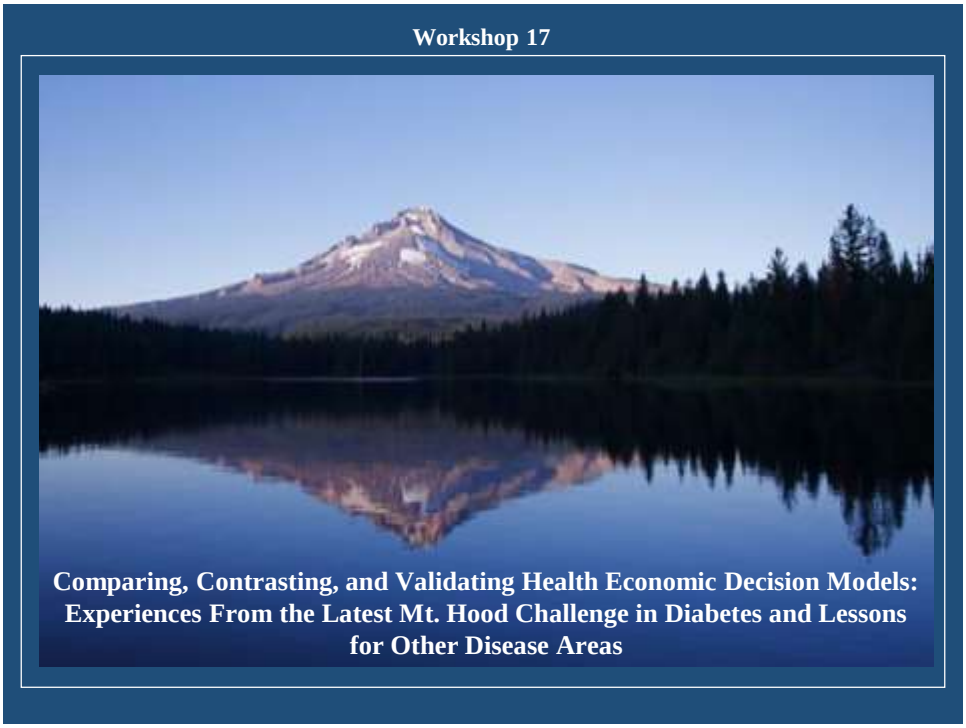


Workshop 17

Comparing, Contrasting, and Validating Health Economic Decision Models: Experiences From the Latest Mt. Hood Challenge in Diabetes and Lessons for Other Disease Areas

Michael Willis, PhD
Talitha Feenstra, PhD
Mark Lamotte, MD
Alan Brennan, PhD

ISPOR 20th Annual European Congress
Glasgow, SCOTLAND

November 8, 2017

Mt. Hood Challenge

Disclosures

- Michael Willis is an employee at The Swedish Institute for Health Economics and a developer of The Economic and Health Outcomes Model of T2DM (ECHO-T2DM). ECHO-T2DM is proprietary software. No funding or consultant fees were involved in this presentation.
- Talitha Feenstra works at the University Medical Centre Groningen and at the Dutch National Institute for Public Health and the Environment (RIVM), and co-developed the MICADO diabetes model. For the current presentation she has no conflicts of interest. The COPD modellers' meetings have been organized by the steering committee of which she is a member and were sponsored by: GSK; Novartis; BI; Takeda; Pfizer/BI NL; Nycomed.
- Mark Lamotte is an employee at QuintilesIMS and leader of the QuintilesIMS Core Diabetes Model team. QuintilesIMS received license fees and consulting fees for the use of the CDM. The current project was however done independent from any funding.
- Alan Brennan is an employee of University of Sheffield, has been involved in developing the Sheffield Type 2 Diabetes Model, The Sheffield Type 1 Diabetes Model and the SPHR Diabetes prevention model. He reports no conflicts of interest for this workshop.

Prepare for Interactive Component

- Click on your App for ISPOR Glasgow
- Click More
- Click Live Polling / Q&A
- Go to W17 – Comparing, contrasting … Mt Hood Challenge

Ask your questions and vote for questions on the APP

ISPOR/SMDM
Best Practices for Model Validation[1]

- **Face validity:** Activities establishing extent to which a model, its assumptions, and applications for which it is used reflect accurately current scientific evidence (as judged by experts)
- **Verification:** Activities establishing extent to which model calculations are correctly implemented, including thorough testing, de-bugging, and 'stress-testing' with extreme input values to expose errors of logic and programming
- **Cross-Validation:** Simulate same standardized scenarios with different models, comparing and contrasting results and investigating differences
  - A cornerstone of the Mt. Hood Challenges in T2DM
- **External Validation:** Test concordance between model predictions and observed outcomes for real patients (e.g., key RCTs)
  - Dependent outcomes (from data used n model construction) vs. Indepedendent (from studies not used in models)
- **Predictive validation:** Prospective form of external validation in which the study has not yet been conducted, thus ensuring that the external validation is blinded to the analysts
  - While "strongest" form of evidence, this type of validation requires conditions that are relatively rare

[1] A series of 7 ISPOR Task Force Reports published in *Value in Health* 15 (2012).

