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Review article

A systematic review of the cost-effectiveness of community and population interventions to reduce the modifiable risk factors for dementia

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ABSTRACT

Dementia is a leading global cause of morbidity and mortality. Evidence suggests that tackling modifiable life-course risk factors could prevent or delay a significant proportion of cases. Population- and community-based approaches change societal conditions such that everyone across a given community is more likely to live more healthily. We systematically reviewed economic studies of population- and community-based interventions to reduce modifiable lifecourse risk factors for dementia. We searched Medline, EMBASE, Web of Science, CINAHL, PsycInfo, Scopus, Econlit, ERIC, the British Education Index, and Google, on 03/03/2022. We included cost-effectiveness, cost-benefit, and cost-utility studies, provided that the direct outcome of the intervention was a modifiable risk factor for dementia, and was measured empirically. Quality appraisal was completed using the Consensus on Health Economic Criteria checklist. A narrative synthesis was performed. We included 45 studies, from 22,749 records identified. Included studies targeted smoking (n = 15), education (n = 10), physical inactivity (n = 9), obesity (n = 5), air pollution (n = 2), traumatic brain injury (n = 1), and multiple risk factors (n = 3). Intervention designs included changing the physical/food environment (n = 13), mass media programmes (n = 11), reducing financial barriers or increasing resources (n = 10), whole-community approaches (n = 6), and legislative change (n = 3). Overall, interventions were highly cost-effective and/or cost-saving, particularly those targeting smoking, educational attainment, and physical inactivity. Effects were observed in high- (e.g. USA and UK) and low- and middle-income (e.g. Mexico, Tanzania, Thailand) countries. Further research into the direct effects of targeting these risk factors on future dementia prevalence will have important economic, social and policy implications.

1. Introduction

Dementia is a leading global cause of morbidity and mortality, with an increasing burden in low- and middle-income countries (LMIC) [1]. However, studies from high income countries (HIC) have reported significant reductions in age-specific incidence in recent generations [2], offering empirical evidence that, though dementia is strongly related to ageing, a proportion could be delayed or even prevented.

The 2020 Lancet Commission on Dementia [3] proposes 12 potentially modifiable, lifecourse risk factors for dementia (MLRFfD) – early-

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life low education; mid-life hearing loss, traumatic brain injury, hypertension, excess alcohol, and obesity; and late-life smoking, depression, social isolation, physical inactivity, air pollution, and diabetes. Based on relative risks and the prevalence of these risk factors, their eradication would theoretically reduce dementia incidence around the world by up to 40 %. Given the absence of effective disease-modifying treatments for dementia [4,5], affordable actions to tackle the modifiable risk factors for dementia, particularly in LMICs, are considered a public health priority [6].

Interventions targeting disease risk factors can be characterised by whether they attempt to change individuals' (usually individuals deemed at high-risk of disease) behaviours directly, by giving them information about their risk and the steps they can take to reduce that risk ('the individual approach'); or to change the societal conditions which make populations more likely to make healthier choices ('the population approach') [7]. Population approaches provide potential equity and efficiency benefits over individual approaches [7]. This is particularly important when dealing with a disease and risk factors that are highly, and globally increasingly, prevalent, with a faster rate of increase in LMICs [8].

A previous study [9] modelled the cost-effectiveness of four interventions against MLRFfD with outcomes justified only through potential reductions in dementia incidence. It found that smoking cessation programmes and hearing aid provision could be cost-saving, anti-hypertensives could be cost-effective, but a diabetes prevention intervention was unlikely to be cost-effective despite being clinically effective. The interventions all followed 'the individual approach'. A lifecourse approach would be more nuanced – for example, hearing loss can result from poor occupational hearing protection, diets high in salt from early life are associated with mid-life hypertension, with both conditions strongly related to inequalities.

Population approaches to dementia risk reduction are a public health priority, but have been underutilised to date [8]. Here, we systematically review cost-effectiveness studies of interventions to reduce MLRFfD, including only interventions following 'the population approach'.

2. Methods

The systematic review protocol is registered on Prospero (ID CRD42022311235).

2.1. Eligibility criteria

Adapted from Thomas et al. [10], we defined community- and population-level interventions as: measures applied to populations, groups, areas, jurisdictions, or institutions with the aim of changing the social, physical, economic, or legislative environments to make them less conducive to the development or maintenance of the MLRFfD.

We included cost-effectiveness, cost-benefit, and cost-utility studies of community- and population-level interventions to reduce the prevalence of MLRFfD. Simulation studies of hypothetical interventions, and non-quantitative studies were excluded.

We did not require studies to demonstrate a change in dementia prevalence or costs *directly*, instead we included studies where at least one of the reported outcomes of the intervention was a named MLRFfD from the 2020 Lancet Commission on dementia [3]. We did not restrict the period of lifecourse targeted (e.g. there was no upper age limit for recipients of more formal education; and no lower age limit for smoking cessation interventions). For air pollution, we only included studies that measured a change to Nitrogen Dioxide (NO_2), Fine Particulate Matter ($PM_{2.5}$), or Carbon Monoxide (CO), as these are the specified pollutants in the Lancet Commission [3].

2.2. Search strategy

We searched Medline and EMBASE via Ovid, Web of Science Core Collection, CINAHL PsycInfo, Econlist, ERIC and the British Education Index via Ebsco and Scopus, searching titles and abstracts, and subject headings where possible, for economic study terms AND MLRFfD terms AND prevention terms AND community/population terms. To search the grey literature, we used Google. Full details of the search strategy are included in Appendix A. Searches were undertaken on 03/03/22.

2.3. Study selection, quality assessment, and data extraction

Article titles and abstracts were imported into the Rayyan QCRI webtool [11]. Two reviewers independently screened titles and abstracts, retrieved full texts of potentially relevant articles, and assessed eligibility for inclusion.

Two reviewers independently assessed study quality, using the Consensus on Health Economic Criteria (CHEC) checklist [12]. An answer of yes was recorded as "1" (i.e. methodological quality indicator present), no as "0" (indicator not present), and where the question was not of relevance to the study as "n/a". Discrepancies were resolved by discussion in the first instance and by a third reviewer where necessary.

Data extraction was performed using a pre-defined extraction template that collected information on country of intervention, intervention design, target population, costs of intervention, intervention outcome measures, economic analytic methods, findings, and a description of significant study strengths and limitations.

All currencies were converted to 2022 US Dollars using CCEMG–EPPI-Centre Cost Converter [13], applying International Monetary Fund Purchasing Power Parities estimates.

2.4. Data synthesis

Given the heterogeneous nature of the studies, prohibiting meta-analysis, a narrative synthesis was conducted, grouping the studies by target MLRFfD and intervention design.

3. Results

We identified 50,041 studies (Fig. 1). After removing 27,292 duplicates, 22,749 unique records were screened for inclusion. We excluded 21,922 records at the title or abstract stage, leaving 827 records for full-text review. Of these, 45 [14–58] met the inclusion criteria (44 from database searches, and one [55] from grey literature).

3.1. Description of included studies

A description of the included studies is in Appendix B, grouped by targeted MLRFfD.

The most commonly targeted risk factors were smoking (n = 15 studies), education (n = 10), physical inactivity (n = 9), and obesity (n = 5). A small number of studies targeted air pollution (n = 2), and traumatic brain injury (n = 1). Three studies targeted multiple risk factors, including combinations of obesity, hypertension, diabetes, alcohol, smoking, and physical inactivity. We identified no studies that targeted hearing loss, depression, or social isolation; and no studies that reported changes to dementia prevalence directly.

Intervention designs varied across studies. Smoking studies utilised mass media-type interventions (n = 10) [15,16,18–21,24,25,27,28] aimed at changing sociocultural norms and publicising cessation support (sometimes centred around a specific cessation event (n = 2) [18,19]), tobacco control plans (n = 3) targeting either state-wide legislative changes [17,23] or community-wide action [14], and national Quitline services (n = 2) [22,26]. Education interventions focused on reducing financial barriers to education (n = 4) [50,55–57], providing additional resources (e.g. books, salary costs of extra teaching staff, or

