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ORIGINAL ARTICLE

Characteristics, treatment and disease burden among stage 3–4 chronic kidney disease patients with and without type 2 diabetes in Finland during 2016–2022

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ABSTRACT

Background. Real-world evidence on the management of chronic kidney disease (CKD) with and without type 2 diabetes (T2D) is limited. This study described the characteristics, treatment and disease burden in patients with stage 3–4 CKD with and without T2D in Finland.

Methods. This cohort study used data from primary and hospital care in five municipalities in Finland to identify adults with stage 3–4 CKD, defined as having either one estimated glomerular filtration rate (eGFR) measurement of 15–59 mL/min/1.73 m^2 followed by a second measurement taken ≥90 days later, or a registered CKD diagnosis. Prevalence was determined on 31 December 2022, and a cohort of incident stage 3–4 CKD patients was followed from the first date fulfilling eligibility criteria since 1 January 2016 (index) until death or 31 December 2022, and analyzed by T2D status.

Results. The prevalence of stage 3–4 CKD was 6.3%. Among the 12 474 incident stage 3–4 CKD patients, the majority were non-T2D (73%). The median age was similar for non-T2D and T2D CKD patients, respectively. Baseline albuminuria screening was 9% among non-T2D and 53% among T2D. The use of kidney-protective treatments at index was also lower in non-T2D patients (47%), compared with T2D patients (69%). The use of kidney-protective treatments remained unchanged during 12 months after index. Healthcare resource utilization was high, and CKD or heart failure contributed considerably more to the all-cause healthcare costs than atherosclerotic diseases, regardless of T2D status. In both CKD subgroups, 10% had died within 1 year.

Conclusions. In Finland, CKD is highly prevalent and associated with high risks and low use of albuminuria testing and kidney-protective medications. Most CKD patients were non-T2D, which showed lower use of preventive management and similar risks compared with T2D patients. These findings call for an urgent need for improved awareness and risk management, especially in non-T2D CKD patients.

Keywords: chronic kidney disease, healthcare resource use, hospitalization, mortality, type 2 diabetes

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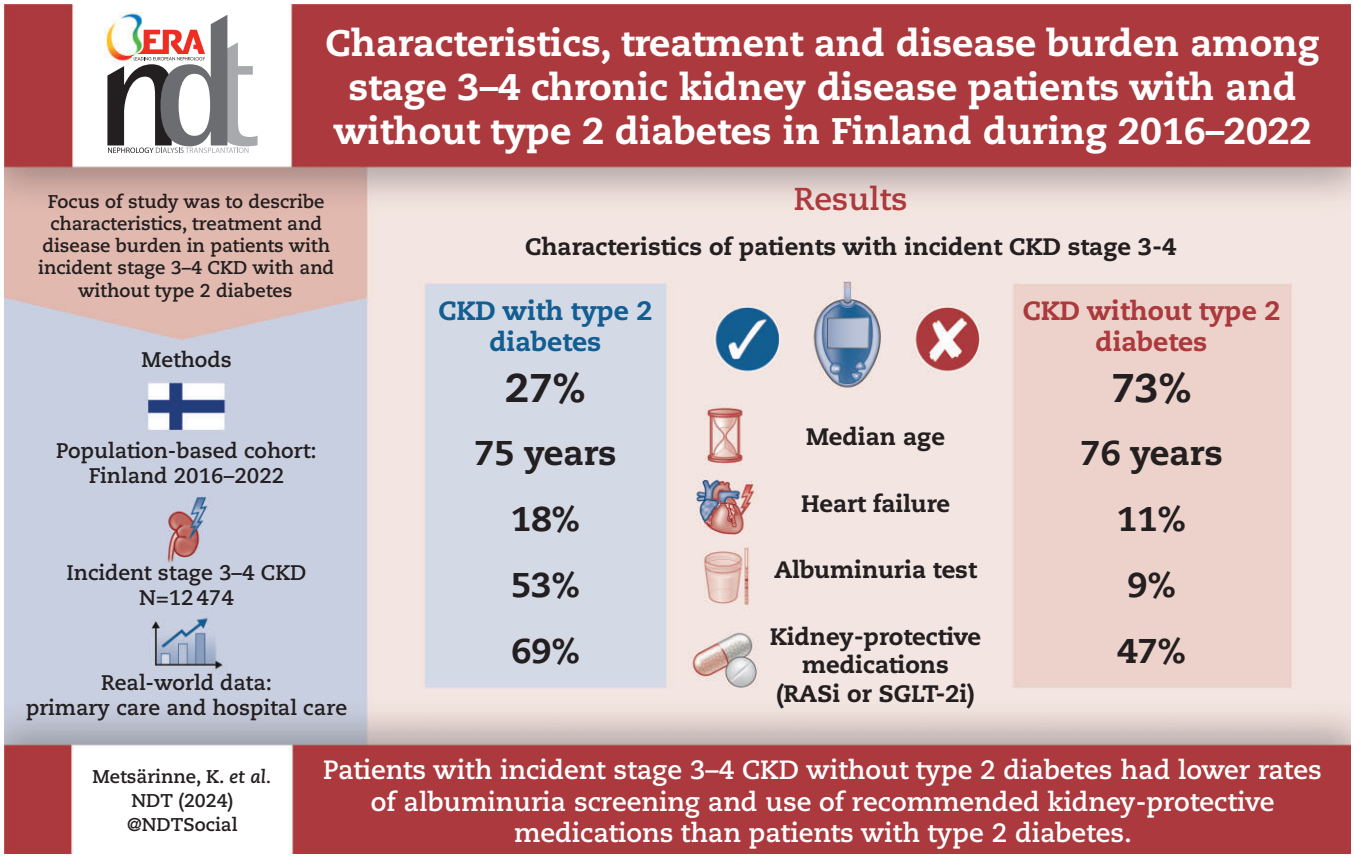
GRAPHICAL ABSTRACT



KEY LEARNING POINTS

What was known:

- Guidelines recommend monitoring kidney function at least annually in at-risk patients [especially in type 2 diabetes (T2D)] and to use renin–angiotensin system and sodium-glucose cotransporter 2 inhibitors as first-line chronic kidney disease (CKD) treatments.
- Too few patients with T2D undergo regular monitoring. The prevalence and management of non-T2D CKD and non-T2D patients at risk of CKD is less clear.

