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ASSUMPTIONS

The below list details a summary of assumptions that have been made in the presented analysis:

- Transition probabilities between health states defined by CKD stages were derived using monthly transition count data assuming last observation carried forward (i.e. patients were assumed to remain in a CKD stage until an observation indicating that they had moved).
- Patients were assumed to discontinue dapagliflozin at an annual rate of 6.2% per annum in this analysis.
- Acute decline in kidney function events were assumed to incur costs associated with a single outpatient visit to reflect the likelihood of increased monitoring following a rapid decline in kidney function; no additional costs were considered to minimize the risk of double-counting with increased management costs associated with more advanced CKD stage.
- The cost of an incidence of volume depletion at £33.00 is assumed to be one GP visit.
- The cost of additional monitoring visits was applied to dapagliflozin arm only; one visit assumed at baseline and after 12 months if patients remain on treatment.
- Patients treated with dapagliflozin were assumed to require additional monitoring following initiation of therapy, incurring costs associated with an outpatient visit at model initiation and at one year if they remained on treatment.
- EQ-5D-5L responses were mapped to EQ-5D-3L applying the mapping function developed by van Hout et al.,[1] in line with NICE technology assessment guidelines and assuming that reported domain scores within individual questionnaires were uncorrelated.

- Patients were assumed to discontinue treatment with dapagliflozin upon receipt of a kidney transplant but were assumed to remain on treatment upon initiation dialysis with associated relative costs and treatment effects.
- Acute decline in kidney function events were assumed to result in no additional utility decrement as loss in quality of life associated with more advanced CKD is independently captured through health state utility values.

MORTALITY AND EVENT INCIDENCE

Parametric survival equations fitted to DAPA-CKD individual patient data are used to estimate the incidence of all-cause mortality. Adjusted and unadjusted parametric survival equations have been included for the overall DAPA-CKD trial population in addition to key subgroups of interest. The parameterisations for the adjusted mortality equations are shown in Supplemental Table 4. CKD stages G3a and G3b (eGFR 30-60 mL/min/1.73m^2) were pooled for analysis to increase statistical power, as there was little differentiation observed in outcomes between patients with eGFR 30-60 mL/min/1.73m^2 in the DAPA-CKD trial. A formal expert elicitation has been conducted previously to inform and validate the long-term extrapolations of mortality.[2]

To ensure that the mortality predictions accounted for the long-term increase associated with ageing, derived risk equations were supplemented with country-specific life tables, such that the probability of death in the general population was applied if it exceeded the predicted probability of death. However, due to the increased mortality risk in patients with CKD, the age-specific mortality rates were rarely applied. Patients with eGFR >60 mL/min/1.73m^2 (CKD stage G1 and G2) were subject to age-specific mortality risk after 15 years, whilst those in the transplant health state after 19 years. Patients in all other health states were subject to the risk of mortality derived from the risk equation throughout the modelled time horizon.

Candidate variables for the parametric survival model were selected to align with those influencing subgroups in the DAPA-CKD trial pre-defined subgroups. These included age, sex, race, type 2 diabetes status, eGFR, UACR, systolic blood pressure, history of heart failure, history of myocardial infarction, history of stroke, smoking status, BMI, haemoglobin, serum potassium, aetiology of CKD and geographic location. The initial a pool

of candidates was subjected to a forward variable selection process conditioned on inclusion of treatment arm and time-updated eGFR respectively to capture the impact of dapagliflozin versus placebo and the expected effect on mortality of increasing eGFR category (that is, worsening CKD stage) on mortality. Each candidate variable is added in turn and only the variable leading to the greatest decrease in Akaike information criterion (AIC) is retained. The process is repeated until no further decrease in AIC is achieved. In the model base case, mortality is taken to follow a Gompertz distribution.

Unlike mortality, patients may experience multiple hospitalizations for HF or acute decline in kidney function events, as such survival analysis is inappropriate. Therefore, the incidence of hospitalization for HF and acute decline in kidney function events were estimated using generalised estimating equations (GEEs) to account for dependence between outcomes.

Similarly to the approach for survival analysis, models were adjusted for covariables that improve model fit with the target metric minimisation of the quasi-likelihood under the independence model information criterion (QIC), and the addition of a time variable to account for any potential trends in the observed data (Supplemental Figure 4). Validation included: visual inspection, relative measures of fit (QIC), k-fold cross validation, clinical expert opinion on the plausibility of included covariables, their effect, and extrapolation.

HEALTH-RELATED QUALITY OF LIFE

EQ-5D-5L responses were first mapped to EQ-5D-3L, applying the mapping function developed by van Hout et al.[1] in line with NICE guidelines.[3] Responses were then converted to utility index scores using published country specific utility tariffs for the UK, Germany and Spain, respectively, for EQ-5D health states, derived using the time trade-off method described in Dolan et al.[4-6]

Using these data, linear mixed-effects models, consisting of fixed and random components, were derived to predict patient-reported utility values to account for the clustering of multiple questionnaires per patient. Regression models were adjusted for important patient demographic characteristics, such as age, sex, type 2 diabetes status and UACR > 1,000 mg/g, and the incidence of adverse clinical outcomes disease severity jointly. The fixed effects coefficients were used for modelling; utilities used in the model (marginal means for health states and event utility decrements) are provided in Table 2.

MODEL VALIDATION

Validation and verification has been conducted to ensure correct implementation, and that the model reliably reproduces outcomes observed in the DAPA-CKD clinical trial. The following exercises have been undertaken to ensure that the model is robust:

- Model equations and parameters have been validated against their source to ensure that there were no transcription errors.
- Input derivation has been reviewed to ensure that there were no issues with their implementation.

