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CKD-PC risk model for CKD progression: Validation and association with outcomes in the FIDELITY population

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INTRODUCTION

- Early diagnosis and risk stratification is vital to reduce chronic kidney disease (CKD)-related morbidity and mortality, and associated complications[1]
- Assessing the risk of CKD progression can help guide therapy to those at the highest risk[1]
- The Chronic Kidney Disease Prognosis Consortium (CKD-PC) developed risk models to predict the risk of 40% decline in estimated glomerular filtration rate (eGFR) or kidney failure (CKD progression) over 2–3 years in the general population[2]
  - However, the utility of risk models in contemporary pivotal clinical trials is unknown

AIM

- To assess the performance of the CKD-PC model for CKD progression in a contemporary clinical population using the FIDELITY pooled dataset
- To evaluate the efficacy of finerenone using categories of 3-year CKD progression predicted risk

METHODS

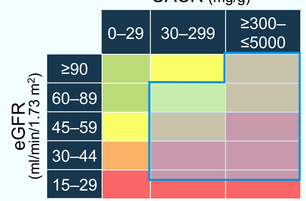
Population (FIDELITY)

- Individual patient-level data from FIDELITY, a prespecified pooled dataset from the FIDELIO-DKD and FIGARO-DKD trials[3]
  - Adults with albuminuric CKD and type 2 diabetes (T2D) and on maximum tolerated dose of a renin–angiotensin system inhibitor, randomised 1:1 to finerenone or placebo (**Figure 1**)

Outcome evaluated

- **CKD progression**: kidney failure, a sustained ≥40% decrease in eGFR from baseline over ≥4 weeks, or kidney-related death

Figure 1. Combined eGFR and UACR inclusion criteria in FIDELIO-DKD and FIGARO-DKD



eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio.

Evaluation of CKD-PC risk model performance

- Risk factors for CKD progression included in the model were[2]:
  - Age, sex, body mass index, systolic blood pressure; use of antihypertensives, oral diabetes medications, insulin; history of heart failure, coronary heart disease, atrial fibrillation; smoking status; eGFR, albuminuria, glycated haemoglobin
- Evaluation metrics included area under the curve (AUC) and the Brier score. Calibration plots were created to compare the observed risk with the CKD-PC model-predicted risk by **deciles of 3-year CKD progression risk**
  - Both discrimination and calibration were evaluated in the overall population and stratified by treatment assignment (finerenone vs placebo)

CKD progression risk and its association with CKD progression in FIDELITY

- Patients were categorised in quartiles (Q) based on their 3-year risk of CKD progression at baseline
- The effect of finerenone vs placebo on a composite kidney outcome was evaluated by risk Qs

RESULTS

Baseline characteristics of the FIDELITY pooled dataset (Table 1)

- Median follow-up was 3.1 years

Table 1. Selected baseline characteristics of the total FIDELITY population and by predicted kidney risk quartiles*

Baseline characteristics	Total (N=13,026)	Q1 <10% (n=3242)	Q2 10–15% (n=3242)	Q3 15–24% (n=3242)	Q4 >24% (n=3242)
Age, year	64.8 ± 9.5	63.8 ± 10.8	65.7 ± 9.2	65.6 ± 8.8	63.9 ± 9.0
Sex, male	9088 (69.8)	2511 (77.5)	2319 (71.5)	2135 (65.9)	2092 (64.5)
HbA1c, %	7.7 ± 1.4	7.4 ± 1.2	7.7 ± 1.3	7.8 ± 1.4	7.9 ± 1.43
Systolic blood pressure, mmHg	136.7 ± 14.2	131.2 ± 13.4	135.9 ± 13.8	138.0 ± 13.6	141.9 ± 13.9
Body mass index, kg/m²	31.3 ± 6.0	30.7 ± 5.8	31.0 ± 5.8	31.5 ± 6.0	32.0 ± 6.3
Smoking status, current	2093 (16.1)	571 (17.6)	568 (17.5)	485 (15.0)	457 (14.1)
History of HF, yes	1007 (7.7)	50 (1.5)	106 (3.3)	256 (7.9)	589 (18.2)
History of CAD, yes	9054 (69.5)	2933 (90.5)	2583 (79.7)	1979 (61.0)	1521 (46.9)
History of atrial fibrillation, yes	1106 (8.5)	206 (6.4)	262 (8.1)	317 (9.8)	315 (9.7)
eGFR, ml/min/1.73 m²	57.6 ± 21.7	70.0 ± 22.0	62.3 ± 20.6	54.3 ± 19.2	43.7 ± 14.9
Median UACR, mg/g (Q1–Q3)	514.7 (197.8–1147.1)	121.7 (54.7–370.7)	362.1 (161.1–697.0)	607.3 (357.5–1070.0)	1532.7 (939.7–2429.9)
Oral anti-diabetes medications, yes	9954 (76.4)	2849 (87.9)	2636 (81.3)	2419 (74.6)	2006 (61.9)
Insulin and analogues, yes	7630 (58.6)	1269 (39.1)	1842 (56.8)	2110 (65.1)	2375 (73.3)

