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Identification and expert panel rating of key structural approaches applied in health economic obesity models

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A B S T R A C T

Objectives: This study aims to assess the key structural modelling approaches applied in published obesity models, and to provide an expert consensus to improve the methodology and consistency of the application of decision-analytic modelling in obesity research.

Methods: Using a previously published systematic literature search as basis, ten individual interviews, and a face-to-face expert panel meeting were conducted. Within the expert panel meeting, the interview findings were presented and discussed, rated and where possible consensus statements were obtained. In particular, five topics of interest were assessed: time horizon, model type, obesity-related clinical events simulated, event simulation approaches and external event validation.

Results: In addition to generic modelling standards, several obesity-specific recommendations were generated: Simulating a lifetime horizon was regarded as optimal (100% agreement); Ideally, both short and long-term results should be presented (100%); Using a risk equation approach for simulating the clinical events was the most preferred approach (60%) followed by applying a body mass index (BMI) related relative risk to a base risk estimate (30%); Continuous BMI approaches were preferred (100%); An individual patient/microsimulation state transition model was regarded as preferred modelling approach (90%); Discrete event simulation (DES) was regarded as the most flexible approach for building an obesity model but it was recognised as complex, and more difficult to build, populate and to disseminate; Performing an external validation was rated as important (100%).

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Conclusions: The obtained insights, discussion and consensus can provide valuable information for developing decision-analytic models to generate high-quality and transparent economic evidence for obesity interventions.

List of Abbreviations

Abbreviation	Meaning
BMI	Body mass index
CHD	Coronary heart disease
DES	Discrete Event Simulation
EuHEA	European Health Economic Association
HEA	Health Economic Assessment
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
RR	Relative risk
STM	State transition model
T2D	Type 2 diabetes
UKPDS	United Kingdom Prospective Diabetes Study
WHO	World Health Organization

Introduction

Obesity, a major public health concern, is a multifactorial disease, caused by both environmental and genetic factors [1], that has reached epidemic proportions globally [2]. The worldwide prevalence of overweight and obesity has doubled since 1980 to an extent that nearly a third of the world's population is now classified as overweight or obese [3]. A common measure to define obesity is the body mass index (BMI), which is obtained by a person's weight in kilograms divided by the square of his height in meters (kg/m^2). According to the WHO definition, a BMI $\geq$ 25 and $<$ 30 in adults is overweight; a BMI $\geq$30 in adults is obesity [2].

In 2015, high BMI contributed to 4.0 million deaths, which represented 7.1% of the deaths from any cause; it also contributed to 120 million disability-adjusted life-years, which represented 4.9 of disability-adjusted life-years from any cause among adults globally [4] Both overweight and obesity are associated with the incidence of multiple co-morbidities including type II diabetes, cancer and cardiovascular diseases [5].

These considerable health impacts of obesity are accompanied with a substantial economic burden, which highlights that there is an urgent need for public health measures in order to save societal resources [6]. Due to this considerable economic impact health economic evaluations are quite commonly applied in the context of obesity prevention and management. Such evaluations allow decision makers to make an informed judgement on the health economic impact of an intervention, by assessing the additional benefits of funding an intervention relative to its additional costs [7]. As shown in systematic reviews [8,9] decision analytic modelling has commonly been used to evaluate the long-term economic consequences of obesity prevention and therapy measures. In the context of these obesity related decision models the key structural aspects are of fundamental influence as they are impacting all outcomes simulated by the model, including clinical parameters & events, quality of life, direct and indirect costs and hence the whole spectrum of relevant economic consequences [10].

Previously, it was shown that there are huge variations in the structural modelling approaches focusing on the prevention and therapy of obesity [8,9] and up to now no consensus meeting on the structural aspects of obesity models has been performed. This makes it difficult for researchers to select an appropriate approach when designing a model, and subsequently for policy makers and stakeholders to assess the quality of an applied model, intended to inform political or medical decision making.

The aim of this study is therefore to assess and measure expert group consensus for key structural modelling approaches of obesity models, and to provide information and recommendations for modellers and decision makers.

Methods

On the basis of a previously published systematic literature review [8,9], the key structural approaches applied in published obesity models were identified.

