



Preventing dementia by promoting physical activity and the long-term impact on health and social care expenditures



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ABSTRACT

Background. Preventing dementia has been proposed to increase population health as well as reduce the demand for health and social care. Our aim was to evaluate whether preventing dementia by promoting physical activity (PA) a) improves population health or b) reduces expenditure for both health and social care if one takes into account the additional demand in health and social care caused by increased life expectancy.

Methods. A simulation model was developed that models the relation between PA, dementia, mortality, and the use of health care and social care in England. With this model, scenarios were evaluated in which different assumptions were made about the increase in PA level in (part of) the population.

Results. Lifetime spending on health and social care related to dementia was highest for the physically inactive (£28,100/£28,900 for 40-year-old males/females), but spending on other diseases was highest for those that meet PA recommendations (£55,200/£43,300 for 40-year-old males/females) due to their longer life expectancies. If the English population aged 40–65 were to increase their PA by one level, life expectancy would increase by 0.23 years and health and social care expenditures would decrease by £400 per person.

Conclusions. Preventing dementia by increasing PA increases life expectancy and can result in decreased spending overall on health and social care, even after additional spending during life years gained has been taken into account. If prevention is targeted at the physically inactive, savings in dementia-related costs outweigh the additional spending in life years gained.

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Introduction

Dementia, often called the “most feared disease,” has a huge societal burden in terms of disability and mortality as well as usage of health care, informal care, and institutional long-term care (WHO, 2012; Wimo et al., 2013; Schaller et al., 2014). Total annual costs for dementia in the United Kingdom (UK) were recently estimated at £22.7 billion, or £27,600 per patient, of which 54% consisted of costs for informal care and 40% of costs for long-term care (Luengo-Fernandez et al., 2010). As a way of countering the burden of dementia, it has been proposed to invest more in its prevention (Yaffe et al., 2014), especially relevant given that there has been virtually no progress in the treatment of the disease. Although epidemiological research has identified several modifiable risk factors for the onset of dementia, targeting physical inactivity (PA) seems to be the factor that has the greatest potential in terms of reducing dementia prevalence (Barnes and Yaffe, 2011; Norton et al., 2014).

When answering the question of whether preventing dementia will reduce the demand for health care, it is not sufficient to look at savings in dementia-related costs only. As dementia substantially increases mortality risk, preventing dementia will increase life expectancy (Rait et al., 2010; Ganguli et al., 2005; Brodaty et al., 2012; Xie et al., 2008). Increased life expectancy for such people exposes them to other diseases and/or disabilities that also result in health and social care use (Bonneau et al., 1998). Consequently, preventing dementia may lead to a reduction in dementia-related costs in the short run but to higher costs in the long run, because of additional costs occurring in the additional life years that people live. Many studies evaluating the effects and costs of preventive interventions include only those future costs related to the risk factor or disease being investigated which may lead to false claims that prevention will reduce the demand for health care (Bonneau et al., 1998; Barendregt et al., 1997; van Baal et al., 2008). However, given that dementia is one of the most costly diseases, it is worthwhile investigating whether preventing dementia could result in cost savings in the long run even if costs of competing diseases in life years gained are taken into account.

The aims of the current study were to estimate the burden of dementia in England associated with physical inactivity and assess the potential health benefits and changes in health care and social care

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expenditures associated with increasing PA levels using a dynamic modeling approach. In doing so, we explicitly took into account the costs that might be a result of increased life expectancy.

Methods

Model structure

To model the impact of PA on dementia and health and social care expenditures, a Markov-type model was developed distinguishing the following states: two health states (“no dementia” and “dementia”) and the state “death”. Each health state was further stratified by gender, age, and physical activity level. PA level was divided into four classes: “inactive,” “low activity,” “some activity,” and “meets recommendations,” based on the classification used in the 2012 English National Health Survey (Bridges et al., 2013). The level of PA was modelled to have an impact on the risk of developing dementia and the risk of dying. Compared to no dementia, having dementia was associated with an increase in mortality and an increase in the use of health and social care. This model structure has been applied previously in other simulation models describing the link between risk factors, chronic diseases, and mortality (van Baal et al., 2006; Hoogveen et al., 2010; Boshuizen et al., 2012). Fig. 1 displays the basic structure of the model employed in this study.

