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Relation of physical activity time to incident disability in community dwelling adults with or at risk of knee arthritis: prospective cohort study

Dorothy D Dunlop,[1] Jing Song,[1] Pamela A Semanik,[2] Leena Sharma,[1] Joan M Bathon,[3] Charles B Eaton,[4] Marc C Hochberg,[5] Rebecca D Jackson,[6] C Kent Kwoh,[7] W Jerry Mysiw,[6] Michael C Nevitt,[7 8] Rowland W Chang[1]

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[1]Institute for Public Health and Medicine Center for Healthcare Studies, Feinberg School of Medicine, Northwestern University, 750 Lakeshore Drive, Chicago, IL 60611, USA
[2]Rush University Medical Center, Chicago
[3]Columbia University College of Physicians and Surgeons, New York, NY, USA
[4]Brown University, Pawtucket, RI, USA
[5]University of Maryland, Baltimore, MD, USA
[6]Ohio State University, Columbus, OH, USA
[7]University of Arizona College of Medicine, Tucson, AZ, USA
[8]University of California at San Francisco, San Francisco, CA, USA
Correspondence to: D Dunlop
ddunlop@northwestern.edu

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- Research: Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study (*BMJ* 2013;347:f5577)
- Research: Training practitioners to deliver opportunistic multiple behaviour change counselling in primary care: a cluster randomised trial (*BMJ* 2013;346:f1191)
- Research: Effectiveness of physical activity promotion based in primary care: systematic review and meta-analysis of randomised controlled trials (*BMJ* 2012;344:e1389)
- Research: Effect of exercise referral schemes in primary care on physical activity and improving health outcomes: systematic review and meta-analysis (*BMJ* 2011;343:d6462)

STUDY QUESTION

Is objectively measured time spent in light intensity physical activity related to incident disability independent of moderate-vigorous activity time and other predictors of risk of disability in adults with or at risk of knee osteoarthritis?

SUMMARY ANSWER

Greater daily time spent in light intensity physical activities was significantly related to a reduced risk of developing disability and a reduced risk of disability progression, independent of the time spent in moderate or vigorous activities and other predictors of disability risk.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Physical activity guidelines recommend engaging in moderate-vigorous intensity physical activity, but whether that intensity is needed to reduce disability is not known. The findings of this study suggest that more time spent being physically active reduces the risk of disability even if the intensity of activity is not increased.

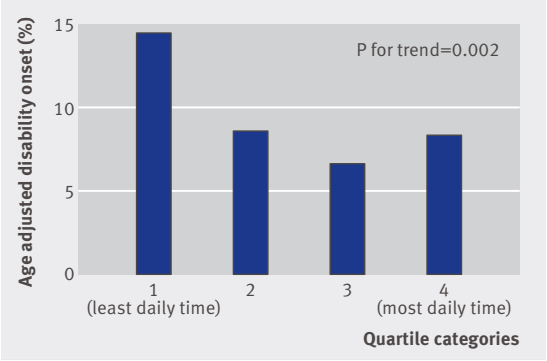
Participants and setting

We studied a cohort of 1680 community dwelling adults at risk for disability onset. These participants had no baseline disability in instrumental or basic activities of daily living, were aged 49 years or older, and had osteoarthritis of the knee or risk factors for knee osteoarthritis. The disability progression cohort included 1814 adults (1680 without baseline disability plus 134 with baseline mild/moderate disability).

Design, size, and duration

This was a prospective multisite cohort study with two year follow-up conducted in 2008-12 at Baltimore, Maryland; Columbus, Ohio; Pittsburgh, Pennsylvania; and Pawtucket, Rhode Island, USA. Participants came from a subcohort of the Osteoarthritis Initiative who were enrolled in an accelerometer monitoring substudy. Disability was ascertained from limitations in instrumental and basic activities of daily living at baseline and two years. The primary outcome was incident disability. The secondary outcome was progression of disability defined by a more severe level (no limitations or limitations in instrumental activities only, in one or two basic activities, or in three or more basic activities of daily living) at two years compared with baseline.

Age adjusted percentage of incident disability according to quartile categories of light physical activity



Main results

We documented 149 cases of new disability in instrumental or basic activities of daily living over two years of follow-up. Less incident disability and less disability progression were significantly related to increasing quartile categories of daily time spent in light intensity physical activities (disability onset hazard ratios: 1.00, 0.62, 0.47, and 0.58, P for trend=0.007; progression hazard ratios 1.00, 0.59, 0.50, and 0.53, P for trend=0.003), when controlled for moderate-vigorous activity time, socioeconomic factors (age, sex, race/ethnicity, education, income), and baseline health factors (comorbidities, depressive symptoms, obesity, smoking, lower extremity symptoms and function, and knee assessments: osteoarthritis severity, pain, symptoms, previous injury).

