PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	**Impact of Walking on Life Expectancy and Lifetime Medical Expenditure: The Ohsaki Cohort Study**
AUTHORS	Nagai, Masato; Kuriyama, Shinichi; Kakizaki, Masako; Ohmori-Matsuda, Kaori; Sone, Toshimasa; Hozawa, Atsushi; Kawado, Miyuki; Hashimoto, Shuji; Tsuji, Ichiro

VERSION 1 - REVIEW

REVIEWER	***Julien Dumurgier*** INSERM U708, Neuroepidemiology, La Pitié-Salpêtrière, Paris, France. No competing interests.
REVIEW RETURNED	26-Jul-2011

THE STUDY	A follow-up of 13 years is mentionned, I think it is rather 12 years (january 1 1995 through december 31 2007) ? There is no mention of lost to follow-up or missing data during the follow-up. Was the vital status known for all the 27,738 participants at the end of the study ? Hypertension has been shown to be associated with poorer motor function and lower walking speed. The prevalence of hypertension appears to be low in the study population (around 20% for subjects aged 40 years and over). Is it a specificity of Japanese population ? Was a measurment of blood pressure used to define the hypertension ? The variable "time spent walking" has been used as a dichotomized variable (<1 hour versus > 1 hour). This choice is not discussed. Does other coding have been considered (maybe sex-dependant) ?
RESULTS & CONCLUSIONS	Age is an important variable associated to the gait. In table 1, the mean age by categories should be added. My major concern is about the differences observed between sex. Results are significant only for men, not for women. This point has to be clearly mentionned in the abstract and in the discussion, and has to be discussed. Has an analysis been performed in the overall population ? In the discussion, it is mentionned that walking speed has been associated with a lower risk of cardiovascular disease. It is true, but things are maybe more complex, and this relation may be bidirectional : cardiovascular disease may lead to poorer motor performance, partly explained by cerebrovascular aging and brain white matter hypersignal.

REVIEWER	***Ramon Luengo-Fernandez DPhil*** Senior Researcher Health Economics Research Centre Department of Public Health University of Oxford UK
REVIEW RETURNED	28-Jul-2011

GENERAL COMMENTS	I found this study very interesting, especially the testing of the assumption to whether increases in life expectancy were associated with increased healthcare costs. My comments to the authors are: 1) Abstract, results section. The authors should make clear in the abstract that the life expectancy and lifetime medical expenditure relate to people who were 40 years of age. As it stands, it appears to suggest that was the average life expectancy for all participants in the study (some of which were aged 79 years). 2) Methods, page 9, Time spent walking. The authors should provide more details in this crucial variable, and more details on how participants were categorized into the <1 or > 1 hour. For example, as a walker myself, I walk over 2 hours daily during the weekday, but less than 1 hour during the weekends. How would I be categorized in this study? 3) Methods, page 11. For the covariates, was history of stroke, hypertension, diabetes etc… established from self-report or from data obtained from the NHI, or any other medical database? In addition, it is unclear why the sentence on covariates is referenced. The authors should explicitly report why this reference is found to be relevant here. 4) Results, page 13. It would be interesting to know in which sectors of the healthcare system were costs incurred, e.g. visits to the doctor, hospitalisations, medications, etc… This would provide valuable information as to whether there were important differences in the types of healthcare resources consumed. E.g. did walkers consume less of everything, or were the savings due to walkers avoiding hospitalisations for major events (e.g. MI or stroke)? 5) Results, page 15. As with the abstract, the authors should make clear in the abstract that the life expectancy and lifetime medical expenditure relate to people who were 40 years of age. 6) Discussion, page 16, 1st paragraph. The authors should report that the 2.7% decrease in medical expenditures found in female walkers was statistically non-significant. 7) Discussion. The authors should report some of the implications of their research. With around 50% of the study sample in this study walking less than 1 hour a day, how could walking levels increase, what are the barriers to walking, etc… 8) Discussion. The authors did not touch in their discussion why they found statistically significant differences for men but not for women. Some discussion around this area should be provided.

VERSION 1 – AUTHOR RESPONSE

Comments from Dr. Julien Dumurgier
1. A follow-up of 13 years is mentioned, I think it is rather 12 years (January 1 1995 through December 31 2007) ?

[Authors' reply]
Thank you for your suggesting.
A follow-up of 13 years is correct.
1 year follow-up: January 1 1995 through December 31 1995
2 year follow-up: January 1 1995 through December 31 1996
3 year follow-up: January 1 1995 through December 31 1997

12 year follow-up: January 1 1995 through December 31 2006
13 year follow-up: January 1 1995 through December 31 2007

2. There is no mention of lost to follow-up or missing data during the follow-up. Was the vital status known for all the 27,738 participants at the end of the study ?

