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Costs and Consequences of Chronic Kidney Disease in People with Diabetes in Portugal: A Modelling Study

Custos e Consequências da Doença Renal Crónica em Pessoas com Diabetes em Portugal: Um Estudo de Modelação

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ABSTRACT

Introduction: Chronic kidney disease is the fastest-growing chronic disease in terms of prevalence and one of the biggest causes of global mortality according to the Global Burden of Disease Collaboration. This study aimed to project the natural disease progression of this disease in people with diabetes, and to quantify the costs and consequences in the Portuguese context. This was achieved by developing an analytical model reflecting the epidemiology of chronic kidney disease and integrating the various stages of disease progression.

Methods: A population-based cohort Markov model was used, to follow an adult cohort of people with diabetes and chronic kidney disease as they progressed through different risk categories, in annual cycles, over a period of 50 years. The model considered the natural progression of chronic kidney disease through 18 risk categories based on the KDIGO classification system, as well as the probability of patients receiving renal replacement therapy, including dialysis and kidney transplantation, and the probability of death. Each stage is associated with an annual cost and a disability weight, so the model allowed survival, years lived with disability and lifetime costs to be estimated for the entire population with chronic kidney disease and for patients in different risk categories.

Results: Over the cohort´s lifetime, the model estimated, for the total population with chronic kidney disease and diabetes, an average survival of 8.62 years, with 0.59 years lived with disability, and an average cost of €24 613. These figures correspond to a loss of more than 410 000 years lived with disability and a total lifetime cost of 17.0 billion euros. The progression of this disease was associated with lower survival, more years lived with disability and higher costs.

Conclusion: The results of this study characterize the natural progression of chronic kidney disease in people with diabetes *mellitus* type 2, as well as the associated costs and consequences in the national context. Since diabetes *mellitus* type 2 is a risk factor for chronic kidney disease, it is expected that the real impact will be greater than estimated in the coming decades. Analysis by risk level shows that progression of the disease is associated with worse outcomes.

Keywords: Diabetes Mellitus, Type 2; Disability-Adjusted Life Years; Health Care Costs; Kidney Failure, Chronic

RESUMO

Introdução: A doença renal crónica é a doença crónica com maior crescimento de prevalência, e uma das maiores causas de mortalidade global de acordo com o *Global Burden of Disease Collaboration*. O presente estudo teve como objetivo projetar a evolução desta doença em pessoas com diabetes, de modo a quantificar os custos e consequências no contexto português. Tal foi conseguido através do desenvolvimento e parametrização de um modelo analítico refletindo a epidemiologia da doença renal crónica e integrando os vários estádios de progressão da doença.

Métodos: Foi utilizado um modelo populacional de coorte com uma mecânica de Markov, onde pessoas com diabetes e doença renal crónica foram seguidas ao longo de 50 anos, em ciclos anuais, sendo registada a sua progressão através das diferentes categorias de risco da doença renal crónica. O modelo considerou a progressão natural da doença renal crónica através de 18 categorias de risco baseados na matriz de estadiamento de KDIGO, bem como a probabilidade de os doentes receberem terapêutica de substituição renal, designadamente, diálise e transplantação renal e a probabilidade de morte. A cada estádio estão associados um custo anual e um ponderador de incapacidade, pelo que o modelo permitiu estimar a sobrevivência, os anos de vida perdidos por incapacidade (*years lived with disability*), e os custos incorridos ao longo da vida, para a totalidade da população e para doentes em diferentes categorias de risco.

Resultados: Durante o tempo total de evolução da coorte, o modelo estimou, para a população total com doença renal crónica e diabetes, uma

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sobrevivência média de 8,62 anos, com 0,59 anos perdidos por incapacidade, e um custo médio *lifetime* de €24 613. Estes valores correspondem a mais de 410 mil anos de vida perdidos por incapacidade e um custo total, ao longo da vida, de 17,0 mil milhões de euros. A análise por nível de risco demonstra que a progressão da doença renal crónica está associada a menor sobrevivência, mais anos perdidos por incapacidade e maiores custos.
Conclusão: Os resultados deste estudo caracterizam a progressão natural da doença renal crónica em pessoas com diabetes *mellitus* tipo 2 bem como os custos e consequências associados no contexto nacional. Sendo a diabetes *mellitus* tipo 2 um fator de risco da doença renal crónica, é expectável que nas próximas décadas o impacto real seja maior do que o estimado. A análise por nível de risco permite verificar que a progressão da doença está associada a piores resultados.
Palavras-chave: Anos de Vida Ajustados por Deficiência; Diabetes Mellitus Tipo 2; Doença Renal Crónica; Custos Médicos

