Health policy

Modelling the impact of physical activity on public health: a review and critique

--Manuscript Draft--

Manuscript Number:	HEAP-D-20-00243R2
Article Type:	Review/Comparative article
Keywords:	physical activity; Health economic modelling; public health, cost-effectiveness, structural uncertainty; decision-analytic modelling
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Abstract:	Background While several reviews have assessed economic evaluations of physical activity in public health and, in most cases, found the interventions to be cost-effective, the validity of the conclusions reached depends on the appropriateness of the modelling methods used in the individual studies. Objective To provide an overview and critique of modelling approaches and key structural assumptions used in applied studies to estimate the impact of physical activity on health. Methods Electronic databases were systematically searched for relevant model-based economic evaluations. A thematic approach was used to assess the modelling studies. The critique determined the appropriateness of the modelling frameworks and plausibility of key structural assumptions. Results Twenty-five models were identified. Cohort models were most frequently used. High variability in the modelling of downstream diseases was found across studies analysing similar populations. Structural assumptions regarding the dynamics of change of physical activity were unrealistic in most cases. Heterogeneity was addressed in only a few studies, while health equity concerns were, at best, acknowledged by authors. Conclusions This literature is predominantly characterised by modelling approaches that may not adequately address the complexities associated with representing the physical activity behaviour- population health process. A consensus on how to model the impact of physical activity on public health and development of a reference model could help reduce these sources of uncertainty.

Dear Editors,

I want to thank the reviewers for their comments and suggestions. We believe that by addressing them, the article has improved substantially. We have focused the article and this is now also reflected in the title and abstract. In the Revision notes file, a detailed response to each of the reviewers' comments has been included.

Please let me know of your decision at your earliest convenience, thank you.

With my best regards,

Paolo Candio

Modelling the impact of physical activity on public health: a review and critique

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Paolo Candio was supported through the White Rose PhD Studentship Network scheme as part of the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care Yorkshire and Humber (NIHR CLAHRC YH). Laura Bojke was supported by the NIHR CLAHRC YH and the NIHR Applied Research Collaboration Yorkshire and Humber (ARC YH). The views expressed in this publication are those of the authors and not necessarily those of the NHS or the Department of Health.

This manuscript has not been published elsewhere. We have no conflict of interest to disclose. Declarations of interest: none. As corresponding author, I confirm that the manuscript has been read and approved for submission by all the named authors. In terms of contributions, Paolo Candio retrieved the articles, processed the data and wrote the draft manuscript, David Meads cross-checked the included and excluded papers and all the authors contributed to the writing of the manuscript.

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Highlights

- The common assumption of no decay of intervention effect over time is unrealistic
- Health equity concerns have not been incorporated into the models
- Development of a reference model could help reduce variability in modelling approaches

Modelling the impact of physical activity on public health: a review and critique

ABSTRACT

Background While several reviews have assessed economic evaluations of physical activity in public health and, in most cases, found the interventions to be cost-effective, the validity of the conclusions reached depends on the appropriateness of the modelling methods used in the individual studies.

Objective To provide an overview and critique of modelling approaches and key structural assumptions used in applied studies to estimate the impact of physical activity on health.

Methods Electronic databases were systematically searched for relevant model-based economic evaluations. A thematic approach was used to assess the modelling studies. The critique determined the appropriateness of the modelling frameworks and plausibility of key structural assumptions.

Results Twenty-five models were identified. Cohort models were most frequently used. High variability in the modelling of downstream diseases was found across studies analysing similar populations. Structural assumptions regarding the dynamics of change of physical activity were unrealistic in most cases. Heterogeneity was addressed in only a few studies, while health equity concerns were, at best, acknowledged by authors.

Conclusions This literature is predominantly characterised by modelling approaches that may not adequately address the complexities associated with representing the physical activity behaviour- population health process. A consensus on how to model the impact of physical activity on public health and development of a reference model could help reduce these sources of uncertainty.

Keywords: physical activity, economic evaluation, modelling, public health.

INTRODUCTION

The finite resources available to decision makers dictates that commissioning of interventions ought to be based not only on the grounds of effectiveness, but also on cost-effectiveness[1]. To support reimbursement decisions concerned with funding interventions where there are multiple options, economic evaluation is typically used[2].

Several studies have reviewed the cost-effectiveness evidence for promoting physical activity (PA) in the general population and found the interventions to provide value for money in most cases[3-7]. However, methodological reviews have highlighted a number of challenges related to the economic evaluation of public health interventions, including PA[8-11]. Covering all elements of the evaluation, from research design of the intervention to the statistical and economic analyses, these challenges have previously been grouped into four broad categories: attribution of effects, measuring and valuing outcomes, intersectoral costs and consequences and incorporating equity concerns.

A recent review examined how the four methodological challenges above have been addressed in applied studies, across two categories of PA interventions (targeted PA and sedentary behaviour)[11]. Confirming previous findings[8-10], this review found an overall poor quality of reporting and marked inconsistencies in the methods applied across economic evaluations, providing a series of recommendations for the design, analysis and appraisal of economic evaluations.

The existing methodological reviews did not provide a critique on the appropriateness of the modelling approaches used to estimate the impact of changes in PA on population health. More specifically, they did not comment on the appropriateness of structural features of the modelling approach and if these aligned with the fundamental nature of the behaviour-population health process they were designed to represent [12,13]. This is important as the lack

of adequate structure and unrealistic model assumptions can hinder the validity of cost-effectiveness findings [14].

Challenges in modelling the impact of physical activity on public health

More specifically, in terms of measuring effectiveness, a number of challenges in modelling healthy behaviours for public health economic evaluations, including PA, have been discussed in the literature [14,16]. These challenges derive from key complexities of the behaviour – population health process, which require the use of form of modelling, and include: 1) the link to multiple chronic diseases; 2) a dynamic nature of behaviour and 3) heterogeneous response to the intervention.

A recent scientific report[17], which forms the basis of the current UK PA guidelines[18], describes the relationship between PA and the downstream risk of disease, by assessing the relevant available evidence from systematic reviews and meta-analysis against five criteria (i.e. applicability, generalisability, risk of bias or study limitations, quantity and consistency and magnitude and precision of effect). This report confirmed that there was strong evidence suggesting a link between PA and metabolic (e.g. type II diabetes), cardiovascular (e.g. coronary heart disease and stroke), genetic mutation (e.g. colorectal and breast cancer), mental (e.g. depression) and geriatric (e.g. falls) conditions. In addition, disease probabilities may not be independent from one another. For instance, the risk of type II diabetes has been associated with risk of colorectal and breast cancers, mainly due to shared risk factors, among which PA plays a major role[19].

From a modelling standpoint, this complexity represents a technical problem in that a heathy individual faces a number of different competing and complementary disease risks at any given time, based on the individuals' PA level and other personal characteristics. Furthermore, some disease risks which will be affected by changes in PA habits in the short

term (e.g. psychological benefits[20]), while others will take some time before occurring (e.g. colorectal cancer incidence[21]).