The starting population of the model was the population of England in 2012 specified by gender, age, PA level, and disease status. The model simulated the annual changes in the population over time due to changes in PA level, incidence of dementia, and mortality. Cycle length of the model was 1 year, indicating that changes in the population took place on an annual basis. The time horizon of the analysis was life-time.

The demographic, epidemiological, and cost input parameters for the model were derived from multiple sources. Relative risks describing the relation between PA and the onset of dementia as well as mortality were taken from published meta-analyses (Sofi et al., 2011; Samitz et al., 2011). All other input parameters of the model were derived from English data sources. Cost parameters in the model were derived from studies using large administrative datasets (Kasteridis et al., 2014; Georghiou et al., 2012). We refer to the supplementary file for a more detailed description of the model and the data sources used to estimate parameters of the model.

Calculating costs with the model

Health and social care costs related to dementia were estimated within the model by multiplying dementia prevalence numbers by the annual costs per dementia patient specified by age and gender. Besides age and gender, a distinction has been made between dementia costs in the last year of life and “other years.” This has been done as health and social care expenditures are known to be concentrated in the last phase of life (de Meijer et al., 2011; Wong et al., 2011; Seshamani and Gray, 2004).

To calculate health-care costs for all “other” diseases, the numbers of survivors without dementia estimated within the model were multiplied by age- and gender-specific per capita average costs for all other diseases. Here again, we

made a distinction between costs in the last year of life and other years. Because lower levels of PA are related to a higher mortality risk compared to “meeting recommendations” with respect to PA, the annual health care and social care costs for an inactive person are higher (van Baal et al., 2011). In this way, costs were made indirectly to depend on PA level because no studies in the UK related PA level to health care use. All costs were expressed in 2012 prices.

Current practice scenario

In the current practice scenario, the model was run for a lifetime horizon assuming that persons did not change their physical activity level, so inactive people remained inactive till they died, low active people remained low active till they died, etc. Outcomes for the model projections over time were life expectancy, years with dementia, health care costs defined as costs borne by the National Health Service (NHS)(dementia versus other diseases), and social care costs (dementia versus other diseases) specified for each PA class.

Intervention scenarios

In addition to the current practice scenario, several intervention scenario analyses were run in which the assumption was made that part of the population would become more active. An increase in PA was hypothesized to result in a lower new incidence of dementia, lower mortality, lower dementia-related costs, but higher costs for other diseases compared to the current practice scenario. To illustrate the potential impact of an increase in physical activity level, three different intervention scenario analyses were performed for a cohort of 1000 people (500 males and 500 females) aged 40 at baseline assuming that 1) an inactive cohort would become low active, 2) a low active cohort would become somewhat active, and 3) a somewhat active cohort would become more active and would thus meet recommendations.

In addition, two different intervention scenario analyses were performed at a population level showing the impact of changes in physical activity level in the English population aged 40–65 assuming that 4) everyone were to increase their physical activity level by one class and 5) everyone would meet recommendations. For all scenario analyses, a lifetime horizon was used.

Sensitivity analysis

Probabilistic sensitivity analysis (PSA) was performed to translate uncertainty surrounding the input parameters into uncertainty around the outcomes of the model. In addition to the PSA, several one-way sensitivity analyses were performed to estimate the impact of key model parameters or assumptions on the outcomes.