KEY MESSAGES

- This study was aimed at filling the gap in data on the costs and outcomes of chronic kidney disease (CKD) in patients with diabetes in Portugal. To the best of our knowledge, this is the first study on this subject regarding the Portuguese context.
- The lifetime costs and outcomes associated with CKD in patients with diabetes can be significant.
- The progression of CKD is associated with lower survival, more years lost due to disability, and higher costs for the healthcare systems.
- Delaying the progression of CKD will lead to health gains and lower follow-up costs.
- The model was parameterized using the best evidence available for the Portuguese context.

INTRODUCTION

A 20.9% estimated prevalence of chronic kidney disease (CKD) has been found in Portugal.[1] It is defined as the presence of sustained structural or functional abnormalities of the kidney for more than three months, with health implications. The disease progression may lead to stage 5 CKD, requiring renal replacement therapy (RRT).[2]

CKD is one of the most frequent outcomes of type 2 diabetes *mellitus* (T2DM), affecting 20% - 40% of patients.[1,3–5] Therefore, the increasing prevalence of CKD is partly due to the increasing incidence of T2DM as well as greater longevity, related to the available therapeutic advances. However, different risk factors are involved in etiology, including the duration of T2DM, adequate control of blood glucose levels, high blood pressure, dyslipidemia, and a history of kidney disease.[6]

CKD is associated with an increased risk of cardiovascular morbidity, premature mortality, and reduced quality of life.[7,8] According to the Global Burden of Disease study, CKD ranked 29th on the list of causes of global mortality in 1990, rising to 18th place in 2019.[9–11] It is also estimated that CKD will become the fifth leading cause of years of life lost globally by 2040.[12]

Annual costs of €344 billion associated with CKD and RRT have been found in a study carried out in 31 countries/regions, with a significant part of the total costs due to RRT-related costs.[13]

The early detection and appropriate treatment of CKD are crucial for delayed progression and improvement of the clinical outcomes by reducing complications, including cardiovascular events and progression to stage 5 CKD requiring RRT.[14]

Data on the national epidemiology of CKD are scarce. The RENA study was published by Vinhas *et al.* in 2020 and is the most recent study characterizing the prevalence of CKD in Portugal,[1] involving a group of adult patients followed in primary care and a 20.9% prevalence was found. This figure compares with the European average rate (18.1%) found in a review and meta-analysis of CKD prevalence studies. A study carried out in 31 countries/regions has estimated the cost associated with CKD and RRT at €344 billion per year, with a significant part of total costs arising from RRT-related costs.[13]

This study was aimed at the assessment of the progression of CKD in Portuguese patients with diabetes, in addition to the quantification of the costs and outcomes through the development and parameterization of a Markov model integrating the different stages of the disease. Estimates for the entire population and for patients in different risk categories were considered. In this context, we aimed at increasing the knowledge on CKD in Portuguese patients with diabetes, particularly as regards the outcomes in terms of survival, years of life lost due to disability, and costs.

METHODS

Description of the model

A Markov model was developed, aimed at assessing the progression of CKD in Portuguese patients with diabetes in addition to the costs and outcomes, with annual cycles, showing the epidemiology and natural progression of CKD through different risk categories (low, moderate, high, or very high). The characterization of CKD progression in different risk categories was based on the Kidney Disease: Improving Global Outcomes (KDIGO) staging overview, based on the glomerular filtration rate (GFR) and albuminuria

Table 1 – KDIGO: CKD prognosis

				Albuminuria (mg/g)		
				A1 Normal to mildly increased < 30	A2 Moderately increased 30 – 300	A3 Severely increased > 300
Glomerular filtration rate (mL/min/1,73 m²)	G1	Normal	≥ 90	G1A1	G1A2	G1A3
	G2	Mildly decreased	60 - 89	G2A1	G2A2	G2A3
	G3a	Mildly to moderately decreased	45 - 59	G3aA1	G3aA2	G3aA3
	G3b	Moderately decreased	30 - 44	G3bA1	G3bA2	G3bA3
	G4	Severely decreased	15 - 29	G4A1	G4A2	G4A3
	G5	Kidney failure	< 15	G5A1	G5A2	G5A3

Source: KDIGO (2013)

levels.[14] Eighteen possible categories are included, based on different combinations of GFR and albuminuria levels. The KDIGO guidelines are shown in Table 1. In addition, two stages regarding patients on RRT are included in the model, namely 'dialysis and kidney transplantation' and 'death' stages.