In particular, five inter-related topics of interest were assessed: time horizon, model type, obesity-related clinical events simulated, event simulation approaches and external event validation. These features represent the structural aspects of models listed within the Phillips reporting checklist [11] which are not related on the quality of research reporting (as e.g. statement of the decision problem or statement of scope / perspective etc.). Additionally these features showed a huge variation in published obesity models [8,9].

The findings from the systematic literature review were then used to guide the topic content of the subsequent ten individual interviews. Data from the combined interviews were then presented and discussed at a face-to-face group meeting in order to derive consensus statements with respect to the key structural approaches applied in published obesity models.

Systematic literature search

The interviews and the group meeting were informed by a previously published systematic review [8,9] that was performed in the PubMed Database and the NHS Economic Evaluation Database, following the PRISMA guidelines [12]. Three different searches were combined: one for health economic evaluations, one for decision models and one for obesity. Eligible studies were original research articles on decision models for full health economic assessment in the context of obesity; the definitions from Drummond et al. [13] (health economic assessments), from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force [14] (decision models), and from the WHO criteria [2] (obesity) were applied in order to define eligible studies. In total 4,293 studies were identified via the database searches, and were reviewed. From these 142 articles were selected for full-text review; of which 87 papers met the inclusion criteria. Of those, 72 models simulated obesity associated events. The rationale for this selection is on one hand to investigate the selected event simulation approaches. On the other hand the rationale is to enable performing and investigating external validations of the event projections made by these models, which increases the credibility of the modelling approaches for researchers, physicians and decision makers.

For more details on the literature search, the eligibility criteria and the literature selection please refer to the published systematic review [8,9].

Box 1
Interview questions and definitions of event simulation approaches.

Interview Questions:

- Which time horizon would you rate as the minimum acceptable for a health economic obesity model?
- Which time horizon would you rate as optimal for a health economic obesity model?
- Which (obesity associated) events would you rate as the minimum acceptable to be included into a health economic obesity model?
- Which (obesity associated) events would you rate as optimal to be included into a health economic obesity model?
- Which model type would you prefer for a health economic obesity model?
- Why would you prefer this model type?
- Which event simulation approach would you prefer for a health economic obesity model? Please rank the top 3 approaches that you would prefer (1 = most preferred one to 3 = least preferred but still preferred one)
- Why would you prefer the top rated (#1) event simulation approach?
- Would you suggest to use different approaches for different events (consider coronary heart disease, type 2 diabetes, stroke)? If yes – why?
- How important do you rate an external validation for a health economic obesity model?

Definitions of Event Simulation Approaches

- Risk Equation / Change in Risk Factors: E.g. Framingham / UKPDS equations – the base risk is calculated as an equation of risk factors and the intervention effect is simulated by the change of risk factors
- Disease Incidence Estimate / BMI related relative risk (RR): Any kind of incidence estimate (e.g. age-specific; gender-specific incidence etc.) is used as base risk and the intervention effect is simulated by applying a BMI related relative risk to the base risk
- BMI Function / Change in BMI: Base risk is calculated as function of the BMI which is directly influenced by the intervention effect on the BMI
- Disease Incidence Estimate / Obesity related RR: Any kind of incidence estimate (e.g. age-specific; gender-specific incidence etc.) is used as base risk and the intervention effect is simulated by applying an obesity status related relative risk (e.g. BMI <30 non-obese; BMI ≥30 obese) to the base risk
- BMI Group Function / Change in BMI Group: Base risk is calculated as function of specific BMI groups (e.g. < 25 normal weight; 25-30 overweight; 30-35 moderate obese; ≥ 35 severe obese etc.) which is directly influenced by the intervention effect on the BMI group
- Disease Incidence Estimate / BMI Group related RR: Any kind of incidence estimate (e.g. age-specific; gender-specific etc.) is used as base risk and the intervention effect is simulated is simulated by applying a BMI group related relative risk to the base risk

Individual interviews

Several health economic experts, with in-depth experience in decision analytic modelling and/or economics of obesity (using a convenience sampling), were requested to participate in an Expert panel meeting during the European Health Economic Association (EuHEA) conference 2018 in Maastricht, and ten (of twenty-two contacted) agreed to participate the meeting and to perform a 60-minute individual preparation interview beforehand. Within this interview the outcomes of the previously published systematic review, related to the key structural aspects (time horizon, model type, obesity-related clinical events simulated, event simulation approaches and external event validation) were presented via a web-based platform, and related to each of the key structural aspects of a model specific questions were asked.