While PA habits generally tend to be stable over adulthood[22], a decline in PA is typically associated with older age[23]. Evidence has also shown that natural fluctuations in PA can occur due to seasonality effects or particular life phases[24]. Furthermore, it is also reasonable to expect that different individuals not only will react heterogeneously, in terms of change in behaviour to the same level of exposure, but also that behaviour changes will be sustained at different rates over time[25]. Although the magnitude of effect will depend on the type of intervention, assuming that the changes induced by the intervention over the short term will remain constant over time is likely to be unrealistic, whereas rebound trajectories are generally more likely to occur[26].

Finally, it is important to take into account heterogeneity in natural history of the PA behaviour-health process and intervention effects on this process for two main reasons: to reduce the risk of inducing bias in the cost-effectiveness results and to align the modelling approach to the objectives of the decision-makers the model is aimed to inform[2,12]. Public health decision-makers have a prominent goal of reducing existing health disparities in the population, for instance associated with socio-economic factors[27], reflecting the value that society places on lessening unfair inequalities alongside improving health[28,29].

Modelling frameworks available to analysts

There has been a wealth of research dedicated to generating taxonomies of the mathematical / epidemiological paradigms available to health economic modellers[30-32]. This has also reflected on their properties to inform model-based economic evaluations in public health. These frameworks have been broadly categorised into cohort and individual level approaches

and based on their ability to formally capture time-dependent effects and interactions between individuals and the environment[32].

Briefly, cohort-level approaches are generally simpler than individual level frameworks. In ascending order of modelling capacity, with decision trees and comparative risks assessments (CRAs) neither time nor interactions can be explicitly considered. Markov chains, which can be implemented at both an individual and a cohort level, can instead represent time in the process explicitly as a sequence of transitions between states. More complex are discrete time events and agent-based models which, despite their ability to formally represent changes in states over time and interactions between individuals (the latter), using either discrete and continuous time frameworks, have seen limited application in public health[32].

Beside the suitability of the modelling framework, the way these methods are implemented in practice (i.e. what structural assumptions are made) can affect the validity of cost-effectiveness findings[15]. Comparably to how the National Institute of Health and Care Excellence (NICE) evaluates models included as part of manufacturers submissions[33], previews attempts to critique the plausibility of key structural assumptions of the models have been made in other public health evaluation settings[10,16]. To date, no methodological review has focussed on investigating these issues within the PA literature. The present paper aims to fill this gap.

METHODS

Details regarding the search strategy, eligibility criteria, study screening and selection methods are described in Appendix I**.** In brief, model-based economic evaluations of PA interventions were identified within the published literature, from database inception to April 2019. Given the review focus, only full economic evaluations were included (i.e. cost-utility,

cost-benefit, cost-consequences and cost-benefit analyses). A literature search of four electronic databases (MEDLINE, EMBASE, SportDiscus and EconLit) was conducted, with free-text terms, synonyms, spelling variants, abbreviations and indexing terms related to the three concepts of economic evaluation, model and physical activity being used to identify relevant articles.

Data extraction forms were developed by adapting existing templates suggested by review guides [34,35]. These forms were designed to extract information on what modelling frameworks were applied and what key structural assumptions of the models relating to the three complexities discussed above (i.e. the link of physical inactivity to multiple chronic diseases; a dynamic nature of PA behaviour and heterogeneous response to the intervention) were made for estimation of the intervention impact on population health.

As recommended for methodological reviews[34,35], methods were summarised using a thematic approach. For reference, an overview of the modelling studies is first presented. This includes details on the decision contexts and mathematical frameworks used for economic evaluation, based on a classification recently suggested[32]. The second part of the review critiqued the base-case structural assumptions of the models in terms of their plausibility against the existing available evidence. While these assumptions are often interrelated, an evaluation of how the related complexities have been handled in practice is presented. The following questions thus formed the basis of the extraction process, under four themes:

- Modelled downstream disease risk:
    - what and how diseases associated with PA have been modelled?
- Dynamic nature of PA:
    - does the model allow for natural fluctuations in PA levels over time?;

- what assumptions have been made with regard to the link between exposure and change in PA / gains in health?;
- what assumptions have been made with regard to time-dependency of intervention effects?;

- Reflecting heterogeneity:
  - how differences in intervention impacts between individual characteristics have been reflected?
- Incorporating health equity concerns:
  - how intervention impacts on existing health inequalities have been modelled?

RESULTS

Included studies

Figure 1 shows a PRISMA flow diagram of the literature search and selection process. Twenty-five papers met the selection criteria. Table 1 provides an overview of the modelling studies. Eleven papers based their analyses on primary data from the UK, seven from the USA, four from Australia and one each from Belgium, Canada and The Netherlands. The majority of studies focused on adults (>=18 years, n=20), four analyses focused only school pupils, and two included a mixed population (adults and children). Interventions based on universal approaches to promotion were explored in the majority of studies (18/25).

Modelling frameworks

Eighty percent of the studies (n=20) employed aggregate-level approaches, nine of which used untimed modelling methods (eight CRAs and one decision-tree). Eleven analyses were based on discrete-time frameworks, with two multiple cohort lifetable approaches[36,37], and

Markov chain modelling being used the most frequently. Of the five individual-level models, two were Markov chains[38,39], one applied a system of linear equations using a cross-sectional regression analysis approach[40], one a microsimulation approach[41] (although no details were reported in terms of Markovian assumptions or interaction-levels) and one study developed a discrete event simulation model[42].

Modelling of downstream disease risk

Table 2 summarises the key structural assumptions made in order to estimate the impact of changes in PA on public health. The majority of studies (n=23) evaluated the impact of interventions on chronic diseases and conditions associated with PA, with eight of these studies not stating which diseases were considered. The number of chronic diseases ranged from one to seven, with one study modelling 32 disease combinations[43].

Except for one study which focused on Osteoporosis[38], all the models selected Type II diabetes and at least one cardiovascular disease (either a type of Stroke or Coronary Heart Disease). Eleven models included at least one cancer (i.e. Colon, Colorectal, Breast, Lung and Kidney) and only two studies considered impacts on mental health outcomes, specifically, depression. Only one study[44] included exercise-related injuries among the consequences. For those studies focussing on adults from the general population (n=14), the majority (n=8) selected five chronic conditions. In addition, while the models evolved over time in terms of disease selection, except for one study which applied random search method to calibrate disease risk parameters[42], none of the models took into account synergistic and compensatory effects between disease risks.

Thus, none of the reviewed models would be able to reflect the currently available evidence on the associated chronic disease risk, therefore, not adequately capturing the impact of

changes in PA, either due to a narrow evaluation scope and/or lack of adjustments for interaction between diseases.

Dynamics of physical activity

Natural course of PA

Except for two studies that developed a natural history model from PA available from a country-level surveillance system [45 46,] none of the models accounted for natural fluctuations in PA levels over time. Baseline PA states were assumed to be stable, also when long-term time horizons were considered, 15/25 evaluations with time horizons equal to or longer than 30 years). Furthermore, transitions between the highest and the lowest levels of PA were not allowed.