Seminal Mount Hood Challenge

- Analysts involved with the IMIB Model and the Global Diabetes Model (GDM) at the Timberline Lodge on the slopes of Mount Hood in Oregon, USA in August 2000
- Methods
  - IMIB and GDM were loaded with 12 sets of identical T2DM patients and simulated for 20 years
  - Survival, MI, stroke, diabetic retinopathy, albuminuria, and amputation rates were extracted and compared (i.e., cross-validation)
  - Differences were explored and explanations sought (and documented)
- Results
  - "Both models generated realistic results and appropriate responses to changes in risk factors" (Brown et al, 2000)
  - There were important numerical differences (especially costs), however, but could be explained by differences in model architecture and CVD risk engines
- Importantly, there was an agreement to repeat the Challenge and to invite more modeling groups

MH Challenges Have Occurred Roughly Every Two Years Since

- For anyone interested in diabetes health economics or epidemiology
  - Clinical medicine, academia, pharmaceutical industry, reimbursement decision makers, or government agencies
- Theme varies, but recurring activities include simulating standardized scenarios
- Beginning in 2010, scope was broadened to include abstract submissions and presentations as well
- Attendance has ranged between 70 and 90 participants

	Place	Date	Participating Models	Theme
MH1	Mt. Hood, Oregon	August 2000	2	Original MH Challenge
MH2	San Francisco, California	June 12, 2002	6	Improving reliability, validity and usefulness of computer simulation models of diabetes
MH3	Oxford, England	August 30-31, 2003	6	Predicting future complications, costs, and lifespan for five pre-specified patients and five standardized treatments
MH4	Basel, Switzerland	September 2-4, 2004	7	(1) Introduce external validation using CARDS study data, (2) simulate DCCT data for T1DM modeling, and (3) estimate outcomes for a precisely defined hypothetical person with type 2 diabetes, with and without glycemic control
MH5	Malmö, Sweden	September 19-20, 2010	8	(1) Validation against recent clinical trial outcomes and (2) capturing uncertainty
MH6	Baltimore, Maryland	June 7-8, 2012	8	(1) Validation against new clinical trial and observational data outcomes with emphasis on "blinding" and (2) exploration of 2nd order uncertainty in modeling standardized scenarios
MH7	Stanford, California	June 17-19, 2014	10	(1) Simulating the new Look AHEAD results, (2) predicting mortality after major events, and (3) exploring ethnicity-related variability in the models (suitability of models geographically)
MH8	St. Gallen, Switzerland	September 16-18, 2016	10	(1) Transparency of simulations and results and (2) communicating outcomes

https://www.mthooddiabeteschallenge.com/

Mt. Hood Challenge

The Next Mount Hood Challenge

https://www.mthooddiabeteschallenge.com/

Mt. Hood Challenge

Mount Hood Challenges Mission

- Knowledge sharing and improved communication:
  - Between modeling groups
  - Between model developers, model users, and consumers of modeling results
- Improve quality of research, set (voluntary) minimum standards
  - Publication of conference proceedings (Brown et al [2000], The Mount Hood 4 Modeling Group [2007], Palmer et al [2013])
  - A web page that contains historical information on previous Challenges, an information repository for diabetes models, user-submitted publication lists, and more (**https://www.mthooddiabeteschallenge.com/**)
  - Mt. Hood participants worked on ADA "*Guidelines for Computer Modeling of Diabetes and Its Complications*" (*Diabetes Care* 27 [Summer 2004])
  - Recommendations for minimum reporting standards under submission (Dr. Lamotte will discuss shortly)
- Platform that promotes external auditing of diabetes modeling
  - Lift perceived credibility to outside actors who often see diabetes models as "black boxes"

How Do MH Challenges Work in Practice?

- Organizing committee chooses theme and venue
  - Preferably with support of a local university or health economics consultantcy
- Simulation Challenges are defined and distributed to participants (and placed on line to aid recruitment of new modeling groups)
- Modeling groups perform simulations and submit results in advance of congress date
- Abstract submission for short presentations open to all meeting participants (volunteers review abstracts and set up an afternoon of parallel presentation sessions)
- The Challenges (1.5 days):
  - Each participating modeling group presents key model details (briefly)
  - Challenge results are presented globally (were previously presented by each model group individually, but led to time-consuming duplication)
  - Considerable time is reserved for discussion of the results, debate, and consensus building
- Invited speakers/submitted abstracts and presentations:
  - Invited speakers address key issues related to the congress theme
  - Accepted abstracts are presented to share insight in areas of active research

Management Challenges

- Administration/Finances (always a challenge!!):
  - Not for profit
  - Funding via participation fees (with some corporate donations in early conferences)
  - Universities have been leveraged to handle financial aspects
- Human resource requirements are extensive:
  - Time to organize the meeting (both content and logistics)
  - Time for modelers to run simulations and submit documentation
  - Time for someone to organize results across modeling teams and present to group/moderate subsequent discussin
- Don't overemphasize "Challenge"
  - Competitions (e.g., for best fit) de-emphasize cooperation
  - Blinded vs. unblinded challenges
- Intellectual Property
  - Recognize where cooperation/sharing begins and ends
  - Focus on common goals: code-sharing/full transparency may work in some areas, but in many settings it doesn't
  - Ensure that groups feel comfortable with sharing and that submitted results are not used without consent elsewhere
- Creating interest
  - Need minimum number of participants to cover fixed costs (and keep conference fees reasonable)
  - Sites/timing generally linked to big diabetes meetings (ADA, EASD) to reduce travel costs

Some Features of Diabetes That Perhaps Helped Precipitate the MH Challenges

- Complicated pathophysiology
  - DM models must capture disease progression, in which multiple risk factors (including blood glucose and blood pressure) can impact on a wide variety of co-morbid and interdependent health outcomes like cardiovascular disease, renal failure, amputation, and blindness
  - Need for these models to be multi-application, otherwise prohibitively expensive
  - Many consider the models to be black boxes; engendering trust is crucial and the DM field was early to realize the importance (necessity) of model validation
- Big disease prevalence
  - Relative abundance of data
  - Critical mass of interested and knowledgable researchers
  - Mix of different actors with different role; perhaps making cooperation easier?
- Presence of engaged individual researchers
  - Among others, Philip Clarke (University of Melbourne) and Andrew Palmer (University of Tasmania)
- Where similar factors exist for other disease areas, they should be leveraged
- Where differences exist, alternative solutions might be warranted

