Economics Modelling and Diabetes: The Mount Hood Five Challenge

Clinical Research Centre, Skåne University Hospital in Malmo, 18th & 19th September 2010.

Conference Program

Sponsors:

The Organising Committee of Mount Hood Five Challenge Conference in Malmo 2010 would like to thank the following sponsors for their generous contributions.

Detailed results of the challenges have been removed from the program, but a summary is published in Palmer AJ, Clarke P, Gray A, Leal J, Lloyd A, Grant D, Palmer J, Foos V, Lamotte M, Hermann W, Barhak J, Willis M, Coleman R, Zhang P, McEwan P, Betz Brown J, Gerdtham U, Huang E, Briggs A, Carlsson KS, Valentine W. Computer modeling of diabetes and its complications: a report on the Fifth Mount Hood challenge meeting. Value in Health. 2013 Jun;16(4):670-85. doi: 10.1016/j.jval.2013.01.002. Epub 2013 Apr 18.

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Economics, Modelling and Diabetes: The Mt Hood Five Challenge, Malmo 2010

Location

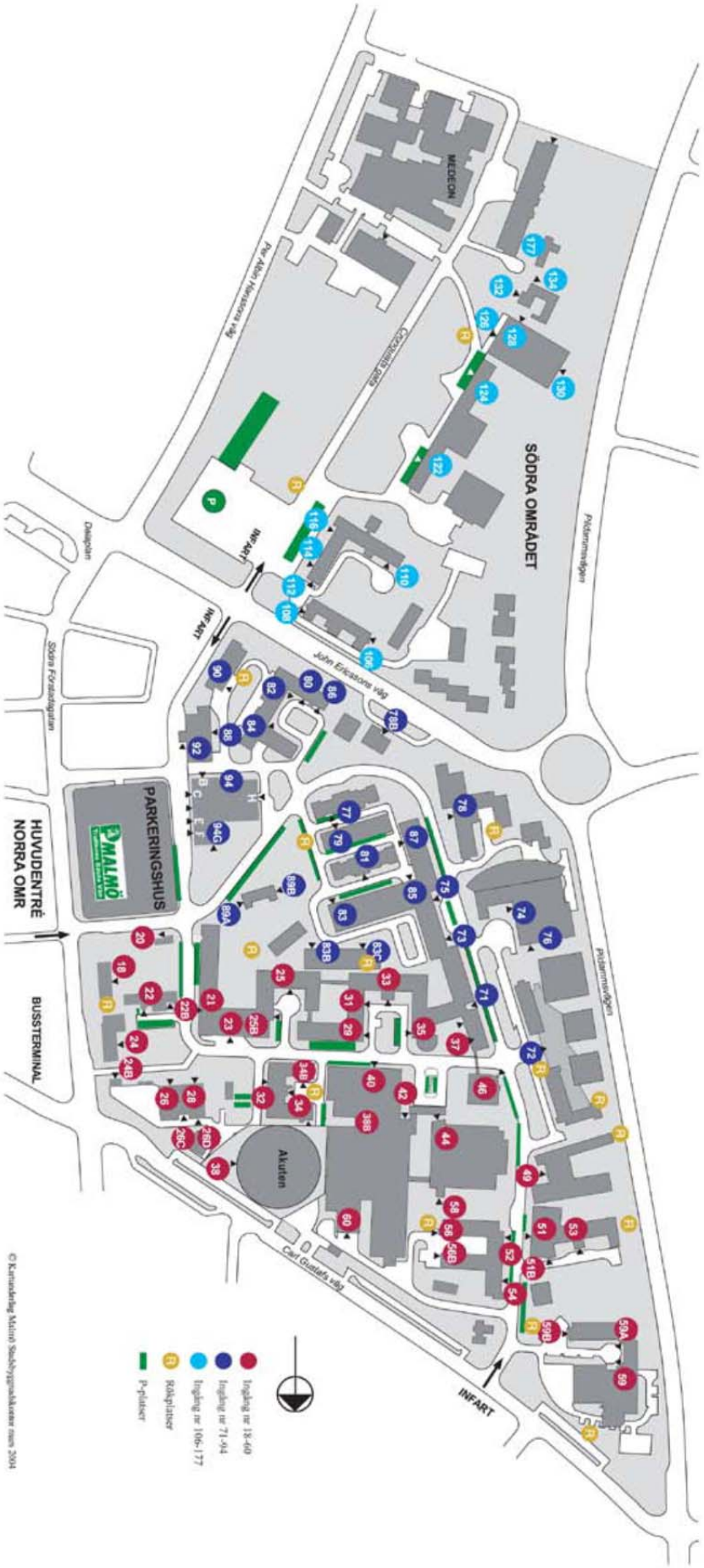
The symposium will be held at the Clinical Research Center (CRC) Skåne University Hospital in Malmö (SUS). Use Entrance 72, Skåne University Hospital in Malmö (see map next page). CRC is 200 metres on the right from the entrance of the hospital complex.

