Producción de **investigación**

Agregando **valor** a la toma de decisiones con datos del **mundo real**

2022

2023

CAC
Cuenta de Alto Costo

Fondo Colombiano de
Enfermedades de Alto Costo

Producción de investigación 2022 – 2023:
Agregando valor a la toma de decisiones con datos del mundo real

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Abreviaturas

CAC:	Cuenta de Alto Costo.
DM:	Diabetes mellitus.
ERC:	Enfermedad renal crónica.
EPQR:	Enfermedad poliquística renal.
TFG:	Tasa de filtración glomerular.
HbA1c:	Hemoglobina glicosilada.
HDL:	Por sus siglas en inglés, lipoproteína de alta densidad.
IC:	Intervalo de confianza.
IETS:	Instituto de evaluación tecnológica en salud.
LDL:	Por sus siglas en inglés, lipoproteína de baja densidad.
TAS:	Tensión arterial sistólica.
TRR:	Terapia de reemplazo renal.
VIH:	Virus de inmunodeficiencia humana.
PVV:	Personas que viven con el VIH.

Introducción

La investigación en políticas públicas en salud genera diversos análisis sobre los componentes de sus sistemas, como la prestación de los servicios y la gestión del riesgo, las tecnologías médicas, el talento humano, el financiamiento, y el liderazgo y la gobernanza. El objetivo de este tipo de investigación es promover la cobertura, la calidad, la eficiencia y la equidad de los sistemas sanitarios (1). El uso de la ciencia para tomar decisiones médicas (medicina basada en la evidencia) se ha convertido en una parte importante de la práctica clínica. Sin embargo, aún se deben aumentar los esfuerzos para seguir el ritmo de los avances científicos en la adopción y la toma de decisiones (2).

La investigación puede dar forma a las políticas en salud en desarrollo por su potencial de añadir objetividad y evidencia (3). Para esto, se requiere la producción de investigación relevante y oportuna que sea accesible y que sea entregada por entidades confiables (4). En este sentido, el trabajo que realiza la Cuenta de Alto Costo (CAC) en la generación del conocimiento cobra importancia para apoyar la toma de decisiones en salud.

En este documento se compilan los productos de investigación publicados, los pósters y las ponencias realizadas durante el 2022 y el 2023 por la CAC, en alianza con la academia, las asociaciones científicas y con los expertos clínicos para responder a algunas preguntas de interés clínico y de gestión que enriquecen el conocimiento de la salud de la población colombiana con enfermedades de alto costo, y promover el acceso equitativo de la información a todos los actores del sistema de salud, sin restricciones de uso.

Enfermedad renal crónica

CAC
Cuenta de Alto Costo

Fondo Colombiano de
Enfermedades de Alto Costo

ERC, HTA Y DM

Achievement of treatment goals among adults with diabetes in Colombia, 2015 - 2019: Results from a national registry

Autores: Carlos O. Mendivil, Mateo Amaya-Montoya, Juliana A. Hernández-Vargas, Nathaly Ramírez-García, Camila Romero-Díaz, Agustín Pérez-Londoño, Valentina Guatibonza-García, Lizbeth Acuña-Merchán.

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Trabajo colaborativo con la academia (Universidad de los Andes) como actores de interés.

Objetivo: evaluar el logro de las metas terapéuticas de hemoglobina glicosilada (HbA1c), la presión arterial y colesterol en los pacientes con diabetes en el marco del aseguramiento en salud colombiano entre el 2015 y el 2019.

Principales hallazgos:

- En Colombia, sólo uno de cuatro pacientes con diabetes mellitus (DM) alcanzó los tres objetivos esenciales en el manejo.
- Durante el periodo de estudio, y de manera constante, alrededor del 50% y del 80% de los pacientes alcanzaron el objetivo de la HbA1c (meta: < 7%) y de la presión arterial sistólica (meta: < 130mmHg), respectivamente.
- El logro de los objetivos de colesterol LDL mejoró entre un 5% y un 7% en estos cuatro años, indicando un área de mejora para la gestión del riesgo cardiovascular en esta población.

Relevancia de los hallazgos:

- Estos resultados representan una llamada a la acción para abandonar la inercia terapéutica y perseguir de forma más activa el objetivo multicomponente en todos los pacientes con diabetes. Esto aportará beneficios en términos de reducción de la morbilidad y la mortalidad por complicaciones diabéticas.

Comentario del autor experto:

Dr. Carlos Olimpo Mendivil

La diabetes es una enfermedad que ocasiona una enorme carga de morbimortalidad y costos, que en su mayoría se pueden evitar alcanzando tres simples metas, llamadas el "ABC" de la diabetes (Hemoglobina A1c (HbA1c), *Blood pressure* [presión arterial] y *Cholesterol* [colesterol LDL y no HDL]). En un seguimiento de 4 años a más de 1.300.000 pacientes con diabetes en el marco del aseguramiento colombiano, encontramos que el alcance de meta de HbA1c se ha mantenido estable en un valor cercano a 50%, mientras que el alcance de meta de presión arterial sistólica se ha mantenido en un valor cercano a 80%. En la única meta en que se vio un progreso importante fue en la de colesterol LDL, que aumentó en 6 puntos porcentuales hasta 49%. Sin embargo, tal vez el hallazgo más sorprendente y relevante fue que hay una gran discrepancia según la raza: en pacientes de ascendencia negra, el logro de meta de HbA1c viene descendiendo a lo largo del tiempo, y el de colesterol LDL no ha mejorado. Así, nuestros resultados ponen de manifiesto la necesidad de estrechar el seguimiento y prevenir la inercia terapéutica, además de facilitar el acceso a valoración y medicamentos, especialmente en las personas afrodescendientes en el país.

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Achievement of treatment goals among adults with diabetes in Colombia, 2015–2019: Results from a national registry

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ABSTRACT

Aims: To assess the achievement of essential treatment goals among patients with diabetes in Colombia.
Methods: We analyzed data from a nationwide registry of all individuals with diagnosed diabetes, hypertension or CKD assisted by the health system. We explored the prevalence of treatment goals (HbA1c < 7% [<53 mmol/mol], systolic blood pressure (SBP) < 130 mmHg and LDLc < 100 mg/dL), and their variations by race and type of health insurance, between July 1, 2015, and June 30, 2019.
Results: We studied 1 352 846 patients with diagnosed diabetes. The prevalence of HbA1c < 7% (<53 mmol/mol) remained steady at 52%, systolic blood pressure (SBP) < 130 mmHg was also stable at 80–82%. Meanwhile, the prevalence of both LDLc < 100 mg/dL and non-HDLc < 130 mg/dL increased by 6 percentage points. Achievement of the triple HbA1c + SBP + LDLc goal was only 21.4% in 2015, increasing to 24.4% by 2019. Goal achievement was consistently lower among patients of black race, especially for HbA1c (5% lower than other races), but also for the SBP, LDLc and joint goals. Patients under third-party insurance reached better HbA1c, SBP, and LDLc control.
Conclusions: Achievement of treatment goals of patients with diabetes in Colombia remains substantially low, despite improvements in LDLc control.

1. Introduction

Diabetes mellitus (DM) is a highly prevalent chronic disease, whose complications impose a heavy burden of death, disability, and costs worldwide, especially in low and middle-income countries (LMIC) [1]. There is sufficient observational and interventional evidence to prove that strict control of glycemic levels, blood pressure, and plasma lipids greatly reduces the risk of micro and macrovascular complications in people with DM [2-4]. Among the multiple targets of DM treatment proposed by different national and international guidelines, the three most commonly recommended goals involve controlling HbA1c, blood pressure, and plasma LDL (or non-HDL) cholesterol [5-7]. Further, timely intensive treatment of the different metabolic disturbances and attainment of treatment goals improves survival [8,9] and leaves a legacy effect that lasts for many years [8-11]. However, achievement of basic DM treatment goals remains persistently low, even in advanced economies [12,13], and in many LMIC the situation is essentially unknown.

Some factors, either intrinsic to the patient or related to the local social and cultural environment, could have an impact on all these treatment targets. One such factor is the type of health insurance, as this may influence the frequency of patientś contact with health professionals, access to preventive education, laboratory measurements, medications, procedures, and emergency visits [14,15]. Race or ethnicity has also been associated with DM treatment goals and outcomes in different populations [16-18], particularly in Latin America.

Colombia is a LMIC of 50 million inhabitants, located in the northern tip of South America, that has recently experienced a notorious increase in the prevalence of both obesity (current estimate in urban adults 36.2% for overweight, 21.3% for obesity) [19] and DM (current estimate

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in urban adults 10.1%) [20]. Recent large, population-based studies of diabetes prevalence in Colombia are scarce, but the International Diabetes Federation estimates the current prevalence of diabetes in the country at 9.9% [21], using extrapolations from prior data and from similar countries. As in most of Latin America, there is very limited information about the prevalence of goal achievement among patients with DM in Colombia, or about how it is evolving over time.

With this context, this study aimed to describe the prevalence of achievement of essential treatment goals (the so-called ABC of diabetes, for Hb**A**1c, **B**lood pressure, and LDL **C**holesterol) among patients with DM registered in a nationwide, centralized database of people with diagnosed DM served by the Colombian health system between 2015 and 2019. We also aimed to explore the variation of goal achievement across categories defined by type of health insurance, self-reported race, and prior diagnosis of hypertension.

2. Methods

2.1. Data sources

We analyzed data from people diagnosed with DM who were reported by health insurers and providers to the Colombian National Registry of Chronic Kidney Disease (NRCKD) between July 1st, 2015, and June 30th, 2019. The NRCKD is managed by the High-Cost Diseases Colombian Fund (" Fondo Colombiano de Enfermedades de Alto Costo" - CAC in Spanish) and has been operating since 2008 through a resolution from the Colombian Ministry of Health [22]. The NRCKD aims to assess the burden of CKD and its most common precursors (hypertension and DM) as well as access to health services related to prevention, diagnosis, and control across the country.

The NRCKD is an administrative and passive registry with a national scope because almost 99% of the population is affiliated to the national healthcare system [23], and their insurers are required to report patients living with hypertension, diabetes, or chronic kidney disease (CKD) to the registry [22]. When a new case enters the NRCKD, a complete registration is done; for previously reported cases, data are updated every year. For each variable entered in to the NRCKD, the value is the last measurement of that variable within the observation period. The NRCKD undergoes a data auditing process to ensure the validity of the information. The first step involves the use of an algorithm to identify mistakes in the reporting process. After this, an experienced team compares the reported information with clinical records by a well-established data monitoring process in a representative stratified sample of cases with hypertension and/ or DM with or without CKD, and in all registries from patients under renal replacement therapy [24]. If any inconsistency is identified, the real data on clinical records are captured.

2.2. Eligibility and variables

All adults with DM reported to the NRCKD between July 1st, 2015 and June 30th, 2019, were eligible for the analyses. For each year of the study, we excluded from the analyses all individuals less than age 18 years at the start of the study year. The presence of a diagnosis of DM or hypertension was analyzed as reported to the NRCKD (Y/N as defined by the treating physician). Data from the NRCKD were also used to classify participants in terms of age, sex, race or ethnic group, and insurance status. The database also contains data on weight, height, date of DM/ hypertension diagnosis (used to estimate the duration of each disease), and laboratory values including creatinine, which was used to estimate glomerular filtration rate (eGFR). Body-mass index (BMI) was classified as recommended by the World Health Organization [25]. We estimated eGFR using the Modified Diet for Renal Disease (MDRD) equation, which has been found to be more accurate than other equations to estimate glomerular filtration among patients with DM [26]. Due to heterogeneity in the units employed for reporting, we only had reliable data on urinary albumin excretion rate, either as urinary albumin concentration (in mg/L) or urinary albumin/creatinine ratio (UACR, in mg/g) from 2017 onwards. Based on eGFR, CKD stages were defined as follows: stage 1: GFR $>$ 90 mL/min; stage 2: GFR: 60–90 90 mL/min; stage 3: GFR: 30–60 90 mL/min; stage 4: GFR 15–30 90 mL/min and stage 5: GFR: $<$15 mL/min [27].

The Colombian health system has three health insurance types: The third-party payer ("*régimen contributivo*") is run by private insurers ("*Empresas Promotoras de Salud*" – *EPS*) akin to the Health Management Organizations (HMOs) of other countries, in this regimen each employee and employer make a monthly contribution to pay for an insurance policy. There is also state-run insurance ("*régimen subsidiado*") for people without employment or below a poverty threshold, in this case the state pays for the whole of the insurance policy to a different type of insurer (mostly "*Administradoras de Régimen Subsidiado* – *ARS*"). Finally, a few public institutions have a different health system for their employees, among them some large public universities (*régimen especial*) and the security forces (police and armed forces – *régimen de excepción*) [28]. We classified the insurance type into three categories as third-party, state, or special/exceptional. However, since 98–99% of insured belong to the first two categories, most comparisons only involve third-party vs. state insurance.

The standard reporting includes self-reported race, with the categories: 1. Indigenous, 2. Gipsy, 3. "Raizal" from the San Andrés and Providencia archipelago, 4. "Palenquero" from the San Basilio village, 4. Black, mulatto, Afro-Colombian or Afro-descendant, and 6. None of the above. For the analyses presented in this paper, we collapsed categories 3, 4, and 5 into a single category called "black", and analyzed self-reported race as black vs. all others. We made this decision because in Colombia as in several other South American countries, a large degree of racial blending makes it difficult to draw clear lines between races. Consequently, very few individuals ($<$1% in any given year) reported identifying themselves as being indigenous or gipsy. Hence, we considered more robust to collapse categories 3, 4 and 5 into a single "black race" category, and all other races into a separate category.

Analyzing each reporting year, we benchmarked our results against treatment goals recommended by the International Diabetes Federation, the American Diabetes Association, and the Latin American Diabetes Association - ALAD [11-13]. Treatment goals were HbA1c $<$ 7% ($<$53 mmol/mol), systolic blood pressure (SBP) $<$ 130 mmHg, and controlled plasma LDL cholesterol (LDLc) and non-HDL cholesterol (non-HDLc). For LDLc and non-HDLc, we analyzed both a less strict goal of LDLc $<$ 100 mg/dL and non-HDL $<$ 130 mg/dL, and a stricter goal of LDLc $<$ 70 mg/dL and non-HDL $<$ 100 mg/dL. We defined the joint triple goal as HbA1c $<$ 7% ($<$53 mmol/mol) plus SBP $<$ 130 mmHg and LDLc $<$ 100 mg/dL. We also report the proportion of patients with diabetes with a UACR $<$ 30 mg/g.

2.3. Data analysis

Quantitative variables were presented as means and standard deviations, categorical variables are presented as absolute and relative frequencies. The trend in the proportion of patients achieving each goal was tested with the *p*-value from a Cochran-Armitrage test for trend in goal achievement across follow-up years. All statistical analyses were performed in Stata version 13 (StataCorp LP, College Station, Texas, USA).

2.4. Ethical considerations

In order to protect privacy, data are anonymized through the use of a database-specific individual ID. This study presents no risk for the participants and no informed consent or ethical approval was required. In Colombia, the legislation allows the use of clinical data on high-cost diseases reported by health insurers for analyses that may positively impact the follow-up and control of such diseases. Confidentiality was guaranteed throughout the information processing (reporting,

managing, and analysis). This research was based on anonymized secondary data sources and did not include any private information that could make any subject identifiable.

3. Results

More than a million adults with diagnosed diabetes were analyzed in each study year. The number of individuals registered per year increased by more than 28% between July 2015 and June 2019. Throughout the study period, we observed a larger proportion of women (58–59%), mean age remained around 63 years. There was also a slight but consistent increase in the proportion of patients aged 60 or older (Table 1). The majority of patients were insured through a third-party payer, although there was a steady increase in the proportion under state insurance, which by 2019 represented about a third of all patients in the registry. The proportion of people with DM self-recognized as black or Afro-Colombian race remained steady at around 7%. As compared to July 2015, the proportion of overweight participants increased, whereas that of normal weight participants decreased, by June 2019. The combined prevalence of overweight and obesity did not change sizably, remaining steady at about 72%. Mean values of HbA1c, SBP, and LDLc were also relatively constant across the follow-up, while mean non-HDLc dropped by approximately 5%. Close to 90% of all participants throughout the study fell into the CKD 1 and 2 stages of the KDIGO classification. The proportion of patients with reported data on treatment goals increased steadily over the study period from 97.1 to 99.4% for BMI, from 59.5 to 69.6% for HbA1c, from 90 to 96.1% for blood pressure, and from 63.5 to 65.4% for plasma lipids (Table 1).

Table 1
Characteristics of adults with diagnosed diabetes treated in the Colombian health system, 2016–2019. 2016 corresponds to data registered between July 2015 and June 2016, and so on. Data are means (SD) unless indicated otherwise. SBP: Systolic blood pressure, DBP: Diastolic blood pressure. LDLc: LDL cholesterol, non-HDLc: non-HDL cholesterol. CKD stage classified according to the KDIGO classification.

Variables	2016 n = 1 006 676	2017 n = 1 095 515	2018 n = 1 301 353	2019 n = 1 290 866
Demographic				
Age (years)	62.4 (13.5)	62.6 (13.4)	62.9 (13.3)	63.1 (13.2)
Age group in years (%)				
<40	5.2	5.1	4.9	4.7
40–49	10.9	10.6	10.2	9.9
50–59	24.3	24.2	23.7	23.5
60–69	28.6	28.9	29.2	29.7
70–79	20.7	20.7	21.2	21.4
≥80	10.3	10.5	10.9	10.9
Sex n (%)				
Female	58.1	58.3	58.8	58.9
Male	41.9	41.7	41.2	41.1
Diabetes duration (years)	5.0 (4.9)	5.3 (5.0)	5.6 (5.1)	5.6 (5.2)
Diagnosed hypertension (%)	72.3	71.4	76.7	74.6
Health insurance type (%)				
Third-party payer	69.1	66.8	68.9	64.5
State	29.9	31.8	30.1	34.1
Other	0.96	1.36	0.99	1.41
Race (%)				
Black	6.7	7.0	6.8	7.0
Other	93.3	93.0	93.2	93.0
Clinical				
n for body-mass index	977 370	1 083 833	1 290 059	1 282 682
body-mass index (Kg/m^2)	28.0 (5.3)	28.0 (5.1)	28.2 (5.1)	28.3 (5.1)
body-mass index category (%)				
Normal weight	28.3	28.8	27.8	27.3
Overweight	38.9	39.8	39.8	40.0
Obesity	32.8	31.4	32.3	32.7
n for blood pressure	906 310	1 028 729	1 253 496	1 240 687
SBP (mmHg)	124.3 (14.4)	124.6 (14.4)	124.6 (14.2)	124.5 (14.2)
DBP (mmHg)	76.5 (8.8)	76.5 (8.7)	76.4 (8.7)	76.2 (8.6)
n for HbA1c	599 186	715 756	810 449	898 586
HbA1c (% of total Hb)	7.43 (1.95)	7.38 (1.95)	7.38 (1.94)	7.41 (1.87)
HbA1c (mmol/mol)	58	57	57	57
n for blood lipids	639 434	713 082	793 008	844 463
LDLc (mg/dL)	109.4 (39.2)	109.3 (39.1)	110.2 (38.9)	109.7 (38.8)
Non-HDLc (mg/dL)	142.2 (46.6)	141.6 (46.7)	139.0 (46.5)	135.2 (46.4)
n for CKD stage	1 006 676	1 095 515	1 301 353	1 290 866
CKD stage (%)				
1	59.2	59.9	61.2	59.2
2	30.4	30.0	28.6	30.0
3A	5.89	5.67	5.60	6.10
3B	2.30	2.22	2.35	2.29
4	0.80	0.82	0.77	0.77
5	1.50	1.42	1.51	1.58

3.1. Achievement of treatment goals in the complete sample

The majority of persons with diabetes were overweight or obese. The proportion of patients with an HbA1c measurement increased from 59.5% in 2016 to 69.6% in 2019. Among those with HbA1c measurements, only a little more than half achieved an HbA1c below 7% (<53 mmol/mol) in any given year. There was a small positive change in the percentage of patients achieving this HbA1c goal between 2016 and 2017, but this trend was reversed by 2019 (Table 2). More than 80% of participants had a SBP below 130 mmHg in any given year, but there was no improvement over the study period. Meanwhile, goals related to blood lipids improved consistently. There was a 6-point increase in the percentage of patients achieving LDLc < 100 mg/dL, and a 4.5-point increase in those achieving the stricter goal of LDLc < 70 mg/dL. Similarly, there were marked improvements in achievement of a non-HDLc < 130 mg/dL or < 100 mg/dL. The linear trends in changes of all these lipid parameters were statistically significant (Table 2).

There was also a positive evolution in the goal of UACR below 30 mg/g, which experienced an increase of over 10% between 2017 and 2019 (Table 2). The triple goal of controlled HbA1c, SBP, and LDLc was achieved by only 21.4% of patients in 2016, a fraction that increased by a small amount every year up to 24.4% in 2019.

3.2. Achievement of treatment goals in patients with diabetes and hypertension

Compared to patients with DM but without hypertension, patients with diagnosed DM and hypertension had higher proportions of achievement of the HbA1c goal (5–8% higher in different years) but, as expected, they had a lower achievement of the SBP goal in all years (10–12% lower). These patients also had higher achievement of the blood lipids goals and of the triple goal, even if only by a small margin (1–4%). The trend towards improved achievement of the triple ABC goal was significant among patients with DM and hypertension, but not among those without hypertension (Table 3).

3.3. Achievement of treatment goals in patients of black race

Patients of black or Afro-Colombian race had systematically lower levels of HbA1c goal achievement. The gap in this indicator between black patients and patients of other races went from two percentage points in July 2015 to five in June 2019 (Fig. 1, Panel A). They also had lower rates of SBP control. In the case of LDLc < 100 mg/dL, black patients started with better control relative to patients of other races. However, their improvement over the study period was much smaller, so that by 2019 black patients were two percentage points below patients of other races (Fig. 1, panel C). Further, the overall trajectory of the triple goal followed opposite directions in patients of black race and in

Table 2
Changes over time in treatment goals among adults with diagnosed diabetes treated in the Colombian health system, 2016–2019. 2016 corresponds to data registered between July 2015 and June 2016, and so on. Data are percentages of study participants in each period (95% CI). BMI: Body-mass index, UACR: Urinary albumin/creatinine ratio, expressed as mg albumin / gram of creatinine. SBP: Systolic blood pressure, LDLc: LDL cholesterol. * *p*-value from a Cochran-Armitrage test for trend in goal achievement across follow-up years.

