

ESM Methods

Mixed linear model construction

Time was scaled within individuals such that dapagliflozin was initiated at $t = 0$. Dapagliflozin use was modelled as categorical duration of dapagliflozin exposure at 3-month intervals, with no exposure (i.e. pre-initiation observations) specified as the reference category. In order to control for serial autocorrelation between measurements, all models were fitted with a continuous autoregressive correlation structure (CAR1), explicitly allowing for correlation between measurements that exponentially decayed the further apart they were in time (see supplement for further details).

All linear mixed regression models were of the form

$$y_{it} = \beta_0 + \beta_1 time_{it} + \beta_2 drugcategory_i \dots \beta_n X_n + v_{0i} + v_{1i} time_{it} + \varepsilon_{it}$$

$$\begin{bmatrix} v_{0i} \\ v_{1i} \end{bmatrix} \sim N \left\{ \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_{v_0}^2 & \sigma_{v_0 v_1} \\ \sigma_{v_0 v_1} & \sigma_{v_1}^2 \end{bmatrix} \right\}$$

$$\varepsilon_{it} \sim N(0, \Sigma_\varepsilon)$$

for observation at time t within individual i where β_0 represents the population-level intercept, β_1 represents the population-level longitudinal slope, β_2 represents the estimated effect of dapagliflozin at the time category of observation, and $\beta_n X_n$ represents additional covariates. The random effects v_{0i} and v_{1i} represent the individual-specific deviations in intercept and longitudinal slope respectively for individual i , which are drawn from a multivariate normal distribution. The residual error term ε_{it} conforms to a CAR1 autoregressive correlation structure with covariance matrix Σ_ε .

Initial models featured time (years), dapagliflozin exposure, and baseline value of the respective clinical outcome as fixed effects by default. All models specified individual-specific intercepts and individual-specific longitudinal slopes as random effects. Models were then further adjusted for time-invariant baseline characteristics of: age; gender; duration of diabetes; baseline HbA_{1c}, baseline weight, and baseline SBP (where not already included in the model by default); smoking status; number of diabetes drug classes received at dapagliflozin initiation; exposure to insulin at dapagliflozin initiation; ever-exposure to CVD drugs;

and prior CVD; as well as month of observation to control for potential seasonality. Covariate-adjusted models were restricted to those with complete covariate data only. Models were constructed for all dapagliflozin users, and on-licence users alone.

ESM Table 1: Rationale of International Classification of Diseases (ICD)-10 codes used in safety analysis

Cardiovascular-related outcome	(ICD)-10 code
<i>Chronic ischemic heart disease</i>	<ul style="list-style-type: none"> • I20.0 Unstable angina pectoris • I21 ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction • I22 Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction • I23 Certain current complications following ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction (within the 28 day period) • I24 Other acute ischemic heart diseases • I25 Chronic ischemic heart disease
<i>Cerebrovascular disease</i>	<ul style="list-style-type: none"> • I63 Cerebral infarction
<i>Heart failure</i>	<ul style="list-style-type: none"> • I11... Hypertensive heart disease with (congestive) heart failure • I13.0 Hypertensive heart and renal disease with (congestive) heart failure • I13.2...Hypertensive heart and renal disease with both (congestive) heart failure and renal failure • I25.5...Ischaemic cardiomyopathy • I42... Cardiomyopathy • I50 Congestive heart failure
<i>Cardiac arrhythmia</i>	<ul style="list-style-type: none"> • I48 Atrial fibrillation and flutter • I49 Other cardiac arrhythmias
<i>Coronary Revascularisation Procedures</i>	<ul style="list-style-type: none"> • Z95.1 Presence of coronary artery bypass graft • Z98.61 Coronary angioplasty status
<i>Revascularisation procedures</i>	<ul style="list-style-type: none"> • K40-K46...coronary artery bypass procedures • K48-K50... other coronary artery bypass procedures and angioplasty • K75, ...more coronary angioplasty procedures • L29, & L30... carotid artery procedures • L31... more coronary artery procedures (excluding L31.2, angiogram without intervention)
Diabetic ketoacidosis	(ICD)-10 code
<i>DKA</i>	<ul style="list-style-type: none"> • E10.0... Diabetes Mellitus with coma, only if evidence of hyperglycaemia elsewhere in coding • E10.1...Diabetes mellitus with ketoacidosis
Lower limb amputation	(ICD)-10 code
<i>Lower limb amputations and limb saving procedures</i>	<ul style="list-style-type: none"> • L51, L52... all iliac artery bypass procedures • L53.1... iliac artery repair