[Authors' reply]
Thank you for your important comment and suggesting the better terms.
We described about lost follow-up in materials and methods section.

[Changes in the revised manuscript]
[Page 9, Lines 17-18]
Study participants (16.3%) were lost to follow-up, thus their vital status was unknown..

3. Hypertension has been shown to be associated with poorer motor function and lower walking speed. The prevalence of hypertension appears to be low in the study population (around 20% for subjects aged 40 years and over). Is it a specificity of Japanese population ? Was a measurment of blood pressure used to define the hypertension ?

[Authors' reply]
Thank you very much for your pertinent and important comment.
Mean age of study participants was 57.3 years in men and 57.7 years in women.
In the 1995 National Nutrition Survey conducted by the Ministry of Health Welfare, Japan, the prevalence of hypertension in men and women was 25.6% and 18.6% in aged 50-59 years, respectively.
(We started follow-up in 1995.)
Then, we consider that the prevalence of hypertension in our participants is appropriate for Japanese population.

We defined hypertension by self-reported history of hypertension.
We describe it in materials and methods section.

[Changes in the revised manuscript]
[Page 10, Lines 15-16]
The data of all covariates was obtained from self-administered questionnaire.

4. The variable "time spent walking" has been used as a dichotomized variable (<1 hour versus > 1 hour). This choice is not discussed. Does other coding have been considered (maybe sex-dependant) ?

[Authors' reply]
Thank you for suggesting the better terms.
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 hour or more" "30 minutes - 1 hour" or "30 minutes or less". In Japan, the Ministry of Health, Labour and Welfare recommended to walk ≥1 hour per day in Exercise and Physical Activity Reference for Health Promotion 2006.
(http://www.nih.go.jp/eiken/programs/pdf/epar2006.pdf)
Then, we divided the participants into two groups according to the time spent walking daily: <1 hour and ≥1 hour.

[Changes in the revised manuscript]
[Page 8, Lines 9-16]
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 hour or more" "30 minutes - 1 hour" or "30 minutes or less". In Japan, the Ministry of Health, Labour and Welfare recommended to walk ≥1 hour 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 hour and ≥1 hour.

5. Age is an important variable associated to the gait. In table 1, the mean age by categories should be added.
[Authors' reply]
Thank you very much for your pertinent and important comments.
We added mean age in table 1.

[Changes in the revised manuscript]
Please see Table 1.

6. My major concern is about the differences observed between sex. Results are significant only for men, not for women. This point has to be clearly mentioned in the abstract and in the discussion, and has to be discussed. Has an analysis been performed in the overall population?

[Authors' reply]
Thank you for suggesting the better terms.
We clearly mentioned and discussed about non-significantly association in women in the abstract and the discussion sections.

We did not analyze in the overall population. Since both life expectancy and lifetime medical expenditure were entirely different between men and women, the impact of walking upon those two variable should be considered for men and women, separately.

[Changes in the revised manuscript]
[Page 3, Lines 17-20]
The multiadjusted life expectancy for those who walked ≥1 hour per day was 44.81 years, being significantly lower by 1.38 years in men (p=0.0073) in men and 57.78 years in women, being non-significantly lower by 1.16 years in women (p=0.2351).

[Page 4, Lines 2-5]
The multiadjusted lifetime medical expenditure for those who walked ≥1 hour per day was £99,423.6, being significantly lower by 7.6% in men (p=0.0048) and £128,161.2, being non-significantly lower by 2.7% in women (p=0.2559).

[Page 4, Lines 8-10]
Encouraging people to walk may extend life expectancy and decrease lifetime medical expenditure, especially men.

[Page 14, Lines 19- Page 15, Lines 3]
In men, the multiadjusted life expectancy of those who walked ≥1 hour per day was 44.81 years (95% CI; 43.66-45.94), which was significantly longer by 1.38 years (p=0.0073) than for those who walked <1 hour per day (43.43 years; 95% CI; 42.39-44.41). In women, the same results were observed, although the differences did not reach statistical significance.

[Page 15, Lines 5- 12]
The multiadjusted lifetime medical expenditure for participants who walked ≥1 hour per day was £99,423.6 (95% CI; 92,515.9-106,694.7), being significantly lower by 7.6% (p=0.0048) than for those who walked <1 hour per day (£107,544.2; 95% CI; 101,234.0-114,044.6). In women, the multiadjusted lifetime medical expenditure for participants who walked ≥1 hour per day was £128,161.2 (95% CI; 111,335.0-148,494.7), being non-significantly lower by 2.7% (p=0.2559) than for those who walked <1 hour per day (£131,766.8; 95% CI; 115,902.4-150,714.3).