Goal	2016	2017	2018	2019	Change across time period (%)	*p*-value for linear trend *
Normal weight (BMI 18.5–25.0 Kg/m^2)	28.3 (28.2–28.4)	28.8 (28.7–28.9)	27.8 (27.7–27.9)	27.3 (27.2–27.4)	−1.0	0.53
HbA1c < 7% (<53 mmol/mol)	52.0 (51.9–52.1)	53.0 (52.9–53.1)	53.1 (53.0–53.2)	52.1 (52.0–52.2)	+0.1	0.95
Systolic blood pressure < 130 mmHg	81.4 (81.3–81.5)	80.5 (80.4–80.6)	80.8 (80.7–80.9)	80.9 (80.8–81.0)	−0.5	0.82
LDL cholesterol < 100 mg/dL	44.7 (44.6–44.8)	46.3 (46.2–46.4)	46.8 (46.7–46.9)	50.7 (50.6–50.8)	+6.0	0.009
LDL cholesterol < 70 mg/dL	15.2 (15.1–15.3)	16.2 (16.1–16.3)	17.6 (17.5–17.7)	19.7 (19.6–19.8)	+4.5	0.005
Non-HDL cholesterol < 130 mg/dL	42.3 (42.2–42.4)	43.3 (43.2–43.4)	45.4 (45.3–45.5)	49.0 (48.9–49.1)	+6.7	0.002
Non-HDL cholesterol < 100 mg/dL	17.7 (17.6–17.8)	18.0 (17.9–18.1)	20.1 (20.0–20.2)	23.3 (23.2–23.4)	+5.6	<0.001
UACR < 30 mg/g	–	59.3 (59.2–59.4)	65.6 (65.5–65.7)	69.8 (69.7–69.9)	+10.5	<0.001
Joint goal: HbA1c < 7% (<53 mmol/mol) + SBP < 130 mmHg + LDLc < 100 mg/dL	21.4 (21.3–21.5)	22.7 (22.6–22.8)	23.5 (23.4–23.6)	24.4 (24.3–24.5)	+3.0	<0.001

those of other races: It deteriorated in the former while steadily improving in the latter (Fig. 1, Panel D). The result was a widening gap, that reached a maximum by 2019.

3.4. Achievement of treatment goals by insurance type

Almost 99% of adults with DM were affiliated to the third-party or state insurance, so comparisons are focused on these two groups. In general, patients under third-party insurance reached better HbA1c, SBP, and LDLc control, in most years by an ample margin (Fig. 2, panel A). In particular, the gap in LDLc control between insurance types widened with time, from four percentage points in 2016 to almost ten in 2019 (Fig. 2, Panel C). Consequently, achievement of the triple goal was always better for patients under third-party insurance in all study years.

4. Discussion

In this study based on a nationwide registry of patients with diagnosed diabetes served by the Colombian health system between July 2015 and June 2019; we found a quite low prevalence of diabetes treatment goal achievement in general, although there were important improvements concerning blood lipid goals. Only slightly more than half of patients reached their HbA1c goal, a figure that remained almost static throughout the study period. Achievement of blood pressure goals was generally better at about 80%, but also showed no signs of improvement. Thus, the observed improvement in the proportion of patients reaching the ABC joint goal was driven almost exclusively by the improvement in LDLc levels.

Achievement of LDL and non-HDL cholesterol goals improved by 5–7% in these four years, probably indicating increased screening, diagnosis, and treatment of blood lipid disorders for patients with diabetes. Only about one in every four patients with diabetes reached the three basic goals of the ABC of diabetes: HbA1c < 7% (<53 mmol/mol), SBP < 130 mmHg, and LDLc < 100 mg/dL, this triple-goal indicator showed a small yet statistically significant increase over the study period. We also found that patients of black race were less likely to reach any of the standard treatment goals, and, in the case of HbA1c, the prevalence of goal achievement among them is actually worsening. People with diabetes insured through a third party displayed sizably and systematically better rates of achievement for each of the individual goals, and for the triple goal.

There is great disparity among the studies reporting achievement of glycemic goals in diabetes in Latin America, with values ranging from nearly 4 to 54% [29]. However, a common finding has been that socioeconomic status, or the availability and type of health insurance are strong correlates of diabetes quality of care and goal achievement [29,30]. In comparison to other studies outside the sub-continent, we found a prevalence of good glycemic control remarkably lower than in the USA [13] or Switzerland [31], but similar to those in the UK [32], Denmark [33], or Japan [34]. Likewise, a population-based study of Catalonian patients with diabetes followed between 2007 and 2013, found a proportion of individuals reaching the HbA1c < 7% target remarkably similar to ours (52.2–55.6%, *versus* 52–53% in our study) [35]. It is noteworthy, however, that these nationwide data from Colombia compare relatively well to what has been reported for 49 developing countries by the IDMPS (International Diabetes Management Practices Study) study: The proportion of participants with HbA1c < 7% (<53 mmol/mol) decreased from 36% in 2005 to 30.1% in 2017 [36].

Concerning SBP goals for diabetes, the percentage of achievement in Latin America has ranged between 25 and 67% [29], while that for LDLc < 100 mg/dL has ranged from 12 to 52.6% [29]. In these two aspects, our results from Colombia compare somewhat favorably (80–82% for SBP, 45–50% and on the rise for LDLc), on the understanding that comparability is limited because data from other countries have been collected at different timepoints and most of them do not come from nationwide registries. Having said that, we cańt rule out that extraneous factors are leading us to overestimate SBP control. For example, it has been shown that clinicians tend to round down blood pressure measurements in routine practice, a problem for registries like ours, in which blood pressure measurement technique is not standardized [37]. Achievement of the triple goal in Colombia, low as it seems, is better than the estimated 9.9% for other Latin American countries [29]. In the United States, the last report estimated 22.2% of patients with diabetes to reach the triple goal of HbA1c, SBP < 130 mmHg and blood lipids (in this case non-HDL < 130 mg/dL) [14]. Within this context, the situation on achievement of diabetes treatment goals in Colombia is comparable to that in many other countries, but there is still ample room for improvement.

One of the most evident findings was that participants of black race had a persistently lower prevalence of goal achievement, and that for some goals this gap was actually widening. An analysis of the cascade of diabetes care using data from the US National Health and Nutrition Examination Survey between 2005 and 2016 found that non-Hispanic black individuals had 43% lower odds of reaching the triple goal

Table 3
Changes over time in treatment goals among adults with diagnosed diabetes treated in the Colombian health system, 2016–2019, by diagnosed hypertension status. 2016 corresponds to data registered between July 2015 and June 2016, and so on. Data are percentages of study participants in each time period (95% CI). BMI: Body-mass index, UACR: Urinary albumin/creatinine ratio, expressed as mg of albumin / g of creatinine. SBP: Systolic blood pressure, LDLc: LDL cholesterol. * *p*-value from a Cochran-Armitrage test for trend in goal achievement across follow-up years.

Patients with diabetes and hypertension						
Goal	**2016**	**2017**	**2018**	**2019**	**Change across time period (%)**	***p*-value for linear trend ***
Number of patients with diabetes and hypertension	732 706	781 900	998 633	962 925	–	–
Normal weight (BMI 18.5–25.0 Kg/m^2)	27.0 (26.9–27.1)	27.2 (27.1–27.3)	26.2 (26.1–26.3)	26.0 (25.9–26.1)	−1.0	0.52
HbA1c < 7% (<53 mmol/mol)	54.0 (53.9–54.1)	54.6 (54.5–54.7)	54.4 (54.3–54.5)	53.9 (53.8–54)	−0.1	0.94
Systolic blood pressure < 130 mmHg	78.4 (78.3–78.5)	77.0 (76.9–77.1)	78.0 (77.9–78.1)	77.8 (77.7–77.9)	−0.6	0.89
LDL cholesterol < 100 mg/dL	46.7 (46.6–46.8)	48.3 (48.2–48.4)	48.6 (48.5–48.7)	53.0 (52.9–53.1)	+6.3	0.007
LDL cholesterol < 70 mg/dL	16.3 (16.2–16.4)	17.9 (17.8–18.0)	18.8 (18.7–18.9)	21.4 (21.3–21.5)	+5.1	0.003
Non-HDL cholesterol < 130 mg/dL	44.5 (44.4–44.6)	45.7 (45.6–45.8)	46.8 (46.7–46.9)	51.4 (51.3–51.5)	+6.9	0.002
Non-HDL cholesterol < 100 mg/dL	19.1 (19.0–19.2)	19.9 (19.8–20.0)	21.2 (21.1–21.3)	25.1 (25.0–25.2)	+6.0	<0.001
UACR < 30 mg/g	–	61.5 (61.4–61.6)	63.6 (63.5–63.7)	68.4 (68.3–68.5)	+6.9	<0.001
Joint goal: HbA1c < 7% (<53 mmol/mol) + SBP < 130 mmHg + LDLc < 100 mg/dL	22.5 (22.4–22.6)	23.3 (23.2–23.4)	24.7 (24.6–24.8)	25.4 (25.3–25.5)	+2.9	<0.001
Patients with diabetes, without hypertension						
Goal	**2016**	**2017**	**2018**	**2019**	**Change across time period**	***p*-value for linear trend ***
Number of patients with diabetes and without hypertension	273 970	313 615	302 720	327 941	–	–
Normal weight (BMI 18.5–25.0 Kg/m^2)	31.6 (31.5–31.7)	32.8 (32.7–32.9)	33.2 (33.1–33.3)	31.1 (31.0–31.2)	−0.5	0.86
HbA1c < 7% (<53 mmol/mol)	45.9 (45.8–50.0)	49.1 (49.0–49.2)	48.9 (48.8–50.0)	46.6 (46.5–46.7)	+0.7	0.79
Systolic blood pressure < 130 mmHg	90.2 (90.1–90.3)	89.5 (89.4–89.6)	90.4 (90.3–90.5)	90.4 (90.3–90.5)	+0.2	0.72
LDL cholesterol < 100 mg/dL	44.7 (44.6–44.8)	46.3 (46.2–46.4)	46.8 (46.7–46.9)	50.7 (50.6–50.8)	+6.0	0.009
LDL cholesterol < 70 mg/dL	15.2 (15.1–15.3)	16.2 (16.1–16.3)	17.6 (17.5–17.7)	19.7 (19.6–19.8)	+4.5	0.006
Non-HDL cholesterol < 130 mg/dL	42.3 (42.2–42.4)	43.3 (43.2–43.4)	45.4 (45.4–45.5)	49.1 (49.0–49.2)	+6.8	0.001
Non-HDL cholesterol < 100 mg/dL	17.7 (17.6–17.8)	18.0 (17.9–18.1)	20.1 (20.0–20.2)	23.3 (23.2–23.4)	+5.6	<0.001
UACR < 30 mg/g	–	52.8 (52.7–52.9)	78.0 (77.9–78.1)	75.3 (75.2–75.4)	+22.5	<0.001
Joint goal: HbA1c < 7% (<53 mmol/mol) + SBP < 130 mmHg + LDLc < 100 mg/dL	22.2 (22.1–22.3)	23.5 (23.4–23.6)	22.1 (22.0–22.2)	21.4 (21.3–21.5)	−0.8	0.53

compared to non-Hispanic whites [38]. As in our study, there was no sign of this racial divide getting better over time. A mixed-methods study of the association between race and several diabetes indicators in the state of North Carolina, USA, found that black patients with diabetes had 25% lower odds of reaching an HbA1c < 8% (64 mmol/mol), and 58% greater odds of an HbA1c > 9% (>75 mmol/mol) relative to white patients. They also had 25% lower odds of reaching the LDLc goal, and 34% lower odds of reaching the SBP < 130 mmHg goal [39]. In a study that evaluated racial differences in risk factor control among ambulatory patients from different ethnic minorities in California (Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese, Hispanic/Latino or Black/African American), black race was most strongly associated with lower odds of achieving HbA1c, SBP and LDLc goals [40].

Thus, health disparities on diabetes goal achievement impacting persons of black race seem to be a commonality across the Americas, and effective public health measures must be taken to counter them.

Another remarkable finding was the persistently higher prevalence of goal achievement among patients insured through a third-party, relative to those with state insurance. Several prior studies, however, have documented a strong association between health insurance type and diabetes control. A longitudinal analysis of US NHANES data between 1999 and 2016 found an enormous gap in goal achievement between patients with diabetes with vs without health insurance. The difference reached 23 percentage points for the HbA1c goal, 12 points for the LDLc goal and seven points for the SBP goal [41]. Further, goal achievement can vary widely among health systems within the same country and regime, as been documented in the US [42]. Likewise, a study of metabolic control among patients with diabetes in Thailand found that those under the Civil Servant Medical Benefit (a special health insurance regime available only to a small fraction of the population), almost doubled the rate of achievement of the triple goal relative to patients under the Universal Coverage or Social Health Insurance schemes [43]. The importance of the existence and type of health insurance for diabetes control has also been proven in Latin America: A study derived from the Mexican National Health and Nutrition Survey found that patients with diabetes affiliated to a public health insurance scheme (*Seguro Popular* – Peoplés Insurance), were significantly more likely to have appropriate glycemic control than uninsured patients by a margin exceeding five percentage points [14].

According to law, all Colombian citizens have full coverage of health-related expenses including direct ambulatory and hospital medical care, drugs, and complementary tests, independent of their insurance scheme or their level of contribution to the system. Our results, nonetheless, show that in practice the indicators of treatment success do differ

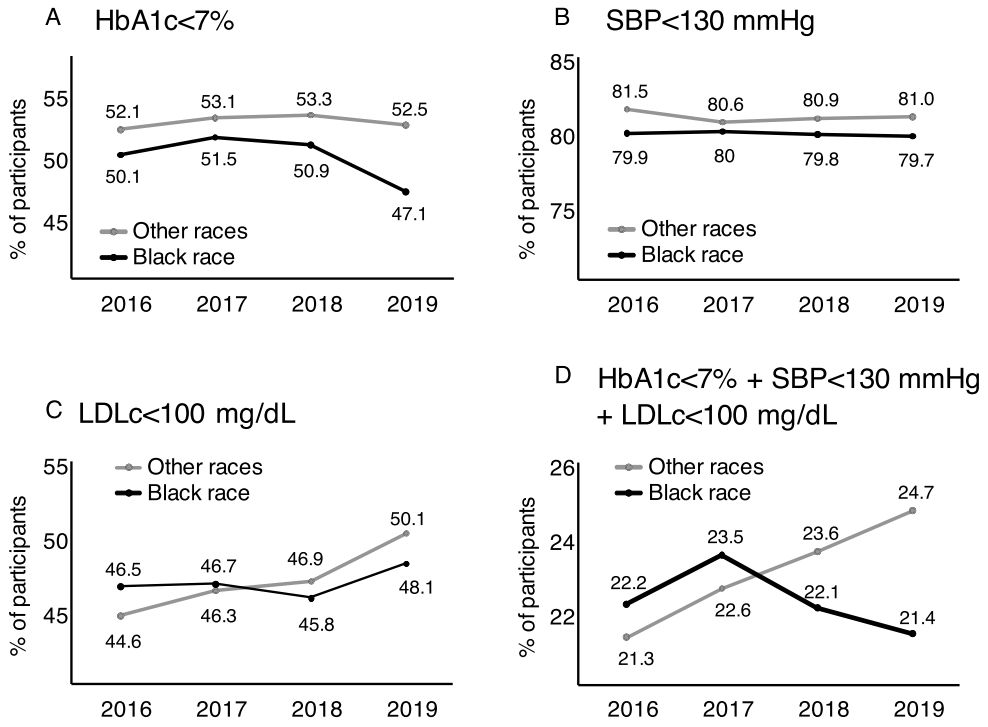

Fig. 1. Achievement of the glycated hemoglobin A1c, systolic blood pressure and LDL cholesterol goals, in patients of black race compared to patients of other races, 2016–2019. 2016 corresponds to data registered between July 2015 and June 2016, and so on.

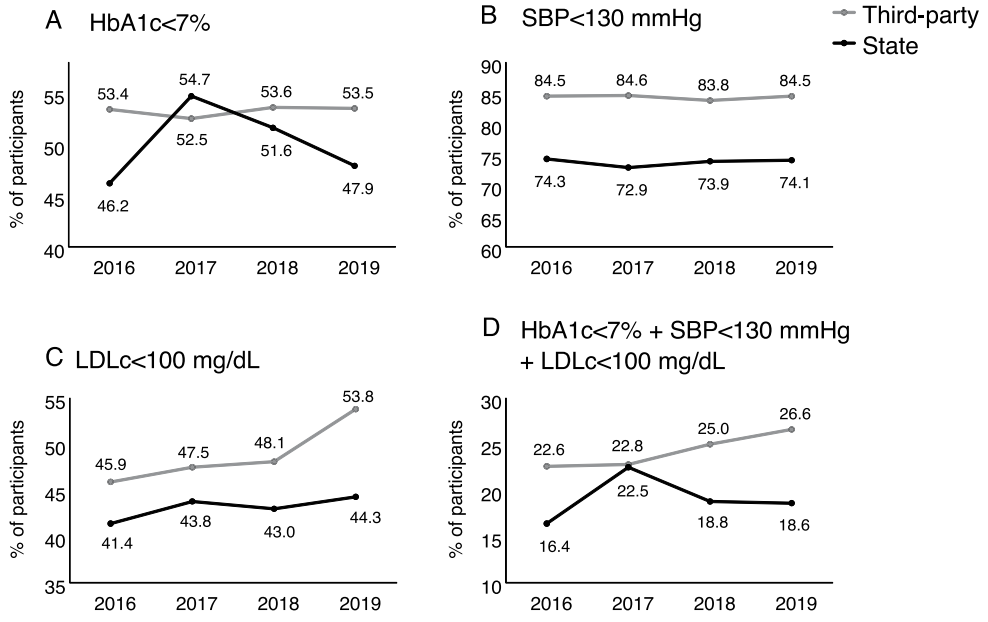

Fig. 2. Achievement of the glycated hemoglobin A1c, systolic blood pressure and LDL cholesterol goals, by type of insurance, 2016–2019. 2016 corresponds to data registered between July 2015 and June 2016, and so on.

significantly according to the type of insurance. It has been proposed that mixed managed competition models like the one established in Colombia since 1993 may face particular challenges related to insurerś purchasing and managed care mechanisms, and to differences in living conditions that correlate with the type and availability of insurance and with risk factors for diabetes complications [23]. The consistent finding of a markedly different prevalence of goal attainment for citizens of the same country who happen to be covered by different health regimes represents a palpable source of inequality in health. Although this phenomenon is not unique to Colombia, the identification and confrontation of its origins should be a public health priority.

We observed an interesting trend of more patients being registered in

the database throughout the study period, an increase of almost 300 000 people. While the increase in the number of patients with diabetes entering the database could signal an increased prevalence of diabetes in the Colombian population, there are other possible reasons for these increases. These include not only a possible higher prevalence, but also better health coverage, migration from rural to urban areas (where contact with the health system tends to be more frequent), increased awareness about the importance of periodic health checkups, and perhaps even a more exhaustive reporting effort on the part of insurers. Immigration into Colombia is rather small (about 9 per 1000 inhabitants - [44]), so this is unlikely to be an important factor influencing the number of persons with diabetes.

Our study has important strengths. First, the NRCKD is an extensive, national registry that reflects the real-world patterns of access and the effectiveness of the health system in achieving goals among people diagnosed with diabetes all over the country. Furthermore, the data analyzed underwent a well-established data monitoring process to guarantee their validity and reliability. Clearly, the main limitations of our analyses are also intrinsic to the nature of NRCKD. Among them, reporting of data is undertaken passively (ie. by insurers and providers to the central database), and despite it being legally mandated, under-reporting on the side of insurers or providers cannot be entirely ruled out. In addition, and despite a standardized data auditing process, misclassification bias cannot be ruled out either because the primary source of information is clinical records. There is also the concern that many persons with diabetes have not been diagnosed and hence are not in contact with the health care system, we have no information on the status of such undiagnosed population. We did not have information on antidiabetic medications received, albeit arguably the effect of such interventions is largely evident in glycemic control, which we did register. Similarly, we did not have information on lifestyle variables like physical activity or smoking, which could be important correlates of metabolic control indicators. Another relevant limitation is that our database does not distinguish between patients with type 1 or type 2 diabetes. Prior studies have documented a positive association between the presence of depression symptoms and poor control in Colombian patients with diabetes [45], this is also an element worth investigating in future research on metabolic control in Colombia.

In conclusion, our results show that achievement of the fundamental glycemic, blood pressure and LDLc goals is still considerably low in Colombia, and that only LDLc control is improving over time. Patients of black race or on state insurance have even lower rates of goal achievement. Since we already have all the diagnostic and therapeutic measures to achieve these goals for most patients in usual clinical practice, our results constitute a call to action to abandon clinical inertia and more actively and aggressively pursue the multicomponent goal in each and every patient with diabetes. This will ultimately yield enormous benefits in terms of reduced morbidity and mortality from diabetes complications.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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ERC, HTA Y DM

Regional variability of glycemic control among adults with diabetes mellitus in Colombia

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Objetivo: evaluar la asociación entre la región de residencia y los niveles de HbA1c en los adultos con DM en el marco del sistema de salud colombiano entre el 1° de julio de 2018 al 30 de junio de 2019.

Principales hallazgos:

- En el marco del aseguramiento colombiano, 3 de cada 5 personas tienen medición de HbA1c, de los cuales el 52,07% alcanzan la meta < 7%.
- Los niveles de HbA1c fueron significativamente mayores en hombres comparados con mujeres y en la región "otros departamentos" (Amazonas, Arauca, Casanare, Guainía, Guaviare, Putumayo, San Andrés y Providencia, Vaupés y Vichada).
- En la población afiliada al régimen subsidiado, el resultado promedio de la HbA1c fue mayor comparado con el contributivo.

Relevancia de los hallazgos:

- Se resalta la importancia de la DM como un factor de riesgo metabólico para condiciones como la obesidad y la enfermedad renal crónica (ERC).
- Estos hallazgos revelan la necesidad de fortalecer los programas de identificación y seguimiento de la DM.

Comentario del autor experto:

Dr. Miguel Urina Triana

Tener información relacionada con todas las personas con diabetes reportadas en el marco del Sistema General de Seguridad Social en Salud de Colombia ofrece la oportunidad de comprender las características de esta población en riesgo y así identificar los desafíos que enfrenta el sistema de salud y determinar acciones para mejorar los resultados de salud y contribuir a la sostenibilidad financiera del sistema.

Este estudio identificó que en Colombia tres de cada cinco personas con diabetes mellitus tuvieron al menos un resultado de HbA1c en el último año. Solo el 52,07% de los diabéticos con este examen cumplieron el objetivo de mantenerse por debajo del 7%. Los pacientes con DM residentes en la región "otros departamentos" y las personas afiliadas al régimen subsidiado mostraron un menor control de la hemoglobina glucosilada. Es necesario fortalecer los programas de promoción de la salud y prevención de enfermedades considerando la DM como un factor de riesgo metabólico para afecciones como la obesidad y la enfermedad renal crónica. Los estudios futuros deberían identificar los determinantes sociales de estas diferencias entre regiones.

tiempo completo y sin constantes interrupciones. El regreso a clases presenciales deberá considerar el rezago educativo de todos los niños y en especial aquéllos con mayores desventajas sociales. Hacemos un llamado a nuestros colegas salubristas y epidemiólogos a ser más vocales sobre este tema; esto implica comunicar mejor los riesgos del Covid-19 en niños, visibilizar su impacto en la educación y bienestar de los niños y apoyar a las autoridades para diseñar medidas de mitigación en escuelas que sean viables y efectivas.

