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Discussion Paper

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Abstract

The Sheffield Type 1 Diabetes Policy Model is a patient-level simulation model of type 1 diabetes and its associated complications, which was developed as part of the National Institute for Health Research Dose Adjustment for Normal Eating (DAFNE) research programme. The aim of this paper is to describe the conceptual modelling, model implementation, and model validation phases of the Sheffield Type 1 Diabetes Model development process. The model is highly flexible and has broad potential application to evaluate DAFNE, other diabetes structured education programmes, and other interventions for type 1 diabetes.

Introduction

Type 1 diabetes is a metabolic disorder characterised by an almost total deficiency in insulin that leads to higher than normal levels of glucose in patients' blood (termed poor glycaemic control). Once patients are diagnosed with type 1 diabetes they must remain on insulin replacement therapy for their lifetime. Type 1 diabetes is associated with long-term microvascular complications (neuropathy, nephropathy, retinopathy, and macular oedema) and macrovascular complications (myocardial infarction (MI), heart failure (HF), stroke, and angina) which can lead to serious consequences such as limb amputation, blindness, disability and death. These diabetes-related complications account for most of the increased morbidity and mortality associated with type 1 diabetes[1]. The risk of long-term complications is related to patients' glycaemic control, which is most commonly assessed using glycosylated haemoglobin (HbA1c), an average measure of blood glucose levels over time. Patients with type 1 diabetes are also at risk of acute complications: hypoglycaemia (excessively low blood glucose caused by taking too much insulin) and diabetic ketoacidosis (DKA) (high levels of ketones in the blood caused by high blood glucose levels). Both long-term and acute diabetic complications are associated with substantial healthcare costs and affect patients' quality of life (QoL) and their mortality risk.

In the UK it is recommended that all patients with type 1 diabetes are offered a structured education programme (SEP) to support their diabetes self-management[2]. The only SEP in the UK currently meeting the nationally agreed criteria is the Dose Adjustment For Normal Eating (DAFNE) course[3]. DAFNE is a five-day outpatient SEP aimed at providing adults with type 1 diabetes with the skills and confidence to estimate the carbohydrate content of meals and adjust their insulin doses to match food portions[4]. A randomised controlled trial (RCT) of 169 patients with type 1 diabetes demonstrated that DAFNE significantly improved HbA_{1c}, dietary freedom and overall QoL compared with no DAFNE, without increasing the rate of hypoglycaemia[5]. A published cost-effectiveness analysis of DAFNE compared with no DAFNE suggested that the intervention was cost-effective and would pay for itself within five years[6]. The National Institute for Health Research (NIHR) funded a five-year research programme to investigate in more detail the factors affecting the success of DAFNE[7]. The programme, entitled "Improving Management of Type 1 Diabetes in the UK: The DAFNE Programme as a Research Test-bed", was underpinned by health economic analyses.

The health economic analyses underpinning this research programme included the development of a new health economic model to evaluate the cost-effectiveness of evolving forms of the DAFNE intervention. This research was undertaken at the University of Sheffield. The aim of this paper is to describe the conceptual modelling, model

implementation, and model validation phases of the Sheffield Type 1 Diabetes Model development process. The paper first outlines how the model was conceptually designed, then describes how it was implemented in the simulation software Simul8® and the key features of the model and its inputs. The results of the internal validation are provided. Finally the paper presents a discussion of the strengths and weaknesses of the Sheffield Type 1 Diabetes Model.

Conceptual Modelling

The conceptual modelling phase of the model development process included two workshops with clinical and social science experts in diabetes, a systematic review of published models of type 1 diabetes, and structured decision making by researchers at the University of Sheffield. An initial workshop (Workshop 1) was held in June 2009 with invited clinical diabetes specialists (including a nurse specialist) and the University of Sheffield DAFNE health economics team to understand the natural history of type 1 diabetes. The next stage of the conceptual modelling process was a systematic review of previously published cost-effectiveness models of type 1 diabetes. A total of 65 papers, relating to 32 individual cost-effectiveness models, were selected for inclusion in the review (details available from the authors on request). A draft model structure including all potential diabetes-related complications was then developed based on the systematic review of previous cost-effectiveness models. In July 2010, the University of Sheffield DAFNE health economics team conducted a second workshop (Workshop 2) with clinical experts to discuss the results of the review and the proposed conceptual model. The final conceptual model was developed after discussions in the workshop and is as shown in Figure 1.