	<ul style="list-style-type: none">• L53.2... open embolectomy of iliac artery• L53.8...Other specified other open operations on iliac artery• L53. 9...Unspecified other open operations on iliac artery• L54... Transluminal operations on iliac artery• L58, L59... All bypass of femoral artery• L60... All reconstruction of femoral artery• L62.1 Endarterectomy of femoral artery and patch repair of femoral artery• L62.2 Endarterectomy of femoral artery NEC• L63.1 ...Percutaneous transluminal angioplasty of femoral artery• L63.2... Percutaneous transluminal embolectomy of femoral artery• L63.5... Percutaneous transluminal insertion of stent into femoral artery• L66.1... Percutaneous transluminal arterial thrombolysis and reconstruction• L66.2... Percutaneous transluminal stent reconstruction of artery• L66.5... Percutaneous transluminal balloon angioplasty of artery• L66.7... Percutaneous transluminal placement of peripheral stent in artery• X09–11... amputation of leg, foot and toe
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ESM Table 2: Safety analysis of exposure to dapagliflozin

Outcome	Cases	Cases among exposed	Cases among unexposed	Follow-up exposed	Follow-up unexposed	Ever/Never Exposure			Cumulative Exposure		
						HR	95% CI	P-Value	HR	95% CI	P-Value
Cohort Total <i>n</i> =238,876	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	Years	Years						
CVD Cohort		8205 (3.4)	230,671 (96.6)	6942	763,805						
CVD Events	23,253 (9.7)	111 (0.5)	23,142 (99.5)								
Minimal model						0.71	(0.53-0.95)	0.02	0.97	(0.71-1.3)	0.84
Full model						0.70	(0.52-0.94)	0.02	0.95	(0.70-1.30)	0.75
DKA Cohort		8516 (3.6)	230,360 (96.4)	7233	800,189						
DKA events	677 (0.3)	13 (1.9)	664 (98.1)								
Minimal model						1.49	(0.62-3.57)	0.37	0.90	(0.36-2.26)	0.82
Full model						1.43	(0.59-3.44)	0.43	0.88	(0.35-2.25)	0.79
Amputation Cohort		8503 (3.6)	230,373 (96.4)	7214	797,954						
Amputation Events	2051 (0.9)	28 (1.4)	2,023 (98.6)								
Minimal model						1.36	(0.75-2.48)	0.32	1.05	(0.58-1.91)	0.86
Full model						1.29	(0.71-2.36)	0.41	1.03	(0.57-1.88)	0.91

Minimal model adjusts for age, sex and diabetes duration.

Full model adjusts for age, sex, duration, smoking, blood pressure, HbA_{1c}, BMI, Cholesterol, Albuminuria, Retinopathy, prior myocardial infarction, prior stroke and prior heart failure. Full model covariates imputed for the following levels of missingness: BMI (23%), HbA_{1c} (6%), blood pressure (4%), cholesterol (6%), weight (24%) and eGFR (5%).

Excludes person time during or after exposure to canagliflozin and empagliflozin.

HR = Hazard ratio for ever never and each year of cumulative exposure.

CI = Confidence interval (Lower 95% to Upper 95% confidence bounds).

