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Projected cost-effectiveness of exenatide once weekly versus exenatide BID for the treatment of type 2 diabetes in the UK

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AIM

- Type 2 diabetes mellitus imposes a considerable and increasing burden on healthcare resources,[1,2] largely as a result of long-term complications associated with hyperglycaemia.
- Therapy for type 2 diabetes mellitus therefore aims to achieve and maintain recommended targets for glycaemic control.[3,4]
- Long-term, add-on treatment with the glucagon-like peptide-1 (GLP-1) receptor agonist exenatide was associated with sustained improvements in glycaemic control and cardiovascular risk factors, and progressive weight loss during at least 3 years of follow-up.[5]
- The aim of this analysis was to estimate the cost-effectiveness of treatment with exenatide once weekly (EQW) compared with that of exenatide twice daily (BID) in patients with type 2 diabetes in the UK.

METHODS

- The published and validated IMS CORE Diabetes Model (CDM)[6,7] was used to make 50-year projections of clinical and cost outcomes based on pooled DURATION-1 and DURATION-5 baseline patient characteristics and study results.
  - These studies had similar methodology and were randomised comparisons of EQW and exenatide BID.
- The model simulates disease progression by combining 15 inter-dependent Markov-based sub-models to determine the occurrence and time to onset of diabetes-related complications, life years gained and quality-adjusted life years (QALYs); and also projects costs.

Base case assumptions

Simulation cohort:

- Pooled data from patients with type 2 diabetes mellitus managed with dietary modification and exercise and/or oral antidiabetic medications enrolled in the 30-week DURATION-1 (N=295)[8] and 24-week DURATION-5 (N=252),[9] phase 3, randomised, open-label clinical trials.
- Baseline diabetes-related medical histories were based on data from the NICE CG87 cohort.[10,11]
  - For diabetes complications not reported in the CG87 cohort, a baseline prevalence rate of zero was assumed.

Perspective of the analysis:

- The analysis has been conducted from the UK national health service payer perspective.

Time horizon:

- A 50-year time horizon was used.

Primary outcome:

- The cost-effectiveness of EQW compared with exenatide BID as measured by the incremental cost per QALY gained.

Patient characteristics at baseline:

- Table 1 shows pooled baseline characteristics of patients enrolled in DURATION-1 and DURATION-5.

Treatment pathway:

- Patients received by subcutaneous injection either EQW 2 mg or exenatide 10 µg BID for 5 years. After 5 years all patients were switched to insulin glargine for the remainder of the 50-year period or until death, whichever came first.

Costs:

- Complication costs were derived when possible from the UK Prospective Diabetes Study (UKPDS). Remaining complication and drug costs were derived from published sources and expressed in 2010 UK Pounds.
  - An annual discount rate of 3.5% was applied to both costs and outcomes, in line with NICE recommendations.

Table 1. Patient characteristics

	EQW	Exenatide BID
	N=277	N=270
Gender, n (%) male	159 (57.4)	143 (53.0)
Age, mean (SD), years	55.6 (10.4)	55.1 (9.9)
Ethnicity, n (%)		
Caucasian	204 (73.6)	175 (64.8)
Hispanic	53 (19.1)	61 (22.6)
Black	15 (5.4)	28 (10.4)
Asian	5 (1.8)	6 (2.2)
Weight, mean (SD), kg	99.5 (19.8)	98.4 (20.4)
BMI, mean (SD), kg/m^2	34.2 (5.3)	34.1 (5.3)
HbA_{1c}, mean (SD), %	8.4 (1.0)	8.3 (1.1)
Duration of diabetes, mean (SD), years	6.9 (5.4)	6.8 (4.9)
Total cholesterol, mean (SD), mg/dl	178.1 (44.7)	188.4 (49.9)*
High-density cholesterol, mean (SD), mg/dl	43.7 (10.1)	46.2 (10.9)**
Low-density cholesterol, mean (SD), mg/dl	97.5 (35.8)	109.1 (41.7)**
Triglycerides, mean (SD), mg/dl	213.8 (205.2)	185.7 (119.8)
Systolic blood pressure, mean (SD), mmHg	129.0 (14.1)	128.6 (13.5)

*EQW, exenatide once weekly; SD, standard deviation; BMI, body mass index; HbA_{1c}, glycated haemoglobin. * p < 0.05, ** p < 0.01; two sample t-test.*

METHODS CONT.

Key treatment-associated changes:

- Projected effects of EQW and exenatide BID on key patient outcomes were determined using pooled data from DURATION-1 and DURATION-5 (Table 2) applied for the first year, then progressed according to data from the UKPDS or Framingham study.

Statistical analyses:

- Data were analysed both deterministically (base case results), for which simulated cohorts of 1,000 patients were repeated through 1,000 iterations to generate results, and using probabilistic sensitivity analyses (PSA), which were performed for a cohort of 25,000 patients and 500 iterations.
  - All results are presented as mean values with standard deviation (SD), standard error (SE) and/or 95% confidence intervals (CIs).
  - Projected treatment group differences are expressed as EQW minus exenatide BID.