Declaración de conflicto de intereses. Los autores declararon no tener conflicto de intereses.

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Regional variability of glycemic control among adults with diabetes mellitus in Colombia

Dear editor: The information related to all diabetic patients reported in the framework of the Colombian General System of Social Security in Health offers the opportunity to understand the characteristics of this population at risk and thus identify the challenges faced by the health system and determine actions to improve health outcomes and contributing to the financial sustainability of the system.[1] The geographic proximity between regions, and differences in social and economic development, can influence access and quality of health services, which means that there may be variations in the glycemic control of patients with diabetes mellitus (DM) that must be explored and described to direct strategies according to regional needs.[2,3]

We conducted a cross-sectional study to evaluate the association between the region of residence and HbA1c levels among adults with DM who received care within the Colombian health system from July 1, 2018, to June 30, 2019. Data were reported by insurers to the High-Cost Diseases Colombian Fund, in compliance with the resolution 2 463 of 2014 stated by the Colombian Ministry of Health and Social Protection.[4]

During the study period, 1 284 048 adults had been diagnosed with DM, of these 68.62% had a report of HbA1c level, which constitute the population analyzed in this study. The mean age was 64.90 years (SD±12.89) and 59.03% of patients were women. The median HbA1c for both men and women was 6.90%

(IQR=6.20-8.00%). The HbA1c target (<7%) was achieved in 52.39 of women and 51.60% of men (p<0.001).

The region "other departments" had the highest median HbA1c (7.20%; IQR=6.20-9.10%), where 50.41% were covered by state insurance. The lowest median was observed in the central region (median: 6.80%; IQR=6.20-7.90%) and in Bogotá, D.C. (median: 6.80%; IQR=6.30-7.80%), where 77.35 and 87.21% of patients had private insurance, respectively.

HbA1c levels was significantly higher in men than women and in the "other departments" region compared to the other regions. In the population covered by public insurance, the HbA1c average was higher than in the population covered by private insurance (table I).

In conclusion, in Colombia three out of five people with diabetes mellitus had at least one HbA1c result in the last year. Only 52.07% of diabetics with HbA1c testing met the target of staying below 7%. Patients with diabetes mellitus living in the "other departments" region, and people affiliated with the state insurance showed less glycosylated hemoglobin control. Health promotion and disease prevention programs need to be strengthened by considering DM as a metabolic risk factor for conditions such as obesity and chronic kidney disease. Future studies should identify the social determinants of these differences between regions.

Declaration of conflict of interests. The authors declare that they have no conflict of interests.

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Table I

RESULTS OF MULTIPLE LINEAR REGRESSION MODEL TO ESTABLISH ASSOCIATION BETWEEN HB1AC AND REGION OF RESIDENCE IN ADULT POPULATION WITH DM, ADJUSTING FOR COVARIATES INCLUDED. COLOMBIA, 2019

Variable	*Coefficient*	*95%CI*		p *value*
		Lower limit	*Upper limit*	
Region				
Other departments*				
Bogotá, D.C	-4.71	-5.28	-4.13	<0.001
Caribbean	-4.14	-4.71	-3.56	<0.001
Central	-5.04	-5.61	-4.47	<0.001
Eastern	-2.95	-3.54	-2.36	<0.001
Pacific	-4.66	-5.23	-4.08	<0.001
Sex				
Female*				
Male	0.11	0.01	0.20	0.029
Age (years)	-0.26	-0.26	-0.26	<0.001
BMI (kg/m^2)	-0.12	-0.13	-0.11	<0.001
Health system insurance coverage				
Private*				
Public	2.62	2.49	2.74	<0.001
Other	-1.57	-2.06	-1.09	<0.001

* Reference category
95%CI: 95% confidence interval; BMI: body mass index; number of observations: 879 657; kg: kilograms; m: meters; DM: diabetes mellitus.
Departments that conform each region of Colombia grouped according to the definition of the National Administrative Department of Statistics for the year 2019: Caribbean: Atlántico, Bolívar, Cesar, Córdoba, La Guajira, Magdalena and Sucre. Bogotá, D.C.: Bogotá, D.C. Central: Antioquia, Caldas, Caquetá, Huila, Quindío, Risaralda y Tolima. Eastern: Boyacá, Cundinamarca, Meta, Norte de Santander, Santander. Other departments: Amazonas, Arauca, Casanare, Guainía, Guaviare, Putumayo, San Andrés y Providencia, Vaupés y Vichada. Pacific: Cauca, Chocó, Nariño y Valle del Cauca.

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ERC, HTA Y DM

Situación de la enfermedad renal crónica en Colombia

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Trabajo colaborativo con la academia (Universidad Simón Bolívar), el Instituto de Evaluación Tecnológica en Salud (IETS), y expertos clínicos pertenecientes a la Asociación Colombiana de Nefrología (ASOCOLNEF).

Objetivo: describir la situación de la ERC en el marco del aseguramiento colombiano entre el 1° de julio de 2020 al 30 de junio de 2021.

Principales hallazgos:

- A junio de 2021, se informaron 5.347.829 casos con ERC o sus precursoras, DM o HTA.
- La prevalencia cruda de ERC fue de 1,7%, y una incidencia cruda de 3,05 casos por 1.000 habitantes.
- Se informaron 42.712 casos con terapia de reemplazo renal (TRR), de los cuales el 58,3% estaban en hemodiálisis.

Relevancia de los hallazgos:

- Esta información permite tener un panorama claro del comportamiento de la ERC en las distintas regiones de Colombia con el fin de plantear oportunidades de mejora en la atención.
- Se reconocen importantes oportunidades de mejora, como la optimización del diagnóstico, el acceso a los servicios y su calidad, la generación de conciencia de cuidado por parte de todos los actores del sistema de salud, y finalmente, el uso de terapias innovadoras para una mejor prevención y tratamiento de la ERC.

Comentario de los autores expertos:

Dr. Jorge Rico Fontalvo y Dra. Erika Yama Mosquera

Este artículo es muy importante porque describe de manera detallada y actualizada cómo es la verdadera realidad de la situación de la enfermedad renal crónica (ERC) en Colombia y sus enfermedades precursoras. En el escrito, se reportan los datos oficiales de incidencia, prevalencia en todos los estadios de la enfermedad, incluyendo los pacientes en diálisis y trasplante renal. Compara los datos reportados de manera oficial en Colombia con los datos estimados a nivel mundial, resaltando que en Colombia hay un importante subregistro de la enfermedad renal, situación que tiene varias explicaciones. Así mismo, en el artículo se detallan algunos aspectos relacionados con las terapias de soporte renal en Colombia, en donde la hemodiálisis es la modalidad más usada. En cuanto al trasplante renal, se describen los datos epidemiológicos importantes de Colombia, incluyendo su frecuencia por año y se resalta cómo durante la pandemia, cayó de manera importante la donación y los trasplantes en general, incluyendo el renal. Además, el escrito resalta el número aproximado de nefrólogos que hay en Colombia y se compara con el resto de América Latina. Estamos en este aspecto, por debajo de la media.

Por otro lado, es también importante que en el artículo se resalta que, en Colombia, y con el apoyo de las sociedades científicas afines, se han hecho guías, consensos y documentos en los que se han establecido los protocolos de manejo de nuestros pacientes con ERC. También, resaltamos de manera importante los costos que se derivan de la enfermedad renal en el país. Teniendo en cuenta que la ERC y las enfermedades precursoras suponen un importante riesgo y carga económica y social para los sistemas de salud, se detallan los costos aproximados calculados para Colombia. Por último, y no menos importante, se hace énfasis en las barreras relacionadas con la enfermedad renal. Los invitamos a leer de manera detallada este manuscrito porque en él podrán conocer en detalle la situación actual de la enfermedad renal crónica en Colombia.

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ARTÍCULO ORIGINAL

Situación de la enfermedad renal crónica en Colombia

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Resumen

Introducción: *La enfermedad renal crónica (ERC) es un importante problema de salud pública en todo el mundo. Según el Atlas Mundial de Salud Renal, la prevalencia estimada de ERC en Colombia para el año 2021 fue del 10.7%.* **Objetivo:** *Describir la situación de la ERC en Colombia.* **Metodología:** *Estudio descriptivo, retrospectivo, que analiza los datos disponibles sobre la ERC en Colombia.* **Resultados:** *Para junio de 2021 se reportaron 5,347,829 personas con ERC y sus precursoras, diabetes mellitus (DM) e hipertensión arterial (HTA). La prevalencia cruda de ERC fue del 1.7%; la incidencia de ERC fue de 3.05 casos nuevos por 1,000 habitantes. Hay un importante subregistro de ERC. Se informaron 37,751 casos fallecidos con HTA o DM con ERC concomitante. Se reportaron 42,712 pacientes en terapia de reemplazo renal, el 58.3% en hemodiálisis. Además, se reportaron 7,816 pacientes con trasplante renal. Del total de recursos dispuesto para enfermedades de alto costo, la cohorte de ERC y precursoras consume cerca del 48%.* **Conclusiones:** *La ERC en Colombia constituye una de las principales causas de morbilidad y mortalidad, sobre todo en grupos con comorbilidades como DM e HTA.*

Palabras clave: *Enfermedad renal crónica. Cuenta Alto Costo. Hemodiálisis. Diálisis peritoneal. Trasplante renal.*

Situation of chronic kidney disease in Colombia

Abstract

Introduction: *Chronic kidney disease (CKD) is a major public health problem throughout the world. According to the World Atlas of Kidney Health, the estimated prevalence of CKD in Colombia for the year 2021 was 10.7%.* **Objective:** *To describe the situation of CKD in Colombia.* **Methodology:** *Descriptive, retrospective study that analyzes the available data on CKD in Colombia.* **Results:** *By June 2021, 5,347,829 people with CKD and its precursors, diabetes mellitus (DM) and hypertension, were reported. The crude prevalence of CKD was 1.7%; the incidence of CKD was 3.05 new cases per 1000 inhabitants. There is a significant underreporting of CKD. A total of 37,751 deaths with hypertension or DM with concomitant CKD were reported. 42,712 patients on renal replacement therapy were reported, 58.3% on hemodialysis. In addition, 7,816 renal transplant patients were reported. Of the total resources available for high-cost diseases, the CKD cohort and precursors consume about 48%.* **Conclusions:** *CKD in Colombia is one of the main causes of morbidity and mortality, especially in groups with comorbidities such as DM and hypertension.*

Keywords: *Chronic kidney disease. High Cost Account. Hemodialysis. Peritoneal dialysis. Kidney transplant.*

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Introducción y generalidades

La enfermedad renal crónica (ERC) es un importante problema de salud pública en todo el mundo[1]; la prevalencia mundial es alta, oscilando en los adultos entre un 11 y 13%, y la mayoría de los pacientes diagnosticados se encuentran en la etapa 3 de la clasificación propuesta en 2012 por la *Kidney Disease Improving Global Outcomes* (KDIGO)[2,3].

Según el Atlas Mundial de Salud Renal de la Sociedad Internacional de Nefrología (ISN-GKHA), para el año 2021 la prevalencia media de ERC en América Latina fue del 9.9% (intervalo de confianza del 95% [IC95%]: 8.75-11.1%) y, para Colombia la prevalencia estimada fue del 10.7%[3]. En América Latina, también hay un Registro Latinoamericano de Diálisis y Trasplante Renal (LADRTR), a cargo del Comité de Registro de la Sociedad Latinoamericana de Nefrología e Hipertensión (SLANH). En Colombia, para el año 2022, el Departamento Administrativo Nacional de Estadística (DANE) estimó que la población colombiana superó los 51.6 millones de habitantes[4]; basándonos en estos datos, en Colombia existirían aproximadamente 5 millones de personas con algún grado de ERC para 2022.

Enfermedad renal crónica en Colombia

Colombia es un país con una población aproximada de 51.6 millones de habitantes con gran diversidad cultural y geopolítica, con una expectativa de vida promedio de 77 años (Proyección DANE 2020); el crecimiento anual de la población es del 0.7%, y el sistema de salud ha logrado una cobertura casi universal (96%), financiado bajo modalidad mixta de recursos privados y estatales.

Desde 2007, preocupados por la alta prevalencia e impacto de enfermedades prevalentes emergentes, particularmente ERC y las precursoras, el Ministerio de Salud y Protección Social reglamentó el Fondo Colombiano de Enfermedades de Alto Costo o Cuenta de Alto Costo (CAC); esta entidad tiene a cargo el diseño e implementación del sistema de información de las enfermedades definidas como de alto costo dentro de las que podemos incluir la ERC, así como la evaluación, seguimiento de su comportamiento en las diferentes regiones del país y desempeño de las aseguradoras y prestadores en el proceso de atención para garantizar el acceso efectivo de los servicios cubiertos por el sistema de salud. En el año 2008, la CAC realizó por primera vez un reporte nominal de las personas con enfermedad renal y sus principales precursoras: hipertensión arterial (HTA) y diabetes *mellitus* (DM), el reporte se sigue informando con periodicidad anual, y se nutre de información de obligatorio reporte por parte de los aseguradores y entidades prestadores de servicios de salud de diálisis, prediálisis, trasplante renal y de asistencia en los primeros niveles de atención, de las enfermedades precursoras. De esta manera actualmente se dispone de los datos de una cohorte abierta constituida desde hace 14 años de más de cinco millones (5,000,000) de personas con ERC, HTA o DM, en donde la analítica de *big data* ha permitido incursionar en la construcción de modelos de predicción de la ERC para una mejor planeación de la atención de estos pacientes con un enfoque preventivo.

Los informes de la CAC de la ERC son de acceso público y se implementó un modelo de pago por resultados con ajuste que ha permitido mejorar la calidad del registro y atención de nuestros pacientes. Al democratizar esta información no solo se identifica el cumplimiento, sino también se reconoce la buena práctica de las instituciones y se suministra información para ajustar las políticas públicas basadas en evidencia, relacionadas con estas enfermedades.

Prevalencia de enfermedad renal crónica y enfermedades precursoras

El reporte de la CAC de este año incluye información de datos de 1 julio de 2020 a 30 junio de 2021; se reportaron 5,347,829 personas con ERC o sus precursoras, DM e HTA; el promedio de edad para los casos analizados fue 63.7 años (desviación estándar [DE]: ± 14.57) con una prevalencia cruda del 1.75% para un total de 889,123 presentando un incremento del 4.6% respecto a 2019. Se informaron cerca de 4.9 millones de personas con HTA con una prevalencia cruda del 9.64% y alrededor de 1.5 millones de personas se reportaron con DM, con una prevalencia del 3.1%. De las personas reportadas con ERC, el 44.30% (n = 393,848) se encontraban en los estadios 1 y 2, el 34.22% (n = 304,273) en el estadio 3, 16.84% en estadio 4 y el 4.64% (n = 41,246) en el estadio 5. En el 15.20% (n = 23,515) fue por DM y en el 14.61% (n = 22,603) por enfermedad vascular renal (HTA), otras causas representan el 58.9% y un 10% no tienen etiología definida, lo que supone un reto para realizar un diagnóstico etiológico oportuno (Figs. 1 y 2).

En los estadios prediálisis, tanto la DM como la misma ERC son más frecuentes en las mujeres, esta situación se invierte en los estadios 5, diálisis y trasplante donde la prevalencia es mayor en el sexo masculino;

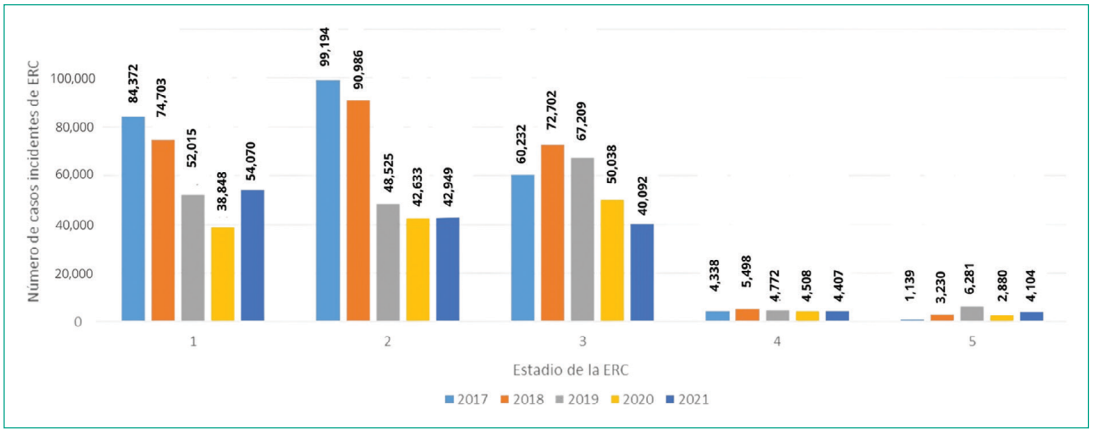

Figura 1. Situación de la enfermedad renal crónica (ERC) en Colombia 2020-2021.

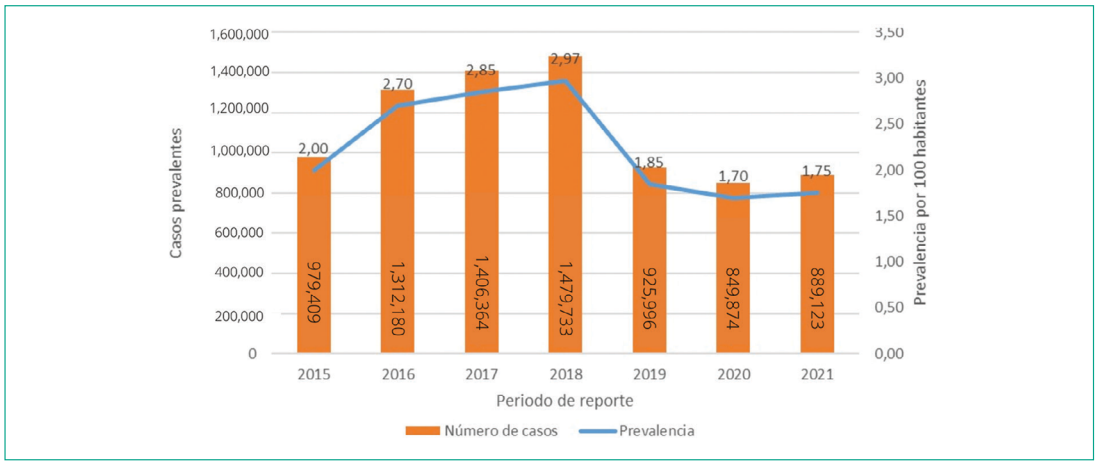

Figura 2. Prevalencia de la enfermedad renal crónica por 100 habitantes, Colombia 2015-2021.

esta situación es similar a la ocurrida en otras latitudes, fenómeno que ha llamado la atención de las diferentes sociedades mundiales revelando posibles circunstancias de equidad en el acceso o condiciones fisiológicas no bien definidas.

A pesar de este esfuerzo y la obligatoriedad del registro y atención, más de la mitad de los pacientes reportados como ERC, no tienen exámenes de seguimiento y son clasificados como indeterminados o no estudiados. Para el caso de albuminuria, similar a lo reportado en otros países, se tiene una escasa disponibilidad de este recurso alcanzando un reporte de menos del 30% de datos. Todos estos aspectos indudablemente que afectan el reporte final ocasionando un subregistro.

Incidencia de enfermedad renal crónica

Para el periodo de estudio se reportaron 154,688 casos nuevos de ERC**,** lo que significa una incidencia de 3.05 casos nuevos por 1,000 habitantes, sin variación con respecto al periodo anterior; el 60% de los casos nuevos son mujeres. La capital, Bogotá DC, fue la entidad territorial que reportó la mayoría de los casos, seguido de Antioquia y Valle del Cauca. La mayoría de los casos incidentes están en el estadio 3 (Fig. 3).

En cuanto a la mortalidad, se informaron 37,751 casos fallecidos con HTA o DM con ERC concomitante, datos que aumentaron en más de un 57% con respecto al año anterior, efecto relacionado probablemente con

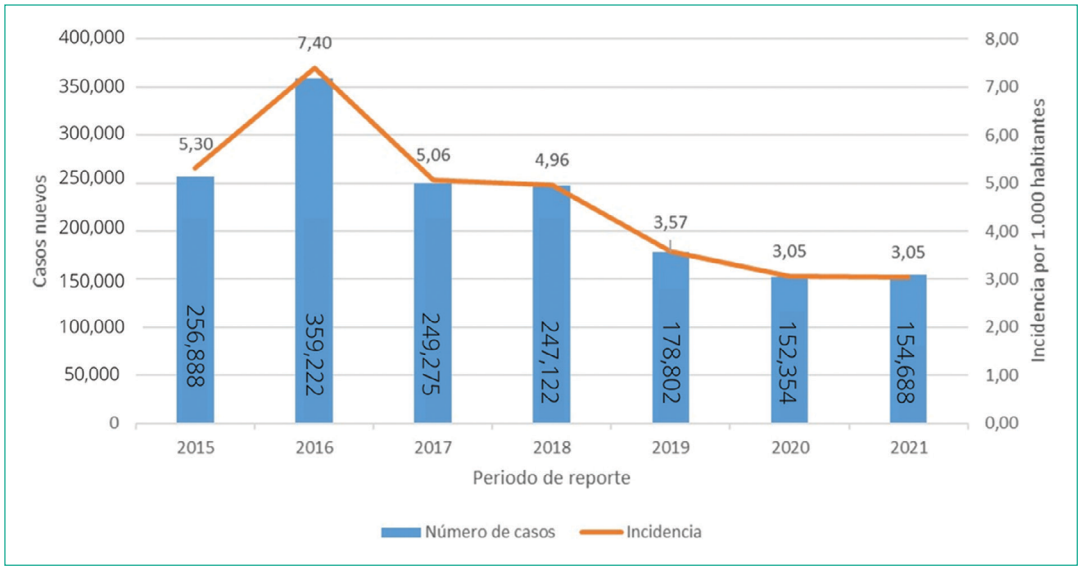

Figura 3. Tasa de incidencia de la enfermedad renal crónica por 1,000 habitantes, Colombia 2015-2021.

la pandemia de enfermedad por coronavirus 2019 (COVID-19). Durante este periodo llama la atención que el 24.57% de los casos fallecidos no tenía estadificación estimada durante el periodo, de igual manera, posiblemente esté también asociado a las dificultades de seguimiento a las personas observada durante la pandemia de COVID-19.