Registration

Registration will be from 8:30am onward on Saturday 18th September. The conference will conclude at 12:45pm Sunday 19th September.

Mt Hood 5 Organising Committee

Philip Clarke, University of Sydney (Chair)
Jonathan Brown, International Diabetes Federation
Ulf Gerdtham, Lund University
Alastair Gray, Oxford University
Bill Herman, University Michigan
Elbert Huang University of Chicago
Andrew Palmer, University of Tasmania
Katarina Steen Carlsson, Lund University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List of participants
List of participants

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William Willis, Johnson and Johnson
Michael Willis, Swedish Institute for Health Economics
Veronique Wyffels, Johnson and Johnson
Ping Zhang, Centre for Disease Control and Prevention

Economics, Modelling and Diabetes:

Mount Hood 5 Challenge

Day 1	Saturday 18th September 2010		
8:30-9:15am	**REGISTRATION**		
9:15-9:30am	**Welcome – A/Prof Philip Clarke & Prof Ulf Gerdtham** **Location: Clinical Research Centre AULA**		
9:30-11:00am	***Mt Hood Five: Validation Challenges*** **Chair: Prof Andrew Palmer** 8 Groups presenting a (very brief) overview of their model & interpretation of major validation results (15 minutes per model) CORE/IMS Model Michigan Model IHE model UKPDS Outcomes Model UKPDS Risk Equation CDC/RTI model Cardiff Model EBMI **Location: Clinical Research Centre AULA**		
11:00-11:30am	***Tea and Coffee***		
11:30am-12:30pm	***Discussion of Validation Results*** **Chair: Prof Bill Herman** **Location: Clinical Research Centre AULA**		
12:30-1:30 pm	***Lunch***		
1:30-3:00pm	**Conference session 1** 4 Abstracts (20 minutes each) **CRC Seminarierum 2**	**Conference session 2** 4 Abstracts (20 Minutes each) **CRC Seminarierum 3**	**Conference session 3** 4 Abstracts (20 Minutes each) **CRC Seminarierum 6**
3:00-3:30pm	***Tea and Coffee***		
3:30-4:30pm	**Conference session 4** 3 Abstracts (20 minutes each) **CRC Seminarierum 2**	**Conference session 5** 3 Abstracts (20 Minutes each) **CRC Seminarierum 3**	**Conference session 6** 2 Abstracts (20 Minutes each) **CRC Seminarierum 6**
4:30-5:30pm	**Business meeting: Where to next with Mt Hood?** Chair: A/Prof Philip Clarke **Location: Clinical Research Centre AULA**		
7:00pm onwards	**CONFERENCE DINNER** "RETRO" located at Norra Skolgatan 24 in Malmö (at the Hotel More)- 500 metres from conference centre Maximum Seating for 90 persons		

Economics, Modelling and Diabetes:

Mount Hood 5 Challenge

Day 2	Sunday 19th September 2010
9:00-11:00am	***How should we deal with uncertainty in diabetes models?*** Chair: **Dr Elbert Huang** **Prof Andy Briggs:** Key issues surrounding capturing and reporting uncertainty (45 minutes) Overview of Mt Hood 5 Uncertainty Challenge results & discussion by participating modelling groups (75 Minutes) **Location: Clinical Research Centre AULA**
11:00-11:30am	***Tea and Coffee Break***
11:30am-12:15noon	***What have the Mt Hood 5 challenges revealed*** Further discussion of challenges & discussion of write-up of proceedings Chair: Jonathan Brown **Location: Clinical Research Centre AULA**
12:15noon-12:45pm	**Key challenges for future diabetes models- Wrap up session** Chair: Dr Katarina Steen Carlsson General discussion **Location: Clinical Research Centre AULA**
12:45-1:30pm	***Lunch (close)***

Mt Hood 5 Challenges

Mt Hood 5 Challenges (as distributed to modelling groups)

The Mt Hood 5 challenge will be in two parts. The first part will involve validation of outcomes of several recent clinical trials, using baseline information on patients and the effect of interventions on intermediate risk factors such as HbA1c. The second challenge will be on how models deal with uncertainty. Modelling groups can choose to participate in either or both challenges.

