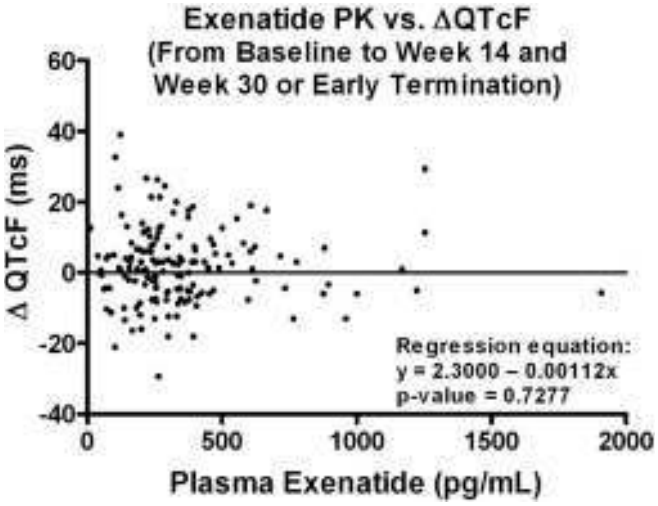
tients with the highest exenatide concentrations or renal insufficiency (n=55). Concentration-QTc analysis did not demonstrate a correlation between exenatide concentration and ΔQTcF (Figure).
Conclusion: In this study, exenatide once weekly treatment did not affect cardiac repolarization, measured by the QTcF interval, in patients with type 2 diabetes.



Clinical Trial Registration Number: NCT00308139

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The risk of heart failure among patients receiving exenatide twice daily versus other glucose-lowering medications for diabetes: a matched retrospective analysis of the GE Healthcare EMR data
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Background and aims: Exenatide twice daily (ExBID), a glucagon-like peptide-1 (GLP-1) receptor agonist, has demonstrated improvements in cardiovascular risk factors in patients with diabetes. We hypothesized that the addition of ExBID to other glucose-lowering therapies may reduce the risk of developing heart failure, defined as diagnosis of ICD-9 code 428 or brain natriuretic peptide >100 pg/mL. This retrospective matched cohort study used data obtained from the national Medical Quality Improvement Consortium of ambulatory medical practices (>14,000 providers) that use Centricity Office from GE Healthcare IT as their electronic medical record.
Materials and methods: Patients with diabetes receiving a prescription for glucose-lowering therapy (ExBID, insulin [INS], and/or other [OTH, excluding ExBID and INS]) between 1 Jan 2005 and 30 Sept 2010 were identified (n = 778,408). Therapies may have been prescribed serially or concomitantly. Patients using ExBID were randomly matched 1:1 to patients not receiving ExBID based on gender, 10 year age band, follow-up time, and any use of thiazolidinediones. Odds ratios (OR) were calculated using conditional logistic regression models with and without adjustment for weighted Charlson Comorbidity Index (CCI), a disease severity measure.
Results: Without adjustment for CCI, the rate of heart failure (affected/total) among patients that received ExBID+INS+OTH was 4.15 vs 8.88 for INS+OTH (OR = 0.41; 95% CI = 0.33-0.50). The rate of heart failure among patients that received ExBID+OTH was 1.54 vs 2.34 in matched controls (OR = 0.66; 95% CI = 0.58-0.75). After adjustment for CCI, risk of heart failure for patients who received ExBID+INS+OTH was 57% lower vs INS+OTH (OR = 0.43; 95% CI = 0.40-0.47; n = 48,184). With adjustment for CCI, the risk of heart failure for patients who received ExBID+OTH was 38% lower vs OTH (OR = 0.62; 95% CI = 0.54-0.70; n = 53,354). Finally, in a model adjusting for CCI that included all patients that received ExBID vs all non-ExBID controls, the risk of heart failure was 51% lower (OR = 0.49; 95% CI = 0.46-0.52; n = 101,538).
Conclusion: In this analysis the addition of ExBID to glucose-lowering regimens for the treatment of diabetes was associated with reduced risk of developing heart failure.

