The Cost and Productivity Consequences of Non-Severe Hypoglycaemic Episodes in Patients Treated with Sulfonylurea or DPP4 Dual Combination Oral Therapy

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Introduction

- Hypoglycaemia is a substantial healthcare burden in terms of resource utilization, costs and quality of life for people with type 2 diabetes [1].
- Non-severe hypoglycaemia episodes (NSHE) occur more frequently than severe episodes and account for the majority of hypoglycaemic burden; recent data has quantified the per-event costs of NSHE in terms of productivity loss and out-of-pocket (OOP) expenses [2].
- The aim of this study was to assess the implications for cost effectiveness (CE) associated with the inclusion of NSHE related indirect costs; illustrated by comparing the CE of sulfonylurea (SU) versus DPP-4 based dual combination blood glucose lowering regimens.

Methods

- The IMS CORE Diabetes Model (CDM, version 8.5) a validated and widely used simulation model [3,4] was initiated with baseline characteristics derived from NHANES (Table 1) and dual therapy and efficacy profiles for metformin + sulfonylurea (M+SU) versus metformin + DPP-4 (M+DPP4) obtained via a mixed treatment comparison [5] (Table 2). Mean duration on 2nd line therapy was set to 4 years with both cohorts escalating to a basal insulin regime.
- Published data was used to obtain workplace productivity costs, out-of-pocket (OOP) expenses and estimates of the frequency of NSHE [2]. This provided a mean weighted productivity cost for each NSHE of $26.43 for NSHE during working time (applied to 10.8% of subjects), $31.12 for NSHE outside working hours (applied to 8.5% of subjects) and $55.16 for nocturnal NSHE (applied to 14.1% of subjects). Mean OOP expenses were $35.56.
- We based this analysis on the profile of patients who reported NSHE frequency of 'daily' to "about 1/week" which was self-reported in 24.9% of T2DM patients surveyed [2]. Consequently, we modeled a scenario in which the impact of experiencing 52 NSHE per year was compared to a scenario with no NSHE to assess the impact of NSHE on overall cost-effectiveness.
- Health state utilities for type 2 diabetes and its complications were derived wherever possible from the UKPDS [6] Disutility values for major and minor hypoglycaemic events were -0.0118 and -0.0035, respectively, based on data published by Currie et al. [7].
- Cost of complications were taken from Pelletier et al. [8] and reported in Table 3; therapy costs reflect wholesale acquisition cost and are in USD. Future costs and benefits were discounted at 3%.

Table 1: Baseline demographics, risk factors and complications of patients in the simulated cohort.

Variable	Mean (SD)
Demographics	
Age (years)	56 (9.53)
Sex (% male)	0.56
Duration diabetes (years)	6 (2.35)
BMI (kg/m^2)	32.44 (6.3)
Racial characteristics	
% White	27
% Black	27
% Hispanic	42
% Asian	4
Risk factors	
HbA1c (%)	8.21 (0.54)
SBP (mm Hg)	132.8 (22.89)
Total cholesterol (mg/dl)	209.31 (44.5)
HDL cholesterol (mg/dl)	47.99 (14.12)
Smoker (%)	18
Pre-existing complications	
% history of myocardial infarction	9
% history of angina	9
% history of stroke	6
% history of heart failure	6
% history of microalbuminuria	28.2
% history of gross proteinuria	7.6
% history of end stage renal disease	0.4
% history of BDR	22.5
% history of PDR	3
% history of severe vision loss	2.2

Source: NHANES. SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; HDL, high density lipoprotein; BDR, background diabetic retinopathy; PDR, proliferative diabetic retinopathy

Results

- Overall, the model predicts modest gains in discounted life expectancy (0.02 years) and more substantial quality adjusted life expectancy gains (0.61 QALE) when comparing M+DPP4 versus M+SU with the greater QALE gain being driven by hypoglycaemia disutility.
- Scenarios including and excluding NSHE demonstrate the tangible impact of productivity costs and OOP expenses on total predicted costs with an incremental cost of $1,387 obtained when including NSHE costs, and $8,613 when excluding NSHE costs. Predictably, this substantially impacts the estimated cost-effectiveness results; with the incremental cost effectiveness ratio (ICER) increasing from $2,282 to $14,169 when including and excluding NSHE respectively (Table 4).
- Figures 1 and 2 reflect this finding in the ICER scatterplots and cost effectiveness acceptability curves.