In addition, the outcomes observed in the trial have been compared against modelled predictions. Supplemental Figure 2 provides a validation of predicted mortality under different distributions to Kaplan Meier data from the DAPA-CKD clinical trial. All distributions validate well to the trial, however Gompertz was the distribution with the best fit to the data. To ensure that long term extrapolations of survival are estimated by the model, Supplemental Figure 3 provides the predicted survival for patients on dapagliflozin and placebo.

Validation to acute decline in kidney function and hospitalisation for heart failure events in the trial was conducted for each considered subgroup. Supplemental Figure 4 demonstrates that the model performed well when predicting outcomes observed in the trial.

Fluctuations in eGFR measurements are common, and when taken in isolation, corresponding CKD stages could be misrepresented. To ensure that the model is not sensitive to CKD transitions, cost and utilities associated with CKD stage G3a (45-59ml/min/1.73m^2) were assumed for all CKD stages prior to kidney failure. In addition, eGFR was assumed to have an equivalent impact in risk equations prior to kidney failure. These alterations did not

materially affect the study conclusions, with ICERs of $7,997, $18,111 and $11,025 in the UK, Germany and Spain, respectively.

Additionally, the time spent in each CKD stage compared with progression in the trial is presented in Supplemental Figure 1, further demonstrating the reliability of the monthly transitions.

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SUPPLEMENTAL TABLES

Supplemental Table 1. Patient profile

Variable		Mean (SE)	Distribution*
Patient characteristics	Age (years)	61.84 (0.18)	Normal
	Female	0.33 (0.01)	Beta
	BMI (kg/m^2)	29.52 (0.09)	Normal
	Race: White	0.53 (0.01)	Beta
	Race: Black or African American	0.04 (0.00)	Beta
	Race: Other	0.08 (0.00)	Beta
	Smoker	0.14 (0.01)	Beta
Clinical characteristics	CKD G1 (eGFR ≥90)	0.00 (0.00)	Beta
	CKD G2 (eGFR 60-89)	0.11 (0.00)	Beta
	CKD G3a (eGFR 45-59)	0.31 (0.01)	Beta
	CKD G3b (eGFR 30-44)	0.44 (0.01)	Beta
	CKD G4 (eGFR 15-29)	0.14 (0.01)	Beta
	CKD G5 (pre-KRT; eGFR <15)	0.00 (0.00)	Beta
	Dialysis	0.00 (0.00)	Beta
	Transplant	0.00 (0.00)	Beta
	UACR: 30-300 mg/g	0.10 (0.00)	Beta
	UACR: ≥300 mg/g	0.90 (0.00)	Beta
	Type 2 diabetes	0.68 (0.01)	Beta
	Glomerulonephritis	0.16 (0.01)	Beta
	Angiotensin-converting enzyme inhibitors	0.27 (0.01)	Beta
	Angiotensin receptor blockers	0.56 (0.01)	Beta
	Mineralocorticoid receptor antagonists	0.05 (0.00)	Beta
	Diuretic	0.37 (0.01)	Beta
	Potassium	4.65 (0.01)	Normal
	Systolic blood pressure	137.08 (0.27)	Normal
	Haemoglobin	12.83 (0.03)	Normal
Patient history	Prior heart failure	0.11 (0.00)	Beta
	Prior myocardial infarction	0.09 (0.00)	Beta
	Prior stroke	0.07 (0.00)	Beta

BMI: body mass index; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; KRT: kidney replacement therapy; SE: standard error; UACR: urine albumin-to-creatinine ratio
**Distributions define the values that are sampled in probabilistic sensitivity analysis*

Supplemental Table 2. CKD transition matrix - dapagliflozin and standard therapy

	CKD G1	CKD G2	CKD G3a	CKD G3b	CKD G4	CKD G5	Dialysis	Kidney transplant	Reference
Months 0-4									
CKD G1	0.586 (0.076)	0.219 (0.064)	0.049 (0.033)	0.049 (0.033)	0.024 (0.024)	0.024 (0.024)	0.024 (0.024)	0.025 (0.024)	DAPA-CKD trial[7]
CKD G2	0.018 (0.005)	0.709 (0.016)	0.246 (0.015)	0.019 (0.005)	0.003 (0.002)	0.003 (0.002)	0.001 (0.001)	0.001 (0.001)	
CKD G3a	0.001 (0.001)	0.079 (0.006)	0.749 (0.009)	0.162 (0.008)	0.008 (0.002)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	
CKD G3b	0.001 (0.000)	0.005 (0.001)	0.079 (0.004)	0.812 (0.006)	0.102 (0.005)	0.001 (0.000)	0.000 (0.000)	0.000 (0.000)	
CKD G4	0.001 (0.001)	0.003 (0.001)	0.006 (0.002)	0.143 (0.008)	0.843 (0.008)	0.004 (0.001)	0.001 (0.001)	0.001 (0.000)	
CKD G5	0.063 (0.060)	0.125 (0.080)	0.062 (0.058)	0.124 (0.080)	0.375 (0.118)	0.125 (0.080)	0.063 (0.059)	0.062 (0.059)	
Dialysis	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.995 (0.0995)	0.005 (0.0005)	Sugrue et al.[8]*
Kidney transplant	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.007 (0.0007)	0.993 (0.0993)	
Months 4+									
CKD G1	0.891 (0.017)	0.070 (0.014)	0.009 (0.005)	0.015 (0.007)	0.006 (0.004)	0.003 (0.003)	0.003 (0.003)	0.003 (0.003)	DAPA-CKD trial[7]
CKD G2	0.005 (0.001)	0.909 (0.004)	0.078 (0.004)	0.006 (0.001)	0.002 (0.001)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	
CKD G3a	0.001 (0.000)	0.025 (0.001)	0.913 (0.003)	0.059 (0.002)	0.002 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	
CKD G3b	0.000 (0.000)	0.001 (0.000)	0.025 (0.001)	0.938 (0.002)	0.035 (0.001)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	
CKD G4	0.000 (0.000)	0.000 (0.000)	0.001 (0.000)	0.035 (0.002)	0.952 (0.002)	0.010 (0.001)	0.001 (0.000)	0.000 (0.000)	
CKD G5	0.001 (0.001)	0.002 (0.001)	0.002 (0.001)	0.001 (0.001)	0.027 (0.005)	0.920 (0.008)	0.045 (0.006)	0.002 (0.001)	
Dialysis	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.995 (0.0995)	0.005 (0.0005)	Sugrue et al.[8]*
Kidney transplant	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.007 (0.0007)	0.993 (0.0993)	