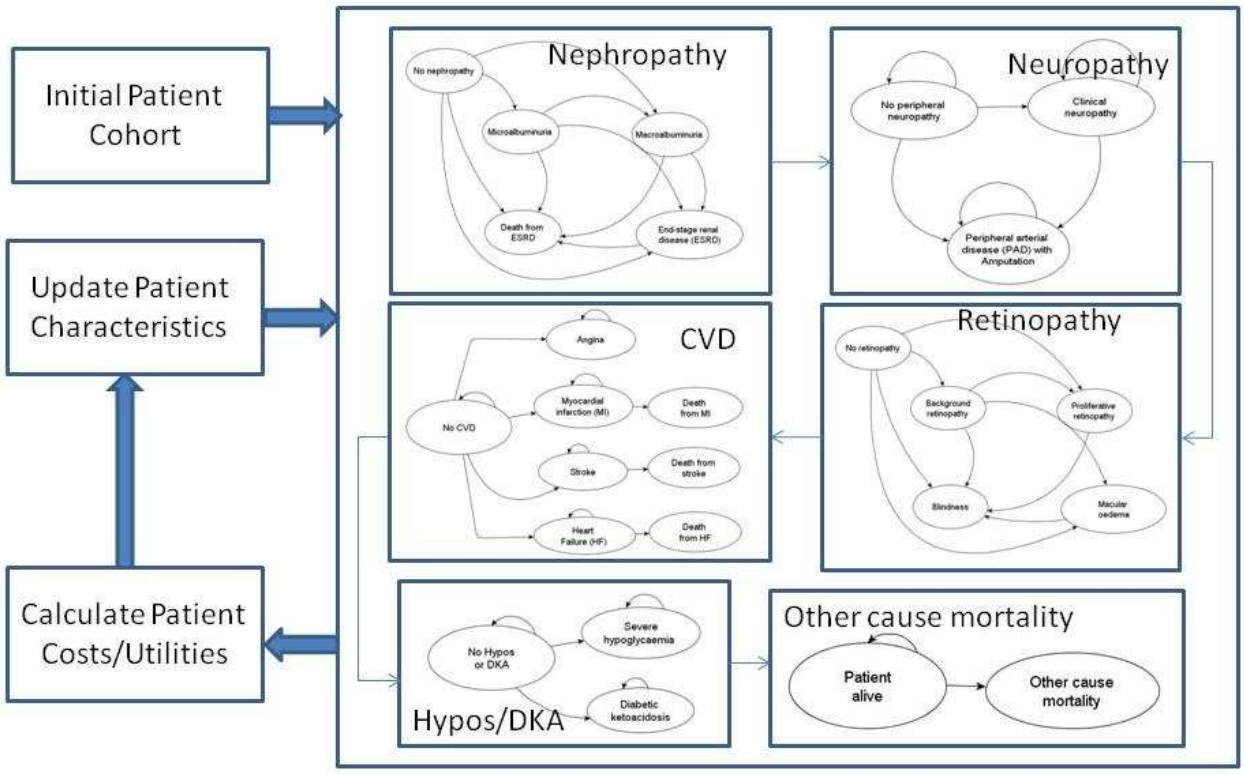
Model Description

The Sheffield Type 1 Diabetes Model is a flexible and comprehensive long-term simulated patient-level Markov model incorporating the most up-to-date methodologies (such as capturing parameter uncertainty, time profile of patient characteristics and including patient behaviour) to allow a number of cost-effectiveness evaluations.

The Sheffield Type 1 Diabetes model consists of a series of sub-models simulating the progression of each of the diabetic complications, acute complications and mortality in a given population with type 1 diabetes. The model allows each simulated patient to develop multiple complications and for the incidence of these complications to be dependent upon simulated patients' individual characteristics. The individual patient characteristics include demographics (age, gender and duration of diabetes), clinical variables (HbA1c, high density lipoprotein (HDL), smoking status, blood pressure and cholesterol), existing diabetes-related

complications and treatment status. The complications included in the model are nephropathy, retinopathy, neuropathy, severe hypoglycaemia, MI, stroke, HF and angina while the adverse events included hypoglycaemia and DKA, as shown in Figure 1. The progression of long-term diabetic complications are modelled using transition probabilities with an annual time cycle and the adverse events are modelled as annual incidence, for each individual patient based on their characteristics (patient behaviour can also be incorporated in the model by updating HbA1c and other variables over time). Each health state is associated with an annual cost and a utility value which is combined with the number of annual time cycles the patient spends in that health state to estimate costs and quality-adjusted life years (QALYs). Some disease progression events are associated with a one-off transition cost that is incurred in the transition year. Costs and QALYs are summed across time and patients to provide total and average cost and QALY estimates for use in cost-effectiveness analyses.