All groups participating in challenges will be expected to supply data in structured format at least two weeks prior to the meeting (4th September 2010). To facilitate this we will circulate a spreadsheet to report the results by the end of June. The required information will include: primary and secondary outcomes; assumed risk factor time paths; summary statistics for baseline population. This information will be circulated to all participants of Mt Hood 5 in material which will be available at the conference.

Any questions regard challenges should be addressed to philipc@med.usyd.edu.au.

Challenge 1: Validation of recent clinical trials

To expand on the validation exercise from Mt Hood 4, we seek external validation again 3 recent clinical trials that have examined interventions that attempt to modify key risk factors for complications of type 2 diabetes. For each of these clinical trials modelling groups will attempt to predict the outcome using information on the baseline characteristics of the population and information contained in the publications concerning these trials.

If groups have access to additional information that is no public (e.g. patient level data) this should not be used to produce the primary results, but could used to produce an additional set of results to examine whether model performance could be improved with access to additional data.

For all these studies the validation exercise will involve predicting the primary and as many secondary endpoints as possible at the end of the study. Results should be reported as the proportion of patents that experience each type of event (i.e. so as to match reported outcomes in the papers below).

Three studies will be used in the challenge:

Lipid lowering intervention: ASPEN (Efficacy and Safety of Atorvastatin in the Prevention of Cardiovascular End Points in Subjects With Type 2 Diabetes), which was reported in DIABETES CARE, VOLUME 29, NUMBER 7, JULY 2006.

Glucose lowering intervention: ADVANCE study (Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes, NEJM Volume 358:2560-2572 June 12, 2008 Number 24 .

Blood Pressure lowering intervention: ACCORD blood pressure arm (Accord Study group, Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus, NEJM, N Engl J Med 2010;362:1575-85.

Finally as an optional additional challenge:

Glucose lowering intervention from ACCORD study (N Engl J Med 2008;358:2545-59.)

If anyone has difficulty obtain these articles please let me know.

Challenge 2: Capturing uncertainty in simulation models.

An important aspect of simulation modelling is to understand and report the uncertainty surrounding of any results produced by the model. The purpose of the second challenge is to understand how different simulation model deal with uncertainty.

1. Understanding the degree of random variation in simulation model.

   This first simulation will only apply for models that have some probabilistic aspect to them such as Monte Carlo simulation models.

   For a person with characteristics defined in Table 1 run them through 1000 simulations of their history of complications over their remaining lifetime. Each simulation should involve a different set of random numbers. For each of the 1000 simulations report whether they have experience one of the following events at 5 years; 20 years; lifetime outcomes.

   Myocardial infarction;
   Stroke;
   Heart failure;
   Blindness;
   Amputation;
   Renal failure;
   Death from any cause.

2. Understanding the degree of parameter uncertainty in the model

   Assume there are two groups of 1000 identical patients with the characteristics reported in Table 1. One group receives an intervention that permanently lowers HbA1c by 0.5% from time paths it would have taken without the intervention.

Simulate these interventions and report estimates the proportion of individuals that will experience one of the following events at 5 years; 20 years and for lifetime outcomes*. Also report 95% confidence intervals around these estimates.*

Myocardial infarction;
Stroke;
Heart failure;
Blindness;
Amputation;
Renal failure;

Finally estimate life expectancy and QALYs differences and the differences in health care costs (where possible using the cost of complications reported in Table 2). Report 95% CI around these results;

Optional additional challenge:

Repeat the same exercise for:

1. Systolic Blood pressures reduction of 10mmHg;
2. Increase in HDL cholesterol of 0.4 (mmol/l);

Table 1: Characteristics of a hypothetical patient

Characteristic	"Input value"
Ethnicity	White
Gender	Male
Age (y)	55
Duration of diabetes (y)	5
BMI (Kg/m2)	30
Current smoker	N
Current risk factors	
Chol (mmol/l)	5.2
HDL (mmol/l)	1.2
Sys BP (mmHg)	133.6
Dias BP (mmHg)	85.6
HbA1c (%)	7.49
No prior complications	