CKD: chronic kidney disease; SE: standard error
** Mean values from transition probabilities identified in the Sugrue et al.*
All values are expressed a mean (SE), with mean values representing monthly transition probabilities. Standard errors represent the variability applied in the probabilistic sensitivity analysis.

Supplemental Table 3. CKD transition matrix - placebo and standard therapy

	CKD G1	CKD G2	CKD G3a	CKD G3b	CKD G4	CKD G5	Dialysis	Kidney transplant	Reference
Months 0-4									
CKD G1	0.375 (0.084)	0.313 (0.081)	0.156 (0.064)	0.031 (0.030)	0.031 (0.030)	0.031 (0.030)	0.031 (0.030)	0.031 (0.030)	DAPA-CKD trial[7]
CKD G2	0.009 (0.003)	0.770 (0.014)	0.195 (0.013)	0.016 (0.004)	0.004 (0.002)	0.002 (0.002)	0.002 (0.002)	0.001 (0.001)	
CKD G3a	0.002 (0.001)	0.070 (0.005)	0.774 (0.009)	0.149 (0.007)	0.004 (0.001)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	
CKD G3b	0.002 (0.001)	0.004 (0.001)	0.084 (0.005)	0.826 (0.006)	0.082 (0.005)	0.001 (0.001)	0.001 (0.000)	0.000 (0.000)	
CKD G4	0.001 (0.001)	0.002 (0.001)	0.005 (0.002)	0.127 (0.008)	0.856 (0.009)	0.007 (0.002)	0.001 (0.001)	0.001 (0.001)	
CKD G5	0.043 (0.041)	0.174 (0.077)	0.043 (0.042)	0.044 (0.042)	0.175 (0.077)	0.348 (0.097)	0.130 (0.068)	0.043 (0.041)	
Dialysis	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.995 (0.0995)	0.005 (0.0005)	Sugrue et al.[8]*
Kidney transplant	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.007 (0.0007)	0.993 (0.0993)	
Months 4+									
CKD G1	0.884 (0.020)	0.075 (0.016)	0.015 (0.007)	0.011 (0.006)	0.004 (0.004)	0.004 (0.004)	0.004 (0.004)	0.004 (0.004)	DAPA-CKD trial[7]
CKD G2	0.004 (0.001)	0.915 (0.004)	0.072 (0.004)	0.008 (0.001)	0.002 (0.001)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	
CKD G3a	0.000 (0.000)	0.023 (0.001)	0.910 (0.003)	0.064 (0.002)	0.003 (0.001)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	
CKD G3b	0.000 (0.000)	0.001 (0.000)	0.026 (0.001)	0.931 (0.002)	0.041 (0.001)	0.000 (0.000)	0.001 (0.000)	0.000 (0.000)	
CKD G4	0.000 (0.000)	0.001 (0.000)	0.001 (0.000)	0.028 (0.001)	0.954 (0.002)	0.014 (0.001)	0.002 (0.000)	0.000 (0.000)	
CKD G5	0.001 (0.001)	0.001 (0.001)	0.001 (0.001)	0.002 (0.001)	0.038 (0.005)	0.910 (0.008)	0.044 (0.005)	0.003 (0.002)	
Dialysis	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.995 (0.0995)	0.005 (0.0005)	Sugrue et al.[8]*
Kidney transplant	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	0.000 (0.000)	*0.000 (0.000)*	*0.000 (0.000)*	0.007 (0.0007)	0.993 (0.0993)	

CKD: chronic kidney disease; SE: standard error
** Mean values from transition probabilities identified in Sugrue et al.*
All values are expressed a mean (SE) , with mean values representing monthly transition probabilities. Standard errors represent the variability applied in the probabilistic sensitivity analysis.

Supplemental Table 4. Parameterisations of adjusted all-cause mortality parametric (Gompertz) survival equations

Covariate	Coefficient (95% CI)	p-value
Shape	0.00026 (-0.00; 0.00)	0.216
Rate	0.00069 (0.00; 0.01)	0.357
Dapagliflozin	-0.36597 (-0.62; -0.11)	0.005
Age	0.03436 (0.02; 0.05)	<0.001
Female	-0.36049 (-0.64; -0.08)	0.012
Race: Black or African American	0.63375 (-0.04; 1.30)	0.064
Race: White	0.81962 (0.43; 1.21)	<0.001
Race: Other	0.84351 (0.36; 1.33)	0.001
BMI	-0.02235 (-0.05; 0.00)	0.065
eGFR <15*	1.47894 (0.76; 2.20)	<0.001
eGFR 15-30	0.53771 (-0.04; 1.12)	0.069
eGFR 30-60	0.28160 (-0.28; 0.84)	0.322
Haemoglobin	-0.22982 (-0.31; -0.15)	<0.001
Glomerulonephritis	-0.45994 (-1.03; 0.11)	0.112
Systolic blood pressure	-0.00930 (-0.02; -0.00)	0.011
Potassium	-0.16838 (-0.39; 0.05)	0.136
Prior heart failure	0.81752 (0.51; 1.13)	<0.001
Prior myocardial infarction	0.37557 (0.03; 0.72)	0.031
Prior stroke	0.47429 (0.08; 0.87)	0.018
AIC	5061.78	

