A systematic review of the cost-effectiveness of lifestyle modification as primary prevention intervention for diabetes mellitus type 2

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ABSTRACT

BACKGROUND: diabetes is one of the leading causes of death, and has a huge economic impact on the burden of society. Lifestyle interventions such as diet, physical activity and weight reducing are proven to be effective in the prevention of diabetes. To encourage policy actions, data on the cost-effectiveness of such strategies of prevention programmes are needed.

METHODS: a systematic review of the literature on the cost-effectiveness of prevention strategies focusing on lifestyle interventions for diabetes type 2 patients. A weighted version of Drummond checklist was used to further assess the quality of the included studies.

RESULTS: six studies met the inclusion criteria and were therefore considered in this paper. Intensive lifestyle intervention to prevent diabetes type 2 is cost-effective in comparison to other interventions. All studies were judged of medium-to-high quality.

CONCLUSIONS: policy makers should consider the adoption of a prevention strategy focusing on intensive lifestyle changes because they are proven to be either cost-saving or cost-effective.

Key words: Diabetes; Prevention; Cost-effectiveness; Lifestyle

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INTRODUCTION

Diabetes mellitus is one of the top ten causes of death for both low and high-income countries [1]. An interaction of genetic predisposition along with behavioural and environmental risk factor was found to be a reason for diabetes mellitus type 2 (DMT2) [2]. Even though it is not yet known what role genetics play in occurrence of diabetes, the literature shows strong evidence that evitable risk factors like overweight and lack of physical activity are the main determining, non-genetic factors of DMT2 [3-7]. The worldwide increase of the prevalence of diabetes mellitus type 2, and the importance of obesity and lack of physical activity, as stated by the WHO [8] increase the need of prevention strategies and policy implications to be taken. Caring for diabetes and the

subsequent complications is expensive [9], however some interventions have the ability to reduce the burden of the disease. One possible primary prevention strategy relies on lifestyle modification i.e., changed dietary habits, increased physical activity, maintaining or reducing body weight. In the last years several randomised, controlled clinical trials have investigated the impact of changing diet and physical activity on the prevention of type 2 diabetes. The Finnish Diabetes Prevention Study (DPS) as well as many other studies [10-12], demonstrated a clinically significant impact of lifestyle changes in the decrease of diabetes. However, resources are scarce and it is important to review if the adoption of such a prevention strategy is cost-effective. The aim of this study is to systematically review the existing English literature available from 2007 to 2012 on the cost-effectiveness of lifestyle changes as a primary prevention intervention for diabetes mellitus.

RESEARCH DESIGN AND METHODS

This systematic review was performed following the PRISMA statement [13]. Studies were identified by searching NCBI's PubMed database and SCOPUS database. Following keywords were used to search the database for appropriate literature indicating diabetes: diabetes OR diabetes mellitus OR diabetes AND mellitus OR diabetes insipidus OR diabetes AND insipidus; indicating cost-effectiveness: cost-benefit analysis OR cost-benefit AND analysis OR cost-effectiveness OR cost AND effectiveness; indicating prevention: prevention AND control OR prevention OR prevention and control OR prevention; indicating lifestyle: life AND style OR lifestyle OR life style.

Inclusion and exclusion criteria

Criteria for inclusion in the review were the following: original cost-effectiveness analysis or other full economic analysis; primary intervention by changing lifestyle (e.g. by diet and/or physical activity); prevention strategy for diabetes type 2 patients; pharmacotherapy or no intervention was a comparator to lifestyle intervention; outcomes were presented as Quality Adjusted Life Years (QALYs) gained or as Life Years Gained (LYGs); original publication language was English; published between January 2007 and February 2012; diabetes type 2. Studies were excluded if the lifestyle intervention was combined with therapy, or if they were compared with treatments such as gastric bypass surgery or therapeutic or enteral nutrition.