Within each annual cycle, it is assumed that transitions between KDIGO categories are limited to changes of one level in GFR and/or albuminuria. Therefore, for example, a patient in category G3aA2 can only transition to the KDIGO categories shown in Fig. 1.

The Markov model showing the possible transitions to one of the stages is shown in Fig. 1. The model projects the evolution of the cohort over 50 years, considering a 4% update rate in accordance with the latest methodological guidelines for economic evaluation studies of health technologies for the Portuguese context.[16] Each stage is associated with an annual cost and a disability weight, allowing for the estimation of survival, years lost to disability, and lifetime costs.

Study population

The estimation of the costs and outcomes of CKD involves parameterizing the model with the prevalence of diabetes and CKD in the Portuguese population in 2021, according to the distribution across each stage of the model.

Identification of clinical data

The CKD natural progression model is based mainly on national data from the following sources: a) the RENA study;[1] b) an analysis carried out by the authors based on data from the Regional Health Administration Information System of the Regional Health Administration of Lisbon and The Tagus Valley (*Sistema de Informação da Administração Regional de Saúde de Lisboa e Vale do Tejo* - SIARS); c) an analysis carried out by the authors based on data from the Beatriz Ângelo Hospital (HBA); d) information released by the Chronic Kidney Disease Registry Office (*Gabinete de Registo de Doença Renal Crónica* - GRDRC) of the Portuguese Society of Nephrology regarding patients on RRT;[17] e) an international study on mortality in patients with chronic kidney disease;[18] f) a panel of experts on resource consumption by patients with CKD; g) the Hospital Morbidity Database; and h) official sources on unit costs.

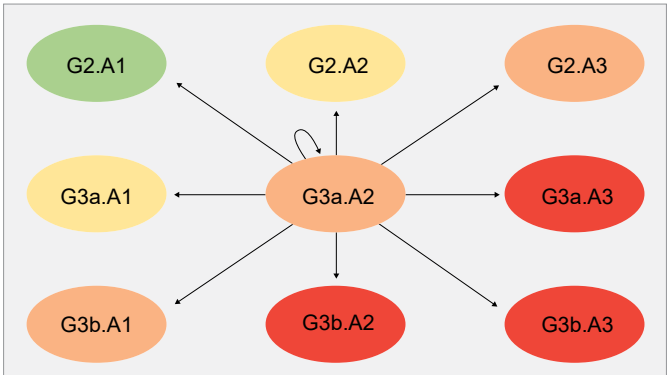

Figure 1 – Analytical decision model diagram

Prevalence of CKD and distribution by stages

Data from different sources were used to estimate the distribution of CKD prevalence across the different stages of the model.

A mixed approach was used for the estimation of the distribution of CKD prevalence by KDIGO risk categories combining data on distribution by GFR levels described in the RENA study[1] with data on distribution by albuminuria levels estimated from the HBA database.

An estimated 20.9% prevalence rate of CKD based on GFR [95% confidence interval (95% CI): 6.5% - 35.3%] and a 32.0% prevalence rate of diabetes in patients with CKD (95% CI: 26.5% - 37.5%) were found in the RENA study by Vinhas *et al.*[1] involving a group of 3,135 adult patients (aged 18 or over). A 20.72% prevalence rate by CKD KDIGO staging categories (G1A1 to G5A3) was found.

Annual information on the follow-up of patients with CKD referred to the Nephrology Service from February 2012 to December 2017 is included in the HBA database. Within this period, 1,267 patients (mean age 72 years, 56% male) were included in the analysis and followed up for a three-year median period. Data analysis was carried out by the authors and allowed for the estimated distribution of this population by CKD KDIGO stages, as well as a longitudinal analysis for the estimation of the probabilities of transition between KDIGO stages and the probabilities of RRT onset.[19]

Estimates from the GRDRC of the Portuguese Society of Nephrology (2019) were used as a source of prevalence by RRT stage, showing a dialysis prevalence rate of 1,301.50 per million people and a kidney transplantation prevalence of 706.94 per million people.