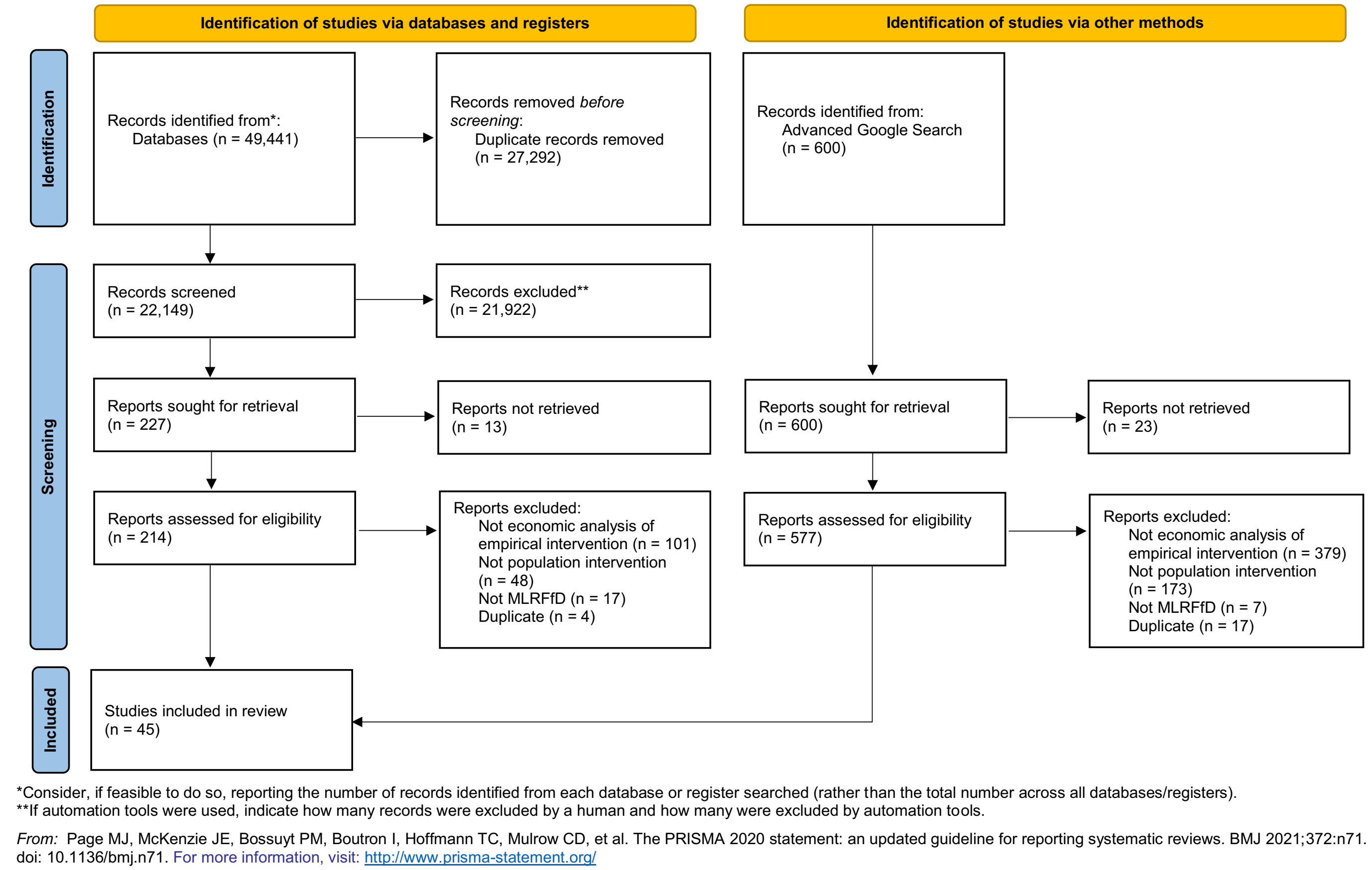

Fig. 1. PRISMA flow diagram.
*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: https://doi.org/10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/.

free school meals) to resource-constrained schools and students (n = 3) [49,52,58], holistic pre-school and early school years' support to children and parents from deprived backgrounds [51], training teachers to become champions of child-centred education [54], and additional remedial education for academic underachievers [53]. Physical inactivity studies focused on built environment changes (n = 5) [32,33,35,36,39] such as construction of new/improved walking and cycling paths [32,35,39] or temporary closure of streets to motorised vehicles [36], altering the school environment (n = 2) [31,34], free leisure centre access [37], and mass media campaigns [38]. Obesity studies investigated school-based programmes that altered the food environment, the curriculum, opportunities for physical activity, and/or home-based activities (n = 3) [40–42], and community-based programmes that engaged local restaurants/takeaways and schools, and provided and promoted physical activity opportunities (n = 2) [43,44]. Those targeting multiple risk factors were either workplace-based, changing the food environment, providing physical activity opportunities, and wellness checks with lifestyle counselling (n = 2) [45,46], or community-based, working with local eateries to make menu choices healthier and providing smoke-free spaces, and changing the built environment to be more conducive to physical activity [47]. Both air pollution interventions reduced the financial barriers to adopting cleaner fuels, either for heating [29] or cooking [30]. The single head injury study [48] provided cost-effectiveness estimates for three different interventions (legislative, community-based, and school-based) designed to increase bicycle helmet usage amongst young people.

Of the 45 included studies, over half predominantly targeted younger people (children and/or teenagers) (n = 25), including all ten education [49–58] and all five obesity studies [40–44], six smoking studies [14,15,17,24,27,28] three physical inactivity studies [31,34,38], and the head injury study [48]. The remaining studies targeted either adults, or the whole population. Ten of the included studies were performed in LMICs, including education studies (n = 4) set in Mexico [49], Senegal [58], Kenya [54], and Tanzania [52]; air pollution studies (n = 2) from Nepal, Kenya and Sudan [30], and China [29]; and single studies on smoking from Thailand [26], physical inactivity from Columbia and Mexico [36], obesity from China [40], and multiple risk factors from South Africa [46].

Economic analytic designs of the included studies can be classified into four types. The simplest design, used in 12 studies [16,20,31–33,38,45,46,49,52,54,58], expressed the cost of the intervention per outcome measure achieved (e.g. cost per quitter, or cost per extra year of schooling). Six studies [17,23,50,51,53,56] performed return on investment (ROI) calculations without the need for modelling of long-term intervention benefits, either by performing the analysis long enough after the intervention took place to allow for direct measurement of the outcomes [17,23,50,51] (e.g. Lightwood et al. directly measured changes in health costs associated with changes to tobacco consumption over two decades [17,23]); or by using an outcome that was directly measurable as a result of the intervention (federal aid received due to extra enrolees) [56]. The remaining studies took the empirically observed changes due to the intervention and modelled the long-term effects, usually using pre-existing chronic disease models, or applying estimates from observational data about the various advantages associated with extra education (e.g. higher salaries). Of these, nine studies [14,15,18,19,21,22,28,40,48] modelled long-term changes in either life-years gained, quality-adjusted life years (QALYs) gained, or deaths avoided. The remaining 18 studies [24–27,29,30,34–37,39,41–44,47,55,57] modelled future cost savings (often as a result of the modelled benefits) and presented ROIs from either societal or healthcare perspectives.

Quality assessment findings are shown in Appendix C. The CHEC items that were least often satisfied were Q17: "Does the study discuss the generalizability of the results to other settings and patient/client groups?" (n = 16 studies did this) and Q18: "Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?" (n = 20). In contrast, all studies (n = 45) satisfied Q3: "Is a well-defined research question posed in answerable form?", and all but two (n = 43) satisfied Q6: "Is the actual perspective chosen appropriate?". The average score out of a possible 19 (considering n/a answers as a 0), was 13.6 (range 5–18) across studies, indicating good overall quality of the evidence base. In general, the analytic designs were clear and reasonable, but a small number of studies lacked sufficient detail [34,36] or contained significant issues with the methodology [35,38].

3.2. Narrative synthesis of findings

Summaries of the intervention costs, key findings, and strengths and limitations of included studies are included in Tables 1, 2, and 3, respectively, grouped by risk factor targeted.

3.2.1. Smoking

The ten studies of mass media anti-smoking campaigns [15,16,18–21,24,25,27,28] reported generally positive results. Four [24,25,27,28] studies forecasted cost-savings, with societal ROIs as favourable as $174 per $1 spent over a long-term time horizon [27]. A further four studies [15,18,19,21] reported cost per life-year gained, with results ranging from $137 [18] to $1136 [15]. It was notable that campaigns using digital media were much cheaper to produce and broadcast than those using the television, and demonstrated comparable results [20].

Other smoking interventions also produced favourable results. Two studies examining state-level tobacco control plans across two decades reported ROIs of 50:1 and 10:1 for California [23] and Arizona [17] respectively. Two studies examining national Quitlines forecasted an ROI of between 6:1 and 9:1 in Thailand [26] and a cost per life-year gained of $58–417 in Sweden. Finally, a multi-faceted community intervention reported a cost of $6033 per life-year gained.

3.2.2. Education

Of the seven studies reporting the effect of removing financial barriers to accessing education [50,55–57], or improving the resources available [49,52,58], six [49,52,55–58] reported positive economic outcomes. In the USA, efforts to encourage and financially support young people to access higher education yielded a benefit-to-cost ratio of 8:1 [55] and forecasted net savings of $835 million from additional tax revenue and other societal benefits over 40 years [57]. Provision of free school meals in Senegal cost $7 per 1 % increase in test scores [58], whilst in Tanzania, an extra 1.45 years of schooling was enjoyed for every $114 spent – with particular benefits to young girls [52]. The provision of holistic pre-school and early school years' support to children from deprived backgrounds in USA yielded an ROI of between 4:1 and 11:1 [51].

3.2.3. Physical inactivity

All nine physical inactivity studies [31–39] reported favourable economic results, though the weak methodology of some studies limited the confidence in the findings [34,36]. Of those studies investigating changes to the built environment, ROIs ranged from 2:1 [36] to 11:1 [39] for road closures and infrastructure provision respectively; and

Table 1
Intervention costs of included studies.