Bias, confounding, and other reasons for caution

These observational study findings may be influenced by reverse causation or confounded by factors associated with unmeasured baseline disability. These concerns are mitigated by restriction of analyses to people free of disability at baseline, assessment of subsequent disability status two years later, and control for baseline function, which is arguably a precursor of disability. The threshold used to identify light intensity activity may influence the strength of associations found.

Generalisability to other populations

The sample was composed of adults with or at high risk of developing knee osteoarthritis, which influences the generalisability of these results. However, the relation between light activity time and incident disability was independent of the severity of knee osteoarthritis, knee pain, and the presence of knee symptoms.

Study funding/potential competing interests

The National Institute for Arthritis and Musculoskeletal Diseases and the Falk Medical Trust funded this study. Publicly released Osteoarthritis Initiative data were funded through a public-private partnership comprising five National Institutes of Health contracts. Private funding partners include Merck Research Laboratories, Novartis Pharmaceuticals Corporation, GlaxoSmithKline, and Pfizer.

Physical capability in mid-life and survival over 13 years of follow-up: British birth cohort study

Rachel Cooper,[1] Bjørn Heine Strand,[2] Rebecca Hardy,[1] Kushang V Patel,[3] Diana Kuh[1]

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[1]MRC Unit for Lifelong Health and Ageing at UCL, London WC1B 5JU, UK
[2]Norwegian Institute of Public Health, N-0473 Oslo, Norway
[3]Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, USA
Correspondence to: R Cooper
rachel.cooper@ucl.ac.uk

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bmj.com
- News: Regular exercise increases brain's memory region in older women, Canadian study shows (*BMJ* 2014;348:g2672)
- Research: Objectively measured physical capability levels and mortality: systematic review and meta-analysis (*BMJ* 2010;341:c4467)

STUDY QUESTION

Are objective measures of physical capability in mid-life associated with all cause mortality?

SUMMARY ANSWER

Standing balance time, chair rise speed, and grip strength at the age of 53 are associated with all cause mortality rates over 13 years of follow-up.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Systematic reviews and meta-analyses have provided evidence of associations between better performance in objective tests of physical capability and lower all cause mortality rates in older people living in the community. The current study shows that, even in mid-life, objective assessment of physical capability can identify those people less likely to achieve a long and healthy life.

Participants and setting

Men and women from the MRC National Survey of Health and Development, a socially stratified sample of people born across England, Scotland, and Wales in March 1946 who have been followed up prospectively.

Design, size, and duration

The analysis included 2766 study participants whose physical capability had been assessed at age 53 (in 1999) and who were linked to the NHS central register for mortality notification. Using Cox proportional hazards regression models we tested the associations of each of the three individual measures of physical capability (grip strength, chair rise speed, and standing balance time), a composite physical capability score, and the number of tests participants were unable to perform with subsequent hazards of all cause mortality. Follow-up time was from March 1999 until confirmed death from any cause, emigration, or the end of March 2012. Adjustments were made for sex, body size, socioeconomic position, lifestyle factors, and health status.

Mortality rate and hazard ratio for mortality according to performance on tests of physical capability at age 53 (n=2766; 177 deaths)