Lessons from other disease areas

COPD Modelling meetings other initiatives

Talitha Feenstra,

Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

University Medical Center Groningen

Mt. Hood Challenge

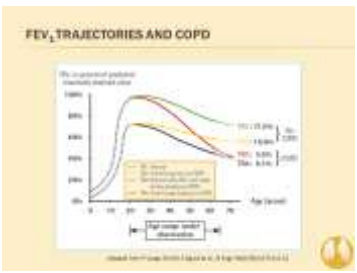
Short intro to Chronic Obstructive Pulmonary Disease

GOLD 2017

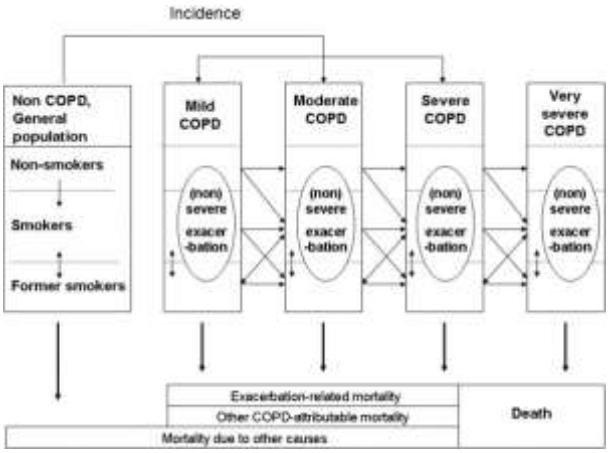
Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

Chronic disorder

- Lung function decline
- Respiratory symptoms
- Exacerbations
- Comorbidities
- Increased mortality



Mt. Hood Challenge



COPD modellers meetings

- Almost annual meetings since 2011 (now 5 in total)
- Most recent was February 2017
- Inspired by Mount Hood Challenges
- Wish to validate Dutch COPD model
- Main organizer: Martine Hoogendoorn (EUR/iMTA)
- Contact:t.l.feenstra@umcg.nl or hoogendoorn@imta.eur.nl

Mt. Hood Challenge

12 models have participated at least once

- NL: Dynamic population COPD Progression model (Hoogendoorn et al)
- US: Dynamic Cohort COPD model (Hansen et al)
- S: Swedish generic model of disease history and economic impact of COPD (Borg et al)
- DE: The German comprehensive care COPD model (Wacker et al)
- It: Italian COPD population model (Dal Negro et al)
- US Pharmacometric-pharmacoeconomic model (represented by Slejko)
- Takeda global COPD model (Samyshkin et al)
- BI bronchodilator therapy COPD Model (Rutten-van Molken et al)
- IMS/Novartis COPD Markov model (Price et al)
- IMS/Novartis COPD patient simulation model (Asukai et al)
- GSK Galaxy COPD Disease Progression model (Briggs et al)
- GSK ICS/LABA model 2005 (Briggs et al)

Meeting Topics

- 2011: "COPD, towards comprehensive, valid and transparent models to support future decision making"
  - **Presenting structure of models**
  - **Hypothetical scenarios changing model-parameters**
- 2012: "COPD, towards comprehensive, valid and transparent models to support future decision making"
  - **Hypothetical treatment scenarios**
- 2014: "Modelling Personalized COPD Care: economic, societal and regulatory implications"
  - **Scenarios based on trial-data**
  - **Scenarios for subgroups**
- 2015: "Personalized treatment of COPD in relation to economic modelling"
  - **Prediction models for exacerbations**
- 2017: "Treatment adherence and meta-modelling"
  - **Meta-models**

Typical Meeting Activities

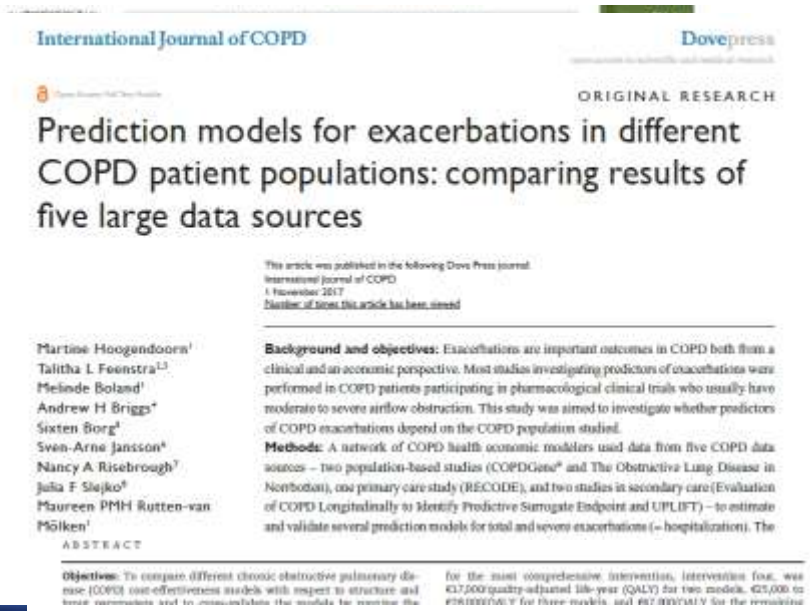
- Model structure
  - Present models
  - Analyze heterogeneity
  - Prediction modeling (exacerbations)
- Investigate essential parameters
  - Scenario analyses
  - Meta-modeling
- Validate against external sources
  - scenario analyses
- External speakers
  - New perspectives