Figure 1. Structure of the Sheffield Type 1 Diabetes Model



Microvascular Complications

The risk of development and progression of nephropathy, neuropathy and retinopathy are modelled according to event rates reported in published randomised controlled trials (RCTs) and observational studies. Cohort Markov models were used to estimate annual

probabilities of transitioning between states within a particular complication, by combining data from multiple sources, assuming a reference HbA1c of 10%. The process was the same for all the microvascular complications (retinopathy, nephropathy, neuropathy and macular oedema) and full details of these methods are available from the authors on request.. For each microvascular complication, patients progress to the more severe health states within each annual time cycle according to the probabilities reported in Table 1. As the probabilities are estimated at the reference HbA1c of 10%, Eastman's method[8] was used to adjust the risk of background retinopathy, macular oedema, proliferative retinopathy, microalbuminuria, macroalbuminuria, and neuropathy for patients with different HbA1c levels (P_{HbA1c}) using the formula:

$$P_{HbA1c} = P_{HbA1c=10}(HbA1c/10)^{\beta} \qquad \text{(Equation 1)}$$

Where is the baseline probabilities $P_{HbA1c=10}$ are as shown in the Table 1 and the coefficients β are as shown in the footnote of Table 1. The rest of the transition probabilities are assumed to be independent of HbA1c levels.

Table 1. Annual probability of microvascular events

Neuropathy

Parameter	Base case value	Source(s)
Annual transition probabilities for microvascular complications		
Healthy to clinically confirmed neuropathy[a]	0.0354	DCCT,[9] Moss et al[10] (WESDR)
Healthy to PAD with amputation	0.0003	
Clinically confirmed neuropathy to PAD with amputation	0.0154	

[a] β coefficient for neuropathy = 5.30

Nephropathy

Parameter	Base case value	Source(s)
Annual transition probabilities for microvascular complications		
Healthy to microalbuminuria[a]	0.0436	DCCT[11], Wong el al[12] (WESDR), UKPDS 33[13]
Healthy to macroalbuminuria[b]	0.0037	
Healthy to ESRD	0.0002	
Healthy to death from ESRD	3.3e-06	
Microalbuminuria to macroalbuminuria[b]	0.1565	
Microalbuminuria to ESRD	0.0133	
Microalbuminuria to death from ESRD	0.0004	
Macroalbuminuria to ESRD	0.1579	
Macroalbuminuria to death from ESRD	0.0070	
ESRD to death from ESRD	0.0884	

[a] β coefficient for microalbuminuria = 3.25

[b] β coefficient for macroalbuminuria = 7.95

Retinopathy and macular oedema

Parameter	Base case value	Source(s)
Annual transition probabilities for microvascular complications		
Healthy to background retinopathy[a]	0.0454	WESDR XXII[14]
Healthy to proliferative retinopathy[b]	0.0013	
Healthy to macular oedema[c]	0.0012	
Healthy to blindness	1.9e-06	
Background retinopathy to proliferative retinopathy[b]	0.0595	
Background retinopathy to macular oedema[c]	0.0512	
Background retinopathy to blindness	0.0001	
Proliferative retinopathy to blindness	0.0038	
Macular oedema to blindness	0.0016	

[a] β coefficient for background retinopathy = 10.10

[b] β coefficient for proliferative retinopathy = 6.30

[c] β coefficient for macular oedema = 1.20

Macrovascular Complications

The risks of fatal and non-fatal macrovascular complications (MI, stroke, HF and angina) are modelled in three stages. First, the annual probability of experiencing any cardiovascular event, P_CVD, is estimated based on patients' characteristics as per Cederholm et al's 5-year cardiovascular risk model[15]:

$$P\_CVD = 1-\exp(-(-(\ln(1 - 5year\_CVD\_risk))/5)*1) \quad \text{(Equation 2)}$$

