Effective interventions for potentially modifiable risk factors for late-onset dementia: a costs and cost-effectiveness modelling study

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Summary

Background The potential economic value of interventions to prevent late-onset dementia is unknown. We modelled this for potentially modifiable risk factors for dementia.

Methods For this modelling study, we searched PubMed and Web of Science from inception to March 12, 2020, and included interventions that: successfully targeted any of nine prespecified potentially modifiable risk factors (hypertension, diabetes, hearing loss, obesity, physical inactivity, social isolation, depression, cigarette smoking, and less childhood education); had robust evidence that the intervention improved risk or risk behaviour; and are feasible to enact in an adult population. We established when in the life course each intervention would be delivered. We calculated dementia incidence reduction from annual incidence of dementia in people with each risk factor, and population attributable fraction for each risk, corrected for risk factor clustering, and how effectively the intervention controls the risk factor. We calculated the discounted value of lifetime health gain and effect on cost (including NHS, social care and carer costs) per person eligible for treatment. We estimated annual total expenditure on the fully operational intervention programme in England.

Findings We found effective interventions for hypertension, smoking cessation, diabetes prevention, and hearing loss. Treatments for stopping smoking and provision of hearing aids reduced cost. Treatment of hypertension was cost-effective by reference to standard UK thresholds. The three interventions when fully implemented would save £1·863 billion annually in England, reduce dementia prevalence by 8·5%, and produce quality-adjusted life-year gains. The intervention for diabetes was unlikely to be cost-effective in terms of effect on dementia alone.

Interpretation There is a strong case for implementing the three effective interventions on grounds of cost-effectiveness and quality-of-life gains, as well as for improvements in general health. The interventions have the potential to remain cost-saving or cost-effective even with variations in dementia incidence and costs and effectiveness of interventions.

Funding Economic and Social Research Council.

Lancet Healthy Longev 2020; 1: e13–20

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Introduction

An estimated 47 million people live with dementia worldwide, and this is predicted to increase to 131 million by 2050.[1] People are living longer than in previous years,[2] particularly in low-income and middle-income countries.[1] The annual global cost of dementia is already estimated to be US$1 trillion,[3] showing how dementia affects individuals, families, and economies.

The incidence of age-specific dementia has decreased in some countries over the past two decades, suggesting that the risk of dementia is modifiable. We calculated a combined population-attributable fraction (PAF) for nine potentially modifiable risks for all-cause dementia from National Institute for Health and Care Excellence and National Institutes of Health guidelines (less childhood education, hearing loss, hypertension, obesity, smoking, physical inactivity, depression, diabetes, and social isolation), finding that up to 35% of all-cause late-onset dementia worldwide might be preventable.[4]

There has been little work on feasibility, effectiveness, or cost-effectiveness of interventions to prevent dementia. Earlier work has not accounted for clustering of risks in individuals—for example, people with obesity more often have hypertension and diabetes than do members of the general population. The best supported intervention is treating cardiovascular risks to prevent cognitive decline. One USA model estimated health-care savings of US$110 billion from a 10% reduction in four risk factors (body-mass index [BMI] ≥25 kg/m²; diabetes; hypertension; cardiovascular diseases, including stroke and heart diseases), although this model did not specify or cost the intervention.[5] A Spanish model of (uncosted) primary prevention interventions resulting in 20% improvements in obesity, hypercholesterolaemia, physical activity, and

Research in context

Evidence before this study

We searched PubMed and Web of Science, from inception to March 12, 2020, with no language restrictions, for effective interventions targeting each of the nine specified potentially modifiable risk factors. We used search terms for each risk factor, combined with terms for interventions or trials, for example, "hypertension", "intervention" OR "trial" OR "treatment". We then searched PubMed from inception to March 12, 2020, for studies investigating the cost-effectiveness of dementia prevention using these interventions. We used search terms "dementia" AND "prevent*" AND "economic" OR "cost" with no restrictions on language or date of publication. We then hand-searched retrieved papers for relevant references. We found one systematic review of interventions targeting cardiovascular risk factors (hypertension, dyslipidaemia, hyperhomocysteinaemia, obesity, or diabetes mellitus) and the effect on cognitive decline or dementia, but this did not include a cost-effectiveness analysis. We found four studies assessing the economic impact of tackling a range of potentially modifiable risk factors on dementia prevalence. Three of these did not account for clustering of risk factors—for example, an individual might have hypertension and diabetes and be physically inactive; nor did they include costs of the interventions. However, they concluded that considerable savings would be associated with reducing risk factors because of the effect on dementia onset and prevalence. A fourth study investigated the effect of a health promotion programme combined with medication for cardiovascular risk factors (hypertension, hypercholesterolaemia, and diabetes) and found that the intervention group had lower costs and a small gain in quality-adjusted life-years (QALYs) over a 20-year period. This study assessed the effect of reducing cardiovascular risk factors and did not account for clustering of risk in an individual.