Reporting of results

In order to make ICERs (Incremental Cost-Effectiveness Ratio) within the different studies comparable, all costs were converted into 2012 Euro using the OANDA Currency Exchange Calculator [14] for yearly average annual exchange rates. Costs already expressed in Euro (€) were also adjusted to 2012 by using the Italian Consumer Price Index [15]. ICERs are then presented in €/QALY or €/LYG and rounded to the nearest hundred Euro.

For the classification of the intervention a threshold approach was used, assuming that an intervention is cost-effective if the ICER is lower than € 20 000-30 000 and cost saving if the costs are lower and health outcomes are better than in the compared intervention.

Results from the included studies are summarised giving an overview of the study population, the intervention, the comparison, where effectiveness data was drawn from, the analytical horizon, the study perspective and the classification of the intervention using the criteria described earlier.

Quality assessment

A weighted version of Drummond checklist was used to further evaluate the quality of the studies included in the systematic review [16, 17]. The checklist was developed to assess the quality of an economic evaluation considering the following sections: study design, data collection, analysis and interpretation of results. All of the 35 items were explored by two independent reviewers for included study. The weighted version assigned a maximum global score of 26 for study design, of 45 for data collection, of 48 for analysis and interpretation of results section, while the global highest available score was 119.

RESULTS

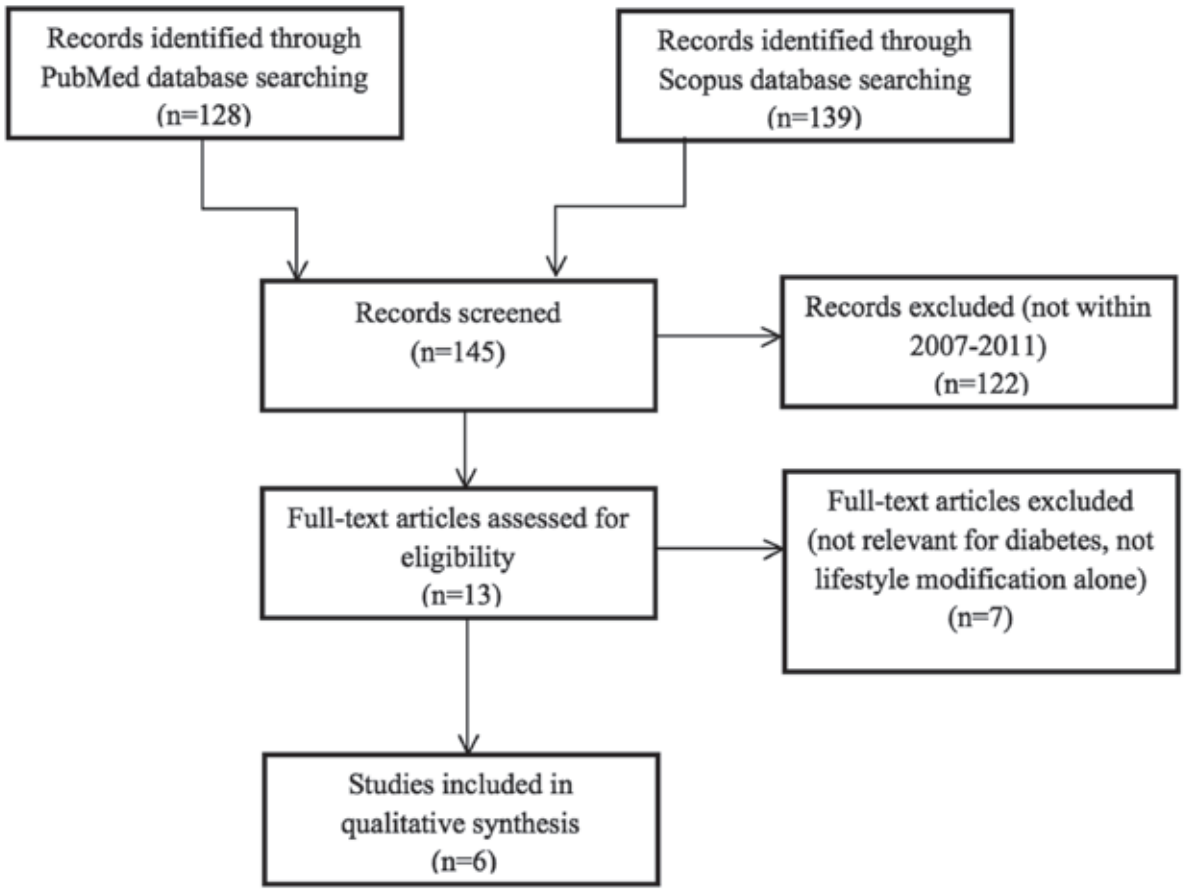
Following this search strategy, 128 studies were found in the PubMed database and 139 in SCOPUS database. All studies were then exported into EndNote. After exclusion of papers published before 2007, 145 abstracts remained for screening. Six studies were identified as being eligible for this review meeting the inclusion criteria. Most of the papers were excluded because they were either not related to diabetes or did not provide the right outcome data (€/QALY or €/LYG) (Figure 1 for the Flow Diagram). A summary of the studies included in this systematic review can be found in Table 1.