Table 2: Default values for costs and utility

	At time of event			In subsequent years	
	Fatal	**Non-fatal**	**Utility decrement**	**Cost**	**Utility decrement**
No Complications	5000	374	0.785	374	0
Non acute CHD	2,696.00	2,696.00	-0.090	891.00	-0.090
MI :	1,366.00	5,199.00	-0.055	856.00	-0.055
Heart failure :	3,007.00	3,007.00	-0.108	1,054.00	-0.108
Stroke :	4,011.00	3,180.00	-0.164	601.00	-0.164
Amputation :	10,354.00	10,354.00	-0.280	598.00	-0.280
Blindness :	1,358.00	1,358.00	-0.074	575.00	-0.074
Renal failure :	30,000.00	30,000.00	-0.263	30,000.00	-0.263

Models Participating in the Challenges

1. **Evidence-Based Medicine Integrator (EBMI)**
2. **Cardiff Model**
3. **CDC/RTI model**
4. **CORE Diabetes Model**
5. **ECHO-T2DM**
6. **Michigan Model**
7. **UKPDS Outcomes Model**
8. **UKPDS Risk Equation**

Model descriptions

Evidence-Based Medicine Integrator (EBMI)

Lead Presenter : Jonathan Betz Brown, MPP, PhD, Portland, OR, USA

Description of the model:

EBMI is a free, open-source medical computation framework that integrates three kinds of knowledge using stochastic discrete-event microsimulation: (1) risk estimates derived from patient data, (2) comparative-effectiveness estimates obtained from randomized clinical trials, and (3) genetic knowledge from basic research. EBMI is designed to be used with electronic medical to identify all potential treatments for every patient and to recommend next treatment steps. It also can generate or accept population data to do management, trial-planning, policy and research studies. EBMI's direct use of local data and RCT results maximizes clinical safety. Assumptions are quickly changeable as new trials appear. The EBMI code and documentation are at http://code.google.com/p/ebmi.
Currently, EBMI simulates all major macro- and microvascular complications of type 2 diabetes, plus associated expenditures and utility effects. Highly detailed protocols use natural dosage increments for all classes of diabetes and CVD treatments, plus user-defined classes. Event-driven protocols are also programmable.
EBMI is designed to safely integrate reliable knowledge with local circumstances, not to predict the results of treatments that have not been trialled (although the user can hypothesize effects). Therefore, the traditional concept that simulators should be validated against trials does not apply to EBMI in the usual way. It is important to demonstrate that EBMI can reproduce the relative effects of treatment trials, and also reproduce local data where it is to be used. The EBMI version used in Mt Hood 5 is derived from, and has been validated against, the Kaiser Permanente Northwest diabetes registry.

Key Publications describing the model:
No publications yet describe the new model-the Evidence Based Medicine Integrator, EBMI, detail. Documentation has been posted to the EBMI open-source code website, http://code.google.com/p/ebmi The following publication uses the new EBMI and includes some description in an appendix:
Shany Blum; Moshe Vardi; Jonathan B Brown; Allen Russell; Uzi Milman; Chen Shapira; Nina S Levy; Rachel Miller-Lotan; Rabea Asleh; Andrew P Levy. Vitamin E Reduces Cardiovascular Disease in Individuals with Diabetes Mellitus and the Haptoglobin 2-2 Genotype. Pharmacogenomics. 2010;11(5):675-684.

Cardiff model

Lead Presenter: Phil McEwan, Cardiff Research Consortium Ltd

Other team members attending:

1. Klas Bergenheim, AstraZeneca

Description of the model:

The Cardiff cost-utility model estimates the long-term economic and health impact of managing patients with Type 2 diabetes mellitus (T2DM). The core model is coded in C++ and linked to a Microsoft Excel front end. The model is a fixed time increment (yearly) stochastic simulation with a 40 year time horizon.
The model utilises the UKPDS 68 outcomes equations to predict macrovascular and microvascular complications. The dynamic profile of modifiable risk factors is controlled via user controllable equations which also includes dynamic changes to weight. The model is designed to evaluate a treatment and control pathway, each of which are comprised of up to three lines of therapy. Therapy escalation is controlled via user defined HbA1c thresholds.
The model incorporates the risk of hypoglycaemia, which is captured in the model using annual rates for the occurrence of symptomatic and nocturnal hypoglycaemic events and an annual probability for the occurrence of severe hypoglycaemic events; these events are associated with immediate cost and utility consequences.
The model is capable of running with mean values, with probabilistic inputs and user-defined data with outputs for costs per life year gained; cost per quality adjusted life year gained in addition to the number, cost and utility consequence of all events occurring within the model.