Where 5year_CVD_risk is given by the equation

$$5year\_CVD\_risk = (1-0.97136^{\exp[0.08426 \times (duration-28.014) + 0.04742 \times (age-duration-16.601) + 0.80050 \times (\log(TC:HDL)-1.1470) + 1.27275 \times (\log(HbA1c(DCCT))-2.0605) + 1.20050 \times (\log(systolic\ BP)-4.8598) + 0.56688 \times (smoker-0.1483) + 0.41995 \times (macroalbuminuria-0.1237) + 1.25506 \times (previous\ CVD-0.0612)]}) \quad \text{(Equation 3)}$$

The P_CVD probability is compared with a random number and if the random number is lower than the estimated probability then the patient is deemed to experience a cardiovascular event. Secondly, for those patients that experience an event, another random number is then used to determine what type of event it was (MI, stroke, HF or angina) using methods outlined in Palmer's 2012 thesis[16], based on data from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study[17]. Given a cardiovascular event, there is a 53% chance that is MI, 28% chance that it is angina, 12% chance that it is HF and 7% chance of stroke, as shown in Table 2. Thirdly, if the event experienced is an MI, stroke or HF, further random numbers are then used to

determine whether the event is fatal using methods outline in Palmer's 2012 thesis[16] and as shown in Table 3.

Table 2 Probability of different cardiovascular events

Parameter	Base case value	Gamma Distribution		Source(s)
		alpha	beta	
MI	0.53	1	0.0053	DCCT/EDIC[17]
Stroke	0.07	1	0.0007	
Angina	0.28	1	0.0028	
HF	0.12	1	0.00126	

Table 3. Probability of dying from cardiovascular events

Parameter	Base case value	Gamma Distribution		Source(s)
		alpha	beta	
MI death in hospital: Men	0.3930	1	0.00393	Sonke et al[18]
MI death in hospital: Women	0.3640	1	0.00364	Sonke et al[18]
MI death within one year: Aged < 65 years	0.1522	1	0.00152	Malmberg et al[19]
MI death within one year: Aged 65-75 years	0.1860	1	0.00186	Malmberg et al[19]
MI death within one year: Aged > 75 years	0.2508	1	0.00250	Malmberg et al[19]
Stroke death within 30 days	0.1240	1	0.00124	Eriksson et al[20]
Stroke death within one year	0.1063	1	0.00106	DCCT/EDIC[17]
HF death within one year	0.0570	1	0.00057	Anselmino et al[21]

Acute Complications

Two acute complications are simulated in the Sheffield Type 1 Diabetes Model: severe hypoglycaemia (defined as a hypoglycaemic event that the person with type 1 diabetes is unable to treat themselves) and DKA. The model parameters on the incidence of these two events were estimated from the DAFNE Research Database and the original DAFNE vs. no DAFNE RCT dataset[22]. Negative binomial models were developed to predict the annual rates and the results of the models are presented in Table 4. These models were inputted into R software to generate 10,000 samples of the number of severe hypoglycaemic and DKA episodes for patients with HbA1c values from 4% to 16% in 0.1% increments. The simulated samples were used to define probability distributions which random numbers were compared to within the model in order to determine how many events each simulated patient

had in each year (based on their HbA1c value and whether they had received DAFNE or not). Full details of these methods are available from the authors on request.

Table 4: Negative binomial models of the annual number of severe hypoglycaemic and DKA episodes

	Coefficient	Standard error	95% confidence interval
Severe hypoglycaemia			
Intercept B_{1H}	0.928	0.553	(-0.155, 2.012)
HbA1c B_{2H}	-0.113	0.064	(-0.259, -0.006)
DKA			
Intercept B_{1K}	-8.108	1.097	(-10.259, -5.958)
HbA1c B_{2K}	0.617	0.115	(0.392, 0.842)

[a] the negative binomial model is Log(number of events) = Intercept B_1 + (B_2*HbA1c) + error

Mortality

Patients can also die due to other causes (than due to ESRD and CVD) and this other cause mortality is modelled based on UK Interim Life Tables from 2008-10[23]. The model compares random numbers to gender- and age-specific annual probabilities of death and if the random number is lower than the probability of death then the patient is simulated to be dead. The model allows for other life tables to be selected e.g. there is an option to select US mortality data used in the CORE model[24] or mortality rates from the EAGLE model[25].

