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Microsimulation modelling to predict the burden of CKD and the cost-effectiveness of timely CKD screening in Belgium: results from the Inside CKD study

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ABSTRACT

Objectives Inside CKD aims to assess the burden of chronic kidney disease (CKD) and the cost-effectiveness of screening programmes in Belgium.

Design Microsimulation-based modelling.

Setting Data derived from national statistics and key literature from Belgium.

Participants Virtual populations of ≥10 million individuals, representative of Belgian populations of interest, were generated based on published data and cycled through the Inside CKD model. Baseline input data included age, estimated glomerular filtration rate (eGFR), urine albumin-creatinine ratio (UACR) and CKD status.

Primary outcome measures Outcomes included the clinical and economic burden of CKD during 2022–2027 and the cost-effectiveness of two different CKD screening programmes (one UACR measurement and two eGFR measurements or only two eGFR measurements, followed by renin-angiotensin-aldosterone system inhibitor treatment in newly diagnosed eligible patients). The economic burden estimation included patients diagnosed with CKD stages 3–5; the screening cost-effectiveness estimation included patients aged ≥45 years with no CKD diagnosis and high-risk subgroups (with cardiovascular disease, hypertension, type 2 diabetes or aged ≥65 years).

Results Between 2022 and 2027, CKD prevalence is estimated to remain stable and substantial at approximately 1.66 million, with 69.9% undiagnosed. The total healthcare cost of patients diagnosed with CKD is expected to remain stable at approximately €2.15 billion per year. The one UACR, two eGFR measurement screening programme was cost-effective in all populations, with an incremental cost-effectiveness ratio of €3623 per quality-adjusted life year (QALY) gained in those aged ≥45 years, well below the estimated willingness-to-pay threshold of €43 839 per QALY gained.

Conclusions Without changes to current practice, the disease burden of CKD in Belgium is predicted to remain substantial over the next few years. This highlights the need for timely diagnosis of CKD and demonstrates that, in line with guideline recommendations, implementing a CKD screening programme involving UACR and eGFR measurements followed by treatment would be cost-effective.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The Inside CKD model uses a dynamic microsimulation that enables modelling of screening scenarios with a high level of granularity.

⇒ Not all required input data were available for Belgium, so proxy data from the UK had to be used in some cases; however, data from the UK may not be representative of Belgium. The updated Kidney Disease: Improving Global Outcomes 2024 guidelines on renin-angiotensin-aldosterone system inhibitor (RAASi) treatment were not used in this study; if these criteria had been used, more patients would have been eligible for RAASi treatment, which would have affected both healthcare costs and CKD progression.

⇒ Sodium-glucose cotransporter-2 inhibitor (SGLT-2i) recommendations based on the updated[7] guidelines were not included in the microsimulation, and so the costs and benefits of SGLT-2i in this model cannot be assessed.

INTRODUCTION

In 2020, the prevalence of chronic kidney disease (CKD) was estimated to be 12.0% in Belgium, with an estimated 63.1% of these patients lacking a CKD diagnosis code in their medical records.[1] The majority (57.9%) of people with CKD (diagnosed and undiagnosed) had CKD stage 3, which is frequently asymptomatic.[1 2] Diabetes is a leading cause of CKD, and albuminuria is an early marker of kidney injury in patients with type 2 diabetes when estimated glomerular filtration rate (eGFR) is completely normal (≥90 mL/min/1.73 m^2).[3] CKD and associated comorbidities, such as cardiovascular disease (CVD), hypertension and type 2 diabetes, impose a substantial clinical and economic burden on the Belgian healthcare system.[1 4 5] To diagnose CKD, guidelines recommend CKD screening programmes that measure both urine albumin-creatinine ratio (UACR) and eGFR.[6 7]

Globally, the economic burden of patients with CKD requiring dialysis or transplantation (renal replacement therapies (RRTs)) is well-established and is projected to amount to US$406.7 billion (~€370 billion) in 2027.[4 8] In Belgium, the reimbursement expenditure for dialysis rose from €206 million in 2000 to almost €336 million in 2008[9] and exceeded €500 million in 2023.[10] In 2020, the annual cost of a patient in Belgium progressing from CKD stage 3a to CKD stage 5 increased by a factor of 3.7 (€2728 vs €10 110).[4] However, the economic burden of early-stage CKD is not well-established.

Individuals with CVD, hypertension and type 2 diabetes are at high risk of CKD.[11] Early CKD diagnosis and management are critical in delaying CKD progression and the development of related complications. Effective screening strategies are crucial to identify early-stage CKD, which is almost always asymptomatic.