We have previously published estimates of population attributable fractions for nine dementia risk factors identified from National Institute for Health and Care Excellence and National Institutes of Health guidelines. They were calculated on the basis of worldwide prevalence estimates and adjusted for clustering of risk factors in the individual. We found that eliminating these nine factors potentially meant that up to 35% of dementia is preventable worldwide. No studies have considered the potential for preventing dementia considering all these risk factors or examined the potential economic consequences.

Added value of this study

We used previously established relative risks for the nine prespecified risk factors associated with dementia (hypertension, diabetes, hearing loss, obesity, physical inactivity, social isolation, depression, cigarette smoking, and fewer years of childhood education) and searched systematically up to March 12, 2020, for effective interventions that were feasible in the adult population. We found interventions for mid-life hypertension and hearing loss, and diabetes and smoking in later life. We then modelled cost-effectiveness for these, considering the effectiveness of the treatments and the clustering of risk factors in individuals. We calculated that stopping smoking and provision of hearing aid led to both cost saving and QALY gains. Treating hypertension proved cost-effective according to standard thresholds at a cost of £9550 per QALY. Preventing diabetes was unlikely to be cost-effective on the basis of its effects on dementia alone. This study provides robust evidence regarding which risk factors for dementia are worth targeting. We also show the benefits of dementia prevention using well established standards of cost-effectiveness while considering clustering of risk factors in an individual.

Implications of all the available evidence

Treating hypertension, stopping smoking, and providing hearing aids to those who need them would eventually reduce the prevalence of dementia by 8·5% and save England £1·863 billion per year (at 2012–13 prices) in health care, social care, and unpaid care costs. These interventions are worth implementing for their effect on dementia alone. If dementia is delayed until very old age, rather than prevented, a compression of morbidity would be anticipated with people living longer without illness and a shorter time with multiple illnesses. These calculations are likely to be generalisable and relevant to other countries considering implementing dementia prevention strategies.

hypertension concluded that dementia prevalence could decrease by 9%, saving €5 billion annually by 2050.[6] Similarly, a model of the effects of increasing physical activity on dementia among middle-aged people (aged 45–64 years) in England concluded that it would be cost-saving in addition to increasing life-expectancy.[7] Only one study costed interventions: a health-promotion programme to lower serum cholesterol and provide pharmacological treatment of hypertension, hypercholesterolaemia, and diabetes in a Swedish and Finnish population;[8] the intervention group had lower costs and gained 0·0511 quality-adjusted life-years (QALYs) over 20 years.[9]

We systematically identified interventions of proven effectiveness in reducing individual risk or risk behaviours, and which were feasible in an adult population. We then modelled, for the first time to our knowledge, potential costs and cost-effectiveness of late-onset (age 65 years and older) all-cause dementia prevention through employing such interventions. We assume some people with each risk factor will already be receiving treatment, estimate how many are not currently receiving treatment, and calculate costs and benefits for the intervention. Focusing on England, we calculate potential costs and savings, accounting for risk clustering in individuals, and associated effects on QALYs.

Methods

Inclusion of interventions and approach to analysis

For this modelling study, we searched PubMed and Web of Science, from inception to March 12, 2020, with no language restrictions, for interventions targeting each of the nine specified dementia risk factors (less childhood education, hearing loss, hypertension, obesity, smoking, physical inactivity, depression, diabetes, and social isolation). We categorised time of treatment as early (younger than age 45 years), mid-life (age 45–64 years), or later life (65 years and older) to maintain consistency with previous evidence.[10] We used search terms for each risk factor, combined with terms for interventions or trials—for example, "hypertension", "intervention" OR "trial" OR "treatment". We then searched PubMed from inception to March 12, 2020, for studies investigating the cost-effectiveness of prevention of dementia using these interventions. We used search terms "dementia" AND "prevent*" AND "economic" OR "cost" with no restrictions on language or date of publication. We then hand-searched retrieved papers for relevant references. One reviewer (NM) checked the articles to ensure that the described interventions met the inclusion criteria, which were robust evidence the intervention reduces or prevents risk or risk behaviour; and are feasible in an adult population.