Mt. Hood Challenge

Meeting Outcomes

- Better understanding of COPD modeling
  - Main drivers of results
  - Different approaches to model same phenomena
- Better model validity
- New methods (external presenters)
- Insights from clinicians
- Great discussions, leading to publications

Mt. Hood Challenge



International Journal of COPD

Dovepress

ORIGINAL RESEARCH

Prediction models for exacerbations in different COPD patient populations: comparing results of five large data sources

This article was published in the following Dove Press journal:
International Journal of COPD
1 November 2017
Number of times this article has been viewed

Martine Hoogendoorn[1]
Talitha L Feenstra[1,2]
Melinde Boland[1]
Andrew H Briggs[3]
Sixten Borg[4]
Sven-Arne Jansson[4]
Nancy A Risebrough[5]
Julia F Slejko[6]
Maureen PMH Rutten-van Mölken[1]

Background and objectives: Exacerbations are important outcomes in COPD both from a clinical and an economic perspective. Most studies investigating predictors of exacerbations were performed in COPD patients participating in pharmacological clinical trials who usually have moderate to severe airflow obstruction. This study was aimed to investigate whether predictors of COPD exacerbations depend on the COPD population studied.

Methods: A network of COPD health economic modelers used data from five COPD data sources – two population-based studies (COPDGene® and The Obstructive Lung Disease in Northotton), one primary care study (RECODE), and two studies in secondary care (Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoint and UPLIFT) – to estimate and validate several prediction models for total and severe exacerbations (= hospitalization). The

ABSTRACT

Objective: To compare different chronic obstructive pulmonary disease (COPD) cost-effectiveness models with respect to structure and

for the most comprehensive intervention, intervention four, was €17,000/quality-adjusted life-year (QALY) for two models, €25,000 to

CANCER: The CISNET Initiative

- Not personally involved
- Consortium, sponsored by NCI from 2000 onwards (https://cisnet.cancer.gov/)
- Range of
  - Cancer sites (BC; LC; Cervical; CRC; Esophagal; Prostate)
  - Interventions (Prevention, screening, treatment, new:diagnosis, biomarkers, palliative care)
  - Countries: seems limited, most US-based models
- Number of participating models varies by site from 3 to 8
- Activities:
  - Modeling same problem with various models: comparative modeling
  - Methodological and technical issues (programmers group)
  - Model registry, allowing selection based on site, model type, etc. https://resources.cisnet.cancer.gov/registry/home/
  - Tools based on the models, for policy makers

Checking the criteria for cancer and COPD

- Complicated pathophysiology:
  - Need for models to be multi-application, otherwise prohibitively expensive
- Big disease prevalence
  - Relative abundance of data
  - Critical mass of interested and knowledgeable researchers
- Presence of engaged individual researchers
- Ability to solve issues of
  - Finances
  - Time of participants
  - Confidentiality

Conclusion

- Cross model validation worth the effort
  - But it is an effort indeed
- Increases separate models' validity
- Increases methodological knowledge of modellers as well as users
- Increases insight in models
  - For model developers
  - For model users

How reproducible are published simulation modeling studies?

Mark Lamotte

IMS Health & Quintiles are now IQVIA™

The modeling groups participating to Mount Hood 8 received the following challenge

- Two published papers were selected
  - **Baxter et al. (2016)**
  - UKPDS 72
- Modelling teams to attempt to replicate the analyses
  - Extract information from the PDFs and Supplementary Appendices provided and load model to "best of ability"
    - ✦If anything contradictory or unclear, the groups were charged with deciding and documenting
  - In the event of data gaps, groups were charged with filling the gaps and documenting
  - Simulate the decision problems in the PDFs
- Submit in advance
  - Brief summary (<300 words) that "could potentially from the methods section of a published paper"
  - Detailed methods section that would be "fully transparent … (and permit a 'blinded' researcher to reproduce … results)"
  - Summary of the data gaps in the PDFs and assumptions required
  - Challenge results

Caveat

- Baxter and UKPDS team were kind enough to act as sacrificial lambs
  - Idea behind challenge was not to criticize the publications, but rather to leverage them to create momentum/direction for standards to promote transparency and replicability in DM modeling

DIABETICMedicine

DOI: 10.1111/dme.13062

Research: Health Economics

Estimating the impact of better management of glycaemic control in adults with Type 1 and Type 2 diabetes on the number of clinical complications and the associated financial benefit

M. Baxter[1], R. Hudson[1], J. Mahon[2], C. Bartlett[2], Y. Samyshkin[3], D. Alexiou[3] and N. Hex[2]

[1]Sanofi, Guildford, [2]York Health Economics Consortium Ltd, University of York, York and [3]IMS Health, London, UK

Accepted 11 January 2016

Abstract

Aim To estimate potential cost avoidance through modest and achievable improvements in glycaemic control in adults with Type 1 or Type 2 diabetes mellitus in the UK healthcare system.

Methods The IMS Core Diabetes Model was used to examine the impact of improved glycaemic control (indicated by reduction in HbA_{1c} level), in a representative cohort of adults with Type 1 or Type 2 diabetes. The cumulative incidence of microvascular and macrovascular complications was modelled across 5-year periods to a 25-year time horizon.

