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Validation of a CKD progression risk prediction model in the FIDELITY dataset population

N. TANGRI[1,2], T. FERGUSON[1,2], S. J. LEON[2,3], S. D. ANKER[4,5], B. PITT[6], P. ROSSING[7,8], L. M. RUILOPE[9–11], A. E. FARJAT[12], Y. M. K. FARAG[13], P. SCHLOEMER[14], R. LAWATSCHECK[15], K. ROHWEDDER[16], G. L. BAKRIS[17]

[1]Department of Internal Medicine, Max Rady College of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada [2]Seven Oaks Hospital Chronic Disease Innovation Centre, Winnipeg, Manitoba, Canada [3]University of Manitoba, Community Health Sciences, Winnipeg, Canada [4]Department of Cardiology (CVK) of German Heart Center Charité; Institute of Health Center for Regenerative Therapies (BCRT), German Centre for Cardiovascular Research (DZHK) partner site Berlin, Charité Universitätsmedizin, Berlin, Germany [5]Institute of Heart Diseases, Wroclaw Medical University, Wroclaw, Poland [6]Department of Medicine, University of Michigan School of Medicine, Ann Arbor, MI, USA [7]Steno Diabetes Center Copenhagen, Gentofte, Denmark [8]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark [9]Cardiorenal Translational Laboratory and Hypertension Unit, Institute of Research imas12, Madrid, Spain [10]CIBER-CV, Hospital Universitario 12 de Octubre, Madrid, Spain [11]Faculty of Sport Sciences, European University of Madrid, Madrid, Spain [12]Research and Development, Clinical Data Sciences and Analytics, Bayer PLC, Reading, UK [13]US Medical Affairs, Bayer US LLC Pharmaceuticals, Whippany, NJ, USA [14]Statistics and Data Insights, Bayer AG, Berlin, Germany [15]Cardiology and Nephrology Clinical Development, Bayer AG, Berlin, Germany [16]Cardio-Renal Medical Affairs Department, Bayer AG, Berlin, Germany [17]Department of Medicine, University of Chicago Medicine, Chicago, IL, USA

INTRODUCTION

- Chronic kidney disease (CKD) affects over 800 million individuals worldwide[1] and is often diagnosed at later disease stages when opportunities to prevent adverse outcomes are limited[2]
- Accurate prediction of individual risk of CKD progression could enhance patient experiences and outcomes
- Klinrisk, a lab-based risk prediction model, has been shown to accurately predict CKD progression in adults at all stages of CKD[3]

AIM

- To validate the Klinrisk model for the prediction of key composite kidney outcomes up to 4 years post-randomisation in FIDELITY, a dataset combining individual patient-level data from two phase III, multicentre, double-blind trials investigating finerenone – a nonsteroidal mineralocorticoid receptor antagonist

METHOD

Population (validation cohort)

This post hoc analysis included all patients from FIDELITY, a prespecified pooled analysis of data from the FIDELIO-DKD (NCT02540993) and FIGARO-DKD (NCT02545049) trials[4]:

- Adults with CKD and type 2 diabetes (T2D) receiving a maximum tolerated dose of a renin–angiotensin system inhibitor
- Randomised 1:1 to finerenone or placebo
- Median follow-up: 3 years

Key composite kidney outcomes

- **Primary**: ≥40% estimated glomerular filtration rate (eGFR) decline or kidney failure
- **Secondary**: ≥57% eGFR decline or kidney failure

Variables used for model predictions

Klinrisk model risk predictions were based on single timepoint (baseline) measures of demographic data and routinely collected laboratory data, including:

- Age and sex
- Complete blood count
- A comprehensive metabolic panel
- Urine albumin-to-creatinine ratio (UACR)
- eGFR

Statistical analyses

- Model **discrimination ability** and **calibration** were calculated using area under the curve (AUC) values, Brier scores and calibration plots in the overall population
- **Sensitivity analyses** examined the accuracy of the models in predicting the secondary outcome and the change in risk score over time
- Kidney Disease: Improving Global Outcomes (KDIGO) heatmap categories were used as the **reference standard**

RESULTS

Baseline characteristics

- Selected baseline characteristics for the 13,026 patients included in the analysis are shown in **Table 1**