This study adds:

- The prevalence of stage 3–4 CKD in Finland is 6.3%.
- Three in four individuals with CKD do not have T2D.
- CKD patients without T2D are also at high risk of morbidity and mortality, but remain neglected in terms of albuminuria screening, diagnosis and kidney-protective treatments.

Potential impact:

- These findings highlight the urgent need for increased awareness and improved risk management among CKD patients
- This study shows that CKD is not only a disease of concern for patients with T2D.
- The alarming findings with lack of albuminuria screening and kidney-protective treatment inertia despite a high disease risk underscore the need for action.

INTRODUCTION

Chronic kidney disease (CKD) is one of the most prevalent non-communicable diseases globally, putting a huge burden on health-care systems. CKD is estimated to affect one in ten individuals worldwide and its prevalence and the burden of associated complications is expected to increase with an aging population [1–5]. Thus, there is an urgent need to raise awareness and improve the management of individuals at risk of CKD [diabetes, high blood pressure, cardiovascular disease (CVD)].

Regular monitoring of kidney function and early detection of albuminuria in at-risk patients is key in prevention of CKD and its progression. Kidney function can be monitored with relatively inexpensive laboratory measurements, including estimated glomerular filtration rate (eGFR) and urine albumin creatinine

ratio (UACR). Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend assessing eGFR and albuminuria annually in patients with diabetes and at least annually in patients with confirmed CKD [6]. Finnish national guidelines recommend annual screening in patients with diabetes and screening every 1–2 years in patients with hypertension, followed by monitoring at least once a year if CKD is confirmed [7, 8]. However, previous reports have shown that too few patients with type 2 diabetes (T2D) undergo regular monitoring [9]. The monitoring among non-T2D CKD and non-T2D at risk of CKD patients is unknown. These patients are heterogenous as several common risk factors exist for CKD [5]. Thus, more data are needed on these patients to fully understand the burden and challenges in the management of CKD.

Early diagnosis of CKD allows prompt initiation of the treatment with kidney-protective medications. Renin–angiotensin system inhibitors (RASi) and sodium–glucose cotransporter 2 inhibitors (SGLT2i) are recommended as first-line CKD treatments, regardless of diabetes status [6], but adherence to these beneficial treatments is less clear.

The aims of the present study were, first, to show the prevalence of stage 3–4 CKD, and second, to describe the patient characteristics, treatment and disease burden in the incident CKD patient population with and without T2D identified in Finnish public healthcare.

MATERIALS AND METHODS

Study design and permissions

This observational study was conducted in accordance with the Declaration of Helsinki and the Act on Secondary Use of Health and Social Data. The study protocol and data requests were approved by the wellbeing services county of Central Uusimaa, Finland, Finnish Social and Health Data Permit Authority, Findata, and Statistics of Finland. Data permission numbers are provided in Supplementary methods.

Study populations, data extraction and study period

The electronic health records of potential CKD patients, identified in primary care in the municipalities of the wellbeing services county of Central Uusimaa (Keusote) and city of Turku, were linked with respective primary and secondary/tertiary care laboratory data (data lakes of Hospital Districts of Helsinki and Uusimaa and Southwest Finland) and national register data. The national data included primary and secondary/tertiary care contacts (the Register of Primary Health Care Visits and the Care Register for Health Care, Finnish Institute for Health and Welfare, THL), reimbursed outpatient medications (Social Insurance Institution Finland, SII), and causes of deaths (Statistics Finland; Supplementary data, Fig. S1). Linkage of individual-level data across different registers was enabled by using the personal identification numbers, and the pseudonymized data were analyzed in a secure data environment. The last data point available was 31 December 2022 (end of study, EOS).

The final study populations included stage 3–4 CKD patients of five Finnish municipalities (Hyvinkää, Järvenpää, Mäntsälä, Pornainen and Turku; two of six Keusote municipalities were excluded due to data quality issues; Supplementary data, Fig. S1).

Stage 3–4 CKD definition

Stage 3–4 CKD was defined as having an eGFR of 15–59 mL/min/1.73 m^2 confirmed by two measurements taken ≥90 days apart, or as having a CKD diagnosis validated with at least one eGFR measurement up to 1 year before or up to 14 days after the recorded diagnosis (Supplementary data, Table S1). Eligible individuals were indexed at the first-ever date fulfilling the confirmed stage 3–4 criteria: date of diagnosis or date of second (confirmatory) eGFR measurement. We excluded individuals aged <18 years at index or patients with records of stage 5 CKD or dialysis or gestational or type 1 diabetes before index date (Supplementary data, Table S1).

Two final study cohorts were formed: prevalent and incident cohorts (Supplementary data, Fig. S1).

Prevalent stage 3–4 CKD patients

The prevalent cross-sectional cohort included all identified stage 3–4 CKD patients on 31 December 2022. The annual point prevalence was calculated as the number of patients alive and still in stage 3–4 CKD on 31 December 2022 reported per 100 000 adult population.

Incident stage 3–4 CKD patients

These CKD patients were indexed at the date of newly detected stage 3–4 CKD between the years 2016 and 2022. The incident cohort was divided in subgroups according to baseline T2D status (T2D vs non-T2D), defined as having a T2D diagnosis (International Classification of Diseases, Tenth Revision E11) or medication (Anatomical Therapeutic Chemical A10) or HbA1c >48 mmol/mol (Supplementary data, Fig. S1).

