STOCHASTIC APPLICATION OF A MODEL FOR INFORMING RESOURCE ALLOCATION DECISION MAKING ABOUT THE IMPLEMENTATION OF CLINICAL PRACTICE GUIDELINES IN DIABETES CARE

TEXT

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Abstract

Background: Decision making about resource allocation for guideline implementation to change clinical practice is inevitably undertaken in a context of uncertainty surrounding the cost-effectiveness of both clinical guidelines and implementation strategies. Recently, a model has been developed in which monetary values are assigned to health outcomes and economic evidence on guidelines and strategies is combined with information on clinical practice to determine the scope of cost-effective guideline implementation. Adopting a net benefit approach, the model overcomes problems with the use of combined ratio statistics when analyzing decision uncertainty concerning clinical practice change.

Aim: To demonstrate the stochastic application of the model for informing decision-making about the adoption of an audit and feedback strategy for implementing a guideline recommending intensive blood glucose control in type 2 diabetes in primary care in The Netherlands.

Methods: An integrated Bayesian approach to comprehensive decision modeling and evidence synthesis is adopted using Markov Chain Monte Carlo simulation in WinBUGS. The effectiveness of audit and feedback is estimated using a pooled, random effects meta-analysis model. Data on other model parameters is gathered from various sources. Decision uncertainty is illustrated using cost-effectiveness acceptability curves (CEACs) and frontier (CEAF).

Results: Decisions about whether to adopt the guidance on blood glucose control and whether to adopt audit and feedback for its implementation alter over the range of maximum values that decision-makers are willing to pay for health gain. Through simultaneously incorporating uncertain economic evidence on both guidance and implementation strategy, the CEACs and CEAF show an increase in decision uncertainty concerning guideline implementation.

Conclusions: The stochastic application in diabetes care demonstrates that the model provides a simple and useful tool for quantifying and exploring the (combined) uncertainty associated with decision-making about adopting guidelines and implementation strategies and, therefore, for informing decisions about the efficient allocation of health-care resources to change clinical practice.

1 Introduction

Diabetes is a common chronic condition that accounts for huge burden of morbidity and mortality through micro and macro vascular complications [1, 2]. Evidence suggests that patients with diabetes benefit from strict control of blood glucose, blood pressure and cholesterol [3-6]. Although several guidelines and diabetes management programs have been developed nationally and locally to achieve better metabolic control, clinical use of guidance on diabetic care does not necessarily follow [7, 8]. Non-adherence to guideline recommendations reduces the efficiency of health care delivery in terms of health and resources forgone. Implementation strategies, such as education, outreach visits, audit and feedback, and reminders, attempt to change guidance adherence [9, 10]. Nonetheless, no single strategy or combination of strategies has been found to be consistently cost-effective [11-13]. Since implementation efforts compete with other health care programs for limited health care resources, decision makers should carefully consider the likely value for money of guideline implementation in diabetes care [14-17].

Economic evaluation based on decision analytic modeling can generate valuable information to aid decision makers allocate scarce health care resources efficiently [18]. Recently, a model for analyzing the scope of cost-effective guideline implementation was developed [19]. By combining evidence from different sources, the model allows the exploring of the investment potential for guideline implementation and the value for money of implementation strategies. By adopting a total net benefit approach, the model overcomes problems with the use of combined implementation cost-effectiveness ratios at patient level [15, 20], e.g. when comparing multiple guidelines and multiple strategies across different clinical settings, or when analyzing the uncertainty associated with decision making about clinical practice change.

In this paper, we demonstrate the stochastic application of the model to inform resource allocation decision-making in type 2 diabetes (non-insulin-dependent) in primary care in The Netherlands by applying it for exploring the economics of implementing a guideline for intensified

blood glucose control by means of audit and feedback. The paper starts with an outline of the modeling approach, providing a detailed description of the model structure, the data input, and the model analysis and implementation. Next, the results of the application of the comprehensive decision model are presented. We conclude with a discussion of the main findings of the analysis, the implications for decision making and some comments on the model and suggestions for its extension.