Key Publications describing the model:

1.McEwan P, Bergenheim K, Yuan Y, Tetlow T, Gordon J. Assessing the Relationship between Computational Speed and Precision: A Case Study Using a Stochastic Simulation Model in Diabetes Care. Pharmacoeconomics. 2010;28(8):665-674.
2.McEwan P, Evans M, Bergenheim K, Yuan Y. Understanding the inter-relationship between improved glycaemic control, hypoglycaemia, and weight change within a long-term economic model. Diabetes, Obesity and Metabolism 2010;12(5):431-6.
3.McEwan P, Evans M, Tetlow T, Bergenheim K, Yuan Y. Population modelling of oral treatment strategies in the glycaemic management of Type 2 diabetes: assessing the trade-off between improved glycaemic control and increased hypoglycaemia and weight gain. Accepted. Diabetes, Obesity and Metabolism 2010;12(7):623-30
4.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 (DiabForecaster). Current Medical Research and Opinion 2006;22(1):121.

The CDC-RTI Diabetes Cost-Effectiveness Model

Lead Presenter: Ping Zhang, PhD
Centers for Disease Control and Prevention Atlanta, GA, USA

Description of the model:

The CDC-RTI Diabetes Cost-Effectiveness Model is a Markov simulation model of disease progression and cost-effectiveness for type 2 diabetes that follows patients from diagnosis to either death or age 95 years.
The model simulates development of diabetes-related complications on three microvascular disease paths (nephropathy, neuropathy, and retinopathy) and two macrovascular disease paths (coronary heart disease and stroke). In the model, progression between disease states is governed by transition probabilities that depend on risk factors and duration of diabetes. Interventions affect the transition probabilities and resulting complications. Model outcomes include disease complications, deaths, costs, and quality-adjusted life-years.

Key Publications describing the model:

1. CDC Diabetes Cost-Effectiveness Group. Cost-effectiveness of intensive glycemic control, intensified hypertension control, and serum cholesterol level reduction for type 2 diabetes. JAMA 2002 May;287(19):2542-2551.
2.Hoerger TJ, Harris R, Hicks KA, Donahue K, Sorensen S, Engelgau M. Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. Ann Intern Med 2004;140(9):689-699.
3. Herman WH, Hoerger TJ, Brandle M, Hicks K, Sorensen S, Zhang P, et al.; Diabetes Prevention Program Research Group. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. Ann Intern Med 2005;142(5):323-332.
4. Hoerger TJ, Hicks KA, Sorensen SW, Herman WH, Ratner RE, Ackermann RT, et al. The cost-effectiveness of screening for prediabetes among overweight and obese U.S. adults. Diabetes Care 2007;30(11):2874-2879.
5.Hoerger TJ, Segel JE, Zhang P, Sorensen SW. Validation of the CDC-RTI Diabetes Cost-Effectiveness Model. RTI Press Methods Report; 2009.

IMS CORE Diabetes Model

Lead Presenter: Adam Lloyd, IMS Health, Health Economics and Outcomes Research (HEOR), London, UK

Other team members attending (name and affiliation):
1. David Grant, IMS Health HEOR, London, UK
2. Volker Foos, IMS Health HEOR, Basel, Switzerland
3. James Palmer, IMS Health HEOR, Basel, Switzerland
4. Martin Knudsen, IMS Health HEOR, Copenhagen, Denmark

Brief Description of the model:

The IMS CORE Diabetes Model is a non-product-specific, diabetes policy analysis tool that performs real-time simulations. The model evaluates intensive or conventional insulin therapy, concomitant oral antidiabetic agents and lipid-lowering therapies, aspirin and angiotensin-converting enzyme inhibitor usage, and screening and treatment strategies for microvascular and end-stage complications. Disease progression is based on a series of inter-dependent Markov sub-models that simulate diabetes-related complications (angina, myocardial infarction, congestive heart failure, stroke, peripheral vascular disease, diabetic retinopathy, macular edema, cataract, hypoglycemia, ketoacidosis, nephropathy and end-stage renal disease, neuropathy, foot ulcer and amputation). Each sub-model uses time-, state- and diabetes type-dependent probabilities derived from published sources, and utilizes tracker variables to overcome the memory-less properties of standard Markov models. The progression of relevant physiological parameters (e.g. glycohemoglobin, systolic blood pressure, triglycerides, body mass index, etc.) is simulated, based on long-term epidemiological data, and event risk is continuously updated based on these risk factors. Analyses, including first- and second-order Monte Carlo simulations, can be performed on patient cohorts with either type 1 or type 2 diabetes, defined in terms of age, gender, baseline risk factors, pre-existing complications and comorbidities. The model is adaptable, allowing the inclusion of new clinical and economic data as it becomes available, and facilitates the investigation of new hypotheses. The creation of country-, health maintenance organization- or provider-specific versions of the model is possible. The reliability of simulated clinical outcomes has been tested, with results validated against those reported by clinical trials and epidemiological studies.