- *Sensitivity analysis 1 (SA1)*. The effect of PA on all-cause mortality in our model was quite small if compared to estimates published by the US Physical Activity Guidelines Advisory Committee (U.S. Department of Health and Human Services, 2008). Therefore, SA1 investigated the impact of using other relative risks for the association between physical activity level and all-cause mortality. Based on data from the US Physical Activity Guidelines Advisory Committee (U.S. Department of Health and Human Services, 2008), RRs compared to being active were calculated to be 0.90 for low activity, 0.80 for some activity, and 0.73 for meets recommendations in SA1.
- *Sensitivity analysis 2 (SA2)*. In our base-case analysis, we assumed that the relative risks of PA on mortality and dementia onset could be applied to all ages. However, there is not that much evidence of the effect of PA on mortality and dementia for the eldest elderly. SA2 investigated the impact of applying the relative risks for all-cause mortality and dementia onset not to the entire age range, but only to ages 90 and below. All relative risk values above the age of 90 were set to one.
- *Sensitivity analysis 3 (SA3)*. A general problem when quantifying the relation between PA and the onset of dementia is that studies do not provide detailed information on how PA is measured and defined. In this sense, the way we used relative risks for the onset of dementia for the different PA classes is a bit arbitrary. Therefore, in SA3, different RRs for PA level in relation to the onset of dementia were used. In the base-case analysis, an RR of 0.65 was applied to both the low and some activity group. In SA3, the assumption was made that the RR of 0.65 only applied to the group with some activity and the RR for the low activity group was then calculated to be 0.89 based on interpolation and the estimated PA in hours per week in the groups.
- *Sensitivity analysis 4 (SA4)*. In SA4, costs for diseases other than dementia were made dependent on age only and not on last year of life as was done

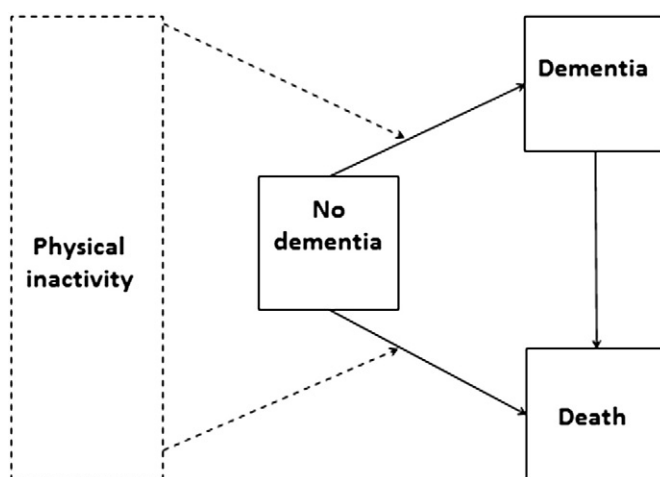


Fig. 1. Model structure.

in the base-case analysis. By making costs solely dependent on age, health and social care spending on other diseases in life years gained are higher (van Baal et al., 2011). This makes results of our analyses more comparable with other modeling studies in the area of prevention.

- *Sensitivity analysis 5 (SA5)*. The impact of discounting effects and costs was explored in SA5. In SA5, we discounted life years and costs at 3.5% annually. This was done as results of our analyses have obvious relevance for cost-effectiveness analyses. NICE guidance for economic evaluation currently dictates this discount rate (National Institute for Clinical Excellence (NICE), 2013).

Results

Table 1 shows the estimated life expectancy, years with dementia, and costs at age 40 years for the different physical activity classes stratified by gender. Compared to a person that meets recommendations with respect to PA, an inactive man/woman can expect to live about one additional year with dementia over his/her entire lifetime because of the higher risk of getting dementia. As a result, the expected lifetime dementia-related health care costs for an inactive man/woman are more than £5000 higher, while the dementia-related social care costs are about £2500 higher. However, due to the 2-year lower life expectancy, an inactive person incurs lower costs for other diseases over his/her lifetime compared to someone who meets recommendations. This difference is bigger for health care expenditures than for social care expenditures.

The potential impact of preventive interventions for a cohort aged 40 years at baseline is shown in Table 2.

From Table 2, it can be seen that in all cohort scenarios, there is an increase in life expectancy. Dementia-related costs decreased in two scenarios, but there was a small increase in costs in the scenario assuming a low active cohort becoming somewhat active. Costs for other diseases, however, increased in all scenarios because of the longer life expectancy. The gain in life years was highest for the scenario assuming inactive people becoming low active. Only in this scenario, the increase in health and social care costs for other diseases was completely compensated by the savings in dementia-related costs, resulting in net cost savings. To better understand the dynamics of prevention, Fig. 2 displays cost differences over time as a result of preventive interventions in the cohort scenarios.