There is consistent evidence for the effect of each risk factor on an individual's subsequent risk of dementia. Our assumption was that treating or eliminating a risk factor would reduce a person's risk of developing dementia to that of someone without the risk factor. Using published figures on dementia incidence and frequency of risk factors, we modelled the effects of treatments on the subsequent risk of dementia. We did not include case-finding for risk factors as our focus is the cost-effectiveness of intervention when provided to people who have already been identified as at risk. We costed interventions, modelled dementia incidence in intervention and control groups, calculated costs and QALYs for those with and without dementia, and assumed transitions between different dementia severities and death. We used all-cause mortality by age and dementia severity to calculate survival to the next year.

Evidence on relative risks in England

We are considering the effect of each risk factor that predisposes to dementia. Our starting point is the PAF, the potential reduction in an illness in the whole population if the risk factor was eliminated. PAF is calculated by multiplying relative risk (RR) of each risk factor by the factor's prevalence. A previous meta-analyses report weighted PAF for each factor and adjusted for clustering (communality)[4] to eliminate the effect of other factors. The RRs we used are therefore "partialled-out"; it is not assumed that individuals have only one risk factor. The formula for calculation of PAF is:

$$\mathrm{PAF}=\frac{p(r-1)}{1+p(r-1)}$$

in which r=adjusted RR, PAF=weighted population attributable fraction, and p=prevalence of risk factor. The required specific RR follows from the weighted PAF, using the equation

$$r=\frac{p(1-\mathrm{PAF})+\mathrm{PAF}}{p(1-\mathrm{PAF})}$$

We identified nationally representative surveys[4] to determine risk factor prevalence in England and to calculate PAF (see appendix p 1).

See Online for appendix

Economic analysis

Our modelling had a societal perspective incorporating the following: intervention cost; annual dementia incidence in people with the risk factor under consideration; reduction in dementia incidence if risk factor is controlled to the extent that the identified intervention shows evidence of effectiveness; annual effect per person with dementia in old age in terms of QALY gain and excess health-care, social, and unpaid care costs; and incremental cost-effectiveness ratio.

We costed interventions using England-specific unit costs 2012–13[11–13] for staff time and drugs[14] (appendix pp 2–3). We focused on incremental effects on dementia risk and prevalence, and did not consider effects on other conditions. We calculated cost-savings from reduced dementia prevalence from up-to-date cost-of-illness figures.[15] Details of annual costs per sector, by age group and dementia stage, and by quality of life and mortality are presented in the appendix (p 4). We established when in the life course each intervention would be delivered and discounted future dementia-associated savings back to present value using annual discount rate of 3·5%, as recommended by the UK Treasury.[16] We did one-way deterministic sensitivity analyses and probabilistic sensitivity analyses using Monte Carlo simulation for each intervention (appendix pp 9–11).

Data, modelling, and incidence of dementia

We used a Markov model previously developed for assessing cost-effectiveness for disease-modifying therapies in Alzheimer's disease.[17] Key inputs in this model are age-specific incidence of dementia in England,[18] three stages of dementia (mild, moderate, and severe), transition rates between stages, excess mortality rates in moderate and severe stages, stage-specific costs (including health, social services, and unpaid care by family), and stage-specific QALY levels[19] (appendix pp 2–7).

We used age-specific average NHS,[18] social care, and unpaid care costs;[20] these relate to the English population as a whole and are, in effect, weighted averages of costs for those with and without dementia (appendix pp 2–7).

To derive costs for those with dementia, we used estimates of age-specific prevalence of dementia from the Cognitive Function and Ageing Study II[21] and age-specific costs[22] accounting for changing stage distribution of dementia with age.