AIC: Akaike information criterion; BMI: body mass index; CI: confidence interval; eGFR: estimated glomerular filtration rate
Confidence intervals define the distribution over which values are sampled in probabilistic sensitivity analysis
**Referent eGFR category > 60 mL/min/1.73m^2*

Supplemental Table 5. Adjusted generalised estimating equations predicting hospitalisation for heart failure events

Covariate	Coefficient (95% CI)	p-value
Intercept	-11.41542 (-14.86; -7.97)	<0.001
Dapagliflozin	-0.64716 (-1.07; -0.23)	0.002
Age	0.04654 (0.02; 0.07)	<0.001
Type 2 diabetes mellitus	0.81195 (0.17; 1.45)	0.013
BMI	0.05873 (0.02; 0.09)	0.001
Race: Black or African American	0.41411 (-0.56; 1.39)	0.405
Race: White	0.65848 (0.01; 1.31)	0.047
Race: Other	-0.35959 (-1.50; 0.78)	0.536
Smoking	0.48239 (0.18; 0.78)	0.002
eGFR < 15	0.87720 (-0.64; 2.39)	0.257
eGFR 15-30	0.85811 (-0.36; 2.07)	0.166
eGFR 30-60	0.33567 (-0.83; 1.50)	0.573
UACR: 30-300 mg/g	1.32207 (-0.70; 3.34)	0.199
UACR: ≥ 300 mg/g	1.63788 (-0.35; 3.62)	0.106
Potassium	-0.43026 (-0.77; -0.09)	0.012
Haemoglobin	-0.15531 (-0.30; -0.01)	0.032
Prior heart failure	1.75096 (1.30; 2.20)	<0.001

BMI: body mass index; CI: confidence interval; eGFR: estimated glomerular filtration rate; UACR: urine albumin to creatinine ratio
Confidence intervals define the distribution over which values are sampled in probabilistic sensitivity analysis

Supplemental Table 6. Adjusted generalised estimating equations predicting acute decline in kidney function events

Covariate	Coefficient (95% CI)	p-value
Intercept	-6.81785 (-8.97; -4.66)	<0.001
Dapagliflozin	-0.30783 (-0.62; 0.01)	0.054
Race: Black or African American	0.55403 (-0.17; 1.28)	0.136
Race: White	0.54789 (0.13; 0.96)	0.010
Race: Other	0.32357 (-0.26; 0.91)	0.277
eGFR < 15	2.12615 (1.35; 2.91)	<0.001
eGFR 15-30	0.61858 (-0.10; 1.34)	0.091
eGFR 30-60	0.01084 (-0.68; 0.71)	0.976
Glomerulonephritis	-0.59022 (-1.18; 0.00)	0.050
Prior myocardial infarction	0.32089 (-0.11; 0.75)	0.143
Potassium	0.25111 (-0.03; 0.53)	0.081
Haemoglobin	-0.14558 (-0.25; -0.04)	0.006
Prior heart failure	0.76177 (0.39; 1.13)	<0.001

BMI: body mass index; CI: confidence interval; eGFR: estimated glomerular filtration rate; UACR: urine albumin to creatinine ratio

Supplemental Table 7. Annual probability of clinical and adverse events

Events	Mean (SE)		Reference
	Dapagliflozin + standard therapy	Standard therapy	
Clinical Events			
Hospitalisation for heart failure	0.008 (0.131)	0.015 (0.185)	DAPA-CKD trial[7]
Acute decline in kidney function	0.014 (0.172)	0.020 (0.210)	
Adverse events			
Volume depletion	0.031 (0.004)	0.021 (0.003)	DAPA-CKD trial[7]
Major hypoglycaemic events	0.003 (0.001)	0.006 (0.002)	
Fractures	0.020 (0.003)	0.016 (0.003)	
Diabetic ketoacidosis	0.000 (0.000)	0.000 (0.000)	
Amputation	0.009 (0.002)	0.010 (0.002)	

SE: standard error

Supplemental Table 8. Base-case discounted health economic results (native currency)

Outcome	Dapagliflozin + standard therapy	Standard therapy	Incremental
United Kingdom			
Total costs	£79,677	£74,717	£4,960
Drug acquisition	£4,386	£509	£3,878
CKD management (pre-KRT)	£26,764	£25,387	£1,377
KRT	£46,061	£46,402	-£341
Adverse events, hospitalisation for heart failure & acute decline in kidney function	£2,465	£2,419	£46
Total QALYs gained	8.681	7.857	0.824
ICER	-	-	**£6,020/QALY**
Germany			
Total costs	€215,119	€200,187	€14,932
Drug acquisition	€6,277	€353	€5,924
CKD management (pre-KRT)	€108,240	€98,977	€9,263
KRT	€96,951	€97,505	-€554
Adverse events, hospitalisation for heart failure & acute decline in kidney function	€3,651	€3,352	€299
Total QALYs gained	10.320	9.318	1.003
ICER	-	-	**€14,891 QALY**
Spain			
Total costs	€138,620	€129,168	€9,452
Drug acquisition	€3,757	€504	€3,254
CKD management (pre-KRT)	€62,787	€56,885	€5,902
KRT	€68,859	€69,003	-€144
Adverse events, hospitalisation for heart failure & acute decline in kidney function	€3,217	€2,777	€440
Total QALYs gained	9.790	8.833	0.957
ICER	-	-	**€9,875/QALY**

