Life expectancy and lifetime medical expenditure in terms of time spent walking

Table 3 shows the life expectancy and lifetime medical expenditure from 40 years of age with 95% CIs according to the categories of time spent walking.

In men, the multiaadjusted life expectancy of those who walked ≥1 h per day was 44.81 years (95% CI 43.66 to

45.94), which was significantly longer by 1.38 years ($p=0.0073$) than for those who walked <1 h per day (43.43 years; 95% CI 42.39 to 44.41). In women, the same results were observed, although the differences did not reach statistical significance.

In spite of their longer life expectancy, their lifetime medical expenditure from 40 years of age was significantly lower in men and non-significantly lower in women. The multiaadjusted lifetime medical expenditure for participants who walked ≥1 h per day was £99 423.6 (95% CI 92 515.9 to 106 694.7), significantly lower by 7.6% ($p=0.0048$) than for those who walked <1 h per day (£107 544.2; 95% CI 101 234.0 to 114 044.6). In women, the multiaadjusted lifetime medical expenditure for participants who walked ≥1 h per day was £128 161.2 (95% CI 111 335.0 to 148 494.7), non-significantly lower by 2.7% ($p=0.2559$) than for

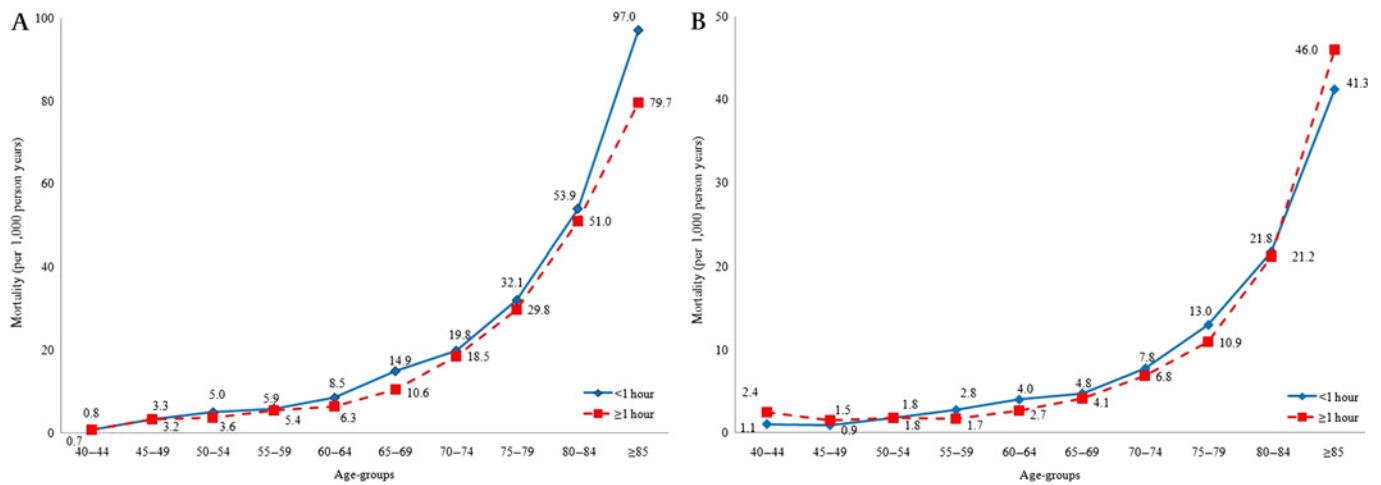


Figure 1 Multiadjusted mortality by time-spent-walking categories in each age group in (A) men and (B) women.

those who walked <1 h per day (£131 766.8; 95% CI 115 902.4 to 150 714.3).

DISCUSSION

The present results indicate that the multiadjusted lifetime medical expenditure from the age of 40 years for those who walked ≥1 h per day was significantly lower by 7.6% in men and non-significantly lower by 2.7% in women than for those who walked <1 h per day. This decrease in lifetime medical expenditure was observed in spite of a longer life expectancy (1.38 years for men and 1.16 years for women) among those who walked ≥1 h per day. Thus, a healthy lifestyle not only extended longevity but also decreased the amount of lifetime medical expenditure, especially men.