- Focus of the challenge was on Type 2 diabetes

Objectives of the Baxter study

- Estimate the potential cost avoidance that may be achieved through reducing complication rates by making achievable, incremental improvements in glycaemic control, when compared with the levels currently delivered in clinical practice
- It is not predicated on any specific therapy, but simply more timely and appropriate interventions to improve care

Mt. Hood Challenge

Savings are reported per HbA1c interval per person and projected to UK population

Table 2: Type 2 diabetes cost reductions per person, and for the total current UK adult population with Type 2 diabetes, from avoided complications for management of HbA_{1c} at treatment levels specified by the National Institute for Health and Care Excellence

HbA_{1c}	5 years	10 years	15 years	20 years	25 years
Adult Type 2 diabetes, per-person cost reductions					
< 59 mmol/mol (7.5%)	£83	£317	£682	£1078	£1280
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£132	£449	£995	£1510	£1678
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£138	£607	£1366	£1999	£2223
> 75 mmol/mol (9.0%)	£105	£622	£1274	£1591	£1559
Adult Type 2 diabetes, total population cost reductions					
< 59 mmol/mol (7.5%)	£146 891 319	£561 018 652	£1 206 986 500	£1 907 817 371	£2 265 311 906
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£41 540 384	£141 300 247	£313 126 383	£475 196 823	£528 066 403
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£58 477 533	£257 216 394	£578 842 824	£847 076 724	£941 996 777
> 75 mmol/mol (9.0%)	£51 933 835	£307 646 148	£630 130 534	£786 921 255	£771 093 801
TOTAL	£298 843 071	£1 267 181 440	£2 729 086 240	£4 017 012 172	£4 506 468 886

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And also on number of complications

Type 2 diabetes	5 years	10 years	15 years	20 years	25 years
Eye disease					
BDR	16,515	39,086	61,222	71,948	68,404
PDR	3,791	8,836	13,083	14,673	14,830
ME	22,544	55,338	87,923	100,391	93,842
SVL	6,215	21,794	37,921	46,768	48,418
Cataract	7,711	16,738	24,844	27,288	25,275
Total	56,777	141,792	224,992	261,069	250,768
Renal disease					
MA	37,844	93,221	143,466	158,051	142,375
ESRD	276	2,183	6,540	11,663	14,524
Nephropathy	31	572	2,108	4,887	7,288
Total	38,151	95,975	152,114	174,601	164,187
Foot ulcers and amputations and neuropathy					
Ulcer	11,088	46,422	87,773	112,120	113,076
Amputation	872	6,695	16,331	25,601	30,449
Neuropathy	110,053	221,893	285,619	274,814	230,104
Total	122,013	275,011	389,723	412,535	373,629
Cardiovascular					
CHF	14,766	32,569	52,270	59,807	52,241
PVD	1,837	4,460	7,312	8,666	8,187
Angina	4,785	10,560	17,048	19,844	16,315
Stroke	4,750	11,274	19,070	18,821	9,605
MI	1,852	3,031	2,190	-721	-3,960
Total	27,991	61,893	97,890	106,416	82,387

Mt. Hood Challenge

A Brief Look at Aggregate Results for Baxter Replication

- The following groups participated:
  - Cardiff, the Cardiff Model;
  - ECHO-T2DM, the Economics and Health Outcomes Model of T2DM;
  - MDM-TTM, Medical Decision Modeling Inc - Treatment Transitions Model;
  - QI-CDM, Quintiles IMS-Core Diabetes Model
  - MMD: Michigan model (only commented on inputs)

Mt. Hood Challenge

Overview of data gaps identified

	Baxter study reported	Model input gaps identified by modelling groups
Baseline characteristics of simulated patients	Refer to IMS Disease Analyser (UK database)	Lack of baseline patient characteristics, Sample size not presented; No point estimates for baseline HbA1c provided within the ranges
Treatment effect / thresholds	Refers to HbA1c treatment intensification levels in Khunti et al.(21) and NICE guidelines(18)	Referred value not present in the paper and count could not be discerned
Effect evolution	Modelling of modification of treatment at HbA1c thresholds indicated by current NICE guidelines (18)	Risk factor evolution for time-dependent parameters not specified; Unclear if there was a treatment algorithm with rescue treatment
Prediction of complications	Quintiles IMS Core Diabetes Model	Choice of rates/equations was not reported and should be for the Core Diabetes Model which has the ability to run different risk equations)
Cost	Supplementary table of direct costs of complications and management costs	Cost for some complications missing (fatal MI, ulcers)

