Economics Modelling and Diabetes: The Mount Hood 2016 Challenge

Kantonsspital of St. Gallen

St. Gallen, Switzerland

16th – 18th September 2016

Contents

Economics, Modelling and Diabetes:

The Mount Hood Challenge, St. Gallen 2016

Conference Centre Map and General Information

Location: The conference will be held at the Kantonsspital of St. Gallen, Rorschacher Strasse 95, 9007 St. Gallen.

Registration for the optional <u>pre-conference workshop</u> will commence at 12.30pm on Friday, 16th September.

Registration for the <u>conference</u> will be from 8.30am onwards on Saturday, 17th September. The conference will conclude at 3.15pm Sunday, 18th September 2016.

Conference registration includes lunches/refreshments and a conference dinner on the evening of 17th September.

Mount Hood Organising Committee 2016

Philip Clarke, The University of Melbourne

Jose Leal, The University of Oxford

Phil McEwan, Health Economics and Outcomes Research Ltd

Andrew Palmer, Menzies Institute, University of Tasmania

Michael Willis, The Swedish Institute for Health Economics

Michelle Tew, University of Melbourne

The organising committee is chaired by Professor Philip Clarke, University of Melbourne and this year's conference is being hosted by Michael Brandle of Kantonsspital St. Gallen.

Thanks are due to:

Michael Brandle and Ruth Perlt-Vögeli for local organising; Nick Woods for assistance with developing the website; Jose Leal, Christian Asseburg and Mike Willis on developing the Challenges; Xinyang Hu and Michelle Tue for the program;

List of Participants

Donna	Ashley	Novo Nordisk
Christian	Asseburg	IHE The Swedish Institute for Health Economics
Jay	Bae	Eli Lilly and Company
Jacob	Barhak	-
Klas	Bergenheim	AstraZeneca
Michael	Brandle	Kantonsspital St. Gallen
Penny	Breeze	University of Sheffield
Alan	Brennan	University of Sheffield
Philip	Clarke	University of Melbourne
Helen	Dakin	University of Oxford
Talitha	Feenstra	RIVM/UMCG
Volker	Foos	IMS Health
James C	Gahn	Medical Decision Modeling Inc.
Michael	Gains	IMS Health
Divina	Glah	Novo Nordisk
Jason	Gordon	Health Economics and Outcomes Research Ltd
Alastair	Gray	University of Oxford
Jens	Gundgaard	Novo Nordisk A/S
William	Herman	University of Michigan
Xinyang	Hua	University of Melbourne
Deanna	Isaman	University of Michigan
Pierre	Johansen	IHE The Swedish Institute for Health Economics
Josh	Knight	University of Melbourne
Shihchen	Kuo	University of Michigan
Neda	Laiteerapong	University of Chicago
Mark	Lamotte	IMS Health Consulting
Jose	Leal	University of Oxford
Philip	McEwan	Health Economics and Outcomes Research Ltd
Balazs	Nagy	SYREON Ltd.

List of Participants (continued)

Bertalan	Nemeth	SYREON Ltd.
Cheryl	Neslusan	Janssen
Patrick	O'Connor	HealthPartners Institute
Katherine	Ogurtsova	Deutsches Diabetes-Zentrum (DDZ)
Andrew	Palmer	University of Tasmania
Dan	Pollard	University of Sheffield
Richard	Pollock	Ossian Health Economics and Communications GmbH
Lei	Qin	AstraZeneca
Samantha	Roberts	University of Oxford
Katrin	Schimke	Kantonsspital SG
Katharina	Schremser	Helmholtz Zentrum München GmbH – German Research Center For Environmental Health
Lei	Si	Menzies Institute for Medical Research
Annabelle	Slingerland	Institute of Public Health
Joel	Smith	University of Oxford
Harry J	Smolen	Medical Decision Modeling Inc.
Oleh	Syarkevych	JSC Farmak
Laszlo	Szilberhorn	SYREON Research Institute Ltd.
Shana	Traina	Janssen
An	Tran Duy	University of Melbourne
Christina	Tzogiou	ZHAW School of Management and Law
William	Valentine	Ossian
Kate	Van Brunt	Eli Lilly & Company
Zoltan	Voko	SYREON Ltd.
Michael	Willis	IHE The Swedish Institute for Health Economics
Josan	Yauw	UMC Utrecht

Pre-conference workshop
Diabetes simulation modelling through the looking glass

16 September 2016 1pm-5pm
A good place for lunch prior to the workshop is ZIA ROSA Pizzeria-Trattoria
St.Gallen (see map)
Building 8, 2nd Floor (see map)

Outline

Introduction to diabetes modelling

- Brief History
- How simulation models work
- Constructing risk equations using individual data

Quality of life and complications

- Collection of Quality of life data: Case studies from UKPDS and ADVANCE studies
- How often and what do we need to collect?
- Heterogeneity in responses across regions
- Should be using levels or changes in Quality of life
- Relationship between utility and mortality
- Quality Adjusted Survival Models
- Role of meta-analysis
- What next?

Costs of treatments and complications

- Changes in the price and expenditure of diabetes therapies: recent evidence
- Options for collecting resource use information
- Analysis of costs in diabetes RCTS
- Costing equations – UKPDS Mk 1 & MK 2
- Sources of costing data in other countries – Sweden, Australia, ADVANCE.
- What next?

Future directions in modelling

- Adapting models across settings
- Calibration risk equations – Framingham indigenous example
- Developing new equations – mortality following events - WA UKPDS example
- LE calculators (Sweden & WA)
- What can we learn from meta-models?

New Developments in Type 1 diabetes

- Burden of the disease: Life expectancy gap in Sweden & Australia
- How a hypo can impact on your life expectancy
- Overview of a new Type 1 diabetes model
- What next?

Speakers

Professor Philip Clarke, was instrumental in the development of both versions of the UKPDS Outcomes Model. More recently he has been involved in the development of a comparable Type 1 diabetes simulation model using data from a large diabetes registry in Sweden. He has also been involved with the economic analyses of the major diabetes clinical trials including the UKPDS, FIELD and ADVANCE studies.

Professor Andrew Palmer was a co-founded CORE, Center for Outcomes Research, in July 2000 and was medical director and CEO until 2005. He developed the CORE diabetes model which has been widely used, particularly to evaluate pharmacutical interventions for the treatment of Type 2 diabetes. He has since developed a diabetes prevention model and has collaborated with Prof Clarke on the development of the Type 1 diabetes model.

Economics, Modelling and Diabetes: Mount Hood Challenge 2016

Conference overview

The Mount Hood Challenge conference focuses on economic aspects of diabetes and its complications. The challenges are developed collectively by an international group of researchers engaged in development of diabetes simulation models for health economic evaluation.