2 Methods

2.1 Clinical setting, diabetes guidance and implementation strategy

In the Netherlands, the prevalence of diabetes is about 2.5%, and about 85% of these patients are estimated to have type 2 diabetes [21]. The majority of these patients are being treated in primary care [22]. To reduce the risk of diabetes-related complications, the Dutch College of General Practitioners (NHG) revised their guidance on glycemic control, formulating recommendations for diagnosis and medication of diabetes mellitus type 2 [23, 24]. In short, the revised guidance on intensified glycemic control recommends to test blood glucose concentrations on a regular basis (i.e. every 3, 6 or 12 months), and the prescribing of, depending on glucose concentrations, metformin, sulphonylureas or thiazolidine and insulin alongside (> 3 months) patient education and advice, diet and physical activities (i.e. conventional therapy). The intensive policy aimed for glycated haemoglobin (HbA_{1c}) < 7%, and, in insulin-treated patients, pre-meal glucose concentrations of 4-7 mmol/l. Based on empiric data from a Dutch study in hospital outpatient clinics [25], current adherence to guideline recommendations on diabetic care is estimated to be 64.1% (with a standard deviation (SD) of 6.4%).

According to the Cochrane Effective Professional and Organisational Change (EPOC) taxonomy, audit and feedback is ‘any summary of clinical performance of health care over a specified period

of time. The summary may also have included recommendations for clinical action. The information may have been obtained from medical records, computerized databases, or observations from patients' [12].

2.2 Comprehensive decision model

For quantifying and exploring the uncertainty associated with decision making about changing diabetes practice in Dutch primary care, we adopted an integrated Bayesian approach to decision modeling and evidence synthesis [18, 26].

2.2.1 Model structure

The structure of the model is derived from the model developed by Hoomans and colleagues [19]. By assigning monetary values to health outcomes (λ) and combining economic evidence on guidelines and implementation strategies with information on the clinical setting (i.e. the duration of guideline use (d_{cg}), the prevalence of disease (p_d), and the number of professionals (n_{hp}) and patients (n_{pt}) targeted), the model establishes the investment potential for implementing guidance on blood glucose control and the value for money of audit and feedback (see Box).

[BOX]

The maximum total investment potential for guidance implementation ($maxTIP_{gi}$) is simply the difference between the total net benefit of guideline use in perfect practice (i.e. assuming 100% adherence to guidance (adr)) and that in current practice, where guideline adherence is less than perfect (adr <1) (see Equation 1a). The investment potential provides a maximum upper bound on resources to be committed to achieve 100% adherence to a cost-effective guideline. Essentially, if a clinical guideline is not deemed cost-effective (with $TNB_{cg} < 0$) but currently implemented into clinical practice (adr > 0), there is a potential to invest in strategies to promote non-adherence to the guidance (see Equation 1b).

The total net benefit of adopting an implementation strategy (TNB_{is}) to change guideline adherence (e.g. audit and feedback) is derived by subtracting the cost of implementation (C_{is}) from the total net benefit of expected change in guidance adherence (Δadr) (see Equation 2). As derived in Equation 3, the sum of the total net benefit of current clinical use of guidance and that of changed guideline use due to implementation efforts yields the expected total net benefit of guideline implementation into clinical practice (TNB_{gi}).

The outline of the model has been described in more detail elsewhere [19].

2.2.2 Data sources and evidence synthesis

Economic evidence on blood glucose control policy. For the economic evidence on the policy for more intensive blood glucose control, we made use of the United Kingdom Prospective Diabetes Study Outcomes Model (UKPDS OM) [27] and the model developed by the CDC Diabetes Cost-effectiveness group [28]. Based on patient-level data from a large-scale randomized clinical controlled trial (UKPDS), both models compared, with model-derived data extrapolation over the lifetime of cohorts of newly diagnosed patients, intensified glycemic control with conventional therapy in terms of cost per quality-adjusted life-year (QALY). The perspective of analysis was that of a health care purchaser, considering only direct health service costs, in the UKPDS OM, and that of the health care system in the CDC model.