CKD is defined by the presence of abnormalities in kidney structure or function for >3 months and classified by eGFR category, albuminuria category and cause.[6] The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines advocate the use of eGFR alongside UACR testing to screen for CKD and predict CKD prognosis.[6 7] Despite this, levels of UACR screening are low, even in patients at high risk of developing CKD.[1 12–14] In Belgium, UACR screening is not widely used in clinical practice because it is only reimbursed by the healthcare system for patients with diabetes; it is estimated that only 11.1% of patients in Belgium with evidence of CKD (based on two pathological eGFR values ≥90 days apart) had received a UACR test.[1]

To address the unavailability of nationwide real-world data on epidemiology and disease burden, the objectives of this study were to use the Inside CKD patient-level microsimulation model[4] to assess (1) the clinical and economic burden of CKD between 2022 and 2027 and (2) the cost-effectiveness of introducing a CKD screening programme based on albuminuria testing (UACR) alongside double eGFR testing in Belgium.

MATERIALS AND METHODS

Model overview

The Inside CKD study uses microsimulation modelling techniques (based on Monte Carlo simulations) to extrapolate the currently available epidemiological information over the long term by generating virtual population cohorts, as described previously.[4 8 15 16]

First, the Inside CKD microsimulation generated a virtual population to emulate the overall Belgian population with baseline health data as well as hazards of incurring CKD, other comorbidities, complications and death. This model predicted both clinical and economic burdens related to various stages of CKD between 2022 and 2027 in Belgium. Second, the microsimulation model created virtual closed cohorts of patients who were not yet diagnosed with CKD, emulating the Belgian population with baseline health characteristics and chances of getting diagnosed with CKD. This model was used to compare the long-term costs and benefits arising from introducing two screening scenarios with interventions: (1) one UACR screening in addition to two eGFR screenings and (2) two eGFR screenings, compared with the current healthcare practice. The screening intervention occurred in year 1 only, and the cohort was followed across their lifetime.[17] The results of this cost-effectiveness analysis were presented using the standardised unit of incremental cost-effectiveness ratio (ICER). C++ was used to code the model.

CKD clinical and economic burden modelling

A virtual population of 20 million individuals, representative of the overall Belgian population (with and without CKD), was generated for 2021. All results were then rescaled to match the projected population size of Belgium, in alignment with UN Population Prospects.[18] Baseline input data, including age, sex, eGFR, UACR, CKD status (no CKD or CKD stages 1–5), risk of developing (or presence of) cardiovascular complications and risk of all-cause death, are shown in online supplemental tables S1–S4. When data for Belgium were unavailable, UK values were used as a proxy because they were available in a more granular mode and were assumed to be the most similar to Belgian values compared with other available sources (online supplemental table S1). Local clinical experts validated the input data.

The virtual individuals were cycled annually for 6 years (2022–2027) through the microsimulation, adjusting the eGFR and UACR values, risk of developing CKD (in those without CKD), risk of CKD progression (in those with CKD), risk of developing cardiovascular comorbidities and risk of all-cause death each year. Healthy individuals may progress to CKD, and those with CKD may progress through CKD stages. Each year, their eGFR and albuminuria measurements are used to estimate the probability of being at a particular CKD stage. As eGFR declines each year, this may result in transitions between CKD stages based on KDIGO stage cut-offs.[15] Annual declines in eGFR to model CKD progression were estimated using data from the DISCOVER CKD study,[19 20] as described previously.[15] UACR values were derived from distributions by age group from the literature.[21] The microsimulation projected, by CKD stage, the prevalence of diagnosed and undiagnosed CKD, the prevalence of associated cardiovascular complications (heart failure, myocardial infarction and stroke) and all-cause mortality.

Healthcare costs directly associated with CKD management and associated complications were only estimated in patients with diagnosed CKD stages 3–5. Direct costs for CKD stages 1 and 2 were not estimated because they could be confounded by costs associated with conditions