Pacientes en estadio 5

Para 2021, se informaron 4,518 personas incidentes con ERC en estadio 5, y se informa una prevalencia de 43,327 casos, la mayor frecuencia de casos se concentra en Bogotá y la región central. El 43% de los casos se documentan en mujeres y el 57% en hombres. La tasa de mortalidad se calculó en 14.55 por cada 100,000 habitantes, siendo la más alta en los últimos años (Fig. 4).

La incidencia nacional de personas en terapia de reemplazo renal (TRR) fue 7.51 casos por cada 100,000 habitantes, la región central presentó mayor proporción de casos nuevos, seguida por la Caribe. Se estima una prevalencia de 85.44 casos por cada 100,000 habitantes.

La terapia más frecuente fue la hemodiálisis (HD), en el 58.3% de los cuales se informan cumplimiento de metas de calidad en cuanto a dosis de diálisis (Kt/V), hemoglobina y albúmina en la mayoría de los pacientes tratados.

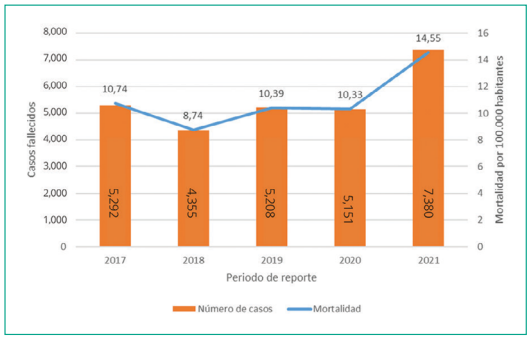

Figura 4. Tasa de mortalidad cruda de la enfermedad renal crónica estadio 5, Colombia 2017-2021.

En diálisis peritoneal (DP) se encuentran el 22.2% las personas, siendo en esta población el control de fósforo el indicador de menor cumplimiento. En terapia médica no dialítica se informa el 1.4% (Fig. 5).

Trasplante renal en Colombia

Para el periodo en estudio se reportaron 7,816 personas trasplantadas, el 61% de sexo masculino, el 18% del total de personas en TRR, con una prevalencia de 154.1 casos/millón de habitantes; la incidencia de trasplantados fue apenas 406 casos, lo cual se explica por

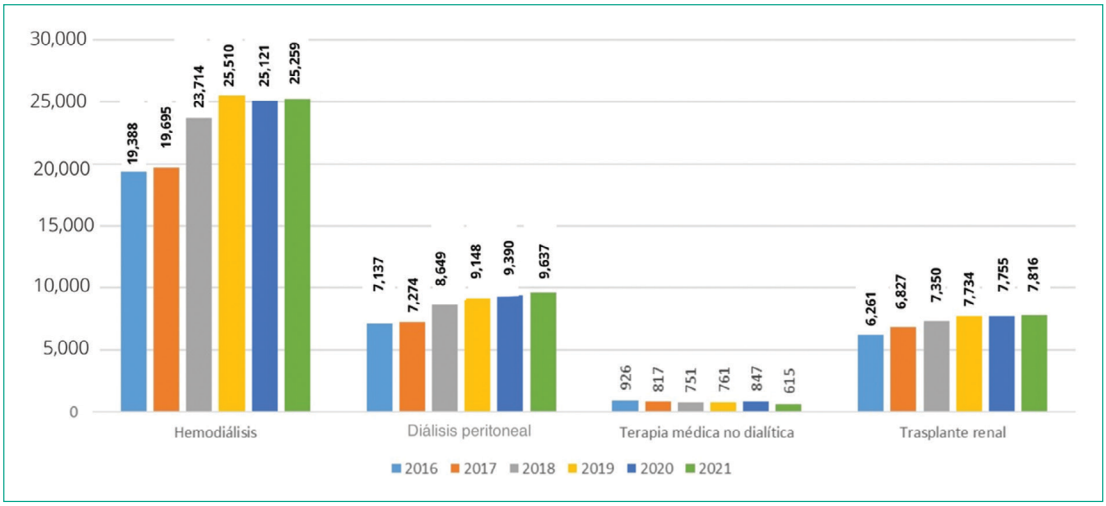

Figura 5. Tendencia de los casos de terapia de reemplazo renal a la fecha de corte de acuerdo con su modalidad, Colombia 2016-2021.

Tabla 1. Resumen de los datos del Sistema Nacional de Información en Donación y Trasplantes, con respecto a trasplante renal de la REDDataINS, del Instituto Nacional de Salud

Órgano/año	2017	2018	2019	2020	2021	Total
Riñón	947	847	932	517	606	3,849
Riñón-corazón	0	2	0	1	0	3
Riñón-hígado	12	7	8	5	5	37
Riñón-páncreas	13	9	7	4	12	45
Total riñón	972	865	947	527	623	3934
Total todos los órganos	1,342	1,184	1,032	800	938	5,296
% Riñón/total órganos	72.43%	73.06%	91.76%	65.88%	66.42%	74.28%

Fuente: Sistema Nacional de Información en Donación y Trasplantes, RedDataINS. Informes años 2017 a 2021. Adaptada de: Instituto Nacional de Salud[6].

los efectos de la pandemia en la donación y trasplante, dicha incidencia cayó de 11.95 casos por millón de población (PMP) a 8.05 PMP (Tabla 1).

De los datos del RedDataINS se observa que el número de trasplantes, tanto renales como para todos los tipos de órganos, venía con una tendencia a la disminución desde el año 2017, cuando se realizaron 972 trasplantes de riñón y, aunque se mantuvo estable durante el año 2019, durante el curso de la pandemia por COVID-19 cayó a menos de 550 trasplantes renales[5].

Por otra parte, el número de pacientes en lista de espera de trasplante renal viene en ascenso desde el año 2017, siendo los pacientes en lista de espera por trasplante renal más del 92% de todos los pacientes que están esperando un órgano desde el año 2017.

Con respecto al número total de pacientes trasplantados renales, al agregar los datos desde el año 2018, tenemos que se han realizado en ese lapso 2,962 trasplantes, de los cuales 2,377 corresponden a trasplantes provenientes de donante cadavérico, lo que representa un 80.25% de todos los trasplantes[5].

Efectos de la pandemia

Durante la emergencia sanitaria por la COVID-19 se evidenció una disminución en la identificación y reporte

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de casos incidentes en un 16% para HTA, un 9.54% para DM y un 11.4% en casos de ERC 5; las regiones con mayor disminución en el reporte de casos nuevos fueron Amazonas y Orinoquia, zonas rurales dispersas que sufrieron mayor aislamiento durante la pandemia. Esta situación se contrasta con el comportamiento global dadas las restricciones de acceso a los servicios y las medidas implementadas por todos los países.

Para el periodo 2020-2021 se evidenció un aumento del 66.78% de casos fallecidos en hipertensos, un 88.16% en diabéticos y un 74.3% en personas con ERC; la mayor mortalidad se observó durante la pandemia entre mayo y septiembre de 2020. Bogotá, y las regiones central y oriental tuvieron los mayores incrementos en mortalidad.

Nefrólogos en Colombia

Según el último reporte del Registro Latinoamericano de Diálisis y Trasplante, en América Latina hay en promedio 19 nefrólogos PMP. En Colombia se reportaron ocho nefrólogos PMP, teniendo un numero de nefrólogos por debajo del promedio de la región[6]. La gran mayoría de nefrólogos en Colombia están concentrados en las cuatro principales ciudades del país: Bogotá, Medellín, Cali y Barranquilla.

Es importante resaltar que bajo el liderazgo de la Asociación Colombiana de Nefrología e Hipertensión Arterial (ASOCOLNEF) se han desarrollado guías de práctica clínica y consensos en relación con la ERC. Algunos de estos documentos también han contado con apoyo de otras sociedades científicas y otros actores de nuestro sistema de salud. A continuación se citan algunos de los más relevantes:

- Guías de práctica clínica para el diagnóstico y tratamiento de la enfermedad renal crónica en Colombia (guías de adopción) elaboradas por el Ministerio de Salud y Seguridad social y por el IETS (Instituto evaluación y tecnologías en salud Colombia). Año 2016[7].
- Consenso colombiano. Manejo de pacientes en diálisis e infección COVID. Año 2020[8].
- Guías colombianas de práctica clínica para enfermedad renal diabética. Año 2021[9].
- Consenso colombiano de expertos sobre recomendaciones informadas en la evidencia para el manejo de la infección por SARS-CoV-2/COVID-19 en adulto mayor multimórbido con enfermedad renal crónica. Año 2021[10].
- Consenso colombiano de expertos sobre recomendaciones basadas en evidencia para el diagnóstico y el tratamiento de alteraciones del metabolismo óseo y mineral en pacientes con enfermedad renal crónica. Año 2021[11].
- Consenso: Recomendaciones sobre la vacunación contra SARS-CoV-2 en pacientes en diálisis y lista de espera de trasplante renal. Año 2022[12].
- Consenso colombiano de expertos sobre recomendaciones basadas en evidencias para el diagnóstico, el tratamiento y el seguimiento de la enfermedad de Fabry con compromiso renal. Año 2022[13].

Indicadores de calidad de atención

En 2016, la CAC lideró con la metodología de consenso y la participación de los expertos clínicos delegados por ASOCOLNEF, la Asociación Colombiana de Medicina Interna, Asociación Colombiana de Diabetes, prestadores de servicios de nefroprotección, organizaciones de pacientes, aseguradoras, instituciones de gobierno e industria farmacéutica, la actualización y definición de indicadores de evaluación y monitoreo de la calidad de la atención en pacientes con diagnóstico de ERC y sus enfermedades precursoras. En este consenso, se resalta el algoritmo de diagnóstico y seguimiento de ERC en los diferentes estadios[14] y se define un rango de cumplimiento aplicable para el país de acuerdo con las políticas de salud definidas, factibilidad de cumplimiento y operación del sistema de salud.

A pesar de estos lineamientos claros se tiene una gran falta de datos, lo que lleva a que el reporte registre un número importante de pacientes con datos no conformes o indeterminados, ya sea porque no se hace la gestión adecuada del algoritmo o no se registran.

De estos datos observamos importantes oportunidades de mejora en el seguimiento: solo el 50% de la población adulta con DM tiene una medición de hemoglobina glucosilada en los últimos seis meses, de estos solo la mitad alcanzan la meta de control del 7%; solo el 66% de las entidades auditadas tienen programas de atención renal con estrategias definidas para personas con enfermedades precursoras y ERC; el 9% de los reportados no tuvo medición de creatinina y el 7% no tuvo medición de tensión arterial durante el último año, lo que pone en evidencia la necesidad de mejorar las intervenciones desde la gestión de riesgo.

Costos de la enfermedad renal crónica en Colombia

La ERC y las enfermedades precursoras suponen un importante riesgo y carga económica y social para el sistema de salud. Se reconoce que del total de

Tabla 2. Costos médicos de la enfermedad renal crónica (ERC) por estadios

Estadio	Costos estimados		Costo promedio/año
ERC 2	Costo total tratamiento estándar		$1.505.407 (350 USD)
	Medicamentos, interconsultas, paraclínicos		
ERC 3	Costo total tratamiento estándar		$1.515.015 (350 USD)
	Medicamentos, interconsultas, paraclínicos		
ERC 4	Costo total tratamiento estándar		$2.506.319 (570 USD)
ERC 5	Diálisis/trasplante/TMND	Hemodiálisis/diálisis peritoneal/acceso/interconsultas/medicamentos	$30.012.324 (6690 USD)

TMND: tratamiento médico no dialítico.
Fuente: elaboración propia a partir de Consejo Directivo del Instituto de Seguros Sociales[17], Rosselli et al.,2013[18] y Dirección de Regulación de Beneficios C y T de A en SaludM de SaludR de Colombia[19].

recursos dispuestos para enfermedades de alto costo, la cohorte de ERC y precursoras consume cerca del 48% del total de recursos destinados[15].

En Colombia, estudios de carga en enfermedad renal crónica para el año 2015 establecen que se gastan en la población renal entre el 1.6 y el 2.7% del producto interno bruto (PIB), teniendo en cuenta que para ese año la inversión en salud fue del 5.73% del PIB[16].

En la tabla 2 se resumen costos promedios anuales estimados en moneda local y USD, incluyendo tratamientos básicos y paraclínicos de requisitos mínimos en los diferentes estadios. Es apremiante establecer estrategias que permitan evitar la progresión a estadios más avanzados, pues conforme avanza la enfermedad es más costosa.

Discusión y conclusiones

Colombia tiene una cobertura en salud mayor del 96%, en donde se tiene un acceso a los tratamientos de diálisis y trasplante en forma universal, igualmente existen los programas de nefroprotección desde los cuales se ha planteado un proceso de mejoría en gestión de riesgo con la intención de lograr indicadores de calidad que permitan reflejar mejoría en los resultados.

En este ejercicio es remarcable el papel del Fondo Colombiano de Enfermedades de Alto costo (Cuenta de Alto Costo), que desde el 2007 realiza la evaluación y monitoreo de la gestión de las entidades en el cumplimiento del proceso de atención con calidad de las personas con ERC y sus precursoras. Esta información permite tener un panorama claro del comportamiento de la ERC en las distintas regiones de Colombia, compararnos con otros países y en este sentido plantear oportunidades de mejora en la atención.

Sin embargo, a pesar de contar con esta información, y ser de los pocos países con uno de los registros de pacientes con ERC más grande y completo en el mundo, se considera que está registrada la morbilidad atendida en el sistema de salud y no toda la morbilidad sentida, lo cual se interpreta como que al comparar las prevalencias estimadas (que suma la morbilidad atendida con la sentida) se tengan menores prevalencias identificadas u observadas en HTA, DM y ERC en relación con las calculadas en el ámbito mundial y en la región latinoamericana, lo cual podrían estar explicado por:

- Diversidad cultural y geopolítica, con una población importante dispersa en áreas rurales apartadas y de difícil acceso como Guajira, Amazonas, Urabá y Orinoquia.
- Uso de medicina tradicional, solicitud de atención solo en fases avanzadas de la enfermedad, carencia en prácticas de autocuidado, miedo al diagnóstico, pocas redes de apoyo y concentración de la atención en grandes ciudades.
- Desconocimiento de las guías de práctica clínica, inercia terapéutica, fallas en interpretación de cuentas, fragmentación en la atención, dificultades para traslados y disgregación de la atención, pocas instituciones ofertan todos los servicios.
- Comparaciones inadecuadas entre estudios: observaciones con muestras de pacientes vs. registros nacionales, en los que se tienen parámetros diferentes que afectan las comparaciones (observaciones vs. esperados), es decir, vida real de los sistemas de salud vs. modelos estadísticos o matemáticos de las prevalencias o incidencias que se esperan. En otro

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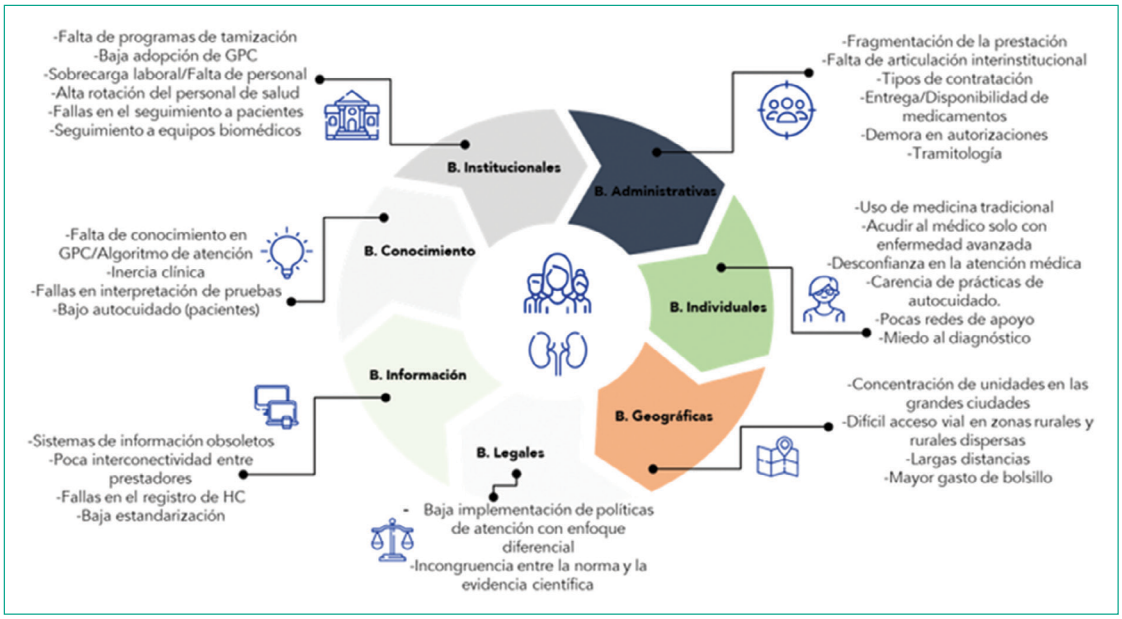

Figura 6. Barreras del proceso de atención en el proceso de nefroprotección. HC: historia clínica; GPC: guías de práctica clínica.

sentido, sería como comparar pacientes con números, y para esto ya existen modelos de corrección que se podrían aplicar para que las estimaciones sean más precisas y cercanas a la vida real de cada país y no tengamos que hacer cálculos con extrapolaciones de estudios de otros países en donde las poblaciones probablemente son diferentes.

A continuación, resaltamos las barreras que se han identificado con respecto a la situación actual de la ERC en Colombia (Fig. 6).

A nivel de los aseguradores, la fragmentación de la prestación ha sido una barrera fundamental que impacta negativamente en el acceso oportuno y por consiguiente efectivo en una proporción de la población, lo cual es un aspecto para mejorar cada vez que se estructure la red de servicios y se identifiquen y analicen los resultados en salud obtenidos. Sin embargo, en cuanto a la gestión de los prestadores, quienes lideran la gestión clínica, la falta de conocimiento y aplicación de la GPC o los algoritmos de diagnóstico en estas enfermedades, e interpretación de pruebas, implica que se puedan generar ineficiencias para el sistema, y deterioro de la calidad de atención del paciente y su calidad de vida.

Un eje importante que se considera un articulador para la toma de decisiones es el sistema de información de registro de historia clínica y pruebas diagnósticas, el cual es uno de los aspectos en los que se ha mejorado, pero no al ritmo que necesitamos y con la suficiente cobertura en todas las regiones del país. Hay sistemas muy precarios, manuales y recursos humanos insuficientes para abordar este problema. Consideramos este aspecto como oportunidad de mejora constante y ágil que se debe incorporar a todo nivel de la operación y estrategia de las entidades.

Respecto a las modalidades de tratamiento, en nuestro país es más frecuente la modalidad de HD como TRR, tal como sucede en la gran mayoría de países en la región, mientras que respecto al trasplante renal, comparados con el promedio de América Latina, estamos cerca de lo reportado.

En América Latina la tasa de trasplante renal reportada fue de 22 PMP, estando entre 1 y más de 60 PMP. Sin embargo, en la gran mayoría de países, el número de trasplantes renales por año es bajo. Argentina, Chile, Uruguay, Brasil y México son los países que están por encima de Colombia en este indicador.

Por otro lado, con respecto al número de nefrólogos PMP estamos muy por debajo del promedio en América Latina y además la gran mayoría están concentrados en las cuatro principales ciudades del país.

Se reconocen importantes oportunidades de mejora, que van desde optimizar el tamizaje en plan de diagnóstico oportuno, mejoría en acceso a los servicios en

cuanto a oportunidad y calidad, conciencia de la importancia de seguimiento por parte de todos los actores: pacientes, médicos, instituciones y aseguradores para facilitar el acceso a las diferentes modalidades de atención y, a su vez, el uso de terapias innovadoras y oportunas para una mejor prevención y tratamiento de la ERC.

Agradecimientos

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Conflicto de intereses

Los autores declaran que no existe conflicto de intereses para este artículo.

Responsabilidades éticas

Protección de personas y animales. Los autores declaran que para esta investigación no se han realizado experimentos en seres humanos ni en animales.

Confidencialidad de los datos. Los autores declaran que han seguido los protocolos de su centro de trabajo sobre la publicación de datos de pacientes.

Derecho a la privacidad y consentimiento informado. Los autores declaran que en este artículo no aparecen datos de pacientes.

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ERC, HTA Y DM

Strong negative association of non-HDL cholesterol goal achievement with incident CKD among adults with diabetes

Autores: Sofía Gnecco-González, Mateo Amaya-Montoya, Lina J. Herrera-Parra, Juliana A. Hernández-Vargas, Nathaly Ramírez-García, Camila Romero-Díaz, Lizbeth Acuña-Merchán, Carlos O. Mendivil.

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Trabajo colaborativo con la academia (Universidad de los Andes) como actores de interés.

Objetivo: evaluar la relación entre el logro de las metas clínicas fundamentales en el manejo de la diabetes en el desarrollo de la ERC incidente en las personas que recibieron atención en el marco del aseguramiento en Colombia y fueron reportadas a la CAC entre el 2015 y el 2019.

Principales hallazgos:

- En el periodo de estudio, se identificaron 125.626 casos nuevos de enfermedad renal crónica (ERC). En esta población, el control de la presión arterial sistólica (meta: < 130 mmHg) y de la HbA1c (meta: < 7%) en el momento de ingreso a la cohorte disminuyó en 21% y 14% respectivamente la posibilidad de desarrollar ERC durante el seguimiento.
- Cuando los pacientes alcanzaron las metas de control clínico de forma sostenida, la disminución en la incidencia de la ERC fue aún mayor. La principal reducción se observó en las personas con diabetes que mantuvieron el colesterol no-HDL por debajo de 130 mg/dL con un 33% menos de casos incidentes de ERC.
- En las personas que cumplieron la triple meta durante todo el seguimiento, es decir, control de la presión arterial, la hemoglobina glicosilada y el colesterol LDL disminuyeron la incidencia de ERC en 32%. Si adicional a esto, mantuvieron un peso normal, la reducción del riesgo fue del 38%.
- El efecto positivo de alcanzar la triple meta (presión arterial, hemoglobina glucosilada y colesterol LDL) y el control del peso fue mayor en las personas de raza negra, con una mayor disminución en los casos nuevos de ERC frente a otras etnias.

Relevancia de los hallazgos:

- Estos hallazgos invitan a los actores del sistema de salud a seguir trabajando conjuntamente para aumentar el número de personas con diabetes que alcanzan la triple meta.
- Se destaca la importancia de realizar un seguimiento más estricto del colesterol no-HDL y el peso con el fin de disminuir los casos nuevos de ERC y las consecuencias asociadas para los pacientes y el sistema de salud.