	Mortality rate per 1000 person years (95% CI)	Adjusted HR for all cause mortality (95% CI)	
		Sex	All covariates*
Fifths of grip strength:			
Unable to do test†	18.63 (11.03 to 31.46)	5.84 (3.01 to 11.36)	4.80 (2.42 to 9.50)
1 (lowest)	8.01 (6.14 to 10.46)	2.42 (1.49 to 3.94)	1.98 (1.20 to 3.27)
2	4.37 (3.06 to 6.26)	1.32 (0.76 to 2.27)	1.27 (0.73 to 2.21)
3	3.77 (2.57 to 5.54)	1.13 (0.65 to 1.99)	1.10 (0.63 to 1.95)
4	4.37 (3.06 to 6.26)	1.32 (0.76 to 2.27)	1.29 (0.75 to 2.22)
5 (highest)	3.33 (3.06 to 6.26)	1.00	1.00
Fifths of chair rise speed:			
Unable to do test†	20.47 (14.47 to 28.94)	6.91 (4.02 to 11.90)	4.28 (2.41 to 7.60)
1 (lowest)	6.43 (4.72 to 8.77)	2.13 (1.27 to 3.59)	1.61 (0.94 to 2.76)
2	4.36 (3.03 to 6.28)	1.44 (0.83 to 2.51)	1.30 (0.74 to 2.28)
3	4.17 (2.82 to 6.18)	1.36 (0.77 to 2.41)	1.21 (0.68 to 2.16)
4	3.94 (2.74 to 5.67)	1.30 (0.75 to 2.26)	1.25 (0.72 to 2.19)
5 (highest)	3.04 (2.00 to 4.62)	1.00	1.00
Fifths of standing balance time:			
Unable to do test†	30.28 (21.53 to 42.59)	12.53 (7.16 to 21.91)	9.61 (5.32 to 17.39)
1 (lowest)	7.84 (5.92 to 10.37)	3.11 (1.84 to 5.25)	2.53 (1.48 to 4.33)
2	2.99 (1.86 to 4.81)	1.17 (0.61 to 2.23)	1.03 (0.54 to 1.98)
3	4.37 (3.14 to 6.09)	1.66 (0.96 to 2.87)	1.65 (0.95 to 2.88)
4	3.38 (2.25 to 5.09)	1.29 (0.71 to 2.36)	1.24 (0.68 to 2.27)
5 (highest)	2.79 (1.80 to 4.33)	1.00	1.00

*Sex, body size (height and BMI), socioeconomic position (occupational class and educational level attained), lifestyle factors (smoking status and leisure activity levels), and health status (cancer, cardiovascular disease, diabetes, severe respiratory symptoms).
†Unable to complete each test for health reasons: 63 for grip strength; 136 for chair rise speed; 99 for standing balance.

Main results and the role of chance

Those participants unable to perform each physical capability test and those in the lowest performing sex specific fifth were found to have higher mortality rates than participants in the highest fifth. Adjustment for baseline covariates partially attenuated associations, but the main associations remained in fully adjusted models. When we compared a series of models including different combinations of the measures using likelihood ratio tests, all three physical capability measures improved the model fit, and a model including all three measures produced the highest estimate of predictive ability (C index 0.71, 95% confidence interval 0.65 to 0.77). The C index estimates the probability of concordance between observed and predicted responses.

Bias, confounding, and other reasons for caution

To minimise the level of potential bias introduced from missing information, we imputed missing values of the covariates in the sample of 2766 with complete data on physical capability and mortality. We ran a series of sensitivity analyses, including exclusion of all deaths that occurred in the first two years of follow-up and those with health problems at baseline; all our main conclusions remained the same. Limitations of our analyses include insufficient statistical power to investigate cause specific mortality and not being able to fully exclude the possibility of residual confounding.

Generalisability to other populations

When physical capability was assessed at age 53, despite losses to follow-up from death, emigration, loss of contact, and permanent refusal, the sample remained representative of the national population born at a similar time in most respects. Our findings are therefore likely to be generalisable to other populations of a similar age in high income countries.

Study funding/potential competing interests

This work was supported by UK Medical Research Council (programme code MC_UU_12019/4) and the Norwegian Institute of Public Health. The funders of the study had no role in the study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit the article for publication.

Discrepancies in autologous bone marrow stem cell trials and enhancement of ejection fraction (DAMASCENE): weighted regression and meta-analysis

Alexandra N Nowbar, Michael Mielewczik, Maria Karavassilis, Hakim-Moulay Dehbi, Matthew J Shun-Shin, Siana Jones, James P Howard, Graham D Cole, Darrel P Francis on behalf of the DAMASCENE writing group

EDITORIAL by Freemantle and Rait

International Centre for Circulatory Health, National Heart and Lung Institute, Imperial College London, London W2 1LA, UK
Correspondence to: A N Nowbar
alexandra.nowbar09@imperial.ac.uk

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- Research: Benefits of β blockers in patients with heart failure and reduced ejection fraction: network meta-analysis (*BMJ* 2013;346:f55)
- Rapid response: Stem cell therapy for acute coronary syndrome (*BMJ* 2011;342:d3527)
- Research: Ticagrelor versus clopidogrel in patients with acute coronary syndromes intended for non-invasive management: substudy from prospective randomised PLATelet inhibition and patient Outcomes (PLATO) trial (*BMJ* 2011;342:d3527)

STUDY QUESTION

Does the number of discrepancies in reports of bone marrow stem cell trials correlate with left ventricular ejection fraction effect size?