Effectiveness of audit and feedback. We conducted a meta-analysis for estimating the effectiveness of audit and feedback, searching the reference lists of relevant systematic reviews plus key articles on implementation research in diabetes care [11-13, 29, 30] for relevant studies. Studies were selected for inclusion whether the strategy was single faceted or accompanied by educational activities or (computerized) reminders. We included studies only if audit and feedback was evaluated in a primary care setting, and was targeted at changing professional behavior

related to diabetic care. Our search yielded only two relevant implementation studies evaluating change in adherence to diabetes guidance [31, 32], of which we extracted data on study details and outcomes (see Table 1).

[TABLE 1]

Cost of audit and feedback. Based on information from the literature [11-13, 29, 30], we initially assumed the cost of audit and feedback to be €100 (€25 SD) per health care professional.

2.3 Model analysis and implementation

2.3.1 Stochastic analysis

To inform decision making about the adoption of intensified blood glucose control and/or audit and feedback to change diabetes practice in The Netherlands, we first established the posterior distributions (i.e. means, standard deviations and 95% confidence intervals) for the relevant model parameters (ΔE_{cg}, ΔC_{cg}, adr, ΔE_{is} and ΔC_{is}) and the expected values for the total net benefit of the guidance (TNB_{cg}), the investment potential for its implementation ($maxTIP_{gi}$), and the total net benefit of implementation (TNB_{is} and TNB_{gi}), given a cost-effectiveness threshold λ of €30,000 per QALY. In addition, we examined these model-derived values over a range of λ's (0 to €40,000 per QALY).

To explore the influence of uncertainty surrounding the different costs and effects relevant for decision making about practice change, we plotted cost-effectiveness acceptability curves (CEACs) and frontiers (CEAFs), generated from model simulation. The CEAC is a plot of the probability that an option to change practice (i.e. guidance and/or its implementation) is cost-effective as a function of λ [33]. The CEAF is constructed from the individual CEACs, depicting the uncertainty associated with the cost-effective options over all values of λ [33].

For simplicity, the model calculations were done under the assumption that the duration of the implementation efforts (d_{is}) was only 6 months.

2.3.2 Sensitivity analysis

Finally, we performed sensitivity analyses to examine whether the cost of implementation influenced the valuations for the total net benefit of implementing guidance on diabetic care and the probabilities that audit and feedback and guidance implementation are cost-effective. To weaken our assumption that the mean cost of audit and feedback are only €100, we set this, subsequently, at €1,000 and €2,500 per health care professional.

2.3.3 Model implementation

To evaluate the comprehensive decision model, we performed Markov Chain Monte Carlo (MCMC) simulation using WinBUGs. We applied multi-parameter evidence synthesis using all relevant data inputs that informed incremental costs and effects of blood glucose control guidance and its implementation. The effectiveness of audit and feedback (ΔE_{is}), in terms of change in guidance adherence (Δadr), was estimated using pooled, random meta-analysis performed on a normal scale. We used non-informative priors for all model parameters. Table 2 summarizes the parameter values, distributions, data sources and priors for all model inputs. All costs are expressed in 2007 € (discounted at a rate of 3.5%).

[TABLE 2]

For all model evaluations to achieve convergence, we used initial 50,000 ‘burn-in’ sample iterations (these values were discarded), with inferences based on further runs of 50,000 iterations. Additionally, model convergence of the MCMC sampler was confirmed by performing

multiple WinBUGS runs for different sets of initial parameter values, track tracing and checking for autocorrelation of relevant parameters.

The implementation of the comprehensive decision model in WinBUGS is outlined in the Appendix.

3 Results

3.1 Stochastic analysis

Table 3 details the posterior distributions for the economic variables of intensified blood glucose control (ΔE_{cg} and ΔC_{cg}), the baseline adherence to glycemic control guidance (adr), and the economic variables of audit and feedback (ΔE_{is} and ΔC_{is}) based on model simulation. In addition, the model-derived expectations regarding the total net benefit of the guidance (TNB_{cg}), the maximum total investment potential to ensure its implementation ($maxTIP_{gi}$), the total net benefit of audit and feedback (TNB_{is}), and that of guidance implementation (TNB_{gi}) are presented, given a cost-effectiveness threshold λ of €30,000 per QALY.