Sensitivity analyses

- Various deterministic sensitivity analyses were performed:
  - The projected effect of EQW on glycated haemoglobin (HbA_{1c}), body mass index (BMI), systolic blood pressure and lipids was adjusted to the upper and lower 95% confidence interval (projected effects of exenatide BID were fixed).
  - Data from each trial were considered individually.
  - Complication costs were varied up and down by 20%.
  - Selected utility values were included or excluded.

Table 2. Key projected treatment-associated changes

	EQW	Exenatide BID
	N=277	N=270
HbA_{1c}, mean (SE), %	-1.71 (0.07)	-1.18 (0.07)
Systolic blood pressure, mean (SE), mmHg	-3.04 (0.76)	-1.83 (0.78)
Total cholesterol, mean (SE), mg/dl	-11.59 (1.75)	-2.14 (1.84)
Low-density cholesterol, mean (SE), mg/dl	-5.02 (1.46)	0.49 (1.53)
High-density cholesterol, mean (SE), mg/dl	0.04 (0.41)	0.07 (0.43)
Triglycerides, mean (SE), mg/dl	-37.60 (9.01)	-5.79 (6.36)
BMI, mean (SE), kg/m^2	-1.04 (0.10)	-0.83 (0.10)
Major hypoglycaemia, events/100 patient years	0	0
Minor hypoglycaemia, events/100 patient years	22.56	57.71

EQW, exenatide once weekly; HbA_{1c}, glycated haemoglobin; SE, standard error; BMI, body mass index.

RESULTS

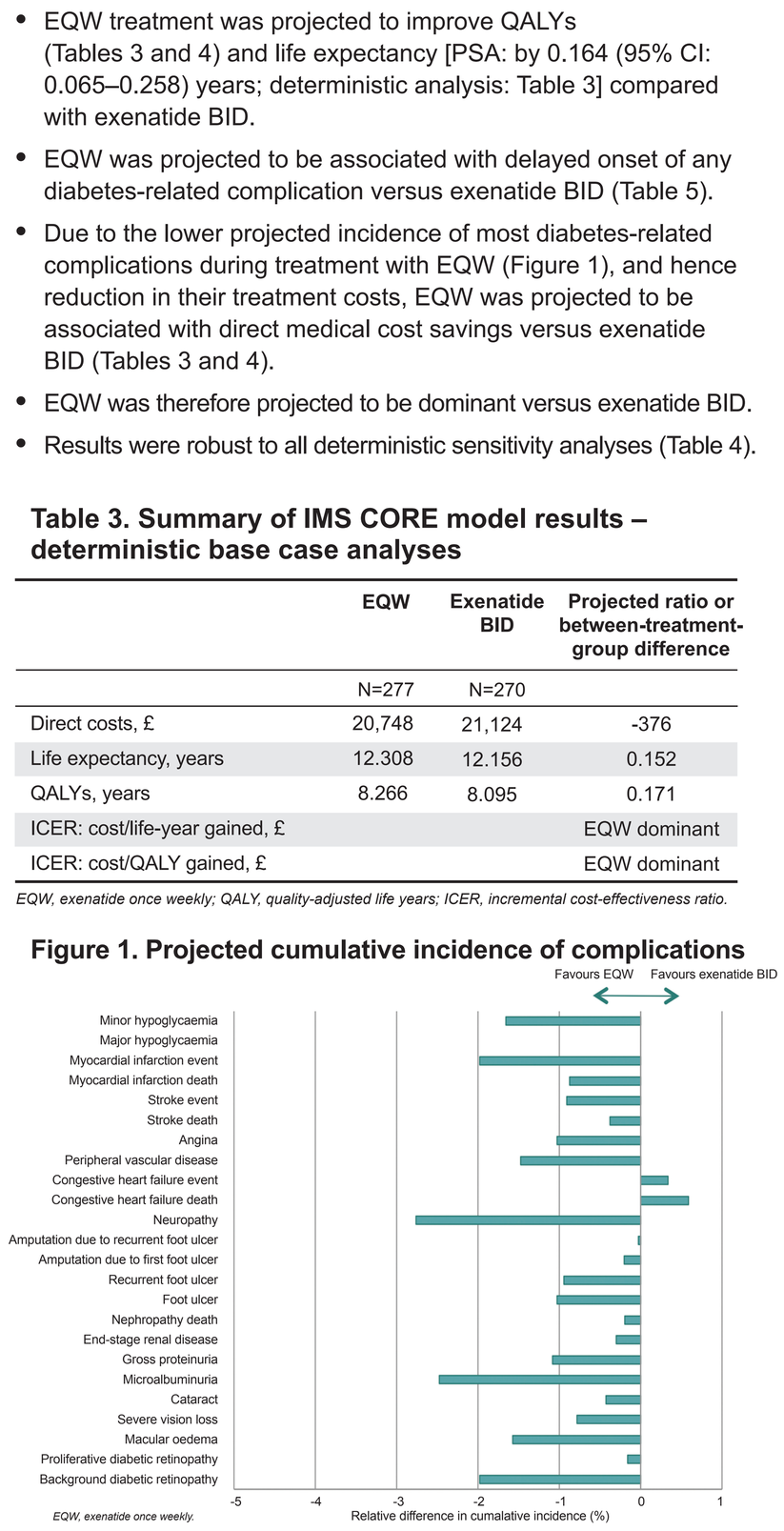
- EQW treatment was projected to improve QALYs (Tables 3 and 4) and life expectancy [PSA: by 0.164 (95% CI: 0.065–0.258) years; deterministic analysis: Table 3] compared with exenatide BID.
- EQW was projected to be associated with delayed onset of any diabetes-related complication versus exenatide BID (Table 5).
- Due to the lower projected incidence of most diabetes-related complications during treatment with EQW (Figure 1), and hence reduction in their treatment costs, EQW was projected to be associated with direct medical cost savings versus exenatide BID (Tables 3 and 4).
- EQW was therefore projected to be dominant versus exenatide BID.
- Results were robust to all deterministic sensitivity analyses (Table 4).