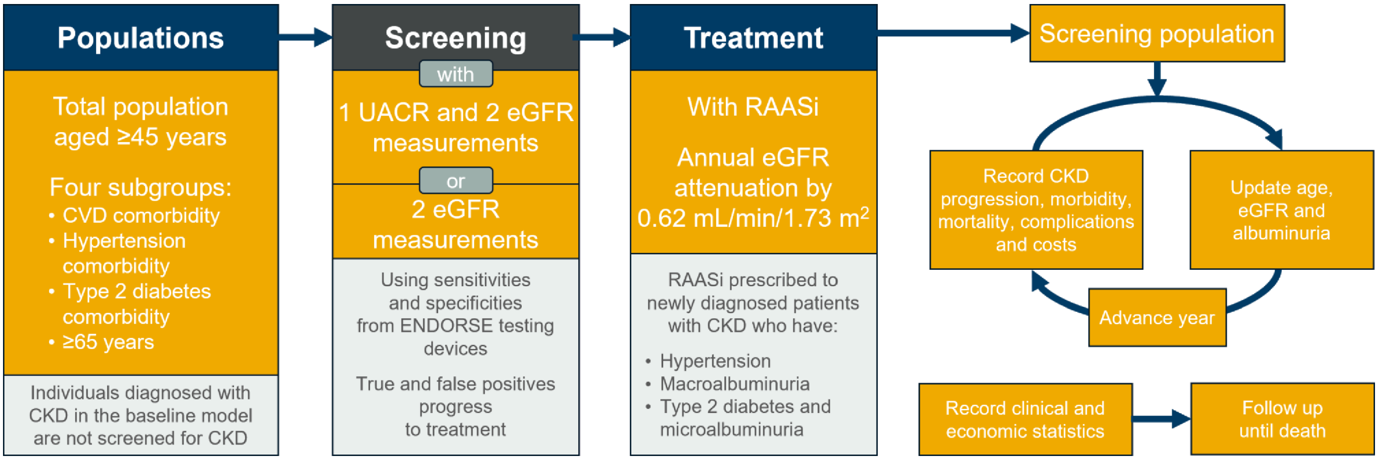

Figure 1 Screening pathway modelling. CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; RAASi, renin-angiotensin-aldosterone system inhibitor; UACR, urine albumin-creatinine ratio.

other than CKD.[4] Costs were also applied individually for those undergoing RRT and, in the cost-effectiveness analysis, for cardiovascular complications (heart failure, myocardial infarction and stroke) associated with all CKD stages. Cost estimates were based on published data and validated by clinical experts. The costs were adjusted to 2022 prices according to the gross domestic product (GDP) deflator from the International Monetary Fund.[22]

Impact and cost-effectiveness of CKD screening scenarios

To assess the impact of CKD screening scenarios (followed by renin-angiotensin-aldosterone system inhibitor (RAASi) treatment in newly diagnosed eligible patients), closed cohorts of individuals without a CKD diagnosis representative of the Belgian population were generated (figure 1). For both the ≥45 years and ≥65 years microsimulation runs, the total population was generated in the start year (2021), before specific eligible cohorts were selected at the end of that same year. Individuals were included if they met the minimum age requirement (45 years or 65 years; no upper age limit) and either had no CKD or undiagnosed CKD. Additional high-risk subgroups of special interest were patients with CVD, hypertension, type 2 diabetes or aged ≥65 years. A sufficient number of simulations were performed to ensure at least 10 million individuals within each high-risk subgroup; results are reported per 100 000 individuals eligible for screening.

Patients were followed up in consecutive yearly cycles and assessed for their chance of developing and being diagnosed with CKD annually. Epidemiological outputs were analysed over a 10-year time horizon (2022–2032); cost-effectiveness outputs were assessed over a time horizon (up to 2086) reflecting a population lifetime, with a maximum age of 110 years. By nature, longer time horizons in cost-effectiveness provide a glance at how cost-effective policies would be in the future (considering the country-specific discounting effect). To help policymakers understand public-health outcomes in the context of investment over the long term, the longer time horizon was chosen.

Although patients in Belgium at high risk of CKD and suspected of having CKD will receive one eGFR test, guidelines define CKD based on structural or functional abnormalities in the kidneys measured >3 months apart. Here, two hypothetical CKD screening strategies were compared with the current clinical practice in Belgium based on KDIGO recommendations: (1) one UACR and two eGFR measurements and (2) two eGFR measurements. A patient was assumed to receive a new CKD diagnosis if (1) both eGFR measurements were <60 mL/min/1.73 m^2 when taken >3 months apart and/or the UACR value >30 mg/g in the first scenario or (2) both eGFR measurements were <60 mL/min/1.73 m^2 when taken >3 months apart in the second scenario. Online supplemental figure S1 presents the first screening strategy of one UACR and two eGFR tests. The second screening strategy differs by replacing the one UACR plus one eGFR test with a single eGFR test.