Table 2 also shows the potential impact of preventive interventions at a population level. If all 40- to 65-year olds in the English population were to maintain their current physical level for their remaining lifetime, the mean life expectancy for this group was calculated to be 30.9 years. Total lifetime health and social care expenditures were calculated to be £60,900 per person. An increase in physical activity by one level for all except those already at the level of meeting recommendations would correspond to an increase in life expectancy of 0.23 years

per person, while lifetime health and social care expenditures per person would decrease by £400. For the scenario assuming that everyone in the population were to increase their physical activity level up to the level of meeting recommendations, the gain in life expectancy per person would be 0.46 years, while lifetime expenditures would increase on average with 100 lb. Note that in this scenario, prediction intervals for total costs are wide and range from – 500 to 700.

Table 3 shows the results for the sensitivity analyses. Estimates of life expectancy at the age of 40 years were strongly influenced by using different RRs for the association between physical activity and all-cause mortality (SA1) which increased life years gained due to increasing physical activity. As a result of higher gains in life expectancy, health care and social care costs in life years gained increased (results not shown) causing a decrease in total cost savings. Assuming no effect of physical activity above age 90 (SA2) only had a small impact on the results. Using different RRs for the association between physical activity and onset of dementia (SA3) also had a substantial impact on gains in life expectancy and cost differences. Cost differences were affected slightly by ignoring the concentration of costs in the last year of life (SA4). Discounting had a big impact on the results and since additional costs in life years gained are discounted heavily, the impact of these costs becomes less pronounced (SA5).

Discussion

This modeling study showed that the economic burden of dementia in England associated with physical inactivity is substantial. Physical inactivity lowers life expectancy and, at a population level, increases the average number of years lived with dementia. Inactive people were also predicted to have the highest lifetime total health and social care expenditures. Although savings in health care and social care are lower than previously suggested, preventing dementia by promoting physical activity could reduce the demand for health and social care even if we take into account costs for other diseases in life years gained. Targeting inactive people in the UK to become low active would increase life expectancy by almost 1 year and total costs would decrease as the savings in dementia-related costs outweigh the additional spending in life years gained. Increasing the physical activity level of people with low or some activity would also increase life expectancy, but total costs would increase slightly.

Limitations

For the current study, it was difficult to find evidence on the dose-response relationship between physical activity and the onset of dementia. Current evidence suggests that the greatest impact from reducing dementia occurs from raising the physical activity from close to zero to the next stage, which is still a low activity level (Sofi et al.,

Table 1

Model predictions for life expectancy, years with dementia, and lifetime costs (×£1000) by physical activity level at the age of 40 years, mean (95% confidence interval).

		Physical activity level			
		Inactive	Low activity	Some activity	Meets recommendations
Males	Life expectancy (years)	38.1 (37.5–38.6)	39.0 (38.5–39.3)	39.5 (39.0–39.8)	40.1 (39.6–40.5)
	Years with dementia	3.4 (2.5–4.8)	2.4 (1.7–3.4)	2.4 (1.8–3.5)	2.4 (1.8–3.4)
	Health care costs, dementia (£1000-)	19.2 (14.1–26.8)	13.3 (9.8–18.9)	13.7 (10.1–19.2)	13.5 (10–18.8)
	Health care costs, other diseases (£1000-)	34.1 (31.3–36)	37.3 (35.2–38.7)	38 (35.8–39.5)	39 (37–40.6)
	Social care costs, dementia (£1000-)	8.9 (6.6–12.3)	6.2 (4.6–8.7)	6.4 (4.7–8.9)	6.3 (4.7–8.7)
	Social care costs, other diseases (£1000-)	3.5 (3.2–3.8)	4 (3.7–4.3)	4.2 (3.9–4.4)	4.3 (4.1–4.6)
Females	Life expectancy (years)	42.0 (41.6–42.4)	42.8 (42.5–43.1)	43.3 (43.0–43.7)	43.9 (43.5–44.4)
	Years with dementia	3.5 (2.8–4.5)	2.5 (1.9–3.2)	2.5 (2.0–3.3)	2.5 (2.0–3.1)
	Health care costs, dementia (£1000-)	19.7 (15.9–25)	13.8 (10.8–18.1)	14.3 (11.2–18.6)	14.1 (11.5–17.6)
	Health care costs, other diseases (£1000-)	41.2 (39.3–42.7)	44.2 (42.6–45.5)	44.8 (43.2–46.2)	45.7 (44.2–47.0)
	Social care costs, dementia (£1000-)	9.2 (7.4–11.6)	6.5 (5.1–8.4)	6.6 (5.2–8.6)	6.6 (5.4–8.2)
	Social care costs, other diseases (£1000-)	7.4 (6.8–7.9)	8.8 (8.2–9.3)	9.1 (8.4–9.6)	9.5 (8.9–10.1)

Table 2
Results of five intervention scenarios compared to current practice (= no change in physical activity level): life years and changes in costs per person.