Data on dementia incidence relate to the whole population. To separate estimates for those with and without each risk factor, we used estimates of prevalence of risk factor (p) and RR of those with the factor compared with those without (r). Incidence in those with the risk factor is given by population incidence factored by the following equation:

$$\text{Incidence with risk factor} = \frac{r}{(pr + 1 - p)}$$

The incidence in those without the risk factor is calculated with the following equation

$$\text{Incidence without risk factor} = \frac{\text{Incidence with risk factor}}{r}$$

Cost per QALY is calculated using the following equation:

$$\text{Cost per QALY} = \frac{\text{Cost of intervention minus saving in cost from reduced incidence of dementia}}{\text{Increase in QALYs}}$$

For cases in which intervention dominates (ie, has better outcomes and lower costs), we quote the result in terms of per-person cost saving and QALY gain. Costs and benefits are those accruing over the individual's lifetime, discounted to the age at which therapy is initiated. For mid-life interventions, we assume the intervention commences in mid-life but continues to end of life: both hearing aids[17] and antihypertensives[23] continue to protect against dementia in later life.

Cost of the average patient's treatment career accounts for death rate during the treatment period, using national average figures[24] plus excess mortality attributable to later stages of dementia.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. RW and RA had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We identified four potential interventions with robust evidence of effectiveness in reducing dementia incidence.

The first potential intervention is for mid-life hypertension. Several studies have shown that antihypertensives treat hypertension effectively, with some showing effects on dementia.[25] A reduction in the risk of dementia is observed even if blood pressure remains above hypertensive thresholds. Calculations of cost used three antihypertensives together if necessary, as recommended by NICE,[26] assuming this would achieve sufficient hypertensive control to eliminate excess dementia risk of mid-life hypertension.

The second potential intervention is for smoking in later life. Smoking cessation reduces risk of dementia.[27] We identified any form of nicotine replacement therapy as the most effective intervention because it is a feasible intervention and commonly used. A meta-analysis showed that the RR of abstinence from smoking for any form of nicotine replacement therapy relative to control was 1·60, with effects largely independent of therapy duration, additional support intensity, or setting.[28] We consider the use of nicotine gum for older people who smoke on the basis of the results of a meta-analysis,[28] in which trial follow-up period was typically 6 months or 12 months. We selected trials with a 12-month follow-up (with low support). There were ten trials with 2751 participants, of whom 323 quit, but 40% of these resumed smoking, leading to a permanent quit rate of 7%.[29]

The third potential intervention is for later-life type 2 diabetes. We identified a lifestyle change intervention to prevent diabetes because to our knowledge there is no evidence that treating diabetes reduces the risk of developing dementia compared with untreated diabetes.[30] The Finnish Diabetes Prevention Study[31] recruited middle-aged, overweight participants with impaired glucose tolerance, following them up for 13 years. The treatment group had a consultation with their general practitioner (GP) yearly, had group physical exercise sessions and seven sessions with a nutritionist in year one, plus four each subsequent year in a continuing individualised lifestyle intervention. The annual incidence of diabetes was 4·5% in the intervention group and 7·2% in the control group.[31]

The fourth potential intervention is for mid-life hearing loss. We chose provision of a hearing aid as the intervention since increasing evidence from longitudinal studies shows that initiating hearing aid use slows memory decline, and continued use reduces dementia risk to that of people without hearing impairment.[31] People with hearing impairment who do not use hearing aids remain at an increased risk of dementia. We assume those with hearing aids avoid the excess risk associated with hearing loss.[32]

We were unable to model interventions for five risk factors for dementia. The first was education; education in England is compulsory through to age 18 years and so we could not increase childhood education to influence future dementia prevalence. The second was obesity; there was an absence of evidence for feasible interventions for the whole obese population that resulted in lowering BMI to below the obesity threshold.

The third was depression; to our knowledge, no evidence suggests that treating depression reduces risk of developing dementia, and no identified interventions exist to prevent depression in the general population. The final two risk factors were low social contact and physical inactivity; evidence for both risk factors was insufficient for effective interventions to be modelled.[33]

Selected risk factors, prevalence of untreated factor at time of potential intervention, RR, and associated PAF are presented in table 1. The effects of each intervention and all interventions combined on QALYs, costs, and dementia prevalence are discussed here, and intervention costs are detailed in the appendix (pp 7–9).