SUMMARY ANSWER

There is an association between the number of discrepancies in trial reports and the effect size of bone marrow stem cells on ejection fraction.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Though autologous bone marrow stem cell therapy has been reported to substantially increase cardiac function, trials have differed in the reported effect sizes. We present a previously undescribed explanatory variable for the discordant effect size between trials of bone marrow stem cell therapy for cardiac function. Trials with fewer discrepancies find smaller effect sizes on ejection fraction, culminating in the few discrepancy-free trials showing a weighted mean effect size of zero.

Selection criteria for studies

We searched PubMed and Embase from inception to April 2013 for randomised clinical trials of autologous bone marrow stem cells in cardiac disease that reported a mean ejection fraction effect size.

Primary outcome

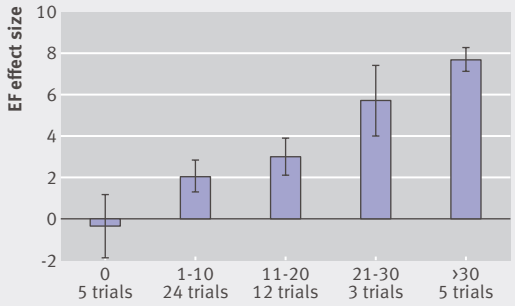
Association between number of discrepancies and weighted mean effect size.

Main results and role of chance

There were over 600 discrepancies in 133 reports from 49 trials. The number of discrepancies correlated with the reported increment in ejection fraction (Spearman's r=0.4, P=0.005). Trials with >30 discrepancies showed a weighted mean effect size of 7.7%. Classes of trials with fewer discrepancies showed progressively smaller ejection fraction effects, culminating in the five discrepancy-free trials showing a weighted mean effect size of −0.4%. In the figure the error bars show only the standard error of the sample size weighted mean effect size across trials in each category. Formal meta-analytical confidence intervals which fully integrate sample size and uncertainty within each trial were available for only a subset of trials (see appendix 10 of the full paper).

There were many types of discrepancies. Some studies reported patients with zero and even negative NYHA classes (which can only be I, II, III, or IV). Graphs sometimes showed data points for more patients than the trial enrolled. In some studies, statistical testing was performed only in the active group, missing highly significant changes in the control group, which, if calculated, showed P values as low as 10^{-108}. Other studies described patients who had died or been lost to survival follow-up, but whose current symptom status was known and were somehow still attending for invasive tests. Proportions given in some studies were incompatible with the reported percentage—for example, 5 of 6 patients reported as 100%. Other stated proportions were impossible for any whole number of patients. Numerous summary statistics were incorrect, including impossibly wide or mathematically impossible standard deviations. Sometimes the mean of a displayed set of numbers was calculated incorrectly. Another trial reported significantly positive results but its later more detailed analysis of the same numbers seems to show no significant effect.

Mean effect size by number of discrepancies



Bias, confounding, and other reasons for caution

We could not blind ourselves to effect size because this was embedded within the report itself. Moreover there could be additional discrepancies that we failed to identify: readers are welcome to report any missed discrepancies via "rapid response." Our method of counting discrepancies is imperfect because there is no universally accepted convention.

Study funding

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Dietary fiber intake and mortality among survivors of myocardial infarction: prospective cohort study

Shanshan Li,[1] Alan Flint,[2] Jennifer K Pai,[3] John P Forman,[4] Frank B Hu,[1 2] Walter C Willett,[1 2] Kathryn M Rexrode,[5] Kenneth J Mukamal,[6] Eric B Rimm[1 2]

[1]Department of Epidemiology, Harvard School of Public Health, 655 Huntington Avenue, Boston, MA 02115, USA
[2]Department of Nutrition, Department of Epidemiology, Boston, MA, USA
[3]Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, MA, USA
[4]Renal Division, Brigham and Women's Hospital, Boston, MA, USA
[5]Department of Preventive Medicine, Brigham and Women's Hospital, Boston, MA, USA
[6]General Medicine, Beth Israel Deaconess Medical Center, Brookline, MA, USA
Correspondence to: S Li
shl607@mail.harvard.edu

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- Editorial: Eat more fibre (*BMJ* 2013;347:f740)
- Research: Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis (*BMJ* 2013;347:f6879)
- Research: Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies (*BMJ* 2011;343:d6617)
- Editorial: Fibre and prevention of chronic diseases (*BMJ* 2011;343:d6938)

STUDY QUESTION

What are the associations of dietary fiber post-myocardial infarction (MI) and changes of dietary fiber from before to after MI with all cause and cardiovascular mortality?