ESM Table 3: Baseline characteristics of dapagliflozin on/off license and never-users

	Off license users	Licensed users	Never-users
N individuals	1335	7231	230,310
Age (years)	63.95 (9.98)	56.56 (9.31)	66.12 (12.05)
Gender (% female)	42.7 (40.1, 45.4)	44.6 (43.4, 45.8)	43.5 (43.3, 43.7)
Duration of diabetes (years)	12.24 (5.95)	11.21 (5.69)	8.96 (6.80)
HbA _{1c} (mmol/mol)	78.36 (17.21)	77.54 (16.37)	58.62 (17.34)
HbA _{1c} (%)	9.32 (1.57)	9.25 (1.50)	7.51 (1.59)
BMI (kg/m ²)	35.74 (7.39)	34.00 (6.72)	31.97 (6.31)
Weight (kg)	101.78 (23.73)	97.03 (21.34)	90.84 (19.81)
SBP (mmHg)	135.92 (17.50)	135.31 (15.14)	132.98 (15.03)
DBP (mmHg)	75.75 (10.27)	76.56 (9.22)	75.06 (9.53)
eGFR (ml/min/1.73m ²)	74.16 (18.76)	81.50 (14.16)	77.99 (21.67)
eGFR <60 ml/min/1.73m ² N (%)	125 (11.58)	116 (2.07)	29238 (15.6)
Ever exposed to CVD drugs (%)	99.4 (99.1, 99.8)	99.0 (98.9, 99.2)	98.2 (98.1, 98.3)
Diabetes drug therapy pre-dapagliflozin initiation (%)			
No therapy	4.4 (3.2, 5.6)	5.6 (5.1, 6.2)	27.1 (26.9, 27.3)
Insulin therapy	8.4 (7.2, 9.6)	7.4 (6.9, 7.9)	7.1 (7.0, 7.2)
Monotherapy	22.8 (20.5, 25.1)	33.7 (32.6, 34.8)	35.9 (35.7, 36.1)
Dual therapy	39.5 (36.8, 42.1)	41.1 (39.9, 42.3)	22.4 (22.2, 22.6)
Triple therapy	17.3 (15.4, 19.2)	10.0 (9.4, 10.6)	7.7 (7.6, 7.8)
≥ Four-class therapy	1.8 (1.3, 2.4)	0.2 (0.2, 0.3)	0.5 (0.4, 0.5)
Clinical albuminuric status (%)			
Normoalbuminuria	74.5 (72.1, 76.9)	75.4 (74.3, 76.5)	78.1 (77.9, 78.3)
Microalbuminuria	22.7 (20.4, 25.0)	22.2 (21.1, 23.3)	18.8 (18.6, 19.0)
Macroalbuminuria	2.9 (2.1, 3.7)	2.4 (2.1, 2.8)	2.8 (2.7, 2.9)
Smoking status (%)			
Current smoker	16.8 (14.8, 18.8)	15.2 (14.5, 16.0)	18.3 (18.1, 18.5)
Ex-smoker	56.9 (54.3, 59.6)	54.0 (52.8, 55.2)	51.8 (51.6, 52.0)
Never smoked	25.8 (23.4, 28.2)	30.6 (29.6, 31.7)	29.3 (29.1, 29.5)
Prior morbidities (%)			
Heart failure	8.0 (6.7, 9.3)	2.1 (1.8, 2.5)	4.6 (4.5, 4.6)
Hypertension	36.0 (33.4, 38.7)	28.0 (26.9, 29.2)	30.6 (30.4, 30.8)
Myocardial infarction	8.3 (6.9, 9.7)	6.3 (5.7, 6.9)	7.2 (7.1, 7.3)
Stroke	2.6 (1.8, 3.4)	2.3 (1.9, 2.6)	3.6 (3.5, 3.6)
Transient ischaemic attack	1.0 (0.5, 1.5)	1.3 (1.0, 1.6)	1.5 (1.5, 1.6)
No retinopathy	74.4 (72.0, 76.8)	75.2 (74.1, 76.2)	79.6 (79.4, 79.7)
Retinopathy status at last screening (%)			
Mild retinopathy	19.3 (17.1, 21.4)	19.3 (18.3, 20.2)	16.6 (16.5, 16.8)
Moderate retinopathy	0.9 (0.5, 1.3)	1.0 (0.8, 1.2)	0.8 (0.7, 0.8)
Referable retinopathy	4.7 (3.7, 5.7)	3.9 (3.5, 4.3)	2.7 (2.7, 2.8)

Note: Data shown are age, sex and diabetes duration adjusted mean (standard deviation) for continuous variables and adjusted proportions (95% CI) for categorical variables. Bold denotes characteristics significantly differing between users/never-users within adjusted linear regression/logistic regression/Chi-squared tests as appropriate, after applying Bonferroni correction for multiple testing.