Table 2: Treatment effects and costs applied in the analysis

	M + SU	M + DPP4
Change in baseline HbA1c (%)	-0.79	-0.8
Change in baseline BMI (kg/m^2)	0.702	0.199
NSHE per year*	52	0
Annual Treatment Cost	$67.6	$2,520.0

Source: McIntosh et al. [5] * Assumed profile based on Brod et al. [2]

Table 3: Cost data for treatment and hospitalisation of type 2 diabetes complications and patient management in the US

Event/item	Year 1	Year 2+
Myocardial infarction	$16,843	$1,546
Angina	$4,686	$553
Congestive heart failure	$12,766	$4,428
Stroke	$7,179	$587
Stroke death (within 30 days of event)	$6,592	
Peripheral vascular disease	$4,109	$1,462
Haemodialysis	$12,024	$8,750
Peritoneal dialysis	$18,023	$15,529
Transplant	$11,215	$6,123
Severe hypoglycaemia	$391	
Non-severe hypoglycemia	$42	
Statins	$49	
Aspirin	$27	
ACE inhibitors	$19	
Screening for MA	$21	
Screening for GRP	$32	
Retinopathy screening	$95	
Foot screening program	$133	
Non-standard ulcer treat (eg. Regranex)	$2,327	
Anti-depression treatment	$615	
Screening for depression	$33	

Conclusion

- The use of glucose lowering therapies that are associated with hypoglycaemia (such as sulfonylurea and insulin) are potentially associated with substantially greater economic consequences for employers and patients compared to those therapies with a low, or negligible, risk of hypoglycaemia (such as DPP-4 based regimes).
- In those patients at risk of hypoglycaemia and of a working age, failing to capture the full range of economic consequences associated with NSHE is likely to result in inflated estimates of cost-effectiveness. This is particularly relevant for NSHE given their relatively high frequency, particularly in patients treated with sulfonylureas and insulin.

Table 4: Summary costs, benefits and incremental cost effectiveness results for metformin + DPP4 versus metformin + sulfonylurea with and without NSHE costs

	Including NSHE Indirect Costs				Excluding NSHE Indirect Costs			
	Metformin + DPP4		Metformin + SU		Metformin + DPP4		Metformin + SU	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Life Expectancy (years)	11.88	0.20	11.86	0.20	11.88	0.20	11.86	0.20
Undiscounted Life Expectancy (years)	16.71	0.34	16.68	0.35	16.71	0.34	16.68	0.35
Quality-Adjusted Life Expectancy (years)	7.51	0.13	6.90	0.13	7.51	0.13	6.90	0.13
Undiscounted Quality-Adjusted Life Expectancy (years)	10.40	0.22	9.74	0.22	10.40	0.22	9.74	0.22
Total Costs	$71,655	$2,349	$70,268	$2,253	$71,617	$2,349	$63,005	$2,229
Difference	**Mean**	**95% LCI**	**95% UCI**		**Mean**	**95% LCI**	**95% UCI**	
Δ Life Expectancy	0.02	0.01	0.03		0.02	0.01	0.03	
Δ QALE	0.61	0.60	0.62		0.61	0.60	0.62	
Δ Total Costs	$1,387	$1,316	$1,458		$8,613	$8,541	$8,684	
Δ Costs/ Δ Life Expectancy	$73,882	-$36,165	$10,823		$458,692	-$354,677	$38,725	
Δ Costs / Δ QALE	$2,282	$2,343	$2,631		$14,169	$14,614	$15,184	

Figure 1: Scatter-plot of incremental costs and effectiveness values with and without NSHE costs applied