	Prevalence, *p* (%)	Adjusted relative risk			PAF (%)
		With vs without the risk factor, r	With risk factor* r/(pr+1–p)	Without risk factor* 1/(pr+1–p)	
Hypertension	22%	1·25	1·18	0·95	5%
Smoking	8%	1·27	1·24	0·98	2%
Diabetes	15%	1·15	1·13	0·98	2%
Hearing loss	8%	1·50	1·36	0·91	9%

Prevalence (*p*) of untreated risk factors at time of potential intervention are presented along with relative risks (r), and PAF adjusted for communality. PAF=population attributable fraction. *Relative to whole population.

Table 1: **Prevalence of risk factors, adjusted relative risk, and PAF**

The target group for treatment of hypertension are those in middle age (46–64 years) with untreated or uncontrolled hypertension. From national surveys, prevalence of untreated or uncontrolled hypertension in mid-life is 22% in England[12] so the intervention was applied to this group. Costs vary with dose and variant of antihypertensives, but as of 2018, combination of three antihypertensives (angiotensin converting enzyme inhibitor, calcium channel blocker, and diuretic) costs £67 a year.[12,15] Allowing for two consultations a year, total annual cost is £141.[15] Discounted lifetime net cost per person treated is £376 and QALY gain is 0·039. Cost per QALY is £9550, which is substantially below the NICE threshold of £20 000 per QALY.[34] Annual expenditure for this treatment for the whole middle-aged population in England with hypertension is £730 million, and dementia prevalence falls by 5%.

8% of older adults (65 years and older) currently smoke and this group is the target patient group for nicotine replacement therapy.[34] This therapy to aid smoking cessation was assumed to be given at age 65 years. The comparator in the meta-analysis on which we rely includes other smoking cessation therapies.[29] Because our target group would not otherwise receive any therapy at all, we use the cost of the intervention for which the participant receives nicotine replacement therapy in addition to support from a health professional. We use an 8-week period (£56 with nicotine gum at £1 a day).[29] A typical upper limit of low support is 30 min with a GP (£114) plus two sessions of 30 min with a practice nurse (£52) per 8 weeks.[29] The intervention both reduces costs and improves quality of life, dominating over the so-called do-nothing option. Discounted cost saving per person treated is £1569 and QALY gain is 0·097. We carried out a threshold analysis of the intervention cost that would deliver a cost up to the NICE threshold of £20 000 per QALY: the cost could increase by 111% and remain below the NICE threshold. The annual cost of delivering the intervention is £12 million a year and the 7% permanent quit rate eventually leads to a reduction of 0·15% in dementia prevalence.

The prevalence of diabetes in people 65 years and older is 15%.[11] The Finnish Diabetes Prevention Study[35] comprised an annual GP visit, at a cost of £34 each (when converted to UK currency), for 6 years. Consultations with a nutritionist (seven in year one, four in subsequent years) were assumed to last for 30 min, remunerated at band 5 professional scale.[14] The duration and frequency of group therapy sessions were not specified in the paper; we assumed a cost of £76 per person per year. The total cost per participant in year one was £232, and £180 per year in subsequent years. We applied the findings to a cohort of overweight 65-year-olds with impaired glucose tolerance. We adopted a stopping rule of diagnosis with dementia or diabetes, or 6 years, whichever came first, because this was the trial duration and benefits were related to this treatment length. Cost per person treated increases by £504 and QALY gain is 0·006. Cost per QALY (£86 000) is above the NICE threshold. The intervention would not be seen by NICE as cost-effective for its effect on dementia.

The lifestyle intervention was expensive because of the number of sessions with a professional; therefore, we carried out a sensitivity analysis using results from a trial of metformin to prevent diabetes. The Diabetes Prevention Research Group recruited adults (mean age 51 (SD 10·7) at high risk of diabetes from impaired glucose tolerance and raised BMI, and randomly assigned them to metformin, placebo, or lifestyle intervention.[36] The annual incidence of diabetes was 5·1% with drug therapy and 6·1% without. Therapy was 850 mg metformin, twice daily, at annual cost of £33.[36] We added one GP consultation per year (cost £34).[15] The results of this sensitivity analysis showed an increase of £423 in lifetime cost per person treated and a QALY gain of 0·002. The cost per QALY (£189 000) is also above the NICE threshold.[14]