ESM Table 4: Percentage change in clinical outcomes by follow-up time in all users

	Baseline	3 months	6 months	9 months	12 months	15 months	18 months	21 months	24 months	27 months	30 months
N users	8566	7554	5468	4044	3082	2282	1601	1124	767	491	283
HbA _{1c} (mmol/mol)											
N users with data (% cohort)	>8550 (>99)	3980 (52.7)	2610 (47.7)	1680 (41.5)	1393 (45.2)	859 (37.6)	640 (40.0)	419 (37.3)	289 (37.7)	165 (33.6)	87 (30.7)
Proportional change (%)	-	-11.56 (16.86)	-12.70 (18.89)	-13.39 (18.21)	-14.56 (17.80)	-13.35 (18.13)	-13.09 (18.95)	-11.27 (18.95)	-11.59 (19.96)	-11.43 (17.54)	-11.94 (21.58)
BMI (kg/m ²)											
N users with data (% cohort)	7787 (90.9)	1905 (25.2)	1415 (25.9)	863 (21.3)	737 (23.9)	436 (19.1)	296 (18.5)	189 (16.8)	149 (19.4)	83 (16.9)	47 (16.6)
Proportional change (%)	-	-2.00 (3.03)	-2.34 (3.54)	-2.43 (3.37)	-2.22 (3.71)	-2.48 (3.73)	-2.41 (3.68)	-2.51 (3.85)	-2.31 (3.42)	-2.63 (3.59)	-2.21 (4.41)
Weight (kg)											
N users with data (% cohort)	7189 (83.9)	1589 (21.0)	1165 (21.3)	726 (18.0)	600 (19.5)	352 (15.4)	255 (15.9)	163 (14.5)	125 (16.3)	64 (13.0)	35 (12.4)
Proportional change (%)	-	-1.98 (2.84)	-2.19 (3.33)	-2.33 (3.33)	-2.20 (3.30)	-1.96 (3.74)	-2.37 (3.36)	-2.64 (3.87)	-2.53 (3.30)	-2.82 (3.40)	-2.11 (3.61)
SBP (mmHg)											
N users with data (% cohort)	8535 (99.6)	2811 (37.2)	2297 (42.0)	1538 (38.0)	1301 (42.2)	836 (36.6)	620 (38.7)	391 (34.8)	286 (37.3)	151 (30.8)	81 (28.6)
Proportional change (%)	-	-2.41 (11.60)	-2.38 (11.33)	-1.77 (12.07)	-1.22 (12.26)	-1.57 (11.98)	-2.40 (12.82)	-2.97 (12.13)	-3.48 (12.25)	-2.09 (13.53)	-4.05 (12.55)
DBP (mmHg)											
N users with data (% cohort)	8535 (99.6)	2808 (37.2)	2297 (42.0)	1537 (38.0)	1301 (42.2)	836 (36.6)	620 (38.7)	391 (34.8)	286 (37.3)	151 (30.8)	81 (28.6)
Proportional change (%)	-	-1.47 (12.76)	-1.51 (12.70)	-1.05 (13.07)	-0.85 (13.20)	-1.45 (12.59)	-2.39 (14.16)	-2.15 (12.20)	-3.64 (12.17)	-3.95 (12.91)	-4.93 (15.11)
eGFR(ml/min/1.73m ²)											
N users with data (% cohort)	8494 (99.2)	3305 (43.8)	2266 (41.4)	1572 (38.9)	1319 (42.8)	825 (36.2)	596 (37.2)	406 (36.1)	288 (37.5)	164 (33.4)	87 (30.7)
Proportional change (%)	-	-1.04 (13.33)	-1.11 (13.24)	-1.02 (13.47)	-0.98 (15.16)	-1.47 (16.45)	-1.51 (11.79)	-3.53 (12.04)	-2.08 (13.16)	-2.74 (12.24)	-2.85 (13.32)

Note: Greater than symbols are used where differences are less than 10 and statistical disclosure control has been applied. Data shown are mean percentage change (SD).