Based on the criteria above, patients were assumed to visit a healthcare professional and receive RAASi if eligible. Eligibility was based on recommendations from the 2012 KDIGO CKD guidelines,[6] where RAASi treatment was initiated if the individual also had hypertension or type 2 diabetes and a UACR value ≥30 mg/g or a UACR value ≥300 mg/g.

The following assumptions were used in the model. In Belgium, 77.7% of people visit a primary care provider at least once a year.[23] Of these, it is assumed that 100% of those aged ≥45 years have access to healthcare, are offered the screening scenario and agree to UACR and eGFR testing. The sensitivity and specificity of the eGFR tests (98.9% and 85.3%, respectively) and the UACR test (95.6% and 96.8%, respectively) were based on published data from the ENDORSE devices.[24] Patients with either true-positive or false-positive screening results progressed to treatment; for patients with false-positive results, treatment was assumed to be stopped after the first year.

The model applied a difference in eGFR decline of 0.62 mL/min/1.73 m^2 per year between patients who received RAASi and patients who did not, based on a meta-analysis by Inker *et al*.[25] The impact of screening with one UACR measurement and two eGFR measurements on the number of new CKD diagnoses in patients aged ≥45 years was projected between 2022 and 2032.

For the cost-effectiveness analysis, costs of screening tests (including primary care visits) and treatment with RAASi (and associated primary care visits) in newly diagnosed patients were included (online supplemental table S5). A discount rate of 3% per year was applied to costs. Quality of life (QoL) of each individual in the model was estimated based on their characteristics, presence of comorbidities and complications. For comorbidities and complications, we assumed that an individual had the lowest utility value of their combination of CKD stage and any comorbid disease. Quality-adjusted life years (QALYs) were calculated using estimated utility weights, based on EQ-5D data (online supplemental table S6). A discount rate of 1.5% per year was applied to QALYs.

ICERs were calculated as the net difference in costs between the screening scenarios and current clinical practice, divided by the difference in QALYs gained by the individuals receiving screening. The cost-effectiveness assessment used a willingness-to-pay (WTP) threshold corresponding to the 2021 Belgian GDP per capita (€43 839 per QALY gained)[26] because Belgium has no formal WTP threshold.

Both screening strategies were assessed in the general population (aged ≥45 years) and in the high-risk subgroups. To assess the robustness of the cost-effectiveness analysis, parametric sensitivity analyses were performed by varying costs and QoL by 10%.

Patient and public involvement

Inside CKD was a microsimulation study of publicly available data; thus, no patients were involved in the conduct of this study.

RESULTS

CKD burden

Baseline characteristics

Online supplemental table S7 shows the baseline characteristics of the total Belgian population used in the model to project the clinical and economic burden of CKD. The total number of diagnosed CKD patients is 520 894 in 2022. This total is dynamic and will change over the microsimulation. Males constituted 49.6% of the population; 46.5% and 19.9% were aged ≥45 years and aged ≥65 years, respectively. The prevalence of CKD was 14.2%; only 31.5% of those with CKD were diagnosed. Among individuals with CKD (diagnosed and undiagnosed), 21.0% had stage 1, 17.0% had stage 2, 55.4% had stage 3, 5.7% had stage 4 and 0.9% had stage 5 disease (including RRT). Of individuals with CKD, 55.8% had hypertension and 19.9% had type 2 diabetes.

Clinical burden of CKD

The number of people with CKD is estimated to remain stable and high at approximately 1.66 million between 2022 and 2027 (figure 2). Between 2022 and 2027, cases of CKD stage 5, including RRT, are estimated to rise from 15 243 to 19 383. Based on the current clinical practice of only testing eGFR in patients at high risk and suspected of CKD, 1.16 million patients (69.9%) with CKD (any stage) will remain undiagnosed in 2027. Most patients (diagnosed and undiagnosed) are expected to