The final distribution of the CKD prevalence across the different stages of the model resulting from the integration of the different data sources is shown in Table 2.

Transition probabilities between stages

KDIGO staging categories

The transition probabilities between KDIGO stages were based on the HBA database. The calculation is based on transitions that occurred between annual cycles, considering all transitions for each patient (i.e., each patient corresponds to a number of transitions equivalent to the years of follow-up and the available information).

Considering stage G1A1 as an example [Table S1 in Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)], 25 annual transitions of patients in this stage were found: 19 patients remained in the same stage, one transitioned to G1A2, and five transitioned to G2A1; no patient has transitioned to G2A2 (which would correspond to a simultaneous change in both GFR and albuminuria). The absence of this transition in data is probably due to the sample size and does not correspond to a zero probability. An adjustment method was implemented, consisting of adding '1' to all possible transitions, to mitigate this effect and to ensure that the model showed an accurate assessment of the natural progression of the disease. This procedure was validated by

Table 2 – Distribution of the prevalence of CKD

		Albuminuria			
		A1	A2	A3	Total
Glomerular filtration rate	G1	0.5%	0.6%	0.8%	1.9%
	G2	15.0%	14.8%	16.6%	46.4%
	G3a	10.7%	15.6%	11.9%	38.1%
	G3b	2.8%	4.2%	3.1%	10.1%
	G4	0.4%	0.9%	0.9%	2.2%
	G5	0.1%	0.1%	0.3%	0.4%
	Dialysis				0.6%
	Transplantation				0.3%
	Total	29.4%	36.0%	33.6%	100.0%[a]

a: corresponds to the sum of the column, including the patients on dialysis and renal transplantation

the clinical experts and ensured that all clinically plausible disease progressions were represented by the model [as shown in Table S1, Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)]. The transition probability matrices between KDIGO stages, estimated through this adjustment, are shown in Appendix 1, Tables S2 to S7 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648).

Transition probability to renal replacement therapy

The probability of transitioning to RRT was also based on HBA data. During the follow-up period, 83 patients were started on dialysis and two underwent kidney transplantation (with no prior dialysis). Considering that transitioning to RRT only occurs in very high-risk patients, and that the probability of transitioning to RRT cannot be lower in higher-risk stages, the estimated transition probability matrices are shown in Appendix 1, Table S8 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648).

Probability of kidney transplantation in dialysis patients

The probability of kidney transplantation in dialysis patients was estimated based on data provided by the GRDRC (2020). A 3.70% - 3.97% percentage of patients undergoing kidney transplantation among dialysis patients has been found. An average value was considered in the model (i.e., 3.85%) [Table S9 in Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)].

Mortality

All-cause mortality by KDIGO stage was estimated, based on the study by Nichols *et al*.[18] This was a real-life data study carried out in the United States (more specifically in Oregon) involving patients presenting with T2DM *vs.* healthy people without T2DM, matched by gender/age, throughout a 7.6-year median follow-up. Increased mortality with increased risk defined by GFR and albuminuria levels has been found at three years. The values were adjusted for the Portuguese reality, considering the relative differences in mortality between the Portuguese population and the Oregon population. The annual mortality probabilities by KDIGO stage are shown in Table S10, Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648).

The estimated mortality rate of patients on RRT was based on data provided by the GRDRC (2020)[17] and the GRSPT (Registry Office of the Portuguese Transplantation Society - *Gabinete de Registo da Sociedade Portuguesa de Transplantação*) (2022).[20] The average value described by the GRDRC (2020) between 2015 (12.0%) and 2019 (13.3%), corresponding to a 12.7% rate was considered as the estimated mortality probability among dialysis patients, [Table S11 in Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)]. The five-year survival data found by the GRSPT (2022)[20] between the 1980s and 2020s corresponded to a 1.3% annual mortality probability, which was considered as the estimated mortality probability in post-transplant patients, [Table S12 in Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)].

Disability weights

Years lived with disability (YLD) were estimated by applying disability weights to each stage of the model, based on the Global Burden of Disease (GBD 2019) study.[11] Therefore, YLDs corresponded to the product of the number of patients at each stage of the model and the disability weights associated with each CKD stage. Weights by severity level or CKD stage are described by the GBD study. For CKD, weights depend on the severity of anemia (except for RRT). According to the GBD study, stages G1 and G2 are not associated with disability, while regarding stages G3 to G5, the average weight was obtained using a weighted average depending on the distribution by severity of anemia in the HBA database. As regards dialysis, the arithmetic mean was calculated. The disability weights used are shown in Table S13 in Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648).