ESM Table 5: Within-person changes in clinical outcomes by 24 months post-initiation among all users, stratified by baseline characteristics

	1 st tertile	2 nd tertile	3 rd tertile
HbA_{1c} (N users with data = 6341)			
~HbA _{1c} (mmol/mol)	[33.00 - 72.00] -2.06 (12.11)	[72.00 - 86.00] -9.65 (13.29)	[86.00 - 166.00] -18.33 (17.67)
~HbA _{1c} (%)	[5.17 - 8.74] -0.19 (1.11)	[8.74 - 10.02] -0.88 (1.22)	[10.02 - 17.34] -1.68 (1.62)
~BMI (kg/m ²)	[15.60 - 31.80] -9.58 (15.66)	[31.80 - 37.24] -10.54 (16.02)	[37.24 - 69.63] -9.68 (16.24)
~eGFR (ml/min/1.73m ²)	[15.18 - 82.33] -8.52 (16.80)	[82.33 - 96.88] -9.93 (15.53)	[96.88 - 163.50] -11.26 (15.39)
~Age (years)	[21.30 - 54.17] -11.44 (16.07)	[54.17 - 62.97] -9.51 (15.43)	[62.97 - 89.91] -8.68 (16.29)
~Duration of diabetes (years)	[0.50 - 6.69] -11.12 (15.79)	[6.69 - 12.00] -9.77 (16.55)	[12.00 - 42.25] -8.73 (15.48)
BMI (kg/m²) (N users with data = 4342)			
~BMI (kg/m ²)	[15.60 - 31.80] -0.39 (0.92)	[31.80 - 37.24] -0.61 (1.06)	[37.24 - 69.63] -0.99 (1.51)
Weight (kg) (N users with data = 3675)			
~Weight (kg)	[38.00 - 90.90] -1.13 (2.40)	[90.90 - 108.00] -1.64 (2.95)	[108.00 - 206.00] -2.69 (4.11)
SBP (mmHg) (N users with data = 6211)			
~SBP (mmHg)	[79.00 - 129.00] +4.68 (12.71)	[129.00 - 140.00] -2.93 (12.41)	[140.00 - 228.00] -14.38 (16.30)
DBP (mmHg) (N users with data = 6210)			
~DBP (mmHg)	[39.00 - 74.00] +3.65 (8.27)	[74.00 - 80.00] -1.73 (7.17)	[80.00 - 184.00] -6.98 (9.80)
eGFR (ml/min/1.73m²) (N users with data= 5964)			
eGFR (ml/min/1.73m ²)	[15.18 - 82.33] +0.61 (10.64)	[82.33 - 96.88] -2.68 (9.73)	[96.88 - 163.50] -3.46 (7.68)
	Male	Female	
HbA_{1c} (N users with data= 6341)			
mmol/mol	-10.50 (15.77)	-8.98 (16.20)	
%	-0.96 (1.44)	-0.82 (1.48)	

Note: Clinical outcomes are given in headers, and baseline characteristics are given in rows. Data are mean (SD) of absolute within-person change from baseline value, unless stated otherwise. Ranges for each tertile are given in square brackets.