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The Association of British Clinical Diabetologists (ABCD) nationwide exenatide and liraglutide audits
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Background and aims: To compare use and efficacy of exenatide and liraglutide in two large scale nationwide audits of real clinical practice.
Materials and methods: Exenatide/liraglutide audits respectively: 128/64 centres across UK submitted anonymised data on 6717/3010 patients during 2007-2009/2009-2010. Previous exenatide users were excluded from liraglutide analysis leaving 2303 patients.
Results: Baseline characteristics of patients are shown in Table 1. All data expressed as exenatide/liraglutide. At 6 months, mean (SE) HbA1c reduction were 0.75(0.04) v 0.93(0.07)% (difference, p=0.040) among 3166 patients. Weight reduction were 6.5(0.1) v 3.7(0.2) kg (difference, p<0.001) among 2790 patients. All HbA1c and weight changes from baseline were significant (p<0.001). Exenatide/liraglutide data for cholesterol reduction were 0.16(0.03)/0.14(0.05) mmol/L, triglycerides reduction were 0.14(0.06)/0.26(0.10) mmol/L and systolic blood pressure reduction were 3.6(0.6)/4.6(0.9) mmHg. These were significant from baseline (at least p<0.05). There was no change in diastolic blood pressure in the exenatide audit but with liraglutide this fell by 1.2(0.5) mmHg (p=0.023). Baseline treatment use(discontinuation) was sulphonylurea 49.5/42.8(6.5/5.3)%, thiazolidinedione 27.1/20.5(13.4/7.5)%, DPP4 inhibitor 2.2/10.9(1.4/9.3)%, insulin 33.9/39(8.1/2.6)%.
Conclusion: These very large audits reveal the effectiveness of these agents in much heavier and more poorly controlled patients than those studied in clinical trials. Patients achieved greater HbA1c reduction but lesser weight reduction in the liraglutide audit as compared with the exenatide audit. However, there were lesser insulin and TZD discontinuation but greater DPPIV inhibitor discontinuation in the liraglutide audit. Contributors might have learnt from the previous use of exenatide to avoid over-reduction of diabetes treatment when initiating liraglutide
Table 1: Baseline characteristics of patients in the ABCD nationwide exenatide and liraglutide audit

	Exenatide	Liraglutide	p-value
n	6717	2303	
Male (%)	54.9	54.1	0.491
Caucasian (%)	84.4	90.4	<0.001
Age (yrs)	54.9 (10.6)	55.4 (11.2)	0.033
Diabetes duration (yrs)	8 (5-13)	9 (5-13)	0.424
HbA1c (%)	9.47 (1.69)	9.32 (1.72)	0.001
Weight (kg)	113.8 (23.4)	111.1 (23.0)	<0.001
BMI (kg/m^2)	39.8 (8.0)	39.1 (7.5)	<0.001
Single oral therapy (%)	21.6	12.0	<0.001
Dual oral therapy (%)	27.6	28.1	0.709
≥3 oral therapy (%)	6.5	17.9	<0.001
On insulin (%)	33.9	39.8	<0.001

Results quoted as mean (SD) and median diabetes duration (inter-quartile range)

Supported by: Eli Lilly Ltd, Novo Nordisk Ltd

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Factors associated with HbA_{1c} and weight changes at 6 months in the Association of British Clinical Diabetologists (ABCD) nationwide exenatide and liraglutide audit
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Background and aims: Treatment with GLP-1 agonists in type 2 diabetes has the advantage of weight loss but they are not effective in every patient. Factors that help predict response to treatment is needed. ABCD conducted two nationwide audits on exenatide and liraglutide based on real clinical practice.

Materials and methods: Patients from both audits were pooled together for analyses. Univariate followed by multivariate analyses were performed to assess for factors that were associated with HbA1c and weight change after GLP-1 agonist treatment. Latest HbA1c and weight changes by 6 months were used as continuous response variables and were assessed against other continuous variables of baseline HbA1c, weight, weight or HbA1c change, patient age, diabetes duration, total insulin dose (logarithm-transformed) and insulin dose reduction. Categorical variables assessed were gender, ethnicity (Caucasian/South Asian/Afro-Caribbean), oral hypoglycaemic agent change (stopped or reduced/unchanged/started or increased) and insulin use (yes/no). To avoid limiting the multivariate analyses to only insulin patients, two models were assessed each for HbA1c and weight change, the first with all significant univariate variables and with the variable insulin use, the second with total insulin dose and insulin dose reduction.
Results: 9020 patients with 5407 and 5245 follow-up HbA1c and weight results were analysed. Univariate analyses showed HbA1c reduction being correlated with higher baseline HbA1c and inversely with baseline weight, weight reduction, diabetes duration, TZD reduction, insulin use, higher insulin dose reduction (all $p<0.001$) and higher daily insulin dose ($p=0.012$). Univariate analyses for weight reduction showed correlation with higher baseline weight, age and diabetes duration, TZD reduction, insulin use and higher insulin dose reduction, and inversely with baseline HbA1c, HbA1c reduction and South Asian or Afro-Caribbean ethnicity (all $p<0.001$). Table 1 shows the results of stepwise regressions analyses. The HbA1c change model had 3982 patients with values of baseline HbA1c and weight, weight change, diabetes duration, TZD reduction and insulin use. The weight change model had 3089 patients with values of HbA1c change, baseline weight and HbA1c, ethnicity, age, diabetes duration, TZD reduction and insulin use. The models accounted for 22.0% and 9.5% of the variance of HbA1c change and weight change respectively.
Conclusion: Besides intuitive factors that affect HbA1c and weight outcomes, insulin-treated patients were found to have less HbA1c reduction but more weight reduction after treatment with GLP-1agonists. Higher total daily insulin dose and longer diabetes duration were also associated with poorer HbA1c reduction. Table 1: Stepwise regression analyses of factors influencing HbA1c and Weight changes among patients treated with exenatide and liraglutide.