CKD: chronic kidney disease; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year

Supplemental Table 9. The effect of alternative treatment discontinuation assumptions

Scenario	Outcome	Dapagliflozin + standard therapy	Standard therapy	Incremental
Discontinuation of dapagliflozin at 3 years	**United Kingdom**			
	Total costs	$103,707	$102,774	$933
	Total LYs gained	10.766	10.461	0.305
	Total QALYs gained	8.096	7.857	0.239
	ICER	-	-	**$3,904/QALY**
	Germany			
	Total costs	$239,867	$236,908	$2,959
	Total LYs gained	11.150	10.833	0.317
	Total QALYs gained	9.602	9.318	0.284
	ICER	-	-	**$10,417/QALY**
	Spain			
	Total costs	$154,533	$152,862	$1,671
	Total LYs gained	11.166	10.846	0.320
	Total QALYs gained	9.105	8.833	0.272
	ICER	-	-	**$6,148/QALY**
Tapering of dapagliflozin discontinuation to 0% over 4 years	**United Kingdom**			
	Total costs	$114,963	$102,774	$12,188
	Total LYs gained	12.038	10.461	1.577
	Total QALYs gained	9.067	7.857	1.210
	ICER	-	-	**$10,072/QALY**
	Germany			
	Total costs	$266,817	$236,908	$29,910
	Total LYs gained	12.518	10.833	1.685
	Total QALYs gained	10.801	9.318	1.483
	ICER	-	-	**$20,166/QALY**
	Spain			
	Total costs	$172,288	$152,862	$19,426
	Total LYs gained	12.550	10.846	1.704
	Total QALYs gained	10.253	8.833	1.420
	ICER	-	-	**$13,676/QALY**

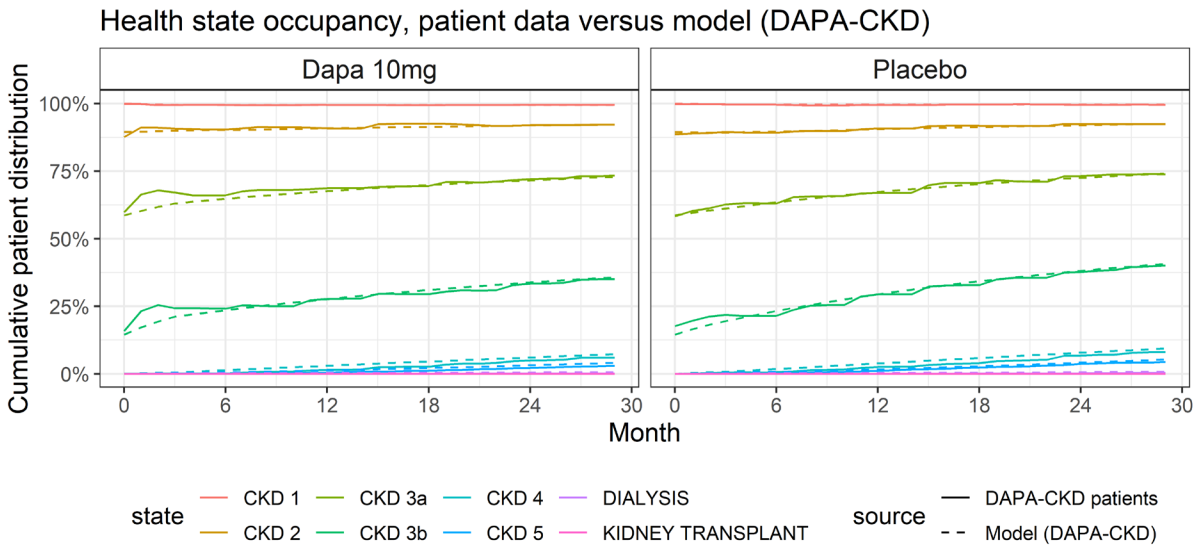
ICER: incremental cost-effectiveness ratio; LY: life year; QALY: quality-adjusted life year; ST: standard therapy