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La enfermedad renal crónica (ERC) es una condición devastadora para el paciente y altamente costosa para el sistema de salud, que es completamente prevenible en la mayoría de los casos, ya que la diabetes y la hipertensión arterial pobremente controladas son sus principales factores de riesgo. Analizamos en una cohorte de pacientes con diabetes de alcance nacional, los factores asociados con el desarrollo de ERC incidente (de nueva aparición), a lo largo de 4 años de seguimiento. La incidencia anual promedio de la ERC en los pacientes con diabetes fue 3,1% (bastante alta), y nos sorprendió hallar que, de las principales metas de tratamiento, el logro de la meta del colesterol no-HDL; fue la que más fuertemente previno la aparición de la ERC (33% menos riesgo si se mantiene la meta). Mantener un índice de masa corporal normal potenció la capacidad de prevención que brindaba el alcance de las otras metas, y mucho más aún en los pacientes de raza negra. Así, el control de lípidos no es solo una condición de prevención cardiovascular, sino que impacta en el cuidado de los riñones y debe ser perseguido también por ese motivo. Los pacientes de raza negra se beneficiaron aún más del logro de las metas que los demás grupos, resaltando la importancia de las consideraciones de equidad y acceso en el tratamiento de la diabetes.

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Clinical Research Article

Strong Negative Association of non-HDL Cholesterol Goal Achievement With Incident CKD Among Adults With Diabetes

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Abstract

Context: The relative importance of the control of different metabolic risk factors for the prevention of chronic kidney disease among patients with diabetes in real life conditions is insufficiently understood.

Objective: We evaluated the effect of the achievement of glycated hemoglobin A_{1c} (HbA_{1c}), systolic blood pressure (SBP), and low-density lipoprotein cholesterol (LDLc) or non–high-density lipoprotein cholesterol (non-HDLc) goals (ABC goals) on the development of incident chronic kidney disease (iCKD) among patients with diabetes.

Methods: In a nationwide registry of all individuals diagnosed with diabetes assisted by the health system in Colombia, we analyzed the association between baseline or sustained goal achievement and development of iCKD over a 4-year follow-up. iCKD was defined as a new occurrence of an estimated glomerular filtration rate less than 60 mL/min/1.73 m^2, hemodialysis, peritoneal dialysis, or kidney transplant.

Results: The study included 998 790 adults with diabetes (56% female, mean age 59). There were 125 626 cases of iCKD. After adjustment for multiple confounders, a baseline SBP less than 130 mm Hg (odds ratio [OR] 0.79 [0.78-0.80]) and a baseline HbA_{1c} less than 7.0% (OR 0.86 [0.85-0.87]) were negatively associated with iCKD. Sustained achievement showed stronger negative associations with iCKD than just baseline achievement. Considering each goal separately, sustained non-HDLc less than 130 mg/dL had the strongest negative association with iCKD (OR 0.67 [0.65-0.69]). Patients who maintained the triple ABC goal over the entire follow-up had 32% (29-34) lower odds of developing CKD, 38% (34-42) if they additionally kept a normal body mass index (BMI). Sustained ABC control including a normal BMI was more strongly associated with a lower incidence of CKD in patients of Black race (OR 0.72 vs 0.89; *P* for interaction = .002).

Conclusion: At the country level, sustained achievement of ABC goals and most especially non-HDLc were associated with substantial reductions in iCKD.

Key Words: diabetes, chronic kidney disease, non-HDL cholesterol, metabolic control, diabetes complications, hypertension

Abbreviations: ADVANCE, Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HbA_{1c}, glycated hemoglobin A_{1c}; iCKD, incident chronic kidney disease; KDIGO, Kidney Disease: Improving Global Outcomes; LDLc, low-density lipoprotein cholesterol; non-HDLc, non–high-density lipoprotein cholesterol; NRCKD, Colombian National Registry of Chronic Kidney Disease; OR, odds ratio; SBP, systolic blood pressure; UAER, urinary albumin excretion rate.

Chronic kidney disease (CKD) is a major health issue worldwide. Progressing CKD leads not only to end-stage renal disease (ESRD) but also to multiple adverse clinical outcomes, including cardiovascular disease, death, and disability [1]. In sharp contrast to other noncommunicable diseases, CKD prevalence seems to be increasing over time. Recent studies from the Global Burden of Disease Collaboration estimate the global prevalence of CKD at 9.1%, an increase of almost 30% over the last 30 years [2]. Low- or middle-income countries bear 80% of the disease burden from CKD [3].

Diabetes is currently the second leading cause of CKD and the top cause of ESRD [4]. In 2019, type 2 diabetes was estimated to have caused 2.5 million incident CKD (iCKD) cases and more than 400 000 deaths. The risk of developing diabetic nephropathy does not follow closely the degree of hyperglycemia, especially among patients with type 1 diabetes [5], indicating that other disturbances must act synergistically with hyperglycemia to promote the development of glomerular and tubular changes that characterize CKD. These alterations include excess plasma free fatty acids, oxidative stress, vascular shear stress induced by transmitted systemic hypertension,

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impaired autoregulation, hyperperfusion or hypoperfusion, and activation of the renin-angiotensin-aldosterone system [6].

This multifactorial pathogenesis suggests that successful and continued control of the main risk factors may substantially affect the appearance of new CKD in people with diabetes. The positive and long-lasting effect of early glycemic control on the development of CKD has been proven for patients with type 1 diabetes in the Diabetes Control and Complications Trial—Epidemiology of Diabetes Interventions and Complications (DCCT-EDIC) study [7], and for patients with type 2 diabetes in the United Kingdom Prospective Diabetes Study (UKPDS) [8]. However, the associations between tight blood pressure or blood lipids control and the risk of iCKD have not been equally robust. This may be due to a host of factors, but it is important to note that treatment goals, pharmacological agents, and guideline adoption have all changed notably since the publication of these milestone trials.

With this background, we aimed to evaluate the association between the achievement of glycated hemoglobin A_{1c} (HbA1c), systolic blood pressure (SBP), and low-density lipoprotein cholesterol (LDLc) or non–high-density lipoprotein cholesterol (non-HDLc) goals, the so-called ABC goals of diabetes, and the development of iCKD in a nationwide sample of nearly all patients with diabetes in the Colombian Health System. We also explored the differential effect of achieving these goals only at baseline vs sustaining them over time, and whether these associations differed in subgroups defined by race or body mass index (BMI).

Materials and Methods

We analyzed data from the Colombian National Registry of Chronic Kidney Disease (NRCKD), a nationwide database of people with diagnosed diabetes, hypertension, or CKD assisted by the Colombian Health System [9]. Data are mandatorily reported by all public and private insurers June 30 of every year, comprising information gathered since July 1 of the preceding year. Each data point registered in the database corresponds to the last measurement within the observation period, for that individual. Since more than 99% of the population is affiliated with the national health care system, the NRCKD has a national scope [9]. The NRCKD ensures data quality and completeness by taking the following steps: Initially an algorithm identifies mistakes in the reporting procedure. Then, an experienced team compares the reported information with clinical records by a well-established data-monitoring process in a representative sample of cases stratified by hypertension, diabetes, and CKD status [10]. If any inconsistency is identified, correct data are captured from clinical records.

Eligibility and Variables

We studied all individuals with diabetes reported to the NRCKD between July 1, 2015, and June 30, 2019. For each study year, people younger than 18 at the start of the year were excluded. We also excluded individuals whose estimated glomerular filtration rate (eGFR) calculated from the first plasma creatinine registered in the NRCKD was less than 60 mL/min, or who had received hemodialysis, peritoneal dialysis, or kidney transplant at the first observation period. The diagnosis of diabetes or hypertension was analyzed as reported to the NRCKD (yes/no [Y/N] as defined by the treating physician). Goals were defined according to the International Diabetes Federation, the American Diabetes Association, and the Latin American Diabetes Association—ALAD [11-13]. Treatment goals were HbA_{1c} less than 7% (< 53 mmol/mol), SBP less than 130 mm Hg, LDLc less than 100 mg/dL, and non-HDLc less than 130 mg/dL. The joint triple goal was HbA_{1c} less than 7% (< 53 mmol/mol), plus SBP less than 130 mm Hg, plus LDLc less than 100 mg/dL. For some analyses, we included BMI between 18.5 and 25.0 as an additional goal.

Data on age, sex, race or ethnic group, type of health insurance, weight, height, and clinical chemistry results were also taken from the NRCKD. BMI was classified as recommended by the World Health Organization [14]. For eGFR, we used the Modified Diet for Renal Disease (MDRD) equation, found to be more accurate than other equations among patients with diabetes [15]. Based on eGFR, CKD stages were defined as follows: stage 1: GFR greater than or equal to 90 mL/min; stage 2: GFR: 60 to less than 90 mL/min/1.73 m^2; stage 3a: GFR: 45 to less than 60 mL/min/1.73 m^2; stage 3b: GFR: 30 to less than 45 mL/min/1.73 m^2; stage 4: GFR 15 to less than 30 mL/min/1.73 m^2; and stage 5: GFR: less than 15 mL/min/1.73 m^2 [16]. Insurance was analyzed according to the 3 categories present in the Colombian Health System: third-party payer (run by private insurers), state insurance, and a special/exceptional health system for the security forces and some public universities [17].

We collapsed the NRCKD race categories "Raizal," "Palenquero," and "Black, Mulatto, Afro-Colombian, or Afro-descendant" into a single category called "Black" and analyzed self-reported race as Black vs all others. We made this decision because very few individuals (< 1% in any given year) identified themselves as belonging to one of the other race categories (indigenous or Roma).

Data Analysis

Quantitative variables are presented as means and SDs, categorical variables as absolute and relative frequencies. For all analyses, the main outcome was iCKD, defined as a new occurrence of any of the following: i, an eGFR less than 60 mL/min/1.73 m^2; ii, start of hemodialysis; iii, start of peritoneal dialysis; or iv, receiving a kidney transplant. All these variables are reliably captured and audited in the NRCKD.

The association between independent variables and incident CKD was evaluated using multivariable logistic regression models. There was a set of potentially confounding variables adjusted for in all models, including sex, age, race, insurance type, and BMI. Additionally, we adjusted for the variables representing goals other than the one being evaluated. Thus, in models to evaluate the association between HbA_{1c} goal and iCKD, we adjusted for the basic set of confounders, plus hypertension status and non-HDLc. When SBP was the main exposure, we adjusted for the basic confounders plus HbA_{1c} and non-HDLc. When one of the plasma lipids was the exposure, we adjusted for basic confounders plus hypertension status and HbA_{1c}. In models simultaneously evaluating all goals, we adjusted only for the basic confounders.

The first group of analyses considered the baseline achievement of each treatment goal as an independent variable. In contrast, a second group considered the sustained achievement of each treatment goal throughout the complete study period. The set of confounders being adjusted for was identical in both cases. We also performed stratified analyses to explore how goal achievement was related to iCKD in subgroups defined by race (Black vs other), and BMI category (normal,

overweight, or obesity). In a last set of analyses, we explored the association between baseline urinary albumin excretion rate (UAER) and the primary outcome. For this purpose, UAER was classified into 3 categories: i, less than 20 mg/L or less than 30 mg/g urinary creatinine; ii, 20 to 200 mg/L or 30 to 300 mg/g; and iii, greater than 200 mg/L or greater than 300 mg/g. The set of confounders adjusted for were the same as in prior analyses. Interactions were tested by the statistical significance of the regression coefficient associated with the multiplicative term between goal achievement status and the stratification variable. All associations are expressed as odds ratios (OR) with 95% CIs. All analyses were 2-sided and performed at a 5% significance level. Statistical analyses were carried out in Stata, version 17 (StataCorp LP).

Ethical Considerations

This research was based on anonymized secondary data sources and did not include any private information that could make any person identifiable. To protect privacy, data were anonymized through the use of a database-specific individual identification. This study has no risk for the participants and no informed consent or ethical approval was required. Colombian legislation (resolution 8430 of 1993 by the Colombian Ministry of Health) allows the use of deidentified clinical data reported by health insurers for analyses that may positively affect the follow-up and control of high-impact diseases. Confidentiality was guaranteed throughout the information processing (reporting, managing, and analysis).

Results

We studied 998 790 adults with diabetes, 56.6% of whom were female. Baseline mean age was 59.5 years, with only small differences in age distribution between sexes (Table 1). More than two-thirds of participants had third-party insurance. Patients of Black race accounted for 7.2% of the study sample, and nearly one-half of participants had a BMI in the obesity range. The prevalence of obesity was almost 5 percentage points higher among women than men. Mean HbA_{1c} was 7.52% (59 mmol/mol), and most patients were in CKD stage 1. Almost a quarter of participants had UAER above 30 mg/g of creatinine or 20 mg/L of urine. Follow-up was 1 year in 99 662 (10.0%), 2 years in 114 445 (11.5%), 3 years in 148 151 (14.8%), and 4 years in 636 532 participants (63.7%). At baseline, most participants (82.5%) attained the SBP goal, while the respective proportions were 52% for the HbA_{1c} goal, 40.7% for the non-HDLc goal, and 43.4% for the LDLc goal. There were 125 626 cases of incident CKD over the study follow-up. The incidence of CKD was 5.6% in 2017, 5.7% in 2018, and 7.0% in 2019, being always about 1.5% higher among women relative to men. The cumulative incidence of each of the renal outcome was as follows: eGFR less than 60 mL/min 12.1%, hemodialysis 0.47%, peritoneal dialysis 0.14%, and kidney transplant 0.01%.

Baseline Measures and Incident Chronic Kidney Disease

Among baseline control measures, an SBP less than 130 mm Hg showed the strongest negative association with iCKD (Table 2). An HbA_{1c} less than 7.0% was associated with reductions in iCKD only after multivariable adjustment (OR 0.86; 95% CI, 0.85-0.87). Plasma LDLc and non-HDLc within recommended thresholds were positively associated with iCKD. Joint achievement of the SBP, HbA_{1c}, and LDLc goal reduced the odds of incident CKD by 6% (95% CI, 5%-8%). Further, participants with good control of these 3 measures plus a normal BMI had 12% lower iCKD (95% CI, 9%-14%).

Analyses by Race

The negative association between baseline SBP goal and iCKD was similar among patients of Black race vs other races (Table 3). Conversely, a well-controlled HbA_{1c} at baseline was much more strongly associated with reduced odds of iCKD among participants of Black race (25% lower in Black race, 14% in other races; P for interaction $< .001$). This translated to a larger effect of achieving the triple goal at baseline for patients of Black race (P for interaction = .050) (see Table 3). The addition of a normal BMI to the triple goal also seemed to provide a larger benefit for patients of Black race (P for interaction = .002).

Analyses by Body Mass Index Category

The protective effect of reaching the SBP goal at baseline was similar in all BMI groups. Interestingly, achieving the HbA_{1c} goal at baseline lowered the odds of iCKD significantly more among patients with normal weight (P for interaction = .001). Consequently, the triple goal at baseline showed a statistically significant stronger negative association with iCKD among those with normal BMI (P for interaction = .001) (Table 4).

Effect of Sustained Risk Factor Control

Attainment of treatment goals at baseline reduced the odds of developing CKD, but the maintenance of such goals over time greatly potentiated this effect. Achieving and sustaining SBP and HbA_{1c} goals over the study follow-up decreased the odds of incident CKD by 28% and 22%, respectively (Fig. 1). Remarkably, a sustained non-HDLc less than 130 mg/dL showed the strongest negative association with incident CKD (OR 0.67; 95% CI, 0.65-0.69). Sustained achievement of the LDLc goal also had a negative association with outcome (OR 0.89; 95% CI, 0.87-0.91). Continued accomplishment of the triple goal reduced the odds of iCKD by 32%. This reduction increased to 38% when a normal BMI was also sustained. Despite the impressive consequences of reaching and keeping risk factors under control, only 5.5% of the study participants sustained the triple goal and only 1.2% of them were able to, in addition, maintain a normal BMI (see Fig. 1).

Baseline Albuminuria and Incident Chronic Kidney Disease

The presence of an abnormal UAER at baseline was substantially associated with iCKD. Relative to those with a UAER in the A1 Kidney Disease: Improving Global Outcomes (KDIGO) category (< 30 mg/g or < 20 mg/L), the multivariable-adjusted OR for the association between a UAER in the KDIGO A2 category (30-300 mg/g or 20-200 mg/L) and iCKD was 1.35 (95% CI, 1.32-1.37; n for model: 573 821). Among those with a baseline UAER in the A3 KDIGO category (> 300 mg/g or > 200 mg/L), the incidence of CKD over the follow-up more than doubled (OR 2.17; 95% CI, 2.10-2.25; n for model: 573 821). The effect of being in category A2 was significantly larger among patients of Black race (OR 1.67; 95% CI, 1.54-1.81 vs OR

Table 1. Baseline characteristics of study participants

	Men (n = 433 219)	Women (n = 565 571)	Total (n = 998 790)
Age, y	59.0 (13.1)	59.8 (13.3)	59.5 (13.2)
Age group, %			
< 40	7.4	6.9	7.1
40-49	15.1	13.4	14.1
50-59	27.9	28.8	28.4
60-69	28.0	27.6	27.8
70-79	16.0	16.6	16.3
≥ 80	5.6	6.8	6.3
Health insurance, %			
Third-party	73.2	63.2	67.5
State	23.3	35.9	31.3
Special/Exceptional	1.5	0.9	1.2
Race, %			
Black	6.6	7.6	7.2
Other	93.4	92.4	92.8
n for BMI	432 204	563 774	995 978
BMI	27.8 (4.8)	28.6 (5.6)	28.2 (5.3)
BMI category, %			
Normal weight	20.6	20.2	20.4
Overweight	32.3	28.1	29.9
Obesity	47.2	51.7	49.7
n for BP	428 210	560 189	988 399
SBP, mm Hg	123.5 (13.6)	123.9 (13.9)	123.7 (13.7)
DBP, mm Hg	76.8 (8.7)	76.6 (8.7)	76.7 (8.7)
n for HbA_{1c}	367 129	467 269	834 398
HbA_{1c}, %	7.59 (2.2)	7.46 (2.1)	7.52 (2.1)
HbA_{1c}, mmol/mol	59	58	59
n for blood lipids	369 658	496 385	866 043
Non-HDLc, mg/dL	140.0 (45.6)	146.3 (46.1)	143.6 (46.0)
LDLc, mg/dL	106.2 (38.0)	113.0 (39.5)	110.1 (39.0)
CKD stage, %			
1	65.7	60.8	63.0
2	34.3	39.2	37.0
Urinary albumin excretion, %			
< 30 mg/g or < 20 mg/L	72.24	78.72	75.85
30-299 mg/g or 20-199 mg/L	23.24	18.12	20.38
≥ 300 mg/g or ≥ 200 mg/L	4.52	3.16	3.76
Hypertension, %	60.9	68.0	64.9

Data are means (SD) unless indicated otherwise. CKD stages were defined according to the KDIGO classification.
Abbreviations: BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; DBP, diastolic blood pressure; HbA_{1c}, glycated hemoglobin A_{1c}; KDIGO, Kidney Disease: Improving Global Outcomes; LDLc, low-density lipoprotein cholesterol; non-HDLc, non–high-density lipoprotein cholesterol; SBP, systolic blood pressure.

1.33; 95% CI, 1.31-1.36 for other races; *P* for interaction < .001). For category A3, the association did not differ by race.

Having a normal weight was associated a greater relative influence of albuminuria on iCKD. The OR for UAER category A2 relative to A1 was 1.41 (95% CI, 1.36-1.46) for patients with normal BMI, 1.38 (95% CI, 1.34-1.42) for those with overweight, and 1.28 (95% CI, 1.24-1.32) for those with obesity (*P* for interaction <.001). Similarly, the OR for category A3 was 2.35 for patients of normal weight (95% CI, 2.19-2.53), 2.18 for those with overweight (95% CI, 2.06-2.31), and 2.06 for those with obesity (95% CI, 1.95-2.18; *P* for interaction <.001).

Discussion

In this prospective study of almost a million people representing the vast majority of patients with diagnosed diabetes in Colombia, we found that strict control of a few fundamental risk factors, and especially of non-HDLc, a frequently neglected target for CKD prevention, may notably affect the

Table 2. Association between measures of diabetes control at baseline and incident chronic kidney disease

Measure of interest	Unadjusted OR	Adjusted OR	n for adjusted model
SBP < 130 mm Hg at baseline[a]	0.74 (0.73-0.75)	0.79 (0.78-0.80)	755 844
HbA_{1c} < 7.0% at baseline[b]	1.00 (0.98-1.01)	0.86 (0.85-0.87)	758 088
Non-HDLc < 130 mg/dL[c]	1.18 (1.17-1.20)	1.05 (1.04-1.07)	758 285
LDLc < 100 mg/dL[c]	1.17 (1.15-1.18)	1.09 (1.07-1.10)	752 056
Joint SBP, HbA_{1c}, and LDLc goal[d]	1.03 (1.01-1.05)	0.94 (0.92-0.95)	719 010
Joint SBP, HbA_{1c}, LDLc, and BMI goal[e]	1.06 (1.03-1.09)	0.88 (0.86-0.91)	719 010

Abbreviations: BMI, body mass index; HbA_{1c}, glycated hemoglobin A_{1c}; LDLc, low-density lipoprotein cholesterol; non-HDLc, non–high-density lipoprotein cholesterol; OR, odds ratio; SBP, systolic blood pressure.
[a]Adjusted for sex, age, race (Black vs other), insurance type, BMI, baseline HbA_{1c}, and baseline non-HDL cholesterol.
[b]Adjusted for sex, age, race (Black vs other), insurance type, BMI, baseline non-HDL cholesterol, and hypertension status.
[c]Adjusted for sex, age, race (Black vs other), insurance type, BMI, baseline HbA_{1c}, and hypertension status.
[d]Adjusted for sex, age, race (Black vs other), insurance type, and BMI.
[e]Adjusted for sex, age, race (Black vs other), and insurance type.

incidence of CKD. We observed a cumulative incidence of CKD of 12.4% over 4 years, corresponding to an average yearly incidence of 3.1%. Recent (2015-2020) data from an electronic health record–based registry in California showed a yearly incidence of CKD between 64 and 81 per 1000 person/years (6.4-8.1%/year) among adults with diabetes [18]. Thus, our results are plausible and comparable to those obtained in other populations.

When considering baseline values individually, SBP control had the strongest negative association with iCKD, but HbA_{1c} control was also a significant predictor. Good HbA_{1c} control seemed to have a significantly stronger association with favorable outcomes among patients of Black race, and among people with a normal BMI. Most important, the continued control of SBP, HbA_{1c}, and LDLc translated into approximately a third less iCKD. Sadly, however, only about 5% of patients achieved this, and only about 1% kept this triple goal plus a normal BMI over the study duration. We were surprised to find that sustained control of non-HDLc had the strongest negative association with iCKD. This result highlights the growing relevance of this metric, and the importance of addressing disturbances of lipoprotein metabolism as a measure to prevent CKD. As expected, the presence of an increased UAER at baseline translated into a higher incidence of CKD, so that it almost doubled when baseline UAER exceeded 300 mg/g or 200 mg/L.