Baseline characteristics

Use of medications was based on at least one reimbursed purchase during the year prior to the index (Supplementary data, Table S2). For laboratory measurements, the closest laboratory value up to 3 years prior to index, or 14 days post-index (see the eligibility criteria) was considered. For estimation of GFR, the CKD Epidemiology Collaboration equation was used [10]. Comorbidities were searched from all available data prior to index (Supplementary data, Table S1).

Clinical outcomes

The following clinical outcomes were reported for the incident cohort as total number of events per 1000 patient years (PYs) during 1 year post index: All-cause and CVD mortality, as well as inpatient hospitalizations due to kidney disease (including acute, chronic, unspecified, diabetic, and hypertensive kidney disease, dialysis, glomerular diseases and renal tubulointerstitial disease), heart failure (HF), cardiorenal disease, myocardial infarction (MI) and stroke (Supplementary data, Table S1). For disease-specific hospitalizations, both main and side diagnoses were considered. Patients without events were followed until EOS, 1 year post-index or death, whichever occurred first. In addition to describing plasma potassium levels at baseline, the cumulative incidence of patients with plasma potassium levels ≥5.5 mmol/L during follow-up was assessed using mean cumulative function from index until maximum 5 years of follow-up, and accounting for death as competing risk.

Costs of healthcare resource use

Healthcare resource use was analyzed based on the data in the Register of Primary Health Care Visits and the Care Register for Health Care (THL) which contain all in- and outpatient contacts of public healthcare in Finland. Respective costs were determined in euros and based on publicly available unit costs of the

healthcare in 2017 [11]. The unit costs include the average costs of examinations, procedures, operations, inpatient medications and overheads estimated for each unit, and the type of contact/visit and occupational group/specialty field [11]. For contacts without relevant cost available, mean cost among all entries with valid cost of same type was used.

Costs were summarized cumulatively using mean cumulative function from index until maximum 5 years of follow-up. Patients were censored at EOS or death, whichever occurred first. Mean cumulative function was fitted separately for all-cause costs, and by disease group (CKD, HF, MI, stroke and peripheral artery disease, and other CVD; Supplementary data, Table S1). Contacts were allocated to disease groups if either the main and/or side diagnoses fulfilled the criteria, thus events could be included in multiple disease groups [1, 12–14].

Utilization of kidney-protective medications

Longitudinal patterns of RASi, SGLT2i and dapagliflozin uptake were determined based on filled prescriptions (Supplementary data, Table S2). On/off treatment status of each patient was followed on daily basis from 6 months prior to index until 12 months post index, death or EOS, whichever occurred first [12]. Dapagliflozin uptake was analyzed from 6 months prior approval for the treatment of CKD until 12 months post-approval. If a new purchase occurred before the previous package had been finished, it was assumed to be used after the previous one. A patient was considered to be off treatment from the last day covered until the collection of a new medication package, if any. The proportion of patients on treatment was defined as the number of patients on treatment divided by patients at risk.

Statistical analysis

All analyses were descriptive and performed using R-4.0.3 [15]. Mean incidence was calculated for the period 2010–2022 with 95% confidence intervals (CIs) derived from Poisson approximation. The presence of monotonic trend was assessed using Mann–Kendall trend test. Standard summary statistics were reported for patient characteristics; mean with standard deviation and/or median with interquartile range for continuous variables, and the number and proportion of patients for categorical variables. Differences were reported using standardized mean differences (SMD), and where more than 10% was considered to represent a significant difference.

RESULTS

Prevalence and incidence

Study cohorts were established based on data from five Finnish municipalities, which together represent approximately 5.7% (0.32 million) of the total Finnish population (5.6 million). In these municipalities in 2022, a total of 16 813 individuals with stage 3–4 CKD were alive and had not progressed to stage 5, representing a prevalence of 6.3% in the total background population of 263 383 adult inhabitants. The mean incidence during 2010–2022 was 750 cases per 100 000 adult population (Supplementary data, Fig. S2).

Baseline characteristics of incident CKD patients

Between January 2016 and December 2022, a total of 12 474 patients were identified with incident stage 3–4 CKD where the majority were non-T2D (73%; $n = 9158$). When comparing non-T2D with T2D patients, they were similar in age (median age, 76 vs 75 years) and eGFR (55 vs 55 mL/min/1.73 m^2) (Table 1). Overall, the utilization of albuminuria testing was low (20%) in patients with newly detected CKD, with a substantial difference between those without and with T2D, 9% and 53%, respectively (SMD 109.7%) (Table 1). The median potassium level at baseline was 4.0 mmol/L, whereas potassium levels ≥5.5 mmol/L at baseline was experienced by 0.4% and 0.8% of patients without and with T2D (SMD –5.9%), respectively (Table 1). Patients without T2D had slightly lower comorbidity burden; 11% vs 18% for HF (SMD –18.7%), 9% vs 14% for myocardial infarction (SMD –15.4%), and 21% vs 25% for atrial fibrillation (SMD –10.2%), respectively (Table 1). Baseline CKD diagnoses were scarce, 13% and 19%, respectively (SMD –15.0%) (Table 1). The proportion of individuals with a recorded CKD diagnosis increased only slightly during the follow-up, with only 25% in non-T2D and 36% in T2D having a recorded CKD diagnosis by the end of follow-up. In patients without T2D, treatment with both kidney- and cardiovascular-protective medications, like RASi/SGLT2i (55% vs 79%, SMD –51.4%) and statins (38% vs 64%, SMD –53.2%), was lower than in patients with T2D (Table 1).

Kidney-protective treatment

At the time of newly detected stage 3–4 CKD, no change in the utilization of kidney-protective medications was observed (Fig. 1; Supplementary data, Fig. S3). The proportions of patients on kidney-protective medications remained unchanged 12 months post-index in both CKD subgroups: 47% in non-T2D and 67% in T2D (Fig. 1).

Post-approval uptake of novel kidney-protective drugs

In a separate analysis of incident CKD patients following the approval of SGLT2i (dapagliflozin) for CKD treatment, the general uptake was very low, i.e. no change in proportions of patients treated with dapagliflozin before and after approval (Fig. 2).