We observed statistically significant differences for men but not for women. Although the differences did not reach statistical significance, the same results were observed for women. The reason why the impact of walking was smaller in women than in men was unknown. In women, other factors such as obesity and postmenopausal change might have a stronger impact on life expectancy and lifetime medical expenditure than walking.

Comparison with other studies

Four studies have addressed the association between physical activity level and life expectancy.¹⁻⁴ Additionally, studies investigating associations between time spent walking,⁵⁻¹³ or distance walked^{17 18} and mortality have consistently shown that participants who have a higher

physical activity have a longer life expectancy and lower mortality than participants who have a lower physical activity. Only one study has reported the association between physical activity and lifetime medical expenditure.⁴ In a simulation study, Keeler *et al* demonstrated that if participants with a sedentary lifestyle had exercised regularly, the additional exercise would have increased their life expectancy by 300 days and saved £1900 in lifetime costs. Even though there is a difference between physical activity and walking, this result is consistent with the present finding that participants who walked ≥1 h per day lived longer and had a lower lifetime medical expenditure.

We previously calculated life expectancy and lifetime medical expenditure in relation to smoking and BMI from age 40 years using the same dataset as that for the present study.²⁴ The results indicated that lifetime medical expenditure was lower for smokers than for non-smokers, reflecting the 3.5-year shorter life expectancy of smokers.²⁴ On the other hand, lifetime medical expenditure was higher for participants who were obese (BMI≥30.0) than for those who were of normal weight (18.5≤BMI<25.0), even though the former lived 2 years less than the latter (Nagai M, Kuriyama S, Kakizaki M, *et al*. Impact of obesity, overweight and underweight on life expectancy and lifetime medical expenditures. *Popul Health Metr*; under review). In fact, both smokers and obese participants had a shorter life expectancy than non-smokers and normal-weight participants, whereas their lifetime medical expenditure was conversely

Table 2 Mortality ratio for time-spent-walking categories in 27 738 participants

Time spent walking	Univariate		Multiadjusted*	
	Mortality ratio (95% CI)	p Value	Mortality ratio (95% CI)	p Value
Men	<1 h	1.00	1.00	
	≥1 h	0.87 (0.80 to 0.94)	0.90 (0.82 to 0.98)	0.0153
Women	<1 h	1.00	1.00	
	≥1 h	0.89 (0.77 to 1.03)	0.95 (0.82 to 1.10)	0.4693

*Adjusted for age groups, smoking status, alcohol drinking, body mass index, self-rated health, sports and physical activity, and history of hypertension, diabetes mellitus, cancer, liver disease and kidney disease.

Table 3 Life expectancy and lifetime medical expenditure at age 40 years for time-spent-walking categories in 27 738 participants

	Time spent walking	Univariate			Multiadjusted*		
		Estimate	95% CI	p Value	Estimate	95% CI	p Value
Men	Life expectancy (years) at age 40 years						
	<1 h	42.41	41.45 to 43.26	0.0004	43.43	42.39 to 44.41	0.0073
	≥1 h	44.19	43.15 to 45.19		44.81	43.66 to 45.94	
	Lifetime medical expenditure (£) at age 40 years						
	<1 h	107 023.2	101 093.6 to 113 066.3	<0.0001	107 544.2	101 234.0 to 114 044.6	0.0048
	≥1 h	94 402.1	87 812.3 to 101 248.0		99 423.6	92 515.9 to 106 694.7	
	Lifetime medical expenditure (£) at age 40 years						
Women	Life expectancy (years) at age 40 years						
	<1 h	52.25	49.79 to 54.92	0.0569	56.62	53.17 to 60.62	0.2351
	≥1 h	54.25	51.38 to 57.48		57.78	54.02 to 62.22	
	Lifetime medical expenditure (£) at age 40 years						
	<1 h	123 553.0	111 619.5 to 137 549.6	0.0644	131 766.8	115 902.4 to 150 714.3	0.2559
	≥1 h	115 896.0	102 406.6 to 131 792.1		128 161.2	111 335.0 to 148 494.7	

*Adjusted for age groups, smoking status, alcohol drinking, body mass index, self-rated health, sports and physical activity, and history of hypertension, diabetes mellitus, cancer, liver disease and kidney disease as same as table 2.