The value of proactive management and simultaneous control of relevant metrics in patients with type 2 diabetes was proven in the Steno-2 study, in which goal-oriented intensive diabetes treatment for 8 years translated into a 61% lower risk of iCKD [19]. Likewise, a later cohort study with noncontemporaneous controls from the same center showed that implementation of goal-based treatment guidelines resulted in a lower incidence of CKD [20]. These impressive results, however, came from a trial of modest size in a very particular population from a single clinic, so their applicability to a broader context was uncertain. Our results confirm that even at the level of an entire country, achievement of the ABC goals may indeed considerably reduce the risk of iCKD. They also position non-HDLc as an important target for CKD prevention in diabetes. Our results seemed to suggest no additional benefit from achieving sustained goals over non-HDLc alone. In reality, variables reflected in treatment goals are correlated between them, so patients who achieve one of them are also more likely to achieve the others, so it is difficult to unequivocally attribute a portion of the overall benefit to a single goal. Also, it is possible that the time frame over which renal benefits are manifested is different for each treatment goal, so that the extra benefit of achieving each additional goal may require a follow-up longer than 4 years.

The importance of early glycemic control for the prevention of advanced CKD was demonstrated by a 5-year observational follow-up of the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) study. In ADVANCE, differences in HbA_{1c} between the intensive and conventional treatment groups had already disappeared by the first posttrial visit. Still, after 9.9 years of total follow-up, intensive glucose control was associated with a 46% long-term reduction in ESRD [21]. In fact, a meta-analysis of more vs less strict glycemic control that included the landmark studies ACCORD, ADVANCE, UKPDS, and VADT found that more intensive glucose control reduced the incidence of total "kidney events" by 20% [22]. These results align with our findings of a 14% lower risk of iCKD for good baseline HbA_{1c} control, and a 22% lower risk for sustained control.

Considering BP control, solid evidence supports its importance in preventing CKD in diabetes. In the RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) study, every 10-mm Hg rise in baseline SBP increased the risk for ESRD or death by 6.7% [23]. Two large, prospective studies from Korea have found substantial increases in the risk of incident CKD with SBP elevations above 130 mm Hg [24, 25]. In our study, SBP control was clearly associated with reductions in CKD, with a larger effect size when this goal was maintained over time.

We were surprised to encounter a small but significant positive association between baseline achievement of lipid goals and iCKD. We believe that this was due to a reverse causation/confounding by indication problem, namely, that patients prescribed lipid-lowering drugs frequently received them because of a higher burden of cardiorenal risk factors or a history of cardiovascular events. Since such patients have lower LDLc and non-HDLc and a higher incidence of CKD, this would manifest itself as a spurious association between lower LDLc and iCKD. Despite this apparently paradoxical association between baseline plasma lipid goals and iCKD, we found a significant negative association between sustained lipid goal achievement and CKD, most notably for non-HDLc. This metric encompasses the cholesterol content of a variety of lipoproteins that contain apolipoprotein B and hence have atherogenic potential. Remarkably, participants who sustained a non-HDLc below 130 mg/dL had 33% less iCKD, the strongest negative association for any individual goal. Several observational studies have documented a lower incidence of CKD among people with reduced concentrations of triglycerides or triglyceride-rich lipoproteins, among them ARIC (Atherosclerosis Risk in Communities)

Table 3. Association between measures of diabetes control at baseline and incident chronic kidney disease, by race

Measure of interest	Race				*P* for interaction
	Black		Other		
Goal	Adjusted OR (95% CI)	n for model	Adjusted OR (95% CI)	n for model	
SBP < 130 mm Hg[a]	0.75 (0.70-0.81)	54 251	0.79 (0.78-0.81)	701 583	.15
HbA_{1c} < 7.0%[b]	0.75 (0.70-0.79)	54 291	0.86 (0.85-0.88)	703 786	< .001
Non-HDLc < 130 mg/dL[c]	1.18 (1.11-1.25)	54 291	1.04 (1.03-1.06)	703 983	< .001
LDLc < 100 mg/dL[c]	1.15 (1.08-1.21)	54 854	1.08 (1.07-1.10)	697 191	.022
Joint SBP, HbA_{1c}, and LDLc goal[d]	0.87 (0.81-0.94)	52 273	0.94 (0.92-0.96)	666 727	.050
Joint SBP, HbA_{1c}, LDLc, and BMI goal[e]	0.72 (0.64-0.82)	52 273	0.89 (0.87-0.92)	666 727	.002

Abbreviations: BMI, body mass index; HbA_{1c}, glycated hemoglobin A_{1c}; LDLc, low-density lipoprotein cholesterol; non-HDLc, non–high-density lipoprotein cholesterol; OR, odds ratio; SBP, systolic blood pressure.
[a]Adjusted for sex, age, insurance type, BMI, baseline HbA_{1c}, and baseline non-HDL cholesterol.
[b]Adjusted for sex, age, insurance type, BMI, baseline non-HDL cholesterol, and hypertension status.
[c]Adjusted for sex, age, insurance type, BMI, baseline HbA_{1c}, and hypertension status.
[d]Adjusted for sex, age, insurance type, and BMI.
[e]Adjusted for sex, age, and insurance type.

Table 4. Association between measures of diabetes control at baseline and incident chronic kidney disease, by body mass index category

Goal	BMI category						*P* for interaction
	Normal weight		Overweight		Obesity		
	aOR (95% CI)	n for model	aOR (95% CI)	n for model	aOR (95% CI)	n for model	
SBP < 130 mm Hg[a]	0.80 (0.77-0.83)	155 901	0.82 (0.80-0.85)	246 096	0.76 (0.74-0.78)	353 847	.07
HbA_{1c} < 7.0%[b]	0.84 (0.82-0.86)	156 668	0.88 (0.86-0.90)	246 677	0.86 (0.84-0.88)	354 743	.001
Non-HDLc < 130 mg/dL[c]	1.02 (0.99-1.05)	156 729	1.04 (1.02-1.07)	246 727	1.08 (1.05-1.10)	354 829	< .001
LDLc < 100 mg/dL[d]	1.04 (1.02-1.07)	154 138	1.09 (1.07-1.12)	241 114	1.10 (1.08-1.13)	356 804	< .001
Joint SBP, HbA_{1c}, and LDLc goal[e]	0.89 (0.86-0.92)	146 829	0.97 (0.94-0.99)	231 054	0.94 (0.92-0.97)	341 127	.001

Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; HbA_{1c}, glycated hemoglobin A_{1c}; LDLc, low-density lipoprotein cholesterol; non-HDLc, non–high-density lipoprotein cholesterol; SBP, systolic blood pressure.
[a]Adjusted for sex, age, race (Black vs other), insurance type, baseline HbA_{1c}, and baseline non-HDL cholesterol.
[b]Adjusted for sex, age, race (Black vs other), insurance type, baseline non-HDL cholesterol, and hypertension status.
[c]Adjusted for sex, age, race (Black vs other), insurance type, baseline HbA_{1c}, and hypertension status.
[d]Adjusted for sex, age, race (Black vs other) and insurance type.

[26], ETDRS (Early Treatment Diabetic Retinopathy Study) [27], and EURODIAB [28]. Furthermore, in the aforementioned ADVANCE trial, high HDLc (which is obviously inversely correlated with non-HDLc) was independently associated with a lower incidence of a composite CKD end point [29]. In post hoc analyses of 2 major diabetes trials, namely ACCORD-Lipid (Action to Control Cardiovascular Risk in Diabetes-Lipid) [30] and FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) [31], therapy with fenofibrate, an agent that strongly reduces non-HDLc, was associated with slower eGFR decline. Our results are in line with the accumulated evidence suggesting that non-HDLc control may provide renal benefits in diabetes, beyond its well-documented role in cardiovascular prevention. It is important to recognize that the information provided by non-HDLc goes beyond what is provided by HDL alone, and they may not always be inversely correlated [32].

We found that sustaining a normal BMI over the study period was associated with a modest additional benefit (~ 6% additional OR reduction) on iCKD, relative to achieving and sustaining just the triple HbA_{1c}/SBP/LDLc goal. Obesity is known to be associated with increased single-nephron GFR [33], which later results in loss of glomerular function. Overweight and obesity have been independently associated with iCKD [34] and ESRD [35], even in the absence of diabetes. Obesity seems to accelerate the age-induced deterioration of kidney function and consequent risk of CKD [36]. A longitudinal study of patients with diabetes in Korea found that both obesity and net weight gain were associated with iCKD over a 12-year follow-up [37]. Similar findings were reported in an observational subanalysis of patients from the ADVANCE trial. The 5-year risk of CKD increased by approximately 4% for each additional BMI point above 25 [38]. Of importance

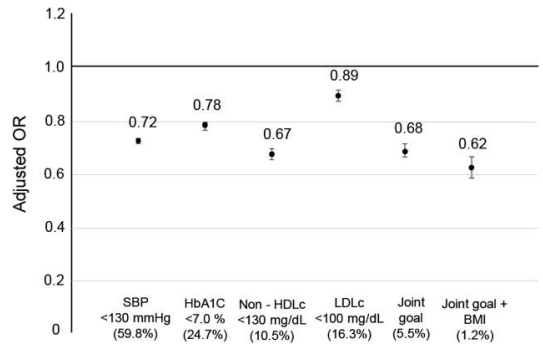

Figure 1. Association between sustained achievement of treatment goals and incident chronic kidney disease. Data are odds ratios (OR) compared to participants not reaching sustained achievement of each goal, adjusted for sex, age, race (Black vs other), insurance type, and baseline body mass index (BMI) (except for the model in which a normal BMI is part of the joint goal). Error bars represent 95% CI. Numbers in parentheses represent the percentage of study participants who sustained achievement of each goal over follow-up.

in the context of our study, overweight and obesity seem to be strong risk factors for CKD among Latino individuals: A retrospective study of Hispanic patients with type 2 diabetes found that excess BMI was more strongly associated with iCKD than even glycemic or BP control [39].

One of the central findings of our study was that, despite the large potential benefit of sustained risk factor control, an appallingly low proportion of patients achieve it in real practice. This is in accordance with findings from Colombia and other Latin American countries [40-42]. Therefore, a major effect on the prevention of CKD in diabetes can be expected from the implementation of strategies to measure, intervene, and closely monitor a few basic measures of treatment success. It is also important to consider that during our period of observation, the use of diabetes medications with specific renoprotective effects (ie, sodium glucose cotransporter 2 [SGLT-2] inhibitors, glucagon-like peptide 1 [GLP-1] agonists) had still not been broadly adopted. Thus, even greater benefits could be expected from the achievement of diabetes treatment goals through the use of newer, kidney-protecting medications.

Study Strengths and Limitations

Our study analyzed the association of treatment goal achievement with iCKD in the overwhelming majority of patients with diagnosed diabetes in an entire country of approximately 50 million inhabitants. Data come from a single, centrally administered registry. Being a database initially designed for the compulsory reporting of CKD and its precursor conditions, data related to kidney function and renal events are documented and audited with special attention. These characteristics endow the results both with large power and generalizability to other countries of a similar demographic and economic background.

Among the limitations, follow-up was only 4 years, which seems short in terms of the pathogenesis of CKD in diabetes. Nonetheless, even in this time span, very clear associations between measures of treatment success and iCKD were evident. The NRCKD does not capture diabetes type, so we do not know what proportion of participants had type 1 vs type 2 diabetes, although current epidemiological data from the region suggest that most patients with diabetes have type 2 diabetes [43]. Also, we did not have reliable data on current medications, so we did not include these important covariates, which could have helped us refine the estimation of the magnitude of the associations. The lack of such information may have introduced residual confounding, which is a possible limitation of our study. In any event, the effect of most of the key medications are reflected in glycemic levels, BP, or plasma lipids, variables that are closer to our end point of iCKD. We decided to analyze UAER as an exposure and not as a CKD end point because we considered eGFR and renal replacement therapies to be the true, unequivocal markers of the appearance of CKD, and thus a more reliable outcome. Finally, the nature of the data deposited in the NRCKD required us to define iCKD according to a single eGFR measurement being below the preestablished threshold.

In conclusion, we found that the successful control of non-HDLc, but also of HbA_{1c}, SBP, LDLc, and BMI, especially when sustained over time, were strongly associated with lower iCKD at a country level. These results have crucial clinical and health policy implications, and support the development of aggressive strategies to control non-HDLc and other essential treatment goals in the majority of patients with diabetes.

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Disclosures

The authors have nothing to disclose.

Data Availability

Restrictions apply to the availability of some or all data generated or analyzed during this study to preserve patient confidentiality or because they were used under license. The corresponding author will on request detail the restrictions and any conditions under which access to some data may be provided.

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ERC, HTA Y DM

Impact of metabolic control on all-cause mortality in a nationwide cohort of patients with diabetes from Colombia

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Trabajo colaborativo con la academia (Universidad de los Andes) como actores de interés.

Objetivo: evaluar la asociación entre el control metabólico sostenido (presión arterial, hemoglobina glicosilada y colesterol LDL) y la mortalidad por cualquier causa en las personas con diabetes reportadas a la CAC entre el 2015 y el 2019 y que recibieron atención en el marco del aseguramiento en Colombia.

Principales hallazgos:

- De las 1.352.846 personas con diabetes analizadas, la meta sostenida de presión arterial sistólica, hemoglobina glicosilada y colesterol LDL se alcanzó en el 57%, 24% y 17%, respectivamente.
- Los pacientes que alcanzaron el control sostenido de la presión arterial sistólica, la hemoglobina glicosilada y el colesterol LDL disminuyeron la probabilidad de morir en 58%, 75% y 72% respectivamente, resaltando la importancia del seguimiento clínico.
- Una reducción del 81% en la mortalidad se observó en las personas que lograron la meta triple de forma sostenida durante el seguimiento. Sin embargo, este grupo solo representó el 5% del total de las personas estudiadas.
- La disminución de la mortalidad en quienes mantuvieron el cumplimiento de la meta triple fue ligeramente menor en los pacientes de raza negra (69%) que en los de otras razas (82%).

Relevancia de los hallazgos:

- Estos resultados soportan la necesidad de trabajar conjuntamente para aumentar el logro de la meta triple de control metabólico en la población con diabetes, logrando con ello más años de vida saludables, mejor calidad de vida y mayor productividad.

Comentario del autor experto:

Dr. Carlos Olimpo Mendivil

Se ha demostrado extensamente que el buen control de las variables metabólicas en los pacientes con diabetes previene el desarrollo de complicaciones micro y macrovasculares, sin embargo, no es claro si eso se traduce en un menor riesgo de morir por cualquier causa, o cuál aspecto del tratamiento tiene un mayor impacto en el riesgo de mortalidad. En el seguimiento de una cohorte nacional de diabetes, examinamos la probabilidad de muerte de las personas que siempre mantuvieron cada parámetro bajo control comparado con quienes no alcanzaron las metas, y encontramos hallazgos sobresalientes: mantener la HbA1c permanentemente por debajo de 7% y conservar el cLDL por debajo de 100 mg/dL durante 4 años produjo 75% y un 72% menor riesgo de morir por todas las causas, respectivamente. Hallamos también que, sólo 5,4% de los pacientes con diabetes en la cohorte alcanzaron las tres metas (HbA1c, LDLc y tensión arterial sistólica – TAS-) de manera concomitante y sostenida. Esas personas tuvieron un 81% menor probabilidad de muerte. Así, el estudio demostró que el seguimiento estrecho y actuación inmediata orientada al alcance de las metas, prolongan la vida de los pacientes con diabetes.

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Impact of metabolic control on all-cause mortality in a nationwide cohort of patients with diabetes from Colombia

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Objective: The magnitude of the mortality benefit conferred by good integral metabolic control in diabetes in not sufficiently known, especially among Latin American patients. We prospectively studied the association between sustained control of blood glucose (HbA1c<7%), systolic blood pressure (SBP) (<130 mmHg) and LDL (LDLc, <100mg/dL) and non-HDL (non-HDLc, <130 mg/dL) cholesterol, and death from any cause among all adult patients with diagnosed diabetes in Colombia.

Methods: We retrospectively analyzed data from a nationwide, centralized, mandatory registry of all patients with diagnosed diabetes assisted by the Colombian health system between July 1, 2015, and June 30, 2019. We estimated the associations of sustained achievement of each goal, and of the joint triple goal (HbA1c + SBP + LDLc) with all-cause death. Associations were assessed after adjustment for sex, age, race, insurance type and BMI in multivariable logistic models.

Results: We studied 1 352 846 people with diabetes. Sustained SBP (OR 0.42 [0.41-0.43]), HbA1c (OR 0.25 [0.24-0.26]) and LDLc (OR 0.28 [0.27-0.29]) control had strong negative associations with death. Moreover, among the 5.4% of participants who achieved joint, sustained metabolic control, the OR for death was 0.19 (0.18-0.21). Importantly, the impact of sustained, joint metabolic control was significantly smaller for patients of black race compared to other races (OR 0.31 [0.23-0.43] *versus* 0.18 [0.17-0.20], p-value for interaction <0.001), mostly at the expense of a smaller impact of LDLc control. The results were similar across body-mass index categories.

Conclusions: Sustained and simultaneous metabolic control was associated with remarkably lower odds of death.

KEYWORDS

diabetes, metabolic control, complications, mortality, Latin America

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1 Introduction

The number of people with diabetes in Central and South America has reached the alarming figure of 32 million patients according to the 2021 version of the International Diabetes Federation (IDF) Atlas (1). This increase is expected to result not only in a heavy burden of disability and costs derived from chronic complications, but also in premature deaths. A large meta-analysis of data from the region found a 2.26-fold increment in all-cause mortality among patients with diabetes compared to the general population (2). The relative growth in the risk of cardiovascular and renal mortality is even more dramatic.

However, the mortality risk imparted by diabetes can presumably be mitigated by metabolic control, measured as the achievement of basic treatment goals. These goals are frequently referred to as the ABC of diabetes (**A**1c, **B**lood pressure and **C**holesterol control). For example, in a long-term observational follow-up from the Diabetes Chronic Complications Trial - Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study of patients with type 1 diabetes, mortality in the intensive treatment group (mean HbA1c 7% [53 mmol/mol]) was comparable to that of the general US population (3). Likewise, an observational follow-up study from the United Kingdom Prospective Diabetes Study (UKPDS) of patients with type 2 diabetes mellitus found that a 0.9% between-groups difference in HbA1c (4) during the active phase translated into 13% lower risk of death from any cause overall, and 27% lower risk among those allocated to intensive therapy with metformin (5).

Adequate blood pressure control is also a major determinant of mortality in diabetes. A meta-analysis including over 100 000 patients with type 2 diabetes concluded that each 10-mmHg lower systolic blood pressure was associated with a 13% reduction in total mortality, equivalent to an absolute reduction of three deaths/1000 patients/year (6). Control of low-density lipoprotein cholesterol (LDLc) also provides a mortality benefit. According to a Cholesterol Treatment Trialists´ Collaboration meta-analysis confined to over 18 000 patients with diabetes who took part in statin trials, all-cause mortality was reduced by 9% per each 38.6 mg/dL (1 mmol/L) decrement in LDLc (7). Further, the Steno-2 trial, despite its limited size, evidenced a very large mortality benefit (46% reduction) from the simultaneous control of the ABC goals in patients with type 2 diabetes over a 13-year follow-up (8).

Despite the clear mortality benefits of actively pursuing metabolic control in diabetes, its achievement remains markedly low. This holds true even in regions with advanced economies like the USA (9), Europe (10–13) and Japan (14). The situation is even more worrisome in Latin America, where the proportion of patients achieving the triple goal has been reported at 9.9% for the entire sub-continent (15) and 25.4% for Colombia (16).

Over the recent years, diabetes seems to be on the rise in Colombia. Despite a scarcity of large population-based data, the prevalence among adult urban residents was estimated at about 10% in 2018 (1, 17). In addition, diabetes holds an important place as a cause of mortality in Colombia (8th place (18)) and countries of a similar sociodemographic and cultural background.

Within this context, we aimed to assess the association between metabolic control and total mortality in a nationwide registry of all patients with diagnosed diabetes served by the Colombian Health System, between 2015 and 2019. We also examined how this association varied according to race and body-mass index (BMI) categories. The exploration and documentation of the impact of metabolic control is a key input to support the design of public health interventions aimed at improving life expectancy among patients with diabetes.

2 Subjects and methods

2.1 Data sources

The Colombian National Registry of Chronic Kidney Disease (NRCKD) is a database of all people with diagnosed diabetes, hypertension or chronic kidney disease who have been assisted by the Colombian Health System. The NRCKD is managed by the High-Cost Diseases Colombian Fund ("*Fondo Colombiano de Enfermedades de Alto Costo*" - CAC in Spanish) and has been operating since 2008 through a resolution from the Colombian Ministry of Health (19). Each new registry cycle starts on July 1 of a year, and ends on June 30 of next year. The NRCKD is a passive registry with a national scope because almost the totality of the population is affiliated to the national healthcare system (19), and insurers are mandated by law to report all eligible patients to the registry (19).

As previously described (16), for each new case entering the NRCKD an initial registration is completed; after which data are updated every year. Each data point registered in the database corresponds to the last measurement of that variable within the observation period. The NRCKD undergoes a data validity auditing process with several steps. The first step involves the use of an algorithm to identify mistakes in the reporting process. Then, an experienced team compares the reported information with clinical records by a well-established data monitoring process in a representative sample of cases stratified by hypertension, diabetes, and CKD status (20). If any inconsistency is identified, real data from clinical records are captured.

2.2 Eligibility and variables

We retrospectively analyzed data on all adults with diabetes reported to the NRCKD between July 1st, 2015 and June 30th, 2019. For each year of the study, we excluded people aged <18 at the start of the study year. The presence of a diagnosis of diabetes or hypertension was analyzed as reported to the NRCKD (Y/N as defined by the treating physician).

Metabolic control goals were defined according to recommendations by the International Diabetes Federation, the American Diabetes Association, and the Latin American Diabetes Association - ALAD (21–23). Treatment goals were HbA1c <7% (<53 mmol/mol), systolic blood pressure (SBP) <130 mmHg, and LDL cholesterol (LDLc) <100 mg/dL. We also analyzed non-HDL cholesterol (non-HDLc) below 130 mg/dL as an exposure. The joint triple goal was HbA1c <7% (<53 mmol/mol) plus SBP <130 mmHg plus LDLc <100 mg/dL.

Data from the NRCKD were used to classify participants in terms of age, sex, race or ethnic group, and insurance status. The database also contains data on weight and height, BMI was classified as recommended by the World Health Organization (24). Plasma creatinine values were used to calculate the estimated glomerular filtration rate (eGFR) using the Modified Diet for Renal Disease (MDRD) equation, which has been found to be more accurate than other equations among patients with diabetes (25). Based on eGFR, CKD stages were defined as follows: stage 1: GFR ≥ 90 mL/min; stage 2: GFR: 60-<90 mL/min; stage 3: GFR: 30-<60 mL/min; stage 4: GFR 15-<30 mL/min and stage 5: GFR: <15 mL/min.