Study	Costs
Smoking (n = 15)	
Allom, 2018	$1.5 million. Includes: costs of producing and broadcasting the campaign materials
Brown, 2014	$10 million footed by Department of Health. Included: $5.8 million on media advertising (TV, radio, press, digital, outdoor, media partnerships), $120k on public relations activity, $859k on local and regional activation of the campaign amongst participating organisations including national Stop Smoking Services, $3.1 million on fees for development, website, and digital tools
Hair, 2019	Total campaign cost: $183 million
Holtgrave, 2009	Total 3-year cost: $496 million. Included $271 million on development and broadcasting costs, $34 million on a summer tour that followed youth music events, $26 million research costs, $81 million in agency fees, and $26 million in litigation costs
Hurley, 2008	$12.1 million over 6 months. 90 % was federal spending, on media advertising, production costs, advocacy, educational materials for smokers, research and evaluation, and administration and national coordination costs. Remaining from state and territory organisations, for: advertising, public relations activities aimed at attracting coverage in local, state-wide or media, telephone counselling and courses to assist people to quit, and distribution of materials through newsletters, community and workplace displays and through health professionals. Federal spend measured directly. State spend on campaign estimated as 50 % of total spend
Kotz, 2011	Total cost: $1.4 million. No details or sources given for this figure
Lightwood, 2008	$2.5 billion spent by state of California on tobacco control policies from 1989 to 2004, data provided by relevant state departments (and from literature/CDC for control states). No further details provided
Lightwood, 2011	$331.2 million spent by state of Arizona on tobacco control education programme, data provided by relevant state departments (and from literature/CDC for control states). No further details provided
MacMonegle, 2018	Total costs of $278.5 million, including: $36 million on planning and development, $223 million on broadcasting costs, $3.4 million on administration, and $14.6 million on evaluation. No detail on sources of costs
Meeyai, 2015	$2.2 million over 4 years. Included salary costs (largest cost component), office rent, promotional resources, evaluation costs, and telephone bills
Mudde, 1999	$4.0 million total cost of development and implementation, funded by grants from Ministry of Public Health and several charities. Group programmes cost-neutral due to cost of manuals
Ross, 2006	$6.1 million, including: expenditures on personnel, consultant fees, equipment, rental space, programme costs, policy enforcement costs, community grants
Sacker-Walker, 1997	$1.2 million, including: salary and fringe benefits for research staff, consultant fees, travel costs, costs of data entry and analysis, production costs, broadcasting costs
Tomson, 2004	$1.0 million, including $700k for staff costs, $295k for services (office rental costs, advertising, computer equipment), $37k for materials (office supplies). Estimated $68k cost to patients for nicotine replacement therapies
Xu, 2015	$57.3 million, including: $8 million for development and execution, $45 million for advertising and broadcasting, and $3.8 million for evaluation
Education (n = 10)	
Acevedo, 1999	$698 for indigenous schools, $443 for rural schools, $78 for urban schools: per pupil cost per year. This includes: library costs, books, training, infrastructure, salary, administration. Biggest costs for infrastructure (though not in urban schools), and learning materials
Anzelone, 2020	$16 per student (messaging) $86 per student (messaging + financial support). $68 per student (additional cost of financial element) – reduced to $48 in 2nd year due to increased federal support. Costs include: materials, stamps, printing, staff costs to administer and design, direct financial grants

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Table 1 (*continued*)

Study	Costs
Azomahou, 2019	$70 per pupil per year from Ministry of Education and World Food Programme: paid for most of canteen/meal costs. $1 per pupil per month required from parents of children for fresh produce e.g. vegetables
Bowden, 2014	$4128/student, and $1.5 billion/national cohort (2 years participation), including: $1.2 billion from national programme, with remainder in local costs. Costs scaled up from interviews with directors from 11 sites across Texas and Florida to the full national level. Costs include: staff costs (75 % of total costs), facilities, materials and equipment, transportation costs
Capper, 1997	$5.7 million, to train 204 staff. With per staff costs in phase II half the costs of phase I. Only staff training costs detailed
Lavy, 2018	$1622 per participant
Reichardt, 2020	$67.7 million per year, including: $36 million on administrative, books, teacher salary, and facilities costs; and $32 million on tuition fees. Per student cost estimated at $2509
Reynolds, 2011	$10,998 per pre-school participant, average length of participation 1.55 years ($7.1k per year). $4899 per school-age participant, average length of participation 2.14 years ($2.6k per year). $16,434 per extended participant (meaning service offered run-through pre-school and school-age support), average length of participation 3.87 years ($6.6k per year). Costs include: outlays for staff, family and community support, administration, operations and maintenance, instructional materials, transportation and community services, schoolwide services, school district support, capital depreciation and interest, and parent opportunity costs
Sabates, 2021	$149 per participant per year. This includes: direct financial support, indirect financial support, educational resources, staff training, school costs
Somers, 1972	$4379, including: $1136 social costs (not detailed), $885 federal government costs (not detailed), $2358 private costs (detailed as forgone earnings, but not clear how this was calculated)
Physical inactivity (n = 9)	
Chapman, 2018	$12.7 million, including: $11 million spent on active travel infrastructure upgrades (e.g. new tracks to connect existing infrastructure better so that whole journeys can be on designated infrastructure). Maintenance costs of $156k/year. Small costs (unlisted) attributed to media and education campaigns
Frew, 2012	$7.9 million/year, including: $7 million on leisure centre fees, $356k on gym estates costs, $267k on administration, and $53k on marketing. Per person annual cost: $68–$133 (depending on 50–100 % usage rate amongst registered individuals). Assumed in the primary model to be £84 in first year, then £46 thereafter
Gesell, 2013	$2.0 incremental cost per child per day. Intervention group total: $1472/child for 12 weeks. Control group: $1351/child for 12 weeks. Facilities costs based on $1 per sq. ft, because these spaces were freely available for this intervention (so costing the opportunity cost of the space usage): $971 per child intervention, $878 controls. Personnel costs: $472 vs. $390. Snacks: $21 vs. $77. Equipment: $7 vs. $5
Kennedy, 2017	$970k for the 19 schools, or $120 per pupil, for 11 years. Equating to $90k per year. Costs included: provincial, regional, and municipal level coordination costs, school-level planning, implementation and monitoring, and maintenance costs (no breakdowns provided)
Knell, 2019	$193 million in total, equating to $250 per meter of sidewalk improvement. Assumed to have 50-year lifespan, resulting in a $3.9 million yearly cost. Costs obtained from city planning officials, and include planning, engineering, construction, and maintenance costs, but breakdowns not given. Census records indicate 1.5 million adults live within 250 m of an improvement site, meaning an annual cost of $2.5 per adult with capacity to benefit
Lal, 2019	$890k design and construction cost. Assumed to last for 20 years with an annual increased maintenance cost of $5.9k/year
Montes, 2012	From Bogota, annual cost $5.1–9.0 million, $71k–124k per event. Consisting of: fixed costs (salaries, logistics) of $1.4million, variable costs (salaries, equipment, dividers) of $767k, and user costs (equipment e.g. bicycles) of $2.9–$6.8 million. Per event costs in other sites: Guadalajara: $21k, Medellin: $10k, San Francisco: $42k
Peterson, 2008	Collected from marketing agency, included production and placement costs. Costs not reported
Wang, 2005	Total annual cost: $476k, cost per trail: $95k. Includes: construction costs of $357k (which is actually 30 times this, but allocated evenly over 30 years), and maintenance costs of $122k/year (with assumed lifetime of 30 years, no discounting). Estimated costs to users of $238 per year for equipment and costs of getting to/from trails, from literature
Obesity (n = 5)	
Brown, 2007	Total costs: $62k (across 4 schools), including: $29k for staff training costs (includes PE teachers, classroom teachers, counsellors/nurse, nutritionist), and $20k promotional costs
Coffield, 2019	$402k over two years, including: $109k for material costs including promotional materials, postage, and donated goods, $29k for equipment, $274k for labour costs including training, and cover, and $30k on facility costs including office space and utilities. Equipment costs were split evenly across a 10-year period with 3 % discount rate and no scrap value
Moodie, 2013	Annual cost $337k, or $60.7k per school community. 64 % of costs were staffing, with other costs for venue hire, resources, and travel. Additional $20k for evaluation costs
Oosterhoff, 2020	Healthcare perspective: HPSF $4.6k per school, $6.27 per child per day. Physical activity schools (PAS) $2.2k per school, $3.03 per child per day. Societal perspective: HPSF $1.35 per child per day. Sum of material costs and time investments. Costs calculated for the steady state, post-implementation into daily practice. Calculated by stakeholder survey/expert opinion using evidence-based template. Separate calculations for healthcare only, and societal perspectives. Societal perspective offset intervention costs by adding potential productivity gain for parents benefiting from the longer school day
Zanganeh, 2021	$167 per child per year. Includes: parents attendance ($116), lunch costs ($40), teachers' time ($7), and materials ($3). Excludes intervention costs
Air pollution (n = 2)	
Feng, 2021	Total cost for 2017 and 2018: $13.3 billion. Costs to households: 44 %. Including 15–50 % of capital costs not covered by subsidy, and more expensive ongoing fuel costs (unclear where data on the costs come from). Costs to government: subsidy costs (part funded by central, and part by local government). Data from official government data
Malla, 2011	Kenya (mostly LPG cooker + smoke hoods, but some lower cost solutions e.g. solar cookstoves): average investment costs $49.74, fuel costs $25.84/year, maintenance $1.99/year; all per household. Nepal (mostly smoke hoods): investment cost $91.53, fuel change costs $0 (remained as wood), maintenance $1.99/year. Sudan (mostly LPG cooker): average investment cost $103.49/10 years, refilling cost $75.59/year, maintenance cost $15.92/year. All capital costs predicted to be incurred only once across 10 years
Head injury (n = 1)	
Hatziandreu, 1995	Legislative: total cost $1.7 million ($23k start up, $51k 4-year maintenance, $1.7 million for helmet purchases). Community: total cost $8.3 million ($142k start up + $508k maintenance + $7.6 million for helmets). School (inflated to cover a whole county): total cost $4.6 million ($222k start up, $3.2million maintenance, $1.2 million for helmets). Programme personnel contacted directly to give costs on: personnel resources (staff and volunteers), materials, advertising. Expansion costs and evaluation costs excluded. Assume 50 % of helmets bought as a result of campaign are worn. So doubled the intervention size to calculate number of new helmets bought. 5 % discounting on costs over 4-year maintenance period
Multiple (n = 3) including: obesity, hypertension, diabetes, alcohol, and smoking	
Johansson, 2009	Total costs for 10-year programme: $5.7 million, equating to $213 per inhabitant in target age group in intervention areas. Consisting mostly of administrative costs and salaries paid by local government, with only $460k estimated as costs to target