Link between exposure and response and its time dependency

All but four models reported that changes in PA and related health gains would be immediate following exposure to the intervention. One study[47] assumed that the intervention could not affect disease risk in the first year ("run-in period"). Other analyses assumed that it would take two years[48], or up to five years[49], for the intervention to reach full effect. Except for one report which reported on the time lag assumed between changes in PA and disease occurrence used in the model[41], none of the other studies provides details regarding time lag to disease.

Time-dependent intervention effects

The majority of models (15/25) assumed implicitly or explicitly that the intervention effect would not decay after the intervention ended (i.e. beyond follow-up assessment period). The remaining 10 analyses assumed a constant and homogeneous decline in effect, ranging from 25% to 100%, up to two years after the intervention ended.

Although lack of data may have driven these choices, the structural assumptions related to the dynamics of change in PA that underlie the current models are underreported and may be unrealistic. While appropriate sensitivity analysis may have helped characterise these complexities for decision-making[2], only a minority of models explored the impact of variations to these base-case structural assumptions (see Table 2).

Reflecting heterogeneity

Ten studies used population average approaches, evaluating the health impact of changes in PA levels in homogeneous groups of inactive / sedentary adults or school pupils. Baseline differences in PA were considered in only nine studies. Three to five levels (i.e. PA states) were defined in these analyses, with part of the models aligning the classification of PA levels to current national-level PA recommendations[37,45,46,51-53]. Twelve studies accounted for heterogeneous health impacts based on at least age or gender, with two analyses also considering ethnicity/race differences[40,42].

Thus, while some degree of heterogeneity has been captured by the reviewed models, only a minority addressed this aspect formally by considering at least basic socio-demographic differences, and in particular, baseline PA level.

Incorporating health equity

None of the reviewed economic models incorporated concerns relating to the distributional impact of the intervention formally into the economic evaluation. Where models accounted for heterogeneous effects, they did not report subgroup analysis which would have allowed for inferences about effects on health inequalities. In only a minority of studies (5/25) equity considerations were discussed.

DISCUSSION AND CONCLUSIONS

Main findings

Complementary to previous reviews[8-11,14], this is the first methodological review to provide an overview and critique of the modelling approaches used in model-based economic evaluations for estimating impacts of changes in PA on public health. This review has shed light on key structural assumptions that underlie the models, which can aid interpretation of the cost-effectiveness findings and highlights model development opportunities.

If, on one hand, economic evaluation guidelines support the notion that model structures should be kept as simple as possible[54,55], models should align to the nature of the process they are intended to represent[12]. While acknowledging that the trade-off between simplicity and internal validity still represents an unresolved challenge for modellers, this literature is predominantly characterised by modelling approaches that may not adequately address the complexities associated with the PA behaviour – population health process they were intended to represent. In addition, key structural assumptions were often unsupported by relevant evidence and based on general rules of thumb.

Minimum modelling standards

Based on the findings from this review, there are a number of areas in which minimum modelling standards should be established. First, modelling of downstream disease risks. The disease selection in the reviewed models does not reflect the current available epidemiological evidence on the relationship between PA and chronic disease. While differences in environmental-level factors may explain differences in magnitude of risk between settings (e.g. countries), disease selection for identified populations should be only based on strong and updated epidemiological evidence. Disease risks are not likely to be

independent from one another, and this should be taken into account, either formally (e.g. using calibration methods) or informally (e.g. by means of scenario analysis).

Second, accommodating for the dynamics of PA. Natural trends in PA levels should be used as baseline data for comparison. Conceptualising PA levels as fixed states is likely to induce bias in the estimations, especially when modelling PA behaviours that are subject to seasonality effects (e.g. gym attendance in summer) or over sensitive life phases (e.g. retirement). However, in scenarios where PA levels are likely to be stable, the decision to incorporate this element into the model needs to be evaluated in light of the trade-off between added complexity and accuracy.

Assumptions regarding time lags and decay of intervention effects over time must also be made explicit. The current lack of data on long-term impacts of PA intervention does not justify the use of unrealistic assumptions. Instead, modelling of PA should include analysis of a range of possible scenarios for adequately reflecting the uncertainty surrounding the decision[2]. The common assumption found across the models of no decay of effect over time is unrealistic, especially when assessing effects over long periods of time. This is likely to result in overestimation of the health benefits of the intervention and undermine the validity of research findings.

Third, reflecting heterogeneity. Models should capture systematic differences in impacts between individual characteristics[56]. Moderator variables should be identified both for the estimation of effectiveness and cost-effectiveness of PA interventions directed at heterogeneous populations. Although sub-group analyses will not always be feasible in practice (e.g. due to small sample sizes), reports should make explicit the reasons for not conducting them. Reports should also include details regarding the gradients in risks between population sub-groups, and how the shape of these gradients is assumed (e.g. curvilinear[57]) when no data were available.

Forth, on the issue of incorporating health inequity concerns. Methods for incorporating such concerns into economic evaluation have only been relatively recently suggested and this may explain why this element is missing in the published studies. Practical considerations related to the use of these methods have been acknowledged[8,58] (e.g. lack of data on sub-groups) and this may impede analysts in undertaking any quantitative assessment such as health inequality impact, opportunity cost or equity weighting analyses[59]. Nevertheless, given the importance of addressing health inequity, it would be reasonable to expect that model structures allowed for capturing differential natural histories and intervention effects between equity-relevant sub-groups (e.g. socio-economic status)[28,29]. Where this is not possible, authors should at least highlight this as a limitation and conduct a qualitative assessment, for instance, by reviewing the background information regarding existing patterns and causes of health inequities)[59].

Finally, there is a need for a better characterisation of the uncertainty related to structural assumptions. A more structured and formal approach to assessing the implications of key structural assumptions on the economic decision should be a minimum requirement. In absence of data, a range of plausible scenarios should be explored, and results be presented as such, rather than just a base-case[60].

Limitations

This review is subject to several limitations. The level of detail presented in the applied studies leads us to conclude that an overall poor quality of reporting was observed, making the assessment of the modelling studies difficult. However, a formal quality assessment was not conducted according to previously defined criteria, limiting the ability of this review to determine a more traditional judgement on study quality. In addition, whilst a detailed systematic search was conducted, this review only included PA interventions, therefore

limiting the generalisability of the findings to economic evaluations of interventions where PA is combined with other technologies or healthy behaviours.

This study focused on the cost-effectiveness literature only, and it is possible that other types of studies, such as epidemiological studies, have addressed some of the complexities discussed. Furthermore, methodological aspects discussed here represent only a proportion of the challenges that are apparent when modelling of impact of different types of PA interventions. Specifically, modelling issues related to compensatory or synergistic effects with other behaviours on the pathway to health improvement, such as dietary patterns, interactions between individuals, and non-health effects of these interventions, have not been addressed in this review and should be the focus of further research.

Concluding remarks

Reaching a consensus on minimum modelling standards, improved reporting of the key model assumptions using the available reporting checklists[61-64] and development of a reference model[65] could help reduce these sources of uncertainty, and therefore support optimal decision-making.

