The full circle: Systematic evaluation, replication and validation of structural health economic modelling approaches: lessons learned in the field of obesity

ISPOR 2023
Annual European Congress,
Copenhagen, Denmark
Poster Session 4 – EE468

Schwander B (1, 2), Nuijten M (3), Evers S (1, 4), Hiligsmann M (1)

(1) CAPHRI - Care and Public Health Research Institute, Maastricht University, Maastricht, The Netherlands
(2) AHEAD GmbH – Agency for Health Economic Assessment and Dissemination, Bietigheim-Bissingen, Germany
(3) a2m - Ars Accessus Medica, Amsterdam, The Netherlands
(4) Trimbos Institute - Netherlands Institute of Mental Health and Addiction, Utrecht, The Netherlands

Introduction

- This research presents the lessons learned of a 5-year research project aiming to increase trust and confidence in selecting and interpreting results related to commonly applied structural approaches used in health economic obesity models [1].
- Obesity is an abnormal or excessive fat accumulation often defined as body-mass-index (BMI) >30 kg/m² [2]. Obesity reached epidemic proportions and is a leading risk for global deaths and morbidities [3].
- Given the high clinical [4] and economic burden [5] of obesity, it is of major interest for healthcare decision makers to identify effective and cost-effective programs or interventions for obesity prevention and therapy.
- Decision analytic modelling is particularly relevant in the case of prevention and therapy of obesity due to the chronic nature of the obesity associated morbidities (e.g. diabetes, coronary heart disease, stroke, osteoarthritis and specific cancer types) and the related mortality.