With respect to the choice of a specific event simulation approach, different definitions were first obtained from the systematic review [9] and are presented, together with the interview questions, in Box 1.

The individual interview data were then analysed quantitatively in MS Excel and summarized in a MS PPT presentation in order to serve as basis for the discussions at the expert panel meeting.

Expert panel meeting

The face-to-face expert panel meeting was performed as satellite event of the EuHEA conference in Maastricht, on July 13th 2018. Within this meeting, the interview results relating to each question were presented and discussed, with the aim of reaching a group consensus or to capture the variance in opinion for each item. Within this meeting the key structural aspects, were discussed in detail with a specific focus on obesity-specific criteria. After the meeting the results were summarized and sent to the expert panel members for further comment and approval.

The results from this expert panel meeting are presented below, together with the results of the individual interviews and the key results from the systematic literature review.

Table 1
Time Horizon – Systematic literature search and expert interview outcomes.

Time Horizon	Literature Review (n=87 models)	Expert Interviews (n=10 experts)	
		Minimum	Optimal
< 20 years	23%	20%	10%*
≥ 20 and < lifetime	14%	20%	10%*
Lifetime	63%	60%	100%*

* 2 experts provided 2 different answers: ≥ 20 years in adults / lifetime in younger subjects; ≥ 10 years / lifetime optimal

Results

Time horizon

Table 1 presents the outcomes linked to the choice of time horizon for all published models identified in the review, and for the expert group opinion.

In the expert panel meeting, it was agreed that a lifetime horizon is optimal for a health economic obesity model (100% agreement)) and it was further agreed that both short- and long-term results should be presented (100% agreement). Short-term / trial period simulations may indeed also be interesting for practitioners / physicians, and are less susceptible to assumptions such as the sustainability of the intervention effect size and the natural course / development of BMI over time, including potential weight-regain post intervention.

Obesity associated events

Table 2 illustrates the findings from the literature review with respect to obesity-associated events (based on the 72 studies that have simulated obesity-associated events) alongside the findings from the expert interviews. Most of the published models simulated coronary heart disease (CHD) (≈83%; 60 of 72), type 2 diabetes (T2D) (≈74%), and stroke (≈67%). A minority of the models simulated cancer (≈35%), osteoarthritis (≈24%), hyperlip-

Table 2
Obesity associated events – Systematic literature search and expert interview outcomes.

Obesity Associated Events	Literature Review* Outcomes (n=72 models)	Expert Interviews Outcomes (n=10 experts) (Minimum acceptable events)*		
		ChD, T2D and, Stroke	ChD, T2D, Stroke and Cancer	ChD, T2D, Stroke, Cancer and HT
Coronary heart disease (ChD)	83%			
Type 2 Diabetes (T2D)	74%	50%*	20%*	
Stroke	67%			10%*
Cancer	35%			
Hypertension (HT)	11%			
Osteoarthritis	27%			
Hyperlipidaemia	11%			
Peripheral arterial disease	10%			

* no definite answer was provided by 2 experts (n=20%) - in general those events with strongest association / causal relationship to obesity should be included

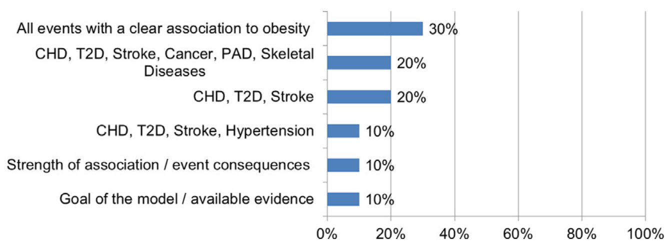

Fig. 1. Which (obesity associated) events would you rate as optimal to be included into a health economic obesity model?

idaemia (≈11%), hypertension (≈11%), and peripheral arterial disease (≈10%).

