A health economic evaluation of the EDGE study using the IMS Core Diabetes Model

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BACKGROUND

- The observational, non-interventional EDGE (Effectiveness of Diabetes control with vildaGliptin and vildagliptin/mEtformin) study showed that vildagliptin is effective in patients with type 2 diabetes mellitus (T2DM) who have suboptimal glycemic control on metformin monotherapy in the real-world setting, confirming the results of previous randomized clinical trials (RCTs).
- Cost-effectiveness evaluations are typically based on RCT data, which offer high internal validity and are the gold standard in evaluating efficacy and short-term safety.
- Nevertheless, RCTs lack external validity and generalizability and there is a growing trend towards the complementary use of real-world data.

OBJECTIVE

- To perform a health economic evaluation of the EDGE study using an established diabetes outcomes model.

METHODS

- This study used the IMS Core Diabetes Model (CDM)[1,2], a validated[3] and established diabetes model, to evaluate the costs and outcomes of metformin + vildagliptin (M+V) compared to metformin + sulfonylurea (M+S), based on data derived from the EDGE study worldwide.
- EDGE was a prospective, 1-year, worldwide, 'real-life' observational, non-interventional study, which compared the effectiveness and safety of treatment intensification with vildagliptin vs other oral anti-diabetics, as per clinical judgment, in patients with T2DM inadequately controlled with monotherapy, across five world regions (East Asia, Europe, India, Latin America and the Middle East)[4].
- M+V was associated with HbA1c and BMI changes of –1.19% and 0.199kg/m^2, respectively. Corresponding data for M+S were –0.99% and 0.707kg/m^2, respectively.
- Published network meta-analysis data were used to populate the CDM with hypoglycemia rates and effectiveness data for basal insulin (BI) rescue therapy (applied to both arms at HbA1c threshold levels of 7.5%), and was associated with HbA1c and BMI changes of –0.82% and 0.545kg/m^2, respectively[5].
- Annual rates of hypoglycemia were estimated from odds ratios obtained from the same systematic review[5]; 8.22, 1.05 and 5.2 for M+S, M+V and BI add-on therapy to metformin vs. metformin monotherapy, respectively.
- The background risk of hypoglycemia with metformin monotherapy was sourced from the UKPDS 73[6]; 1.7 and 0.3 events per 100 patient-years for symptomatic and severe episodes, respectively.
- Annual treatment costs were expected to be $67.6, $2,520.0 and $1,869.7 for M+S, M+V and BI, respectively, based on wholesale acquisition costs (WAC) obtained from standard US list prices (2012). **Table 1** and **Table 2** summarize the key demographics and effectiveness data modelled.
- The model was run over a lifetime using standard CORE model costs ($ US) and health utilities, with costs and benefits discounted at 3.0%.

Table 1. Key baseline demographics

Demographics	Mean (SD)
Age (years)	57.8 (11.8)
Sex (% male)	54.8
Duration of diabetes (years)	5.5 (5.2)
BMI (kg/m^2)	29.0 (5.1)
HbA1c (%)	8.2 (1.3)

Table 2. Efficacy and treatment costs for M+V, M+S and BI

Treatment effects applied	M+V	M+S	BI
Change in HbA1c (%)	–1.19%	–0.99%	–0.82%
Change in BMI (kg/m^2)	0.199	0.707	0.545
Symptomatic hypoglycemia	1.785*	13.974*	8.84*
Severe hypoglycemia	0.315*	2.466*	1.56*
Annual treatment costs ($ US)	2,520	67.6	1,869.7

*Derived from odds ratios applied to baseline metformin reference group;
M+S = metformin + sulfonylurea; M+V = metformin + vildagliptin; BI = basal insulin

RESULTS

- Predicted quality-adjusted life expectancy (QALE) was 11.14 and 11.07 years in patients treated with M+V and M+S, respectively (**Table 3**).
- Total direct costs were estimated at $90,788 and $85,692 for patients treated with M+V and M+S, respectively (**Table 3**).
- Incremental differences between M+V and M+S were 0.07 for QALE and $5,096 for total costs, yielding an incremental cost-effectiveness ratio (ICER) of $72,800 (**Table 4**).
- Differences in total costs were predominantly therapy-related (**Figure 1**).

Table 3. Summary of costs and benefits for M+V versus M+S obtained from the CDM

	M+V			M+S		
	Mean	95% LCL	95% UCL	Mean	95% LCL	95% UCL
Life expectancy (years)	16.57	16.562	16.582	16.53	16.523	16.543
Undiscounted life expectancy (years)	25.53	25.509	25.55	25.43	25.412	25.453
Quality-adjusted life expectancy (years)	11.14	11.129	11.142	11.07	11.066	11.079
Undiscounted quality-adjusted life expectancy (years)	16.63	16.619	16.645	16.51	16.503	16.529
Direct costs ($ US)	90,788	90,716	90,859	85,692	85,621	85,762

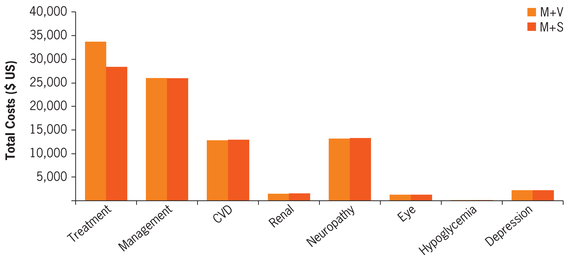
LCL = lower control limit; M+S = metformin + Sulfonylurea; M+V = metformin + vildagliptin; UCL = upper control limit

Table 4. Incremental cost-effectiveness results for M+V versus M+S obtained from the CDM

Difference [(M+V) - (M+S)]	Mean	95% LCL	95% UCL
Δ Life expectancy (years)	0.039	0.025	0.052
Δ QALE (years)	0.063	0.504	0.072
Δ Total costs ($ US)	5,096	4,996	5,195
Δ Costs/Δ QALE	$72,800	–	–

LCL = lower control limit; M+S = metformin + sulfonylurea; M+V = metformin + vildagliptin; UCL = upper control limit

Figure 1. Distribution of costs in patients treated with M+V and M+S



CVD = cardiovascular disease; M+S = metformin + sulfonylurea; M+V = metformin + vildagliptin

DISCUSSION

- The economic analysis of real-life observational studies provides useful data to quantify the extent to which new interventions provide value for money in clinical practice.
- Furthermore, the analysis of patient-level data from studies like EDGE would further enhance this output by providing clinicians and payers with data on both patient and geographic characteristics associated with maximum treatment-related health economic value.

CONCLUSIONS

- In the real-world setting, compared to sulfonylureas, vildagliptin was estimated to be cost effective using US ICER thresholds.
- These data further highlight the potential role of real-world data in assessing health economic value.

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Conflict of interest
PM declares no conflicts of interest and has not received funding in connection with this work.
ME has received speaker honoraria from Novartis, Novo Nordisk and Sanofi; research awards from Novo Nordisk and Sanofi; and is a member of the advisory panel for Novartis, Novo Nordisk and Sanofi.
VF declares no conflicts of interest and has not received funding in connection with this work.
PMP is employed by and owns shares in Novartis.

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