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Table 1: Overview of the modelling approaches used

Reference	**Country / time of analysis**	**Population**	**Universal / targeted approach** (target group)	**Analysis sample**	**Evaluation time horizon**	**Individual / aggregate level**	**Timed / untime modelling**	**Modelling paradigm**
66 Amarasinghe et al., 2010	Australia, 2003	Western Australia	Targeted (physically inactive)	national prevalence data	lifetime	Aggregate level	Untimed	CRA
47 Anoyke et al., 2013	UK, 2011	Adults	Targeted (physically inactive)	100,000 healthy inactive adults aged 33	lifetime	Aggregate level	Timed	Markov chains
48 Barrett et al., 2015	USA, 2014	US school pupils aged 6-11 y, N=18.5 million	Universal (school)	2015 population, no other details specified	10 y	Aggregate level	Timed	Markov chains
67 Beale et al., 2012	UK, 2007	Adults	Targeted (physically inactive)	1,000 sedentary adults	10 y	Aggregate level	Timed	Markov chains
	UK, 2006	Adults	Targeted (physically inactive)	1,000 sedentary adults	30 y	Aggregate level	Untimed	CRA

49 Cavill et al., 2011	UK, 2009	not specified	Universal (resident population)	N=not specified, 16 y+	10 y	Aggregate level	Untimed	CRA
36 Cobiac et al., 2009	Australia, 2003	Australia population	Simulated multiple interventions, universal and targeted	Population age/gender distribution	lifetime	Aggregate level	Timed	Multiple cohort life-table approach
41 Cradock et al., 2017	USA, 2016	School children	Universal (school)	2015 population, no other details specified	10 y	Individual level	Timed	Microsimulation
50 Dallat et al., 2014	Northern Ireland (UK), 2009	N=110,600, 16 y+	Universal (resident population)	Prevalence data	41 y	Aggregate level	Untimed	CRA
68 De Smedt et al., 2012	Belgium, 2009	N=245,000, adults 25-75 y	Universal (resident population)	N=266 adults 25-75 y who improved PA level	20 y	Aggregate level	Timed	Markov chains
51 Frew et al., 2012	UK, 2010	City adult population	Universal (resident population)	N=not specified, population of adults 16-70 y, no other details provided	lifetime	Aggregate level	Timed	Markov chains

39 Goyder et al., 2014	UK, 2012	Sedentary adults from deprived areas	Targeted (physically inactive, middle-aged, from deprived socio-economic backgrounds)	N=500,000 age/gender matched individuals	lifetime	Individual level	Timed	Markov chains
43 Gulliford et al., 2014	UK, 2010	National population	Targeted (physically inactive)	N=262,704 inactive adults> 30 y	5 and 10 y	Aggregate level	Timed	Markov chains
40 Guo and Gandavarapu, 2009	USA, 2001	County population	Universal (resident population)	N=438,881	10 y	Individual level	Untimed	System of linear equations
69 Montes et al., 2012	USA, Mexico, Colombia, 2010	National population	Universal (resident population)	N=not specified, 16 y+	5 and 10 y	Aggregate level	Untimed	CRA
70 Moodie et al., 2009	Australia, 2001	Primary school children	Universal (school)	N=15,680 average school pupils 5-7 y	lifetime	Aggregate level	Untimed	CRA
44 Munro et al., 2004	UK, 1994	Older adults	Universal (resident population)	N=10,000 adults>=65 y	10 y	Aggregate level	Untimed	CRA

38 Nshimyumukisa et al., 2013	Canada, 2008	Women>=40y	Universal (resident population)	N=500,000, women>= 40 y	5 and 10 y	Individual level	Timed	Markov chains
52 Over et al., 2012	The Netherlands, 2009	National population 20-65 y	Targeted (physically inactive)	N=not specified, population 20-65 y	lifetime	Aggregate level	Timed	Markov chains
53 Pringle et al., 2010	UK, 2006	Adults	Simulated multiple interventions, universal and targeted	N=not specified, population 10+ y	lifetime	Aggregate level	Untimed	Decision-tree
46 Roux et al., 2008	USA, 2004	Adults 25-64 years	Simulated multiple interventions, universal and targeted	N=not specified, adult population 25-64 years	lifetime	Aggregate level	Timed	Markov chains
45 Roux et al., 2015	USA, 2004	Adults 50-64 years	Simulated multiple interventions, universal and targeted	N=not specified, adult population 50-64 years	lifetime	Aggregate level	Timed	Markov chains
42 Gc et al., 2018	UK, 2011	Adult population	Universal (resident population)	N=10,000 representative sample	10 y	Individual level	Timed	Discrete event simulation

71 Verhoef et al., 2009	UK, 2014	not specified	Targeted (physically inactive)	N=1025, inactive adults>18 y	lifetime	Aggregate level	Timed	Markov chains
72 Wang et al., 2005	USA, 1998	National population	Universal (resident population)	N=not specified, trail users	30 y	Aggregate level	Untimed	CRA
37 Zapata-Diomedi et al., 2017	Australia, 2013	City population	Universal (resident population)	N=860,000, adult residents	lifetime	Aggregate level	Timed	Multiple cohort life-table approach

Note: CRA=comparative risk assessment, y=years

Table 2: Critique of the reviewed studies

		Dynamics of change in PA					
Reference	**Modelled downstream disease risks**	**Natural course of PA**	**Time lag to health benefit**	**Decay of intervention effect over time**	**Reflecting heterogeneity (details)**	**Incorporation of health equity**	**Uncertainty assessment**
66 Amarasinghe et al., 2010	T2D, HD,STR,CC,DEP	PA as a fixed state	not specified	different constant rates of compliance	average individual, 2 levels of PA	not specified	not specified
47 Anoyke et al., 2013	T2D,CHD,STR	PA as a fixed state	1 year run-in period	100% constant, benefits accrue for the first 10 years over lifetime	average individual, 2 levels of PA	not specified	not specified
48 Barrett et al., 2015	obesity	PA as a fixed state	2 years to full effect on BMI	100% constant, benefits accrue over the whole TH	not specified	discussed implementation issues potentially increasing inequalities	not specified
67 Beale et al., 2012	T2D,CHD,STR	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	average individual, 2 levels of PA	not specified	not specified
	not specified	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	average individual, 2 levels of PA (adjustment for age, gender, ethnicity, employment status, education level, income, marital status, smoking status, alcohol	not specified	not specified

					consumption, and body mass index)		
49 Cavill et al., 2011	not specified	PA as a fixed state	5 years	100% constant, benefits accrue over the whole TH	average individual, 2 levels of PA (proportion of cyclists)	not specified	not specified
36 Cobiac et al., 2009	T2D, CHD,IHD, STR, BRC	PA as a fixed state	not specified	Sustained for the first year, but decay exponentially at a rate of 50% per annum thereafter	age, gender and 2 levels of PA	not specified	one-way SA (dissipation of effect size)
41 Cradock et al., 2017	obesity	PA as a fixed state	not specified for base-case analysis, 2 to 20 years in SA	100% constant, benefits accrue over the whole TH	body mass index, 2 levels of PA	not specified	not specified
50 Dallat et al., 2014	T2D, IHD, STR,CC,BRC	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	age, gender and 2 levels of PA (walking time)	not specified	one way SA (time lags)
68 De Smedt et al., 2012	T2D,CHD,STR, CC	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	age, gender, 3 levels of PA (national recommendations)	not specified	50% of intervention effect after the first year in SA
51 Frew et al., 2012	T2D, CHD, STR, CRC, BRC	PA as a fixed state	not specified	Decline of 100% after the 2 years, benefits accrue over the whole TH	age, gender and quintiles of PA	sub-group analysis is limited because of sample size	one-way SA (dissipation of intervention effect on part of the sample)
39 Goyder et al., 2014	not specified	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	age, gender and PA (within the "at risk", three levels)	not specified	not specified