A major focal point of the conference will be a comparison of health economic diabetes models both in terms of their structure and performance. This conference builds on six previous diabetes simulation modelling conferences that have been held since 1999.

The theme of the 2016 Challenge will be how to improve the transparency of simulation models. It will feature both challenges and debates on how this can best be achieved. The conference will also focus on how best to convey information on health outcomes to clinicians and patients.

Speakers will include:

- **Rod Jackson**, University of Auckland, contributing a long history in developing tools to explain cardiovascular risk.
- **Amanda Adler**, Addenbrooke's Hospital (Cambridge) chair of NICEs Technology Appraisal committee.
- **Barrie Chubb,** Regional Health Economics Manager, Novo Nordisk.

The conference will also have open sessions on all aspects of the health economics of diabetes.

Economics, Modelling and Diabetes:
Mount Hood Challenge 2016

Guest Speakers

Professor Rod Jackson

Rod Jackson is a professor of epidemiology at the University of Auckland, New Zealand. He is medically trained, has a PhD in epidemiology and is a fellow of the New Zealand College of Public Health Medicine.

He has 35 years of research experience in cardiovascular disease epidemiology. In the 1990s he led the development of New Zealand's absolute risk-based clinical guidelines for managing CVD risk factors. For the past 15 years his research has been mainly focused on CVD risk prediction and its application in clinical practice. He leads a 'big-health data' research programme that generates very large cohort studies from web-based clinical decision support systems linked to national health databases to implement, monitor and improve CVD risk assessment and management in primary and secondary care. He has published over 270 papers in peer-reviewed journals.

Amanda Ingham Adler

Amanda Ingham Adler trained in economics, medicine and epidemiology. She chairs a multi-disciplinary Technology Appraisal Committee at the National Institute for Health Excellence (NICE) and is a consultant physician at Addenbrooke's Hospital, Cambridge. Her clinical work involves patients' in-hospital, in out-patient clinics, and in the community. She holds an honorary position with the MRC Epidemiology Unit, Institute of Metabolic Sciences, Cambridge University.

Barrie Chubb

Barrie Chubb undertook his health economic training at City University in 2006, and has since worked as a health economist for Novo Nordisk.

In his time there Barrie has been involved in a number of submissions to all of the UK HTA authorities (NICE, SMC and AWMSG) as well as the NCPE in Ireland for diabetes therapies. Barrie's current role is that of 'Regional Health Economics Manager', in the European Health Economics and Outcomes Research team.

Areal Kantonsspital St.Gallen

Standort St.Gallen

Parkplatzsituation
Kantonsspital St.Gallen
Ideal ist die Anreise mit dem öffentlichen Verkehr. Die Anzahl Parkplätze auf dem Areal des Kantonsspitals St.Gallen ist beschränkt.

Auf dem Areal stehen kostenpflichtige Kurzzeit-Parkplätze zur Verfügung.

Auf dem Parkdeck Böschenmühle, angrenzend an das Spitalareal, gibt es weitere Parkplätze. Zudem stehen Parkplätze im nahegelegenen öffentlichen Parkhaus Cityparking des Athletik-Zentrums zur Verfügung.

Weitere Informationen
071 494 11 11 oder www.kssg.ch

Öffentliche Verkehrsmittel

Stadtbus VBSG
Die Stadtbusse halten an der Rorschacherstrasse beim Kantonsspital St.Gallen (Haltestelle Kantonsspital) und an der Lindenstrasse (Haltestelle Spitalstrasse).

Linie 1	(Stephanshorn)
Linie 4	(Guggeien)
Linie 7	(Achslen)
Linie 11	(Mörschwil)
Linie 10	(Abacus-Platz)

Postauto
Die Postautokurse von und nach Rehetobel/Heiden, Eggersriet/Heiden und Goldach-Rorschach/Rorschacherberg, Tübach und Engelburg halten an der Haltestelle Kantonsspital.

Bahn
Ab Bahnhof St.Gallen-St.Fiden ist der Fussweg mit Schildern: «Spitäler/Kantonsspital» gekennzeichnet.

Auto
Über die Autobahnausfahrt «St.Fiden/Spitäler» oder via Innenstadt über die Steinachstrasse.

Kantonsspital St.Gallen
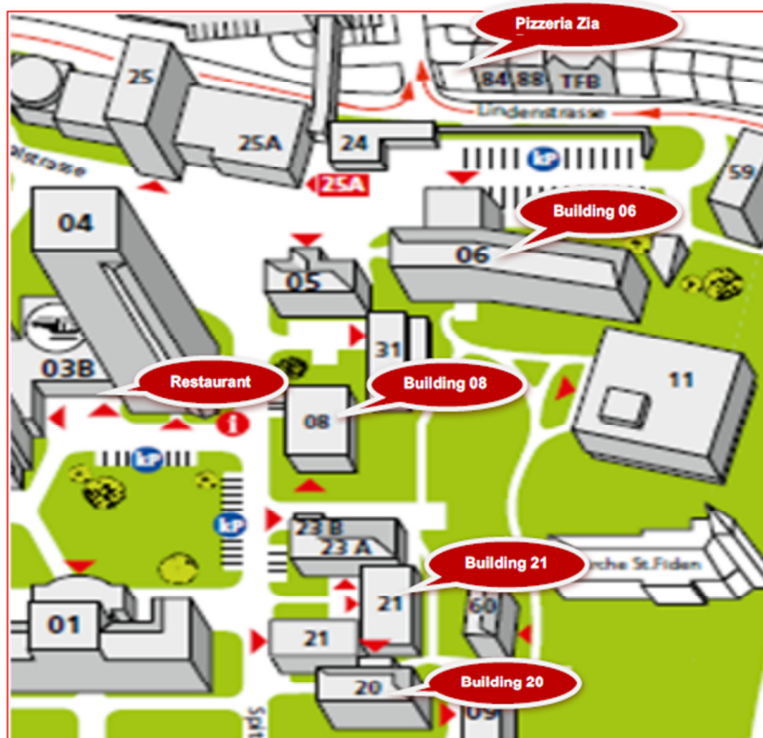
Building 21 – Lecture Hall
- Registration
- Plenary sessions
- Workshop
- Breaks
- Lunches

Building 06 / 4th floor
- Workshop

Building 20 / 1st floor
- Workshop

Building 08 / 2nd floor
- Optional Workshop : A Master Class in Diabetes Stimulation Modelling

Economics, Modelling and Diabetes:
Mount Hood Challenge 2016

Day 1	Saturday 17th September 2016		
8:30-9:00am	REGISTRATION		
9:00-9:10am	**Welcome –** Prof Philip Clarke, University of Melbourne **Location:** Building 21- Lecture Hall		