Supplemental Table 10. Deterministic sensitivity analysis

Scenario	UK				Germany				Spain			
	Cost	QALYs	LYs	Cost/ QALY	Cost	QALYs	LYs	Cost/ QALY	Cost	QALYs	LYs	Cost/ QALY
Base case	$6,823	0.824	1.068	$8,281	$17,671	1.003	1.134	$17,623	$11,186	0.957	1.143	$11,686
Model time horizon (10 years)	$3,992	0.67	0.862	$5,957	$11,416	0.807	0.904	$14,151	$6,896	0.768	0.909	$8,974
Model time horizon (Lifetime)	$6,823	0.824	1.068	$8,281	$17,671	1.003	1.134	$17,623	$11,186	0.957	1.143	$11,686
Cost discounting (0.00%)	$13,224	0.824	1.068	$16,050	$30,219	1.003	1.134	$30,137	$19,476	0.957	1.143	$20,348
Cost discounting (6.00%)	$4,459	0.824	1.068	$5,411	$10,852	1.003	1.134	$10,822	$6,751	0.957	1.143	$7,053
Benefit discounting (0.00%)	$6,823	1.339	1.749	$5,094	$17,671	1.527	1.736	$11,575	$11,186	1.459	1.752	$7,667
Benefit discounting (6.00%)	$6,823	0.608	0.784	$11,228	$17,671	0.693	0.779	$25,507	$11,186	0.661	0.785	$16,920
Adverse events (excluded)	$6,626	0.825	1.068	$8,034	$17,197	1.003	1.134	$17,137	$10,592	0.958	1.143	$11,057
Adverse events (included)	$6,823	0.824	1.068	$8,281	$17,671	1.003	1.134	$17,623	$11,186	0.957	1.143	$11,686
Sub population: T2DM	$6,882	0.815	1.058	$8,444	$17,606	0.985	1.115	$17,869	$11,195	0.944	1.128	$11,859
Sub population: No T2DM	$6,646	0.842	1.09	$7,897	$17,731	1.037	1.171	$17,106	$11,150	0.984	1.173	$11,330
Sub population: eGFR <45	$6,565	0.856	1.109	$7,670	$17,534	1.044	1.178	$16,801	$11,110	0.993	1.183	$11,193
Sub population: eGFR >=45	$7,158	0.775	1.007	$9,234	$17,739	0.939	1.063	$18,897	$11,246	0.903	1.08	$12,450
Sub population: Age <65	$6,735	0.837	1.085	$8,041	$17,903	1.032	1.167	$17,340	$11,237	0.979	1.168	$11,473
Sub population: Age >=65	$4,706	0.624	0.806	$7,535	$11,029	0.702	0.789	$15,705	$9,475	0.837	0.998	$11,323
Health state costs (80% of mean)	$6,538	0.824	1.068	$7,934	$15,610	1.003	1.134	$15,567	$9,822	0.957	1.143	$10,263
Health state costs (120% of mean)	$7,107	0.824	1.068	$8,626	$19,732	1.003	1.134	$19,678	$12,549	0.957	1.143	$13,110
Event costs (80% of mean)	$6,849	0.824	1.068	$8,312	$17,695	1.003	1.134	$17,647	$11,201	0.957	1.143	$11,702
Event costs (120% of mean)	$6,795	0.824	1.068	$8,248	$17,647	1.003	1.134	$17,599	$11,172	0.957	1.143	$11,671
Adverse event costs (80% of mean)	$6,783	0.824	1.068	$8,232	$17,576	1.003	1.134	$17,528	$11,067	0.957	1.143	$11,562
Adverse event costs (120% of mean)	$6,861	0.824	1.068	$8,327	$17,766	1.003	1.134	$17,717	$11,304	0.957	1.143	$11,811
Intervention costs (80% of mean)	$5,846	0.824	1.068	$7,096	$16,315	1.003	1.134	$16,271	$10,466	0.957	1.143	$10,935
Intervention costs (120% of mean)	$7,798	0.824	1.068	$9,465	$19,026	1.003	1.134	$18,974	$11,905	0.957	1.143	$12,439
Comparator costs (80% of mean)	$6,807	0.824	1.068	$8,263	$17,662	1.003	1.134	$17,614	$11,173	0.957	1.143	$11,673
Comparator costs (120% of mean)	$6,836	0.824	1.068	$8,297	$17,679	1.003	1.134	$17,631	$11,199	0.957	1.143	$11,699

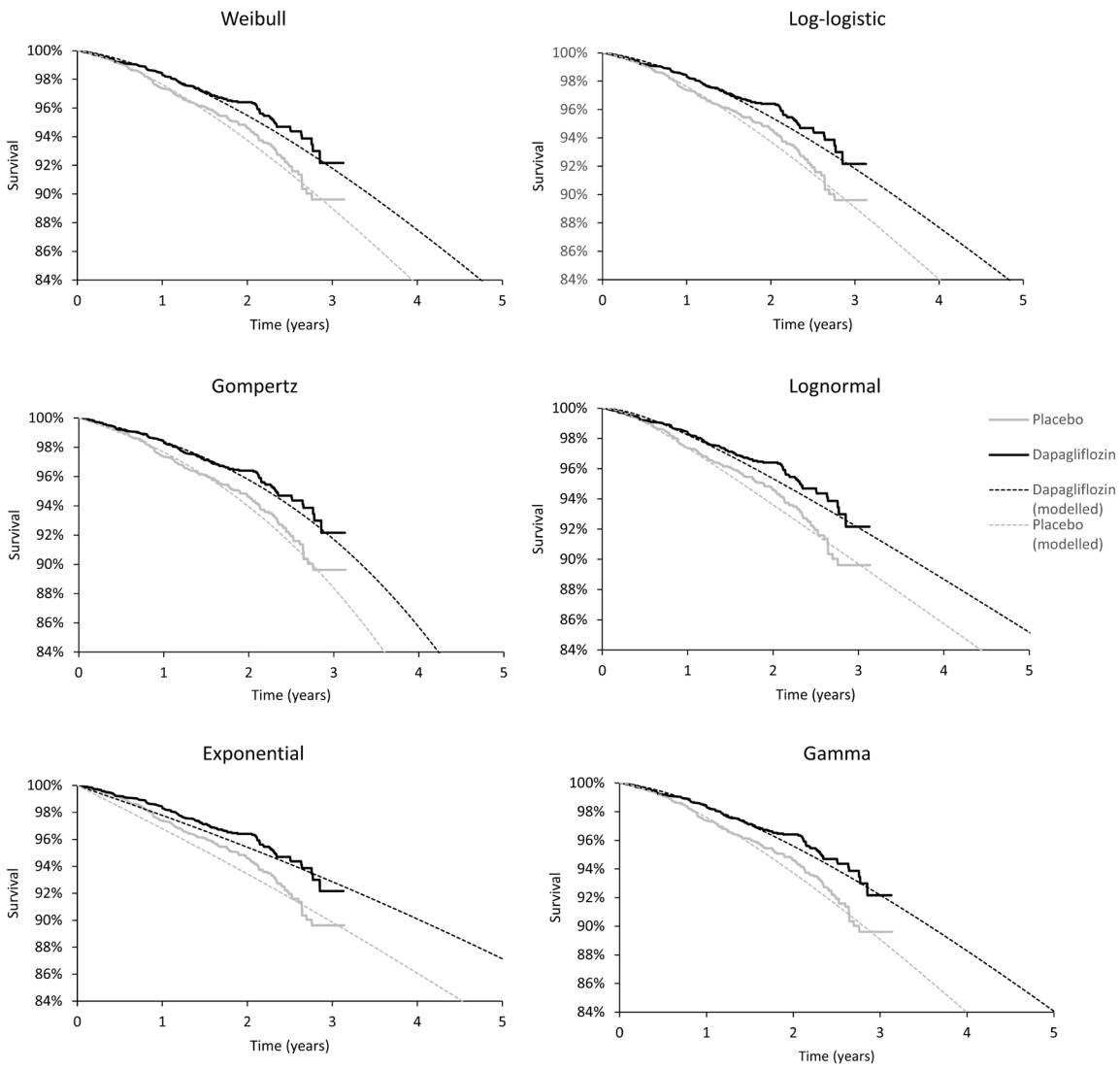
Health state utility (80% of mean)	$6,823	0.659	1.068	$10,352	$17,671	0.802	1.134	$22,032	$11,186	0.766	1.143	$14,611
Health state utility (120% of mean)	$6,823	0.989	1.068	$6,900	$17,671	1.137	1.134	$15,546	$11,186	1.145	1.143	$9,772
Event disutility (80% of mean)	$6,823	0.824	1.068	$8,281	$17,671	1.003	1.134	$17,623	$11,186	0.957	1.143	$11,686
Event disutility (120% of mean)	$6,823	0.824	1.068	$8,279	$17,671	1.003	1.134	$17,622	$11,186	0.957	1.143	$11,686
Adverse event disutility (80% of mean)	$6,823	0.824	1.068	$8,279	$17,671	1.003	1.134	$17,620	$11,186	0.957	1.143	$11,685
Adverse event disutility (120% of mean)	$6,823	0.824	1.068	$8,282	$17,671	1.003	1.134	$17,625	$11,186	0.957	1.143	$11,689
Discontinuation (0.00%)	$14,061	1.391	1.814	$10,106	$34,543	1.706	1.938	$20,251	$22,449	1.634	1.96	$13,742
Discontinuation (10.00%)	$4,667	0.63	0.815	$7,407	$12,443	0.764	0.861	$16,297	$7,766	0.728	0.867	$10,659