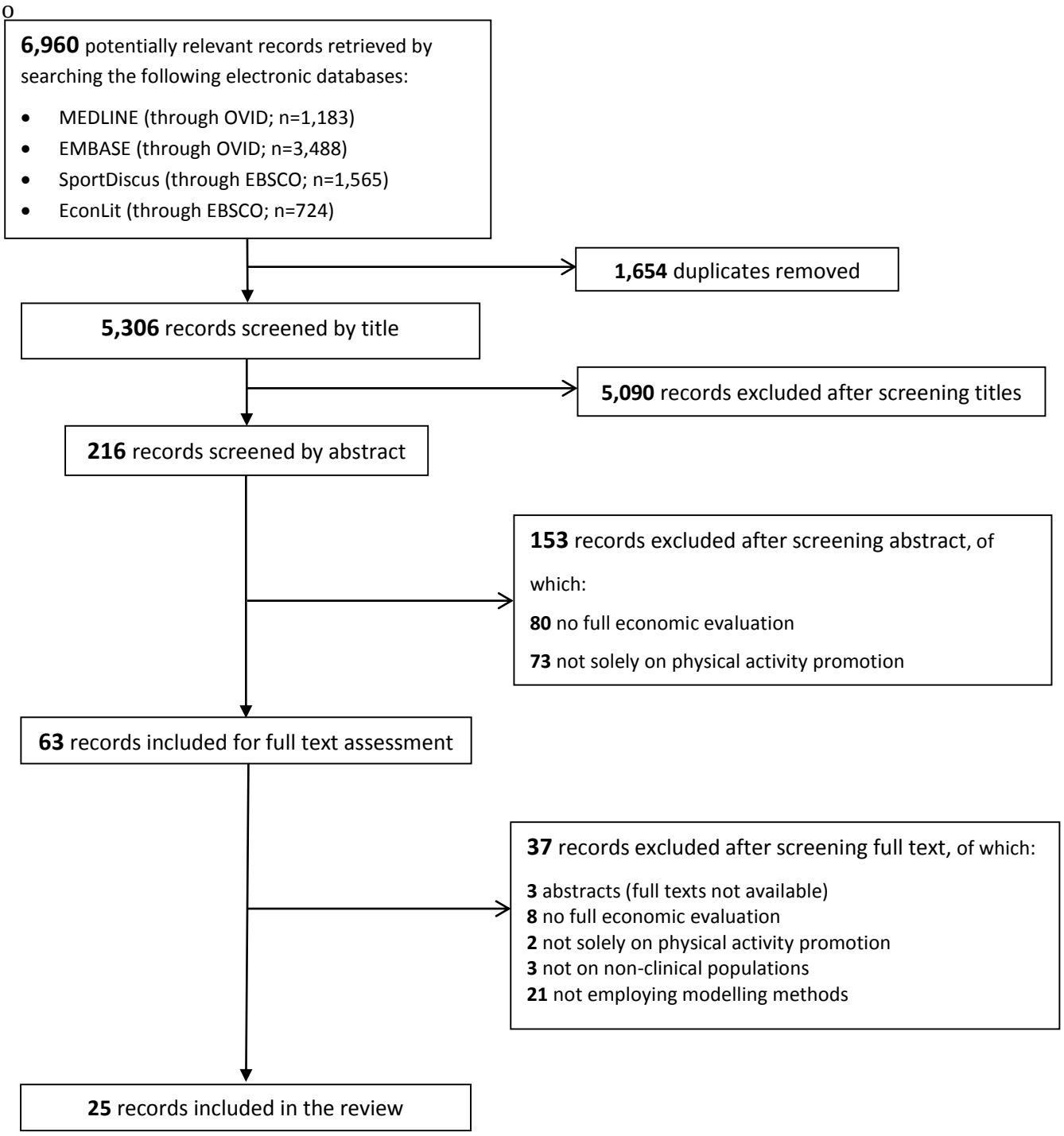
43 Gulliford et al., 2014	T2D, CHD, STR, CRC + DEP interaction (32 combinations)	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	age, gender, depression status and 3 levels of PA (walking/biking time)	not specified	not specified
40 Guo and Gandavarapu, 2009	obesity	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	age, gender, race, employment status, 2 levels of PA	not specified	not specified
69 Montes et al., 2012	not specified	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	average individual, 2 levels of PA (proportion of active commuters to school)	not specified	not specified
70 Moodie et al., 2009	obesity	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	average individual, 2 levels of PA	discussed implementation issues potentially increasing inequalities	not specified
44 Munro et al., 2004	not specified	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	average individual, 2 levels of PA	not specified	not specified
38 Nshimyumukisa et al., 2013	Osteoporosis	PA as a fixed state	not specified	explicit constant at 25% after 18 weeks, benefits accrue over the whole TH	age and 3 levels of PA (national recommendations)	not specified	not specified
52 Over et al., 2012	not specified	PA as a fixed state	not specified	50% constant, benefits accrue over the whole TH	average individual, 3 levels of PA (national recommendations)	not specified	not specified

53 Pringle et al., 2010	T2D, CHD,STR,CC	PA as a fixed state	not specified	explicit 33% to 50% of decline in effect after year 2, benefits accrue over the whole TH	age, gender,4 levels of PA - national recommendations	not specified	not specified
46 Roux et al., 2008	T2D,CHD,STR, CRC,BRC	natural history model	not specified	explicit 33% to 50% of decline in effect after year 2, benefits accrue over the whole TH	age, gender and 4 levels of PA (national recommendations)	sub-group analysis is limited because of lack of data	one-way SA (dissipation of intervention effect)
45 Roux et al., 2015	T2D,CHD,STR, CRC,BRC	natural history model	not specified	100% constant, benefits accrue over the whole TH	gender and 4 levels of PA (national recommendations)	sub-group analysis is limited because of lack of data	one-way SA (dissipation of intervention effect)
42 Gc et al., 2018	T2D, HD,STR,BRC, LUC,CC, KDC	PA as a fixed state	not specified	Sustained for the first year, but decay exponentially at a rate of 55% per annum thereafter	age, sex, ethnicity and 3 levels of PA	not specified	one-way SA (dissipation of effect size)
71 Verhoef et al., 2009	T2D,CHD,STR	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	average individual and 3 levels of PA (national recommendations)	not specified	not specified
72 Wang et al., 2005	not specified	PA as a fixed state	not specified	100% constant, benefits accrue over the whole TH	average individual, 2 levels of PA	not specified	not specified
37 Zapata-Diomedi et al., 2017	T2D, IHD,STR,CC,BRC	PA as a fixed state	not specified	gradual increase, benefits accrue over the whole TH	Household-level: age, gender, geographical location and 2 levels of PA	not specified	not specified

Note: BRC=breast cancer, CC=colon cancer, CHD=coronary heart disease, DEP=depression, CRC=colorectal cancer, HD=heart disease, KDC=kidney cancer, IHD=ischaemic heart disease, LUC=lung cancer, PA=physical activity, SA=sensitivity analysis, STR=stroke, T2D=type II diabetes, TH= time horizon, y=years.