9:10-11:00am	*Mt Hood 2016: Transparency Challenge*
	 Chair: Philip Clarke, University of Melbourne
	 Overview: Outline of the challenge & results
	 Groups presenting a (very brief) overview of their model & how they would make their simulations transparent (5 Minutes per model)
	     ECHO-T2DM
	     IMS CORE Diabetes Modelling Group
	     Medical Decision Modelling (MDM)
	     Michigan Model for Diabetes
	     The Reference Model
	     UKPDS Outcomes Model		

11:00-11:30am	*Tea and Coffee*		
11:30am-12:30pm	*General discussion of Validation Results* Chair: Alastair Gray, University of Oxford Location: Building 21 Lecture Hall		
12:30-1:30 pm	*Lunch*		
1:30-3:00pm	**Conference session 1** Lecturer Hall (20 Minutes each)	**Conference session 2** Building 06 4th Floor (20 Minutes each)	**Conference session 3** Building 20 1st floor (20 Minutes each)
3:00-3:30pm	*Tea and Coffee*		
3:30-5:00pm	**Conference session 4** Lecturer Hall (20 Minutes each)	**Conference session 5** Building 06 4th Floor (20 Minutes each)	**Conference session 6** Building 20 1-st floor (20 Minutes each)
5:00- 6:00pm	**Business meeting: Where to next with Mt Hood? Lecture Hall.** Chair: Prof Philip Clarke		
7:00pm onwards	**CONFERENCE DINNER** Restaurant Falkenburg (http://www.falkenburgsg.ch)		

Day 2	Sunday 18th September 2016
9:20-11:00am	Challenge 2: What can we learn from comparing "Outcome tables" **Location: BUILDING 21- LECTURE HALL** Chair: Amanda Adler, NICE.
11:00-11:30am	*Tea and Coffee Break*
11:30am-12:30	**Making the results of models understandable to clinicians and the patients Speaker** **Chair:** Neda Laiteerapong, University of Chicago Plenary Speaker: Prof Rod Jackson, University of Auckland
12:30-1:30pm	*Lunch*
1:30-2:30	**Special Session: Creating new models diabetes models** Chair: Mike Willis, IHE. Speakers: Philip Clarke- Type 1 models William Valentine - Type 1 models Josh Knight – CVD models Xinyang Hua – Calibrating CVD risk in an indigenous population
2:30-3pm	**What have we learned – general discussion**
3:00-3:15	*Wrap up- CLOSE (Afternoon Coffee to finish)*

Mount Hood 2016

Challenges

Challenge #1: TRANSPARENCY

Motivation

How reproducible are published simulation modelling studies? What is the best way to describe a simulation so that it can be reproduced? For this challenge we have selected two published papers. The purpose of this challenge is to determine how easy it is to reproduce the simulations undertaken in these studies. Beyond the level of agreement, the main point of this challenge assist in the development of checklist for documenting simulations. The ultimate purpose is to develop reporting guidelines that Mt Hood would publish collectively.

Instructions

1. The replication transparency challenge consists of attempting to replicate two studies: the UKPDS 72 and Baxter et al. 2016.
   - P. M. Clarke, A. M. Gray, A. Briggs, R. J. Stevens, D. R. Matthews, R. R. Holman, on behalf of the UK Prospective Diabetes Study (UKPDS) Cost-utility analyses of intensive blood glucose and tight blood pressure control in type 2 diabetes (UKPDS 72) Diabetologia, May 2005, Volume 48, Issue 5, pp 868-877 (can be downloaded from: http://link.springer.com/article/10.1007%2Fs00125-005-1717-3)
   - M. Baxter, R. Hudson, J. Mahon, C. Bartlett, Y. Samyshkin, D. Alexiou andN. Hex 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, Diabetes Medicines, Online: 15 APR 2016: DOI: 10.1111/dme.13062

2. For each of the published cost-effectiveness applications, please read the study publications carefully and carry out the following:
   a. Extract the information and load model to the best of your ability and judgment.
      i. If anything is contradictory or unclear, you decide, but document it (naming this Section 1 in your documentation).
   b. Document gaps (call this Section 2 in your documentation).
   c. Continue loading model using complementary sources.

      i.   First, use other publications from the same study (for example, other UKPDS in the case of UKPDS 72).

      ii.   It may be necessary to obtain inputs from other sources if they are not reported, or to convert inputs to other units etc.

     iii.   Document fully the sources of all your inputs and any assumptions that were required, and document any gaps of necessary information. Note whether the missing information relates to differences in model design.

   d. If your group published the study in question, try to replicate the analysis using only publically available information, and not any proprietary or other information available to you!

3. Simulate the same decision problems using your model. Note that UKPDS 72 includes three separate analyses: (i) blood glucose control with metformin in overweight patients; (ii) intensive blood glucose control; (iii) tighter blood pressure control. Please focus only on intensive blood glucose control. If you have time, you can try to replicate the other interventions. For the Baxter paper, there are separate analyses for T1DM and T2DM. Please focus on T2DM, but feel free to simulate T1DM as well.

4. *Result extraction:* Extract the relevant results from your simulations into the provided Excel file for capturing outcomes.

5. *Documenting your methods:* Prepare two summaries describing the simulations you have undertaken:
   - A brief summary (less than 300 words) that could potentially form the methods section of a published paper
   - A detailed methods section that you believe would document the simulation you have undertaken so that it is fully transparent (for a working definition of transparent, assume that you describe your model in sufficient details that would enable an informed but "blinded" researcher (i.e. a researcher not having access to simulated results) to reproduce your results.

6. Prior to the meeting:

a. Submit the result Excel file ("Challenge 1 Results Reporting Template.xls").
b. Submit the documentation (Sections 1 and 2), being sure to include a summary of what you think are the gaps in the existing methods contained in the published studies
c. Submit the two methods sections of how you would document your simulations

7. Deadline: Please submit the results by September 4th, 2016.

Challenge #2: COMMUNICATING OUTCOMES

Background

A few years ago the UKPDS Outcomes model was used to produce some Life Expectancy tables (Jose Leal, Alastair M. Gray, Philip M. Clarke, Development of life-expectancy tables for people with type 2 diabetes. European Heart Journal, Volume 30, Issue 7, 2009 http://eurheartj.oxfordjournals.org/content/30/7/834).

The purpose of this challenge is two-fold. The first is for modelling groups to produce comparable outcome tables using their own models for people with Type 2 (and where models are available for Type 1 diabetes). These tables are a method for communicating outcomes to clinicians and patients. They are also intended to promote transparency as they enable comparisons of models across a broad range of standardised simulations, i.e. a standard set of simulations for patients with a wide variation in characteristics would allow users to understand what risk factors drive variations in model outcomes.

