The role of patient level data in assessing health economic value: a case study using EDGE and the core diabetes model

PRM111

Foos V,[1] McEwan P,[2] Evans M,[3] Paldanius P[4]

[1]IMS Health, Basel, Switzerland; [2]Health Economics and Outcomes Research, Monmouth, United Kingdom; [3]University Hospital Llandough, Cardiff, United Kingdom; [4]Novartis Pharma AG, Basel, Switzerland

BACKGROUND

- The observational, non-interventional EDGE (Effectiveness of Diabetes with vildaGliptin and vildagliptin/mEtformin) study showed that vildagliptin is effective in patients with type 2 diabetes mellitus (T2DM) who have suboptimal glycaemic 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 patient-level data (PLD).

OBJECTIVE

- To perform a health economic evaluation based on data from EDGE study using an established diabetes outcomes model and PLD drawn from the cohort worldwide.

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 + sulphonylurea (M+S), based on data derived using PLD drawn 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]
- Due to cohort size limitation when running PLD through the CDM we extracted 6,000 patients treated with M+S (from a total available of 6,032 and a cohort of 6,000 patients with M+V were randomly drawn from the total number treated 18,325). **Table 1** reports the key baseline demographic profiles for both cohorts.

Table 1. Key baseline demographics

Demographics	M+V	M+S
Age, years – Mean (SD)	59.2 (11.3)	56.9 (11.5)
Sex, % male	50.6	55.5
Duration of diabetes, years - Mean (SD)	7.2 (6.5)	5.8 (4.8)
BM, kg/m^2 – Mean (SD)	30.0 (5.1)	28.7 (4.8)
HbA1c, % – Mean (SD)	8.1 (1.4)	8.2 (1.3)

M+V=metformin + vildagliptin; M+S=metformin + sulphonylurea; BMI=body mass index

- M+V was associated with HbA1c and BMI changes of –1.33% and –0.76 kg/m^2, respectively. Corresponding data for M+S were –1.05% and 0.0 kg/m^2, respectively (**Table 2**).

Table 2. Efficacy and safety of M+V and M+S

Efficacy and safety	M+V	M+S
Change in HbA1c, %	–1.33	–1.05
Change in BMI, kg/m^2	–0.76	0
Symptomatic hypoglycaemia, Number of events	1.785*	13.974*
Severe hypoglycaemia, Number of events	0.315*	2.466*

M+V=metformin + vildagliptin; M+S=metformin + sulphonylurea; *=per 100 patient years

- Published network meta-analysis data were used to populate the CDM with hypoglycaemia rates and effectiveness data for basal insulin (BI) rescue therapy (applied to both arms at HbA1c threshold levels of 8.5%), and was associated with HbA1c and BMI changes of –0.82% and 0.545 kg/m^2, respectively.[5]
- Annual rates of hypoglycaemia were estimated from odds ratios obtained from the same systematic review;[5] OR=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 hypoglycaemia with metformin monotherapy was sourced from the UKPDS 73 analysis;[6] 1.7 and 0.3 events per 100 patient years for symptomatic and severe hypoglycaemic episodes, respectively.
- Annual therapy costs applied were M+S £106.79 (Year 1) then £110.51 Year 2+ and M+V £410.53 (Year 1) £412.00 (Year 2+) as given in **Table 3**. Therapy escalation at HbA1c level of 8.5% was modeled assuming insulin glargine + metformin (cost £899.51 Year 1, £806.84 Year 2+).

Table 3. Treatment costs for M+V and M+S

Treatment Costs	M+V	M+S
Annual treatment costs	£411.00	£107.00
Year 1	£410.53	£106.79
Year 2+	£412.00	£110.51

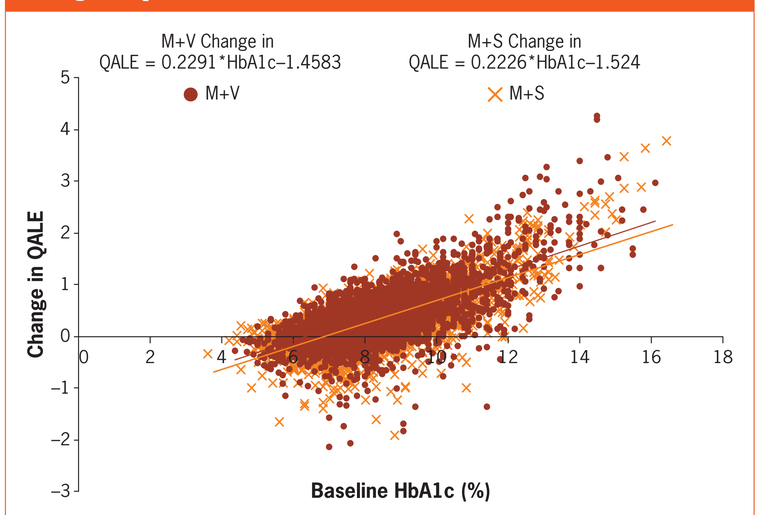
Therapy escalation at HbA1c of 8.5% was modeled assuming insulin glargine + metformin (cost £899.51 year 1, £806.84 year 2+) with the following parameters applied: change in HbA1c –0.82%; change in BMI +0.545; number of symptomatic hypoglycaemia events 8.84*; number of severe hypoglycaemia events 1.56* (*=per 100 patient years); M+V=metformin + vildagliptin; M+S=metformin + sulphonylurea

- Multivariate regression analysis of PLD output from CDM was undertaken using R 2.15.2. United Kingdom costs (£) and health benefits were discounted at 3.5%.