Figure 1 PRISMA flow diagram of the literature search and selection process

Figure 1 PRISMA flow diagram of the literature search and selection process



Revision Notes (without Author details)

Reviewer: 1	Comment	Response
	* None of the studies accounted for natural fluctuation in PA levels over time. I agree that the PA models should consider or at least discuss this issue. However, whether to include this in the model also depends on factors such as time horizon of the analysis, model cycle length (e.g. monthly vs annual), and study population (e.g. young adults). Incorporating this into models to evaluate PA intervention in adults that are known to have stable PA habits and with a short time horizon would additionally add complexity. This aspect is not well reflected in the discussion.	**Answer: thanks for this comment.** The Discussion section has been edited to include *"However, in scenarios where PA levels are likely to be stable, the decision to incorporate this element into the model needs to be evaluated in light of the trade-off between added complexity and accuracy. "*
	* Page 6, line 29 - please spell out NICE.	**Answer:** NICE spelt out
	* There are still issues with referencing. The main text cites references up to #65, but the reference list includes 72 papers.	**Answer:** The reason for this is that not all of the 25 reviewed studies are directly cited within the manuscript, so the difference in 7 references is given by those studies.
	* Table 1 - it is hard to link the reference # with the study in column 1. Suggest adding author name, i.e. Amarasinghe et al66 to improve readability. Did the authors of ref#67 use two times of analysis, i.e. 2007 and 2006?	**Answer:** Added authors' name to reference numbers to improved readibility in both Table 1 and 2. Yes, the authors of ref#67 (Beale et al., 2012) use two times of analysis, namely, 2007 and 2006.
	*There is inconsistent use of country names (United Kingdom, UK, US and USA). Please use them consistently throughout the paper.	**Answer:** corrected to UK and USA
	* Figure 1 - total number of studies for two boxes (n=153 and n=37) do not match. Suggest replacing EE with economic evaluation. Check all acronyms and remove if not using them more than five times in the paper.	**Answer:** Total number of studies for the n=153 and n=37 boxes corrected. Replaced all acronyms, including EE, with their corresponding full words.
	* Table 2, column 2 heading - what does 'other' refer in 'Modelled downstream disease risks /other'?	**Answer:** "/other" removed

Modelling the impact of physical activity on public health: a review and critique

ABSTRACT

Background While several reviews have assessed economic evaluations of physical activity in public health and, in most cases, found the interventions to be cost-effective, the validity of the conclusions reached depends on the appropriateness of the modelling methods used in the individual studies.

Objective To provide an overview and critique of modelling approaches and key structural assumptions used in applied studies to estimate the impact of physical activity on health.

Methods Electronic databases were systematically searched for relevant model-based economic evaluations. A thematic approach was used to assess the modelling studies. The critique determined the appropriateness of the modelling frameworks and plausibility of key structural assumptions.

Results Twenty-five models were identified. Cohort models were most frequently used. High variability in the modelling of downstream diseases was found across studies analysing similar populations. Structural assumptions regarding the dynamics of change of physical activity were unrealistic in most cases. Heterogeneity was addressed in only a few studies, while health equity concerns were, at best, acknowledged by authors.

Conclusions This literature is predominantly characterised by modelling approaches that may not adequately address the complexities associated with representing the physical activity behaviour- population health process. A consensus on how to model the impact of physical activity on public health and development of a reference model could help reduce these sources of uncertainty.

Keywords: physical activity, economic evaluation, modelling, public health.

INTRODUCTION

The finite resources available to decision makers dictates that commissioning of interventions ought to be based not only on the grounds of effectiveness, but also on cost-effectiveness[1]. To support reimbursement decisions concerned with funding interventions where there are multiple options, economic evaluation is typically used[2].

Several studies have reviewed the cost-effectiveness evidence for promoting physical activity (PA) in the general population and found the interventions to provide value for money in most cases[3-7]. However, methodological reviews have highlighted a number of challenges related to the economic evaluation of public health interventions, including PA[8-11]. Covering all elements of the evaluation, from research design of the intervention to the statistical and economic analyses, these challenges have previously been grouped into four broad categories: attribution of effects, measuring and valuing outcomes, intersectoral costs and consequences and incorporating equity concerns.

A recent review examined how the four methodological challenges above have been addressed in applied studies, across two categories of PA interventions (targeted PA and sedentary behaviour)[11]. Confirming previous findings[8-10], this review found an overall poor quality of reporting and marked inconsistencies in the methods applied across economic evaluations, providing a series of recommendations for the design, analysis and appraisal of economic evaluations.

The existing methodological reviews did not provide a critique on the appropriateness of the modelling approaches used to estimate the impact of changes in PA on population health. More specifically, they did not comment on the appropriateness of structural features of the modelling approach and if these aligned with the fundamental nature of the behaviour-population health process they were designed to represent [12,13]. This is important as the lack

of adequate structure and unrealistic model assumptions can hinder the validity of cost-effectiveness findings [14].

Challenges in modelling the impact of physical activity on public health

More specifically, in terms of measuring effectiveness, a number of challenges in modelling healthy behaviours for public health economic evaluations, including PA, have been discussed in the literature [14,16]. These challenges derive from key complexities of the behaviour – population health process, which require the use of form of modelling, and include: 1) the link to multiple chronic diseases; 2) a dynamic nature of behaviour and 3) heterogeneous response to the intervention.

A recent scientific report[17], which forms the basis of the current UK PA guidelines[18], describes the relationship between PA and the downstream risk of disease, by assessing the relevant available evidence from systematic reviews and meta-analysis against five criteria (i.e. applicability, generalisability, risk of bias or study limitations, quantity and consistency and magnitude and precision of effect). This report confirmed that there was strong evidence suggesting a link between PA and metabolic (e.g. type II diabetes), cardiovascular (e.g. coronary heart disease and stroke), genetic mutation (e.g. colorectal and breast cancer), mental (e.g. depression) and geriatric (e.g. falls) conditions. In addition, disease probabilities may not be independent from one another. For instance, the risk of type II diabetes has been associated with risk of colorectal and breast cancers, mainly due to shared risk factors, among which PA plays a major role[19].

From a modelling standpoint, this complexity represents a technical problem in that a heathy individual faces a number of different competing and complementary disease risks at any given time, based on the individuals' PA level and other personal characteristics. Furthermore, some disease risks which will be affected by changes in PA habits in the short

term (e.g. psychological benefits[20]), while others will take some time before occurring (e.g. colorectal cancer incidence[21]).