	Life years gained	Dementia-related costs (in £)		Costs due to other diseases (in £)		Total costs (in £)
		Health care costs	Social care costs	Health care costs	Social care costs	
<i>Cohort scenarios (aged 40 year at baseline)</i>						
1. Inactive cohort becomes low active	0.82 (0.62/1.02)	−5900 (−8000/−4000)	−2700 (−3700/−1800)	3100 (2300/3900)	900 (700/1200)	−4600 (−6600/−2800)
2. Low active cohort becomes somewhat active	0.54 (0.31/0.77)	400 (200/600)	200 (100/300)	700 (400/900)	200 (100/300)	1500 (800/2100)
3. Somewhat active cohort becomes more active and meets recommendations	0.59 (0.29/0.93)	−200 (−2600/2000)	−100 (−1200/900)	1000 (−200/2100)	300 (−100/700)	900 (−1300/2900)
<i>Population scenarios (40–65 years old)</i>						
4. Everyone would increase their physical activity level by one class	0.23 (0.17/0.29)	−1000 (−1300/−700)	−400 (−600/−300)	700 (500/800)	300 (300/400)	−400 (−700/−100)
5. Everyone would meet recommendations	0.46 (0.3/0.62)	−900 (−1600/−300)	−400 (−700/−100)	1000 (600/1300)	500 (300/700)	100 (−500/700)

2011). The impact of using different RRs for the onset for dementia showed that life expectancy of the low activity group decreased, while lifetime total costs increased compared to the base case. The most important other assumption tested in the sensitivity analysis was the use of different RRs for the association between physical activity and all-cause mortality which had a strong impact on life expectancy and years lived with dementia. Overall, the impact of the assumptions tested was limited and did not change the main conclusions.

In terms of the cost estimates used in our analyses, these were derived from a relatively small region in England and although we

adjusted total spending to match the English average, we could not assess whether the distribution among diseases is representative. Finally, we limited our cost analyses to publicly funded spending on health and social care and did not take into account costs of informal care. In England, some institutional care for people with dementia is paid for by the person or their family, and some by the local government. However, the rules governing the proportions change from one local authority to another, so it has been simpler to assume that the government pays the whole institutional care bill. Since the cost of informal care at home and the amounts paid for institutional care will vary approximately linearly with the prevalence of dementia, changes to the prevalence due to changes in physical activity at a younger age will impact in approximately the same way on informal care, on family payment of institutional care, and on government payment of institutional care. Thus, the costs of these components will all rise or fall uniformly as the prevalence of dementia rises or falls. As a result, including the costs of informal care is unlikely to influence the direction of the results though it would change the magnitude of the costs or the costs saved.

Comparison with previous studies

At least three other modeling studies have investigated the association between physical activity and the onset of dementia (Barnes and Yaffe, 2011; Nepal et al., 2010; Zhang et al., 2011). Based on the input of our model, the population attributable risk caused by physical inactivity was estimated to be about 20%, which is in line with two of these studies (Barnes and Yaffe, 2011; Nepal et al., 2010). Results of the other study could not be compared to the current study, because in that study, physical inactivity was included as one of seven risk factors that were combined into one overall risk score (Zhang et al., 2011). In comparison with previous studies on the costs of dementia in England, our results are fairly similar and major differences can be explained by a) we did not include costs of informal care and b) other studies did not include spending during life years gained (Luengo-Fernandez et al., 2010; UK, 2007; Wübker et al., 2014).