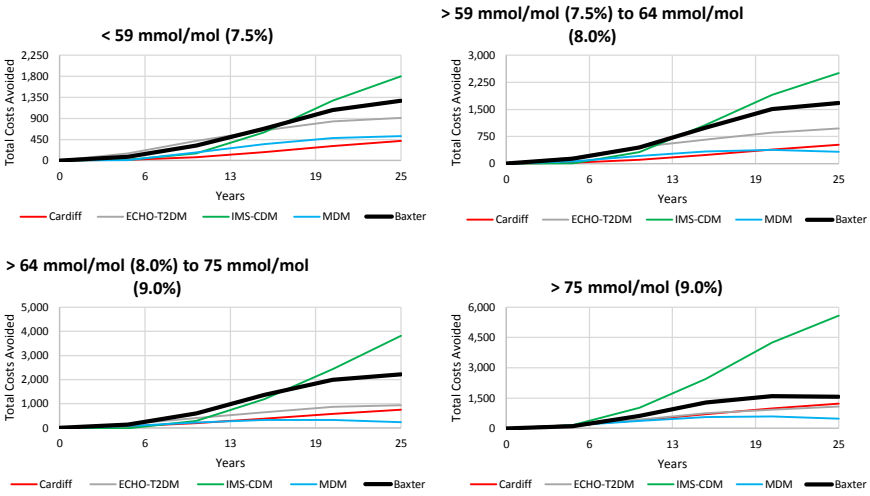
Mt. Hood Challenge

Cost savings per HbA1c and per patient

	Baxter study	Participating modelling groups			
		Cardiff	ECHO-T2DM	MDM-TTM	QI-CDM
< 59 mmol/mol (7.5%)					
5 years	£83	£16	£154	£7	£13
10 years	£317	£73	£418	£174	£151
15 years	£682	£179	£644	£353	£605
20 years	£1,078	£307	£838	£484	£1,283
25 years	£1,280	£422	£911	£521	£1,799
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)					
5 years	£132	£26	£170	£60	£9
10 years	£449	£104	£457	£208	£317
15 years	£995	£235	£658	£337	£1,069
20 years	£1,510	£385	£860	£379	£1,906
25 years	£1,678	£518	£976	£324	£2,503
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)					
5 years	£138	£68	£157	£83	-£16
10 years	£607	£201	£412	£218	£294
15 years	£1,366	£384	£651	£329	£1,198
20 years	£1,999	£580	£869	£331	£2,440
25 years	£2,223	£748	£942	£236	£3,810
> 75 mmol/mol (9.0%)					
5 years	£105	£160	£150	£146	£169
10 years	£622	£402	£427	£372	£1,019
15 years	£1,274	£697	£750	£561	£2,442
20 years	£1,591	£993	£923	£584	£4,255
25 years	£1,559	£1,231	£1,088	£476	£5,590

Mt. Hood Challenge

Costs Avoided per Patient, by HbA1c



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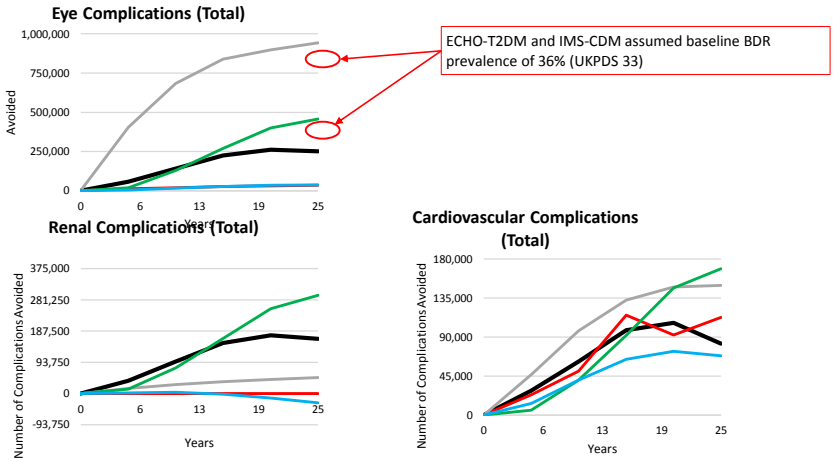
Complications Avoided, for Full Population



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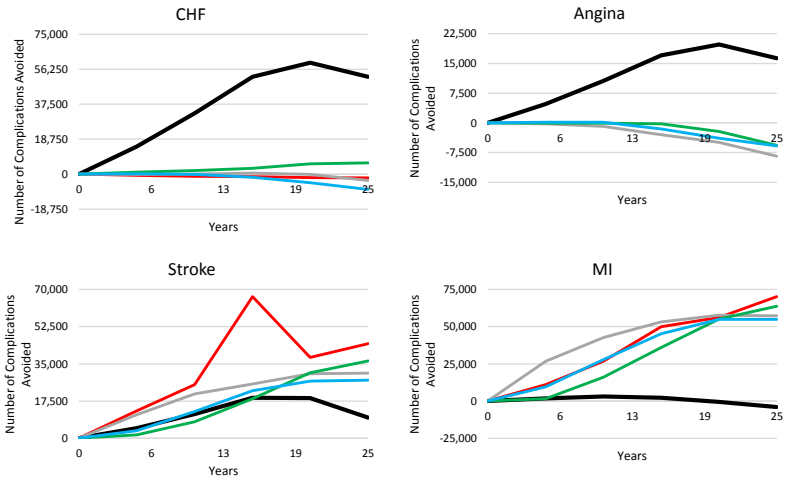
Complications avoided for individual cardiovascular complications



Mt. Hood Challenge

Possible reasons why we see differences ….

Mt. Hood Challenge

Hypothesis #1

Differences in assumed baseline patient characteristsics may matter

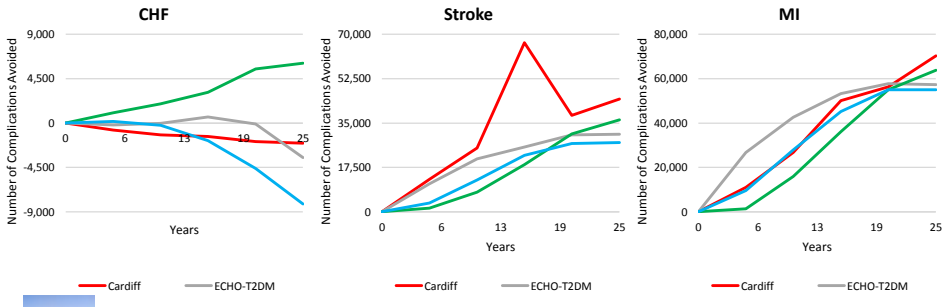
- Baseline patient characteristics were poorly reported
  - Baseline HbA1c was in four brackets (<59, 59-64, 64-75, and >75 mmol/mol or <7.5%, 75-8%, 8-9%, and >9.0%)
  - Mean HbA1c (and SD) were not given,
  - No on other covariates.
  - Assumptions varied across groups:
    - Cardiff assumed fixed initial HbA1c of 7.0%, 7.75%, 8.5% and 9.5%, for each of the four brackets
    - ECHO-T2DM used distributions from NHANES: mean HbA1c 6.35%, 7.68%, 8.43%, 10.60%
    - QI-CDM sources baseline HbA1c from NICE guideline
    - Various assumptions regarding other covariates, which were set to the same values in all HbA1c subgroups (Cardiff, QI-CDM) or to subgroup- varying values (ECHO-T2DM)
- Unclear what effect this had on results