From the expert interviews, with regard to the question on the minimum acceptable events to be included in a health economic obesity model (presented in Table 2), in 50% of cases only CHD, T2D and stroke were named as "minimum acceptable events" in 20% of cases accompanied by cancer and in 10% accompanied by hypertension; whereas in two cases no definite answer was given due to the rationale that "in general those events with strongest association / causal relationship to obesity should be included". Related to the question on the events to be included in a health economic obesity model in the optimal world (presented in Fig. 1) the picture was more diverse.

In 40% of cases it was stated that all events with a clear association with obesity should be included. One expert stated that this clear association should be combined with the severity of event consequences. In 50% of cases, CHD, T2D and stroke were named (alone or in combination with other diseases), whereas by one expert no definite answer was given as it was claimed that it depends on the goal of the model and on the available evidence.

During the expert panel, several discussions around these obesity associated events took place (please refer to discussion part), but it was not possible to achieve consensus on the whole. However, finally there was general agreement that those events with a strong statistical association to obesity combined with a clear clinical causal relationship to obesity should be included in the optimal case.

Model type

Table 3 presents the results concerning the appropriate model type.

In the expert interviews, in 90% of cases a state transition model was named as the preferable approach, and, within these responses - 60% suggested a state transition model alone, and 30% also recommended a DES as an alternative model type to consider. Only one expert (10%) recommended DES alone.

On the question "why a specific model type was preferred?" the following rationales were provided by the experts:

- "STM is adequate to simulate the three major health impacts (T2D, CHD and stroke);
- STM is most practicable for event based simulation;
- STM is the most familiar approach (for health economists and stakeholders);
- STM is the most familiar approach - and individual patient simulation enables; building in specific memory;
- An individual patient simulation STM is preferred as it is possible to include a kind of memory".

In three cases both the DES and the STM were preferred by the experts, for the following reasons:

- "Memory is an important factor (as time with obesity / related morbidity impacts event risk) - therefore a DES would be preferred or a STM on a patient level with included memory states;
- Due to competing risks a DES / STM using a microsimulation approach will be preferred (for DES not all data might be available);
- DES might be scientifically the best approach but difficult to build, inform and to explain. STM might be the most accepted approach".

For one participant the DES alone was preferred as

- "DES allows considering timing of events which is important due to the inter-event dependencies".

Within the expert panel, a consensus was reached in the form of the following two statements:

- An individual patient / microsimulation STM is regarded as preferred approach for an obesity model;
- DES is regarded as the most flexible approach however DES is complex, difficult to build, to inform and to explain (to stakeholders).

Event simulation approach

Within the expert interviews the experts were asked to rank a list of potential modelling approaches identified from the systematic review. The results are presented in Table 4 and in Fig. 2, respectively. The risk equation approach was the most preferred approach (60% rated this as number one, followed by BMI-related RR (30% rated this as number one) and one expert felt it difficult to rank the approaches.

- The reasons for the number one rating for the Equation / Change in Risk Factors were:

Table 3
Model type – Systematic literature search and expert interview outcomes.

Model Type	Literature Review (n=87 models)	Expert Interviews (n=10 experts)
State Transition Model (STM)	85%	60%
Discrete Event Simulation (DES)	2%	10%
Decision Tree Model	13%	–
STM or DES (expert rating)	–	30%

*3 experts rated both STM and DES as suitable - depending on the data availability (for the DES model)

Table 4
Event simulation approach – Systematic literature search and expert interview outcomes.

Event Simulation Approach	Literature Review (n=72 models)	Expert Interviews (n=10 experts) – Ranking (#1, #2, #3)
Risk Equation / Change in Risk Factors	32%	#1 (60%): #2 (10%); #3 (20%)
Disease Incidence Estimate / BMI related relative risk (RR)	21%	#1 (30%): #2 (40%); #3 (0%)
BMI Function / Change in BMI	12%	#1 (0%): #2 (20%); #3 (20%)
Disease Incidence Estimate / Obesity related RR	12%	
BMI Group Function / Change in BMI Group	9%	
Disease Incidence Estimate / BMI Group related RR	7%	
Others / Others	7%	

* 3 experts rated both STM and DES as suitable - depending on the data availability (for the DES model)