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Table 1 (*continued*)

Study	Costs
	groups' own expenses and time spent. Cost data from reviewing programme documentation, and interviewing key stakeholders. Acknowledged that many smaller events difficult to cost, so sensitivity analysis included 300 % higher costs.
Schouw, 2020	Total cost for 2-year intervention: $4.2k, or $1.20 per individual per year. Including: $2.3k for physical activity (e.g. equipment costs), $822 for catering, and $1.2k for health and wellness services. Excluded research costs
Erfurt, 1992	Total costs over 3 years/annual cost per employee: Site A: $175k/$35.77 Site B: $952k/$79.48 Site C: $476k/$62.64 Site D: $389k/$78.04 Including: salary costs and equipment costs. No discounting/cost inflation reported. N.B. workforce size partially driving per employee costs (1.6k, 4.0k, 2.5k, 1.7k, respectively)

costs per increase in metabolic equivalent of a task (MET) hour was estimated at $0.54 from sidewalk improvements [32] and $0.45 from a park refurbishment [33]. Providing free leisure centre access in the UK was predicted to be cost-effective at $711 per QALY [37].

3.2.4. *Obesity*

The five obesity studies [40–44] reported mixed results. Of those focusing only on changes to the school environment, a study from USA reported small cost-savings over a 50-year time horizon [42], and studies from the Netherlands and China reported cost-effectiveness at $27.7k/QALY [41], and $22.9k/QALY [40] respectively, though the former extrapolated non-significant trends in body mass index (BMI) changes from the original trial. One whole-of-community study reported an ROI of 1.5:1, over a 10-year horizon in USA [43], whilst the other reported a cost per disability adjusted life year avoided of $29.6k [44], though sensitivity analysis allowing for some intervention waning over time pushed the estimate just over the national Australian threshold for cost-effectiveness at the time.

3.2.5. *Air pollution*

Both air pollution studies reported positive ROIs from interventions to subsidise [29] and/or provide [30] cleaner heating/cooking technologies, with benefit-to-cost ratios of 4.5:1 in China [29], 1.4:1 in Kenya, 21.4:1 in Nepal, and 2.5:1 in Sudan [30] arising from reduced disease and fuel costs.

3.2.6. *Head injury*

The costs per year life-year gained from the three different interventions to promote helmet use amongst children were reported as $1.7k for the legislative intervention, $1.7k for the community-based intervention, and $6 million for the school-based intervention [48]. However, the surveys used to estimate changes in helmet use associated with the interventions were not adequately reported.

3.2.7. *Multiple risk factors*

The two workplace-based interventions targeting multiple risk factors [45,46] only reported changes in risk factor prevalence per dollar spent. In both cases, large reductions were possible for small amounts of money ($3–4 USD per unit decrease in risk factor prevalence), largely because of the very high prevalence of risk factors in the first place. The community-based prevention programme from Sweden reported largely null findings from the intervention itself, resulting in a similar picture from the economic analysis [47].

Table 2
Key findings of included studies, grouped by risk factor targeted.

Study	Key findings
Smoking (n = 15)	
Allom, 2018	Online display (OD) only was most cost-effective ($137 per weighted score), followed by combination of OD + online video (OV) ($613). Television (TV) alone was least cost-effective ($7013). Full cost/outcome for OD only: $5/unique website view, $650/Quitline call, $2843/QuitCoach registration
Brown, 2014	October 2012 9.6 %, vs. 6.6 % year average, whereas October 2007–11, lower than year averages. Regression interaction term: OR1.79 (1.20–2.68). Additional 4.15 % (0.94–7.37) attempts attributable to Stoptober. No evidence it brought forward quits from November/December. No three-way interaction between October, quit attempts, and socioeconomic status, sex, or age. ICER: $959 ($216–$1699) per life year gained. Estimated that Stoptober resulted in extra 8817 extra permanent quitters (95 % CI 1992-15,641) in England. Extra attributable LYs gained: 10,400 (2349-18,450)
Hair, 2019	Conservative scenario: health cost savings: $183 million, QALYs saved: 150,588, cost per QALY: $1214 (cost-effective). Base-case: health cost savings: $3.5 billion, QALYs saved: 150,588, cost-saving, societal ROI: 174:1. Optimistic: health cost savings: $3.5 billion, QALYs: 253,848, cost-saving
Holtgrave, 2009	Conservative scenario: cost savings: $1.2 billion, QALYs saved: 178,290, cost per QALY: 6584 (cost-effective). Base-case: cost savings: $2.9 billion, QALYs saved: 178,290, cost-saving. Optimistic: cost savings: $8.5 billion, QALYs: 1.1 million, cost-saving
Hurley, 2008	Reduction in smoking point prevalence: 1.4 %. Equating to 900,000 people nationally. Total healthcare cost savings: $887.7 million. Net cost saving: $875.6 million. 323,000 extra life years, 407,000 more QALYs. Therefore, intervention dominant. Remained dominant if number of quitters halved. Dominant for time horizons from 5 years onwards
Kotz, 2011	9.2 % of smokers attempted a quit in April 2007–09, compared to 6.4 % in March/May (difference 2.8 %, p = 0.001). 0.07 % of English smokers permanently quit in response to the intervention between 2007 and 09. ICER per LY, by age-group: aged <35: $206, 35–44: $148 (95 % CI £90–£419), 45–54: $138, 55–64: $176. If long-term quitters halved: 35–44: $297 ($179–$836)
Lightwood, 2008	Increase of one cigarette pack purchase per capita per annum associated with a $38 increase in per capita healthcare costs. Every $1 spent on tobacco control by state associated with a 0.261 decrease in per capita cigarette consumption. Estimated total savings in health expenditure in California of $121.2 billion from 1989 to 2004. Estimated 3.6 billion fewer packs of cigarettes sold in total. Ratio of benefits to costs 50:1
Lightwood, 2011	Increase of one cigarette pack purchase per capita per annum associated with a $27.5 increase in per capita healthcare costs. Every $1 spent on tobacco control by state associated with a 0.190 decrease in per capita cigarette consumption. Estimated total savings in health expenditure in Arizona of $2.3 billion from 1996 to 2004. Estimated 200 million fewer packs of cigarettes sold in total. Ratio of benefits to costs 10:1 (95 % CI 2:1–21:1)
MacMonegle, 2018	Estimated that campaign resulted in 175,941 fewer long-term smokers. Cost per LY saved: $2363. Cost per QALY: $1508. Costs averted: individuals: $169k per person, $29.3 billion total; family members: $28k per person, $4.5 billion total; societal costs: $8k per person, $1.1 billion total. Total: $205k per person, $36 billion total. ROI = 4:1 (societal), 128:1 (all costs)
Meeyai, 2015	% abstinent at 7 days, 1, 3 and 6 months were: 51.6 %, 49.9 %, 38.0 %, 33.1 %, respectively. Projected to 19.5 % at 12 months. Scaling up this equates to 7215 quitters over 4 years. Cost per completed counselling $38. Cost per quit (at 12 months): assuming 0 % would have quit otherwise: $301, assuming 1/3 would have quit otherwise: $469. 57,238 life years saved. Equating to $38 per life year (0 % assumption), $59 (33 % assumption). Cost savings from quitters (human capital) of $1602 per quitter or $19.6 million total (0 % assumption reported only). ROIs: 9.01 (0 %), 7.17 (20 %), 5.78 (33 %)
Mudde, 1999	88 % of non-pretested smokers recalled campaign, 45 % could reproduce a name/description of a campaign element. Estimate 4.5 % of smokers that quit because of the campaign. Applying

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Table 2 (*continued*)