Treatment Effectiveness

HbA1c is the primary method of accounting for treatment effects in the model. However, intervention effects on other risk factors such as blood pressure, cholesterol or severe hypoglycaemia can also be incorporated and the profiles of the risk factors over time can be updated annually. HbA1c change as a result of an intervention has an impact on the risk of developing several microvascular complications and this effect is modelled based on Eastman's method[8] of adjusting the risk for changes in HbA1c levels as outlined above. For macrovascular complications, the coefficients for HbA1c, HDL, smoking status, blood pressure or cholesterol used in Cederholm et al[15] were used to adjust the probability of any cardiovascular event. Finally, the effect of interventions on outcomes such as hypoglycaemia and DKA can be input directly into the model by the user.

Utilities

The model calculates long-term QALYs by using utility values for the health states from the literature, reported in Table 5. Each health state is associated with a disutility value

(negative) which is added to the baseline utility to estimate the utility in the given health state. In case of multiple complications, the utilities are estimated by aggregating the disutilities of the multiple complications to the baseline utility. The lifetime QALYs for each patient are estimated based on patients' life expectancy and their corresponding annual utilities. The model has the flexibility to use alternative utility values as inputted by the model user.

Table 5: Base case utility parameters

Health state or event	**Utility**	**Beta distribution**		**Source(s)**
		Alpha	**Beta**	
Baseline utility values				
Male with type 1 diabetes and no complications	0.672	3022.176	1475.11	Coffey[26]
Utility decrements				
Complications or covariates	**Disutility**	**Gamma Distribution**		**Source(s)**
		Alpha	**Beta**	
Female with type 1 diabetes and no complications	-0.033	17.01563	0.001939	Coffey[26]
Blindness	-0.208	256	0.000813	Assumption
Macroalbuminuria	-0.017	2.89	0.005882	Coffey[26]
ESRD	-0.023	0.725652	0.031696	Coffey[26]
Clinically confirmed neuropathy	-0.055	30.25	0.001818	Coffey[26]
PAD with amputation	-0.116	25.43667	0.004561	Coffey[26]
Background retinopathy	-	-	-	Assumption
Proliferative retinopathy	-	-	-	Assumption
Macular oedema	-	-	-	Assumption
MI (assumed equal to HF)	-0.058	6.950413	0.008345	Coffey[26]
Stroke	-0.018	0.669421	0.026889	Coffey[26]
HF	-0.058	6.950413	0.008345	Coffey[26]
Angina	-0.090	24.00912	0.003749	UKPDS 62
Severe hypoglycaemia	-0.071	Samples	Samples	Walters et al[27]
DKA (assumed equal to severe hypo but without ongoing utility decrement due to fear of hypos)	-0.001	Samples	Samples	Walters et al[27]

Costs

The model calculates long-term costs by using health state costs values from the literature, as presented in Table 6. Each health state is associated with an annual cost which is combined with the number of annual time cycles the patient spends in that health state to estimate the costs. In case of multiple complications, the costs are estimated by aggregating the annual costs of the different complications. Some disease progression events are also associated with a one-off transition cost that is incurred in the transition year. All costs have been inflated to 2010/11 prices using Personal Social Services Research Unit inflation indices[28]. The model has the flexibility to use alternative cost profiles as inputted by the model user.

Table 6: Base case health state and transition costs

	Mean Costs	Gamma Distribution		Source
		Alpha	Beta	
Microalbuminuria (ongoing)	£34	100	0.34	BNF[29], McEwan et al[30]
Macroalbuminuria (ongoing)	£34	100	0.34	BNF[29], McEwan et al[30]
ESRD (ongoing)	£23,275	100	232.75	NHS Reference Costs[31]
Clin Conf Neuropathy	£258	100	2.58	Currie et al[32]
Clinical Neuropathy	£258	100	2.58	Assumed equal to clinical confirmed neuropathy
Diab foot syndrome	£2,713	100	27.13	NHS Reference Costs[31]
PAD with amputation (year 1)	£6,878	100	68.78	NHS Reference Costs[31]
PAD with amputation (ongoing)	£418	100	4.18	McEwan et al[30]
Background Retinopathy	£138	100	1.38	McEwan et al[30]
Proliferative Retinopathy	£630	100	6.30	McEwan et al[30]
Macular edema	£630	100	6.30	Assumed equal to proliferative retinopathy
Blindness (year 1)	£1,509	100	15.09	UKPDS 65[33]
Blindness (ongoing)	£494	100	4.94	UKPDS 65[33]
First MI (year 1)	£6,465	100	64.65	UKPDS 65[33]
Second MI	£6,465	100	64.65	UKPDS 65[33]
Final MI	£6,465	100	64.65	UKPDS 65[33]
MI (ongoing)	£861	100	8.61	UKPDS 65[33]
Fatal MI	£2,001	100	20.01	UKPDS 65[33]
First Stroke (year 1)	£4,154	100	41.54	UKPDS 65[33]
Second Stroke	£4,154	100	41.54	UKPDS 65[33]
First Stroke (ongoing)	£532	100	5.32	UKPDS 65[33]
Fatal Stroke	£5,414	100	54.14	UKPDS 65[33]
HF (year 1)	£3,637	100	36.37	UKPDS 65[33]
HF (ongoing)	£1,117	100	11.17	UKPDS 65[33]