Key Publications describing the model:

Palmer AJ, Roze S, Valentine WJ, et al. The CORE Diabetes Model: projecting long-term clinical outcomes, costs and cost-effectiveness of interventions in diabetes mellitus (types 1 and 2) to support clinical and reimbursement decision-making. Current Medical Research and Opinion 2004; 20: S5-S26.

Palmer AJ, Roze S, Valentine WJ, et al. Validation of the CORE Diabetes Model against epidemiological and clinical studies. Current Medical Research and Opinion 2004; 20: S27-S40.
Pratoomsoot C, Smith HT, Kalsekar A, et al. An estimation of the long-term clinical and economic benefits of insulin lispro in Type 1 diabetes in the UK. Diabetic Medicine 2009; 26: 803-814.
Sullivan SD, Alfonso-Christnacho R, Conner C, Hammer M, Blonde L. A simulation of the comparative long-term effectiveness of liraglutide and glimepiride monotherapies in patients with type 2 diabetes mellitus. Pharmacotherapy 2009; 29(11): 1280-1288
Palmer JL, Knudsen MS, Aagren M, Thomsen TL. Cost-effectiveness of switching to biphasic insulin aspart from human premix insulin in a US setting. Journal of Medical Economics 2010; 13:212-220.

ECHO-T2DM

Lead Presenter: Michael Willis, IHE, Sweden

Other team members attending:
1. Ulf Persson, IHE, Sweden
2. Christian Asseburg, ESiOR Oy, Kuopio, Finland; and Department of Pharmacy, University of Eastern Finland, Finland
3. Cheryl Neslusan, J&J Pharmaceutical Services, LLC, USA
4. Jianming He, J&J Pharmaceutical Services, LLC, USA

Description of the model:

ECHO-T2DM is a (2nd order) stochastic, micro-simulation model that consists of Markov health states representing the development and consequences of key micro- and macrovascular complications. Specifically, a cohort of hypothetical T2DM patients is generated from a probability distribution of initial patient characteristics (both demographic and health-related). HbA1c is the core driver of the model, affecting both outcomes and changes in treatment. These patients are initially treated with one of two user-specified treatment paradigms and their evolving health and treatment needs are simulated annually until the end of the user-defined time horizon or death (if occurring sooner).
Patient health is recorded using health states that capture the existence and severity of retinopathy, of nephropathy, of neuropathy, and of CVD (as defined in the UKPDS), updated on an annual basis.
Diabetes treatment is governed by an algorithm that seeks to maintain user-defined HbA1c treatment thresholds. User-defined inputs control the algorithm, which is, thus, quite flexible. Treatment affects HbA1c, but can also affect BMI, SBP, and lipid values. Treatments can be escalated or discontinued and new agents added to meet HbA1c goals. Treatments can also cause AE's, including importantly hypoglycemic events, which can lead to discontinuation or non-compliance.
The model applies costs to both blood glucose control and to treatment of the diabetic complications that arise, both event costs and state costs. The model also calculates QALYs for each of the simulated patients, using QALY decrements for each of the diabetic complications. The model outcomes consist of incidence rates for each of the complications and AEs, ICERs, Net Monetary Benefits, and the Cost-Effectiveness Acceptability Curve.