Two studies by Galani et al. [18, 19] focusing on lifestyle intervention were conducted on both obese and overweighed population groups in Switzerland. Effectiveness data was taken from the Finnish Diabetes Prevention Study (DPS) [20]. By developing a Markov model with seven states over a lifetime horizon they estimated that prevention strategies based on lifestyle interventions could be cost-effective from the societal perspective but depended on sex, age group and threshold values. However the results of the two studies were quite different. The study result of 2007 [18] was that in borderline groups the cost/QALY was € 47/QALY for females and € 228/QALY for males. In the study conducted only one year later [19], the ICERs were much higher, coming up to € 3 200/QALY for females and € 1 600/QALY for males at the age of 30 with overweight. The difference might result from the different population and age considered in the result, but this still has to be considered when interpreting the results.

Icks et al. [21] investigated the cost-effectiveness of the Diabetes Prevention Program (DPP) in a real-world setting in

FIGURE 1

THE SEARCH STRATEGY AND FLOW DIAGRAM FOR DATABASES SEARCH



Germany, getting their effectiveness data both from the DPS and literature review. They conclude that even though the lifestyle intervention program was more cost effective than metformin, before implementing such a strategy efforts should be made to improve patient participation to achieve better clinical and cost-effectiveness, because acceptance of and adherence to the intervention is low and the drop- out rate is high. ICERs were calculated from the societal and healthcare perspective and were reported as € 31 000/