RESULTS

- Overall predicted life expectancy (LE) and quality-adjusted life expectancy (QALE) was 16.24 years and 11.01 years respectively.
- The relationship between baseline HbA1c and predicted change in quality adjusted life expectancy (QALE) as predicted by the CDM for M+S versus M+V is shown in **Figure 1**. Greater gains in QALE were observed in both M+S and M+V as baseline HbA1c increased.

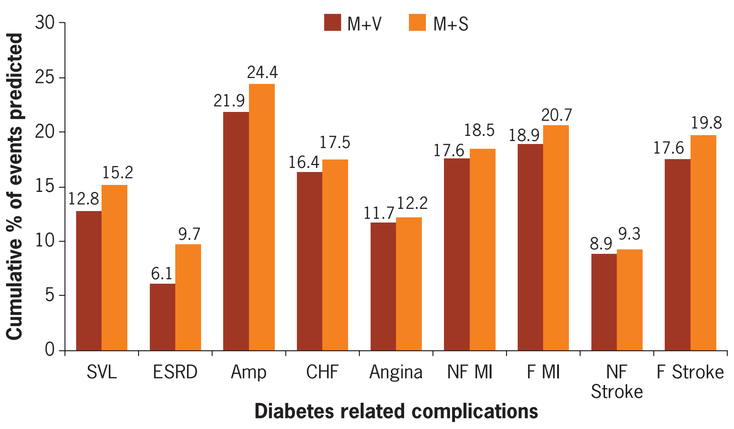
Figure 1. Relationship between baseline HbA1c and predicted change in QALE for M+V and M+S



Linear regression fits are shown for M+V and M+S separately; QALE=quality adjusted life expectancy; M+V=metformin + vildagliptin; M+S=metformin + sulphonylurea

- In multivariate analysis, adjusting for baseline characteristics, total costs were £28,512 (M+S) and £27,507 (M+V); this cost saving favouring M+V was driven by reduced complications and a longer time to insulin intensification compared to M+S (**Table 4a**).
- M+V was associated with an increase in QALE (0.12 years, p<0.001) and LE (0.08 years, p<0.001) compared to M+S (**Table 4b and 4c respectively**).
- Gains in LE and QALE favouring M+V were driven by an 8.6% and 6.8% reduction in the cumulative incidence of major micro-vascular and cardiovascular complications. **Figure 2** shows the reduction on the cumulative incidence of complications as predicted by the CDM.

Figure 2. Cumulative percentage of events predicted over a lifetime for M+V and M+S



SVL=severe vision loss; ESRD=end stage renal disease; Amp=amputations; CHF=congestive heart failure; NF=non-fatal; F=fatal; MI=myocardial infarction

M+V=metformin + vildagliptin; M+S=metformin + sulphonylurea

Table 4. Multivariate regression analysis

	Estimate	SE	t value	Pr (>|t|)
(a) Predicted lifetime costs (£)				
Intercept	28512.18	131.23	217.26	<2e-16***
Age, years	–586.75	6.87	–85.46	<2e-16***
Duration of diabetes, years	222.67	13.50	16.50	<2e-16***
Male	–1951.51	147.81	–13.20	<2e-16***
Baseline HbA1c, %	1061.26	55.76	19.03	<2e-16***
Baseline BMI, kg/m^2	42.99	14.84	2.90	0.00378**
M+V versus M+S	–1005.74	148.58	–6.77	1.36e-11***
Residual standard error=7976 on 11993 degrees of freedom; Multiple R-squared=0.4203; Adjusted R-squared=0.42; F-statistic=1449 on 6 and 11993 degrees of freedom; p-value ≤2.2e-16				
(b) Predicted change in quality adjusted life expectancy (QALE)				
Intercept	0.300	0.005	57.86	<2e-16***
Age, years	–0.003	0.000	–10.21	<2e-16***
Duration of diabetes, years	–0.001	0.001	–2.05	0.03999*
Male	–0.016	0.006	–2.67	0.00754**
Baseline HbA1c, %	0.223	0.002	101.34	<2e-16***
Baseline BMI, kg/m^2	0.001	0.001	1.22	0.22412
M+V versus M+S	0.124	0.006	21.23	<2e-16***
Residual standard error=0.3148 on 11993 degrees of freedom; Multiple R-squared=0.484; Adjusted R-squared=0.4837; F-statistic=1875 on 6 and 11993 degrees of freedom; p-value ≤2.2e-16				
(c) Predicted change in life expectancy (LE)				
Intercept	0.249	0.005	47.77	<2e-16***
Age, years	0.002	0.000	8.12	5.13e-16***
Duration of diabetes, years	–0.002	0.001	–3.44	0.000591***
Male	–0.022	0.006	–3.69	0.000225***
Baseline HbA1c, %	0.205	0.002	92.79	<2e-16***
Baseline BMI, kg/m^2	0.000	0.001	–0.36	0.716257
M+V versus M+S	0.077	0.006	13.09	<2e-16***
Residual standard error=0.3148 on 11993 degrees of freedom; Multiple R-squared=0.484; Adjusted R-squared=0.4837; F-statistic=1875 on 6 and 11993 degrees of freedom; p-value ≤2.2e-16				

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

M+V=metformin + vildagliptin; M+S=metformin + sulphonylurea; SE=standard error

CONCLUSION

- In the real-world setting, vildagliptin was estimated to be associated with lower overall costs and additional health benefit compared to sulphonylureas. These data further highlight the potential role of real-world data in assessing health economic value.

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Paldanius P is employed by and owns shares in Novartis.

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