[TABLE 3]

The mean incremental effectiveness (ΔE_{cg}) and cost (ΔC_{cg}) of glycemic control are estimated to be 0.16 QALYs (95% confidence interval -5.01% to 5.34%) and €4132 (€1439 to €6812), respectively. Consequently, the incremental cost-effectiveness ratio of the clinical guideline ($ICER_{cg}$) is estimated to be approximately €25,000 per QALY, with an expected baseline adherence to the guidance (adr) of 62.55% (16.30% SD). The estimated change in guidance adherence due to audit and feedback (ΔE_{is}) is 17.75% (31.59% SD) at an expected expense (ΔC_{is}) of €99.50 (€37.11 SD).

If decision makers are willing to pay €30,000 per QALY, the guidance on intensified blood glucose control is deemed cost-effective (with a TNB_{cg} of €317.3 million (95% confidence interval -€63,000 to €63,310), and there is expected to be considerable potential to invest in its implementation ($maxTIP_{gi}$) (€113.1 million (-€24,080 to €24,190)). The adoption of audit and feedback for implementation would yield an additional net benefit (TNB_{is}) of €20.1 million (-€96.98 to €121.400), and the total net benefit of adopting and implementing glycemic control in diabetes practice (TNB_{gi}) in the Netherlands is estimated to be €231.5 million (-€39,160 to €40,490).

[FIGURE 1]

Figure 1 shows that the decisions about whether to adopt guidance on intensified blood glucose control and about whether to adopt audit and feedback for its implementation alter over the range of values for λ. Given that the guidance is expected to enact both additional QALYs and additional costs, standard care is preferred to 'guided' care for values of λ less than the $ICER_{cg}$. As a consequence, there is value associated with promoting non-adherence to guidance (i.e. 64.1% currently) in diabetes practice, which is quantified in the positive values for $maxTIP_{gi}$, TNB_{is} and TNB_{gi} for λ less than ≈€25,000 per QALY. The investment potential for guideline de-implementation ($maxTIP_{gi}$) falls as λ increases, and turns zero for the $ICER_{cg}$. At this value for λ, decision makers ought to be indifferent about whether the guidance is implemented. The total net benefit of audit and feedback (TNB_{is}) and that of guidance de-implementation (TNB_{gi}) also vary with λ. While implementation strategies cost money to enact, TNB_{is} turn negative for values of λ around the $ICER_{cg}$. For values of λ larger than ≈€25,000 per QALY, the implementation investment potential ($maxTIP_{gi}$), the value of adopting audit and feedback (TNB_{is}) and the value of implementing the guideline (TNB_{gi}) rise as a result of the total net benefit to be gained from enhancing adherence to the cost-effective guidance on blood glucose control in Dutch diabetes practice (where $TNB_{cg} > 0$)).

Comment [B1]: . In effect, the more monetary value is associated with health gain, the more net benefits (with health care provision costs being equal) is gained from clinical use of guideline recommendations.

Figure 2a, 2b and 2c illustrate the uncertainty associated with decision making about changing diabetes practice.

In Figure 2a, we plotted the probability that blood glycemic control is cost-effective as a function of λ. The figure shows that there is considerable uncertainty associated with the decision about whether to adopt the guidance, with the maximum probability that guidance adoption is the correct decision not exceeding 60%.

Figure 2b illustrates the decision uncertainty surrounding the adoption of audit and feedback to change adherence to diabetes guidance by health care professionals. The estimates for the probabilities that this implementation strategy is cost-effective are derived by reading in data on rather than iteratively deriving estimates of the mean effectiveness ($\Delta\bar{E}_{cg}$) and cost ($\Delta\check{C}_{cg}$) of glycemic control in the model simulations (see Appendix). As a result, the V-shaped curve reflects the uncertainty surrounding only the economic evidence on audit and feedback. Given the relatively low implementation cost, the probabilities that the strategy is cost-effective are fairly high for both low and high values for λ. As decision makers are more or less indifferent about the clinical use of diabetic guidance for values of λ around the $ICER_{cg}$, any resources committed to implementation activities are expected to be not cost-effective and therefore the CEAC falls.