Table 3. Summary of IMS CORE model results – deterministic base case analyses

	EQW	Exenatide BID	Projected ratio or between-treatment-group difference
	N=277	N=270	
Direct costs, £	20,748	21,124	-376
Life expectancy, years	12.308	12.156	0.152
QALYs, years	8.266	8.095	0.171
ICER: cost/life-year gained, £			EQW dominant
ICER: cost/QALY gained, £			EQW dominant

EQW, exenatide once weekly; QALY, quality-adjusted life years; ICER, incremental cost-effectiveness ratio.

Figure 1. Projected cumulative incidence of complications



EQW, exenatide once weekly.

RESULTS CONT.

Table 4. Sensitivity analyses (treatment differences)

Parameter	QALYs	Cost (£)	ICER (£/QALY)
Base case – deterministic analyses	**0.171**	**-376**	**EQW dominant**
Deterministic sensitivity analyses			
HbA_{1c} upper CI for EQW	0.203	-487	EQW dominant
HbA_{1c} lower CI for EQW	0.145	-241	EQW dominant
SBP upper CI for EQW	0.197	-373	EQW dominant
SBP lower CI for EQW	0.155	-335	EQW dominant
Lipids upper CI for EQW	0.197	-427	EQW dominant
Lipids lower CI for EQW	0.156	-254	EQW dominant
BMI upper CI for EQW	0.176	-380	EQW dominant
BMI lower CI for EQW	0.166	-374	EQW dominant
Complication costs increased 20%	0.171	-525	EQW dominant
Complication costs decreased 20%	0.171	-228	EQW dominant
No hypoglycaemia disutility	0.165	-376	EQW dominant
No BMI disutility	0.175	-376	EQW dominant
No nausea disutility	0.169	-377	EQW dominant
Injection site reaction disutility included	0.167	-376	EQW dominant
Treatment frequency and flexibility utility benefits included	0.298	-376	EQW dominant
DURATION 1 trial data alone	0.111	-119	EQW dominant
DURATION 5 trial data alone	0.216	-572	EQW dominant
PSA results, (95% CI)	**0.178 (0.103–0.249)**	**-305 (-715–35)**	**EQW dominant (-5,786–185)**

QALY, quality-adjusted life years; ICER, incremental cost-effectiveness ratio; HbA_{1c}, glycated haemoglobin; EQW, exenatide once weekly; CI, confidence interval; SBP, systolic blood pressure; BMI, body mass index; PSA, probabilistic sensitivity analysis.

Table 5. Projected time alive and free of complications (years)

	EQW	Exenatide BID	Difference
	N=277	N=270	
Any complications	**4.93**	**4.47**	**0.46**
Background diabetic retinopathy	12.62	12.19	0.43
Proliferative diabetic retinopathy	17.13	16.83	0.30
Microalbuminuria	13.79	13.17	0.62
Gross proteinuria	17.23	16.86	0.37
End-stage renal disease	17.65	17.35	0.30
Foot ulcer	16.39	16.04	0.35
Amputation	17.40	17.09	0.31
Neuropathy	11.79	11.18	0.61
Peripheral vascular disease	16.77	16.34	0.43
Congestive heart failure	15.78	15.50	0.28
Angina	16.46	16.07	0.39
Myocardial infarction	15.35	14.93	0.42
Stroke	15.12	14.77	0.35
Cataract	16.59	16.26	0.33
Macular oedema	16.14	15.67	0.47
Severe vision loss	16.97	16.60	0.37

EQW, exenatide once weekly.

CONCLUSIONS

- In the UK setting, EQW was projected to be associated with greater improvements in long-term clinical outcomes than exenatide BID when pooled results of DURATION-1 and DURATION-5 were considered.
- The lower incidence of most diabetes-related complications in EQW-treated patients was projected to result in lower costs over a patient's lifetime with EQW when compared with exenatide BID.
- Limitations: Patients were switched to insulin glargine after five years; intermediate end points (e.g. HbA_{1c}, systolic blood pressure, lipids, BMI) were used to project long-term outcomes; intervention effects were applied in the first year only.

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