While PA habits generally tend to be stable over adulthood[22], a decline in PA is typically associated with older age[23]. Evidence has also shown that natural fluctuations in PA can occur due to seasonality effects or particular life phases[24]. Furthermore, it is also reasonable to expect that different individuals not only will react heterogeneously, in terms of change in behaviour to the same level of exposure, but also that behaviour changes will be sustained at different rates over time[25]. Although the magnitude of effect will depend on the type of intervention, assuming that the changes induced by the intervention over the short term will remain constant over time is likely to be unrealistic, whereas rebound trajectories are generally more likely to occur[26].

Finally, it is important to take into account heterogeneity in natural history of the PA behaviour-health process and intervention effects on this process for two main reasons: to reduce the risk of inducing bias in the cost-effectiveness results and to align the modelling approach to the objectives of the decision-makers the model is aimed to inform[2,12]. Public health decision-makers have a prominent goal of reducing existing health disparities in the population, for instance associated with socio-economic factors[27], reflecting the value that society places on lessening unfair inequalities alongside improving health[28,29].

Modelling frameworks available to analysts

There has been a wealth of research dedicated to generating taxonomies of the mathematical / epidemiological paradigms available to health economic modellers[30-32]. This has also reflected on their properties to inform model-based economic evaluations in public health. These frameworks have been broadly categorised into cohort and individual level approaches

and based on their ability to formally capture time-dependent effects and interactions between individuals and the environment[32].

Briefly, cohort-level approaches are generally simpler than individual level frameworks. In ascending order of modelling capacity, with decision trees and comparative risks assessments (CRAs) neither time nor interactions can be explicitly considered. Markov chains, which can be implemented at both an individual and a cohort level, can instead represent time in the process explicitly as a sequence of transitions between states. More complex are discrete time events and agent-based models which, despite their ability to formally represent changes in states over time and interactions between individuals (the latter), using either discrete and continuous time frameworks, have seen limited application in public health[32].

Beside the suitability of the modelling framework, the way these methods are implemented in practice (i.e. what structural assumptions are made) can affect the validity of cost-effectiveness findings[15]. Comparably to how the National Institute of Health and Care Excellence (NICE)~~NICE~~ evaluates models included as part of manufacturers submissions[33], previews attempts to critique the plausibility of key structural assumptions of the models have been made in other public health evaluation settings[10,16]. To date, no methodological review has focussed on investigating these issues within the PA literature. The present paper aims to fill this gap.

METHODS

Details regarding the search strategy, eligibility criteria, study screening and selection methods are described in Appendix I**.** In brief, model-based economic evaluations of PA interventions were identified within the published literature, from database inception to April 2019. Given the review focus, only full economic evaluations were included (i.e. cost-utility,

cost-benefit, cost-consequences and cost-benefit analyses). A literature search of four electronic databases (MEDLINE, EMBASE, SportDiscus and EconLit) was conducted, with free-text terms, synonyms, spelling variants, abbreviations and indexing terms related to the three concepts of economic evaluation, model and physical activity being used to identify relevant articles.

Data extraction forms were developed by adapting existing templates suggested by review guides [34,35]. These forms were designed to extract information on what modelling frameworks were applied and what key structural assumptions of the models relating to the three complexities discussed above (i.e. the link of physical inactivity to multiple chronic diseases; a dynamic nature of PA behaviour and heterogeneous response to the intervention) were made for estimation of the intervention impact on population health.

As recommended for methodological reviews[34,35], methods were summarised using a thematic approach. For reference, an overview of the modelling studies is first presented. This includes details on the decision contexts and mathematical frameworks used for economic evaluation, based on a classification recently suggested[32]. The second part of the review critiqued the base-case structural assumptions of the models in terms of their plausibility against the existing available evidence. While these assumptions are often interrelated, an evaluation of how the related complexities have been handled in practice is presented. The following questions thus formed the basis of the extraction process, under four themes:

- Modelled downstream disease risk:
    - what and how diseases associated with PA have been modelled?
- Dynamic nature of PA:
    - does the model allow for natural fluctuations in PA levels over time?;

- what assumptions have been made with regard to the link between exposure and change in PA / gains in health?;
- what assumptions have been made with regard to time-dependency of intervention effects?;

- Reflecting heterogeneity:
  - how differences in intervention impacts between individual characteristics have been reflected?
- Incorporating health equity concerns:
  - how intervention impacts on existing health inequalities have been modelled?

RESULTS

Included studies

Figure 1 shows a PRISMA flow diagram of the literature search and selection process. Twenty-five papers met the selection criteria. Table 1 provides an overview of the modelling studies. Eleven papers based their analyses on primary data from the ~~United Kingdom~~UK, seven from the USA, four from Australia and one each from Belgium, Canada and The Netherlands. The majority of studies focused on adults (>=18 years, n=20), four analyses focused only school pupils, and two included a mixed population (adults and children). Interventions based on universal approaches to promotion were explored in the majority of studies (18/25).

Modelling frameworks

Eighty percent of the studies (n=20) employed aggregate-level approaches, nine of which used untimed modelling methods (eight CRAs and one decision-tree). Eleven analyses were

based on discrete-time frameworks, with two multiple cohort lifetable approaches[36,37], and Markov chain modelling being used the most frequently. Of the five individual-level models, two were Markov chains[38,39], one applied a system of linear equations using a cross-sectional regression analysis approach[40], one a microsimulation approach[41] (although no details were reported in terms of Markovian assumptions or interaction-levels) and one study developed a discrete event simulation model[42].

Modelling of downstream disease risk

Table 2 summarises the key structural assumptions made in order to estimate the impact of changes in PA on public health. The majority of studies (n=23) evaluated the impact of interventions on chronic diseases and conditions associated with PA, with eight of these studies not stating which diseases were considered. The number of chronic diseases ranged from one to seven, with one study modelling 32 disease combinations[43].

Except for one study which focused on Osteoporosis[38], all the models selected Type II diabetes and at least one cardiovascular disease (either a type of Stroke or Coronary Heart Disease). Eleven models included at least one cancer (i.e. Colon, Colorectal, Breast, Lung and Kidney) and only two studies considered impacts on mental health outcomes, specifically, depression. Only one study[44] included exercise-related injuries among the consequences. For those studies focussing on adults from the general population (n=14), the majority (n=8) selected five chronic conditions. In addition, while the models evolved over time in terms of disease selection, except for one study which applied random search method to calibrate disease risk parameters[42], none of the models took into account synergistic and compensatory effects between disease risks.

Thus, none of the reviewed models would be able to reflect the currently available evidence on the associated chronic disease risk, therefore, not adequately capturing the impact of

changes in PA, either due to a narrow evaluation scope and/or lack of adjustments for interaction between diseases.

Dynamics of physical activity

Natural course of PA

Except for two studies that developed a natural history model from PA available from a country-level surveillance system [45 46,] none of the models accounted for natural fluctuations in PA levels over time. Baseline PA states were assumed to be stable, also when long-term time horizons were considered, 15/25 evaluations with time horizons equal to or longer than 30 years). Furthermore, transitions between the highest and the lowest levels of PA were not allowed.