[Page 16, Lines 1-4]
The present results indicate that multiadjusted lifetime medical expenditure from the age of 40 years for those who walked ≥1 hour 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 hour per day.

[Page 16, Lines 7-8]
Thus, a healthy lifestyle not only extended longevity, but also decreased the amount of lifetime medical expenditure, especially men.

[Page 16, Lines 9-14]
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 stronger impact on life expectancy and lifetime medical expenditure than walking.

[Page 20, Lines 4-5]
This intervention may extend life expectancy without apparently increasing lifetime medical expenditure, especially men.

7. In the discussion, it is mentioned that walking speed has been associated with a lower risk of cardiovascular disease. It is true, but things are maybe more complex, and this relation may be bidirectional : cardiovascular disease may lead to poorer motor performance, partly explained by cerebrovascular aging and brain white matter hypersignal.

[Authors' reply]
Thank you for suggesting the better terms.
We agreed that the association between walking speed and risk of cardiovascular disease is

bidirectional. However, we exclude the participants who have history of cardiovascular disease from study participants. Then, the reverse causation due to cardiovascular disease may not remain in our study.

Comments from Ramon Luengo-Fernandez DPhil

1. Abstract, results section. The authors should make clear in the abstract that the life expectancy and lifetime medical expenditure relate to people who were 40 years of age. As it stands, it appears to suggest that was the average life expectancy for all participants in the study (some of which were aged 79 years).

[Authors' reply]
Thank you very much for your pertinent and important comments.
We described more clearly about the life expectancy and lifetime medical expenditure in Abstract.

[Changes in the revised manuscript]
[Page 3, Lines 16-Page 4, Lines 5]
Participants who walked ≥1 hour per day have longer life expectancy from 40 years of age than participants who walked <1 hour per day. The multiadjusted life expectancy for those who walked ≥1 hour per day was 44.81 years, being significantly lower by 1.38 years in men (p=0.0073) in men and 57.78 years in women, being non-significantly lower by 1.16 years in women (p=0.2351). In spite of their longer life expectancy, participants who walked ≥1 hour per day required lower lifetime medical expenditure from 40 years of age than participants who walked <1 hour per day. The multiadjusted lifetime medical expenditure for those who walked ≥1 hour per day was £99,423.6, being significantly lower by 7.6% in men (p=0.0048) and £128,161.2, being non-significantly lower by 2.7% in women (p=0.2559).

2. Methods, page 9, Time spent walking. The authors should provide more details in this crucial variable, and more details on how participants were categorized into the <1 or > 1 hour. For example, as a walker myself, I walk over 2 hours daily during the weekday, but less than 1 hour during the weekends. How would I be categorized in this study?

[Authors' reply]
Thank you for your pertinent and important comments.
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 hour or more" "30 minutes - 1 hour" or "30 minutes or less". As mentioned method section, we had previously evaluated and reported the validity of self-reported time spent walking (Tsubono et al. J Epidemiol 2002: 12; 305-309). We did not ask walking time per day separately divided into weekday and weekends. In Japan, the Ministry of Health, Labour and Welfare recommended to walk ≥1 hour per day in Exercise and Physical Activity Reference for Health Promotion 2006. (http://www.nih.go.jp/eiken/programs/pdf/epar2006.pdf in English)
Then, we divided the participants into two groups according to the time spent walking daily: <1 hour and ≥1 hour. We describe above sentence in materials and methods section.

[Changes in the revised manuscript]
[Page 8, Lines 9-16]
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 hour or more” “30 minutes - 1 hour” or “30 minutes or less”. In Japan, the Ministry of Health, Labour and Welfare recommended to walk ≥1 hour 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 hour and ≥1 hour.

3. Methods, page 11. For the covariates, was history of stroke, hypertension, diabetes etc… established from self-report or from data obtained from the NHI, or any other medical database? In addition, it is unclear why the sentence on covariates is referenced. The authors should explicitly report why this reference is found to be relevant here.

[Authors’ reply]
Thank you very much for your pertinent and important comment.
The data of all covariates was obtained from self-administered questionnaire. We mentioned it in the materials and methods section.

We used the same covariate and category to keep consistency with reference because this previous study is the same data set with the present study. We already reported the association between time spent walking and medical expenditure per month. Present study was an extension of the previous study.