SUPPLEMENTAL FIGURES



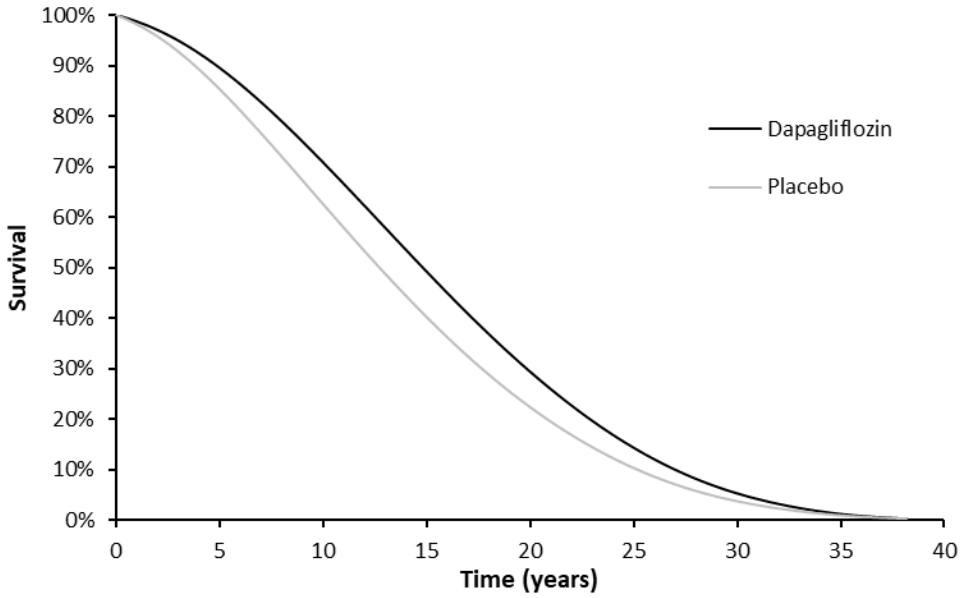
Supplemental Figure 1. Stacked area plot of predicted (dashed line) and observed (solid line) patient distribution in CKD stages in the model and DAPA-CKD trial, respectively.

The proportional occupancy in each CKD stage-defined health state is designated by the distance between each line for both predicted and observed cases.

