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Natural evolution of chronic kidney disease in diabetic patients: costs and consequences in Portuguese reality

Silva Miguel L[1], Almeida E[2], Ascenção R[3], Alves R[4], Bigotte Vieira M[5], Falcão L[2], Pestana M[6], Raposo J[7], Santos J[8], Silva AP[9], Matias J[1], Duarte G[3], Costa J[3], Borges M[1,3]

[1]IQVIA Portugal, Lisboa, Portugal; [2]Hospital Beatriz Ângelo, Lisboa, Portugal; [3]Laboratório de Farmacologia Clínica e Terapêutica, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal; [4]Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; [5]Centro Hospitalar Universitário de Lisboa Central, Lisbon, Portugal; [6]Centro Hospitalar Universitário de São João, Porto, Portugal; [7]Associação Protectora dos Diabéticos de Portugal, Lisbon, Portugal; [8]Centro Hospitalar Universitário de Santo António, Porto, Portugal; [9]Centro Hospitalar Universitário do Algarve, Faro, Portugal.

Corresponding author: luis.silvamiguel@iqvia.com

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Background & objectives

- Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. CKD is classified according to cause, glomerular filtration rate (GFR) (categories G1 to G5), and albuminuria (categories A1–A3) [1]. One of the main risk factors for the development of CKD is type 2 diabetes mellitus (DM2), which is responsible for approximately two thirds of cases [2]. On a global scale, it is estimated that patients with CKD and DM2 have lost 8,1 million disability-adjusted life years (DALY) in 2017 [3].
- The objective of this study was to evaluate the impact of kidney disease on people with diabetes and estimate the related costs and consequences in Portugal for a lifetime period.

Methods

An original **Markov model** based on the KDIGO staging, and incorporating three additional stages (dialysis, kidney transplantation and death), was developed to estimate survival, years lost due to disability (YLD), and costs incurred by diabetic patients with CKD throughout life. The model runs in yearly cycles with half-cycle correction. KDIGO stages are described in Table 1.

Table 1. KDIGO matrix for the prognosis of CKD.

GFR categories (ml/min/1,73 m²) Description and range			Persistent albuminuria categories Description and range: A1 Normal to mildly increased < 30 mg/g < 3 mg/mmol	A2 Moderately increased 30-300 mg/g 3-30 mg/mmol	A3 Severely increased > 300 mg/g > 30 mg/mmol
G1	Normal or high	≥ 90	G1.A1	G1.A2	G1.A3
G2	Mildly decreased	60 - 89	G2.A1	G2.A2	G2.A3
G3a	Mildly to moderately decreased	45 - 59	G3a.A1	G3a.A2	G3a.A3
G3b	Moderately to severely decreased	30 - 44	G3b.A1	G3b.A2	G3b.A3
G4	Severely decreased	15 - 29	G4.A1	G4.A2	G4.A3
G5	Kidney Failure	< 15	G5.A1	G5.A2	G5.A3

Green, low risk (if no other markers of kidney disease, no CKD); Yellow, moderately increased risk; Orange, high risk; Red, very high risk. GFR, glomerular filtration rate

The **prevalence** of CKD was sourced from a cross-sectional Portuguese study: 20.9%, with 32.0% of CKD patients having diabetes [4].

KDIGO staging was based on the same study [4], combined with data from a Portuguese public hospital (Hospital Beatriz Ângelo, HBA). The estimated distribution is shown in Table 2.

Table 2. Distribution of patients by KDIGO stage.

	A1	A2	A3	Total
G1	0.5%	0.6%	0.8%	1.9%
G2	15.2%	14.9%	16.7%	46.8%
G3a	10.8%	15.7%	12.0%	38.5%
G3b	2.8%	4.2%	3.2%	10.2%
G4	0.4%	0.9%	0.9%	2.2%
G5	0.1%	0.1%	0.3%	0.4%
Total	29.7%	36.4%	33.9%	100%

Transition probabilities were estimated using a longitudinal database from HBA. This database includes data collected between 2012 and 2017 on 1,267 patients, with an annual observation until progression to dialysis or kidney transplant, lost to follow-up, or death. A median follow-up of 3 years was achieved. This database was complemented with official data regarding patients under renal replacement therapy [5].

All-cause **mortality** was based on a real-world study [6] that estimated mortality rates per KDIGO stage. As this study was developed in Oregon (United States of America), published rates were adjusted for the Portuguese population. All-cause mortality for patients with end stage renal disease was based on official Portuguese data [5, 7].

Utilities: Disability weights were derived from a Global Burden of Disease Study [8]. Stages G1 and G2 are not associated to any disability.

Costs: Portuguese specific resource use was sourced from multiple sources including primary health care and specialized care microdata, as well as published literature. Resources were valued according to publicly available national unit cost data - national legislation (Portaria nº 207/2017) and official national drug cost database (Infomed).

Table 3. Disability weights and annual costs by KDIGO stage.

	Average disability weights	Annual costs: A1 First year	A1 Following years	A2 First year	A2 Following years	A3 First year	A3 Following years
G1	0.000	504 €	504 €	524 €	524 €	524 €	524 €
G2	0.000	562 €	562 €	570 €	570 €	570 €	570 €
G3a	0.004	798 €	485 €	916 €	596 €	1,332 €	972 €
G3b	0.004	820 €	507 €	935 €	615 €	1,350 €	990 €
G4	0.111	1,147 €	1,127 €	1,255 €	1,235 €	1,685 €	1,656 €
G5	0.577	1,435 €	1,403 €	1,543 €	1,511 €	2,058 €	2,021 €
Dialysis	0.593			27,502 €	25,120 €		
Kidney transplant	0.024			68,709 €	7,273 €		

Results

- The model allows to estimate the natural evolution of CKD in people with diabetes. It is mainly based on Portuguese real-life data, so it reflects Portuguese reality.
- Results include life years, years of life lost due to disability, and costs, stratified by KDIGO stage.
- For the global population with CKD and diabetes, the model estimates a mean survival of 8.62 years, 0.59 YLD, and a mean lifetime cost of 24.6 thousand euros per patient.
- Overall, considering the entire cohort with CKD and diabetes, a loss of 410 thousand YDL and a total cost of 17,046 million euro were estimated.

Table 4. Life years, years of life lost due to disability and costs.

Risk group	Distribution of patients	Results per patient: Life years	YLD	Costs	Total costs (million €)
All patients	100%	8.62	0.59	24,613 €	17,046
Low risk	16%	10.54	0.42	18,058 €	1,946
Moderate risk	26%	9.21	0.49	19,964 €	3,593
High risk	36%	8.30	0.56	22,721 €	5,617
Very high risk	22%	6.95	0.84	32,691 €	4,934

Conclusions

This study is based on real world data, therefore reflecting national reality. The results show that disease progression is associated with worse results. Comparing very high-risk patients with low-risk, on average, life expectancy reduces 34%, YLD double and costs increase approximately by 81%. Therefore, a delay in the progression of the disease would lead to clinical gains and lower costs.

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