The Colombian health system has three health insurance types: Third-party payer ("*régimen contributivo*"), run by private insurers ("*Empresas Promotoras de Salud*" – *EPS*); state-run insurance ("*régimen subsidiado*"), run by a different type of insurer (mostly "*Administradoras de Régimen Subsidiado - ARS*) and a special/exceptional health system for the security forces and employees of some public universities (*régimen especial/régimen de excepción*) (26). We studied insurance type using these three categories.

For the effects of this study, we collapsed the NRCKD race categories "Raizal", "Palenquero" and "Black, Mulatto, Afro-Colombian or Afro-descendant" into a single category called "black" and analyzed self-reported race as black vs. all others. We made this decision because very few individuals (<1% in any given year) identified themselves as belonging to one of the other race categories (indigenous or Roma).

2.3 Data analysis

For descriptive analyses of baseline clinical and demographic characteristics, quantitative variables are presented as means and standard deviations, categorical variables as absolute and relative frequencies. For all analyses, the main outcome was death from any cause, inferred from the variable "date of death", reported by insurers to the NRCKD as the date registered in the death certificate if the patient died during the observation year, or as missing if the patient was still alive. This information was double-checked against the data warehouse of the social protection integrated information system (SISPRO) of the Colombian Ministry of Health and Social Protection. In the case of a discrepancy, the Colombian database of death certificates was consulted.

The association between metabolic control goals as explanatory variables and death from any cause as outcome was evaluated using multivariable logistic regression models. There was a set of potentially confounding variables adjusted for in all models, including sex, age, race, insurance type and BMI. Additionally, we adjusted for the variables representing goals other than the one being evaluated. Thus, in models to evaluate the association between HbA1c goal and mortality, we adjusted for the basic set of confounders, plus hypertension status and non-HDLc. When SBP was the main exposure, we adjusted for the basic confounders plus HbA1c and non-HDLc. When one of the plasma lipids was the exposure, we adjusted for basic confounders plus hypertension status and HbA1c. In models evaluating the triple metabolic goal, we only adjusted for the basic confounders.

We performed two types of analyses, a first group considering as independent variable baseline metabolic control, and a second group modelling the effect of sustained metabolic control throughout the complete study period. The set of confounders being adjusted for was identical in both groups of analyses. Additionally, we performed stratified analyses to explore how metabolic control was related to mortality in subgroups defined by race (black vs other), and BMI category (normal, overweight or obesity). Interactions were tested by the significance of the regression coefficient associated to a multiplicative interaction term between goal achievement status and the stratification variable. All associations are expressed as Odds Ratios (OR) with 95% confidence intervals. To explore the robustness of findings and sort out reverse causation, we performed a sensitivity analysis of metabolic control and mortality excluding participants with CKD stages 4 or 5 at baseline. All analyses were performed at a 5% significance level, and all reported significance tests are two-tailed. Statistical analyses were performed in Stata version 17 (StataCorp LP, College Station, Texas, USA).

2.4 Ethical considerations

This research was based on anonymized secondary data sources and did not include any private information that could make any subject identifiable. To protect privacy, data were anonymized through the use of a database-specific individual ID. Because the study involved only secondary retrospective analyses of an anonymized database, it did not qualify as human subjects research as was exempted from IRB review. Confidentiality was guaranteed throughout the information processing (reporting, managing, and analysis).

3 Results

We studied 1 352 846 adults with diagnosed diabetes from the NRCKD, mean age was 60.8 years, 42.3% were male, 6.6% reported their race as black and almost four of every five patients were overweight or obese. Average systolic and diastolic blood pressure levels were within the normal range, while HbA1c was well above 7%. Mean LDLc and non-HDLc also exceeded recommended thresholds. Most participants were in CKD stage 1, and had a urinary albumin excretion rate (UAER) below 30 mg/g of urinary creatinine or 20 mg/dL. Diagnosed hypertension was highly prevalent (Table 1). Follow-up duration was four years in 59.0% of participants, three years in 15.4%, two years in 12.7%, and one year in 12.9%. As compared to men, a larger proportion of women had a BMI in the obesity range.

3.1 Baseline metabolic control and mortality

There were 107 839 deaths over the entire follow-up (total cumulative mortality 7.97%). The variable whose baseline control was most strongly associated with lower mortality was a SBP<130 mmHg, an association that persisted and actually became stronger after multivariable adjustment (OR 0.72, 95% CI 0.71-0.74)). Glycemic control with HbA1c<7% at baseline was associated with only 3% lower odds of mortality in univariate analysis, but after adjustment

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TABLE 1 Baseline characteristics of study participants.

Variables	Men (n=572 383)	Women (n=780 463)	Total (n=1 352 846)
Age (yrs)	60.2 (13.6)	61.3 (14.0)	60.8 (13.9)
Age group (%)			
<40	7.2	6.8	7.0
40-49	13.9	12.0	12.8
50-59	25.8	25.4	25.6
60-69	27.5	27.2	27.3
70-79	17.8	18.9	18.5
≥80	7.7	9.7	8.9
Health insurance (%)			
Third-party payer	70.6	59.8	64.4
State	27.4	38.9	34.0
Special/Exceptional	2.0	1.3	1.6
Race (%)			
Black	6.3	6.8	6.6
Other	93.7	93.2	93.4
n for BMI	567 768	772 671	1 340 439
BMI (Kg/m^2)	27.6 (4.8)	28.3 (5.6)	28.0 (5.3)
BMI category (%)			
Normal weight	21.2	20.9	21.1
Overweight	31.3	27.2	28.9
Obesity	47.5	51.9	50.0
n for blood pressure	553 722	757 425	1 311 147
SBP (mmHg)	124.1 (14.3)	124.4 (14.6)	124.3 (14.5)
DBP (mmHg)	76.7 (8.9)	76.6 (8.9)	76.7 (8.9)
n for HbA1c	444 573	587 212	1 031 785
HbA1c (% of total Hb)	7.55 (2.12)	7.45 (2.05)	7.49 (2.08)
HbA1c (mmol/mol)	59	58	58
n for blood lipids	449 351	620 820	1 070 171
Non-HDLc (mg/dL)	139.1 (46.1)	146.1 (47.0)	143.2 (46.8)
LDLc (mg/dL)	105.5 (38.3)	112.6 (40.0)	109.6 (39.5)
CKD stage (%)			
1	64.1	59.3	61.3
2	26.0	28.4	27.4
3A	5.6	8.0	7.0
3B	2.2	2.7	2.5
4	0.8	0.8	0.8
5	1.3	0.8	1.0
Urinary albumin excretion (%)			
<30 mg/g or <20 mg/dL	69.1	76.2	73.2

(Continued)

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TABLE 1 Continued

Variables	Men (n=572 383)	Women (n=780 463)	Total (n=1 352 846)
30-300 mg/g or 20-199 mg/dL	25.0	19.8	22.1
>300 mg/g or ≥200 mg/dL	5.9	4.0	4.8
Hypertension (%)	62.7	69.4	66.6

The year 2016 corresponds to data registered between July, 2015 and June, 2016, and so on. Data are means (SD) unless indicated otherwise. BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; LDLc, LDL cholesterol; non-HDLc, non-HDL cholesterol; CKD stage was classified according to the KDIGO classification.

for confounders the negative association grew stronger (18%, 95% CI 17-19%). Patients who achieved the joint triple goal at baseline had significantly lower mortality (OR 0.85, 95% CI 0.83-0.87).

3.2 Sustained metabolic control and mortality

The effect of sustaining basic diabetes treatment goals largely exceeded that of achieving them only at baseline. In models adjusted by sex, age, race, insurance type and baseline BMI, sustained SBP and HbA1c control were associated with 58% lower and 75% lower odds of death, respectively (Figure 1). Sustained control of LDLc under 100 mg/dL also showed a strong negative association with mortality (OR 0.28 [0.27-0.29]). When we used the stricter 70 mg/dL cLDL goal, sustained LDLc control was associated with 75% lower odds of all-cause mortality (OR 0.25, 95% CI 0.23-0.27). When the three metabolic goals were achieved and sustained, the decrease in the odds of mortality was 81% (79-82%) (Figure 1). Unfortunately, only 5.4% of study participants both achieved and sustained this degree of metabolic control. When a non-HDLc <130 mmHg substituted LDLc<70 mg/dL in the triple goal, the results were quite consistent, maintenance of this joint goal was associated with an adjusted OR for mortality of 0.19 (95% CI 0.17-0.21). Sustained control of albuminuria (urinary albumin excretion rate<30mg/g creatinine or <20 mg/L), was associated with a multivariable-adjusted OR for total mortality of 0.26 (95% CI: 0.24-0.27).

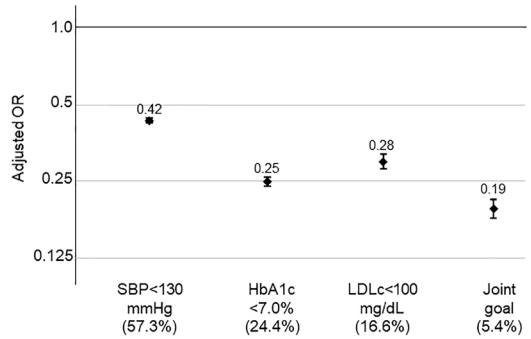

FIGURE 1
Association between sustained metabolic control and mortality. Data are odds ratios compared to participants not reaching sustained achievement of each goal, adjusted for sex, age, race (black vs other), insurance type and baseline BMI. Error bars represent 95% confidence intervals. Numbers in parentheses represent the percentage of study participants who sustained control of each goal over study follow-up.

3.3 Sustained metabolic control and mortality, by race

The positive effect of SBP control did not differ by between patients of black race and those of other races (*p-value* for the interaction 0.32). By contrast, the beneficial effect of sustained glycemic control was significantly smaller for patients of black race (OR 0.39, 95% CI 0.34-0.45 for black race; OR 0.24, 95% CI 0.25-0.25 for other races, *p-value* for interaction <0.001) (Table 2). However, the largest difference according to race existed in the relationship of sustained lipid control and mortality, the impact being much larger for patients of non-black race. The reduction in the OR for sustained control of non-HDLc was 30% for black patients and 73% for patients of other races (*p-value* for interaction<0.001). In the case of sustained LDLc control, the figures were 59% lower odds for black patients, and 73% lower odds for patients of other races (*p-value* for interaction <0.001). In consequence, the reduction in the odds of death with sustained achievement of the triple goal was 69% for black patients, and 82% for patients of other races (Table 2).

3.4 Sustained metabolic control and mortality, by BMI category

There was no significant difference in the association between sustained SBP control and mortality for patients with a BMI in the normal, overweight or obesity range (*p-value* for interaction 0.54, Table 3). Conversely, sustained glycemic control was most negatively associated with mortality among patients with obesity (*p-value* for interaction <0.001). While sustained control of LDLc had a similar impact in all BMI categories, non-HDLc control also had a greater impact in the obesity category (*p-value* for interaction 0.001). Remarkably, the effect of sustained joint metabolic control on mortality was similar across BMI categories, with no significant interaction (Table 3).

3.5 Sensitivity analyses excluding advanced CKD at baseline

Given that individuals with advanced CKD may experience reductions in blood pressure, glycemic levels and/or plasma lipids towards the end of life (leading to the so-called reverse causation

TABLE 2 Association between sustained metabolic control and mortality, by race.

	Race						
	Black			Other			
Sustained metabolic control goal	aOR (95% CI)	n for model	Events for model	aOR (95% CI)	n for model	Events for model	*p-value* for interaction
SBP < 130 mmHg †	0.42 (0.38-0.46)	58 400	2 373	0.42 (0.41-0.43)	771 052	35 273	0.32
HbA1c < 7.0% ‡	0.39 (0.34-0.45)	52 802	2 398	0.24 (0.23-0.25)	715 101	36 082	<0.001
Non-HDLc < 130 mg/dL §	0.70 (0.57-0.85)	48 499	2 174	0.27 (0.26-0.29)	651 802	34 389	<0.001
LDLc < 100 mg/dL §	0.41 (0.35-0.48)	54 822	2 382	0.27 (0.26-0.28)	704 675	34 960	<0.001
Joint SBP, HbA1c and LDLc goal ¶	0.31 (0.23-0.43)	56 036	2 801	0.18 (0.17-0.20)	753 074	43 779	0.003
Joint SBP, HbA1c, LDLc and BMI goal *	0.35 (0.21-0.59)	58 763	3 060	0.22 (0.19-0.25)	799 878	48 556	0.10

aOR, Adjusted Odds Ratio. † Adjusted for core confounders (sex, age, race [black vs other], insurance type and BMI), baseline HbA1c and baseline non-HDL cholesterol. ‡ Adjusted for core confounders, baseline non-HDL cholesterol, and hypertension. § Adjusted for core confounders, baseline HbA1c, and hypertension status. ¶ Adjusted only for core confounders, except BMI. * Adjusted only for core confounders, except BMI.

problem), we performed a sensitivity analysis of sustained goal achievement and mortality excluding participants at CKD stages 4 or 5 at baseline. The results were generally consistent with those for the complete study sample. The OR for mortality according to sustained control of each variable were 0.50 (0.49-0.51) for SBP, 0.25 (0.24-0.26) for HbA1c, 0.27 (0.26-0.29) for LDLc, and 0.21 (0.19-0.23) for the triple goal (Table 4).

4 Discussion

In this large scale, nationwide retrospective study of people with diabetes in Colombia, we found a very strong negative association between good metabolic control and death from any cause. Sustained control of SBP was associated with up to 58% lower odds of death, HbA1c control with 75% lower odds, and LDLc control with 72% lower odds. A powerful finding was that the continuous achievement of the triple metabolic goal was accompanied by an 81% reduction in total mortality. The inclusion of either LDLc or non-HDLc as lipid parameter in the joint goal produced very similar results.

Several trials have compared more versus less strict blood pressure control in diabetes, most notably the UKPDS-38 (27) and ACCORD-BP (28) trials. Even though UKPDS-38 found significant reductions in total diabetes complications, the effect on total mortality was not significant. Likewise, in ACCORD-BP there was a significant reduction in strokes with tighter SBP control, but not a mortality

TABLE 3 Association between sustained metabolic control and mortality, by body-mass index category.

	BMI category									
	Normal weight			Overweight			Obesity			
Sustained metabolic control goal	aOR	n for model	Events for model	aOR	n for model	Events for model	aOR	n for model	Events for model	*p-value* for interaction
SBP < 130 mmHg†	0.39 (0.37-0.41)	172 555	12 024	0.46 (0.45-0.48)	269 179	13 674	0.40 (0.39-0.42)	387 708	11 948	0.54
HbA1c < 7.0% ‡	0.26 (0.24-0.28)	158 861	12 708	0.28 (0.26-0.29)	249 311	14 100	0.21 (0.20-0.22)	359 731	11 672	<0.001
Non-HDLc < 130 mg/dL §	0.32 (0.28-0.37)	139 739	11 804	0.38 (0.33-0.44)	222 025	13 365	0.27 (0.25-0.30)	338 516	11 394	0.001
LDLc < 100 mg/dL §	0.28 (0.26-0.30)	160 056	12 491	0.29 (0.27-0.31)	240 728	13 302	0.28 (0.26-0.30)	358 699	11 549	0.98
Joint SBP, HbA1c and LDLc goal ¶	0.17 (0.14-0.20)	170 598	15 838	0.23 (0.20-0.27)	260 990	16 724	0.18 (0.16-0.21)	377 500	14 018	0.54

aOR, Adjusted Odds Ratio (95% CI). † Adjusted for sex, age, race (black vs other), insurance type, baseline HbA1c and baseline non-HDL cholesterol. ‡ Adjusted for sex, age, race (black vs other), insurance type, baseline non-HDL cholesterol, and hypertension status. § Adjusted for sex, age, race (black vs other), insurance type, baseline HbA1c and hypertension status. ¶ Adjusted for sex, age, race (black vs other) and insurance type.

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TABLE 4 Association between metabolic control and mortality, excluding patients in CKD stages 4 or 5 at baseline.

Sustained treatment goal	Adjusted OR	n for adjusted model	Events for adjusted model
SBP < 130 mmHg†	0.50 (0.49-0.51)	812 077	32 387
HbA1c < 7.0%‡	0.25 (0.24-0.26)	752 097	33 744
Non-HDLc < 130 mg/dL§	0.32 (0.30-0.34)	687 398	32 541
LDLc < 100 mg/dL§	0.27 (0.26-0.29)	744 879	33 399
Joint SBP, HbA1c and LDLc goal¶	0.21 (0.19-0.23)	790 844	40 356
Joint SBP, HbA1c, LDLc and BMI goal*	0.26 (0.23-0.31)	839 558	45 008

† Adjusted for core confounders (sex, age, race [black vs other], insurance type and BMI), baseline HbA1c and baseline non-HDL cholesterol. ‡ Adjusted for core confounders, baseline non-HDL cholesterol, and hypertension. § Adjusted for core confounders, baseline HbA1c, and hypertension status. ¶ Adjusted only for core confounders. * Adjusted only for core confounders, except BMI.

effect, although the study was underpowered for total mortality. Nonetheless, the previously mentioned meta-analysis of blood pressure control trials in diabetes found a continuous negative relationship between achieved SBP and mortality (6). Our results support the idea that in usual practice conditions, achievement of this SBP goal does translate into lower risk of death among patients with diabetes.

Concerning glycemic control, the UKPDS documented a monotonic negative relationship between achieved HbA1c and adjusted total mortality rate (29). Later studies have found this association to be strongest among patients with low glucose variability (30). We had the very interesting finding that sustained glycemic control had a negative relationship with mortality four times larger than just baseline control. In a recent observational study in Israel, patients newly diagnosed with type 2 diabetes who experienced an early reduction followed by a sharp, progressive increment in HbA1c had an 83% higher risk of death over a five-year period, relative to those with stable, controlled HbA1c levels (31). These results highlight the importance of active HbA1c monitoring and avoidance of clinical inertia in diabetes management. Our results were markedly different for baseline *versus* continued lipid control, the protective effect being present only for the sustained control of LDLc or non-HDLc. A similar problem had been reported in a nationwide study of the association between statin use and cancer mortality in Denmark (32). Our results emphasize the importance of strict and continuous LDL and non-HDL control among people with diabetes.

Next to the impressive effect of joint and sustained metabolic control, an alarming result was that only 5.4% of patients achieved this fundamental treatment objective. Globally, better metabolic control has been held responsible for recent downward trends in mortality among patients with diabetes (33), despite the increase in diabetes prevalence (34). Recent analyses of data from the U.S. Veteran Administration warehouse found that control of each additional ABC goal was associated with a significant improvement in mortality (35). Thorough metabolic control is feasible and provides substantial benefits, every possible effort should be made to achieve it in all patients with diabetes.

Data from several countries indicate that patients of black race have increased rates of diabetes complications (36). In the United States, African American patients with diabetes are four times more likely to have end-stage renal disease than non-Hispanic whites (37), a difference that can be explained only partially by disparities in socioeconomic status or access to healthcare (36). In our study, black race was an important modifier of the relationship between metabolic control and mortality. Compared to other races, patients of black race derived the same benefit from sustained SBP control, but significantly less benefit from achievement of the HbA1c, non-HDLc or LDLc goals, or of the joint triple goal. The Heart Outcomes Prevention Evaluation (HOPE)-3 trial, found no evidence of a differential effect of LDLc control with rosuvastatin on major cardiovascular events in patients of black race compared to other races (38). In fact, in the very large ALLHAT-LLT study, patients of black race seemed to derive *larger* coronary heart disease reductions from LDLc control (39). Thus, it might be that in our particular population a lower LDL among people of black race acts as a marker of other risk factors for mortality like social or economic deprivation. This hypothesis, however, will need to be tested in future studies.

We also found that good metabolic control provides large benefits in patients of *any* BMI. Importantly, our central findings remained essentially unaltered in sensitivity analyses excluding patients in baseline CKD stages 4 or 5.

4.1 Study strengths and limitations

Our study is based on a large, nationwide, centrally administered database of compulsorily reported and constantly audited data. In addition, the primary outcome of death from any cause is verified against official government sources. Limitations of the study include its relatively short follow-up for metabolic control to impact mortality. Also, we could not differentiate between patients with type 1 or type 2 diabetes, and metabolic control may have a numerically different impact in these two patient populations. In addition, the NRCKD database does not collect data on current medications, except for angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. Arguably, however, most of the effects of antidiabetic, antihypertensive or lipid lowering drugs should be manifest in the values of SBP, HbA1c or blood lipids, which we did analyze. As in most registry-based studies of chronic diseases, the exact date of start of diabetes was not known, so we could not include diabetes duration as a covariate in our models.

In conclusion, our results showed that successful control of fundamental variables has a strong negative association with mortality in diabetes. Despite the existence and availability of the

lifestyle and pharmacological means to attain these goals, they are still not being achieved by the overwhelming majority of patients. Widespread pursuit of tight metabolic control may yield large benefits in terms of mortality in diabetes.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

CM: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Supervision, Visualization, Writing - original draft, Writing - review & editing. MA-M: Data curation, Formal analysis, Methodology, Visualization, Writing - original draft; Writing - review & editing. JH-V: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Software, Writing - original draft; Writing - review & editing. NR-G: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Software, Writing - original draft; Writing - review & editing. LH-P: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Software, Writing - original draft; Writing - review & editing. VG-C: Data curation, Formal analysis, Methodology, Writing - original draft; Writing - review & editing. CR-D: Data curation, Formal analysis, Methodology, Writing - original draft; Writing - review & editing. AP-L: Data curation, Formal analysis, Methodology, Writing - original draft; Writing - review & editing. LA-M: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Software, Writing - review & editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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ERC, HTA Y DM

Autosomal dominant polycystic kidney disease in Colombia

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Trabajo colaborativo con la academia (Fundación Universitaria Sanitas) como actores de interés.

Objetivo: describir la prevalencia de la enfermedad poliquística renal (EPQR) y sus características clínicas en las personas que reciben TRR a nivel nacional, departamental y en las ciudades principales, en el marco del aseguramiento colombiano entre 2015 y 2019.