Identification and measurement of costs

The costs of CKD were based on the perspective of the National Health Service (*Sistema Nacional de Saúde* - SNS), including all direct medical costs related to hospitalization, emergency episodes, in addition to outpatient consultations, diagnostic tests, and pharmacological treatment. The quantification of resources consumed at different stages, namely KDIGO stages G3a.A1 to G5.A3 and RRT stages, was carried out using two main sources: the SIARS database and a panel of experts.

Costs across KDIGO staging categories

The costs associated with patients in KDIGO stages with low risk of progression to CKD (normal GFR or slightly decreased GFR ≥ 60 mL/min/1.73 m^2) attending primary care were estimated from an analysis made by the authors using the SIARS database (unpublished work). This analysis allowed for the identification and quantification of the use of consultations, diagnostic tests, and associated medication.

The data from SIARS included 20,652 adult patients registered with the Lisbon and Tagus Valley Regional Health Administration, with at least one consultation recorded between January 1, 2018, and December 31, 2018, and diagnosed with T2DM; the clinical records regarding 12,270 patients from these allowed for their distribution by KDIGO[14] categories, in addition to the definition of a pattern of resource consumption for each stage. Among these, 9,102 patients were classified in categories G1A1 and G2A1, with no clinical criteria for CKD. The remaining 3,168 patients were classified in KDIGO staging categories of moderate or high risk.

No patients in stage A3 were found in the SIARS; therefore, the values obtained for stage A2 were considered. SIARS data were also used to quantify the medication consumption in patients with GFR corresponding to stages G3a and G3b.

The estimated costs for each stage are shown in Table S14, Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648).

The annual costs associated with the follow-up of patients in high risk KDIGO stage (G3a.A1 to G5.A3 with GFR < 60 mL/min/1.73 m^2) were estimated by a nationally representative panel of experts. The panel members independently responded to specific questions regarding the pattern of healthcare consumption by completing a questionnaire sent by email. The questionnaire included questions regarding the use of consultations, emergency episodes, hospitalizations, diagnostic tests, and medications. A simple average was calculated.

Based on the panel of experts, resources consumed during the transition to lower GFR levels were identified. Therefore, the costs of follow-up within the first year at each stage are different from the costs of follow-up within the subsequent years [Appendix 1, Table S15 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)].

Costs of renal replacement therapy

The costs of resources consumed by dialysis patients were estimated from Order No. 12-A/2020,[21] that was used for the definition of the price of dialysis per week and per session, with differences regarding the presence of vascular access or without it. A weighted price was calculated based on the values established in Order No. 12-A/2020, leading to a single price and weighted by the prevalence rate of each stage (GRDRC, 2020). In addition, complementary information from the expert panel was used to estimate the resources at RRT onset, including the placement of the initial vascular access for hemodialysis and the placement of a catheter for peritoneal dialysis.

The estimate of the costs of kidney transplantation was based on a real-life data study[22] considering resource consumption and incentives for transplantation. The value reported by the authors for 2010 was updated taking inflation into account. The annual costs per RRT stage are shown in Table S16, Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648).

Assessment of resources

The estimated costs of the resources described by the panel of experts were based on official sources. The 2017 Hospital Morbidity Database was used to estimate the cost of hospitalizations, including inpatient episodes of adult patients that were coded according to the International Classification of Diseases – 10th revision (ICD-10-CM/PCS).[23] Detailed information on the calculation of hospitalization costs is available in Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648). The costs of medications dispensed by hospital pharmacies were obtained from the Public Health Procurement Catalog (*Catálogo de Aprovisionamento Público da Saúde*).[24] The lowest-cost intervention was selected due to the presence of different alternatives within the same therapeutic class. The costs of outpatient drugs were estimated based on IQVIA data for 2021. From these data, packages of reduced sizes and dosages were excluded, as they were not considered representative of the treatment of chronic diseases. For each therapeutic class, the weighted average costs were calculated based on sales volume and price per package (price without value added tax), assuming a 90% therapeutic adherence. The unit costs of other healthcare resources (consultations, emergency care without hospitalization, and diagnostic tests) are based on the prices defined by Ordinance No. 254/201, September 7.[2]

RESULTS

Survival (years of life), YLD, and cumulative costs throughout the model period by risk group, are shown in Table 3; patients at high risk of progression to CKD have shown a lower life expectancy and higher YLD and costs. On average, a 34% reduction in life expectancy, a two-fold increase in years lost due to disability, and an 81% increase in costs have been found when comparing the results of very high-risk patients with low-risk patients,

The estimates for the overall population are shown in Table 4. The model estimates an average survival of 8.62 years, with 0.59 YLD, and an average cost of €24,613, over the total lifetime of the modelled population. Considering the entire cohort, a loss of more than 410,000 YLD and a total lifetime cost of approximately €17 billion are expected.