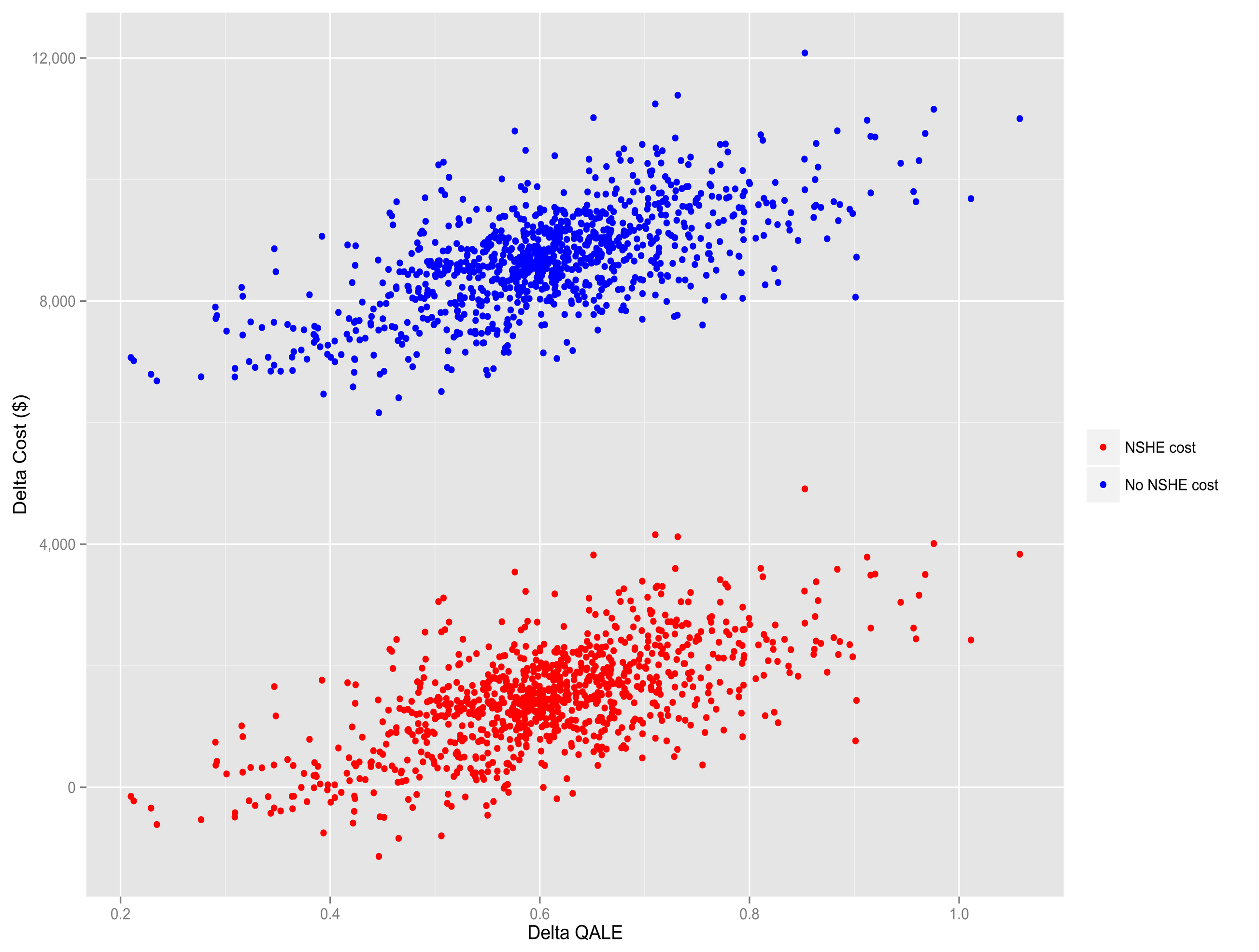
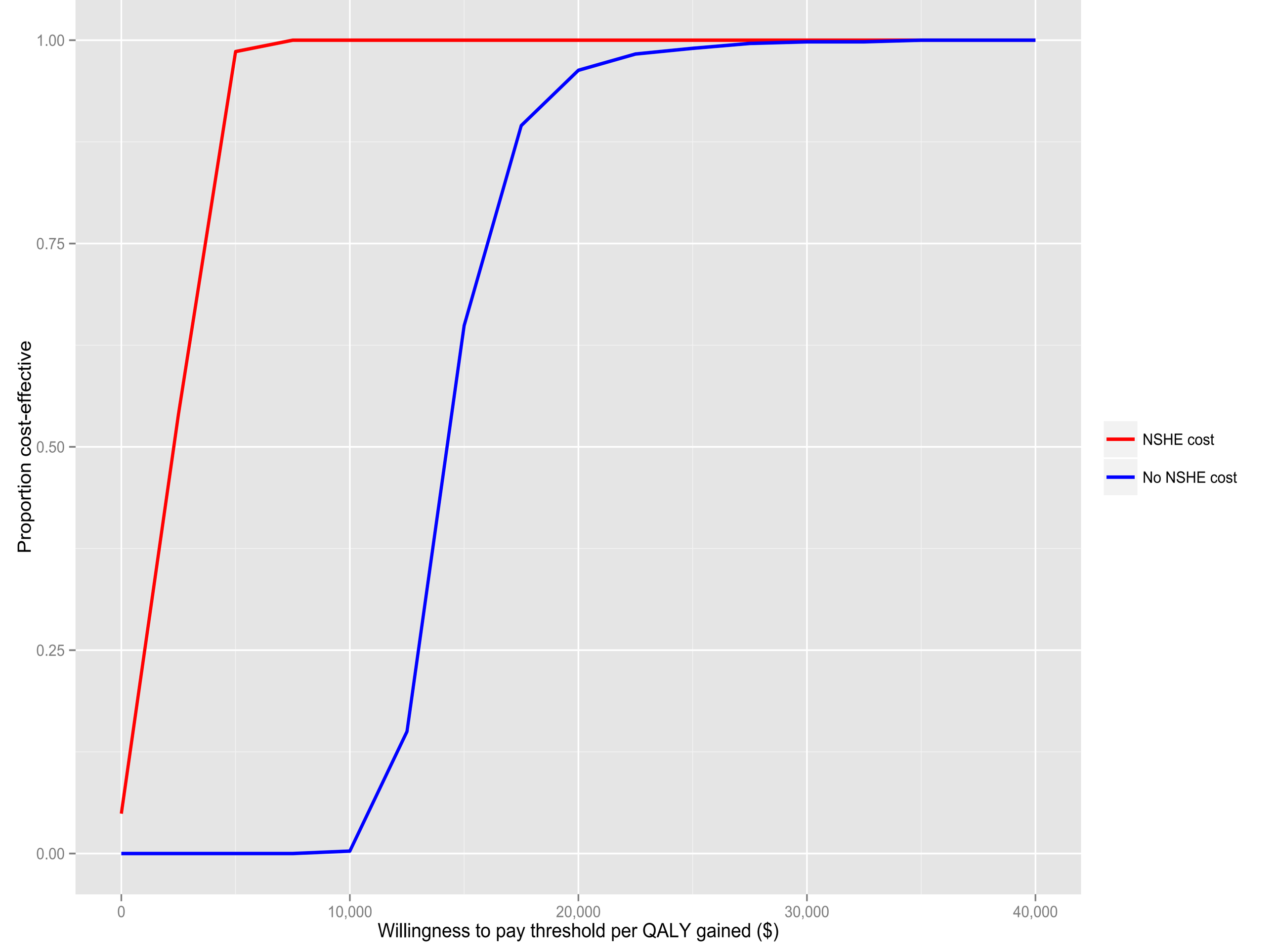


Figure 2: Cost effectiveness acceptability curves for the cost per quality adjusted life years gained with and without NSHE costs applied



References

[1] Williams et al. J Diabetes Complications. 2012;26(5):399-406
[2] Brod et al. Value Health. 2011;14(5):665-71
[3] Palmer et al. Curr Med Res Opin 2004;20:S27–40
[4] Palmer et al. Curr Med Res Opin 2004;20:S5–S26
[5] McIntosh et al. Open Medicine 2011;5(1):e38
[6] Clarke et al. Med Decis Making 2002;22:340–349
[7] Currie et al. Curr Med Res Opin 2006;22:1523–1534
[8] Pellitier et al. Appl Health Econ Health Policy 2008; 6 (2-3)

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