ESM Table 6: Follow-up measurements and changes in clinical outcomes through time for **licensed** dapagliflozin use

	Baseline	3 months	6 months	9 months	12 months	15 months	18 months	21 months	24 months	27 months	30 months
N users	7231	6418	4698	3499	2681	1980	1390	982	685	437	249
HbA_{1c}											
N users with data (% cohort)	>7220 (>99)	3365 (52.4)	2234 (47.6)	1446 (41.3)	1204 (44.9)	736 (37.2)	547 (39.4)	356 (36.3)	256 (37.4)	142 (32.5)	76 (30.5)
Absolute change * (mmol/mol)	-	-10.75 (14.32)	-11.88 (16.15)	-12.06 (15.51)	-13.29 (15.25)	-11.79 (15.29)	-11.84 (15.65)	-10.19 (14.75)	-10.67 (15.95)	-9.68 (13.97)	-9.82 (17.35)
Absolute change * %	-	-0.98 (1.31)	-1.09 (1.48)	-1.10 (1.42)	-1.22 (1.40)	-1.08 (1.40)	-1.08 (1.43)	-0.93 (1.35)	-0.98 (1.46)	-0.89 (1.28)	-0.90 (1.59)
BMI (kg/m²)											
N users with data (% cohort)	6605 (91.3)	1608 (25.1)	1184 (25.2)	731 (20.9)	630 (23.5)	374 (18.9)	259 (18.6)	167 (17.0)	131 (19.1)	69 (15.8)	40 (16.1)
Absolute change *	-	-0.76 (1.11)	-0.89 (1.27)	-0.94 (1.26)	-0.87 (1.38)	-0.91 (1.36)	-0.87 (1.37)	-1.02 (1.57)	-0.83 (1.25)	-0.96 (1.42)	-0.79 (1.70)
Weight (kg)											
N users with data (% cohort)	6110 (84.5)	1347 (21.0)	990 (21.1)	607 (17.3)	511 (19.1)	302 (15.3)	220 (15.8)	143 (14.6)	108 (15.8)	54 (12.4)	32 (12.9)
Absolute change *	-	-2.13 (3.15)	-2.47 (3.64)	-2.51 (3.62)	-2.45 (3.59)	-2.09 (4.05)	-2.65 (3.83)	-3.15 (4.59)	-2.50 (3.74)	-2.97 (4.24)	-2.16 (4.57)
SBP (mmHg)											
N users with data (% cohort)	7203 (99.6)	2372 (37.0)	1944 (41.4)	1308 (37.4)	1106 (41.3)	709 (35.8)	524 (37.7)	331 (33.7)	250 (36.5)	126 (28.8)	70 (28.1)
Absolute change *	-	-4.16 (15.75)	-4.13 (15.34)	-3.20 (16.37)	-2.71 (16.48)	-2.97 (16.16)	-4.13 (17.39)	-4.75 (16.22)	-5.23 (16.74)	-3.30 (18.54)	-5.16 (17.53)
DBP (mmHg)											
N users with data (% cohort)	7203 (99.6)	2369 (36.9)	1944 (41.4)	1307 (37.4)	1106 (41.3)	709 (35.8)	524 (37.7)	331 (33.7)	250 (36.5)	126 (28.8)	70 (28.1)
Absolute change *	-	-1.78 (9.89)	-1.88 (9.69)	-1.30 (9.81)	-1.53 (9.91)	-1.77 (9.49)	-2.69 (10.91)	-2.01 (9.24)	-3.03 (9.82)	-3.05 (10.12)	-4.00 (11.64)
eGFR (ml/min/1.73m²)											
N users with data (% cohort)	7166 (99.1)	2755 (42.9)	1918 (40.8)	1345 (38.4)	1122 (41.9)	701 (35.4)	504 (36.3)	342 (34.8)	247 (36.1)	140 (32.0)	77 (30.9)
Absolute change *	-	-1.42 (9.06)	-1.42 (9.33)	-1.46 (9.68)	-1.64 (9.37)	-2.05 (10.18)	-1.92 (8.94)	-3.63 (9.81)	-2.83 (10.90)	-3.62 (10.39)	-2.89 (10.36)

Note: Greater than symbols are used where differences are less than 10 and statistical disclosure control has been applied.