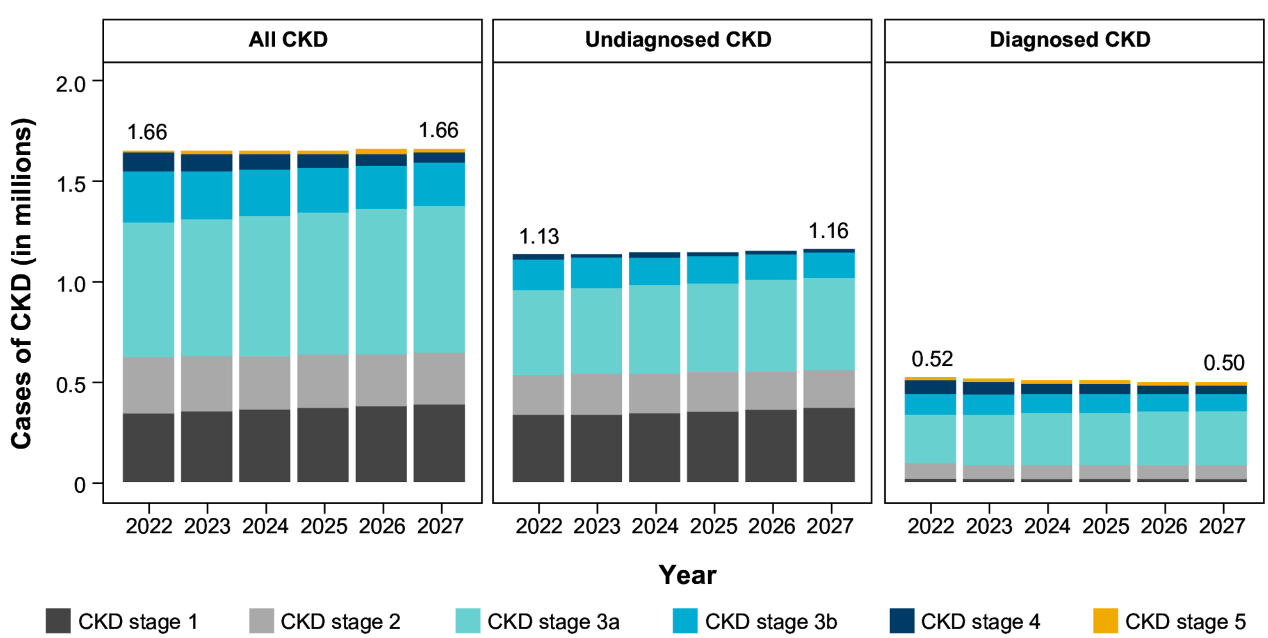

Figure 2 Number of people with chronic kidney disease (CKD) in Belgium, by CKD stage. CKD stage 5 includes patients receiving renal replacement therapy (RRT). CC BY 2024. Figure adapted from Chertow *et al*[16]; Appendix 1 (Poland). This work is licensed under a Creative Commons Attribution Licence https://creativecommons.org/licenses/by/4.0/.

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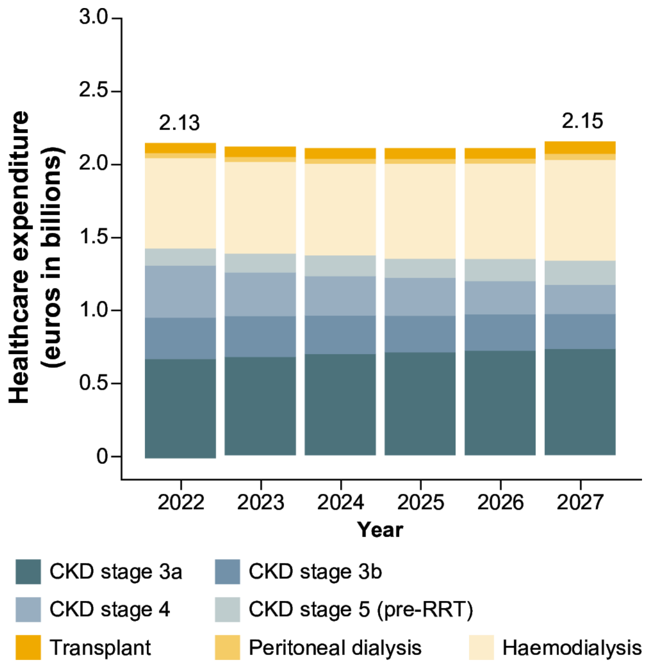

Figure 3 Healthcare costs associated with diagnosed CKD. CKD, chronic kidney disease; RRT, renal replacement therapy.

have CKD stage 3 (56.9% in 2027); a minority (4.5% in 2027) will have late-stage CKD (stages 4/5, including RRT).

Between 2022 and 2027, the number of patients to be diagnosed with CKD and a comorbidity, such as heart failure, myocardial infarction and stroke, is expected to remain high, with 25 057, 14639 and 14627 patients predicted to have heart failure, myocardial infarction or a stroke, respectively, by 2027 (online supplemental figure S2).