Risks of clinical outcomes

Patients with newly detected stage 3–4 CKD had 10% risk of all-cause mortality within the first year, irrespective of diabetes status (Supplementary data, Fig. S4); 101 and 103 deaths per 1000 PYs in non-T2D and T2D CKD, respectively (Fig. 3). Accordingly, CVD mortality rate was 29 and 40 deaths per 1000 PYs. The risk of severe complications requiring hospitalization was mainly driven by cardiorenal diseases, like CKD or HF, and less by atherosclerotic CVDs, like MI, stroke or peripheral artery disease. A similar pattern of event rates was observed in patients with and without T2D (Fig. 3). All-cause hospitalization rate was high in both CKD subgroups: 551 and 707 events per 1000 PYs in non-T2D and T2D, respectively.

Throughout follow-up, the proportion of patients with potassium levels ≥5.5 mmol/L, was twice as high among T2D patients compared with non-T2D patients (Supplementary data, Fig. S5).

Healthcare costs per patient

During 5 years, the total all-cause accumulated healthcare costs per patient were 13 000 euros (95% CI 12 000–14 000 euros) in non-T2D and 18 000 euros (95% CI 16 000–20 000 euros) in T2D (Supplementary data, Fig. S6). Cardiorenal complications (CKD or HF) contributed considerably more to the all-cause healthcare costs than the atherosclerotic CVD complications (Fig. 4). This pattern was similar irrespective of diabetes status. As expected, hospitalizations contributed to the costs already 1 year before

Table 1: Baseline characteristics of individuals with incident stage 3–4 CKD in Finland 2016–2022.

Variable	All	Non-T2D	T2D	SMD (%)[d]
N	12 474	9 158	3 316	
Age (years), median (IQR)	76 (70; 82)	76 (70; 83)	75 (69; 81)	8.2
Females, *n* (%)	7448 (60)	5772 (63)	1676 (51)	25.4
Comorbidities, *n* (%)[a]				
CKD diagnosis	1850 (15)	1224 (13)	626 (19)	–15.0
Myocardial infarction	1261 (10)	808 (8.8)	453 (14)	–15.4
Stroke	1893 (15)	1366 (15)	527 (16)	–2.7
Peripheral artery disease	633 (5.1)	385 (4.2)	248 (7.5)	–14.0
Atrial fibrillation	2743 (22)	1909 (21)	834 (25)	–10.2
Any heart failure	1654 (13)	1053 (11)	601 (18)	–18.7
Cancer	2566 (21)	1906 (21)	660 (20)	2.3
Laboratory measurements[b]				
Blood hemoglobin (g/L), median (IQR)	135 (123; 145)	135 (124; 145)	132 (121; 144)	11.1
Missing/not measured	112 (0.9)	90 (1)	22 (0.7)	3.5
Plasma potassium (mmol/L), median (IQR)	4.00 (3.90; 4.30)	4.00 (3.90; 4.30)	4.00 (3.90; 4.40)	–15.8
Plasma potassium <5.0 mmol/L, *n* (%)	11 631 (95)	8576 (96)	3055 (93)	13.9
Plasma potassium ≥5.0 mmol/L, *n* (%)	593 (4.9)	357 (4.0)	236 (7.2)	–13.9
Plasma potassium ≥5.5 mmol/L, *n* (%)	60 (0.5)	33 (0.4)	27 (0.8)	–5.9
Plasma potassium ≥6.0 mmol/L, *n* (%)	23 (0.2)	11 (0.1)	12 (0.4)	–4.9
Missing/not measured	250 (2)	225 (2.5)	25 (0.8)	13.6
eGFR (mL/min/1.73 m^2), median (IQR)	55 (50; 58)	55 (50; 58)	55 (49; 58)	11.1
eGFR 45–60 mL/min/1.73 m^2, *n* (%)	10 781 (86)	7993 (87)	2788 (84)	9.3
eGFR 30–45 mL/min/1.73 m^2, *n* (%)	1405 (11)	973 (11)	432 (13)	
eGFR 15–30 mL/min/1.73 m^2, *n* (%)	288 (2.3)	192 (2.1)	96 (2.9)	
UACR categories (mg/mmol), *n* (%)				27.8
A1 (<3 mg/mmol)	1926 (76)	650 (84)	1276 (73)	
A2 (3–30 mg/mmol)	480 (19)	93 (12)	387 (22)	
A3 (>30 mg/mmol)	123 (4.9)	34 (4.4)	89 (5.1)	
Missing/not measured	9945 (79.7)	8381 (91.5)	1564 (47.2)	109.7
Pharmacological treatments, *n* (%)[c]				
Statins	5585 (45)	3474 (38)	2111 (64)	–53.2
RASi	7640 (61)	5078 (55)	2562 (77)	–47.4
SGLT2i	420 (3.4)	0 (0)	420 (13)	–53.8
SGLT2i and/or RASi	7693 (62)	5078 (55)	2615 (79)	–51.4

[a]Based on all available data prior to index.
[b]The closest laboratory value up to 3 years prior to index (or 14 days post-index, see eligibility criteria). The numerical categories of UACR and plasma potassium indicate the proportion to the total number of assessed patients for whom the respective data was available.
[c]Based on data recorded 1 year prior to index.
[d]Absolute SMD of >10% is considered to represent a significant difference.
For laboratory variables that are missing/not measured, the SMD is calculated as binary variable for missing vs non-missing.
IQR, interquartile range.

index and remained the main driver across the follow-up time (Supplementary data, Fig. S7).

DISCUSSION

This study showed that the prevalence of stage 3–4 CKD was as high as 6.3%. Moreover, we showed that newly detected stage 3–4 CKD patients were at high risk of dying and having severe clinical events, irrespective of diabetes status. Overall, CKD patients had high all-cause healthcare costs, and cardiorenal complications (CKD or HF) contributed considerably more to the healthcare costs than atherosclerotic diseases, with similar pattern among non-T2D and T2D CKD patients, respectively. The majority of all CKD patients were non-T2D patients, which, compared with T2D patients, were more neglected in terms of albuminuria screening and utilization of recommended kidney-protective medications.