Key Publications describing the model:
1. Asseburg C, Willis M, Persson U, et al, "Validation of the IHE/J&J Economic Simulation Model of Type 2 Diabetes Mellitus (T2DM)", Presented at the 14th Annual ISPOR International Meeting, May 18, 2009.
2. Willis M, Assesburg C, Neslusan C, et al, "The Economic Importance of Metabolic Memory in the Treatment of Type 2 Diabetes Mellitus (T2DM)", Presented at the ADA Annual Congress, Orlando, USA, 2010.
3. Asseburg C, Willis M, He J, et al, "The Impact of Adherence on the Costs And Benefits of Intensive lifestyle Management (ILM) in Overweight and Obese Patients

at High risk for Type 2 Diabetes Mellitus (T2DM)", Presented at the 14th Annual ISPOR International Meeting , Orlando, USA, 2009.
4. Willis M, Asseburg C, Neslusan C,et al, “The Economic Impact of Weight Loss for Patients with Newly Diagnosed Type 2 Diabetes Mellitus (T2DM) in the US”, Presented at the 15th Annual ISPOR International Meeting, Atlanta, USA, 2010.
5. He J, Willis M, Asseburg C, et al, "Simulation of the Chinese Diabetes Treatment Guideline Using IHE/JJPS Type 2 Diabetes Model", Presented at the 7th world Congress, iHEA, Beijing, 2009.

Michigan Model for Diabetes

Lead Presenter: Jacob Barhak Ph.D.
Application Systems Analyst / Programmer Senior Department of Biostatistics School of Public Health University of Michigan

Other team members attending:
1. William H. Herman , MD, MPH - Director of the Michigan Diabetes Research and Training Center (MDRTC), University of Michigan 2.

Description of the model:

The Michigan Model for Diabetes has been substantially revised and is implemented using newly-developed software that models chronic diseases. This software provides an environment for model design, estimation and simulation, as well as a convenient Graphical User Interface (GUI) to: 1) define parameters; 2) define populations; 3) generate populations from distributions; 4) create a new disease model or modify an existing model; 5) simulate the behavior of a given base population using a defined model enhanced by a set of simulation rules; 6) analyze and report simulation results. These capabilities support models expressed as multiple nested extended Markov sub-processes. It uses Monte-Carlo to simulate disease progression.
Thus the software system is very general and can accommodate many chronic disease models in the same software environment, which enables it to compare and contrast results from alternative models.

The current version of the software simulates disease progression in the following disease processes: diabetes, diabetic nephropathy, diabetic neuropathy, diabetic retinopathy, cardiovascular disease (CVD), and cerebrovascular disease. It calculates costs and health utility scores for user-specified periods of time. Among other options, the user can specify frequency of examination, which results in diagnosis, and rate of compliance with treatment, which affects rate of disease progression.

The Michigan Model for Diabetes is publicly available under a General Public License (GPL). Model and software, as well as its validation results, can be downloaded from the Michigan Diabetes Research and Training Center (MDRTC) web site:
http://www.med.umich.edu/mdrtc/cores/DiseaseModel/index.html

We will present a description of the model and its validation, and an example of its results.

Key Publications describing the model:

[1] Zhou H, Isaman DJM, Messinger S, Brown MB, Klein R, Brandle M, Herman WH: A Computer Simulation Model of Diabetes Progression, Quality of Life, and Cost. Diabetes Care 28:2856-2863, 2005. DOI:
10.2337/diacare.28.12.2856

[2] Barhak J., Isaman D.J.M., Ye W., Lee D.: Chronic disease modeling and simulation software. Journal of Biomedical Informatics, Article in Press, Published online 2010, DOI:10.1016/j.jbi.2010.06.003
[3] Coffey JT, Brandle M, Zhou H, Marriott D, Burke R, Tabaei BP, Engelgau MM, Kaplan RM, Herman WH: Valuing health-related quality of life in diabetes. Diabetes Care 25:2238-2243, 2002. DOI:
10.2337/diacare.25.12.2238
[4] Brandle M, Zhou H, Smith BRK, Marriott D, Burke R, Tabaei BP, Brown MB, Herman WH: The direct medical cost of type 2 diabetes.
Diabetes Care 26:2300-2304, 2003 DOI: 10.2337/diacare.26.8.2300
[5] Isaman, D.J.M., Herman, W.H., & Brown, M.B. A discrete-state and discrete-time model using indirect estimates. Statistics in Medicine
2006 25(march): 1035-1049. DOI: 10.1002/sim.2241

UKPDS Outcomes Model

Lead Presenter: Prof Alastair Gray, Health Economics research Centre, University of Oxford

Other team members attending:
1. Jose Leal, Health Economics research Centre, University of Oxford
2. Philip Clarke, Sydney School of Public Health, University of Sydney

Description of the model:

UKPDS Outcomes Model (UKPDS OM) is a widely used simulation model for type 2 diabetes based on patient level data from the United Kingdom Prospective Diabetes Study. It models the first occurrence of each of the seven diabetes-related endpoints (MI, angina, stroke, heart failure,amputation, renal failure and blindness in one eye) and to death in order to estimate expected QALYs. In brief, the UKPDS OM is based on an integrated system of parametric equations which predict the annual probability of any of the above endpoints occurring and Monte Carlo methods to predict the occurrence of events.