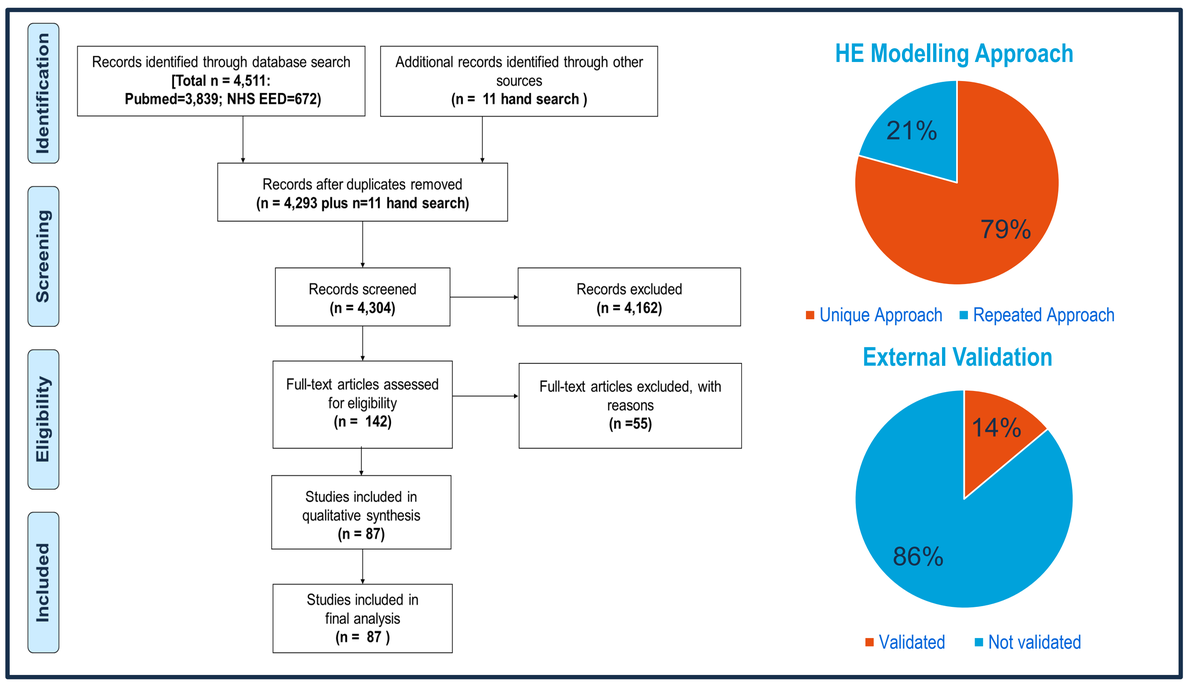
Methods

- A three-step process was followed:
  1. First a systematic review was performed to determine commonly applied health economic modelling approaches.
  2. Second a replication of high-quality health economic models was performed in TreeAge Pro and the reproduction success was evaluated.
  3. Third, using the successfully replicated models, we performed an external validation and health economic result comparison using state of the art methods.

Results

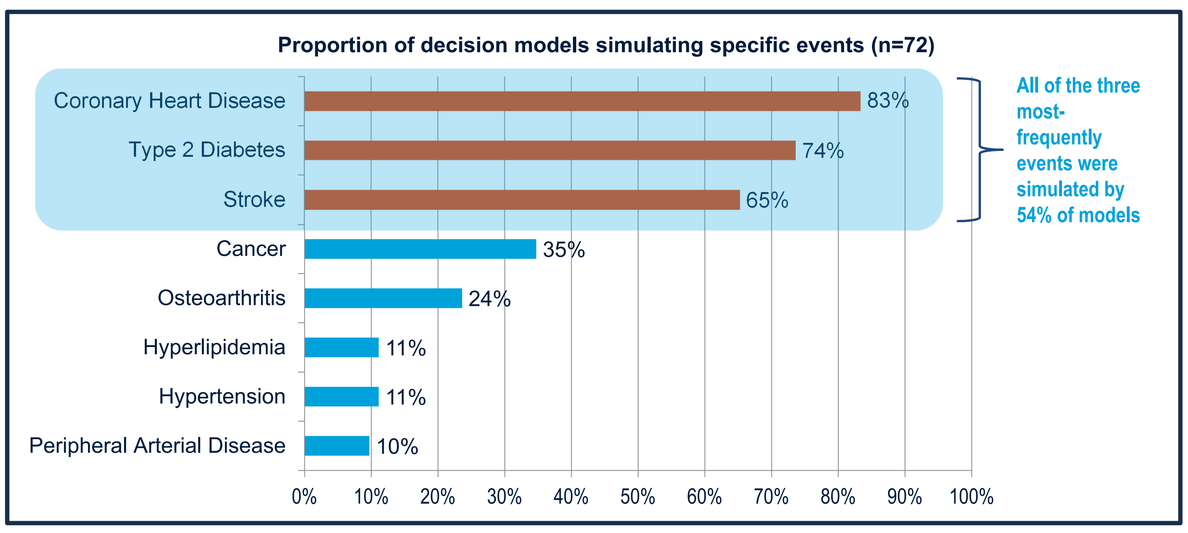
- Of 87 included papers reflecting health economic obesity models, 69 (79%) applied unique modelling approaches, but only for a minority (14%) an external validation was performed; as presented in Figure 1.