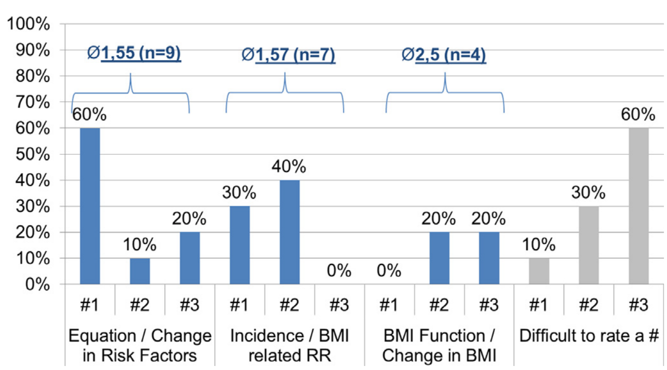

Fig. 2. Outcomes of the interview question: *Which event simulation approach would you prefer for a health economic obesity model? (Rank 1-3).*

- *"Method is quite robust, widely validated and widely used;*
- *Quite valid (accepted) approach and most commonly used;*
- *Not everything might be explainable by change in BMI and therefore it may be important to consider further risk factors;*
- *Risk equation approach describes the whole nature of a chronic disease;*
- *Risk equation approach takes into account inter-event dependencies;*
- *Risk equation approach is widely applied and health economists are most familiar with this;*
- *Familiar approach, well know, risk equations are also used in clinical guidelines; for the others it is the key question how strong the association between BMI and risk is".*

The reasons for the number one rating for the Incidence / BMI related RR were:

- "Most valuable / simple to set up events driven models for obesity;
- BMI related RR is preferred as always small changes are taken into account;
- Continuous BMI approaches are preferred against categorical approaches (there was 100% agreement on this statement in the expert panel)".

Furthermore, in the interviews, the experts were asked whether they would suggest using different approaches for different events if considering CHD, T2D, and stroke. With regard to this question, 90% answered with "no"; whereas 40% mentioned that not necessarily different approaches need to be applied and 50% answered that consistent approaches (if applicable) are preferred. One expert found it difficult to rate this topic and gave no answer.

External validation

External validation was defined as comparing the model's results with actual event data [15]. External validation involves simulating events that have occurred, such as those in clinical trials or epidemiologic studies, and examining how well the model results compare.

According to the systematic review, only ten published model-based health economic assessments in obesity included an external event validation (14%; 10 of 72).

Within the individual interviews the experts were asked how important they rate an external validation with possible answers being: "essential", "very important", "important", "less important", "not important" or "other" (please specify). All experts (100%) rated the external validation as "important"; 60% "very important" and 20% as "essential". These findings were confirmed during the expert panel.

Summary of key recommendations

A summary of key recommendations generated as a result of the expert interviews combined with the expert panel meeting are presented in Table 5.

Discussion

Focusing on the key structural aspects outlined in the Philips checklist [11], this paper presents the main findings relevant to obesity models that have been identified (systematic literature search), rated (expert interviews) and discussed (expert panel). The expert panel meeting resulted in specific modelling recommendations that go beyond the findings from the systematic literature research, which is also representing the novelty of this research.

Table 5
Overview of key expert recommendations by key structural aspect.

Key Structural Aspect	Expert panel recommendations
Time Horizon	Simulating a lifetime horizon was regarded as optimal for an obesity model (100% agreement) Ideally, both short and long-term results should be presented (100% agreement)
Obesity Associated Events	No consensus was possible on which clinical events to be included in a health economic obesity model There was general alignment that those events with a strong association to obesity combined with a clear causal relationship to obesity should be included in the optimal case
Model Type	An individual patient/microsimulation state transition model was regarded as preferred modelling approach (90% agreement) Discrete event simulation (DES) was regarded as the most flexible approach for building an obesity model but DES was recognised as complex, as more difficult to build, populate and to disseminate (to stakeholders)
Event Simulation Approach	Using a risk equation approach for simulating the clinical events was the most preferred approach (60%) followed by applying a body mass index (BMI) related relative risk to a base risk estimate (30%) Continuous BMI approaches were preferred (relative to categorical ones) (100% agreement)
External Validation	100% of experts rated the external validation at least important

The main findings by key structural aspect are discussed in detail below; each topic starts with a summary of outcomes of the expert panel meeting and these outcomes are then discussed and set into perspective by reflecting the complex circumstances and considerations related to each aspect. The latter discussion points are mainly driven by statements obtained during the expert panel meeting, which were accompanied and completed on the basis of related literature.