	HbA1c reduction, stepwise regression among 3982 patients		Weight reduction, stepwise regression in 3089 patients	
Factor	Adjusted T-value	Adjusted p-value	Adjusted T-value	Adjusted p-value
Baseline HbA1c	30.44	<0.001	-5.94	<0.001
Baseline Weight	-3.79	<0.001	13.29	<0.001
HbA1c change	-	-	-	NS
Weight change	-	NS	-	-
Age	-	-	2.06	0.040
Diabetes duration	-4.16	<0.001	3.25	0.001
Ethnicity	-	-	-	NS
TZD reduction	-7.96	<0.001	7.02	<0.001
Insulin use	-10.02	<0.001	7.06	<0.001
	Stepwise regression among 1134 patients		Stepwise regression among 1002 patients	
Total insulin dose (log)	-3.6	<0.001	-	NS
Insulin dose reduction	-3.5	<0.001	9.21	<0.001

Supported by: Eli Lilly Ltd and Novo Nordisk Ltd

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Life-years, QALYs, costs and numbers needed to treat associated with exenatide once weekly versus insulin and pioglitazone treatment for type 2 diabetes: an Archimedes model simulation

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Background and aims: Exenatide once weekly (ExQW) is a glucagon-like peptide-1 (GLP-1) receptor agonist that improves glycaemia in patients with type 2 diabetes (T2DM) while potentially eliciting weight loss and improvement in cardiovascular risk factors (blood pressure and plasma lipids). In published trials, ExQW resulted in superior reduction in HbA1c compared to maximum daily doses of sitagliptin and pioglitazone (PIO) on metformin (MET) background, and to titrated insulin glargine. We used the Archimedes Model, a validated, clinically detailed model of physiology, disease, and healthcare delivery, to explore potential long-term benefits of ExQW and to evaluate savings from ExQW that might be achieved through reduced healthcare expenditures.
Materials and methods: We simulated 20 y of treatment (reported annually) in a virtual population (n = 24,878) based on individuals with T2DM drawn from the National Health and Nutrition Examination Survey who were on MET±sulphonylureas and who had not yet advanced to insulin (mean age 57 y, BMI 33 kg/m^2, weight 94 kg, duration of T2DM 9 y, baseline HbA1c 8%). The potential effects of 3 different treatment regimens were modeled at simulation start: 1) advancement to insulin at HbA1c ≥8% (treat to target HbA1c <7%), 2) addition of PIO, and 3) addition of ExQW. ExQW's effect on HbA1c, weight, blood pressure, and lipids was derived from four Phase 3 ExQW clinical trials. Direct medical costs (inpatient, outpatient, ambulatory, treatments) inflated to 2010 USD were derived from the Medicare Current Beneficiary Survey, as well as Medicare Part D data, www.drugstore.com, and published literature. Since ExQW is investigational, antidiabetic therapy costs for ExQW, insulin, and PIO were excluded from the analysis.
Results: At 20 y, undiscounted life years for ExQW, insulin, and PIO were 16.06, 15.87, and 15.81, respectively; quality-adjusted life years (QALYs) were 13.72, 13.52, and 13.46, respectively. Similar gains for ExQW over insulin and PIO were seen at 5 y and 10 y as well. ExQW demonstrated per person-year savings of $465 and $327 vs insulin and PIO, respectively, at 5 y, $528 and $415 at 10 y, and $556 and $539 at 20 y. The numbers of patients needed to treat to prevent one major adverse cardiovascular event (composed of myocardial infarction, stroke, and cardiovascular death) were 94, 53, and 43 for ExQW therapy vs insulin at years 5, 10, and 20, respectively, and 147, 104, and 90 for ExQW vs PIO.
Conclusion: These simulations showed increased life-years and QALYs for ExQW vs insulin and PIO, as well substantial healthcare cost savings. Use of ExQW reduced direct medical costs by $300 to $560 vs insulin and PIO per person year throughout the 20 y simulation period. These explorations through simulation modeling provide early indication of the potential of ExQW and underscore the need for confirmation through real-world clinical trials.