Study	Key findings
	to the whole Dutch population: 187,000 quit because of the campaign. This produces a cost per quitter of $22
Ross, 2006	$5799 per avoided smoking initiation. $6033 per life-year gained. Compliance rates amongst tobacco vendors improved from 64 % at baseline to 94 % at outcome (methods for ascertainment not detailed)
Sacker-Walker, 1997	Prevalence rate 20.4 % in intervention cities, compared to 25.9 % in controls. $1212 (95 % CI $854–$2084) per avoided smoking initiation. $1136 (95 % CI $727–$2072) per life-year gained
Tomson, 2004	8503 new callers to Quitline, 4021 recorded on database, 1131 agreed to participate and completed 12-year outcome survey. 354 (31 %) quit at 12 months. Cost per quitter $1551–$2005. 2400 life years saved. Cost per year of life gained was $58 (0 % discounting), $199 (3 %), $417 (5 %)
Xu, 2015	Campaign attributable long-term quits: 100,000 (95 % CI 95,592-104,409). Life years added: 98,676 (93,704-228,182). QALYs gained: 154,382 (147,015-161,750). Premature deaths avoided: 13,638 (12,988-14,289). Cost per quit: $574 ($550–$597). Cost per life year: $585 ($550–610). Cost per QALY: $370 ($358–$394). Cost per premature death avoided: $4194 ($3991–$4397)
Education (n = 10)	
Acevedo, 1999	Significant improvements in Spanish scores, compared to controls, for children in Indigenous and rural schools. Students in urban schools improved, but significantly less than the control. Indigenous school costs increased 38 % for a 42 % attributable increase in scores (ratio +11 %). Rural schools 24 % cost increase, 17 % test score increase (ratio −30 %). Urban schools 4 % increase in costs, 15 % worsening of test performance (ratio −445 %)
Anzelone, 2020	26 % of control students enrolled in summer courses, 32 % of enhanced messaging students enrolled, 38 % of financial support students enrolled. Credits earned: 1.31 (control), 1.53 (+0.22) (messaging), 1.83 (+0.52) (financial). One year later, the difference in total credits earned was maintained as 0.21 and 0.51, respectively. Prior term pass rates: 86 % control, 83 % messaging, 82 % financial. Summer course pass rates: 76 % control, 74 % messaging, 75 % financial. Enrolment in the fall term: 55 % control, 55 % messaging, 55 % financial. ROI: messaging only = +$60/year (SE 18, p = 0.001), messaging + financial = +$82/year (SE 18, p < 0.001)
Azomahou, 2019	6.8 % (intention to treat), 11.3 % (compliers only) point increase in maths score, and 5.9 % (ITT), 9.7 % (compliers only) point increase in French score, compared to controls. Non-significant effects on enrolment and dropout, but intervention significantly increased the repetition rate by 1.96 % points. Cost per additional 1 % increase in test score: $6.2 (maths), $7.2 (French)
Bowden, 2014	High school completion rate increased by 9 % points (Texas) and 14 % points (Florida), compared to controls. Within-state post-secondary education enrolment increased by 18 % (Texas) and 15 % (Florida), compared to controls. $41,651/extra high school graduate. $39,140/extra post-secondary enrolment. $22,144/extra year of schooling. Ratio of additional lifetime earning to cost per student: 7.62
Capper, 1997	Statistically significant improvements in all three tests for group 1 (10–20 % point improvements over controls), and in around half of tests for group 2. Group 3 performed the same or worse than control schools. However, after adjusting for relevant sociodemographic factors, results become non-significant. Aggregated across all test scores, group 1 outperformed controls by 16 %, group 2 by 5 %, group 3 by 5 %. Equating to a cost per % increase per pupil of group 1: $49, group 2: $104, group 3: $52
Lavy, 2018	Significant 13 % point increase in matriculation, significant 7.6 % point increase in ever enrolment, significant 20 % relative increase in completed years of education, significant 4.5 % point increase in likelihood of marriage. Non-significant changes to annual earnings. Monthly earnings $1106, 20 % income tax, therefore costs recovered within 8 years
Reichardt, 2020	Intervention group saw a 15 %-point increase in enrolment, and a 19 % point increase in completion rate (n = 4000 extra completers). Total revenues and savings over 40-year time horizon: $835 million, state: $305 million, federal: $530 million
Reynolds, 2011	Pre-school intervention associated with significant improvements in following domains: 7 %-point increase in high school completion, 0.3 years of extra education, less remedial education, reductions in criminal justice and social services interactions, reductions in substance misuse and smoking. Non-significant reduction in depressive symptoms (12.8 % vs. 17.4 %, p = 0.057). School intervention associated with significant improvement in high school completion rate (79.1 % vs. 75.4 % p = 0.14), and less remedial education (15.4 % vs. 21.3 % p = 0.02) but all other domains non-significant. Extended intervention associated with significant improvements in following domains: 4.6 %-point increase in high school completion, 0.2 years more education, remedial education, less depressive symptoms, some criminal justice/social services interactions. ROI: pre-school 11:1 (90 % CI 4.1–18.1), school-age: 4:1 (−3:1–12:1), extended 8:1 (0:1–17:1)
Sabates, 2021	Girls who received financial support increased their test scores by 1.10 SDs in maths, and 0.58 SDs in English, relative to matched controls. Odds of drop out for girls receiving financial support reduced by 25 % (relative) to matched controls. Cost per additional SD of English score: $152 weighted school average, $505 for girls receiving direct financial support, $58 for girls receiving non-direct financial support. Additional years of schooling per $114 spent is 1.45 weighted school average, 0.43 for girls receiving direct financial support, 3.76 for girls not receiving direct financial support. Sensitivity analysis adding weighting for reduction in dropout rates improves cost per additional SD of English score to $105, and additional years of schooling per $114 to 2.10 (but these are only reported for school average)
Somers, 1972	No significant benefit for likelihood of high school graduation or years of high school completed overall, however, significant effects were found for ethnic minority groups (African Americans, and Native Americans). Significant increased likelihood of attending college, but not university. Non-significant effects on post-tax income to individuals. Social average benefits estimated as $485.4 million
Physical inactivity (n = 9)	
Chapman, 2018	Net changes (intervention - controls from 2010 to 2013, cumulative). Increase in active travel trips: 17.3 million, or 30 %. Equating to 34.5 DALYs and 2 deaths saved. Decrease in motorised trips: 5.3 %. Meaning a 1.21 % reduction in KM travelled as a % of total trips; equating to 4.87 million less KM travelled, saving 1149 t of carbon. Health benefits: $138 million. CO_2 reduction benefits: $2.2 million. Benefit:cost ratio: 11.1
Frew, 2012	Physical activity levels increased by 15 %, percentage of participants scoring as physically inactive dropped by 9 %. Assuming increased physical activity sustained over 5 years: extra QALYs: 0.06, cost per QALY: $711 per QALY. Sensitivity analysis increasing time horizon to 10 years results in a dominant intervention. Sensitivity analysis with 50 % weaning of intervention effect by 1 year showed a cost per QALY of £3272 (5-year time horizon)
Gesell, 2013	Time spent doing physical activity: 6 % point increase in intervention group, 6.8 % point decrease in controls. Moderate/vigorous physical activity: 2.8 % point increase compared to 0 % change in controls (p = 0.002). $2 per 15.4 % point increase in any physical activity, 14.7 % point increase in MVPA
Kennedy, 2017	Car trips decreased by 2.8 % in the mornings, and 1.4 % in the afternoons. Walking and cycling increased by 1.3 % in the morning and 0.6 % in the afternoon (not clear if these are relative or absolute increases, and what makes up the shortfall in between them). Vehicle KM travelled reduced by 192,224 km, resulting in 41.7 t of greenhouse gas emissions and 1.7 t of air pollutants avoided (all per year). Walking increased by 1.3 million min, and cycling by 2 million min (both per year). Net societal benefit of $1.7 million per 11 years, producing a cost-benefit ratio of 1.8:1
Knell, 2019	Living near a sidewalk improvement project associated with mean increase in MET hours per year of 203.3 h (95 % CI -33.0,

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Table 2 (*continued*)