Time horizon

With regard to the time horizon of a health economic obesity model, it was possible to obtain clear expert recommendations. However, there were some interesting viewpoints expressed during the expert panel mostly around the question of whether or not a short term (e.g. trial period) simulation should be performed and presented. One key consideration in this context was that practitioners, physicians and stakeholders might be (additionally) interested in short term results and it is recommended that health economists also take into account the information needs of the health care personnel involved and also the requests / preferences of policy makers and other stakeholders. From a scientific point of view the key reasons for presenting short term / trial period outcomes (in addition to lifetime) were to present the impact of lifetime extrapolations as well as the practical need to determine whether the model adequately replicates the underlying study/trial results (internal validation). The key issues of extrapolation named in the context of obesity were the sustainability of the effect size (e.g. weight or BMI reduction and the related regain over time) and the natural course/development of weight / BMI over time, which is often based on a limited time-horizon, which again requires extrapolation to lifetime. These key issues of extrapolation were the key drivers for recommending an additional presentation of short term / trial period results.

Obesity associated events

The discussions around obesity-associated events to be modelled reflected some divergent views but there was general alignment among the experts that those events with a strong association to obesity combined with a clear causal relationship to obesity should be included in the optimal case. In contrast to the causal relationship of a specific event the strength of association could be more easily assessed, as the odds ratio or relative risk based on the best case could be extracted from prospective cohort studies. In a systematic review and meta-analysis of Guh et al. 2009 [5] the relative risk of various obesity associated events was presented and results by prospective cohort study and pooled results were provided, by gender and weight status (overweight / obese). According to the pooled results for obesity the strongest RR based associations in females (defined as RR≥2 in subjects with a BMI ≥ 30) were obtained for T2D (RR=12.41), CHD (RR=3.10), Gallbladder Disease (RR=3.08), Endometrial Cancer (RR=2.86), Kidney Cancer (RR=2.64), Hypertension (RR=2.42), osteoarthritis (RR=2.19) and congestive heart failure (RR=2.06) [5]. For males the strongest RR based associations (defined as RR≥2 in subjects with a BMI ≥ 30) were obtained for T2D (RR=6.74), osteoarthritis (RR=4.20), pancreatic cancer (RR=2.29) and asthma (RR= 2.19); the association to CHD in males (RR=1.75) was not that pronounced as in females (RR=3.10) [5]. Furthermore the association of obesity and stroke was not that pronounced with a RR of 1.50 in females and a RR of 1.68 in males [5]. Hence looking at the results of the systematic review (T2D, CHD and stroke are the most frequently included events within health economic obesity models) it is clear that not only the strength of association is important but also the severity and consequences of the specific events need to be considered, which was also discussed and determined as a selection criteria during the expert panel meeting, and might explain the brought inclusion of CHD and stroke into the health economic obesity models, as both events are potentially leading to mortality or disability. Furthermore from a health economic perspective the absolute incidence of events plays a role, as a strong obesity-association that is observed only in a very small number of patients, might have less impact on the cost-effectiveness than an event with a weak obesity-association that is observed in many patients.

The answer on the strength of statistical association, the severity and the absolute incidence of events are much easier to be answered than the question on the causal clinical relationship to obesity. The passage from obesity to T2D is caused by a progressive defect in insulin secretion coupled with a progressive rise in insulin resistance. Both insulin resistance and defective insulin secretion appear very prematurely in patients with obesity, and both worsen similarly towards diabetes [16], therefore the causal relationship is well understood. Also, there is good evidence on the causal relationship between obesity and CHD, and obesity and stroke and insulin resistance has been identified as the primary mechanism driving the progression of cardio-metabolic diseases (such as CHD and stroke) [17]. For different types of cancer the causal relationship is more challenging to capture and it remains unclear how obesity impacts the aetiology of cancer, which itself is not fully understood [18]. Hence, many researchers might have not included cancer as an obesity associated event within the model. If including only those events, for which there is clear evidence of a causal relationship, T2D, CHD and stroke would be an adequate minimum selection to be simulated within a health economic model. In this context it is recommended that the inclusion of events for which the causal relationship to obesity is not yet fully understood is investigated within scenario analyses.

