**SUPPLEMENTARY MATERIAL**

**Table 1. Costs Of Medications and Type 2 Diabetes-Related Complications Applied in the Model (2013 SEK)**

| | Cost 1st year | Subsequent years | Reference |
|---|---|---|---|
| Metformin | 774 | 774 | http://www.tlv.se/ |
| Liraglutide (1.2mg daily) | 12183 | 12183 | http://www.tlv.se/ |
| Exenatide (2mg once weekly) | 12838 | 12838 | http://www.tlv.se/ |
| Sitagliptin (100mg daily) | 5453 | 5453 | http://www.tlv.se/ |
| Saxagliptin (5mg daily) | 5453 | 5453 | http://www.tlv.se/ |
| Vildagliptin (50mg daily) | 2314 | 2314 | http://www.tlv.se/ |
| NPH insulin 40 IU | 2523 | 2523 | http://www.tlv.se/ |
| NPH insulin 60 IU | 3784 | 3784 | http://www.tlv.se/ |
| Lancet | 142 | 142 | http://www.tlv.se/ |
| Test strip | 855 | 855 | http://www.tlv.se/ |
| ACE-inhibitors 20mg/day | 773 | 773 | http://www.tlv.se/ |
| Statin 20mg/day | 497 | 497 | http://www.tlv.se/ |
| Fibrate | 1646 | 1646 | http://www.tlv.se/ |
| BDR | 1139 | 1139 | http://www.skane.se/srvn |

| | | | |
|---|---|---|---|
| PDR | 26838 | 1139 | http://www.skane.se/srvn |
| ME | 38526 | 12842 | http://www.skane.se/srvn |
| Severe visual loss | 8610 | 3675 | 1 |
| Symptomatic neuropathy | 8341 | 16684 | http://www.apoteket.se, http://www.tlv.se/ |
| Peripheral vascular disease | 73581 | 7358 | 2 |
| Lower extremity amputation | 252648 | 7358 | 2 |
| End-stage renal disease | 496319 | 743,470 | http://www.skl.se |
| Ischemic heart disease | 94251 | 3394 | 3 |
| Myocardial infarction | 79,921 | 1708 | 3 |
| Stroke | 163543 | 147130 | 4 |
| Congestive heart failure | 62852 | 4812 | 3 |
| Mild hypoglycaemia | 22 | - | 5 |
| Moderate hypoglycaemia | 88 | - | 5 |
| Major hypoglycaemia | 1435 | - | 5 |

ACE, angiotensin-converting-enzyme; BDR, background diabetic retinopathy; ME, macular edema; PDR, proliferative diabetic retinopathy;

**Table 2A. Utility Decrement of Health States Applied in the Model**

| Health State | Utility decrement | Reference |
|---|---|---|
| T2DM without complications | 0.817 | 6 |
| Stroke, first and subsequent | -0.111 | 6 |
| Ischemic heart disease | -0.052 | 6 |
| Myocardial infarction, first and subsequent | -0.055 | 7 |
| Congestive heart failure | -0.042 | 8 |
| End stage renal disease | -0.114 | 6 |
| Blindness | -0.057 | 9 |
| Neuropathy | -0.084 | 9 |
| Peripheral vascular disease | -0.061 | 9 |
| Amputation | -0.272 | 9 |
| Macroalbuminuria | -0.048 | 9 |
| Mild hypoglycaemia | -0.005 | 10 |
| Moderate hypoglycaemia | -0.006 | 10 |
| Major hypoglycaemia | -0.053 | 10 |

T2DM, type 2 diabetes

**Assumptions for Loss of Production for Type 2 Diabetes-Related Complications**

In the absence of published results, the authors made the following assumptions regarding relative loss of production compared to the average in the population by age and gender:

• −100% at end-stage renal disease;

• −50% at severe visual loss; lower extremity amputation (in current cycle); stroke (in current cycle); at second year and onwards after a second stroke; respectively;

• −25% at second year and onwards after lower extremity amputation; ischemic heart disease; all stages of myocardial infarction; in the second year after a stroke and until a subsequent stroke event; congestive heart failure; respectively.

The loss of production, and hence the indirect costs in absolute numbers, will thus depend age and gender of the cohort.