The low-risk population corresponds to 15.6% of the

population of patients with CKD. In this population, longer survival (10.54 years per patient), lower YLD (0.42 per patient), and lower costs (€18,100 per patient) are estimated. In aggregate terms, CKD is estimated to lead to a loss of 44,800 YLD and a €1.9 billion cost [Table S17, Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)].

Regarding the moderate-risk population (26.0% of the population), average survival is estimated at 9.21 years, with 0.49 YLD, and an average cost of €20,000 per patient. A total loss of 87.8 thousand YLD and costs of 3.6 billion euros are estimated for this population [Appendix 1, Table S18 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)].

An estimated 8.30-year average survival, 0.56 YLD, and an average cost of €22,700 per patient are estimated in high-risk patients. High-risk patients were mostly found (35.7%); therefore, in aggregate terms, these are associated with the poorest outcomes: 138,200 years of life lived with disability and total costs of €5.6 billion [Table S19 in Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)].

The very high-risk patients are associated with the poorest average outcomes, with an average survival of 6.95 years, a loss of 0.84 YLD, and an average cost of €32,700 per patient. This subgroup represented 21.8% of the population with CKD, showing a loss of 126,500 YLD and total costs of €4.9 billion [Table S20, Appendix 1 (*Apêndice* 1: https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/22573/15648)].

DISCUSSION

This study was aimed at assessing the progression of CKD in patients with diabetes, allowing for the quantification of costs and outcomes in the Portuguese context. This was achieved by developing a Markov model that integrates the different stages of disease progression. The model was parameterized with data reflecting the Portuguese reality, using the best available evidence.

The estimates regarding the natural progression of CKD, as well as survival, years lost due to disability, and associated costs were based on the most current data, including non-aggregated values for the different risk categories based on the KDIGO international matrix. During the total progression time of the cohort, an average survival of 8.62 years, with 0.59 years lost due to disability, and an average cost of €24,613 were estimated by the model for the total population with CKD and T2DM.

These figures correspond to a loss of more than 410,000 YLD and a total lifetime cost of approximately €17 billion. The analysis by risk level showed that disease progression is associated with lower survival, more years lost due to disability, and higher costs for the SNS. The model results show that a delay in the progression of CKD will lead to health gains and lower follow-up costs.

The study was also aimed at filling the gap in data on the costs and outcomes related to patients with CKD and diabetes in Portugal and is an innovative analysis in the national context. However, it has some limitations, including the absence of a single database allowing to reach the prevalence rate of CKD distributed by KDIGO categories, leading to the need to use a mixed approach and combined data from different sources, information regarding patients attending primary care (distribution based on GFR from Vinhas *et al.*, 2020) and secondary care (distribution based on albuminuria values obtained from the HBA database). The estimated values based on the available sources are naturally influenced by the context in which they are performed. There are some limitations regarding the RENA study,[1] particularly related to the geographical representativeness and sociodemographic characteristics of the sample. In fact, the predominance of Caucasian patients, who are relatively older, and the absence of participants from the Northern region and the Algarve may prevent the generalization of the results to the Portuguese population.

The distribution by albuminuria levels seems more accurate when obtained from a hospital-based study in which, on the one hand, patients in low-risk KDIGO stages are included, and on the other hand, more patients in stages with lower GFR will be followed. In addition, the availability of longitudinal data from the HBA database allowed for the estimation of the distribution of albuminuria for each GFR level over time, providing the transition probabilities of the model. These data had limitations due to the sample size

Table 3 – Results by level of risk

Risk group	Weight in patients with CKD	Average survival (years), per patient	YLD, per patient	Lifetime costs, per patient	Total costs by risk group
Total population	100.0%	8.62	0.59	€24 613	€17 045 827 148
Low risk patients	15.6%	10.54	0.42	€18 058	€1 946 152 022
Moderate risk patients	26.0%	9.21	0.49	€19 964	€3 592 737 068
High risk patients	35.7%	8.30	0.56	€22 721	€5 617 401 877
Very high-risk patients	21.8%	6.95	0.84	€32 691	€4 934 120 620

