# Modelling the effect of multi-indication treatment in patients with multimorbidity using population-scale linked electronic health records to inform healthcare policy and decision-making

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## Introduction

Healthcare decision-making has previously focussed on developing recommendations for single conditions. However, standardised care for each chronic condition in isolation can be inappropriate for individuals living with multiple long-term conditions known as multimorbidity, and may lead to unnecessary polypharmacy. This work is motivated by recent National Institute for Health and Care Excellence (NICE) recommendations on the use of a Sodium-Glucose Cotransporter-2 (SGLT2) inhibitor in three commonly co-existing long-term conditions: type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD), and heart failure (HF).

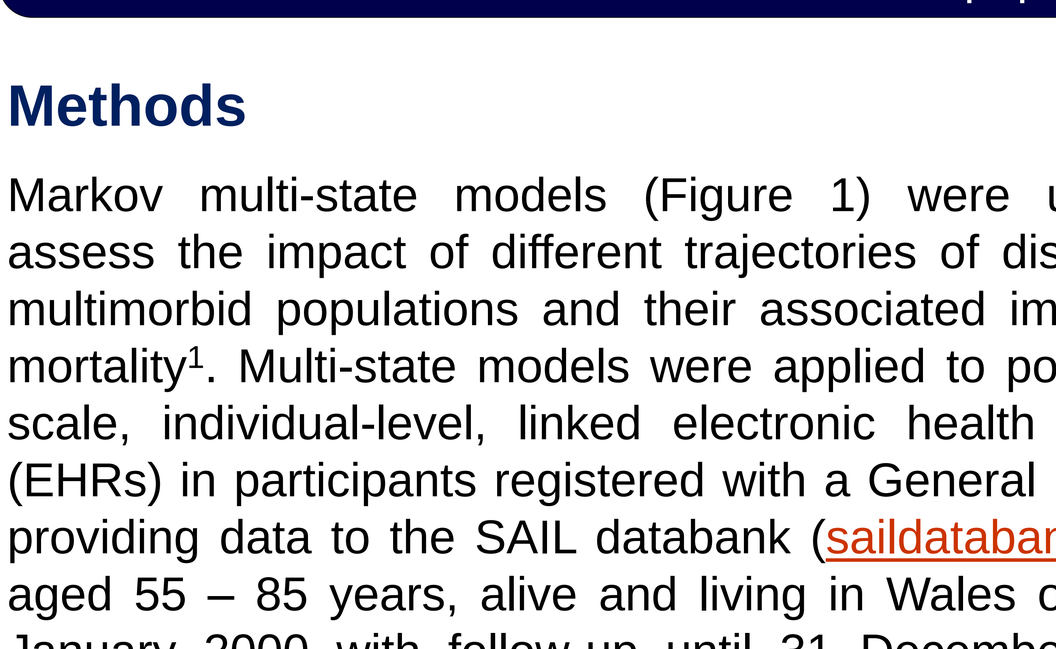
**Objective**

To develop a modelling framework to estimate the effect of a multi-indication treatment in multimorbid populations.

## Methods

Markov multi-state models (Figure 1) were used to assess the impact of different trajectories of disease in multimorbid populations and their associated impact on mortality[1]. Multi-state models were applied to population scale, individual-level, linked electronic health records (EHRs) in participants registered with a General Practice providing data to the SAIL databank (saildatabank.com), aged 55 – 85 years, alive and living in Wales on the 1 January 2000 with follow-up until 31 December 2012, Welsh residency break, or death.

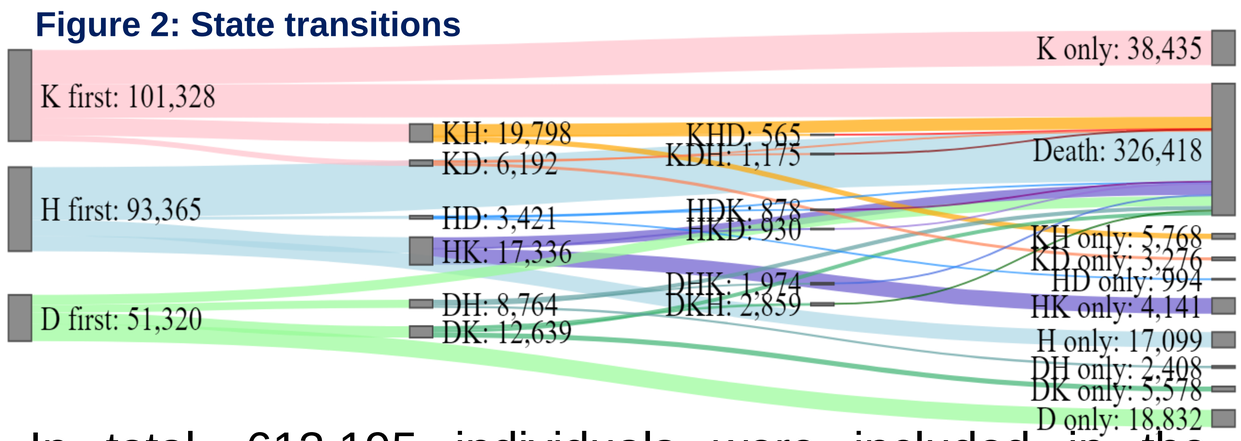
**Figure 1: Multistate model**




Separate baseline hazards, adjusted for age at entry into the health state, were estimated using Weibull regression models. Hazard ratios of treatment effects were obtained from published randomised controlled trials in subgroups of multimorbid populations, and implemented in a patient-level simulation to compare treated and untreated populations.

## Results

**Figure 2: State transitions**




In total, 613,195 individuals were included in the analysis. In terms of first indication, 101,328 participants developed CKD, 93,365 developed HF, and 51,320 developed T2DM (Figure 2). SGLT2 inhibitors increased the estimated mean life-expectancy from 0.02 (95%CI: -0.02 to 0.05) to 1.44 (95%CI: 1.12 to 1.74) years in multimorbid T2DM, CKD and HF, with the largest gain in estimated mean life-expectancy for individuals with HF followed by T2DM [HF>T2DM]. The estimated gain in life-expectancy for individuals treated with a SGLT2 inhibitor was less than 0.5 years for individuals with T2DM, CKD and HF in different temporally ordered sequences. The estimated mean time to develop HF increased by 3.1 (95%CI: 3.00 to 3.24) and 1.34 (95%CI: 1.12 to 1.56) years in individuals with CKD [CKD>HF], and CKD followed by T2DM [CKD>T2DM>HF].

## Conclusions

There is an increasing need to appraise interventions in multiple long-term conditions to identify optimal treatment strategies and reduce polypharmacy in multimorbid populations.

Multistate models applied to linked EHRs allowed for a more rigorous assessment of treatment effects in multimorbid populations for healthcare decision-making.

**[1]** Owen R, *et al.* Temporal sequencing in multimorbidity using population-scale linked data for 1.7 million individuals with 20-year follow-up: Research Square, 2022. https://doi.org/10.21203/rs.3.rs-1537576/v1

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