Study	Key findings
	439.6) on self-report, and −4.5 h (−47.8, 38.8) on accelerometer. Cost-effectiveness $0.01 annual cost of sidewalk improvement, per MET h gained per year per person (self-report), and $0.54 (accelerometer). Cost-effectiveness threshold: $0.21. Therefore: cost-effective using self-report, but non-cost-effective using accelerometer data
Lal, 2019	Net gain between baseline and last follow up: 114k MET/h/year (95 % CI 80k–146k), with greatest increases amongst children. This was similar to the observed difference between baseline and immediately after completion of playground, indicating sustained change over 1 year. Cost per MET h gained was $0.45 ($0.34–$0.61), indicating cost-effectiveness. Using observations from across the park: net gain 131k; cost $0.66 ($0.18–$0.33) per MET h gained
Montes, 2012	Bogota: annual number of users varied between 239k and 557k (cyclists), 247k and 577k (pedestrians), 30k and 71k (other). With 102k–239k (cyclists), 72k–168k (pedestrians), and 10k–24k (others) estimated to be meeting physical activity guidelines. This produced an estimated annual health benefit of $88 per user, with a benefit to cost ratio of 3:1–4:1. Ratios for other sites: Guadalajara: 2.5, Medellin: 1.8 San Francisco: 2.3. Almost all sensitivity analyses produced smaller but positive benefit to cost ratios. Mean annual benefit of mortality avoided ranged from $85k to $85 million across sites and assumptions
Peterson, 2008	30 % recognised no ads, 13 % of them intent to change, 10 % changed behaviour. 10 % recognised billboards only, 53 % intent to change, 44 % changed. 34 % recognised TV adds only, 42 % intent, 33 % changed. 44 % recognised all 3, 66 % intent, 58 % changed. All categories combined: 77 % recognised something, 55 % intent, 45 % changed. Billboard only: cost per person to see ad $3.17, cost for intent $5.98, cost for outcome $7.20. TV only: cost per person to see ad $14.09, cost for intent $32.77, cost for change $44.46. All 3: $9.87 reach, $15.50 intent, $16.91 change. Overall: $5.64, $9.87, $12.69
Wang, 2005	225,351 estimated annual uses averaged across the 5 trails. $0.43 average cost per use. 0.43 * 156 = $67.08 + $238 for equipment and travel = $305. Estimated health benefit associated with this is $895, giving an ROI of 2:1. Sensitivity analyses all produced ROIs above $1
Obesity (n = 5)	
Brown, 2007	Girls: prevalence of BMI > 85th centile from baseline to year 3 30 %→32 % in intervention group. Controls 26 %→39 %. Boys: 40 %→41 % (intervention), 40 %→49 % (controls). Cases of adult obesity prevented: 15. QALYs saved: 8.6. Medical costs averted: $51k. Labour costs averted: $107k. Net total benefits: $96k
Coffield, 2019	Children: BMI Z-score decreased by an average of 0.057 (95 % 0.04, 0.08). Parents: BMI decreased by average of 0.411 (0.097, 0.725) over the 2-year intervention. Benefits: $671k over 10 years. Net benefits: $227k. ROI: 1.5:1 (over 10 year return period). ROI remained positive until >76.2 % of the treatment effect dissipated over the 10 year period (i.e. an annual depreciation rate of 7.62 %)
Moodie, 2013	BMI change intervention group: 18→19.7 (+1.7). BMI change control group: 17.9→19.2 (+1.3). Average change in BMI from baseline to follow up, for intervention group compared to controls, adjusted for age, height at follow up, gender, duration between measurements, and clustering by school: −0.28 (−0.7, 0.15) p = 0.2. 10.2 DALYs averted. $27.1k costs averted. $29.6k per DALY averted. 73.2 % chance this falls within Australian benchmark of $50k per DALY averted. If 50 % intervention waning, no longer within cost-effectiveness threshold. If only 50 % recipients benefit, then point estimate falls just within cost-effectiveness threshold
Oosterhoff, 2020	BMI z-score changes (vs. controls): PAS: −0.066 (−0.13, 0.00). HPSF: −0.083 (95 % CI-0.15, 0.02). Lifetime productivity benefits per child (vs. controls): $334 (PAS), $407 (HPSF). Lifetime QALYs per child: +0.032 (PAS), +0.039 (HPSF). Lifetime cost per QALY gained: $82.4k (PAS Vs. controls), $348.4k (HPSF Vs. PAS). Using the societal cost perspective: $27.7k (HPSF Vs. controls). HPSF dominant over PAS under societal cost perspective. Sensitivity analyses under the various scenarios: Scenario 2: fourfold increase in cost per QALY for both interventions vs. controls. Scenario 3: two to threefold increase. Scenario 4: minimal effect for PAS, but HPSF becomes dominant over controls
Zanganeh, 2021	Difference in change in BMI: −0.13 (−0.26, 0.00) p = 0.048 (unadjusted model); −0.13 (−0.026, −0.01) p = 0.041 (adjusted). Difference in change in QALYs for children: 0.004 (0.000–0.007) p = 0.034 (unadjusted), 0.004. (−0.000, 0.008) p = 0.056 (adjusted). Difference in change in QALYs for adults: 0.002 (−0.002, 0.006) p = 0.329 (unadjusted), 0.002 (−0.002, 0.007) p = 0.421 (adjusted). Cost per QALY $23.0k. Sensitivity analysis increase cost per QALY to $23.2k
Air pollution (n = 2)	
Feng, 2021	11 million homes changed heating source through this scheme by the end of 2018. PM2.5 reduced by between 7 and 9 μg/m^3 across the different areas, all significant at p < 0.001. Health economics benefits of $33.9 billion, over the 2 years. Net benefits of $10.9 million. Average benefit to cost ratio of 4.5:1 across the areas
Malla, 2011	Absolute change in mean 24 h CO concentrations (ppm) in kitchen: Kenya: −6.5 ppm (3.81, 9.19) p < 0.001, Nepal: −11.30 ppm (7.90, 14.60) p < 0.001, Sudan: +0.10 ppm (−0.82, 0.63) p = 0.791. In Sudan they had gas supply issues, forcing many households to go back to charcoal. Post-hoc analysis excluding charcoal-using households, there was a 10 % reduction (assumed absolute reduction as per others). Reductions in personal exposure calculated as: 65 % (Kenya), 80 % (Nepal), and estimated as 40 % (Sudan). ARLI cases averted during next 10 years: 232 (Kenya), 314 (Nepal), 138 (Sudan). COPD cases avoided: 0.83, 0.62, 1.11. Net present value per household over 10 years: $1262 (Kenya), $38 (Nepal), $293 (Sudan). IRR%: 19.0 %, 429.3 %, 61.8 %. ROI: 1.4.1 (Kenya), 21.4.1 (Nepal), 2.5.1 (Sudan)
Head injury (n = 1)	
Hatziandreu, 1995	Helmet wearing from original sources: legislative: 4 %→47 %. Community: 5 %→33 % School: 2 %→8 %. Cost per injury/death avoided: legislative: $66k/$31.8 million, community: $67k/$32.8 million, school: $257k/$116.3million. Cost per year of life saved: legislative: $1.7 million, community: $1.7 million, school: $6.0 million. Sensitivity analyses show fairly stable results, with legislative intervention always the most cost-effective, and the school-based always the least
Multiple (n = 3) including: obesity, hypertension, diabetes, alcohol, and smoking	
Johansson, 2009	Results for changes in risk factors are reported separately for areas and by sex, with no significance testing reported. Generally, risk factors increased across time in all groups. No consistent trend in change in risk factors between intervention and control groups (i.e. no clear evidence of intervention effectiveness). As a result, half the intervention groups (still split by area and sex) had more QALYs gained than controls, and half didn't. In conclusion, no evidence of effectiveness or cost-effectiveness
Schouw, 2020	Significant improvements in alcohol, healthy eating, physical activity, BP, cholesterol. Non-significant trend for smoking. No discernible effect on psychosocial measures, BMI, glucose, waist circumference, sick leave. $2.45 per 10.2 mmHg reduction in systolic blood pressure, and 0.45 mmol/L reduction in total cholesterol
Erfurt, 1992	Relative % reduction in presence of risk factors: Site A: 35 % (39 % moderate), site B: 32 % (36 % moderate), site C: 44 % (48 % moderate), site D: 45 % (51 % moderate). % risk reduction per $2: site B dominated by site A (risk factor reduction −3 %), site C: 0.68 % (0.68 % moderate), site D: 0.48 % (0.57 % moderate). Cost per 1 % risk reduction: site C: $2.99 ($2.99), site D: $4.23 ($3.52)

4. Discussion

4.1. Summary of key findings

We identified 45 studies reporting an economic analysis of

Table 3
Strengths and Limitations of included studies, grouped by risk factor targeted.