YLD: years lived with disability

Table 4 – Results for the global population

a) Average survival (years), per patient			
	A1	A2	A3
G1	0.21	0.17	0.10
G2	0.57	0.46	0.41
G3a	0.61	0.84	0.49
G3b	0.74	0.82	0.60
G4	0.37	0.56	0.53
G5	0.02	0.04	0.10
Dialysis			0.53
Transplantation			0.46
Years of life			8.62

b) YLD, per patient			
	A1	A2	A3
G1	0.00	0.00	0.00
G2	0.00	0.00	0.00
G3a	0.00	0.00	0.00
G3b	0.00	0.00	0.00
G4	0.04	0.06	0.06
G5	0.01	0.02	0.06
Dialysis			0.31
Transplantation			0.01
YLD			0.59

c) Costs (€), per patient			
	A1	A2	A3
G1	107	89	50
G2	320	262	232
G3a	348	572	540
G3b	376	505	597
G4	424	693	879
G5	23	59	209
Dialysis			13 498
Transplantation			4830
Costs (€)			24 613

d) Results, per cohort	
Average survival (years)	5 967 968
YLD	410 203
Costs (€)	17 045 827 148

YLD: years lived with disability

and therefore requiring an adjustment method validated by the clinical experts.

Another limitation concerns the lack of information on mortality in patients with CKD in the Portuguese population.

However, the model was based on the best evidence available in literature.

Despite the limitations related to the methodology, this study has provided relevant information for the Portuguese reality, improving the knowledge on CKD in Portuguese patients with diabetes, particularly as regards the outcomes in terms of survival, years lost due to disability, and costs.

CONCLUSION

The results of this study have shown the natural progression of CKD in patients with T2DM, as well as the associated costs and outcomes nationwide. Considering T2DM as a risk factor for CKD, a greater impact is expected throughout the coming decades than what is estimated. The analysis by risk level showed that the disease progression is associated with poorer outcomes. Direct public investment towards reducing the impact of T2DM and CKD is therefore imperative, including early diagnosis of CKD and outcomes in patients with T2DM, as well as strategies to reduce the natural progression of CKD and to approach all associated comorbidities.

AWARDS AND PREVIOUS PRESENTATIONS

Oral presentation: Edgar Almeida *et al*. Staging and prediction of CKD progression. Oral presentation at the *"Nefrologia em Diálogo: Para Um Diagnóstico e Intervenção Precoce Na Doença Renal Crónica"* event of the Portuguese Society of Nephrology held in Coimbra on the 9th of March 2023 (World Kidney Day).

Poster presentation: L. Silva Miguel *et al.* "SA45 Natural Evolution of Chronic Kidney Disease in Diabetic Patients: Costs and Consequences in Portuguese Reality" at the ISPOR Europe 2023 event held in Copenhagen, 12-15 November 2023.

AUTHOR CONTRIBUTION

MB, JC, LSM: Study design, development of the analytical model, data collection and analysis, critical revision and

writing of the manuscript.

EA, RA, GSD: Study design, data collection and analysis, critical revision of the manuscript.

RA, MBV, LF, MP, JR, JS, APS: Data collection and analysis, critical revision of the manuscript.

CB, FS: Data collection and analysis, critical revision and writing of the manuscript.

The final version was approved by the authors.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2024 update of the Helsinki Declaration of the World Medical Association.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS

EA was supported by Vifor Pharma, AstraZeneca, BIAL and Bayer for the participation in meetings or travels; EA is the president of the Portuguese Society of Nephrology.

JC has received consulting fees from IQVIA, in addition to support by EAN, IQVIA and ERASMUS PLUS for the participation in meetings or travels; holds a paid or unpaid leadership or fiduciary role in EAN.

MBV has received payments or fees from AstraZeneca, Bayer, Boehringer Ingelheim, Bial and Lilly regarding lectures, presentations, speaker's offices, writing of manuscripts or educational events; MBV has received support from Bayer, Boehringer Ingelheim, Bial and Lilly for the participation in meetings or travels.

The remaining authors declare not having any conflicts of interest related to the manuscript.

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