increased. These differences could be explained by the impact of these risk factors on quality of life. Using prospective data for 16 176 adult Caucasians in the USA,³¹ Reuser *et al* estimated life expectancy and years of life with and without activities of daily-living disability in relation to smoking and BMI, respectively. The results indicated that smoking decreased both life expectancy and years of life with activities of daily-living disability, whereas obesity decreased the former but increased the latter, thus leading to the conclusion that ‘smoking kills, and obesity disables’. Reuser’s conclusion is concordant with the impact of walking on life expectancy and lifetime medical expenditure. Physical activity decreases not only mortality but also disability,^{5–13 17 18 32} leading to lower medical expenditure.³³ For instance, walking has been significantly associated with a lower risk of cardiovascular disease,⁷ stroke,³⁴ coronary heart disease,^{35 36} type 2 diabetes³⁷ and hypertension.³⁸ Consequently, walking also reduces expenditure on medication needed for these conditions.³⁹

Strengths and limitations

This is the first study to have investigated the association between walking, life expectancy and lifetime medical expenditure. A major strength of this study was that we collected individual data on medical expenditure based on a cohort study of survival and medical-care utilisation, and its cost, for all participants,^{19 22 24 28} and the NHI covers almost all medical treatment in Japan. Second, we conducted a 13-year prospective observation of 27 738 Japanese adults aged 40–79 years living in the community who were free of any functional limitations or chronic conditions interfering with physical activity, with an accrued total of 285 342 person-years. Third, in order to reduce bias or reverse causation in that people did not walk because of functional limitations that also required

medical expenditure, we excluded participants who, at the baseline, reported limited physical function or conditions interfering with physical activity. Additionally, to control for confounders, we also included various covariates in our Poisson regression model and linear regression model.

On the other hand, several limitations should also be considered. First, we assessed walking using a simple questionnaire in which we asked the participants to report only the time spent walking and did not ask about walking pace, distance walked or any distinction between walking for exercise and other reasons. Second, a longer time spent walking may be a reflection of performing more vigorous activity, making it difficult to distinguish the impact of walking from other types of physical activity. However, the present result did not change after multivariate adjustment.

Conclusions and policy implication

In summary, lifetime medical expenditure was shown to be decreased in participants who walked ≥1 h per day, despite the fact that they lived longer. Increased longevity resulting from a healthier lifestyle did not necessarily translate into an increased amount of medical expenditure throughout life. However, in the present study, around 50% of study participants walk <1 h per day. To increase their walking time, the recommendation of walking with a pedometer may be useful.⁴⁰ An increase in walking time at the population level would bring about a tremendous change in people’s health and medical cost. A campaign to encourage people to walk for longer and a program to make walking environments safer and more pleasant should be implemented. This intervention may extend life expectancy without apparently increasing lifetime medical expenditure, especially for men.

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Competing interests None.

Patient consent Obtained.

Ethical approval Ethics approval was provided by the Ethics Committee of Tohoku University School of Medicine.

Contributors All authors contributed to the design of the study. MN, SK, MK, KO-M, TS and IT carried out the data collection. MN, SK, AH, MK and SH carried out the data analysis. MN, MK, KO-M, TS, AH, MK and SH wrote the report. SK and IT carried out a critical revision of the manuscript. All authors approved the final version of the report for submission.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	p. 1, 3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	p. 3, 4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	p. 5
Objectives	3	State specific objectives, including any prespecified hypotheses	p. 5, 6
Methods			
Study design	4	Present key elements of study design early in the paper	p. 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p. 7-9
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	p. 7-8
		(b) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p. 8-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	p. 8-11
Bias	9	Describe any efforts to address potential sources of bias	p. 10
Study size	10	Explain how the study size was arrived at	p. 8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p. 10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	p. 9-11
		(b) Describe any methods used to examine subgroups and interactions	-
		(c) Explain how missing data were addressed	-
		(d) If applicable, explain how loss to follow-up was addressed	p. 8, 9
		(e) Describe any sensitivity analyses	p. 9-11-
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	p. 7, 8 p. 7, 8 -
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	p. 12 - p. 12
Outcome data	15*	Report numbers of outcome events or summary measures over time	-
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	p. 13, 14 p. 8, 10 -
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	p. 15
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p. 15-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	p. 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p. 20

* Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.