Instructions

1. Attached, please see a PDF "Development of Life-Expectancy Tables" that contains a table-based analysis that presents (life expectancy over a range of covariate values at baseline) for a typical patient or cohort.

2. Using the attached input values (Excel file "Inputs for Outcome Table.xlsx"), replicate this analysis using your model.
   a. Switch off discounting. Life-time time horizon (or longest time-frame possible).
   b. Set up a simulation matching all inputs in the specified Excel sheet. Note following the UKPDS study, please assume that all risk factor values remain constant.

c. Please use public data from the characteristics of the UKDPS population (e.g. as reported in UKPDS 33), or make plausible assumptions regarding any other risk factor values.

d. If there are computational limitations to run all patients through the model, then focus on patients in rows 61-81.

e. For the covariates (or inputs) that are being varied in the table-based analysis, set up and run your model such that the patient baseline inputs are varied accordingly.

f. Throughout, hold the risk factors constant through life-time (as in the Excel file).

g. Where your model requires different data or data in a different format, document your assumptions, but try to match the instructions as closely as possible.

h. If anything is contradictory or unclear, you decide, but fully document it.

3. Simulate and extract life expectancy, lifetime QALYs (undiscounted) and, if possible, rates of MI, Stroke, CHF, Overall CVD, ESRD, and Amputation.

4. Standard set of tables for reporting results will be circulated to groups registering for the challenge.

5. Prior to the meeting:
   a. Submit the result output capture file which will match that produced in the EHJ tomthood2016@gmail.com.
   b. Submit documentation: The inputs and assumptions required, any gaps in information

6. Deadline: Please submit the results by September 4th 2016.

Models Participating in Challenges

- **Cardiff Model**

- **ECHO-T2DM**

- **Medical Decision Modelling (MDM) – Treatment Transitions Model (TTM)**

- **MICADO**

- **Michigan Model for Diabetes**

- **MMUs Diabetes Model**

- **Reference model**

- **SPHR Diabetes**

- **UKPDS Outcomes Model**

Cardiff Model

Lead Presenter: Phil McEwan

Other team members attending: Jason Gordon

Brief Description:

The Cardiff Model is a fixed-time increment stochastic simulation model programmed in C++ and Visual Basic for Applications. It is designed to evaluate the impact of therapeutic intervention in Type 1 and Type 2 diabetes.

The Type 1 Diabetes Model utilises data from the Diabetes Control and Complications Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) study (microvascular complications) and the Swedish National Diabetes Registry (cardiovascular complications). The Type 2 diabetes model fully implements UKPDS 68 and 82 risk equations.

The model requires specification of demographic and established diabetes specific modifiable risk factors. In both Type 1 and Type 2 models, simulated patients are initialised with baseline profiles and, following the application of a treatment effect, are modelled over a lifetime. Pre-specified HbA1c threshold values, or a specified duration of therapy, may be used to invoke escalation to subsequent therapy lines (up to three in total).

Event costs are applied in the year of occurrence and maintenance costs applied in all subsequent years. The costs of diabetes-related complications are drawn primarily from UKPDS 65 and utilities from UKPDS 62, and supplemented with Type 1-specific data where published. The relationship between both weight change and the frequency and severity of hypoglycaemia on costs and quality of life is also captured.

Model output includes the incidence of microvascular and macrovascular complications, hypoglycaemia, diabetes-specific mortality and all-cause mortality and point estimates of costs, life years and quality adjusted life years in addition to probabilistic cost-effectiveness output.

Key Publications:

McEwan P, Ward T, Bennett H, Bergenheim K. Validation of the UKPDS 82 risk equations within the Cardiff Diabetes Model. Cost Eff Resour Alloc. 2015;13:12. doi: 10.1186/s12962-015-0038-8.

McEwan P, Peters JR, Bergenheim K, Currie CJ. Evaluation of the costs and outcomes from changes in risk factors in type 2 diabetes using the Cardiff stochastic simulation cost-utility model. Current Medical Research and Opinion 2006;22(1):121.

McEwan P, Bennett H, Fellows J, Priaulx J and Bergenheim K. The Health Economic Value of Changes in Glycaemic Control, Weight and Rates of Hypoglycaemia in Type 1 Diabetes Mellitus. 2016. Accepted for publication. PlosOne.

ECHO-T2DM

Lead Presenter: Michael Willis

Other team members attending: Christian Asseburg and Pierre Johansen

Brief Description:

ECHO-T2DM is a stochastic, 2nd order, 'multi-application' microsimulation cost-effectiveness model of treatment intervention in T2DM with Markov health states that reflect different severities of kidney disease, neuropathy, and retinopathy, four types of macrovascular disease, and mortality. The model is programmed in R with Microsoft Excel® interface.

ECHO-T2DM generates parameter values (e.g., treatment effects, unit costs, and risk equation coefficients, and AE rates) for i cohorts drawn from user-defined probability distributions and generates initial patient characteristics including <u>demographics</u> (e.g., age, sex, ethnicity), <u>clinical</u> (e.g., T2DM duration, HbA1c, SBP, BMI, eGFR, serum cholesterol, pulse pressure (PP), ACR, WBC, heart rate, and smoking status), and <u>pre-existing micro- and macrovascular complications</u> (e.g., microalbuminuria, ESRD, symptomatic neuropathy, MI, and stroke) for j hypothetical patients in each cohort. Correlation between the initial characteristics is used to account for observed patterns of risk factor clustering.

The user can choose between four sets of macrovascular risk equations, including UKPDS 68, UKPDS 82, ADVANCE, and the Swedish NDR, and two sets of mortality risk equations (UKPDS 68 and 82). A fully-integrated sub-model of chronic kidney disease (CKD) based on the CDC Model of CKD is implemented in ECHO-T2DM.

For the economic comparison, the user defines anti-hyperglycemic treatment sequences (a sequence starting with the new intervention vs. up to ten comparator sequences, such as current care); in addition, the user can define treatment sequences for hypertension, dyslipidemia, and obesity. The cycle length is one year and the time horizon is user-definable.