These key findings are consistent with previous literature with regard to proportion of T2D among CKD patients [1, 12], underutilization of albuminuria screening [16, 17], treatment inertia [18], cardiorenal risk drivers [1, 12], cardiorenal cost drivers [1, 12] and mortality [16].

To overcome challenges in identification of CKD patients, we used both diagnostic codes and pathological kidney function tests in cohort formation [1], which allowed a more complete assessment of CKD, with an estimated prevalence of 6.3%, being in line with evidence from a previous multi-country study [1]. The prevalence would have been lower if estimated based on diagnostic codes only [17, 18]. In this study, only one in four CKD patients had a recorded diagnosis at end of follow-up. The prevalence of CKD based on eGFR values and CKD diagnoses was in fact close to the prevalence of T2D in Finland, 7% [19]. Thus, CKD should be considered as a common disease, similar to T2D. It is known that CKD is a major risk factor for CV events, even without the presence of T2D [5]. In this study, non-T2D CKD patients showed high 1-year morbidity and similar 1-year mortality to T2D patients. Risks and healthcare costs were driven by cardiorenal complications as compared with atherosclerotic diseases. Therefore, CKD needs to be diagnosed, treated and followed up accordingly, regardless of T2D status. Our findings showed that T2D patients had twice the risk of hyperkalemia during follow-up than non-T2D patients, which is in line with previous studies [20]. Moreover, this could also partly be explained by the higher proportion of RASi

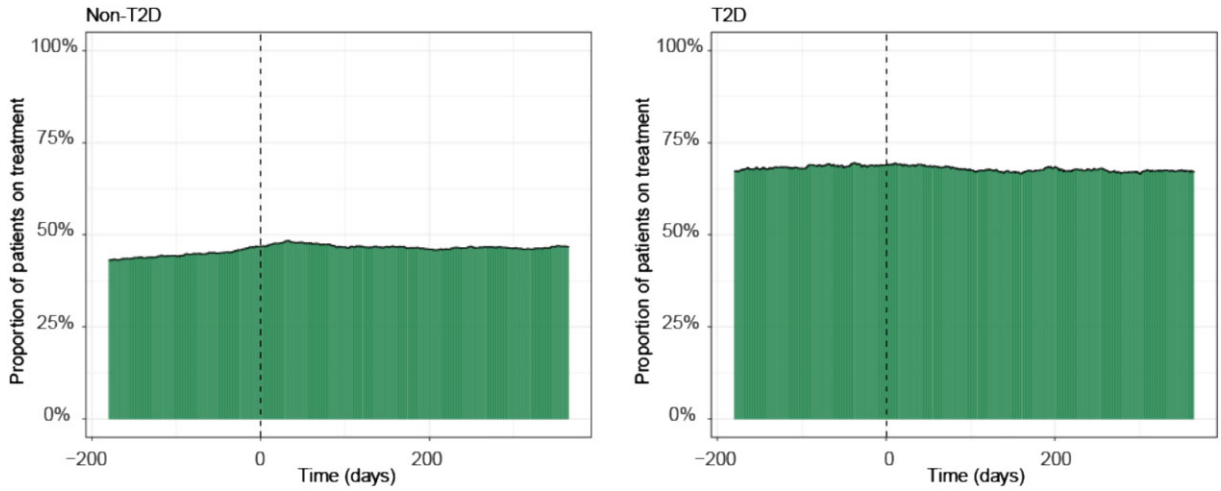


Figure 1: Uptake of RASi and/or SGLT2i in incident stage 3–4 CKD patients, with and without T2D. Uptake was followed on daily basis from 6 months prior to index (Day 0) until 12 months post-index. Each data point represents the proportion of individuals on treatment.

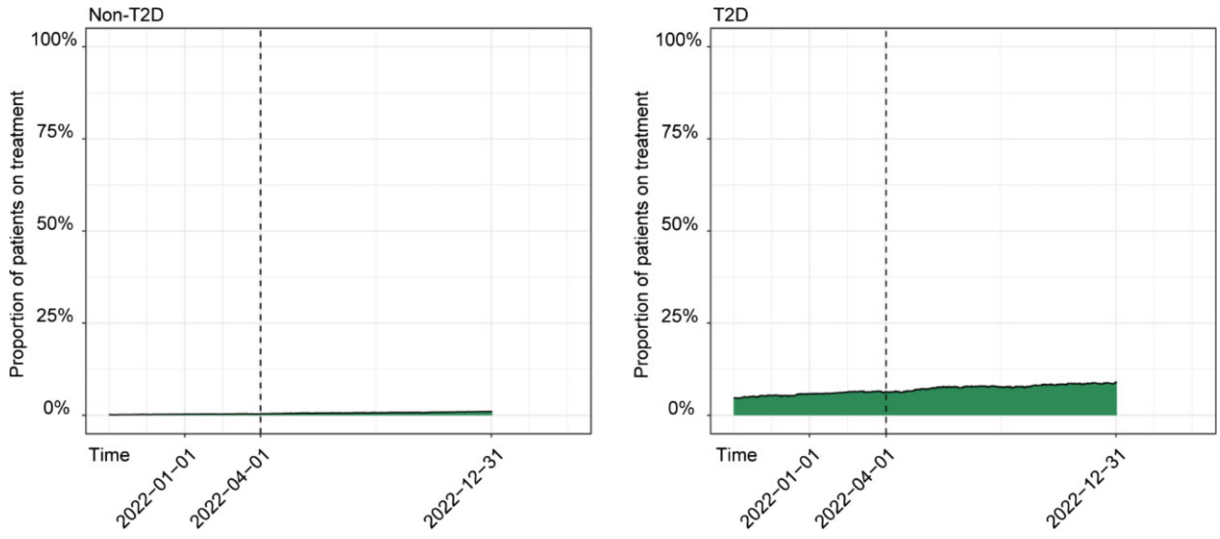


Figure 2: Uptake of SGLT2i, dapagliflozin, pre- vs post-reimbursement approval for the treatment of CKD in Finland (1 April 2022). Uptake was followed on daily basis from 6 months prior to approval (dotted line) until 12 months post-approval. Each data point represents the proportion of individuals on treatment.

prescriptions among T2D patients than non-T2D patients, since RASi is also a well-known risk factor for hyperkalemia, in addition to CKD and T2D [20].