TABLE 1

DESCRIPTION OF THE COST-EFFECTIVENESS STUDIES FOR DIABETES PREVENTION

AUTHOR, YEAR, COUNTRY	INTERVENTION	COMPARISON	AGE, RISK FACTOR	INTERVENTION PERIOD, PERSPECTIVE	EFFECTIVENESS SOURCE	RESULTS AND CONCLUSION	PRICE YEAR, DISCOUNT RATE	SENSITIVITY ANALYSIS	MODEL	CLASSIFICATION
Galani [14], 2007, Switzerland	Lifestyle intervention (DPS)	Standard care	age >= 25; overweight BMI 25-29.9, borderline BMI 30, moderate obese BMI >30	3.2 years, societal	Literature review	€50/QALY for females and €200/QALY for males in borderline group	2006, 3%	Probabilistic	DAM	Cost-effective
Galani [15], 2008, Switzerland	Lifestyle intervention (DPS)	No intervention	Age: 60-74, BMI>24	3.2 years, societal	Literature review	€3 200/QALY (females) and €1 600/QALY (males), 30 years old and overweighted	2006, 3%	Probabilistic	DAM	Cost-effective
Icks [17], 2007, Germany	Targeted screening + lifestyle intervention, targeted screening + metformin	No intervention	Age: 60-74, BMI>24	3 years, societal and healthcare	DPP and literature review	€5 400 healthcare and €31 000 societal perspective per T"DM case prevented by lifestyle intervention	2004, NP	Univariate, probabilistic	DAM	Cost-effective
Lindgren [18], 2007, Sweden	Lifestyle intervention (DPS)	No intervention	Age: 60, BMI >25, fasting glucose >6.1 mmol/L	3 years, societal and healthcare	Single study, (DPS)	With declining effect: societal: €15 600/LYG; healthcare perspective €10 900/LYG; With remaining effect: societal €15 600/LYG, healthcare perspective €1 300/LYG	2000; 3%	Univariate	DAM	Cost-effective
DPP RG [20], 2012, USA	Lifestyle intervention (DPS)	No intervention	Age≥24, BMI>24	3 years, societal and healthcare	DPP and Quality of Well Being Index	€10 000/ QALY	2012; 3%	Probabilistic	No Model	Cost-effective
Neumanm [19], 2012, Germany	PREDIAS and SDPP	No intervention	Individuals at high risk	5 years, societal and healthcare	Literature review	70 year old men: 27 600/ QALY, 70 year old women: 19 400/QALY	NA	Probabilistic	Markov	Cost saving if older age groups are excluded, cost-effective

TABLE 2

QUALITY OF INCLUDED STUDIES

	REFEREE'S CHECKLIST	STUDY ID											
	ITEM	GALANI 2007		GALANI 2008		ICKS 2007		LINDGREN 2007		DPP 2012		NEUMANN 2012	
STUDY DESIGN	(1) The research question is stated	Y	4	Y	4	Y	4	Y	4	Y	4	NC	-
	(2) The economic importance of the research question is stated	Y	3	Y	3	Y	3	Y	3	Y	3	Y	3
	(3) The viewpoint(s) of the analysis are clearly stated and justified	NC	-	Y	4	Y	4	Y	4	Y	4	Y	4
	(4) The rationale for choosing the alternative programmes or interventions compared is stated	N	-	NC	-	Y	4	Y	4	Y	4	NA	-
	(5) The alternatives being compared are clearly described	Y	4	NC	-	Y	4	NA	-	Y	4	NA	-
	(6) The form of economic evaluation used is stated	Y	4	Y	4	Y	4	Y	4	Y	4	Y	4
	(7) The choice of form of economic evaluation is justified in relation to the questions addressed	N	-	Y	3	Y	3	Y	3	Y	3	Y	3
DATA COLLECTION	(8) The source(s) of effectiveness estimates used are stated	Y	4	Y	4	Y	4	Y	4	Y	4	Y	4
	(9) Details of the design and results of effectiveness study are given (if based on a single study)	NA	-	N A	-	NA	-	Y	3	NA	-	NA	-
	(10) Details of the method of synthesis or meta-analysis of estimates are given (overview)	Y	3	Y	3	Y	3	NA	-	Y	3	Y	3
	(11) The primary outcome measure(s) for the economic evaluation are clearly stated	Y	4	Y	4	Y	4	NC	-	Y	4	Y	4
	(12) Methods to value health states and other benefits are stated	Y	4	Y	4	Y	4	Y	4	Y	4	NA	-
	(13) Details of the subjects from whom valuations were obtained are given	Y	3	Y	3	Y	3	Y	3	Y	3	NA	-
	(14) Productivity changes (if included) are reported separately	NA	-	NA	-	NA	-	NA	-	NA	-	NA	-
	(15) The relevance of productivity changes to the study question is discussed	NA	-	NA	-	NA	-	NA	-	NA	-	NA	-
	(16) Quantities of resources are reported separately from their unit costs	Y	3	Y	3	Y	3	Y	3	Y	3	Y	3
	(17) Methods for the estimation of quantities and unit costs are described	NC	-	Y	4	Y	4	Y	4	Y	4	Y	4
	(18) Currency and price data are recorded	Y	3	Y	3	Y	3	Y	3	Y	3	Y	3
	(19) Details of currency of price adjustments for inflation or currency conversion are given	Y	3	Y	3	Y	3	NA	-	Y	3	NA	-
	(20) Details of any model used are given	Y	3	Y	3	Y	3	Y	3	NC	-	Y	3
	(21) The choice of model used and the key parameters on which it is based are justified	Y	4	Y	4	Y	4	Y	4	NC	-	Y	4
ANALYSIS AND INTERPRETATION OF RESULTS	(22) Time horizon of costs and benefits is stated	Y	4	Y	4	Y	4	Y	4	Y	4	N	-
	(23) The discount rate(s) is stated	Y	4	Y	4	NA	-	Y	4	Y	4	Y	4
	(24) The choice of rate(s) is justified	N	-	Y	3	NA	-	Y	3	N	-	Y	3
	(25) An explanation is given if costs or benefits are not discounted	NA	-	NA	-	Y	3	NA	-	NA	-	NA	-
	(26) Details of statistical tests and confidence intervals are given for stochastic data	Y	3	N	-	Y	3	Y	3	NA	-	NA	-
	(27) The approach to sensitivity analysis is given	Y	4	Y	4	Y	4	Y	4	Y	4	Y	4
	(28) The choice of variables for sensitivity analysis is justified	Y	3	Y	3	Y	3	Y	3	Y	3	Y	3
	(29) The ranges over which the variables are varied are stated	Y	3	Y	3	Y	3	NC	-	Y	3	N	-
	(30) Relevant alternatives are compared	Y	3	Y	3	Y	3	Y	3	Y	3	Y	3
	(31) Incremental analysis is reported	Y	3	Y	3	Y	3	Y	3	Y	3	Y	3
	(32) Major outcomes are presented in a disaggregated as well as aggregated form	Y	3	Y	3	Y	3	Y	3	Y	3	Y	3
	(33) The answer to the study question is given	Y	4	Y	4	Y	4	Y	4	Y	4	Y	4
	(34) Conclusions follow from the data reported	Y	4	Y	4	Y	4	Y	4	Y	4	Y	4
	(35) Conclusions are accompanied by the appropriate caveats	N	-	Y	4	Y	4	Y	4	Y	4	Y	4
	Final score	87		94		105		92		96		77	