Fatal HF	£3,637	100	36.37	UKPDS 65[33]
Angina (year 1)	£3,236	100	32.36	UKPDS 65[33]
Angina (ongoing)	£906	100	9.06	UKPDS 65[33]
Hypos	£178	100	1.78	Our calculation
Hypos with Comma	£702	100	7.02	Assumed equal to hypo w/ hosp
Hypos with Hospitalisation	£702	100	7.02	NHS Reference Costs[31]
DKA with Hospitalisation	£1,333	100	13.33	NHS Reference Costs[31]
Cost of a diabetic patient with no complications	£4,212	100	42.12	UKPDS 65[33]

Other Model details

The model was developed in line with the modelling good practice guidelines[34], recommendations from the American Diabetes Association[35] and published checklists for economic evaluation[36,37]. The model uses an annual discount rate of 3.5% as default (for both costs and QALYs, as recommended by NICE[38]). The model takes a health service perspective and uses a lifetime horizon (i.e. until all simulated patients have died) as default but the perspective and time horizon are flexible and can be set by the model user. The model is capable of performing probabilistic sensitivity analysis (PSA) allowing the effects of parameter uncertainty to be captured and the likelihood that interventions are cost-effective to be reported. The decision uncertainty is estimated using probability distributions (or a collection of random samples) for uncertain parameters. Where parameters were correlated and the covariance matrix was known, the random samples were drawn from a multivariate distribution.

Model Flexibility

The model, programmed in Simul8® software, was developed in a flexible manner that allows alternative sets of input data. The user can select whether to perform a deterministic analysis or conduct PSA, whereby model parameters are sampled from probability distributions. The model also has several option dialogs that allow the user to change the time horizon, discount rates for costs and QALYs, patient cohort characteristics, cohort size, treatment effects, and cost and utility sources. The Sheffield Type 1 Diabetes Model is highly flexible to allow for a large number of differing cost-effectiveness analyses to be undertaken.

Model Outputs

The model also allows tracking the history of each of the patients every year which allows easy verification and validation of the model. This includes the patient characteristics (i.e. HbA1c, SBP, HDL, etc), incidence of acute complications (i.e. hypos and DKA), and

microvascular and macrovascular complication status (i.e. disease progression) for each year the patient is alive. The aggregated numbers of patients in different health states are output each year and the total numbers of each event are also output at the end of the lifetime horizon. The costs and utility values, including the split of costs and disutilities by complication, are output for each patient for every year they are alive. The total discounted costs and QALYs are also output at the end of the lifetime horizon. When performing PSA, for the sake of efficiency, the model does not track the history of each patient every year but outputs the total costs, QALYs and the numbers of events in each complication for each PSA run.

Model Verification

Internal verification of the model code (visual logic in Simul8®) was conducted throughout the model implementation process. Patient characteristics and complication statuses were checked to ensure that they were changing as expected, and that patients were following expected routes. The costs and utility value outputs each year were checked against the patient status outputs for face validity. The aggregated outputs were also cross checked against the sum of individual patient outputs. Second-order validation was also conducted, whereby the risk model was internally validated against the data from which it was estimated.

Results

The results of second-order validation, which compared the model results with the data from the studies used to build the model, are as shown in Table 7. For microvascular complications, the normalised differences between model results and the published data ranged between 0-15%, except for the deaths from ESRD (which is more than 50%, but can be attributed to low event rates) and neuropathy events (~ 25%), with most difference less than 10%. For macrovascular complications, the normalised differences between model results and the published data ranged between 0-10%, with most differences less than 5%.