Economic burden of CKD

The total healthcare cost of patients with diagnosed CKD, including RRT, is expected to remain substantial at approximately €2.15 billion per year (figure 3). Although healthcare costs for individuals with CKD stage 3 are low compared with late-stage CKD, the high prevalence of CKD stage 3 results in an annual cost close to €1 billion (figure 3, online supplemental table S8), representing an estimated 45.3% of the total CKD-related healthcare costs in 2027 in the absence of new preventative policy interventions. As expected, RRT imposes substantial costs on healthcare expenditure, constituting an estimated 38.0% of the total CKD-related healthcare costs and 0.2% of GDP in 2027.

Impact and cost-effectiveness of CKD screening scenarios

Baseline characteristics

Online supplemental table S9 shows the baseline characteristics of the patients aged ≥45 years without a CKD diagnosis (overall population) and the high-risk subgroups that were used to assess the impact of screening scenarios in the microsimulation. The total number of simulated individuals were 244.5 million (aged ≥45 years), 24.5 million (CVD), 46.6 million (hypertension), 16.6 million (type 2 diabetes) and 166.2 million (aged ≥65 years). In the overall population, 17.3% had CKD (62.6% had CKD stage 3), 10.0% had CVD (34.3% with CKD, of whom 72.3% had CKD stage 3), 19.1% had hypertension (51.3% with CKD, of whom 69.3% had CKD stage 3) and 6.8% had type 2 diabetes (50.4% with CKD, of whom 60.9% had CKD stage 3). In the subgroup aged ≥65 years, 31.5% had CKD, of whom 70.0% had CKD stage 3.

Cost-effectiveness of screening with one UACR and two eGFR measurements compared with standard practice

Over a lifetime time horizon up to 2086, screening with one UACR and two eGFR measurements followed by RAASi treatment in eligible patients was highly cost-effective in the overall population, resulting in 0.063 QALYs gained per patient compared with current clinical practice, with an additional cost per patient of €228, resulting in an ICER of €3623 (table 1). This was well below the estimated WTP threshold of €43 839 per QALY gained and was expected to be cost-effective by 2023 (online supplemental figure S3); it was also more cost-effective than screening with two eGFR measurements alone. Cumulative QALY and costs over time for screening of the overall population with one UACR measurement and two eGFR measurements and two eGFR measurements are shown in online supplemental figure S4.

Furthermore, screening with one UACR and two eGFR measurements was more cost-effective in the high-risk populations than in the overall population (table 1); sensitivity analyses in the overall population showed that this intervention remained cost-effective when varying individual health utility weights and costs by ±10% (online supplemental figure S5).

Cost-effectiveness of screening with two eGFR measurements compared with standard practice

Screening with two eGFR measurements followed by RAASi treatment in eligible patients in the overall population was cost-effective, resulting in 0.039 QALYs gained per patient, an additional cost per patient of €183 and an ICER of €4755 (table 1). This screening scenario was more cost-effective in the high-risk populations than in the overall population (table 1).

Overall costs

The expected implementation costs of both screening scenarios were analysed to provide a complete economic outlook of the screening implementation in the healthcare system. By 2032, implementation of screening with one UACR and two eGFR measurements was expected to identify an additional 461 CKD cases per 100000 previously undiagnosed individuals compared with current practice (online supplemental figure S6). In the 2022–2032 period, screening with one UACR and two eGFR measurements was expected to incur an additional one-off screening cost of €4.9 million per 100000 individuals

Table 1 Cost-effectiveness* of the different screening scenarios followed by RAASi initiation in eligible patients†

Cohort	Screening with one UACR and two eGFR measurements			Screening with two eGFR measurements		
	Cumulative QALYs gained per patient	Cumulative costs gained per patient (€)	ICER (€)	Cumulative QALYs gained per patient	Cumulative costs gained per patient (€)	ICER (€)
General population ≥45 years	0.06292	227.97	3623	0.03850	183.06	4755
High-risk subgroups						
CVD ≥45 years	0.09905	341.85	3451	0.07221	294.06	4072
Hypertension ≥45 years	0.30544	931.65	3050	0.20164	747.96	3709
Type 2 diabetes ≥45 years	0.23048	688.05	2985	0.11073	461.95	4172
≥65 years	0.10387	341.96	3292	0.07346	285.71	3889

*A WTP threshold of €43 839 was used to assess the cost-effectiveness.
†Patients eligible for RAASi treatment were based on KDIGO 2012 guidelines.[6]
CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ICER, incremental cost-effectiveness ratio (cumulative costs gained per patient divided by cumulative QALYs gained per patient); KDIGO, Kidney Disease: Improving Global Outcomes; QALY, quality-adjusted life year; RAASi, renin-angiotensin-aldosterone system inhibitor; UACR, urine albumin-creatinine ratio; WTP, willingness-to-pay.

screened compared with current clinical practice (online supplemental table S10). Screening with two eGFR measurements was expected to incur an additional one-off screening cost of €4.6 million per 100 000 individuals screened. Subsequent treatment with RAASi in eligible patients was also expected to incur an additional cost of €4.1 million and €2.6 million per 100 000 individuals screened using the one UACR and two eGFR measurements screening scenario and the two eGFR measurements screening scenario, respectively. This is mainly attributable to the higher number of patients being diagnosed following screening who are also eligible for RAASi treatment.