Model type

The model types recommended for a health economic obesity model were either an individual patient / microsimulation STM or alternatively a DES. DES is clearly understood as the most flexible approach for building an obesity model, but it was also recognised as complex, as more difficult to build, populate and to disseminate (to stakeholders). Many shortcomings of (cohort) state transition models can be compensated by an individual patient / microsimulation approaches which enables patient history to be tracked using tunnel states and therefore overcome the Markovian assumption; this is important for obesity as time with obesity and/or obesity associated morbidities impacts the event risk. However, there is still some functionality of DES models that cannot be reproduced by a STM [19]. The DES can simulate interactions amongst individuals or between individuals and the environment [20,21], which might be interesting in obesity prevention models in which the positive effect of an intervention could have a positive effect on the whole community (e.g. on a whole school class or the whole school setting). Furthermore DES is well suited to modelling situations where patients are subject to multiple or competing risks [21,22]. A DES manages the competing and the sequencing of events by generating a future events list, then, for example, selecting the next closest time-to-event to ascertain which event occurs next in the process. This is relevant for obesity as there are several obesity associated events to be simulated. In a STM a transition probability is derived for each mutually exclusive competing health state and these competing health states must be exhaustive, and it requires many health states to achieve a level of detail comparable to DES. In a DES it is also easier to manage multiple events at the same time and to include and exclude events [23]. In the STM the patient is in one of a variety of mutually exclusive health states at any one time, which need to be clearly defined in the model structure, hence including / excluding events is a complex task. Furthermore, DES models can capture a greater level of detail than STM allowing the model to capture more detail regarding uncertainty in the system and including time to event information [21, 22]; this is important for obesity as multifactorial conditions and complex interventions (e.g. in the context of prevention) need to be simulated.

Besides all these advantages it needs to be considered that there are also several disadvantages, which prevent a broad application of DES in the fields of health economics [19]. DES models are generally more complex, require more data (that is often not available), and take more time to develop and run than STM; furthermore this could lead to a DES-induced over-specification [24] where models may become more complex than necessary, which again leads to increased data needs for DES models compared to STM [24].

These issues prevent a broad application of DES in health economics of obesity. The STM is rated as a pragmatic, widely applied, practical, familiar and widely accepted approach by the expert panel. Especially the communication and dissemination of (complex) DES models to stakeholders and policy makers is seen as a key hurdle for a broad application, as usually the model approach needs to be understandable to achieve research impact.

Clinical event simulation

The obtained event simulation approaches are quite diverse but it was possible to identify two preferred approaches by the expert panel namely the risk equation approach (most preferred approach - 60% rated this as number one, and the BMI related RR (30% rated this as number one). Many reasons were provided by the experts why the risk equation approach is preferred. The most prominent ones were that the risk equation approach describes the whole nature of a chronic disease and takes into account inter-event dependencies whereas within the BMI based approach the question remains whether everything can be explained only by the BMI and how strong the BMI association of a specific disease really is. A further point that was highlighted in the expert discussions was that the modellers' decision on the event simulation approach is often driven by data availability. Whereas for the BMI based approach only data on the BMI development (over time) is required, the risk equation approach requires data on all risk factors included in the equation, and is therefore far more data demanding. In the case that data on the risk factors is not available the BMI approach could be the most pragmatic way to estimate the health economic impact of an intervention, although the named limitations need to be considered and extra sensitivity analyses and scenario analysis may be required. Furthermore the experts agreed on the procedure that (if possible) comparable event simulation approaches should be applied for the different events, mainly to have comparable strengths and limitations for the simulation of the different events included in the obesity model.

External validation

The systematic review identified only ten models (of 72 that simulated events) that performed an external validation [9]. As this procedure is a key part of testing the validity of the modelling results with regard to the predictiveness of the event simulation approach, this was in general regarded as a limitation of published obesity models. All the experts rated the external validation as (at least) important for a health economic obesity model and that this should be performed as standard together with the internal validation that is usually performed as part of the internal model testing.

General issues of obesity models

Besides the key structural aspects that were investigated and discussed there are several other aspects that make it a challenge to model health economic assessments in obesity. As already mentioned one key difficulty is that the chronic events associated with obesity require a lifetime horizon and therefore several assumptions related to the sustainability of the effect size and the natural course of weight / BMI. It is recommended that these two factors require clear and transparent handling and need to be investigated in a sensitivity analyses.