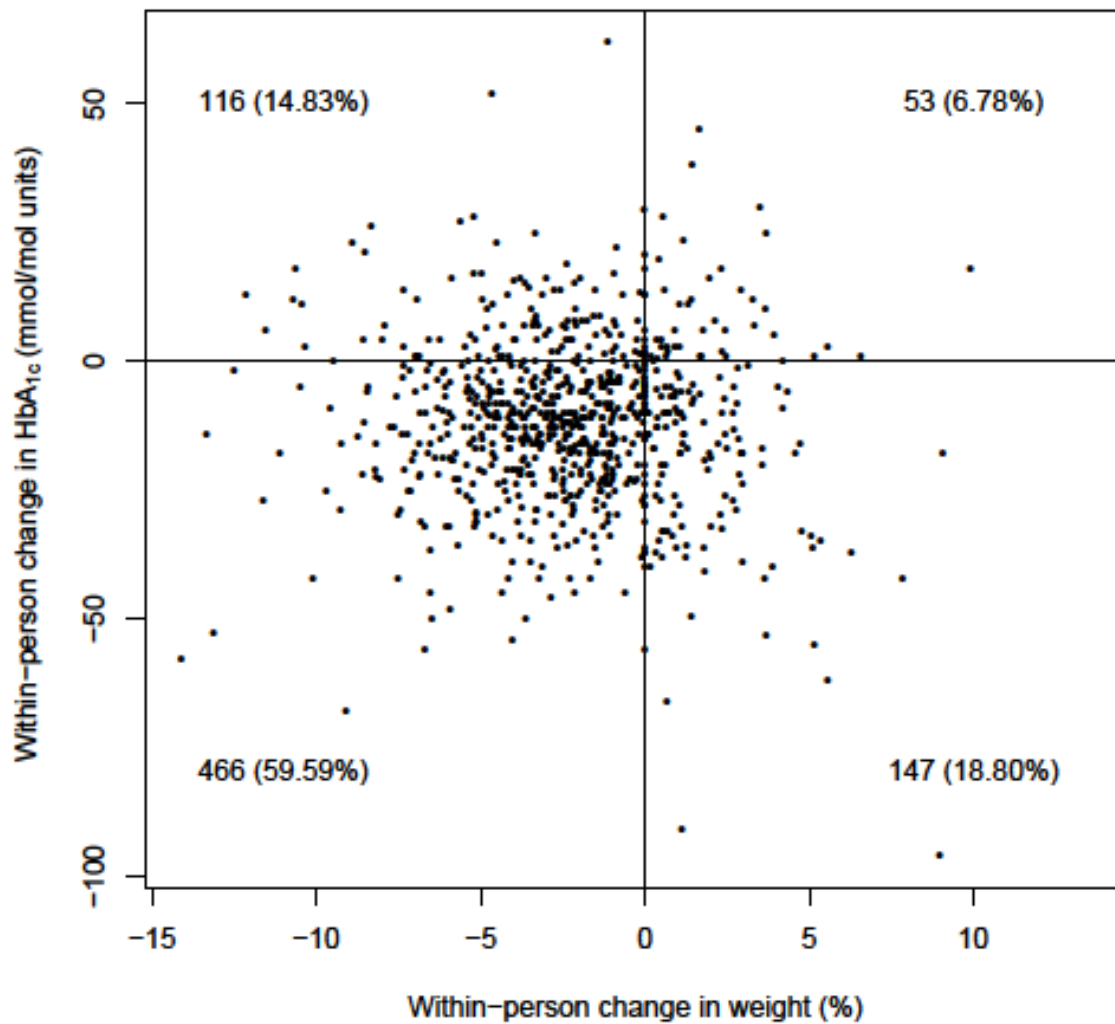
* Data shown are mean (SD) of the absolute within-person average from the baseline value.