Figure 1: Systematic Review on Health Economic Obesity Models



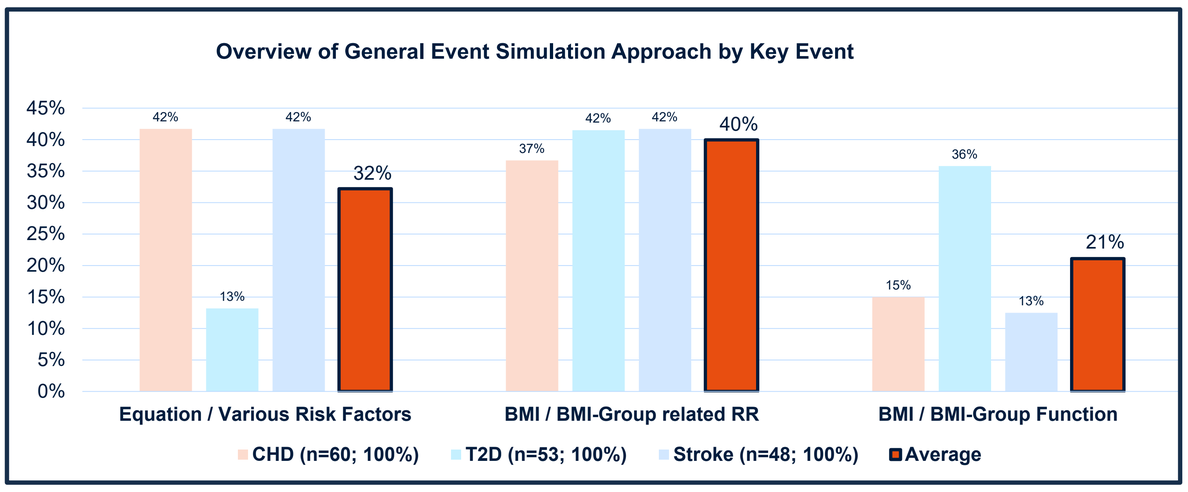
- Furthermore, several methodological variations were identified the most important are presented in Figure 2 and Figure 3 below.
- Most frequently simulated events were coronary heart disease (≈83%), type 2 diabetes (≈74%), and stroke (≈65%), as presented in Figure 2.

Figure 2: Methodological Variations – Type of Events



- As presented in Figure 3 below, three main obesity associated event simulation approaches were identified.

Figure 3: Methodological Variations – Event Simulation Approach



BMI = Body Mass Index, CHD = Coronary Heart Disease, T2D = Type 2 Diabetes, RR = Relative Risk

- In a next step high-quality health economic obesity models were selected (using expert recommendations) and a model replication was performed using TreeAge Pro. The models selected for replication are presented in Table 1.

Table 1: Overview of Obesity Models selected for Model Replication

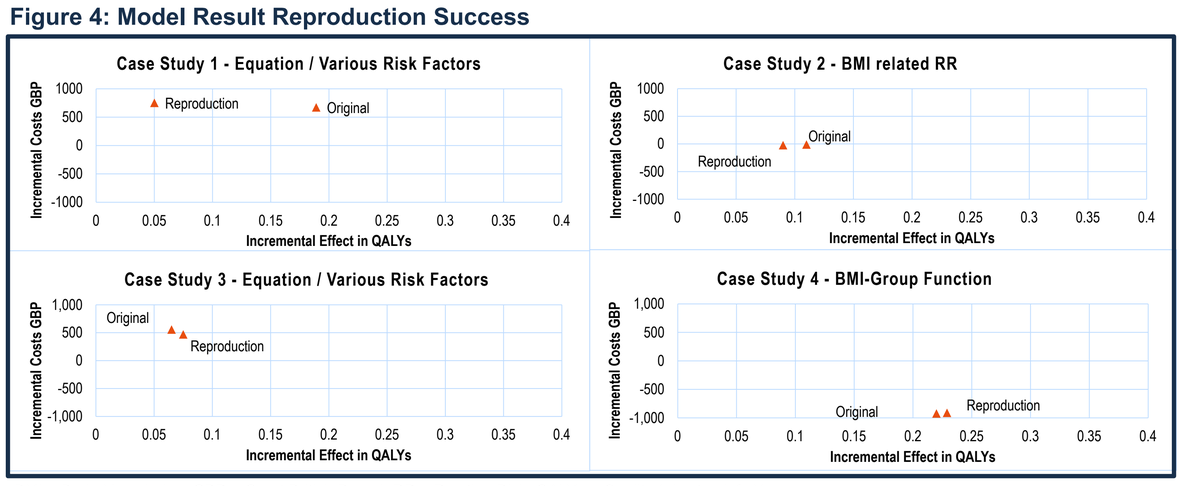
Coding	First Author	Event Simulation Approach	Model Type /Time Horizon / Cycle Length	Events	Country / Perspective	Health Outcomes(s)
Case Study 1	Ara (2012) [6]	**Equation / Various Risk Factors**	STM / Lifetime/ 1-year	**CHD, T2D, Stroke, Death**	UK / NHS	QALYs
Case Study 2	Au (2013) [7]	**BMI related RR**	STM / 40 Years*/ 6 months	**CHD, T2D, Stroke**, CC, OA **Death**	UK / NHS	QALYs
Case Study 3	Caro (2007) [8]	**Equation / Various Risk Factors**	STM / Lifetime/ 1 month	**CHD, Stroke, T2D, Death**	UK / NHS	QALYs
Case Study 4	Meads (2014) [9]	**BMI-Group Function**	STM / Lifetime/ 1-year	**CHD, T2D, Stroke, Death**	UK / NHS	QALYs