Figure 2c shows the CEACs for all relevant options to change diabetes practice, i.e. to adopt guidance and implement it ($PrCE_{gi}$), to adopt the guidance without implementation ($PrCE_{cg}$), to reject the guidance and promote non-adherence ($PrCE_{gdi}$) and to reject the guidance but leave diabetes practice as it is ($PrCE_{cp}$), based on evidence on guidance, adherence and audit and feedback. The CEAF represents the probability that the intervention option deemed cost-effective on the basis of expected total net benefit is in fact cost-effective. Depending on λ, decision makers should choose either to reject the guidance and promote non-adherence (< €25,000 per QALY) or adopt the guidance and ensure its implementation (> €25,000 per QALY). Through simultaneously incorporating uncertainty surrounding the costs and effects of both guidance and

audit and feedback, the individual CEACs and CEAF hereby reflect an increase in decision uncertainty about the adoption and/or implementation of glycemic control. Although of limited relevance in this particular case, the uncertainty associated with information about current adherence to guidance is also reflected. Another important issue is that the comparison of multiple options to change diabetes practice results in a relative large extent of decision uncertainty, which (partially) explains the kink in the CEAC and CEAF around the $ICER_{cg}$.

3.2 Sensitivity analysis

Figure 3a and 3b illustrate the CEACs for the guidance on intensified glycemic control ($PrCE_{cg}$) and audit and feedback ($PrCE_{is}$) and the CEAF for guidance (de-)implementation (CEAF) simultaneously, under the assumption that the mean implementation cost ($\Delta\check{C}_{is}$) are €1,000 or €2,500 per health care professional, respectively. These figures provide comprehensive overviews of the construct and extent of decision uncertainty about the (individual and combined) components of practice change.

Comparing the curves and frontiers in Figure 3a and Figure 3b, it seems evident that the (possible) higher cost of implementation reduces the range of values for λ at which the (de-)implementation of the guidance is worthwhile. For values of λ from approximately €21,000-€23,500 per QALY to the ICERcg, it is more valuable to reject the guidance and leave diabetes practice as it. From the ICERcg to €26,000-€28,000 per QALY, decision makers should adopt the guidance without implementation activities. Outside this range of values for λ (i.e. ≈€21,000 to ≈€28,000 per QALY), the increasing implementation result in lower probabilities that actively changing diabetes practice is indeed cost-effective.

4 Discussion

Main findings of the analysis. In order to provide an efficient allocation of health care resources for improving the primary care of type 2 diabetes in the Netherlands, we applied a comprehensive decision model, which combines evidence from different sources, to determine the scope of cost-effective implementation of guidance on intensified blood glucose control. Depending on the cost-effectiveness threshold (λ), the policy is deemed cost-effective (with an $ICER_{cg}$ of approximately €25,000 per QALY) and there is considerable investment potential ($maxTIP_{gi}$) to ensure its clinical use in diabetes practice. Under the assumption that its expenses are relatively low (€100 per health care professional), audit and feedback is likely to be a cost-effective strategy to change guidance adherence. As illustrated in the CEACs and CEAF, the decisions about guidance adoption and its implementation are associated with a large degree of uncertainty. This is partly caused by combining relatively uncertain economic evidence on both intensified blood glucose control and audit and feedback. Through sensitivity analyses, we found that decisions about the implementation of diabetes guidance and the uncertainty surrounding these decisions will vary with implementation cost.

Interpretation of the main findings. As with any model, its use and the interpretation of results for decision making purposes should be done with caution. First of all, the model results are based on limited evidence on the model parameters, particularly considering the effectiveness of audit and feedback (ΔE_{is}) (only 2 studies were included in the meta-analysis) and its cost (C_{is}) (data was extracted from the literature). Given the missing and/or poorly reported data, assumptions had to be made regarding the distribution, means and variances of various model parameters, e.g. regarding the derived effects and costs of glycemic control in the CDC model [28]. In addition, we made simplifications regarding the model structure and its data input. For instance, we based our estimates for the incremental costs and QALYs of intensive blood glucose control on reported data, whereas the integration of the UKPD OM and/or CDC model into the comprehensive decision model would be more ideal. Finally, the findings from different sources

(i.e. both guideline and implementation trials) are assumed to be transferable not just to the Dutch primary care setting but also to different recommendations for care and disease aspects.