Y=yes; N=not; NC=not clear; NA=not appropriate

QALY and € 5 400/QALY respectively.

In order to assess the economic consequences of a DPS intervention in Sweden, Lindgren et al. [22] created a simulation model, using effectiveness data from the DPS and cost data from Swedish studies. Besides showing that such a program would be both cost-saving from the healthcare perspective and cost-effective form a societal perspective, they also prognosticated an increase of survival and the cost associated with it. ICERs were € 10 900/LYG and € 156 000/LYG, respectively.

A four-state Markov model was used by Neumann et al. [23] with data on transition probabilities from best available evidence, calculating costs from the perspective of society. Their results show that diabetes prevention intervention can be cost-effective, but the outcome is very uncertain and depending on different factors, such as age. QALYs gained through this strategy were low, but the ICER showed cost-effectiveness if initiation of the intervention was at an age of 70 years. For men and women between 30 and 50 years the adoption of the intervention leads to a saving in costs.

In order to assess the cost effectiveness of the DPP, the Diabetes Prevention Program Research Group [24] performed an economic evaluation both from the health care and societal perspective using prospectively collected data on resource utilisation, cost and quality of life. Throughout their study they approved the cost-effectiveness of lifestyle intervention over metformin and the cost-saving compared to placebo. They reported € 19 400/QALY for females and € 27 600/QALY for males for a population aged 70 years.