BMI = Body Mass Index, CHD = Coronary Heart Disease, NHS = National Health Service, T2D = Type 2 Diabetes, RR = Relative Risk, STM = State Transition Model, UK = United Kingdom, QALYs = Quality Adjusted Life Years

Results (continued)

- The model result reproduction success was measured by several factors [10], whereas the visualization of Incremental cost-effectiveness results (see Figure 4 below) was a key factor for evaluating the reproduction success, which resulted in rating case study 1 as a failure and case studies 2, 3 and 4 as success in reproducing results.

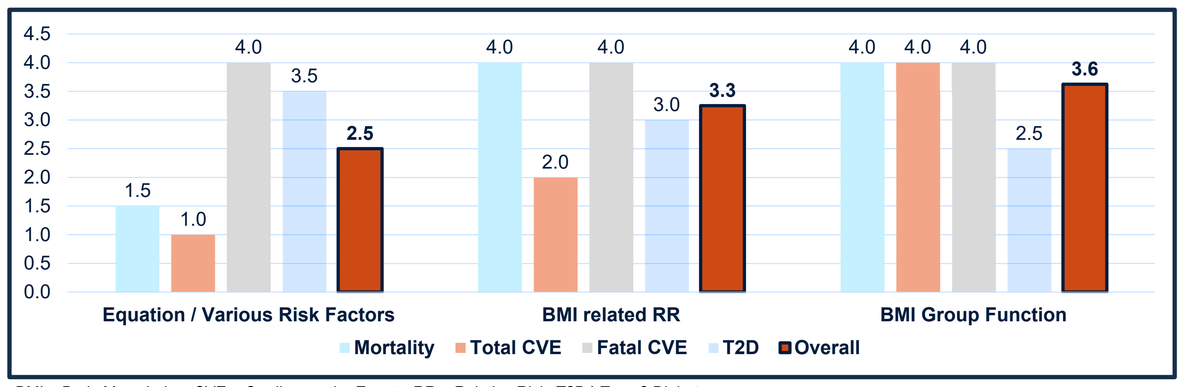
Figure 4: Model Result Reproduction Success



BMI = Body Mass Index, GBP = Great British Pound, RR = Relative Risk, QALYs = Quality Adjusted Life Years

- Using the three successfully replicated models an external validation, using the Swedish obesity subjects (SOS) study [11] was performed.
- These replicated models reflect three main structural event modelling approaches used in obesity: 1) continuous body mass index (BMI) approach; 2) risk equation approach; and 3) categorical BMI-related approach
- Outcomes evaluated were mortality, cardiovascular events, and type 2 diabetes for both the surgery and control arms.
- Concordance between modelling results and the SOS study were investigated by different state of the art measurements and categorized by the grade of deviation observed (from grade 1-4 expressing mild, moderate, severe and very severe deviations), as presented in Figure 5.