Policy relevance

Previous studies took into account only costs related to dementia which obviously decrease if dementia is prevented. Due to the increase in life expectancy, however, costs for other diseases increased. Dementia prevention through increased physical activity, including costs for other diseases in life years gained, still did not lead to cost increases in some scenarios indicating the potential for cost savings through prevention. These results are more informative for decision makers who are concerned with total public spending rather than only spending related to dementia. Including costs of competing risks in life years gained allows better comparison across investments in different diseases (Rappange et al., 2010; van Baal et al., 2016).

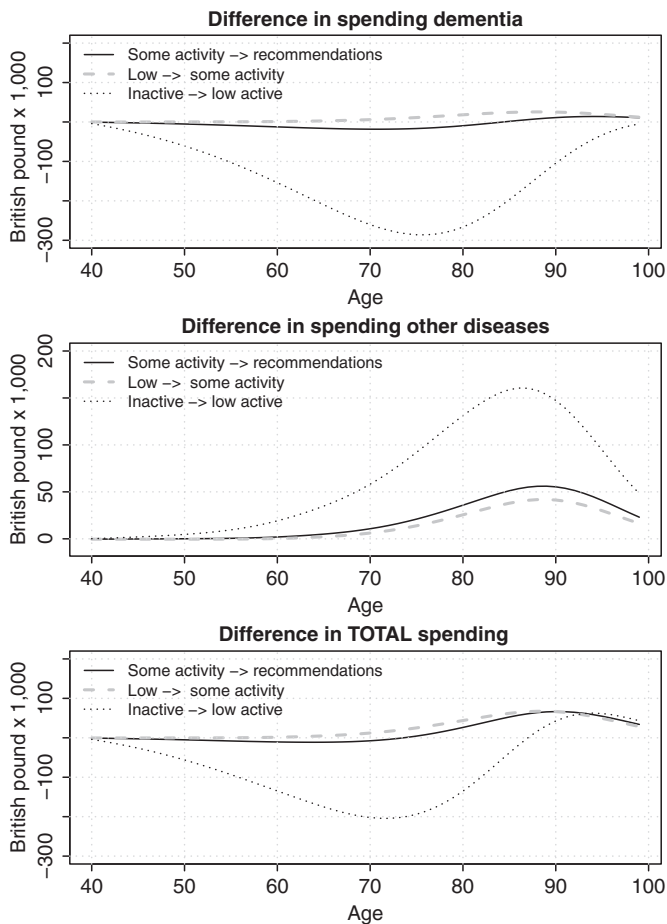


Fig. 2. Effect of three scenarios of increase in physical activity level on the costs for a cohort of people aged 40 years at baseline. Scenario 1: Inactive cohort becomes low active; scenario 2: low active cohort becomes somewhat active; and scenario 3: somewhat active cohort becomes more active and meets recommendations.

Table 3
Change in life years and total costs (the sum of health care costs and social care costs) per person for different sensitivity analyses (SA) for the three different cohort intervention scenarios.

	Inactive cohort becomes low active		Low active cohort becomes somewhat active		Somewhat active cohort becomes more active and meets recommendations	
	Life years gained	Total costs (in £)	Life years gained	Total costs (in £)	Life years gained	Total costs (in £)
Base case	0.81	−4600	0.53	1400	0.58	1000
SA1*	1.44	−2700	1.02	2800	0.83	1600
SA2*	0.76	−4500	0.48	1300	0.53	800
SA3*	0.42	−800	0.92	−2200	0.58	1000
SA4*	0.81	−4600	0.53	1700	0.58	1200
SA5*	0.19	−2100	0.13	300	0.14	100

SA1: Different RRs for the association between physical activity and all-cause mortality (1/0.9/0.8/0.73 instead of 1/0.97/0.91/0.86). SA2: RRs for all-cause mortality and dementia incidence above age 90 were set to 1. SA3: Different RRs for the association between physical activity and dementia (1/0.89/0.65/0.62 instead of 1/0.65/0.65/0.62). SA4: Costs for other diseases dependent on age instead of age and last year of life. SA5 discounting of costs and life years with 3.5% annually.

Whether preventing dementia by targeting risk factors other than physical activity will also result in cost savings depends on how these risk factors are related to dementia and mortality. However, dementia prevention probably diverts people from one expensive later-life trajectory into another expensive later-life trajectory. Including costs of competing risks in life years gained has more impact in the context of smoking cessation when people are diverted from cheap to more expensive later-life trajectories (Barendregt et al., 1997).