Key Publications:

Sabapathy S, Neslusan C, Yoong K, Teschemaker A, Johansen P, Willis M. Cost-effectiveness of Canagliflozin versus Sitagliptin when Added to Metformin and Sulfonylurea in Type 2 Diabetes in Canada. Forthcoming in Journal of Population Therapeutics and Clinical Pharmacology

Neslusan C, Teschemaker A, Johansen P, Willis M, Valencia-Mendoza A and Puig A. Cost-Effectiveness of Canagliflozin versus Sitagliptin as Add-on to Metforminin Patients with Type2 Diabetes Mellitus in Mexico. Value in Health Regional Issues 2015; 8C: 8-19. Published Online: June 03, 2015. http://dx.doi.org/10.1016/j.vhri.2015.01.002

Willis M, Asseburg C & He J. Validation of Economic and Health Outcomes Simulation Model of Type 2 Diabetes Mellitus (ECHO-T2DM). Journal of Medical Economics 2013; 16(8): 1007-1021

Medical Decision Modeling (MDM) – Treatment Transitions Model (TTM)

Lead Presenter: Harry J. Smolen

Other team members attending: James G. Gahn

Brief Description:

The Treatment Transitions Model (TTM) is a Monte Carlo microsimulation model which estimates clinical and economic outcomes for patients with type 2 diabetes mellitus (T2DM) under user-specified treatment paradigms. The TTM simulation begins with creating an individual simulated patient with baseline demographic and clinical characteristics. The baseline characteristics include age, gender, ethnicity, and HbA1c. Clinical characteristics include systolic blood pressure, total cholesterol, high-density (HDL) and low-density lipoprotein (LDL), body mass index (BMI), and estimated glomerular filtration rate (eGFR). Comorbidities estimated from the TTM include nephropathy, neuropathy, retinopathy, stroke, and coronary heart disease.

Based on the comorbidity-related mortality and overall natural mortality, the patient's mortality is estimated. Treatment escalation within TTM is primarily controlled by increases to HbA1c and the sequence of treatments being evaluated. Patients not achieving durable control of their HbA1c are typically subject to drift after a period of time on a specific treatment (a treatment modifiable input). Once a patient's HbA1c fails to decline or remain below the target for a prescribed amount of time (treatment specific), the patient will advance to the next step in their treatment progression. The model user can select the specific treatment progression (i.e., series of treatments) to be evaluated.

In the TTM, event and continuing medical costs are estimated along with pharmacy costs. The TTM also includes estimation of medical costs associated with hypoglycaemic events.

Key Publications:

Smolen HJ, Murphy DR, Gahn JC, Yu X, Curtis BH. The evaluation of clinical and cost outcomes associated with earlier initiation of insulin in patients with type 2 diabetes mellitus. J Manag Care Spec Pharm. 2014 Sep;20(9):968-84. PubMed PMID: 25166296.

Curtis BH, Curtis S, Murphy DR, Gahn JC, Perk S, Smolen HJ, Murray J, Numapau N, Bonner JS, Liu R, Johnson J, Glass LC. Evaluation of a patient self-directed mealtime insulin titration algorithm: a US payer perspective. J Med Econ. 2016 Jun;19(6):549-56. doi: 10.3111/13696998.2016.1141098. Epub 2016 Feb 1. PubMed PMID: 26756804.

S Perk, DR Murphy , JC Gahn, X Yu , and HJ Smolen. Estimating clinical and economic outcomes following a diabetes-related vascular complication. Value in Health. May 2015. Volume 18, Issue 3, Pages A59–A60.

HJ Smolen and X Yu. Using a treatment transition model to evaluate the effects of neglecting Hba1c drift in oral anti-diabetic drugs for type 2 diabetes. Value in Health. May 2015Volume 18, Issue 3, Page A53.

MICADO: Modelling Integrated Care for Diabetes based on Observational data

Lead Presenter: Talitha Feenstra

Other team members attending: Josan Yauw

Brief Description:

Simulation models can assist in comparing the cost-effectiveness of interventions. Most models concentrate on existing diabetes patients. However, the MICADO model was developed for the evaluation of long term cost-effectiveness of interventions in both diabetes patients and the general population. Its basic structure is that of a dynamic population model, with either overlapping birth-cohorts or a cohort of diabetes patients being followed over annual time cycles. MICADO is a Markov-type, multistate transition model linking risk factors to incidence of diabetes and to micro- and macrovascular complications. Being based on GP registry data, as well as other population-wide data sources, it contains a mixed diabetes population of mainly type 2. Microvascular complications modelled are diabetic foot, nephropathy and retinopathy, macrovascular complications modelled are AMI, other CHD, CVA, and CHF. Outcomes are prevalence of complications, and quality of life. Costs are being added. Parameter uncertainty analysis can be performed concerning estimated disease/complication prevalence and treatment effectiveness parameters.

Key Publications:

A. A. W. A. van der Heijden, T. L. Feenstra, R. T. Hoogenveen, L. W. Niessen, M. C. de Bruijne, J. M. Dekker, C. A. Baan and G. Nijpels. "Policy evaluation in diabetes prevention and treatment using a population-based macro simulation model: the MICADO model" 15 JUN 2015 DOI: 10.1111/dme.12811 Diabetic Medicine Volume 32, Issue 12, pages 1580–1587, December 2015

Michigan Model for Diabetes

Lead Presenter: Deanna Isaman

Other team members attending: William Herman, Stanley Kuo, and Michael Brandle

Brief Description:

The Michigan Model for Diabetes (MMD) is a computerized disease model that enables the users to simulate the progression of diabetes over time, its complications (retinopathy, neuropathy and nephropathy), and its major comorbidities (cardiovascular and cerebrovascular disease), and death. Transition probabilities can be a function of individual characteristics, current disease states or treatment states. The model also estimates the medical costs of diabetes and its comorbidities, as well as the quality of life related to the current health state of the subject. MMD is implemented in a disease modeling software, Indirect Estimation and Simulation Tool, programmed in python language.

In contrast to other models, the transition probabilities implemented in the MMD were obtained by synthesizing the published literature. Most of the risk equations adapted in the coronary heart disease sub-model and cerebrovascular disease sub-model are from the UKPDS Outcomes Model I. Transition probabilities were derived by calibrating these equations to contemporary population-based epidemiologic studies and randomized controlled clinical trials.

MMD explicitly models diabetes management strategies and allows users to modify them to match the specific scenarios that they are simulating. Changes in risk factors (HbA1c, BMI, lipid profiles and systolic and diastolic blood pressures) over time in simulated individual patients are determined by both treatment states and aging/disease progression. MMD allows a user to control risk factor changes by defining treatment thresholds and compliance rates for hyperglycemia, dyslipidemia, and hypertension, and compliance to quitting smoking and taking aspirin.