The true prevalence of stage 3–4 CKD in Keusote and Turku municipalities is likely higher than estimated in this study because it depends on the coverage of kidney function screenings. As the cohort comprises patients with eGFR values of 15–59 mL/min/1.73 m^2, there are no patients without a creatinine/eGFR value. Nevertheless, the low coverage of baseline UACR screening in this CKD cohort is in line with observations in T2D patients in several regions in Finland and again confirms the lack of compliance to this important aspect [9, 16]. Early diagnosis of CKD, preferably already in stages 1 and 2, enables the initiation of kidney-protective treatments to slow down the progression of CKD. This underlines how crucial it is to find and inform of ways to improve the screening practice which mainly takes place in the primary care [21]. A more systematic approach to screening for CKD in at risk patients with both the eGFR and UACR measurements is needed.

RASi are the mainstay treatment of diagnosed CKD, with clinical trials showing kidney-protective effects and beneficial cardiovascular risk reduction [22–25]. More recently, clinical trials have shown that SGLT2i reduce the risk of CKD progression and cardiovascular events, regardless of diabetes status [26]. The baseline use of RASi/SGLT2i in 55% of non-T2D CKD patients is therefore extremely low, showing no improvement even after the identification of CKD. These data are in line with previously published European data with over half of the CKD population receiving RASi treatment and only a minority receiving SGLT2i [1]. RASi/SGLT2i treatment inertia suggests there may be a potential for increased use of recommended CKD therapies. The low use of kidney-protective medications may partly result from poor adherence to prescribed treatments. This could be due to several patient- and healthcare-related factors which, however, were not in the focus of the present study. In general, the doctor–patient relationship, shared decision-making, continuous patient education and personalized treatment plans are a few key factors in

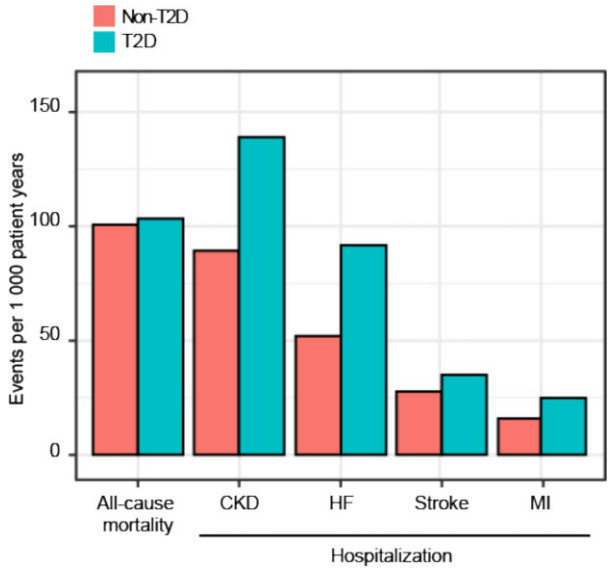


Figure 3: One-year mortality and hospitalization rates in stage 3–4 CKD, with and without T2D. Events reported per 1000 patient years for all-cause mortality and hospitalizations with any main/side diagnosis of CKD, HF, stroke or MI.

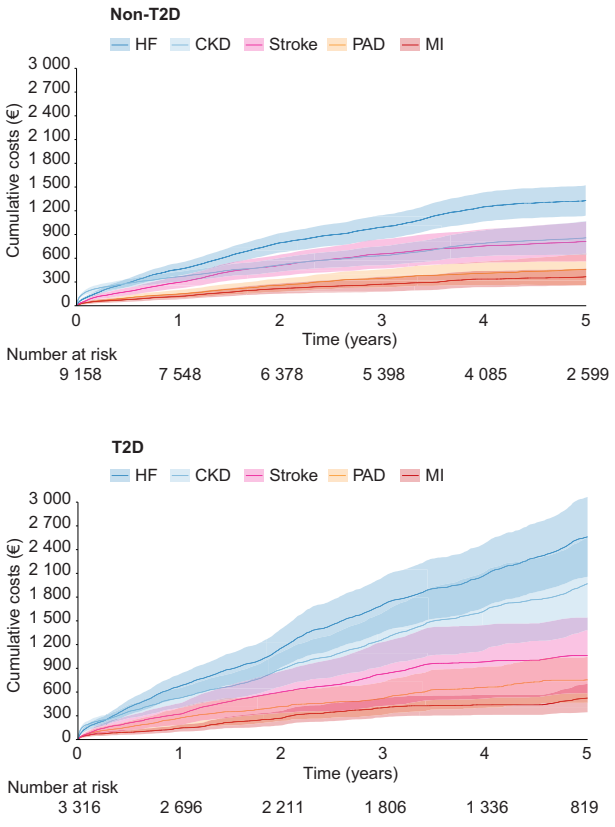


Figure 4: Cumulative direct public healthcare costs per patient in incident stage 3–4 CKD, with and without T2D. Costs associated with HF, CKD, stroke, peripheral artery disease (PAD) and MI as a primary or secondary cause of the contact (one contact may be included in more than one disease group). All costs were reported in euros (€) at 2017 price level. 95% CIs and patients at risk included.

adherence to pharmacological treatments and these aspects should also be studied for CKD treatments [27]. The screening for CKD including testing for UACR in at risk patients as well as the initiation of kidney-protective medications should mostly take place in primary care where both general practitioners (GPs) and nurses follow up and treat these patients. Moreover, CKD patients are often asymptomatic in early stages and therefore problematic symptoms do not prompt patients to take their medication. Therefore, both GPs, nurses and patients need to be educated.