SUMMARY ANSWER

In this prospective study of dietary fiber intake after MI, a greater intake of dietary fiber, especially cereal fiber, was inversely associated with all cause mortality. On average, participants increased dietary fiber intake after MI, and the greater the increase, the lower was the risk of subsequent all cause and cardiovascular mortality.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Dietary fiber is associated with a lower risk of coronary heart disease in healthy populations but it is unclear whether higher consumption of dietary fiber after MI is associated with lower mortality. In this prospective study of survivors after MI, a greater post-MI intake of dietary fiber, especially cereal fiber, was inversely associated with all cause mortality, and an increase in consumption of fiber from the period before to after MI was significantly associated with lower all cause and cardiovascular mortality.

Participants and setting

The Nurses' Health Study and the Health Professionals Follow-Up Study are two large prospective cohort studies of US women and men with repeated dietary measurements. We included 2258 women and 1840 men who were free of cardiovascular disease, stroke, or cancer at enrollment, survived a first MI during follow-up, were free of stroke at the time of initial MI onset, and provided a food frequency questionnaire before and at least one after MI.

Design, size, and duration

We evaluated the associations of dietary fiber post-MI and changes from before to after MI for all cause and cardiovascular mortality using Cox proportional hazards models, adjusting for medication use, medical history, and lifestyle factors, including smoking status.

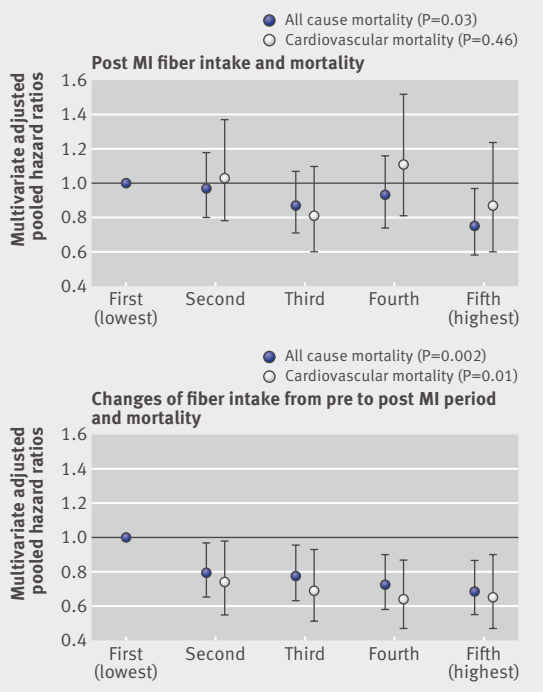
Main results and the role of chance

Higher fiber intake post-MI was significantly associated with lower all cause mortality (comparing extreme fifths of fiber intake, pooled hazard ratio 0.75, 95% confidence interval 0.58 to 0.97). Greater intake of cereal fiber was more strongly associated with all cause mortality (pooled hazard ratio 0.73, 0.58 to 0.91) than were other sources of dietary fiber. An increased fiber intake from before to after MI was significantly associated with lower all cause mortality (pooled hazard ratio 0.69, 0.55 to 0.87).

Bias, confounding, and other reasons for caution

Our food frequency questionnaire is a reliable measure for assessing dietary intake in the previous year but its validity is not known for measuring intake within the same person before and after MI. Our results may be confounded by beneficial factors related to fiber intake; foods that are high in fiber, such as whole grains, fruits, and vegetables, also contain vitamins, minerals, antioxidants, and phytochemicals, which may also be beneficial for health. We performed series sensitivity analyses and showed that only under extreme conditions was the observed inverse association meaningfully attenuated. Even with two of the largest long term prospective post-MI cohorts, we still had limited power to examine cause specific mortality. We were also not able to examine optimal timing for change in diet or potential interactions between dietary fiber and medication use post-MI.

Multivariate adjusted hazard ratios for all cause and cardiovascular mortality according to fiber intake after initial myocardial infarction (MI) and changes from before to after MI



Generalisability to other populations

Our study sample comprised a relatively homogeneous population of US health professionals. The underlying biological mechanisms of beneficial effects of fiber are, however, likely to be similar across different ethnic groups.

Study funding/potential competing interests

This study was supported by National Institute of Health grants AA11181, HL35464, HL34594, HL60712, CA55075, CA87969, and CA055075.