Key Publications:

Ye W, Brandle M, Brown MB, Herman W. The Michigan Model for Coronary Heart Disease in Type 2 Diabetes: Development and Validation (2015). Journal of Diabetes Technology and Therapeutics 17(11) DOI: 10.1089/dia.2014.0304

Herman W, Ye W, Brown MB, Simmons R, Davies M, Khunti K, Rutten G, Sandbaek A, Lauritzen T, Borch Johnsen K, Wareham N (2015) Estimating the public health impact of early detection of type 2 diabetes: a modeling study based on the results of the Anglo-Danish-Dutch Study of Intensive Treatment in People with Screen-Detected Diabetes in Primary Care (*ADDITION-Europe*). Diabetes Care. 38: 1449-1455

R Li, D Bilik, MB Brown, P Zhang, SL Ettner, RT Ackermann, JC Crosson, WH Herman (2013). Medical Costs Associated with Type 2 Diabetes Complications and Comorbidities. *American Journal of Managed Care* 19:421-430.

P Zhang, MB Brown, D Bilik, RT Ackermann, R Li, WH Herman (2012). Health Utility Scores for Persons with Type 2 Diabetes in U.S. Managed Care Health Plans: Results from Translating Research into Action for Diabetes (TRIAD). *Diabetes Care* 35:2250-2256.

Ye W, J. Barhak J, Isaman DJM, Use of Secondary Data to Estimate Instantaneous Model Parameters of Diabetic Heart Disease: Lemonade Method. Information Fusion Volume 13, Issue 2, April 2012, Pages 137-145

Barhak J, Isaman DJM, Ye W, Lee D: Chronic disease modelling and simulation software. Journal of Biomedical Informatics, Volume 43, Issue 5, October 2010, Pages 791-799

Isaman DJM, BarhakJ , Ye W: Indirect Estimation of a Discrete-State Discrete-time model using Secondary Data Analysis of Regression Data. Statistics in Medicine Volume 28, Number 16, Pages 2095 - 2115, 2009.

Zhou H, Isaman DJM, Messinger S, Brown MB, Klein R, Brandle M, et al. A Computer Simulation Model of Diabetes Progression, Quality of Life, and Cost. Diabetes Care. 2005; 28:2856-63.

Brandle M, Zhou H, Smith BRK, Marriott D, Burke R, Tabaei BP, et al. The direct medical cost of type 2 diabetes. Diabetes Care. 2003;26(8):2300-4.

Coffey JT, Brandle M, Zhou H, Marriott D, Burke R, Tabaei BP, et al. Valuing health-related quality of life in diabetes. Diabetes Care. 2002;25(12):2238-43.

MMUs Diabetes Model

Lead Presenter: An Tran-Duy

Other team members attending: Philip Clarke

Brief Description:

The MMUs Diabetes Model is developed to simulate disease progression, predict occurrence of disease-related events and mortality, and estimate life expectancy and quality-adjusted life years in patients with type 2 diabetes. This is a probabilistic discrete-time model based on a set of parametric equations representing changes over time in risk factors and probabilities of events. The model can receive inputs in two forms: (1) vectors of fixed values of age, duration of diabetes, weight, height, total cholesterol, HDL cholesterol, systolic blood pressure and HbA1c, and vectors of fixed indicators of gender, ethnicity, smoking status and history of atrial fibrillation, peripheral vascular disease, ischemic heart disease, congestive heart failure, amputation, blindness, renal failure, ischemic stroke and acute myocardial infarction, or (2) parameters in the probability distributions of these variables.

Given the increasing chance that a patient survives after the first diabetes-related complication, and in anticipation of the availability of rich data coming from on-going and future observational studies (e.g. The Maastricht Study; see Eur J Epidemiol 2014;29:439- 51), this model is designed to allow prediction of repeated occurrence of the same diabetes- related complication and emergence of comorbidities (e.g. depression). The model is programmed in C++ with modern data structures and algorithms to maximize simulation speed and ease of incorporating new events, and minimize maintenance time. Integrated graphical user interfaces will be developed in the future to make the model a stand-alone program.

For the Mt Hood 2016 Challenge, the MMUs Diabetes Model uses the equations reported in the UKPDS Outcome Model (UKPDS 68).

Key Publications:

Not yet available

The Reference Model

Lead Presenter: Jacob Barhak

Other team members attending: None

Brief Description (Max 250 Words):

The Reference Model for Disease Progression is a validation model that employs High Performance Computing (HPC) to combine computational building blocks to best fit multiple populations. Those computational building blocks can be either other published models or assumptions. The Reference Model now employs an assumption engine that allows computational components to compete and cooperate to find better fitting model combination. The Reference Model is composed from multiple competing models, therefore its results show our mutual understanding of disease progression. The MIcro Simulation Tool (MIST) is used to support the model. MIST supports object oriented population generation which allow controlled modelling of populations from statistics and MIST runs over the cloud!

Key Publications:

- J. Barhak, A. Garrett, W. A. Pruett, Optimizing Model Combinations, MODSIM world 2016. 26-28 Apr, Virginia Beach Convention Center, Virginia Beach, VA. Paper: http://www.modsimworld.org/papers/2016/Optimizing_Model_Combinations.pdf Presentation: http://sites.google.com/site/jacobbarhak/home/MODSIM2016_Submit_2016_04_25.pptx
- J. Barhak, The Reference Model for Disease Progression and Latest Developments in the MIST, PyTexas 2015. College Station, TX, 26-Sep-2015. Presentation: http://sites.google.com/site/jacobbarhak/home/PyTexas2015_Upload_2015_09_26.pptx Video: https://www.youtube.com/watch?v=htGRRjia-QQ
- J. Barhak, The Reference Model Uses Modular Population Generation! Object Oriented Population Generation on the Fly with MIST. IMAG Multiscale Modeling (MSM) Consortium Meeting 9-10 September 2015. Poster: http://sites.google.com/site/jacobbarhak/home/PosterModularPopulationGeneration_IMAG_MSM2015_Upload_2015_09_03.pdf
- J. Barhak, The Reference Model uses Object Oriented Population Generation. SummerSim 2015 July 26-29, Chicago IL, USA. Paper: http://dl.acm.org/citation.cfm?id=2874946 Presentation: http://sites.google.com/site/jacobbarhak/home/SummerSim2015_Upload_2015_07_26.pptx
- J. Barhak, Modeling Clinical Data from Publications, SpringSim 2015. April 12 - 15, Alexandria, VA, USA. Paper: http://dl.acm.org/citation.cfm?id=2873011&CFID=575392711&CFTOKEN=46270544 Presentation: http://sites.google.com/site/jacobbarhak/home/SpringSim2015ModelingDataFromPublications_Present_2015_04_13.pptx
- J. Barhak, The Reference Model for Disease Progression – Data Quality Control. 6-10 July 2014, Monterey CA. Paper: http://dl.acm.org/citation.cfm?id=2685666 Presentation:

http://sites.google.com/site/jacobbarhak/home/SummerSim2014_Upload_2014_07_06.pptx