DISCUSSION

The Inside CKD study used microsimulation modelling techniques to generate virtual cohorts of individuals representative of the population of Belgium, which was necessary because robust data on the prevalence and incidence of CKD in Belgium are lacking. These virtual populations were used to project the clinical and economic burden of CKD and the economic impact of implementing guideline-recommended CKD screening programmes. With current clinical practice, the prevalence of CKD is predicted to remain high in Belgium between 2022 and 2027, leading to a substantial financial burden. Of particular concern, more than two-thirds of individuals with CKD are predicted to remain undiagnosed in Belgium, in agreement with published data.[27] Similar results were observed in other countries (68.1%–87.4%).[16]

Across 31 countries/regions, the direct cost of CKD was predicted to rise from $202.4 billion (~€151.8 billion) in 2022 to $220.1 billion (~€165.1 billion) in 2027.[4 8] Our model predicted that almost half of the total CKD-related healthcare costs in 2027 in Belgium will be attributable to individuals with CKD stage 3, most likely due to its high prevalence and the high rate of cardiovascular events in this group.[28] In 2027, the total healthcare cost of patients with diagnosed CKD is predicted to be approximately 5.1% (€2.15 billion) of the expected total annual healthcare expenditure in Belgium, based on healthcare expenditure in 2016.[29]

Identification and treatment of early-stage CKD can slow kidney function decline and reduce the risks of RRT and developing comorbidities.[30] Quick resolution consultations can improve CKD management,[31] but without a formal diagnosis, patients could potentially miss out on guideline-recommended treatments. KDIGO guidelines advocate screening programmes aimed at early detection and treatment of patients with CKD, particularly for high-risk patients.[7] In Belgium, a single eGFR test is typically offered to patients at higher risk of developing CKD according to their full medical assessment. Although this is in line with the 2012 Domus Medica guidelines, these guidelines are under review and are being updated.[32] KDIGO guidelines recommend that CKD screening consist of a dual assessment of eGFR and albuminuria.[33] Albuminuria testing is important to assess kidney damage and CVD risk, particularly in patients at elevated risk, such as those with hypertension or type 2 diabetes.[34 35] Albuminuria testing is complementary and has substantial additional prognostic value to that of eGFR testing alone.[36]

The Inside CKD microsimulation showed that implementation of CKD screening in the general Belgian population (aged ≥45 years) using one UACR and two eGFR measurements (followed by RAASi treatment in eligible patients) would be cost-effective. Gains in QALYs were moderate but associated with relatively low additional costs per patient, well below the estimated WTP threshold. Thus, these low additional costs would be a small investment in the health of the Belgian population and were predicted to be cost-effective within 2 years of implementation. This presents an opportunity to optimise the identification of patients with CKD and provide more patient-centred treatment pathways in Belgium.

Screening with one UACR and two eGFR measurements was also predicted to be cost-effective in subgroups of patients at increased risk of CKD, including individuals aged ≥45 years with CVD, hypertension or type 2 diabetes or those aged ≥65 years. However, limiting a CKD screening programme to those at a more advanced age would reduce the long-term beneficial impact on patients, because improved QoL and delayed disease progression would occur over a longer lifetime in those identified at a younger age. Of note, screening with two eGFR measurements was less cost-effective than screening with one UACR and two eGFR measurements in the overall population and in the high-risk subgroups. This highlights the additional patient benefits of UACR testing if conducted in routine clinical practice in Belgium.