Quality of characteristics included in the study and quality of the included studies

Table 2 reports qualitative evaluation assigned to each included study, according to the 35 items exploring study design, data collection and analysis and interpretation of results. All the studies clearly defined the economic importance of research question (item 2), the form of economic evaluation (item 6), the sources of effectiveness estimates (item 8); in all the studies quantities of resources are reported separately from their unit costs (item 16), currency and prices data are reported (item 18), the approach to sensitivity analysis is given (item 27), the choice of variables for sensitivity analysis is justified (item 28); moreover all the studies compared relevant alternatives (item 30), reported incremental analysis (item 31), answer to the study questions (item 33) and conclusions (item 34). Most studies stated research question (item 1) and the viewpoint of analysis (item 3), justified the form of economic evaluation (item 7), stated the primary outcome measure of economic evaluation (item 11), described methods for quantities and estimation of unit costs (item 17) and details of any model used (item 20), justified the choice of model used (item 21), stated the range over which variables are varied (item 29), gave appropriate conclusions (item 35). Details of the study design were not clearly given by Neumann and al. [23], Galani and al. [18] and Galani and al. [19]. Finally some deficiencies have been highlighted referring to analysis and interpretation of results section. According to the weighted Drummond's scale, the median quality score of selected studies was 93, with a minimum score of 77, and a maximum score of 105 (Table 2). In study design question two studies attained the maximum available score, no maximum available score was attained in data collection section and analysis and interpretation of results.

DISCUSSION

Several studies such as the US DPP [25], the Finnish DPS [11] and the Indian DPP [26] have already presented the efficacy of lifestyle modification. Our systematic review showed that lifestyle modification as a prevention strategy is not only efficient but it is also cost effective and/or in some cases cost saving. If the costs of such an intervention could be further reduced, cost-effectiveness would increase. A possible first step in this direction could be the changing of the setting where the intervention was provided. But also the different methods available (information delivery about lifestyle modifications in groups or on a one-by-one basis) should be evaluated and improved.

However our study has several limitations: first, we included only English-language publications; second, most of these studies rely on different methodologies, include varying types of costs, have different outcomes or measure outcomes differently and have a related

baseline risk which makes the comparison difficult. Also the country setting can influence the outcomes. Another issue that should be considered is that different healthcare systems, population groups and values, clinical practices, incentives to physician, may have an impact on the cost-effectiveness.

We considered a threshold approach for the classification of the cost-effectiveness, however setting a threshold is controversial. Since the UK [27], the USA [28] and Australians [29] all use different thresholds, the WHO recommends basing the decision on the country's GDP [30]. An intervention is considered as cost-effective if the costs per DALYs are 1.3 GDP per capita. Five of the six studies used economic decision models to evaluate the costs, thus providing information at a much lower level than trials in a real world setting. But even with the help of Decision Modelling not all costs, values and criteria that are relevant for decision makers can be captured. Furthermore they are based on assumptions and may not represent the reality due to oversimplification. However DAMs (Decision Analysis Model) have the ability to help to inform policy makers. In the future economic evaluation of diabetes intervention should address the impact in real-world settings, because non-compliance, drop-out rates or attrition rates are very often not considered when evaluating the cost-effectiveness.

Furthermore it would be advantageous to have information about the cost-effectiveness of changes in public policies or public insurance reimbursement.

Eventually the impact of multiple different interventions should be evaluated as well, because in a real-world setting patients follow more than one intervention at the same time.

It is important to keep in mind that cost-effectiveness should not replace decision makers, but should inform them to help them making their decision. Cost-effectiveness is not the only aspect to consider when deciding whether or not to adapt an intervention, because CEAs (Cost-Effectiveness Acceptability) do not take into account the benefits, utility, willingness to pay (both from a personal and a societal perspective), or any social, legal or ethical issues that may occur when adapting the intervention. Although the six studies included in the systematic review are of good quality, some deficiencies have been documented in all the sections. Future studies will need to take better account of the items related to study design, data collection and results from a methodological point of view. This is also necessary to perform comparable and scientifically based economic evaluations.

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