Mt. Hood Challenge

Hypothesis #2

The choice of risk equations may matter

- Unclear what Baxter used
- Cardiff, ECHO-T2DM, QI-CDM all used **UKPDS 82** for the T2DM patients, MDM?
  - Expect reasonably similar incidences of CVD morbidity and mortality?
    - ✦Good for MI, maybe stroke, but complicated by differences in covariate values over time

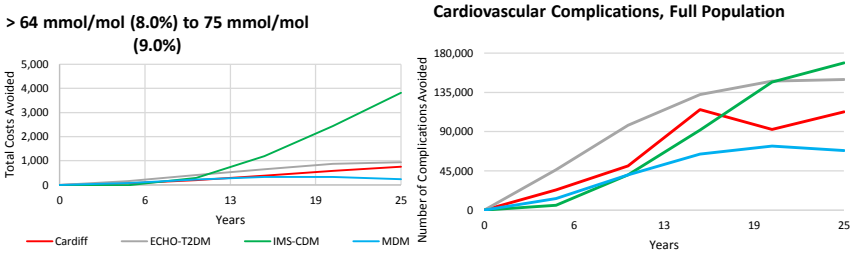


Mt. Hood Challenge

Hypothesis #3

Assumption about downstream treatment intensification may matter

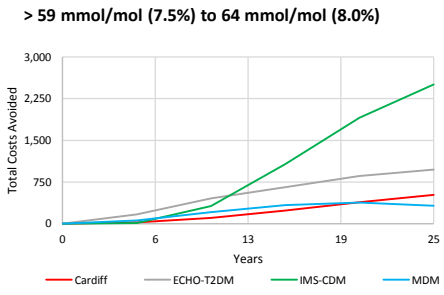
- QI-CDM modeled treatment intensification with additional efficacy, others (probably) did not
- Cardiff applied common HbA1c intensification threshold (7.5%), QI-CDM and ECHO-T2DM had separate threshold for the two arms, MDM?



Hypothesis #4

Differences in assumptions about unit costs may matter

- QI-CDM assumed costs for events other than found in Baxter, whereas other models applied only Baxter
  - Expect higher costs for IMS-CDM
  - Supported, but does not explain what drives differences between other models



Conclusion

- Detailed reporting of data inputs is needed
- If not, results cannot be reproduced
- Reader has a black box feeling
- HTA agencies will not believe us
  - ❾ recommendations!

Mt. Hood Challenge

The Mount Hood Diabetes Modelling Transparency Checklist

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Mt. Hood Challenge

Background & building upon …

- Transparency of model inputs important to reproducibility & credibility of simulation results.
- ISPOR/SMDM Modeling Good Research Practices - "sufficient information to enable the full spectrum of readers to understand a model's accuracy, limitations, and potential applications at a level appropriate to their expertise and needs" (1)
- The ISPOR CHEERS checklist (2), Philips checklist on best practice guideline in model reporting (3), AdViSHE (4).
- American Diabetes Association (ADA) guidelines for computer modeling - "sufficient detail to reproduce model and results" (5)

(1) Caro JJ, Briggs AH, Siebert U, et al. Modeling good research practices—overview a report of the ISPOR-SMDM modeling good research practices task force–1. Medical Decision Making. 2012; 32: 667-77.
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(3) Philips Z, Ginnelly L, Sculpher M, et al. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. Health Technol Assess. 2004; 8: iii-iv, ix-xi, 1-158.
(4) P. Vemer1,2 • I. Corro Ramos3 • G. A. K. van Voorn4 • M. J. Al3 • T. L. Feenstra1,5 PharmacoEconomics (2016) 34:349–361
(5) Guidelines for Computer Modeling of Diabetes and Its Complications. Diabetes Care. 2004; 27: 2262.

Objective

- Eighth Mount Hood Challenge – an exercise to address this
- Diabetes modelling groups attempted to answer 2 questions

  Q1) "how reproducible are published simulation modelling studies?"

  Q2) "what is the best way to describe a simulation so that it can be reproduced?"

Objective:

To develop a diabetes-specific checklist for transparency of input data that can be used alongside general health economic modelling guidelines to improve reproducibility of health economic analyses and simulation model results in diabetes

Method

- Modelling groups examined 2 cases studies
  - Data gaps reported by each group were summarized in a tabular format and compared and contrasted during meeting proceedings.
  - Documented lack of transparency in reporting model inputs including important deficiencies such as baseline patient characteristics, treatment effects, HbA1c evolution, treatment use over time.
  - Modelling groups generally sourced missing information from literature and made different assumptions
- MONDAY meeting after the Challenge
  - Discussed key issues & reached consensus to start draft guidelines
  - Post-meeting, draft paper proposing and motivating a checklist
  - 2 rounds of revision with all authors,
  - Final refined position paper was created - submitted to ViH journal