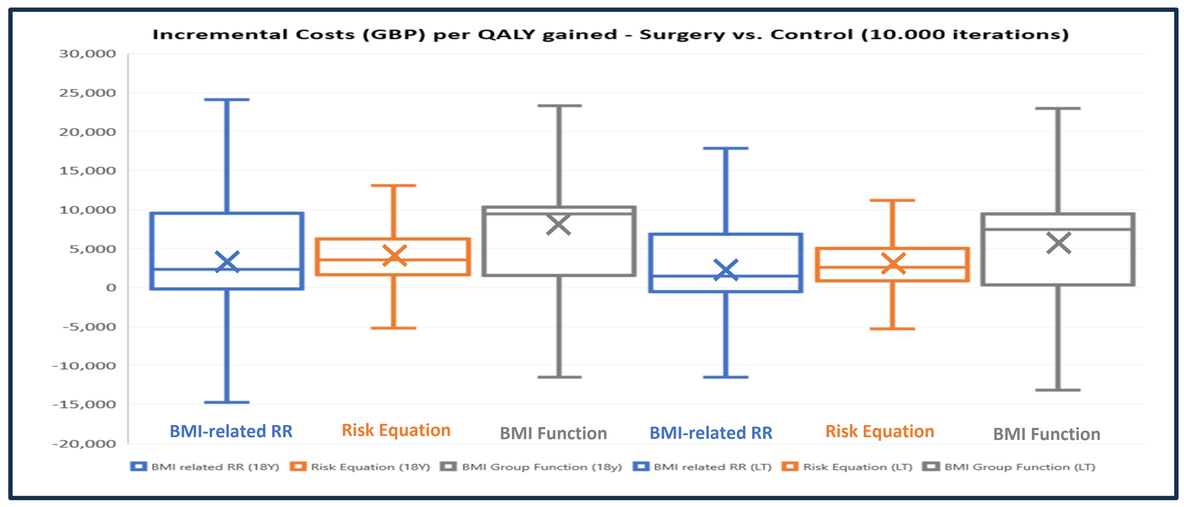
Figure 5: Overview of Grade of Event Result Deviation comparing SOS-Study Events to the Modeling Results (1=mild to 4 very severe deviation)



BMI = Body Mass Index, CVE = Cardiovascular Events, RR = Relative Risk, T2D) Type 2 Diabetes

- Additionally, the cost per quality-adjusted life year (QALY) gained of surgery vs. controls were compared, as presented in Figure 6.

Figure 6: Overview of Incremental Costs per QALY gained comparing the Main Structural Event Modelling Approaches



BMI = Body Mass Index, GBP = Great British Pound, RR = Relative Risk, T2D) Type 2 Diabetes,, QALYs = Quality Adjusted Life Years

- We were able to successfully reproduce the results of three models reflecting those three main approaches.
- In the external event validation, the risk function approach showed the best results, followed by the BMI-related RR risk and the BMI-function approaches.
- Although a variation in the mean incremental cost effectiveness ratio was identified, there was no statistically significant difference identified between the approaches.

Discussion

- The main issue for performing external validations of health economic models, in the context of obesity, is the lack of long-term (intervention) studies.
- Other research teams have used long-term studies performed in non-obese populations, but the question remains whether an external validation based on non-obese cohorts is sufficient to investigate the prognostic validity of a model in the context of obesity.
- Hence, there is a need for additional long-term (intervention) studies in order to obtain a better understanding of the influence of the obesity status on the development and prevention of obesity-associated events.
- It might be interesting for further research to investigate if and how observational long-term studies and real-world evidence related to obese populations could be used for the external validation of health economic obesity models.

Conclusions

- This research identified important aspects related to health economic model reporting, reproduction and validation in general, and key aspects specifically related to obesity associated event simulation.
- Our research could form a basis for evaluating the strengths and weaknesses of different structural event simulation approaches and identified important areas for further research to improve model reporting, reproducibility and credibility.

References

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