It should be noted that we did not analyse specific interventions in this study, and therefore, we cannot conclude whether interventions promoting physical activity are cost-effective or not. However, this study illustrated that, if effective, low-cost incentive-based interventions increasing physical activity have the potential to reduce public spending (O'Malley et al., 2012).

Conclusion

In conclusion, this study showed that the burden of dementia associated with physical inactivity in England is substantial. People who are physically inactive were found to be associated with lower life expectancies, more years lived with dementia, and higher total health and social care costs compared to physically active people. Promoting physical activity in the English middle-aged population has the potential for increasing life-expectancy on average by half a year. Targeting people with very low levels of activity to become more active seems likely to be the most effective option of choice, as results for this scenario analysis showed the highest gain in life expectancy and savings in total expenditures for health and social care.

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Competing Interests

All authors declare that they have no conflicts of interest. No ethics committee approval was required for this study.

Transparency document

The Transparency document associated with this article can be found in online version.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ypmed.2016.01.013>.

References

- Barendregt, J.J., Bonneux, L., Maas, V.d., J., P., 1997. The health care costs of smoking. *N. Engl. J. Med.* 337 (15), 1052–1057.
- Barnes, D.E., Yaffe, K., 2011. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol.* 10 (9), 819–828.
- Bonneux, L., Barendregt, J.J., Nusselder, W.J., Maas, V.d., Paul, J., 1998. Preventing fatal diseases increases healthcare costs: cause elimination life table approach. *BMJ* 316 (7124), 26–29.
- Boshuizen, H.C., Lhachimi, S.K., van Baal, P.H.M., et al., 2012. The DYNAMO-HIA model: an efficient implementation of a risk factor/chronic disease Markov model for use in health impact assessment (HIA). *Demography* 49 (4), 1–25.
- Bridges, S., Doyle, M., Fuller, E., et al., 2013. Health survey for England 2012. *Health, Social Care and Lifestyles*.
- Brodady, H., Seeher, K., Gibson, L., 2012. Dementia time to death: a systematic literature review on survival time and years of life lost in people with dementia. *Int. Psychogeriatr.* 24 (7), 1034–1045.
- de Meijer, C., Koopmanschap, M., Uva, T.B., van Doorslaer, E., 2011. Determinants of long-term care spending: age, time to death or disability? *J. Health Econ.* 30 (2), 425–438.
- Ganguli, M., Dodge, H.H., Shen, C., Pandav, R.S., DeKosky, S.T., 2005. Alzheimer disease and mortality: a 15-year epidemiological study. *Arch. Neurol.* 62 (5), 779–784.
- Georghiou, T., Davies, S., Davies, A., Bardsley, M., 2012. Understanding patterns of health and social care at the end of life. *Nuffield Trust Research Report*.
- Hoogenveen, R.T., Baal, P.H., Boshuizen, H.C., 2010. Chronic disease projections in heterogeneous ageing populations: approximating multi-state models of joint distributions by modelling marginal distributions. *Math. Med. Biol.* 27 (1), 1–19.
- Kasteridis, P., Street, A., Dolman, M., et al., 2014. The Importance of Multimorbidity in Explaining Utilisation and Costs across Health and Social Care Settings: Evidence from South Somerset's Symphony Project.
- Luengo-Fernandez, R., Leal, J., Gray, A., 2010. Dementia 2010. The economic burden of dementia and associated research funding in the United Kingdom. A Report Produced by the Health Economics Research Centre. University of Oxford for the Alzheimer's research trust.
- National Institute for Clinical Excellence (NICE), 2013. Guide to the Methods of Technology Appraisal.
- Nepal, B., Brown, L., Ranmuthugala, G., 2010. Modelling the impact of modifying lifestyle risk factors on dementia prevalence in Australian population aged 45 years and over, 2006–2051. *Australas. J. Ageing* 29 (3), 111–116.
- Norton, S., Matthews, F.E., Barnes, D.E., Yaffe, K., Brayne, C., 2014. Potential for primary prevention of Alzheimer's disease: an analysis of population-based data. *Lancet Neurol.* 13 (8), 788–794.
- O'Malley, G.C., Baker, P.R., Francis, D.P., Perry, I., Foster, C., 2012. Incentive-based interventions for increasing physical activity and fitness. *Cochrane Libr.*
- Rait, G., Walters, K., Bottomley, C., Petersen, I., Iliffe, S., Nazareth, I., 2010. Survival of people with clinical diagnosis of dementia in primary care: cohort study. *BMJ* 341, 3584.
- Rappange, D.R., Brouwer, W.B., Rutten, F.F., van Baal, P.H., 2010. Lifestyle intervention: from cost savings to value for money. *J. Public Health (Oxf.)* 32 (3), 440–447.
- Samitz, G., Egger, M., Zwahlen, M., 2011. Domains of physical activity and all-cause mortality: systematic review and dose–response meta-analysis of cohort studies. *Int. J. Epidemiol.* 40 (5), 1382–1400.
- Schaller, S., Mauskopf, J., Kriza, C., Wahlster, P., Kolominsky-Rabas, P.L., 2014. The main cost drivers in dementia: a systematic review. *Int. J. Geriatr. Psychiatry.*
- Seshamani, M., Gray, A.M., 2004. A longitudinal study of the effects of age and time to death on hospital costs. *J. Health Econ.* 23 (2), 217–235.