- J. Barhak, The Reference Model for Disease Progression uses MIST to find data fitness. PyData Silicon Valley 2014 held at Facebook Headquarters: Abstract: http://pydata.org/sv2014/abstracts/#195 Presentation: http://sites.google.com/site/jacobbarhak/home/PyData_SV_2014_Upload_2014_05_02.pptx Video: https://www.youtube.com/watch?v=vyvxiljc5vA

- J. Barhak, The Reference Model: Improvement in Treatment Through Time in Diabetic Populations, The Fourth International Conference in Computational Surgery and Dual Training. The Joseph B. Martin Conference Center at Harvard Medical School. Boston, MA, USA. December 9-10-11, 2012. Video: http://web.cs.uh.edu/~cosine/?q=node/140 , Presentation: http://www2.cs.uh.edu/~cosine/talks_cosine4/monday/MultidisciplinaryTalks/2_Jacob Barhak.pptx Slides Copy: http://sites.google.com/site/ComputationalSurgery_Presneted_2012_12_LateUploadToOwnWebSite_2014_2_27.pptx

- J. Barhak, The Reference Model for Disease Progression. SciPy 2012, Austin Tx, 18-19 July 2012. Paper: https://github.com/Jacob-Barhak/scipy_proceedings/blob/2012/papers/Jacob_Barhak/TheReferenceModelSciPy2012.rst, Poster: http://sites.google.com/site/jacobbarhak/home/PosterTheReferenceModel_SciPy2012_Submit_2012_07_14.pdf

Contact email: jacob.barhak@gmail.com

SPHR Diabetes

Lead Presenter: Penny Breeze

Other team members attending: Alan Brennan

Brief Description:

The SPHR Diabetes Prevention model is an individual patient simulation model programmed in R. It was developed to evaluate public health interventions to prevent diabetes and cardiovascular disease in the United Kingdom. The model can be used to estimate the long-term costs, life years and QALYs gain in diabetic or non-diabetic populations.

The model combines data from a number of sources to describe longitudinal risk factor trajectories and multiple complications and comorbidities relating to diabetes. BMI, HbA1c, systolic blood pressure, Total and HDL cholesterol trajectories have been estimated based on longitudinal data from the Whitehall II study. After progression to diabetes HbA1c trajectories are estimated using the UKPDS outcomes model.

A three stage diabetes treatment regimen is applied in the model. At diagnosis all patients are prescribed low cost treatments. If HbA1c increases above 7.4% the individual is prescribed the more expensive Gliptins in addition to Metformin. The individual continues to receive insulin above a threshold of 8.5%. Individuals receive opportunistic screening for hypertension and cardiovascular risk.

Cardiovascular events are estimated using the QRISK2 risk score to be representative of the UK population. In addition the risk of cardiovascular disease was assumed to increase with HbA1c for test results greater than 6.5 to reflect observations from the UKPDS. Microvascular events are estimated from the UKPDS2 outcomes model. Other outcomes include Congestive Heart Failure, Breast cancer, Colorectal cancer, osteoarthritis and depression, cardiovascular mortality, cancer mortality and all-cause mortality. All health events incur costs and utility decrements.

Key Publications:

Breeze P, Squires H, Chilcott J, Stride C, Diggle PJ, Brunner E, Tabak A, Brennan A. (2015) A statistical model to describe longitudinal and correlated metabolic risk factors: the Whitehall II prospective study. Journal of Public Health. [Epub ahead of print].

Breeze PR, Thomas C, Squires H, Brennan A, Greaves C, Diggle PJ, Brunner E, Tabak A, Preston L, Chilcott J (2015) Impact of Type 2 diabetes prevention programmes based on risk identification and lifestyle intervention intensity strategies: a cost-effectiveness analysis. Diabetic Medicine. [Epub ahead of print]

UKPDS Outcomes Model

Lead Presenter: Jose Leal, University of Oxford

Other team members attending: Philip Clarke, University of Melbourne, Alastair Gray, University of Oxford

Brief Description (Max 250 Words):

The UKPDS Outcomes Model (UKPDS-OM) is based on patient-level data from the United Kingdom Prospective Diabetes Study (UKPDS). It simulates type 2 diabetic populations modelling the occurrence of eight diabetes-related complications (MI, angina, stroke, heart failure, amputation, renal failure, diabetic ulcer and blindness in one eye) and death to estimate quality-adjusted life expectancy, life expectancy, and costs. In brief, the UKPDS-OM is based on an integrated system of parametric equations that predict the annual probability of any of the above complications and Monte Carlo methods to predict the occurrence of events. The likelihood of the events is based on patient demographics, duration of diabetes, risk factor levels, and history of diabetes-related complications. Different treatment and management strategies are evaluated through their impact on risk factor levels. A key aspect of the model is its ability to capture the clustering or interaction of different types of complications at the individual patient level. The model is a probabilistic discrete-time multi-state model. Patients start with a given health status (e.g., age, sex, duration of diabetes, risk factor values, and no complications) and can have one or more nonfatal complications and/or die in any model cycle. When a patient experiences a complication, their utility is permanently decremented such that they accumulate quality-adjusted life-years at a slower rate. Utility decrements and costs associated with events are estimated from the same patient-level data set. Elements of the UKPDS Outcomes Model have been widely used in many other diabetes simulation models.

Key Publications:

Alva ML, Gray A, Mihaylova B, Leal J, Holman RR. The impact of diabetes-related complications on healthcare costs: new results from the UKPDS (UKPDS 84). Diabetic Medicine 2015;32:459-466

Alva M, Gray A, Mihaylova B, Clarke P. The effect of diabetes complications on health-related quality of life: the importance of longitudinal data to address patient heterogeneity. Health Econ 2014; 23(4):487-500.

Leal J, Hayes AJ, Gray AM, Holman RR, Clarke PM. Temporal Validation of the UKPDS Outcomes Model Using 10-Year Post trial Monitoring Data. Diabetes Care 2013;36:1541-1546

Hayes AJ, Leal J, Gray AM, Holman RR, Clarke PM. UKPDS Outcomes Model 2: a new version of a model to simulate lifetime health outcomes of patients with type 2 diabetes mellitus using data from the 30 year United Kingdom Prospective Diabetes Study: UKPDS 82. Diabetologia 2013;56:1925-1933.

Clarke PM, Gray AM, Briggs A, Farmer AJ, Fenn P, Stevens RJ, Matthews DR, Stratton IM, Holman RR. A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS 68). Diabetologia 2004;47:1747-1759.