This study was based on secondary use of data extracted from Finnish hospital records and national registers. Health, social and administrative registers in Finland are known for their high-quality data and accurate linkage of data from multiple data sources. The study was carried out in public healthcare setting, where patients at risk for kidney function decline are mainly followed up in primary healthcare, with severe complications treated in secondary/tertiary care. Thus, the extraction of patient population from primary care should identify most of the relevant CKD patients treated in public healthcare of assessed municipalities. However, we may have missed individuals with CKD based on diagnostic code only or based on UACR measurements only. Moreover, data for the patients also treated at private care may be incomplete. Emigration from geographical areas of interest was not considered in the analysis of the prevalence of CKD.

Limitations also exist in the analysis of comorbidities, which was dependent on diagnostic code assignments known to be biased due to underreporting. Medication data was derived from purchases and thus might not fully reflect the actual medication utilization. Moreover, Finland's reimbursement situation allowed assessment of dapagliflozin-specific treatments only for a short time period. The study period includes the COVID-19 pandemic, which was associated with a temporary decrease in the number of healthcare visits in Finland [28, 29]. Although this may have impacted patients' prognosis due to delayed diagnosis (Supplementary data, Fig. S2), we did not observe any decline in the uptake of kidney protective medications (SGLT2i and/or RASi) by calendar year of incident CKD (data not shown), but rather a small increased uptake from 2016 to 2022. Lastly, this study included five municipalities and thus may not be completely generalizable across Finland, where e.g. the coverage of albuminuria screening is known to vary by region [30].

CONCLUSIONS

This study shows that CKD is a common disease in Finland, comparable to the prevalence of T2D, but remains neglected in terms of albuminuria screening and kidney-protective RASi/SGLT2i treatments, especially in non-T2D, which showed similar disease pattern as those with T2D. Cardiorenal complications (CKD or HF) contributed considerably more to the all-cause healthcare costs than the atherosclerotic CVD complications. These data call for an urgent need to improve awareness and risk management, especially in the larger, non-T2D group of CKD patients. Similar studies in Finland and more detailed studies assessing ways to improve CKD screening and healthcare/patient adherence to kidney-protective treatments should be carried out in the future.

SUPPLEMENTARY DATA

Supplementary data are available at *Nephrology Dialysis Transplantation* online.

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AUTHORS' CONTRIBUTIONS

All authors contributed to the conception and design of the study. Acquisition of data was done at Medaffcon, and I.T. performed the statistical analyses. K.U.-R., J.B., L.E.F. and I.T. wrote the first draft of the manuscript. All authors thoroughly revised previous versions of the manuscript and have read and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

Only the original register holders or Finnish Social and Health Data Permit Authority can grant rights to third parties to use the data in accordance with the Act on Secondary Use of Health and Social Data. The single-level data cannot be shared.

CONFLICT OF INTEREST STATEMENT

The study was fully sponsored by AstraZeneca, for which L.E.F. and J.B. are employees. K.M. reports fees for consultancy, lecturing and/or advisory board work from Astellas, AstraZeneca, Bayer, Boehringer Ingelheim, Mundipharma, Novartis, Pharmacosmos and Viforpharma. S.B. reports fees for consultancy, lecturing and/or advisory board work and/or support for attending meetings and/or travel from AstraZeneca, Boehringer Ingelheim, Novo Nordisk, Sanofi, Duodecim Medical Society, University of Helsinki/HUS/Department of General Medicine and Primary Health Care. S.B. is a member of the Council for Primary Health Care at the Duodecim Medical Society and a member of the team for National Guidelines for Heart Failure in Finland (published 19.12.23). K.U.-R. and I.T. are employed by Medaffcon Oy (Espoo, Finland), which received payments from AstraZeneca for conducting the study.