- Sofi, F., Valecchi, D., Bacci, D., et al., 2011. Physical activity and risk of cognitive decline: a meta-analysis of prospective studies. *J. Intern. Med.* 269 (1), 107–117.
- U.S. Department of Health and Human Services, 2008. Physical Activity Guidelines Advisory Committee Report.
- UK, 2007. A Report to the Alzheimer's Society on the Prevalence and Economic Cost of Dementia in the UK Produced by King's College London and the London School of Economics.
- van Baal, P.H., Hoogenveen, R.T., Wit, G.A., Boshuizen, H.C., 2006. Estimating health-adjusted life expectancy conditional on risk factors: results for smoking and obesity. *Popul. Health Metrics* 4, 14.
- van Baal, P.H., Polder, J.J., de Wit, G.A., et al., 2008. Lifetime medical costs of obesity: prevention no cure for increasing health expenditure. *PLoS Med.* 5 (2), e29.
- van Baal, P.H.M., Wong, A., Slobbe, L.C.J., Polder, J.J., Brouwer, W.B.F., de Wit, G.A., 2011. Standardizing the inclusion of indirect medical costs in economic evaluations. *Pharmacoeconomics* 29 (3), 175–187.
- van Baal, P.H.M., Meltzer, D., Brouwer, W.B., 2016. Future costs, fixed health care budgets and the decision rules of cost-effectiveness analysis. *Health Econ.* 25 (2), 237–248.
- WHO, 2012. Factsheet on Dementia.
- Wimo, A., Jonsson, L., Bond, J., Prince, M., Winblad, B., International AD, 2013. The worldwide economic impact of dementia 2010. *Alzheimers Dement.* 9 (1), 1–11, e3.
- Wong, A., van Baal, P.H.M., Boshuizen, H.C., Polder, J.J., 2011. Exploring the influence of proximity to death on disease-specific hospital expenditures: a carpaccio of red herrings. *Health Econ.* 20 (4), 379–400.
- Wübker, A., Zwakhalen, S.M., Challis, D., et al., 2014. Costs of care for people with dementia just before and after nursing home placement: primary data from eight European countries. *Eur. J. Health Econ.* 1–19.
- Xie, J., Brayne, C., Matthews, F.E., 2008. Medical Research Council Cognitive Function and Ageing Study collaborators. Survival times in people with dementia: analysis from population based cohort study with 14 year follow-up. *BMJ* 336 (7638), 258–262.
- Yaffe, K., Aisen, P., Albert, M., Anstey, K., 2014. Dementia (including Alzheimer's disease) can be prevented: statement supported by international experts. *J. Alzheimers Dis.* 38, 699–703.
- Zhang, Y., Kivipelto, M., Solomon, A., Wimo, A., 2011. Cost-effectiveness of a health intervention program with risk reductions for getting demented: results of a Markov model in a Swedish/finnish setting. *J. Alzheimers Dis.* 26 (4), 735–744.