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Alternative Email: Philip.clarke@unimelb.edu.au

Website: https://www.dtu.ox.ac.uk/outcomesmodel/

Conference Sessions

(Based on submitted abstracts)

Instructions for Presenters in Conference sessions

- All Presenters will have around 20 minutes each (including 5 minutes questions).

- A laptop computer and projector will be provided for your presentation, using Microsoft PowerPoint software.

- The time allocated for presentation will be 15 minutes. Allow a minimum of one minute per slide, preferably 2–3 minutes.

- Arrive at the meeting room before the session begins and contact the session convener for last-minute instructions or changes in the schedule.

- During your presentation, state the purpose and objectives of the paper, the main concepts and results, and the conclusions. Avoid too much detail.

- Do not exceed the allocated time for your presentation.

- Presenters will be given an opportunity to make a pdf of a paper or slides available on the conference website.

Saturday 17 September 2016 - 1:30-3:00pm

Presenter	Authors	Title	Location (Chair)
Jose Leal	Jose Leal, Peter Eibich, Alastair M Gray, Rury Holman, Alison J Hayes, Philip M Clarke	Life-expectancy and costs for people with type 2 diabetes	**Building 21 Lecture Hall (Andrew Palmer)**
Harry Smolen	JC Gahn, X Yu, S Perk, DR Murphy, and HJ Smolen	Estimating the cost effectiveness of a patient-directed mealtime insulin titration algorithm	
Patrick J. O'Connor	Patrick J. O'Connor MD MA MPH, Todd P. Gilmer Ph.D., JoAnn M. Sperl-Hillen MD, Heidi L. Ekstrom MA, A. Lauren Crain Ph.D	Impact of Improving Diabetes Care on Quality Adjusted Life Expectancy (QALE) and Costs: A 30-Year Perspective	
Neda Laiteerapong	Neda Laiteerapong, Jennifer M. Cooper, Rochelle N. Naylor, Elbert S. Huang	Cost-effectiveness of Individualizing Glycemic Goals for U.S. Adults with Type 2 Diabetes	
Annabelle S. Slingerland	Slingerland AS, Choudhurry R, Redekop WK, Niessen LW	Follow up on the 6th Mount Hood Conference: filling the gap to model type 1 diabetes.	**Building 06-4th Floor (Talitha Feenstra)**
Dan Pollard	Daniel Pollard, Alan Brennan, Jackie Elliott	The estimation of post-treatment HbA1c using a beta regression in the Sheffield Type 1 Diabetes Policy Model.	
Oleh Syarkevych	Olha Zalis'ka, Oresta Piniazhko, Danylo Halytsky Lviv, Oleh Syarkevych	Cost analysis of insulin treatment regimens for patients with type 1 diabetes in the Ukrainian setting	
William Valentine	Pollock RF, Brändle M and Valentine WJ	A Covaried, Target-Based, Patient-Level MOdel of HbA1c Progression in Type 1 Diabetes	
An Tran-Duy	An Tran-Duy, Philip Clarke	Data structures and algorithms for modelling conditionally random events in a probabilistic discrete-time simulation model for type 2 diabetes: exploitation of modern C++ features	**Building 20- 1st Floor (Alatasir Gray)**
Helen A. Dakin	Helen A. Dakin, Rury R. Holman, José Leal, Alastair M. Gray	Combining parameter and sampling uncertainties within diabetes clinical outcome simulation models	
Phil McEwan	Phil McEwan, Volker Foos, Mark Lamotte	Replacing input probability distributions with mean values can bias simulation output: an illustration using the CORE diabetes model.	
Volker Foos	Volker Foos, Phil McEwan, Mark Lamotte	Implications of introducing patient heterogeneity in cost effectiveness modeling	

Saturday 17 September 2016 - 3:30-5:00pm

Title	Authors	Title	
Balazs Nagy	A Zsólyom, L Szilberhorn, B Németh, B Nagy, Z Vokó	Impact of adjusting diabetes treatment pathways according to disease severity – the case of HbA1c and macular oedema	Building 21 Lecture Hall (Patrick O'Connor)
Joel Smith	Joel Smith, John Forbes	Breaking away from central tendencies: Using more flexible and informative economic models of the cost of healthcare for people with type 2 diabetes	
Michael Willis	Michael Willis, Christian Asseburg, Cheryl Neslusan, Andreas Nilsson	The Importance of HbA1c Evolution in Modeling Type 2 Diabetes Mellitus	
Pierre Johansen	Pierre Johansen, Michael Willis, Andreas Nilsson, Christian Asseburg, Cheryl Neslusan,	The Importance of Capturing Cardiovascular Benefits Not Mediated by Traditional Risk Factors in Type 2 Diabetes Mellitus (T2DM) Modeling	
Josan S Yauw	Josan S Yauw, Joline W Beulens, Fariza Badloe[2], Linda M Peelen[1], Giel Nijpels[3], Amber A van der Heijden[3]	Prediction models for the risk of retinopathy in persons with type 2 diabetes. A systematic review	Building 06-4th Floor (Neda Laiteerapong)
Christian Asseburg	Christian Asseburg,[1] Michael Willis,[1] Cheryl Neslusan,[2] Agata Schubert[3]	The Importance of Considering Differences in Network Meta-analyses (NMAs): An Example of Sodium Glucose Co-transporter 2 Inhibitors (SGLT2i)	
Jose Leal	Jose Leal[1], Talitha Feenstra[2], Eva Pagano[3]	Challenges and opportunities for decision modelling from the onset of pre-diabetes onwards	
Xinyang Hua	Xinyang Hua, Thomas Wai-Chun Lung, Andrew Palmer, Lei Si, William H. Herman, Philip Clarke	How consistent is the relationship between improved glucose control and modelled health outcomes for people with type 2 diabetes? A systematic review	
Alastair Gray	Alastair Gray[1], Oliver Rivero-Arias[2], Shelby D Reed[3], Yanhong Li[3], Rury Holman[4], Jose Leal	Can delaying onset of diabetes be cost-effective? A simulation study based on NAVIGATOR data	Building 20- 1st Floor (Alan Brennan)
Christina Tzogioua	Simon Wiesera , Christina Tzogioua, Sascha Hessa, Klaus Eichlera, Marie Azoulayb, Sima Djalalic, Thomas Rosemannc, Michael Brändled	Costs of hypoglycemia in insulin-treated diabetes in Switzerland: a health-economic analysis	
Melat Mamo	Melat Mamo, Meaza Demissie	Self care practice and its associated factors among diabetic patients in AddisAbaba public hospitals, cross sectional study	
Josh Knight	Knight J Clarke P Jackson R	The impact of statins on HbA1c levels in individuals tested in a community setting	