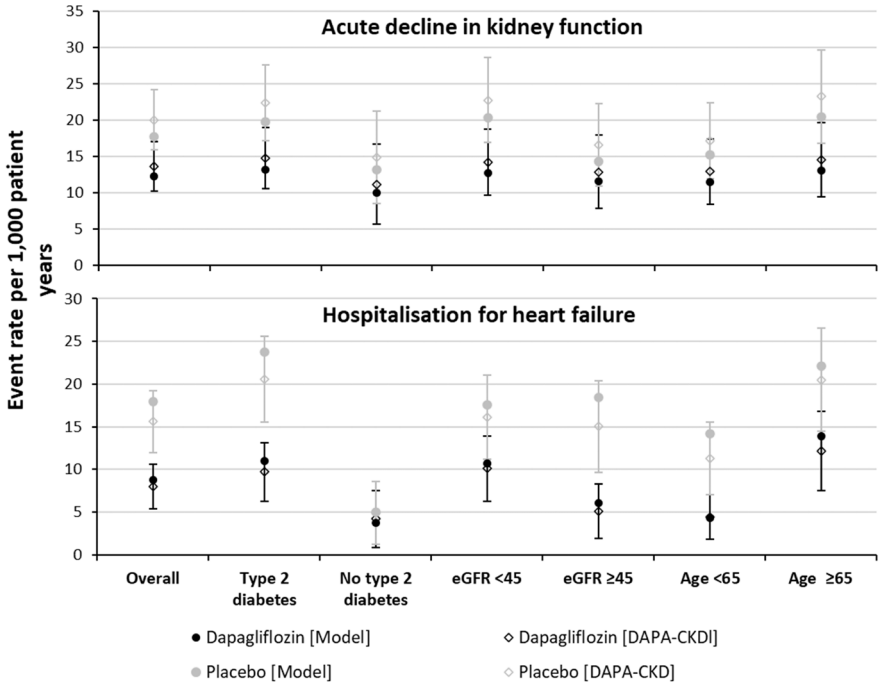


Supplemental Figure 2. Observed (solid line) and predicted (dotted line) incidence of all-cause mortality.

The solid line plots observed data from the DAPA-CKD trial, and the dotted lines represent the parametric functions that have been fitted to the data in each Kaplan-Meier graph.

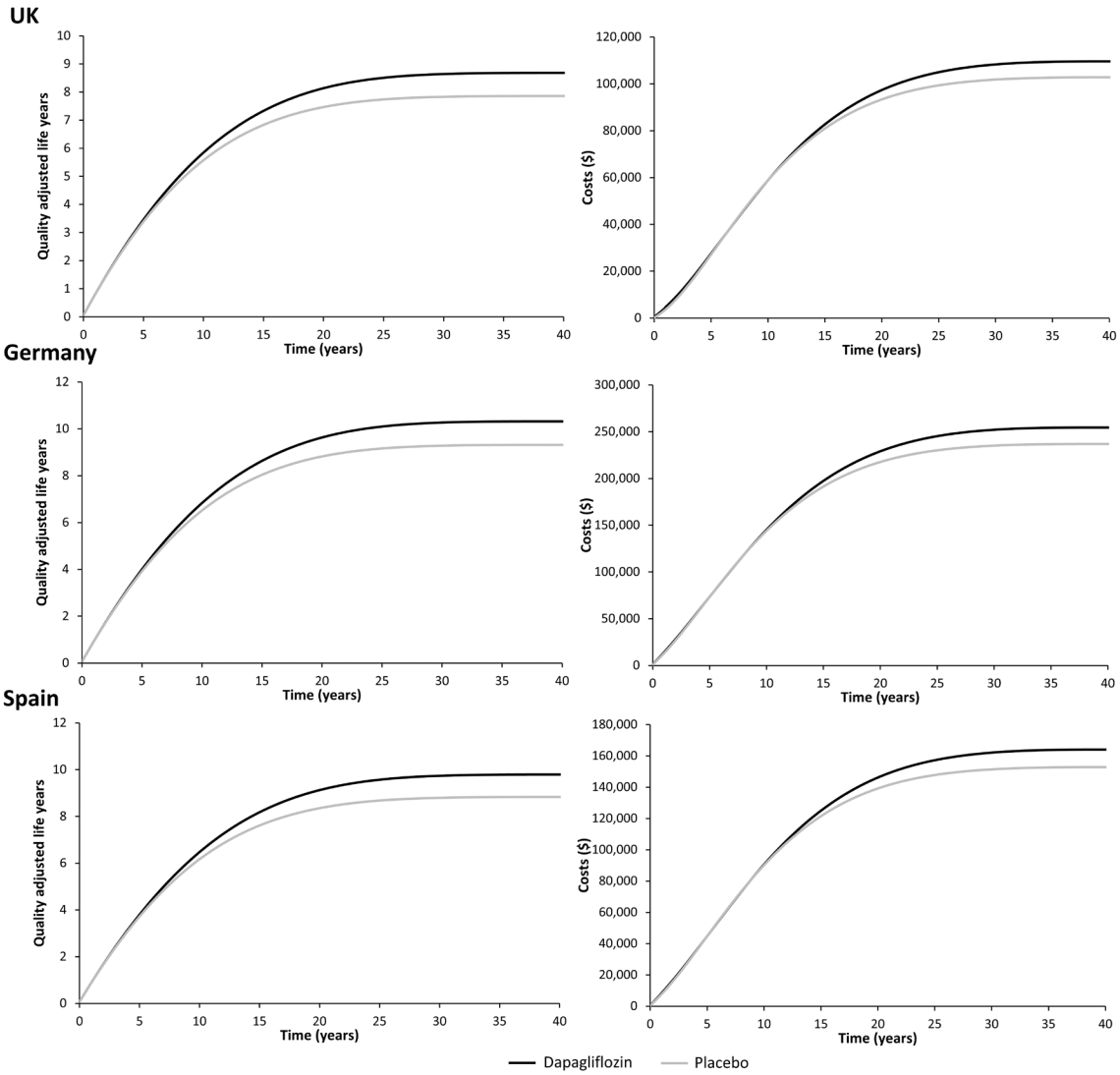


Supplemental Figure 3. Extrapolated mortality rate of patients treated with dapagliflozin and standard therapy versus placebo and standard therapy over a lifetime horizon using a Gompertz survival equation



Supplemental Figure 4. Observed (rhombuses) and predicted (circles) incidence of acute decline in kidney function and hospitalisation for heart failure across subgroups.

Unadjusted model projections were calculated using generalised estimating equations and were compared to observed case data. eGFR: estimated glomerular filtration rate



Supplemental Figure 5. Cumulative accrual of QALYs and total costs (left to right) in patients treated with dapagliflozin and standard therapy (blue) and standard therapy only (grey) in UK, Germany and Spain setting (top to bottom).

QALY: quality-adjusted life year