One other aspect that makes obesity models so diverse is that an intervention might focus either on the therapy or on the prevention of obesity. Whereas prevention measures usually start in younger age groups (e.g. in the school setting), the therapy of obesity could either target young or older age populations. Modelling prevention measures are usually more complex than modelling therapy, as the prevention effect might have a positive influence on the whole community setting, and would hence require simulating interactions amongst individuals or between individuals and the environment, whereas therapy is usually targeted to the patients receiving a specific intervention.

Besides the diversity in the setting and intervention there are quite some challenges related to the understanding of the aetiology of obesity and of obesity associated diseases including so called obesity-paradoxes [25]. Whereas obesity implies increased risk for chronic diseases, it is in fact associated with decreased mortality risk compared with normal weight [25]. Another paradox concerns the observation that when fitness is taken into account, the mortality risk associated with obesity is offset [25]. Furthermore there is a paradox describing the presence of a sizeable subset of individuals with obesity who are otherwise healthy [25]. Even when some obese persons are healthy and for late phase of disease, obesity may be protective, it still is considered an important risk factor in the development of chronic disease. This has been recently stressed in a review on cardiovascular diseases [26]. Modelling may thus have to distinguish several subgroups, depending on time and diseases analysed.

Limitations and implications

As discussed above, challenges around the economic modelling of obesity are not purely structural, and hence one limitation of this study is the focus only on key structural aspects. However, especially as there are many challenges, it is important to offer recommendations on the handling of some key structural aspects when simulating obesity. The rationale for this is that the basic structure of the model is integral, and each decision that is made in the key structural development is carried forward to each calculation step of the model. Therefore the provided consensus on those fundamental structural issues could minimize the challenges modellers, stakeholders and decision makes face, while developing, interpreting and rating model-based health economic assessments in obesity.

For the expert panel, we focused on experts that were attending the EuHEA meeting in Maastricht (2018), as a result of this selection criterion we had only European experts participating. Hence one limitation of this approach was that researches from non-European countries were not able to contribute to this research. Considering that, according to the previously published systematic review, 47% of decision models focused on a European setting, 27% on US setting and 20% on an Australian setting, it would have been interesting to consider additionally the expert opinion of non-European experts. Additionally the limited number of experts (n=10 experts) has to be rated as limitation of our research, therefore it could be interesting to validate our findings on the basis of a larger sample of experts. Accordingly the presented work is not to be seen as a strict guideline for obesity modelling but as a set of information and recommendations that are regarded to be useful for other researchers and decision makers in this field.

Further, in the expert interviews and in the expert panel we only used basic quantitative methods in order to obtain an expert rating and an expert consensus, as the style of questions were not designed to involve more advanced quantitative methods (e.g. discrete choice experiments) or qualitative techniques (such as the Delphi method). Furthermore the set focus on health economists is a limitation related to the composition of the panel. The rationale for selecting health economists was that modelling is primarily driven by this discipline, but as a consequence it was not possible to get a clear expert rating on purely clinical aspects, such as the obesity associated event selection. In case of specialized epidemiologists and / or clinicians the discussion might have moved more into the direction of which events are nowadays considered as clearly obesity associated, a fact that we have tried to resolve by discussing the latest related literature.

Although we have observed consensus on many structural issues, there is no structural approach that covers all needs, and hence related to the decision problem, research question, and according to the data and resource availability there are different structural approaches that were rated as suitable for building a health economic obesity model. Furthermore, depending on the purpose of a health economic evaluation in obesity, researches might take different approaches than those recommended in our paper, if they have a good rationale for doing so.

One key question that remains in this context is, how the application of different approaches to the same decision problem, research question and population might influence the results of the clinical event prediction and subsequently of the whole health economic evaluation – which is seen as a valuable field of future research.

Conclusions

While the working group acknowledges the challenges in achieving consensus, several recommendations for the key structural approaches for a health economic obesity model were developed. The obtained insights, discussion content and consensus can provide valuable information for all decision makers, health economists and modellers for developing decision-analytic models to generate high-quality and transparent economic evidence for obesity interventions.

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