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The Checklist

Table 6 Checklist of reporting model input in diabetes health economics studies

Diabetes Modelling Input Checklist		
Model input	**Checkbox**	**Comments (e.g. justification if not reported)**
Simulation cohort		
Baseline age		
Ethnicity/race		
BMI/weight		
Duration of diabetes		
Baseline HbA1c, lipids and blood pressure		
Smoking status		
Comorbidities		
Physical activity		
Baseline treatment		
Treatment intervention		
Type of treatment		
Treatment algorithm for HbA1c evolution over time		
Treatment algorithm for other conditions, e.g. hypertension, dyslipidaemia, excess weight		
Treatment initial effects on baseline biomarkers		
Rules for treatment intensification, e.g. the cut-off HbA1c level to switch the treatment, the type of new treatment and whether the rescue treatment is an addition or substitution to the standard treatment		
Long-term effects, adverse effects, treatment adherence and persistence and residual effects after the discontinuation of the treatment		
Trajectory of biomarkers, BMI, smoking and any other factors that are affected by treatment		
Cost		
Differentiated by acute event in first year and subsequent years		
Cost of intervention and other costs, e.g. managing complications, adverse events, diagnostics, etc. Please report unit prices and resource use separately and give information on discount rates applied.		
Health state utilities		
Operational mechanics of the assignment of utility values, i.e. utility- or disutility-oriented		
Management of multi-health conditions		
General model characteristics		
Choice of mortality table and any specific event-related mortality		
Choice and source of risk equations		
If microsimulation: number of Monte Carlo simulations conducted and justification		
Components of model uncertainty being simulated (e.g. risk equations, risk factor trajectories, costs, treatment effect), number of simulations and justifications		

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Diabetes Modelling Input Checklist
Simulation cohort

Baseline patient characteristics of simulated cohort should be clearly stated, incl.

- age, sex, ethnicity/race, smoking status,
- body mass index (BMI)/weight, physical activity
- duration of diabetes, baseline HbA1c, lipids and blood pressure levels,
- comorbidities,
- baseline treatments
  - aspirin, statins, ACE-inhibitors/angiotensin II receptor blockers and/or glucose-lowering treatments.
- Baseline characteristics should be presented in a table as mean with standard deviation or as proportion. Statistical distributions for baseline characteristics should be reported in the table.

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Diabetes Modelling Input Checklist
Treatment interventions

1. treatments / algorithms for blood glucose control, hypertension, dyslipidaemia, excess weight etc. for comparator & intervention
2. specify initial impact of treatment(s) on baseline biomarkers
3. rules for treatment intensification and thresholds triggering changes should be specified for HbA1c, blood pressure, lipids, BMI, eGFR
4. specify the set of long-term effects, adverse effects, treatment adherence and persistence, and assumptions on legacy effects i.e. residual treatment effects after the discontinuation of a treatment
5. direct and indirect links from treatment effects on glucose / lipids levels to health outcomes, costs and effectiveness
   e.g. HbA1c directly affects stroke, MI, retinopathy, nephropathy risks,
   . HbA1c indirectly affects mortality through its impact on CVD
6. include effects on biomarker trajectories over time for HbA1c, lipids, blood pressure, BMI, eGFR, smoking

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Diabetes Modelling Input Checklist
Costs & Utilities

Costs of …

- interventions themselves
- being in specific health state and on specific treatments
- complication management should consider timing of events
  e.g. macrovascular complications high cost at the time of the event and lower follow-up management costs
- adverse events, diagnostics
- If a societal perspective is used then specify assumptions e.g. productivity losses through absenteeism, presentism, or early retirement.

Health state utilities (HSUs)

- Methodology for utility for multiple co-morbidities should be stated e.g. 'minimum'(using value of the condition with the lowest utility score), 'additive' (using the arithmetic sum of utility decrements), or 'multiplicative' (using the product of utility decrement factors).

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Diabetes Modelling Input Checklist
General Model Characteristics

1. choice of country-specific life table for all-cause mortality should be stated in methods, and specific event-related mortality must be stated.
2. document the source and details of risk equations used in the model.
3. if using a microsimulation model, authors should report and justify number of Monte Carlo simulations performed per individual.
4. when performing probabilistic sensitivity analysis it is important to document and justify distributions for components (e.g. risk equations, risk factor trajectories and treatment effect).

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Discussion of Usefulness

- Publications -Modellers should document simulation inputs via checklist, and submit as supplementary materials with publications. Journal editors/reviewers permit (or require) inclusion of checklist.
- Use for each application - this is a minimal checklist for typical analyses - for some analyses other things will be needed. It is for each specific application of a model - not a general overall model 'validation' Issue
- "Costs of Transparency" - full transparency requires considerable resources of modellers and consumers of results. The checklist is a pragmatic solution, focused on influential parameters and assumptions.
- Further Work on …
  - Standardised model outputs to enable cross comparison of results
  - Test if checklist increases transparency at a future Mt Hood.
- Conclusion: - improve credibility and clarity. We hope the checklist will inspire modellers in similarly complex fields to promote transparency of inputs & improve reliability of outputs.

Prepare for Interactive Component

- Click on your App for ISPOR Glasgow
- Click More
- Click Live Polling / Q&A
- Go to W17 – Comparing, contrasting … Mt Hood Challenge

Live Content Slide

When playing as a slideshow, this slide will display live content

Poll: 1. Who do you work for?

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Poll: 2a. How important do you think transparency of models is to Decision Makers?

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Poll: 2b. How important do you think transparency of models is to journal editors?

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Poll: 2c. How important is transparency of models to model builders wishing to utilise components of existing models?

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Poll: 3. In your experience is information in a published article enough to replicate the model?

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Poll: 4. Do you agree that the Mt Hood transparency checklist adds value

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Poll: 5. Should a similar transparency exercise be done in other disease areas

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Poll: 6. What disease area do you think would be good priorities ?

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Social Q&A

Workshop 17

Thank you

Michael Willis, PhD
Talitha Feenstra, PhD
Mark Lamotte, MD
Alan Brennan, PhD

ISPOR 20th Annual European Congress
Glasgow, SCOTLAND

November 8, 2017

Mt. Hood Challenge