Notwithstanding the limitations of the model, we found that for reasonable values of λ (> €25,000 per QALY), the expected total net benefit of intensified glycemic control in patients with type 2 diabetes are such that there is considerable value associated with adopting implementation strategies, like audit and feedback, to ensure guidance use in primary practice. In effect, given that current adherence to diabetes guidance is believed not to exceed 65%, there is substantial potential to invest in implementation activities. Although not formally quantified, it also seems worthwhile to acquire more evidence, concerning both the costs and effects of guidance and implementation strategies, to reduce uncertainty associated with the allocation of resources. Ideally, further research is focused on collecting information relevant for and/or transferable to the Dutch setting for diabetes care.

Use and practicality of the decision model. By adopting an integrated Bayesian comprehensive decision modeling approach for establishing the total net benefit of implementing guidance to change clinical practice, decision makers are able to explore the uncertainty associated with decision making about the adoption of clinical guidelines and implementation strategies. The synthesis of all available sources of evidence into a single coherent model can be used to analyze the scope of cost-effective guideline implementation, and to set priorities when confronted with multiple instances of suboptimal practice. In principle, any perspective of analysis can be adopted and the model is easily applicable to other health care areas. In addition to cost-effectiveness planes, CEACs and CEAFs are useful in appropriately representing and interpreting (combined) decision uncertainty about guideline implementation [34]. In effect, the complement of the CEAF provides the probability that the decision is incorrect and the option deemed cost-effective on the basis of the expected values is in fact not cost-effective [33]. It is this error probability which is used within the value of information analysis to determine the potential worth of further research [35]. Of course, for model-based evaluations to be valuable for decision

makers, decision modeling and evidence synthesis needs to be conducted and reported according to best practicable standards of quality, providing adequate disclosure of the data input and modeling assumptions, e.g. concerning the transferability of research findings [14, 20] or the potential selection bias between the target and study population [15].

Comments on the model and suggestions for its extension. Some comments have to be made on the model, inducing suggestions for its extension. Given that methodological guidance on health economic evaluation [36, 37] advocate decision makers to consider all relevant options for clinical practice change, the model should be extended to compare the value for money of audit and feedback with that of other implementation strategies, e.g. education, outreach visits or reminders. In fact, for decision makers to prioritize between alternative uses of health care resources, it should aid in analyzing the economics of the implementation of different sets of guideline recommendations across different settings, diseases or therapies. Considering the common absence of head-to-head trials comparing all relevant options being considered in economic evaluation of clinical practice change, the model should hereby allow for mixed comparison of guidance and/or implementation [26, 38]. Within the model, economic evidence on both guidance and implementation are assumed to be linearly proportionate to guideline adherence. More realistically, it is likely that it will bring increasing implementation cost with increasing adherence to guidance and that there will always be a proportion of non-adherence by health care professionals and patients. The model could be adapted to incorporate a more dynamic relationship between guidance adherence and the costs and effects of guideline implementation. To correctly reflect uncertainty in the data in case of multi-parameter synthesis on clinical practice change, the model hereby also needs to take account of the correlation between parameters [38, 39]. Other methodological challenges would be to use more advanced Bayesian methods that permit the adjustment for baseline adherence rates, the modeling of surrogate outcomes and/or the incorporation of meta-regression or subgroup analysis. Although the decisions about whether to adopt guidelines and/or implementation strategies are central to most decision makers, many also consider the issue of research priorities [35]. Recently, an

analytic framework was presented and applied to establish both the value of implementation (i.e. the investment potential for implementing guidance) and the value of information simultaneously [40, 41]. Following the outline of this framework, our modeling approach could be extended to allow decision makers to establish the expected value of conducting further research.

Conclusions. The stochastic application in diabetes care demonstrates that the model provides a simple and useful tool for quantifying and exploring the (combined) uncertainty associated with decision-making about adopting guidelines and implementation strategies and, therefore, for informing decisions about the efficient allocation of health care resources to change clinical practice.

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