A key aspect of this 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 illness-death model, rather than a Markov model. Patients start with a given health status (e.g. no complications) and can have one or more non-fatal complications and/or die in any model cycle by comparing estimated probabilities with random numbers drawn from a uniform distribution ranging from zero to one to determine whether an event occurs. When a patient experiences a complication, their utility is permanently decremented such that they accumulate QALYs at a slower rate.

Aspects of the UKPDS OM have been widely used in many other diabetes simulation models.

An implementation of the model is available under licence from Oxford University.For further details of the model see http://www.dtu.ox.ac.uk/Outcomesmodel.

Key Publications describing the model:

1.Clarke P. Gray A. Holman R. “Estimating utility values for health states of type 2 diabetic patients using the EQ-5D (UKPDS 62)", Medical Decision Making Vol. 22. pp. 340-349, 2002.
2.Clarke PM, Gray AM, Legood R, Briggs AH, Holman R. “The impact of Diabetes-related Complications on Health Care Costs: Results from the United Kingdom Prospective Diabetes Study”, Diabetic Medicine, Vol. 20, pp.442-450, 2003.

3.Clarke PM, Gray AM, Briggs A, Farmer A, Fenn P, Stevens R, Matthews D, Stratton IM, Holman R. A model to estimate the lifetime health outcomes of patients with Type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 68) Outcomes Model, Diabetologia Vol. 47 pp.1747–1759, 2004.
4.Clarke PM. Gray, A. Briggs A, Stevens R., Matthews D and Holman R. On behalf of the UK Prospective Diabetes Study (UKPDS 72) "Cost utility analyses of intensive blood-glucose and tight blood-pressure control in Type 2 diabetes" Diabetologia. 2005 May;48(5):868-77.
5. Leal J., Gray A.M., Clarke P.M. "Development of life expectancy tables for people with type 2 diabetes", European Heart Journal, 2009 30(7):834-839.

UKPDS Risk Engine

Lead Presenter: Ruth Coleman - University of Oxford

Brief Description of the model:

The UKPDS Risk Engine is a type 2 diabetes specific risk calculator based on over 50,000 patient years of data taken between 1977 and 2007 It is designed to provide estimates and 95% confidence intervals for cardiovascular disease risk in individuals with type 2 diabetes not known to have heart disease.
The risk estimates can be calculated for any given duration of type 2 diabetes based on current age, sex, ethnicity, smoking status, presence or absence of atrial fibrillation, presence or absence of microalbuminuria or worse and levels of HbA1c, systolic blood pressure, total cholesterol and HDL cholesterol.

Key Publications describing the model (list up to five):

1. Stevens RJ, Kothari V, Adler AI, Stratton IM, Holman RR
UKPDS 56: The UKPDS Risk Engine: a model for the risk of coronary heart disease in type 2 diabetes 2001 Clinical Science, 101, pp. 671-679
2. Kothari V, Stevens RJ, Adler AI, Stratton IM, Manley SE, Neil HAW, Holman RR
UKPDS 60: Risk of stroke in type 2 diabetes estimated by the UK Prospective Diabetes Study Risk Engine
2002 Stroke, 33 (7), pp. 1776-1781
3.Stevens RJ, Coleman RL, Adler AI, Stratton IM, Matthews DR, Holman RR
Risk Factors for Myocardial Infarction Case Fatality and Stroke Case Fatality in Type 2 Diabetes: UKPDS 66 2004 Diabetes Care, 27 (1), pp. 201-207
4. Holman RR, Coleman RL, Shine BSF, Stevens RJ Non-HDL cholesterol is less informative than the total-to-HDL cholesterol ratio in predicting cardiovascular risk in type 2 diabetes 2005 Diabetes Care, 28 (7), pp. 1796-1797
5.Stevens RJ, Sweeting TJ Estimation across multiple models with application to Bayesian computing and software development 2007 Statistics and Computing, 17 (3), pp. 245-252