ESM Table 7: Follow-up measurements and changes in clinical outcomes through time for **off-license** dapagliflozin use

	Baseline	3 months	6 months	9 months	12 months	15 months	18 months	21 months	24 months	27 months	30 months
N users	1335	1136	770	545	401	302	211	142	82	54	34
HbA_{1c}											
N users with data (% cohort)	>1320 (>99)	615 (54.1)	376 (48.8)	234 (42.9)	189 (47.1)	123 (40.7)	93 (44.1)	63 (44.4)	33 (40.2)	23 (42.6)	11 (32.4)
Absolute change * (mmol/mol)	-	-8.53 (15.71)	-9.77 (16.91)	-10.28 (16.08)	-11.05 (16.71)	-12.26 (16.34)	-10.45 (19.21)	-8.98 (19.67)	-7.79 (19.58)	-11.61 (18.24)	-17.09 (17.36)
Absolute change * %	-	-0.78 (1.44)	-0.89 (1.55)	-0.94 (1.47)	-1.01 (1.53)	-1.12 (1.49)	-0.96 (1.76)	-0.82 (1.80)	-0.71 (1.79)	-1.06 (1.67)	-1.56 (1.59)
BMI (kg/m²)											
N users with data (% cohort)	1182 (88.5)	297 (26.1)	231 (30.0)	132 (24.2)	107 (26.7)	62 (20.5)	37 (17.5)	22 (15.5)	18 (22.0)	14 (25.9)	<10 (<30)
Absolute change *	-	-0.66 (1.32)	-0.80 (1.74)	-0.72 (1.47)	-0.61 (1.71)	-1.03 (2.08)	-0.80 (1.20)	-0.63 (1.01)	-1.12 (1.55)	-1.39 (1.50)	-1.46 (2.08)
Weight (kg)											
N users with data (% cohort)	1079 (80.8)	242 (21.3)	175 (22.7)	119 (21.8)	89 (22.2)	50 (16.6)	35 (16.6)	20 (14.1)	17 (20.7)	10 (18.5)	<10 (<30)
Absolute change *	-	-1.96 (2.89)	-1.83 (3.94)	-2.61 (4.26)	-1.94 (3.32)	-2.50 (4.96)	-2.39 (3.53)	-1.65 (2.72)	-4.32 (4.58)	-5.31 (4.13)	-6.30 (5.75)
SBP (mmHg)											
N users with data (% cohort)	>1320 (>99)	439 (38.6)	353 (45.8)	230 (42.2)	195 (48.6)	127 (42.1)	96 (45.5)	60 (42.3)	36 (43.9)	25 (46.3)	11 (32.4)
Absolute change *	-	-5.19 (17.93)	-4.41 (17.76)	-4.81 (17.46)	-2.43 (17.46)	-5.03 (18.54)	-6.53 (18.88)	-6.58 (18.72)	-8.90 (20.09)	-10.60 (25.60)	-16.36 (16.26)
DBP (mmHg)											
N users with data (% cohort)	>1320 (>99)	439 (38.6)	353 (45.8)	230 (42.2)	195 (48.6)	127 (42.1)	96 (45.5)	60 (42.3)	36 (43.9)	25 (46.3)	11 (32.4)
Absolute change *	-	-2.44 (11.28)	-1.83 (11.46)	-2.60 (11.20)	-0.41 (10.29)	-2.29 (13.69)	-2.54 (14.29)	-3.95 (15.30)	-7.24 (16.63)	-9.66 (19.36)	-15.36 (33.40)
eGFR (ml/min/1.73m²)											
N users with data (% cohort)	>1320 (>99)	550 (48.4)	348 (45.2)	227 (41.7)	197 (49.1)	124 (41.1)	92 (43.6)	64 (45.1)	41 (50.0)	24 (44.4)	10 (29.4)
Absolute change *	-	-0.82 (9.93)	-1.21 (10.59)	-1.02 (10.92)	-0.60 (11.18)	-1.51 (10.65)	-0.78 (10.38)	-2.71 (11.17)	+0.87 (8.69)	+0.72 (7.97)	-4.96 (15.08)

Note: Greater than and less than symbols are used where differences are less than 10 and statistical disclosure control has been applied.

* Data shown are mean (SD) of the absolute within-person average from the baseline value



ESM Figure 1: Quadrant plot showing the within person changes in weight against the within person changes in HbA_{1c} at 3 months among all those exposed to dapagliflozin.