[Changes in the revised manuscript]
[Page 10, Lines 15-16]
The data of all covariates was obtained from self-administered questionnaire.

4. Results, page 13. It would be interesting to know in which sectors of the healthcare system were costs incurred, e.g. visits to the doctor, hospitalisations, medications, etc… This would provide valuable information as to whether there were important differences in the types of healthcare resources consumed. E.g. did walkers consume less of everything, or were the savings due to walkers avoiding hospitalisations for major events (e.g. MI or stroke)?.

[Authors’ reply]
Thank you very much for your pertinent and important comments.
We would like to show the types of healthcare resources consumed. However, we have information about only inpatient care and outpatient care. Although the National Health Insurance covers almost all medical treatment, we can not obtain its types of healthcare resources consumed.

5. Results, page 15. As with the abstract, the authors should make clear in the abstract that the life expectancy and lifetime medical expenditure relate to people who were 40 years of age.

[Authors’ reply]
Thank you for your pertinent and important comments.
We describe more clearly about your suggestion.

[Changes in the revised manuscript]
[Page 3, Lines 16-20]
Participants who walked ≥1 hour per day have longer life expectancy from 40 years of age than participants who walked <1 hour per day. The multiadjusted life expectancy for those who walked ≥1 hour per day was 44.81 years, being significantly lower by 1.38 years in men (p=0.0073) in men and 57.78 years in women, being non-significantly lower by 1.16 years in women (p=0.2351).

[Page 3, Lines 20-Page 4, Lines 5]
In spite of their longer life expectancy, participants who walked ≥1 hour per day required lower lifetime

medical expenditure from 40 years of age than participants who walked <1 hour per day. The multiadjusted lifetime medical expenditure for those who walked ≥1 hour per day was £99,423.6, being significantly lower by 7.6% in men (p=0.0048) and £128,161.2, being non-significantly lower by 2.7% in women (p=0.2559).

[Page 14, Lines 17- Page 15, Lines 3]
Table 3 shows 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 multiadjusted life expectancy of those who walked ≥1 hour per day was 44.81 years (95% CI; 43.66-45.94), which was significantly longer by 1.38 years (p=0.0073) than for those who walked <1 hour per day (43.43 years; 95% CI; 42.39-44.41). In women, the same results were observed, although the differences did not reach statistical significance.

[Page 15, Lines 4- 12]
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 multiadjusted lifetime medical expenditure for participants who walked ≥1 hour per day was £99,423.6 (95% CI; 92,515.9-106,694.7), being significantly lower by 7.6% (p=0.0048) than for those who walked <1 hour per day (£107,544.2; 95% CI; 101,234.0-114,044.6). In women, the multiadjusted lifetime medical expenditure for participants who walked ≥1 hour per day was £128,161.2 (95% CI; 111,335.0-148,494.7), being non-significantly lower by 2.7% (p=0.2559) than for those who walked <1 hour per day (£131,766.8; 95% CI; 115,902.4-150,714.3).

6. Discussion, page 16, 1st paragraph. The authors should report that the 2.7% decrease in medical expenditures found in female walkers was statistically non-significant.

[Authors' reply]
Thank you for suggesting the better terms.
We mentioned about non-significantly association in women in the discussion sections, 1st paragraph.

[Changes in the revised manuscript]
[Page 16, Lines 1- 4]
The present results indicate that multiadjusted lifetime medical expenditure from the age of 40 years for those who walked ≥1 hour 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 hour per day.

7. Discussion. The authors should report some of the implications of their research. With around 50% of the study sample in this study walking less than 1 hour a day, how could walking levels increase, what are the barriers to walking, etc…

[Authors' reply]
Thank you for your pertinent and important comments.
We describe about implication in discussion section.

[Changes in the revised manuscript]
[Page 19, Lines 18- Page 20, Lines 5]
However, in present study, around 50 % of study participants walks <1 hour per day. To increase their walking time, recommendation of walking with pedometer may be useful. An increase in walking time at the population level would bring about a tremendous change in people's health and medical cost. The campaign to encourage the people walk longer and program to make environment for people to walk more safely and pleasantly should be implemented. This intervention may extend life expectancy

without apparently increasing lifetime medical expenditure, especially men.

7. Discussion. The authors did not touch in their discussion why they found statistically significant differences for men but not for women. Some discussion around this area should be provided.

[Authors' reply]
Thank you for suggesting the better terms.
We discussed about non-significantly association in women in the discussion sections.

[Authors' reply]
[Page 16, Lines 9-14]
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 stronger impact on life expectancy and lifetime medical expenditure than walking.