Link between exposure and response and its time dependency

All but four models reported that changes in PA and related health gains would be immediate following exposure to the intervention. One study[47] assumed that the intervention could not affect disease risk in the first year ("run-in period"). Other analyses assumed that it would take two years[48], or up to five years[49], for the intervention to reach full effect. Except for one report which reported on the time lag assumed between changes in PA and disease occurrence used in the model[41], none of the other studies provides details regarding time lag to disease.

Time-dependent intervention effects

The majority of models (15/25) assumed implicitly or explicitly that the intervention effect would not decay after the intervention ended (i.e. beyond follow-up assessment period). The remaining 10 analyses assumed a constant and homogeneous decline in effect, ranging from 25% to 100%, up to two years after the intervention ended.

Although lack of data may have driven these choices, the structural assumptions related to the dynamics of change in PA that underlie the current models are underreported and may be unrealistic. While appropriate sensitivity analysis may have helped characterise these complexities for decision-making[2], only a minority of models explored the impact of variations to these base-case structural assumptions (see Table 2).

Reflecting heterogeneity

Ten studies used population average approaches, evaluating the health impact of changes in PA levels in homogeneous groups of inactive / sedentary adults or school pupils. Baseline differences in PA were considered in only nine studies. Three to five levels (i.e. PA states) were defined in these analyses, with part of the models aligning the classification of PA levels to current national-level PA recommendations[37,45,46,51-53]. Twelve studies accounted for heterogeneous health impacts based on at least age or gender, with two analyses also considering ethnicity/race differences[40,42].

Thus, while some degree of heterogeneity has been captured by the reviewed models, only a minority addressed this aspect formally by considering at least basic socio-demographic differences, and in particular, baseline PA level.

Incorporating health equity

None of the reviewed economic models incorporated concerns relating to the distributional impact of the intervention formally into the economic evaluation. Where models accounted for heterogeneous effects, they did not report subgroup analysis which would have allowed for inferences about effects on health inequalities. In only a minority of studies (5/25) equity considerations were discussed.

DISCUSSION AND CONCLUSIONS

Main findings

Complementary to previous reviews[8-11,14], this is the first methodological review to provide an overview and critique of the modelling approaches used in model-based economic evaluations for estimating impacts of changes in PA on public health. This review has shed light on key structural assumptions that underlie the models, which can aid interpretation of the cost-effectiveness findings and highlights model development opportunities.

If, on one hand, economic evaluation guidelines support the notion that model structures should be kept as simple as possible[54,55], models should align to the nature of the process they are intended to represent[12]. While acknowledging that the trade-off between simplicity and internal validity still represents an unresolved challenge for modellers, this literature is predominantly characterised by modelling approaches that may not adequately address the complexities associated with the PA behaviour – population health process they were intended to represent. In addition, key structural assumptions were often unsupported by relevant evidence and based on general rules of thumb.

Minimum modelling standards

Based on the findings from this review, there are a number of areas in which minimum modelling standards should be established. First, modelling of downstream disease risks. The disease selection in the reviewed models does not reflect the current available epidemiological evidence on the relationship between PA and chronic disease. While differences in environmental-level factors may explain differences in magnitude of risk between settings (e.g. countries), disease selection for identified populations should be only based on strong and updated epidemiological evidence. Disease risks are not likely to be

independent from one another, and this should be taken into account, either formally (e.g. using calibration methods) or informally (e.g. by means of scenario analysis).

Second, accommodating for the dynamics of PA. Natural trends in PA levels should be used as baseline data for comparison. Conceptualising PA levels as fixed states is likely to induce bias in the estimations, especially when modelling PA behaviours that are subject to seasonality effects (e.g. gym attendance in summer) or over sensitive life phases (e.g. retirement). However, in scenarios where PA levels are likely to be stable, the decision to incorporate this element into the model needs to be evaluated in light of the trade-off between added complexity and accuracy. Assumptions regarding time lags and decay of intervention effects over time must also be made explicit. The current lack of data on long-term impacts of PA intervention does not justify the use of unrealistic assumptions. Instead, modelling of PA should include analysis of a range of possible scenarios for adequately reflecting the uncertainty surrounding the decision[2]. The common assumption found across the models of no decay of effect over time is unrealistic, especially when assessing effects over long periods of time. This is likely to result in overestimation of the health benefits of the intervention and undermine the validity of research findings.

Third, reflecting heterogeneity. Models should capture systematic differences in impacts between individual characteristics[56]. Moderator variables should be identified both for the estimation of effectiveness and cost-effectiveness of PA interventions directed at heterogeneous populations. Although sub-group analyses will not always be feasible in practice (e.g. due to small sample sizes), reports should make explicit the reasons for not conducting them. Reports should also include details regarding the gradients in risks between population sub-groups, and how the shape of these gradients is assumed (e.g. curvilinear[57]) when no data were available.

Forth, on the issue of incorporating health inequity concerns. Methods for incorporating such concerns into economic evaluation have only been relatively recently suggested and this may explain why this element is missing in the published studies. Practical considerations related to the use of these methods have been acknowledged[8,58] (e.g. lack of data on sub-groups) and this may impede analysts in undertaking any quantitative assessment such as health inequality impact, opportunity cost or equity weighting analyses[59]. Nevertheless, given the importance of addressing health inequity, it would be reasonable to expect that model structures allowed for capturing differential natural histories and intervention effects between equity-relevant sub-groups (e.g. socio-economic status)[28,29]. Where this is not possible, authors should at least highlight this as a limitation and conduct a qualitative assessment, for instance, by reviewing the background information regarding existing patterns and causes of health inequities)[59].

Finally, there is a need for a better characterisation of the uncertainty related to structural assumptions. A more structured and formal approach to assessing the implications of key structural assumptions on the economic decision should be a minimum requirement. In absence of data, a range of plausible scenarios should be explored, and results be presented as such, rather than just a base-case[60].

Limitations

This review is subject to several limitations. The level of detail presented in the applied studies leads us to conclude that an overall poor quality of reporting was observed, making the assessment of the modelling studies difficult. However, a formal quality assessment was not conducted according to previously defined criteria, limiting the ability of this review to determine a more traditional judgement on study quality. In addition, whilst a detailed systematic search was conducted, this review only included PA interventions, therefore

limiting the generalisability of the findings to economic evaluations of interventions where PA is combined with other technologies or healthy behaviours.

This study focused on the cost-effectiveness literature only, and it is possible that other types of studies, such as epidemiological studies, have addressed some of the complexities discussed. Furthermore, methodological aspects discussed here represent only a proportion of the challenges that are apparent when modelling of impact of different types of PA interventions. Specifically, modelling issues related to compensatory or synergistic effects with other behaviours on the pathway to health improvement, such as dietary patterns, interactions between individuals, and non-health effects of these interventions, have not been addressed in this review and should be the focus of further research.

Concluding remarks

Reaching a consensus on minimum modelling standards, improved reporting of the key model assumptions using the available reporting checklists[61-64] and development of a reference model[65] could help reduce these sources of uncertainty, and therefore support optimal decision-making.

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