Table 3 shows age-specific expected annual salary adjusted for hours worked and labour force participation in Sweden year 2012 from Statistics Sweden; and annual cost of consumption based on [11] inflated to year 2012 using consumer price index. The salary and the cost of consumption are allowed to vary with age.

**Table 3. Expected Salary Based on Annual Full-Time Salary Weighted for Labour-Market Participation and Average Hours Worked in the Employed Population Age-Group (www.Scb.se) and Annual Cost of Consumption [11] Inflated to Year 2012.**

| Age Interval (years) | Expected Salary (SEK) | Annual cost of Consumption (SEK) |
|---|---|---|
| 0-19 | 3 358 | 162 766 |
| 20-34 | 180 900 | 155 625 |
| 35-49 | 277 340 | 140 342 |
| 50-64 | 246 767 | 173 493 |
| 65-74 | 11 114 | 173 915 |
| 75-84 | 1 261 | 199 149 |
| 85+ | 206 | 298 409 |

SEK, Swedish Krona

**Model Overview**

The Swedish Institute for Health Economics Cohort Model for type 2 diabetes (IHECM-T2DM) is a cohort model developed to estimate the cost-effectiveness of treatment intervention in T2DM. It uses Markov health states in order to capture important microvascular and macro vascular complications and premature mortality that may result from type 2 diabetes. The cycle length is one year and the maximum time horizon is 40 years. The model is highly flexible with most model parameters defined by the user on the input sheet. It can be run with either deterministic settings or stochastic settings in order to account for second-order uncertainty regarding the value of the underlying parameters.

The model was constructed in Microsoft® Excel 2013 (Reading, UK) with the aid of the built in Visual Basic for Applications (VBA). To enhance the flexibility of the model the input sheet contains a large number of parameters, which need to be defined by the user in order to run the model. These include baseline characteristics of the cohort, the treatment algorithm,

unit costs, health utility weights, choice of risk equations and a number of supporting parameters.

The baseline characteristics of the cohort are demographic characteristics, biomarker values and pre-existing diabetic complications; all of which are risk factors for complications and premature mortality. The progression of biomarkers, over time, interact with a user-defined treatment algorithm. When medications fail to control HbA1c adequately, doses can be altered and new medications added. The algorithm also includes possible medications for blood pressure, blood lipids and overweight/obesity.

The micro- and macro vascular health states in the model were selected to include the most important micro- and macro vascular complications related to type 2 diabetes. The model uses two parallel Markov chains. The first Markov chain consists of 120 different microvascular health states and the second Markov chain is made of 100 different macro vascular health states.

The microvascular health states comprise three complications: retinopathy (six stages, i.e., no retinopathy, background diabetic retinopathy, proliferative diabetic retinopathy, macular edema, proliferative diabetic retinopathy & macular edema, and severe vision loss), neuropathy (five stages, i.e., no neuropathy, symptomatic neuropathy, peripheral vascular disease, lower extremity amputation, and post lower extremity amputation) and nephropathy (four stages, i.e., no nephropathy, microalbuminuria, macroalbuminuria, and end-stage renal disease).

The macro vascular health states comprise four complications: ischemic heart disease (IHD), myocardial infarction (MI), stroke, and heart failure (HF). IHD and HF contain two stages (i.e., no event and event) and MI and stroke contain five stages (i.e., no event, first event, post first event, subsequent event, and post subsequent event).

Two identical cohorts are created from the user defined baseline characteristics. Each cohort is assigned a separate treatment algorithm. Treatment effects are applied to the biomarkers and the evolution of biomarkers is modelled annually until the predefined time horizon is reached.

Development and progression of complications and mortality is modelled next to the evolution of biomarkers. Time varying annual transition probabilities govern the progression of the cohort between different health states. The transition probabilities are calculated from the characteristics of the cohort (diabetes duration, demographics, biomarkers, etc.); mortality risk equations from either UKPDS-1 [12] or UKPDS-2 [13]; macro vascular risk equations from either NDR [14], UKPDS-1 [12] or UKPDS-2 [13]; and microvascular risk equations [15-17]. The user decides on choice of equation depending on the context for the research question and the relevant clinical setting.

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Figure 1. 35-year cumulative incidence of type 2 diabetes-related complications for the treatment strategies.