Data are reported as n (%) or mean ± SD unless stated otherwise. *Risk quartiles were based on the patients' 3-year risk of CKD progression as predicted by the CKD-PC model. CAD, coronary artery disease; CKD, chronic kidney disease; CKD-PC, Chronic Kidney Disease Prognosis Consortium; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; HF, heart failure; IQR, interquartile range; SD, standard deviation; UACR, urine albumin-to-creatinine ratio.

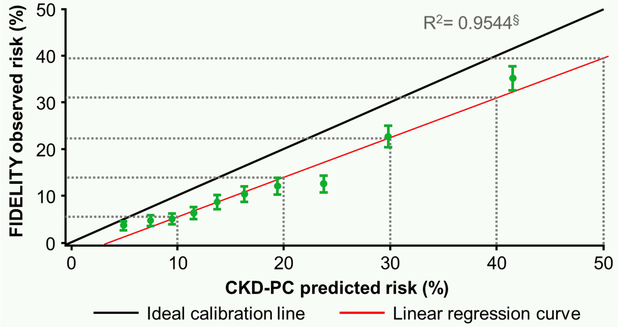
Model performance

- Of the 12,968 patients evaluated*, the median 3-year individual risk of CKD progression was 15.0% (range 0.6–67.3%)
  - AUC score 0.726 (95% confidence interval [CI] 0.712–0.739]
  - Brier score 0.100 (95% CI 0.097–0.103)#
- The predicted 3-year risk was generally slightly higher than the observed risk (**Figure 2**)

*58 patients were excluded due to incomplete data; #Higher AUC scores indicate better risk prediction and lower Brier scores indicate improved accuracy of probabilistic predictions.

Figure 2. Calibration plot for risk of CKD progression‡ at 3 years after randomisation in the FIDELITY population.

‡Kidney failure, a sustained ≥40% decrease in eGFR from baseline over ≥4 weeks, or kidney-related death. §An R^2 value close to one indicates that a linear function between the observed and predicted risk is reasonable. ¶The linear regression equation quantifies the relationship between the predicted and observed risk.
CKD, chronic kidney disease; CKD-PC, Chronic Kidney Disease Prognosis Consortium; eGFR, estimated glomerular filtration rate; R^2, coefficient of determination.



Linear regression equation¶: y = 0.85x – 0.03

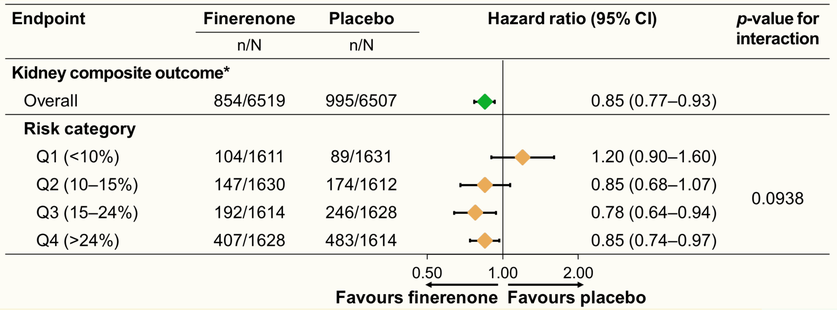
CKD-PC predicted risk, x (%)	FIDELITY observed risk, y (%)
10	5.5
20	14.0
30	22.5
40	31.0
50	39.5

Association of CKD progression risk with outcomes

- Finerenone reduced the risk of CKD progression irrespective of the risk Qs (*p*-interaction = 0.09) with a trend towards greater reduction in the higher risk Qs (3-year risk of CKD progression ≥10%) (**Figure 3**)
- Finerenone treatment also demonstrated a slower decline in eGFR compared with placebo

Figure 3. Efficacy of finerenone in reducing the risk of CKD progression* stratified by the baseline 3-year risk.

*Kidney failure, a sustained ≥40% decrease in eGFR from baseline over ≥4 weeks, or kidney-related death.
CI, confidence interval;
CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; Q, quartile.



CONCLUSIONS

- The CKD-PC risk model accurately predicted CKD progression in a large global clinical trial population of patients with CKD and T2D
- Finerenone reduced the risk of CKD progression across different risk categories predicted by the CKD-PC model

Our findings suggest that the CKD-PC model can be used to identify the patients at high risk of CKD progression and prioritise them for kidney function preserving therapies

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