Although the introduction of screening programmes will inevitably place an additional economic burden on healthcare systems, policymakers must consider whether a screening programme is likely to generate benefits at a reasonable cost.[37] The benefits versus costs of population-wide CKD screening have long been debated.[38] Patient advocates with CKD strongly argue for CKD screening programmes to improve early diagnosis,[33] particularly because early-stage CKD is frequently asymptomatic. In agreement with our findings, modelling studies in overall populations in Germany (aged ≥30 years), the Netherlands (aged ≥45 years) and the USA (aged ≥35 years) found that introducing albuminuria testing in population-wide screening programmes would be cost-effective.[39–41] By contrast, a systematic review of studies assessing the cost-effectiveness of CKD screening in the general adult population concluded that screening programmes were only cost-effective in patients with diabetes and high-risk ethnic groups.[42] However, van Mil *et al* argued that most of the studies included in this systematic review did not consider the positive impact of screening on CVD prevention, the possibility of home-based screening instead of screening in a healthcare setting (reducing costs), or the treatment effect of novel therapeutic agents such as sodium-glucose cotransporter-2 inhibitors (SGLT-2is), finerenone and glucagon-like peptide-1 receptor agonists in relevant patients.[43 44]

Overall, without implementing a CKD screening programme, this microsimulation study highlights the continued high clinical and economic burden that CKD is likely to have on the Belgian healthcare system.

This study has several strengths and limitations. First, it uses a dynamic microsimulation that enables modelling of screening scenarios with a high level of granularity. However, this requires a large volume of detailed input data, not all of which was available for Belgium. Therefore, in some cases, proxy data from the UK were used and further enhanced with expert input. The UK was the closest match to Belgium, according to a data-clustering algorithm and validation by local experts.

Second, the associated costs of screening were limited to primary care and nurse consultations. However, individuals with more severe CKD may be referred to a nephrologist. Such costs were not accounted for in the model, but the total cost of a nephrologist consultation was estimated to be equal to a primary care visit. Furthermore, our results show that most patients with undiagnosed CKD have CKD stages 1–3 and may not need referral to a nephrologist.

Third, the healthcare costs included in the cost-effectiveness analysis did not consider that, because more individuals receive treatment for CKD, the occurrence of cardiovascular events is likely to decrease[45 46] due to the direct cardiovascular effects of RAASi treatment in addition to the reduction in CKD progression associated with RAASi use, thus leading to a potential reduction in costs and improved cost-effectiveness.

Fourth, interventions in this study were limited to RAASi treatment for patients who met the KDIGO 2012 eligibility criteria[6] because the model was developed and run before the 2024 KDIGO update.[7] In this model, RAASi initiation was assumed in patients newly diagnosed with CKD and hypertension, macroalbuminuria (UACR ≥300 mg/g) or type 2 diabetes and microalbuminuria (UACR 30–300 mg/g). The 2024 KDIGO update recommends RAASi treatment in patients with CKD and a UACR of 30–300 mg/g, regardless of diabetes status, which would lead to more patients being eligible for RAASi treatment than the current model predicts.[7] This would subsequently lead to higher costs but likely slow CKD progression and reduce the development of associated complications in more patients. Furthermore, the 2024 KDIGO update also recommends the use of SGLT-2is in subgroups of patients based on the presence of comorbidities (type 2 diabetes and/or heart failure) and their UACR and eGFR levels.[7] SGLT-2is are now reimbursed in Belgium.[47] The model was developed and run before this update and reimbursement; introducing these SGLT-2i recommendations into the microsimulation would incur additional costs. The increased costs would likely be outweighed by the benefits conferred by SGLT-2is, both on renal function decline and other cardiorenal outcomes.[48–51] Indeed, several studies have demonstrated that empagliflozin and dapagliflozin would be cost-effective in patient cohorts with CKD in Europe, Japan and the USA.[39 47 52–54]

Finally, the sensitivity analyses that varied individual health utility weights and costs by ±10% could be viewed as a limitation. However, these analyses were conducted in addition to the sensitivity analyses carried out for the core model[15]; this was deemed a standard, transparent approach to testing the robustness of the model.

CONCLUSIONS

The Inside CKD microsimulation predicts that, with current clinical practice, without the introduction of regular UACR screening, the clinical and financial burden of CKD in Belgium will remain substantial over the next few years. Although the burden of patients with late and severe stages of CKD is well-established, this study projects that CKD stage 3 will also place a substantial burden on the Belgian healthcare system. Policies introducing screening programmes to improve timely diagnosis of early CKD stages, followed by appropriate treatment, are needed to lessen this burden. The implementation of a screening programme with one UACR measurement and two eGFR measurements, followed by initiation of guideline-recommended treatment, would be cost-effective in the Belgian population aged ≥45 years, as well as in patients at high risk of CKD. These results support the implementation of a UACR-based CKD screening programme for the general population in Belgium and can inform policymakers when considering strategies to improve the outcomes of patients with CKD.

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