Study	Strengths and limitations
Smoking (n = 15)	
Allom, 2018	Despite weighting, analysis driven by online clicks only, because other outcomes (calls to Quitline, registration for support) numbers are small, and no clear pattern. Analysis also driven by significant price differences in cost of interventions (OD 10× cheaper than OV or TV)
Brown, 2014	No evidence of differential effect by socioeconomic status but acknowledge power to detect it low. No objective validation of quit status. No empirical data on success rates of quitters. Long-term success rates may be lower for those who attempt to quit following high-profile national campaign, than those who quit without this motivation - not tested in sensitivity analyses. Unclear if results replicable, or if effectiveness of repeated campaigns would wain over time
Hair, 2019	Nil of note
Holtgrave, 2009	Estimate of effectiveness relies heavily on inference, rather than any directly attributable data
Hurley, 2008	Survey results indicated an increase in number of people intending to quit, so 6 month follow up survey may underestimate total effect on smoking prevalence. No evidence of differential effect by age, sex or socioeconomic status but survey not powered to detect this specifically. Assume drop in point prevalence equates to long-term quitters
Kotz, 2011	Smokers reporting a quit attempt in April compared to March/May were comparable on age, sex, and cigarettes smoked per day. Assume smokers quitting in response to national campaign are as likely to achieve long-term abstinence as smokers quitting without that support. Costs cover total UK spend, benefits only England. Only health costs included. No objective validation of smoking cessation, no empirical measurement of long-term quitting
Lightwood, 2008	Model performs well in robustness checks. Adjustment for sociodemographic factors did not significantly affect results
Lightwood, 2011	Nil of note
MacMonegle, 2018	Response and follow up rates for survey not reported (in original paper). Robust to sensitivity analyses
Meeyai, 2015	Callers to Quitline younger, better educated, higher % female, more likely to smoke cigarettes than roll your own, than smokers in general Thai population (as measured by national survey). Within random subsample of Quitline completers, responders more likely to be older, and employed than non-responders. But no difference for likelihood of higher education, prior quit attempt, or quantity of cigarettes smoked at baseline. Amongst responders, no relationship between age or employment with likelihood of success, so reasonable to scale up subsample in the way they did to all Quitline completers. No objective validation of quit status. Model didn't include healthcare savings, so likely underestimate of ROI from a societal perspective
Mudde, 1999	Initial response rates not reported. Retention good, but those lost to follow up younger, less well educated, males, and tended not to smoke roll your own or combination products
Ross, 2006	Funded by a $0.6/pack increase in taxation on cigarettes within Arizona. Explicit aim to change social norms around smoking. Many aspects of the intervention endured 5 years after specific funding elapsed. Conversion to life-years gained assumes non-smokers (who would have otherwise started) will remain non-smokers long-term; and those who would have otherwise started smoking would have remained smokers long-term. Examined in sensitivity analyses
Sacker-Walker, 1997	Conversion to life-years gained assumes non-smokers (who would have otherwise started) will remain non-smokers long-term; and those who would have otherwise started smoking would have remained smokers long-term. Examined in sensitivity analyses
Tomson, 2004	Costs taken from whole sample of 8503 callers, even though outcome data only available for 1131. So likely underestimate of cost-effectiveness (assuming some benefits realised for some of the 7000 callers not captured by this study). Range of sensitivity analyses present effects if abstinence rate reduced, or effect on additional years of life reduced, showing proportional increases in cost per outcome
Xu, 2015	Consider in the discussion that "extra quitters" would generally indicate extra demands on smoking cessation services (which add to the costs of achieving the health gain, but reason that the total cost-effectiveness will still lie well within the national threshold at the time). No follow up measure of abstinence, just the 3-month (immediately post-intervention) measure
Education (n = 10)	
Acevedo, 1999	Analysis assumes that a 1 % increase in funding should achieve at least a 1 % increase in test scores to be 'cost-effective', but without any justification for the valuation. No indication of long-term educational benefit
Anzelone, 2020	Because existing support was means tested, the additional financial support in the intervention was larger for people with higher household income. As a result, the financial intervention resulted in a bigger increase in enrolment for students with higher household income. In this sense, this intervention would be expected to widen socioeconomic educational outcomes, but only because existing interventions were designed to narrow them
Azomahou, 2019	Both genders benefit, but girls test scores benefit slightly more than boys
Bowden, 2014	Large range of costs and effect sizes observed across different sites, suggesting heterogeneous intervention implementation/impact. Costs data collected from 11 sites, including 9 of the 15 sites from the impact evaluation. Costs data collected by interview in 2010, impact evaluation conducted in 2002 (assume intervention remains equally effective)
Capper, 1997	Loss of statistical significance when adjusting for sociodemographics suggests selection bias towards more affluent schools than controls, with no pre-test scores available to compare against. Likely overestimation of effects. "Between 1991 and 1994, the GDP deflator increased from 143.6 to 241.3" but unadjusted costs from across this period used in analysis. National per pupil expenditure at the time was $289. So, this project cost around 15 % extra per pupil to achieve a 1 % improvement in test scores (though there the data collected, and the efforts towards longer term impact should see marginal costs come down over time). Decreasing costs during study, and efforts to make intervention sustainable mean that costs would likely have continued to decrease, whilst outcomes may have exponentially improved with longer time horizon
Lavy, 2018	Number of years of schooling gained continues to increase up to 12 years after the intervention (whilst ever enrolment plateaus after 6 years). Effect sizes significantly greater for students from poorer backgrounds (as measured by parental income). Economic analysis is not compared to a comparison group. No discounting. Intervention didn't significantly increase earnings, so analysis flawed
Reichardt, 2020	Control group matched to treatment group by propensity score matching. Control group sourced from schools where the uptake of concurrent enrolment was low (despite the offer covering these schools). Assumes the extra degree holders from the intervention will enjoy the average benefits of having a degree. Outputs unrealistic
Reynolds, 2011	Biggest savings driven by criminal justice system savings, followed by increased tax revenues, and decreased education costs. Return on investment 4× and 7× higher for most deprived children compared to least deprived, for pre-school and school-aged interventions respectively. Sensitivity analyses removing intangible criminal justice cost reductions (i.e. victim savings) still resulted in a positive, but reduced, ROI
Sabates, 2021	When comparing demographics between intervention schools and control schools (sourced from other districts), they noted the girls in the intervention group had more indicators of dropout risk on average, and therefore they adopted an individual matching approach. This assumes, however, that a poor girl in a poor school does the same as an equally poor girl in a less poor school. Boys attending intervention schools saw improvements in their test scores compared to matched boys in control schools, suggesting spill over effect. Do not consider the effects of reduced dropout in the analysis (partially reported in sensitivity analysis), so likely underestimate of effect
Somers, 1972	Analysis assumes that a 1 % increase in funding should achieve at least a 1 % increase in test scores to be 'cost-effective', but without any justification for the valuation. No indication of long-term educational benefit

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Table 3 (*continued*)

Study	Strengths and limitations
Physical inactivity (n = 9)	
Chapman, 2018	Costs time horizon 20 years, benefits time horizon 40 years. Under various sensitivity analyses varying discounting rate, changes to costs, changes to value of benefits, and intervention weaning the cost benefit ratio still remained positive, however, attenuated to around 8:1
Frew, 2012	46 % follow up rate. Lower follow up rates for older people, but no pattern for sex, ethnicity, deprivation, or baseline BMI. Not clear why 2nd year costs are so much reduced when the vast majority of intervention cost is reimbursing the gyms (which is not a start-up cost but a recurring one). Compared respondents Willingness to Pay at baseline and follow up, increased from median £21 to £36 (study has likely survival bias but this only includes those who were follow up)
Gesell, 2013	High (91 %) follow up rate. Costs do not account for co-production costs, administrative costs, costs of changing bus stops. Co-produced intervention with community: Families provided input about their needs and preferences (e.g., transportation from school to. the community centre, flexibility in pick-up times, homework time, reduction of screen time, and increased physical activity). The city's public school system changed its policy around permissible bus stops allowing buses to deliver students to the community recreation centre to support programme attendance. Groups well matched at baseline for BMI/fitness. Intervention group more males, and more ethnically diverse. Unclear why the controls would be expected to reduce in physical activity over the 12 week study period, though increases in physical activity within intervention group significant in their own right
Kennedy, 2017	Screened 40 schools for inclusion, only included the 19 with >40 % completion of data. Likely selection bias. Unclear data collection methods, but liable to reporting bias and possible seasonal effects. No control group. Assumed 0 % weaning of intervention effect. No evidence of discounting applied. No detail on how societal benefits calculated
Knell, 2019	Comparable demographics between exposed and comparison group. Different participants had shorter/longer between baseline and follow up, and some may have been exposed to completed project before baseline data collected – likely bias towards null. Ongoing rail infrastructure improvements at the time, though this intervention was unsuccessful at increasing rail transport usage in this cohort. No discounting, assume intervention results in immediate (and sustained) healthcare benefit. Assume no weaning over time. Calculation of healthcare cost-effectiveness threshold flawed
Lal, 2019	Comparison park had similar amenities but was in an area of high socioeconomic area (because all parks in lower socioeconomic areas were undergoing improvement works). Sensitivity analysis using observations from across the park had much wider confidence intervals for cost per MET gained than in primary analysis, despite including more observations. Subtracting maintenance costs from comparator park inappropriate because the alternative here was 0 maintenance costs in the intervention park (if no playground built). Observation unlikely to be accurate measure of total changes to daily physical activity. Cost-effectiveness threshold comes from methodology estimating benefits across the lifecourse, costs only modelled here for 20 years
Montes, 2012	Limited data available on collection methods, no data on response rates. No comparison groups, or before/after comparisons. No detail on how they got from: activity done during events, to meeting/not meeting physical activity guidelines. Assumption that person using events and now active will immediately cost health system the average cost of an active person (but would otherwise have cost the average cost of an inactive person). Cost perspective: city. Benefit perspective: city + visitors/tourists. Missing cost data on economic cost of closing roads (e.g. to businesses)
Peterson, 2008	Survey response rate not reported. Nearly 1000 survey responses discarded due to incomplete or improbable data for BMI and weight, suggesting possible issues with data collection. Likely selection bias. Unclear time lag between intervention and outcome. No cost data other than in analysis results. No evidence of sustained behaviour change, no evidence of magnitude of behaviour change, no details on demographic details between intervention responders and non-responders. Numbers in the results table don't add up. No confidence intervals or statistical significance reported
Wang, 2005	No demographic information on users and how representative they are of general population. Spreading construction costs over 30 years. No discounting for costs. Assumption that physical activity increases associated with trails would result in immediate healthcare benefits. Likely overestimation of healthcare cost avoided. Unlikely that someone who uses the trails 156 times a year wouldn't find some form of alternative exercise if trails removed. No differentiation between health benefits of cyclists vs. walkers. No before/after or comparison group
Obesity (n = 5)	
Brown, 2007	High follow up rate, with no differences to those lost to follow up for key characteristics. Of note, even in this (successful) intervention, overweight prevalence static, controls increased. Assumption that those who benefit from intervention will stay at a normal weight after the intervention. Slightly greater per student cost benefit for Hispanic students
Coffield, 2019	Exclude research and evaluation costs from the analysis, but given the approach, the relationship between researchers and the community was likely an important factor in its success. 75 % follow up rate, unclear if those lost to follow up significantly different to those retained. Self-reported BMI changes by parents not likely to be reliable, especially given non-blinded design. Incorporate a waning rate for the effect of the intervention, and test this in sensitivity analyses. Use official sources for estimating intervention benefits in 10 year model, with incremental changes to BMI considered rather than binary 'active'/'inactive' change. COI statement indicates a COI is present
Moodie, 2013	Intervention group: 54 % response rate at baseline, with 84 % retention to follow up (comparison group: 44 % and 83 %). Fundamentally flawed cost-effectiveness analysis as original study produced a non-significant result (in adjusted regression analysis that adjusted for height with an outcome of BMI; basic comparison between groups did not even show a non-significant trend towards effectiveness). Original study was effective for some outcomes (waist circumference, BMI z score (just), but not BMI which is what they plugged into the model). Primary analysis assumed intervention effect maintained indefinitely
Oosterhoff, 2020	Intervention schools more affluent than controls, with significantly less obesity at baseline. 1/3 of patients missing BMI data at baseline. Assumed societal benefit from parents taking up unpaid work from the extended school day seems optimistic. Results examined without this demonstrate non-cost-effective interventions at a WTP threshold of $28k per QALY (unless one assumes increasing effect size until age 20). Outcomes from original 2-year trial non-significant (though clear trend). Trend towards greater benefits to those from low SES backgrounds
Zanganeh, 2021	Inappropriate to adjust for healthy eating and physical activity behaviours in the models; however, adjustment made little difference to outcome
Air pollution (n = 2)	
Feng, 2021	Note that the high cost to residents meant this scheme was generally only taken up by more affluent households. Suggest that the scheme may be tweaked moving forwards by offering greater subsidies to poorer families. No time horizon listed for the health benefits, meaning either they omitted this detail accidentally, or they are expecting the health benefits to have occurred within the 2-year period. Either way it seems from the methods that they assumed a person now benefiting from cleaner air would assume the risk profile of that level of exposure immediately, ignoring any cumulative health damage done to this point. Some data sources unclear
Malla, 2011	Low rates of follow up data for CO in kitchen (37 % Kenya, 25 % Sudan, 65 % Nepal) - on which health outcomes are modelled. No imputation of comparison analysis between those lost to follow up and retained. Economic analysis results (excluding