REFERENCES

1. Sundström J, Bodegard J, Bollmann A. *et al.* Prevalence, outcomes, and cost of chronic kidney disease in a contemporary population of 2·4 million patients from 11 countries: the CaReMe CKD study. *Lancet Reg Health Eur* 2022;**20**:100438. https://doi.org/10.1016/j.lanepe.2022.100438
2. Hill NR, Fatoba ST, Oke JL *et al.* Global Prevalence of chronic kidney disease—a systematic review and meta-analysis. *PLoS One* 2016;**11**:e0158765. https://doi.org/10.1371/journal.pone.0158765
3. Bikbov B, Purcell CA, Levey AS *et al.* Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet North Am Ed* 2020;**395**:709–33. https://doi.org/10.1016/S0140-6736(20)30045-3
4. Jager KJ, Kovesdy C, Langham R *et al.* A single number for advocacy and communication—worldwide more than 850 million individuals have kidney diseases. *Nephrol Dial Transplant* 2019;**34**:1803–5. https://doi.org/10.1093/ndt/gfz174
5. Ronco C, Bellasi A, Di Lullo L. Cardiorenal syndrome: an overview. *Adv Chronic Kidney Dis* 2018;**25**:382–90. https://doi.org/10.1053/j.ackd.2018.08.004
6. Stevens PE, Ahmed SB, Carrero JJ *et al.* KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int* 2024;**105**:S117–314. https://doi.org/10.1016/j.kint.2023.10.018
7. Duodecim. Diabetes Current Care Guideline. Working group set up by the Finnish Medical Society Duodecim and the Finnish Society of Internal Medicine. In Finnish. 2020; Finland: Duodecim Käypä Hoito. Available from: https://www.kaypahoito.fi/hoi50056 (8 January 2023, date last accessed).
8. Duodecim. Duodecim. Hypertension Current Care Guideline. Working group set up by the Finnish Medical Society Duodecim and the Finnish Society of Hypertension. In *Finnish*. 10 September 2020; Finland: Duodecim Käypä Hoito. Available from: www.kaypahoito.fi (26 April 2023, date last accessed).
9. Terveyden ja hyvinvoinnin laitos. Diabetesrekisterin raportti [Internet]. *Terveyden Ja hyvinvoinnin laitos*, Helsinki, 2022; Finland: THL Laaturekisterit. Available from: https://repo.thl.fi/sites/laaturekisterit/diabetesrekisteri/ (10 March 2023, date last accessed).
10. Levey AS, Stevens LA, Schmid CH *et al.* A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;**150**:604–12. https://doi.org/10.7326/0003-4819-150-9-200905050-00006
11. Mäklin M, Kokko P. Terveyden- ja sosiaalihuollon yksikkökustannukset Suomessa vuonna 2017 [Internet]. *Terveyden Ja hyvinvoinnin laitos (THL)*, Report 21/2020. 2020, 1–55. Finland: THL Laaturekisterit. Available from: https://www.julkari.fi/bitstream/handle/10024/142882/URN_ISBN_978-952-343-493-6.pdf?sequence=1&isAllowed=y (11 June 2024, date last accessed).
12. Tangri N, Svensson MK, Bodegård J *et al.* Mortality, health care burden, and treatment of CKD: a multinational, observational study (OPTIMISE-CKD). *Kidney360* 2024;**5**:352–62. https://doi.org/10.34067/KID.0000000000000374
13. Bozkurt B, Savarese G, Adamsson Eryd S *et al.* Mortality, outcomes, costs, and use of medicines following a first heart failure hospitalization. *JACC Heart Fail* 2023;**11**:1320–32.
14. Norhammar A, Bodegard J, Vanderheyden M *et al.* Prevalence, outcomes and costs of a contemporary, multinational population with heart failure. *Heart* 2023;**109**:548–56. https://doi.org/10.1136/heartjnl-2022-321702
15. R Core Team. *R: A Language and Environment for Statistical Computing* [Internet]. 2020. Vienna, Austria: R Foundation for Statistical Computing, 2017. Available from: https://www.r-project.org/ (11 June 2024, date last accessed).
16. Vestergaard AHS, Jensen SK, Heide-Jørgensen U *et al.* Risk factor analysis for a rapid progression of chronic kidney disease. *Nephrol Dial Transplant* 2024;**39**:1150–58. https://doi.org/10.1093/ndt/gfad271
17. Agvall B, Ashfaq A, Bjurström K *et al.* Characteristics, management and outcomes in patients with CKD in a healthcare re-

gion in Sweden: a population-based, observational study. *BMJ Open* 2023;**13**:e069313. https://doi.org/10.1136/bmjopen-2022-069313

18. Sundström J, Norhammar A, Karayiannides S *et al.* Are there lost opportunities in chronic kidney disease? A region-wide cohort study. *BMJ Open* 2024;**14**:e074064. https://doi.org/10.1136/bmjopen-2023-074064
19. Terveyden ja hyvinvoinnin laitos. Diabetesrekisterinraportti. Koko Suomi, tyyppi 2 ja muut. [Diabeteksen esiintyvyys] [Internet]. 2023. Available from: https://repo.thl.fi/sites/nqrdm/viimeisin/DM_koko_suomi2.html (11 June 2024, date last accessed).
20. Thomsen RW, Nicolaisen SK, Hasvold P *et al.* Elevated potassium levels in patients with chronic kidney disease: occurrence, risk factors and clinical outcomes—a Danish population-based cohort study. *Nephrol Dial Transplant* 2018;**33**:1610–20. https://doi.org/10.1093/ndt/gfx312
21. Wolpert EZ, Norman S, Eek D *et al.* How do patients experience chronic kidney disease? A mixed-methods study among patients in Sweden. *J Public Health* 2023;**32**:2015–25. Available from: https://link.springer.com/10.1007/s10389-023-01942-0 (20 June 2024, date last accessed).
22. Lewis EJ, Hunsicker LG, Bain RP *et al.* The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993;**329**:1456–62. https://doi.org/10.1056/NEJM199311113292004
23. Lewis EJ, Hunsicker LG, Clarke WR *et al.* Renoprotective effect of the angiotensin-receptor antagonist Irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;**345**:851–60. https://doi.org/10.1056/NEJMoa011303
24. Brenner BM, Cooper ME, De Zeeuw D *et al.* Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;**345**:861–9. https://doi.org/10.1056/NEJMoa011161
25. Xie X, Liu Y, Perkovic V *et al.* Renin-angiotensin system inhibitors and kidney and cardiovascular outcomes in patients with CKD: a Bayesian network meta-analysis of randomized clinical trials. *Am J Kidney Dis* 2016;**67**:728–41. https://doi.org/10.1053/j.ajkd.2015.10.011
26. Baigent C, Emberson JR,Haynes R *et al.* Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials. *Lancet North Am Ed* 2022;**400**:1788–801. https://doi.org/10.1016/S0140-6736(22)02074-8
27. Huupponen R, Strandberg T. Miten auttaa potilasta sitoutumaan lääkehoitoonsa? *Duodecim* 2020;**136**:223–7.
28. Summanen M, Kosunen M, Kainu V *et al.* COVID-19 hospitalisations and all-cause mortality by risk group in Finland. *PLoS One* 2023;**18**:e0286142. https://doi.org/10.1371/journal.pone.0286142
29. Niemenoja O, Ämmälä AJ, Riihijärvi S *et al.* The impact of Covid-19 of healthcare booking and cancellation patterns: time series analysis of private healthcare service utilisation in Finland. *BMC Health Serv Res* 2024;**24**:383. https://doi.org/10.1186/s12913-024-10987-0
30. Terveyden ja hyvinvoinnin laitos. Diabetesrekisterinraportti. Koko Suomi, tyyppi 2 ja muut. [U-Alb-Kre] [Internet]. 2023. Finland: THL Laaturekisterit. Available from: https://repo.thl.fi/sites/nqrdm/viimeisin/DM_koko_suomi2.html (11 June 2024, date last accessed).

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