Table 7. Results of second order validation

Microvascular Complication	Source	Observed incidence (%)	Modelled incidence (%)
Nephropathy			
Microalbuminuria	DCCT[11]	20%	17%
Macroalbuminuria	Wong el al[12] (WESDR)	33%	27%

ESRD	Wong el al[12] (WESDR)	20%	18%
Death from ESRD	UKPDS 33[13]	0.26%	0.11%
Retinopathy			
BDR	WESDR XXII[14]	80%	64%
PDR	WESDR XXII[14]	39%	40%
ME	WESDR XXII[14]	26%	18%
Blindness	WESDR XXII[14]	2.3%	2.3%
Neuropathy			
Neuropathy	DCCT,[9]	9.3%	11.9%
Amputation	Moss et al[10] (WESDR)	9.6%	9.5%

Macrovascular Complication	**Source**	**Observed % of total events**	**Modelled % of total events**
MI	Cederholm et al,[15] Palmer's thesis[16]	53%	52%
Stroke	Cederholm et al,[15] Palmer's thesis[16]	7%	7%
HF	Cederholm et al,[15] Palmer's thesis[16]	12%	13%
Angina	Cederholm et al,[15] Palmer's thesis[16]	28%	29%
All CVD	Cederholm et al[15]	5.41%	5.61%

Discussion and Conclusions

The Sheffield Type 1 Diabetes Model has several key strengths. Firstly, the model is based on a structured conceptual modelling process that included input from multidisciplinary experts in the fields of clinical diabetes, psychology, diabetes education, and simulation modelling. This structured process ensured that the development of the model was evidence-based and that the model is fit for purpose from a number of disciplinary perspectives. Secondly, the model is highly flexible, allowing users to specify the characteristics of simulated patients, the time horizon, the cohort size, how treatment effects are accounted for, what outcomes are tracked by the model, and whether to run the model deterministically or probabilistically. This high level of flexibility allows the model to be adapted to the user's particular research question, setting, or population of interest and broadens the model's potential applications. Thirdly, the model is a patient-level simulation

which offers the advantage of being able to account for individual differences between patients. Fourthly, the model allows for patients' psychological and behavioural characteristics and their impact on treatment effectiveness to be incorporated into analyses. These two features of the model are particularly useful for investigating heterogeneous populations or subgroups. Finally, the model is structured to facilitate probabilistic sensitivity analysis which accounts for uncertainty in the model parameters and is recommended by several health technology assessment agencies including NICE[38].

Despite its many advantages the Sheffield Type 1 Diabetes Model also has some limitations. The Sheffield Type 1 Diabetes Policy Model used published data from non-UK settings to define risk of long-term complications, some of which are now very old. The risk of long-term macrovascular complications is dependent mainly on HbA1c and the effect of other risk factors is not captured, which might cause bias when evaluating interventions that affect risk factors other than HbA1c. Although the uncertainty in most of the parameters is incorporated into the model, uncertainty in some parameters (e.g. coefficients of the risk equations) is not captured.

Future Research/Planned Analysis

The Sheffield Type 1 Diabetes model was developed as part of the NIHR DAFNE research programme and several model-based evaluations are planned as part of that programme. Firstly, the model will be used to update the cost-effectiveness results reported by Shearer et al[6] to include the effects of DAFNE on long-term incidence of macrovascular as well as microvascular complications. Secondly, the model will be used to evaluate DAFNE delivered one day per week over five weeks compared with original DAFNE (five consecutive days) and thirdly, to evaluate DAFNE plus insulin pumps versus DAFNE plus MDI. The Sheffield Type 1 Diabetes model can also be used to evaluate any (i.e. non-DAFNE) interventions for type 1 diabetes. There are also plans to re-estimate the risk equations from longitudinal data from DAFNE research database and the long-term follow-up data from DCCT/EDIC. Several additions and adaptations to the model are also planned. Planned changes include addition of alternative cost and utility input databases from DAFNE research database and/or RCTs.

Summary

In summary, the Sheffield Type 1 Diabetes Model offers a new whole disease model of type 1 diabetes and its associated complications. The model development process was evidence-based and in consultation with multi-disciplinary experts. The model is highly flexible and has broad potential application to evaluate DAFNE, other diabetes structured

education programmes, and other interventions for type 1 diabetes. The model is under constant development and updating and several adaptations are planned.

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