9% of middle-aged adults (age 45–64 years) have hearing loss at 3 kHz[11] as measured by a pure-tone audiometry screening test. We used this cutoff as it is likely to encompass most age-related hearing loss and to represent those who would benefit from a hearing aid.[11] Of those with midlife hearing loss, 17% currently use a hearing aid, so we considered the effect of providing hearing aids to those with hearing loss who are not using an aid (8% of all middle-aged adults).[37] The cost of supplying and fitting a hearing aid, including follow-up, is £370 and two adjustments annually cost £25 each,[14]

with hearing aids requiring replacement every 3 years. At age 45 years, discounted lifetime cost saving is £607 per person and QALY gain is 0·0798. Cost of therapy could be up to 68% higher without breaching the NICE threshold of £20 000 per QALY. Annual expenditure is £335 million and dementia prevalence eventually falls by 3·3%.

The effects of each and all interventions together on QALYs, costs, and dementia prevalence are substantial (tables 2 and 3). Considered together, treating hypertension in midlife, stopping smoking, and providing hearing aids in later life are associated with QALY gains and lifetime savings per person. This translates into annual net savings in unpaid family care of £1051 million) and social care of £866 million, resulting in total savings of £1863 million when NHS costs are considered. This is in addition to a dementia prevalence reduction of 8·5% (appendix pp 7–9).

The deterministic sensitivity analyses found that the leading influences on cost-effectiveness across all interventions were underlying incidence of dementia, excess risk of dementia for the risk factor, and intervention cost and effectiveness of the intervention (appendix pp 9–17). The cost of unpaid care in the mild stage of dementia is also prominent for all four interventions. If dementia incidence rates at the lower 95% CI are applied, both antihypertensive therapy and hearing aids cease being cost-effective, but hearing aids only marginally so. Smoking cessation remains highly cost-effective but no longer dominates its comparator. Preventing diabetes remains not cost-effective even with incidence rates at upper 95% confidence limits. In a high proportion of probabilistic sensitivity analysis iterations, incremental cost-effectiveness is well below the NICE threshold of £20 000 for smoking cessation and hearing loss, indicating that smoking cessation has 0·03% probability of not being cost-effective at this threshold and treating hearing loss a 16·3% probability of not being cost-effective. At the same £20 000 threshold, anti-hypertensive therapy has 85% probability of being cost-effective, and 97% probability at the £30 000 threshold.

	Intervention	QALY gain	Cost saving (£)	Cost per QALY (£)
Hypertension	Antihypertensive therapy	0·0393	–376	9555
Smoking	Nicotine replacement therapy	0·0967	1569	Dominates
Hearing loss at 3 kHz	Hearing aid	0·0798	607	Dominates
Diabetes	Prevention package	0·0060	–504	86 000

An intervention dominates when it results in better outcomes and lower costs. QALY=quality-adjusted life-year.

Table 2: **Lifetime cost savings and benefit per person treated for each risk factor**

Discussion

To our knowledge, these are the first calculations of potential cost and cost-effectiveness of implementing evidence-based, feasible preventative interventions for dementia. Implementing three measures (treating hypertension, reducing smoking, providing hearing aids) improves health-related quality of life (as measured by QALYs), and reduces annual costs associated with dementia by £1·863 billion, accounting for intervention costs. These QALY gains and cost reductions come to fruition when the programme is fully operational and those treated in mid-life reach late life. Cost of the full intervention programme is £1·077 billion annually. Social care accounts for more savings than does health care. This estimate of cost savings is lower than previously suggested because previous studies omitted intervention costs. Therefore, our estimate is relatively conservative, but probably more accurate given our detailed calculations.

These interventions are cost-effective. Hearing aids and smoking cessation save money while improving quality of life, and are worth implementing for their effect on dementia alone. Additionally, there is huge potential benefit in stopping smoking and administering antihypertensives on cardiovascular health, and personal and other health benefits of hearing improvement. Our cost-effectiveness results are sensitive to perspective: if savings in unpaid care are excluded, interventions other than smoking cessation are not cost-effective by NICE criteria (appendix p 13). On the basis of the effect on dementia without considering effects on other illnesses, interventions to prevent diabetes by lifestyle changes or drug therapy are not cost-effective.