Table 1. Selected FIDELITY baseline characteristics

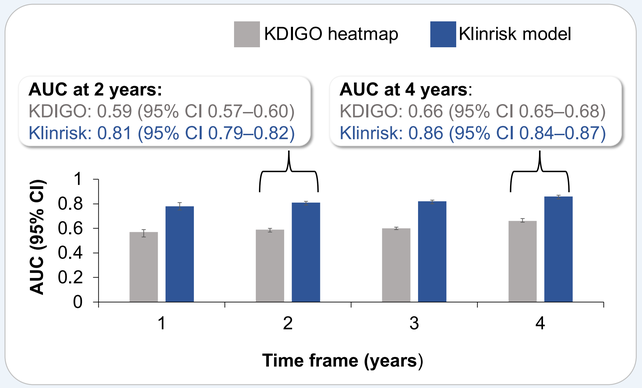
Characteristic, n (%)*	Total, N=13,026
Age, mean (SD)	64.8 (9.5)
Sex, male	9088 (69.8)
Sex, female	3938 (30.2)
Mean eGFR, ml/min/1.73 m^2 (SD)	57.6 (21.7)
Median UACR, mg/g (IQR)	515 (198–1147)

**Data shown as n (%) unless otherwise specified*
eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation; UACR, urine albumin-to-creatinine ratio

Model performance and calibration

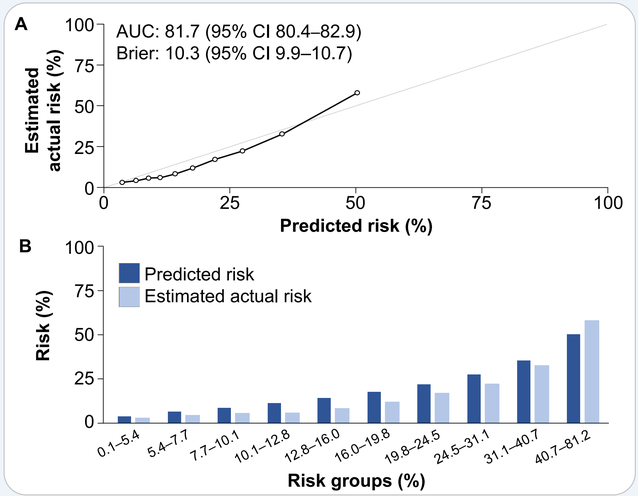
- At 2 and 4 years, 984 and 1795 patients had experienced a primary outcome event, respectively
- The Klinrisk model accurately predicted the primary outcome and outperformed KDIGO heatmap categories (**Figure 1**)
- Calibration was found to be appropriate:
  - Brier score 0.067 (95% confidence interval [CI] 0.064–0.070) at 2 years and 0.115 (95% CI 0.109–0.120) at 4 years
  - Calibration at 3 years is shown in **Figure 2**
- Discrimination accuracy for the secondary outcome was similar to that obtained for the primary outcome (C-statistic 0.88; 95% CI 0.87–0.90 at 3 years)

Figure 1. AUC scores for the primary outcome for years 1 to 4 with Klinrisk model and KDIGO heat map categories



AUC, area under the curve; CI, confidence interval; KDIGO, Kidney Disease: Improving Global Outcomes

Figure 2. Calibration plots for Klinrisk prediction model for the primary composite outcome at 3 years



AUC, area under the curve; CI, confidence interval

CONCLUSIONS

- Based on routinely collected lab data, the Klinrisk machine learning model accurately predicted CKD progression events in a well-characterised population pooled from two global clinical trials
- Prospective implementation of the model in clinical trial enrolment, as well as clinical care pathways, may allow for earlier intervention and improve clinical outcomes for patients with CKD

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CONTACT INFORMATION

Navdeep Tangri
Max Rady College of Medicine, Internal Medicine, Section of Nephrology, University of Manitoba, 2LB19 – 2300 McPhillips Street, Seven Oaks General Hospital, Winnipeg, Manitoba R2V 3M3, Canada
Phone: +1 204 -631-3834; Fax: +1 204-632-3660; ntangri@sogh.mb.ca