(*continued on next page*)

Table 3 (*continued*)

Study	Strengths and limitations
	ratio) are subject to hypothetically, successfully scaling up the intervention by 100 % every year for 10 years
Head injury (n = 1)	
Hatziandreu, 1995	Survey-based estimates of effectiveness unreliable. Helmets made up 90 % of the costs of the legislative and community programmes. Likely that the intense interventions to promote helmet use would also have additional benefit of increasing the number of cyclists, which would decrease healthcare costs further (though over a longer time horizon). Administrative costs associated with legislative intervention not accounted for
Multiple (n = 3) including: obesity, hypertension, diabetes, alcohol, and smoking	
Johansson, 2009	Initial response rate not reported, follow up rate around 50 %. No analysis of those lost to follow up vs. those retained. Impressive to follow up of 10 years. May well have been that earlier measurement timepoints would have shown a benefit, but the intervention waned over time
Schouw, 2020	Participatory action research indicates that the relationship between the research group and the employees is likely a contributory factor to intervention success, therefore these costs should arguably be included (at least in a sensitivity analysis). Additionally, costs to productivity of releasing staff on a Friday to exercise are not costed "because salaries didn't change", but this is lost productivity, which is at a cost to the organisation. Likely Hawthorne effect given lack of control group. Analysis very simplistic and not able to monetise outcomes
Erfurt, 1992	Baseline and follow up response rates high (>80 %). Quite dynamic workforce, with large lay-offs and new staff. 95 % of those screened had at least 1 risk factor at baseline (hypertension, obesity, smoker, physically inactive). Randomising only single sites to each intervention means possibility of organisational quirks shaping outcomes

interventions that aimed to change the social, physical, economic, or legislative environments to make them less conducive to the development or maintenance of the MLRFfD. Overall, these population- and community-based interventions were found to be highly cost-effective, and often cost-saving, particularly in the long-term. The quality of included studies varied, and was reasonable overall.

The most frequently targeted MLRFfDs were smoking (n = 15), education (n = 10), and physical inactivity (n = 9). No studies reported dementia outcomes directly. Common intervention types were changing the physical or food environment (n = 13), mass media programmes aimed at changing the social environment (n = 11), reducing financial barriers or increasing resources available for education, physical activity, or cleaner fuels (n = 10), whole community approaches (n = 6), and legislative change (n = 3).

Compared to studies from HICs, studies from LMICs were as likely to report cost-savings or cost-effectiveness. Of the nine studies that investigated the effect of socioeconomic status within their samples, four [19,23,25,26] found no evidence of a differential effect, three [41,51,53] found the intervention benefited lower socioeconomic groups more, and two [54,56] found the opposite.

4.2. Strengths and limitations

This is the first systematic review focused on economic analyses of interventions applying the population-based approach to reducing the MLRFfD. By focusing on population-based studies, it was feasible to include all MLRFfD, rather than focusing only on a smaller subsample, which is important given the frequency of clustering of risk factors. The high number of unique records screened for inclusion (n = 22,749) indicates the breadth of the search strategy, but population-based approaches can take many forms and it is possible that some relevant papers were missed. Due to the heterogeneity of the included studies, and the narrative synthesis approach, it was not possible to formally assess for publication bias.

Only studies which measured the effect on one of the named MLRFfD from the Lancet Commission [3] were included. This meant studies measuring outcomes that appear earlier on the proposed casual pathways, such as healthy eating (proximal to obesity), salt reduction (hypertension), and electric vehicle usage (air pollution) were excluded. Equally, only studies that considered intervention costs against benefits were included, meaning other economic analytic designs, such as price elasticity studies that are an important component of evaluating taxation policies, were excluded. Those studies that reported shorter-term outcomes but did not apply chronic disease models to predict the long-term health effects of the intervention, will have underestimated the full population health benefit. Importantly, the MLRFfD have been identified using predominantly observational data, meaning that causality cannot be assumed and it is unknown to what extent the described changes in the risk factors would translate into actual changes in dementia prevalence. However, the observed cost-effective reductions in the MLRFfD are valuable to population health in their own right, and any potential reduction in dementia would only increase the population benefit.

We included studies that changed the environments in which people live their lives, interact, work, play and move around. This meant that we excluded screening-based interventions, provision of extra physical activity sessions (e.g. during school time), and education-based interventions if they were not accompanied by some attempt to change the long-term environment to enhance healthier automatic behaviours. However, intervention designs are often complex and nuanced, and inevitably some studies straddle the definitions of the individual and population approaches. It was therefore sometimes challenging to determine whether or not studies met these inclusion criteria.

4.3. Implications

Economic analyses are important to influence policymakers. It is likely that further effective interventions against the MLRFfD exist but have not yet been subject to economic analysis, and therefore were not identified by this review. Existing high-profile reviews of the effectiveness of dementia risk reduction interventions [3,59] focus almost entirely on individual-based approaches. Further research is needed to identify effective population-based approaches to dementia risk reduction by action on MLRFfD across different settings (e.g., HIC and LMIC settings) and groups (e.g., stratified by culture/ethnicity).

Population-based prevention approaches are already known to be generally more efficient and equitable than individual-based approaches for other non-communicable diseases such as cardiovascular disease. It seems likely, from the evidence base presented in this review, that this is also the case for dementia. However, to date these approaches have been under-explored for dementia risk reduction, and the evidence base that underpins the area has been given less attention than individual-based approaches [8]. This study finds that many cost-effective and cost-saving interventions following the population prevention approach have been demonstrated to tackle known MLRFfD, across HICs and LMICs.

We urgently need policy action to replicate, upscale, and improve these interventions for further population health gain. Dementia develops over decades, and as a result, interventions to significantly reduce dementia incidence will take time to demonstrate their full impact. The evidence presented in this review should give policymakers confidence that these investments are worthwhile, and the right policies for the populations they serve.

Contributors

Sebastian Walsh designed the study, piloted and refined the search strategy, completed screening, selection, extraction, and quality appraisal of studies, and drafted the manuscript.

Jacob Brain designed the study, piloted and refined the search strategy, and completed screening, selection, extraction, and quality appraisal of studies.

Naaheed Mukadam designed the study, completed screening, selection, extraction, and quality appraisal of studies.

Robert Anderson completed screening, selection, extraction, and quality appraisal of studies.

Leanne Greene completed screening, selection, extraction, and quality appraisal of studies.

Ishtar Govia completed screening, selection, extraction, and quality appraisal of studies.

Isla Kuhn piloted and refined the search strategy.

Kaarin J Anstey designed the study.

Martin Knapp designed the study.

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Carol Brayne designed the study.

All authors commented on the final draft.

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Appendices. Supplementary data

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