We assumed risk factors cause dementia, so addressing risk factors reduces dementia risk. Evidence from trials suggests that treating hypertension reduces cognitive

	Cost of therapy (millions of £) £m	Savings in NHS treatment (millions of £) £m	Savings in social care (millions of £) £m	Savings in informal care (millions of £) £m	Net cost savings† (millions of £)	Reduction in prevalence of dementia (%)
Antihypertensive therapy	730	–42	497	614	1077	5·0%
Nicotine replacement therapy	12	–1	14	18	31	0·2%
Hearing aid	335	–28	355	423	755	3·3%
Total	1077	–71	866	1051	1863	8·5%

*Costs and savings are per year once the programme is mature, with all those treated in middle age having reached late old age, assuming all eligible are treated. †Net cost savings are a total of NHS treatment savings, social care savings, and savings in informal care, in addition to a small amount of other cost savings.

Table 3: **Total annual costs and savings of chosen interventions***

decline, but for the other risk factors, evidence is observational, although strong, consistent, biologically plausible, and dose-related.[4] Causal links are therefore likely but not proven. We have assumed that interventions reduce but do not eliminate dementia risk.

There will not be full intervention uptake and effectiveness can differ in routine practice from trials. Some people who are hypertensive or with hearing loss or who smoke do not want interventions. Costs and benefits would decrease proportionately with decrease in uptake, but cost-effectiveness would not change because it is independent of uptake.

We have assumed that, if NICE guidelines are followed, controlling hypertension might be possible; however, this might not happen in practice. Some people will not agree to interventions, and others will not adhere to them, possibly because of treatment adverse effects. We have not modelled this, but we advocate established treatments using results from trials. We consider interventions in the whole population, not exploring differences by sex, or in early onset dementia.

Consequently, the interventions might prove less successful in practice than we assume, but there is considerable room for the interventions to absorb reductions in efficacy and remain cost-saving or cost-effective. We did deterministic and probabilistic sensitivity analyses to understand how changes in model assumptions affect our conclusions. We accounted for risk factor communality and used conservative estimates. For hypertension, we costed for treatment with three antihypertensive drugs, which is often unnecessary. We assumed treatment at relatively young ages—for example, many people might not need hearing aids by age 45 years, and so treatment costs would be lower. We used a relatively high threshold for effects of hearing loss on cognition, for increased benefit. Not all the interventions were cost-effective, but our calculations emphasise the potential benefit to people with dementia, their families, and wider society.

These interventions would also be expected to reduce risk of cardiovascular disease and other diseases such as stroke, aside from dementia, but we did not model these, and therefore have underestimated the overall cost-saving effects. A delay of dementia until very old age might decrease morbidity: people could live for more years free of multiple illnesses. Nowadays, reductions in dementia have been in higher socioeconomic groups. Future interventions should also target other groups for greater equity of access and to increase overall benefit.

We have not included costs of promoting increased use of nicotine replacement therapy, hearing aids, or antihypertensives. We started our analysis when people decide on screening for risk factor or start treatment for them.

Our calculations are based on costs in England but our methods are generalisable to other countries. We expect these interventions will be valuable in similar settings. In low-income and middle-income countries with a greater PAF from hypertension, hearing loss, and smoking, they might be even more useful than we hope they will be in the UK.

Contributors

GL and MKn conceptualised and designed the study with NM, RA, CA, MKa and RW. NM did the literature search and review for evidence on interventions and wrote the first draft of the manuscript. RA and RW did the economic modelling and analysis and had full access to all of the data. SGC and MT provided data and expertise on hearing loss. All authors commented on the manuscript.

Declaration of interests

We declare no competing interests.

Acknowledgments

Economic and Social Research Council grants ES/L001780/1 and ES/L001896/1 funded NM and health economist time. NM is funded by an Alzheimer's Society Senior Fellowship, and GL and SGC are supported by UCLH National Institute for Health Research (NIHR) Biomedical Research Centre. SGC receives funding from Alzheimer's Research UK and the European Commission Horizon 2020 Programme. GL receives funding from the NIHR Collaboration for Leadership in Applied Health Research and Care North Thames at Bart's Health National Health Services Trust. MKn receives funding from the NIHR School for Social Care Research. MKn and RW receive funding from NIHR for four Policy Research Units: Adult Social Care, Economics of Health Systems and Interface with Social Care, Policy Innovation and Evaluation, and Older People and Frailty.

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