Principales hallazgos:

- Se analizaron 3.339 personas con EPQR, estimando una prevalencia de periodo de 9,81 casos por 100.000 habitantes entre el 1° de julio de 2015 al 30 de junio de 2019. Entre las personas con TRR, la prevalencia fue de 4,35 casos por 100.000 habitantes.
- Existe una gran variabilidad epidemiológica en las diferentes regiones geográficas del país, con una alta prevalencia en los departamentos de la periferia. La prevalencia estandarizada más elevada se registró en el Valle del Cauca (6,55 casos por 100.000 habitantes). Por otro lado, se identificó que La Guajira tuvo la mayor proporción de pacientes con EPQR en TRR (10,48%).
- De acuerdo al grupo étnico, la mayor prevalencia se estimó para la población ROM con 37,7 casos por 100.000 habitantes, seguido por los afrocolombianos e indígenas con 2,1 y, 0,31 casos por 100.000 habitantes, respectivamente.
- Los pacientes con EPQR en Colombia iniciaron la TRR a una edad media de 52,58 años. El 50% se encontraba en hemodiálisis, el 18% en diálisis peritoneal y el 32% habían recibido un trasplante renal.

Relevancia de los hallazgos:

- Esta caracterización geográfica soporta la toma de decisiones a nivel regional, y apoya la necesidad de buscar activamente estos pacientes y sus familiares para establecer medidas de prevención primaria y secundaria, y terapias tempranas para evitar la progresión a diálisis o trasplante renal.

Comentario del autor experto:

Dr. Camilo Alberto González

La enfermedad renal poliquística autosómica dominante es la causa genética más frecuente de ERC en TRR. Nuestro estudio revela una prevalencia de periodo (2015 a 2019) de 4,35 por 100.000 habitantes en Colombia, 29 de cada 1.000 pacientes en diálisis tiene EPQR y el departamento con la mayor prevalencia es el Valle del Cauca. La EPQR puede ser la entidad con mejor opción de modelo de gestión de riesgo posible. La historia familiar alerta a las personas, el largo tiempo de latencia a la falla renal permite aplicar todos los modelos de predicción, prevención y tratamiento, incluyendo el trasplante anticipado a la diálisis y el ingreso programado TRR. Más detalles en el documento completo.

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RESEARCH Open Access

Autosomal dominant polycystic kidney disease in Colombia

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Abstract

Background Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic cause of chronic kidney disease (CKD) that requires dialysis. Knowing geographical clusters can be critical for early diagnosis, progression control, and genetic counseling. The objective was to establish the prevalence, geographic location, and ethnic groups of patients with ADPKD who underwent dialysis or kidney transplant in Colombia between 2015 and 2019.

Methods We did a cross-sectional study with data from the National Registry of Chronic Kidney Disease (NRCKD) managed by the High-Cost Diseases Fund (*Cuenta de Alto Costo* [CAC] in Spanish) between July 1, 2015, and June 30, 2019. We included Colombian population with CKD with or without renal replacement therapy (RRT) due to ADPKD. Crude and adjusted prevalence rates were estimated by state and city.

Results 3,339 patients with ADPKD were included, period prevalence was 9.81 per 100,000 population; there were 4.35 cases of RRT per 100,000 population, mean age of 52.58 years (± 13.21), and 52.78% women. Seventy-six patients were Afro-Colombians, six were indigenous, and one Roma people. A total of 46.07% began scheduled dialysis. The highest adjusted prevalence rate was in *Valle del Cauca* (6.55 cases per 100,000 population), followed by *Risaralda*, and *La Guajira*. Regarding cities, *Cali* had the highest prevalence rate (9.38 cases per 100,000 population), followed by *Pasto*, *Medellin*, and *Bucaramanga*.

Conclusions ADPKD prevalence is lower compared to Europe and US; some states with higher prevalence could be objective to genetic prevalence study.

Keywords Chronic kidney failure, Polycystic kidney disease, Renal replacement therapy, Dialysis, Kidney transplant

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Background

Autosomal dominant polycystic kidney disease (ADPKD) is characterized by the gradual growth of fluid-filled cysts in both kidneys, leading to increased size, loss of function, and eventually kidney failure [1]. It is the first hereditary cause and the fourth most common cause of the need for renal replacement therapy (RRT) worldwide [2–5]. ADPKD has been described in all ethnic groups, with variable regional prevalence [6–9]. Mutations in the PKD1 and PKD2 genes are the most frequent etiology of the disease [2]. PKD1 is more common and causes up to 85% of cases. However, spontaneous mutations may occur in up to 5% of cases [1, 10]. Kidney failure leads to up to 70% of patients requiring RRT between 40 and 70 years of age, with earlier ages at onset in cases with PKD1 mutations compared to those with PKD2 mutations [4], generating high costs for the health system and reducing the health-related quality of life [2, 4].

Estimating the prevalence of ADPKD is difficult owing to a long asymptomatic period and underdiagnoses caused by the lack of an adequate approach to detecting the disease. The genetic prevalence in small cohorts is as high as 1 per 1,000 population, but population-based studies show a lower prevalence [11]. Latin America does not have enough information in this field. Colombia, where we have multiple origins and genetic mixtures, probably shows a different prevalence than the rest of the world [12].

The main objective of this study was to determine the prevalence of ADPKD in Colombia. However, to avoid selection bias due to the asymptomatic period and underdiagnoses, we included individuals with ADPKD receiving RRT to compare the geographical prevalence and describe their clinical characteristics between 2015 and 2019.

Methods

We conducted a cross-sectional observational study with data from the National Registry of Chronic Kidney Disease (NRCKD) managed by the High-Cost Diseases Fund (*Cuenta de Alto Costo* [CAC] in Spanish) from July 1, 2015, to June 30, 2019. NRCKD is an official registry with a national scope within the framework of the general system of social health insurance (SGSSS in Spanish), taking into account that approximately 97% of the population is covered by this system [13]. All grades (1 to 5 by Kidney Disease, Improving Global Outcomes KDIGO) of CKD must be reported to the NRCKD in Colombia. CKD was defined as glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m2 for at least three months, albumin-to-creatinine ratio > 30 mg/g in two of three spot urine specimens, or abnormal kidney structure by images [14]. The reporting process is legally mandatory [15]. The inclusion criteria were residents of Colombia who were reported to the NRCKD with a diagnosis of CKD with or without RRT (dialysis or kidney transplant) and ADPKD. However, the descriptive analysis was performed only for patients on RRT, contemplating the limitation expected by the underreporting of patients without RRT.

Table 1 Crude prevalence of ADPKD per 100,000 population

	2016	2017	2018	2019	2015–2019
Adults with ADPKD	7.26	9.14	9.12	9.31	9.81
Adults with ADPKD on RRT	3.53	3.98	3.84	3.92	4.35

Each case was identified with a unique registration number to protect the personal information of the participants. Additionally, a structured audit process was carried out to ensure the quality of the information provided by comparing it with the medical records.

The study variables were divided into demographic (age, sex, type of health insurance, ethnicity, states and cities of residence, and follow-up time) and clinical variables (weight, height, serum creatinine, estimated glomerular filtration rate (eGFR) at diagnosis, time since diagnosis of CKD, time since diagnosis of CKD stage 5, time since the start of RRT and its initial modality, potential kidney transplant evaluation and vital status). To ensure the validity and reliability of this study, all patients who met the inclusion criteria were included.

Statistical analysis

The qualitative data is informed as proportions, and the quantitative as the means, medians, and standard deviation or interquartile ranges (IQR). Crude prevalence is presented. The results were presented by georeferenced departments and municipalities. The prevalence was studied for four consecutive years (2015–2019); for each period, cases were included from July 1st of the previous year to June 30th of the year under study. The period prevalence was estimated by taking all new and pre-existing cases of ADPKD in the four years, over the mean or mid-interval population. Data analysis was performed with the statistical package STATA® 13.0 (StataCorp®) and georeferenced with the software Qgisnciv ® 3.2. The prevalence was measured with Microsoft® Excel® version 2019.

Results

A total of 3,339 patients with ADPKD were reported NRCKD (overall period prevalence of 9.81 cases per 100,000 population), of which 1,476 patients were on RRT, for a period crude prevalence between 2015 and 2019 of 4.35 cases per 100,000 population (Table 1).

For the patients on RRT, the mean age at the time of this study was 55.43 years (±12.78 years), and the mean age at the start of RRT was 52.58 years (±13.21 years). The female was predominant, with 779 patients (52.78%). (Table 2). Regarding ethnicity, among the

Table 2 Demographic and clinical characteristics of patients with ADPKD on RRT, Colombia 2016–2019

Description	N = 1,476
Demographics	
Age at study onset in years, mean (SD)	55.43 (12.78)
Age at onset of RRT in years, mean (SD)	52.58 (13.21)
Female sex, n (%)	779 (52.78)
Healthcare insurance affiliation	
Contributory regime, n (%)	1,032 (69.9)
Subsidised regime, n (%)	409 (27.71)
Exceptions (military, police, etc.), n (%)	31 (2.1)
Special (*Ecopetrol*), n (%)	3 (0.2)
Ethnicity	
Indigenous, n (%)	6 (0.41)
Black, mulatto, or Afro-Colombian people, n (%)	76 (5.15)
Clinical characteristics	
Weight in kg, mean (SD)	65.39 (13.79)
Size in cm, mean (SD)	163.02 (9.35)
BMI in kg/m2, mean (SD)	24.51 (4.27)
Serum creatinine level at program admission in mg/dl, median (IQR)	5.29 (1.5-9)
Time with stage 5 CKD in years, median (IQR)	5.46 (2.66–9.36)
Dialysis vintage in years, median (IQR)	4.32 (2.53-7)
Kidney transplant waitlist, n (%)	735 (49.8)
Contraindication for kidney transplantation, n (%)	262 (17.75)
No data about the kidney transplant waitlist, n (%)	479 (32.45)
Renal replacement therapy	
Hemodialysis, n (%)	725 (49.12)
Peritoneal dialysis, n (%)	271 (18.36)
Functioning kidney transplant, n (%)	480 (32.52)
Deaths from any cause, n (%)	226 (15.31)

patients with ADPKD, there were 76 Afro-Colombians patients (5.15%), six indigenous patients (0.41%), and one Roma patient (0.07%), and the remaining 1,393 patients (94.38%) did not have a specific ethnic assignment. Based on the 2018 Colombian ethnicity census, the prevalence of ADPKD on RRT was 2.1 cases per 100,000 population for Afro-Colombians, 0.31 cases per 100,000 population for indigenous, and in the 2,649 (0.008% of the Colombian population) auto-nominated Roma people or gypsy, an overestimated prevalence of 37.7 cases per 100,000 population.

Upon initiation of RRT, only 15.58% belonged to a CKD program. However, 680 patients (46.07%) had a scheduled admission to their first RRT visit, 458 (31.03%) started dialysis by emergency service, and the rest were not reported. The number of deaths during the study period was 226 (15.31%).

At the end of the study, on June 2019, 725 patients were on hemodialysis, and 271 were on peritoneal dialysis. That is, around 29 of every 1,000 patients on dialysis had ADPKD. Functioning kidney transplants were reported in 480 patients (32.52% of RRT patients).

Regarding the geographic distribution of the disease by state (*Departamentos* in Spanish for Colombia) (Fig. 1), the highest standardized prevalence rates were found in *Valle del Cauca* (6.55 cases per 100,000 population), *Risaralda* (6.48 cases per 100,000 population) and *La Guajira* (5.56 cases per 100,000 population). The lowest prevalence rates were reported in Quindío and Caquetá, with 0.57 and 0.08 cases per 100,000 population, respectively. Table 3 shows the adjusted prevalence of CKD on RRT from any cause, caused by ADPKD, and the overall mortality from any cause at some states of extremes of ADPKD prevalence. La Guajira has the highest proportion of ADPKD patients on RRT (10.48%). Overall adjusted mortality of CKD patients on RRT was higher in Valle del Cauca.

Regarding the main cities, Cali had the highest prevalence rate (9.38 cases per 100,000 population), followed by Pasto (8.81 cases per 100,000 population) and Medellin (7.30 cases per 100,000 population).

Discussion

CKD is a public health problem that affects more than 10% of the general population worldwide [16]. ADPKD is the leading hereditary cause [16], responsible for up to 10% of patients with kidney disease on RRT [17, 18]. In Colombia, in 2019, more than 925,996 patients with CKD were reported, with a possible sub-estimated prevalence of 1.8%, of which 4.9% had End-stage Kidney Disease (ESKD) [19]. We suppose the early diagnosis of CKD in Colombia is reduced because of the silent period of the disease, young population composition, cultural perception of preventive medical consultation, and, despite the almost universal health system coverage, dispersed areas have less access to quality health services [20, 21].

Consultations with physicians, including both generalists and specialists in Colombia for 2019 was 2.6 doctor consultations per person, lesser than the average 5.3 for OECD members [22]. Vulnerable socio-economic groups still have obstacles to accessing health care. However, preventive health care consultations in the poorest quintile are rising. Access to healthcare services is more difficult in rural areas inhabited by indigenous communities, who may have beliefs, traditions, and models of healthcare that are different from the Western healthcare model. Indicators such as maternal and neonatal mortality rates tend to be higher in rural areas and for specific population groups (e.g., indigenous and Roma people) [20–22].

Those explain our low ADPKD period prevalence of 9.81 cases per 100,000 population compared to the majority of high-income countries, such as in Europe, where the prevalence is 39.6 per 100,000 population [7], or in the US, which has a prevalence of 42.6 per 100,000 population [11]. On the other hand, in Colombia, the

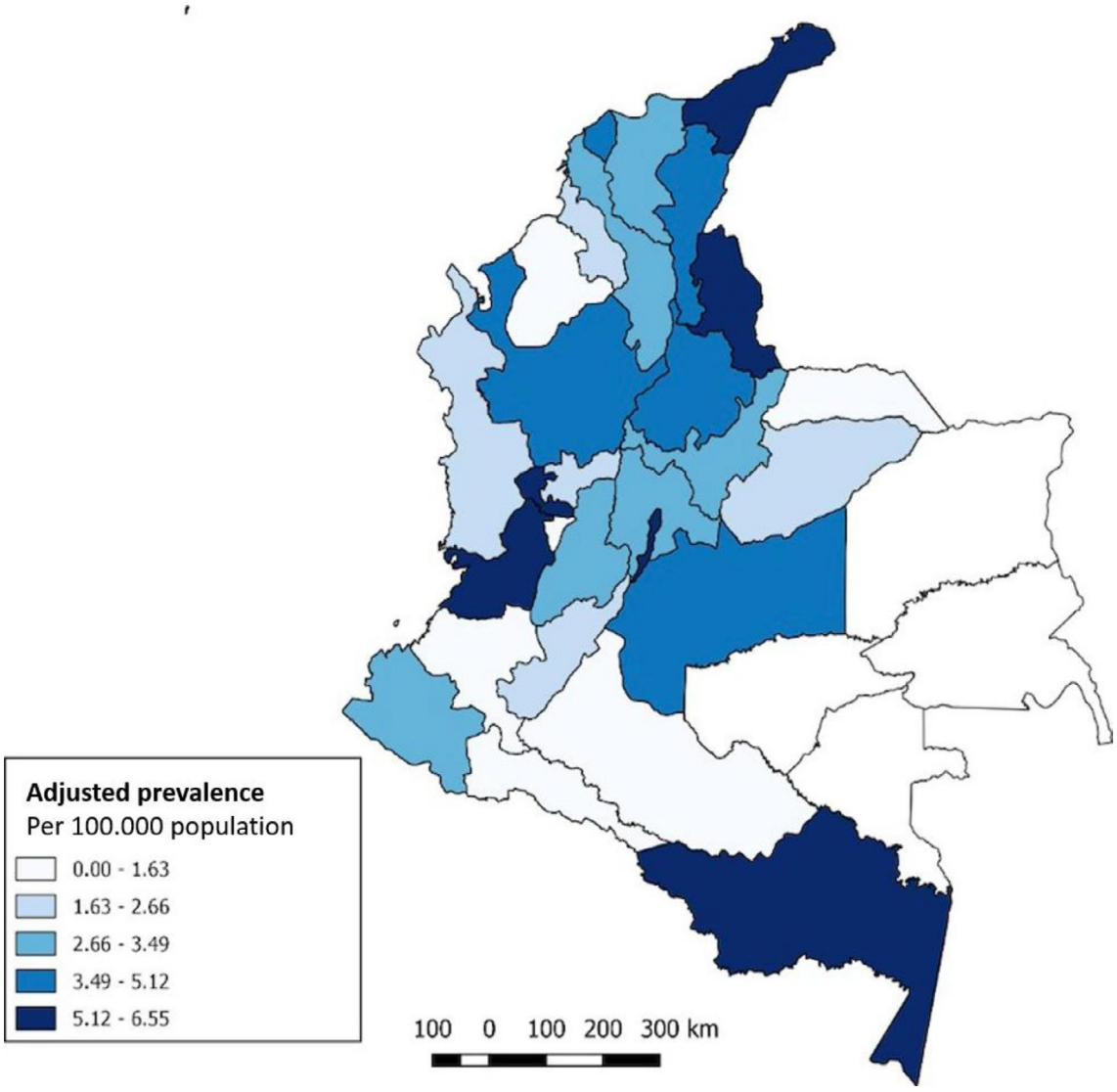

Fig. 1 ADPKD period prevalence on RRT by states (*Departamentos* in Spanish), 2015–2019. (Data source: NRCKD)

prevalence of CKD on RRT are increasing from 77 to 86.13 per 100,000 population between 2016 and 2019 [23], but is at least 2.5 times less than in the US for 2019 [24]. According to our estimation, ADPKD patients who undergo dialysis or kidney transplant was 4.35 cases per 100,000 population, lower than that reported by the ERA-EDTA Registry on RRT from 12 European countries between 1991 and 2010, it shows an increasing ADPKD prevalence from 5.68 to 9.11 per 100,000 population [4].

In Colombia, every 29 patients out of 1,000 on RRT have ADPKD. This prevalence is comparable to Alves EF et al. that showed a prevalence of 10 per 1,000 patients on hemodialysis [9]. Likewise, in Africa, the frequency in the University Clinic of Nephrology and Hemodialysis of Cotonou was estimated at 18 per 1,000 population [25], and in Taiwan, it was estimated at 19 per 1,000 population on dialysis [26]. Moreover, in 2020 in the US, 50 per 1,000 patients were on RRT, 56% were on hemodialysis, 27% were on peritoneal dialysis, and 17% had functional kidney transplantation [24].

The ADPKD patients in Colombia started RRT at an average age of 52.8 years, and these patients were more likely to be women, with around 50% on hemodialysis, 18% on peritoneal dialysis and 32% who had kidney

Table 3 Adjusted prevalence of CKD on RRT from any cause, caused by ADPKD, and CKD overall mortality in 2019 (Per 100.000 population)

	CKD on RRT prevalence		CKD on RRT Mortality
State	**All causes**	**ADPKD, prevalence (%)**	**Death from any cause**
La Guajira	53.05	5.56 (10.48)	5.82
Risaralda	86.62	6.48 (7.48)	7.73
Valle del Cauca	111.07	6.55 (5.90)	11.37
Bogotá D.C	92.11	5.2 (5.65)	8.66
Quindio	92.61	0.57 (0.62)	8.99
Caqueta	48.92	0.08 (0.16)	6.69

Data source: NRCKD

transplantation, similar to the US for the same year. For the US, the median age at the start of RRT between 2001 and 2010 was 55.6 years without changes, but RRT was more frequent among males [3]. For Europe, the mean age at the start of RRT increased from 56.6 to 58.0 years ($p<0.01$) between 1991 and 2010. The increased age at onset of RRT is most likely due to increased access for elderly ADPKD patients or lower competing risks prior to the start of RRT [4].

Our study showed that there is a wide epidemiological variability in the different geographical regions of our country, with a high prevalence in the states and main cities of the periphery, probably related to the effect of georeferenced family clusters, health care access, and the centralization of RRT. That last hypothesis explain the highest prevalence of CKD of any cause in *Valle del Cauca* as well as for ADPKD in TRR. This regional difference coincides with observations in other latitudes, where similar studies have been carried out [27, 28]. The lowest prevalence was found in Quindío and Caquetá, with 0.57 and 0.08 cases per 100,000 population, respectively. Interestingly, Quindío showed one of the lowest prevalence rates compared to Risaralda, which was the department with the second highest prevalence rate (6.48 cases per 100,000 population). These two states have minimal geographical separation, and their cultures are similar; migration during the colonial period likely explains such a markedly different distribution. A low prevalence of ADPKD among indigenous should be caused by a low health care consultation or less probably by fewer frequent genetic PKD mutations. These hypotheses can be clarified with a genetic study, which allows the description of the prevalence of mutations.

Some strengths of this study is the data based on a nationwide registry with audited medical records, estimated prevalence by states and cities; and in the future, it will allow monitoring and even genotyping to group patients and families according to the risk of disease progression, taking into account the mutational profile and establishing primary and secondary prevention measures and early therapies to prevent progression to dialysis or kidney transplantation [29].

Limitations

Given the secondary source of data, a standardized diagnosis of the disease is lacking. For NRCKD the diagnosis was based on nephrologist clinical judgment. Additionally, we lack information on approximately 3% of the population, which is not affiliated to the health care system. Unfortunately NRCKD doesn't have a detailed mortality rate and causes of CKD patients. Similarly, we do not follow up on relatives of reported patients, it is the responsibility of the health provider and insurer within the health system model of Colombia, to actively search for relatives affected by the disease, and to carry out the corresponding notification and intervention.

Conclusions

The prevalence of patients with ADPKD on RRT is lower than in Europe and the US. However, similar to known to Africa and Latin America; the areas with the highest prevalence rates in Colombia are found in *Valle del Cauca*, *Risaralda* and *La Guajira*. It is imperative to carry out the genetic geographic characterization of ADPKD by region.

List of abbreviations

ADPKD	Autosomal dominant polycystic kidney disease
CKD	chronic kidney disease
NRCKD	national registry of chronic kidney disease
CAC	High Cost Diseases Fund (*Cuenta de Alto Costo* in Spanish)
RRT	renal replacement therapy
US	United States of America
eGFR	estimated glomerular filtration rate
IQR	interquartile range
CIOMS	Council of International Organizations of Medical Sciences
SD	Standard deviation
ERA-EDTA	European renal association - European Dialysis and Transplant Association Registry
ESKD	End-stage kidney disease

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Authors' contributions

"JC, CG, NY, MI constructed the protocol and perform the systematic review. JC, CG, LH, AV, MI analyzed and interpreted the patient data. All authors read and approved the final manuscript."

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Data Availability

The data that support the findings of this study are available from High Cost Diseases Fund (*Cuenta de Alto Costo* [CAC] in Spanish), but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from on reasonable request via email to the coauthor: Ana M Valbuena-García: avalbuena@cuentadealtocosto.org.

Declarations

Competing interests
All the authors declared no competing interests.

Ethics approval and consent to participate
the study was approved by the research and ethics committee of *"Fundacion Universitaria Sanitas"* on March 2020, with the code: CEIFUS 414 – 20. This study complied with international regulations (particularly the Declaration of Helsinki and the ethical guidelines for biomedical research prepared by the Council of International Organizations of Medical Sciences, CIOMS). This was a retrospective documentary investigation of secondary database; no intervention was made. It was considered an investigation without risk for the population of interest by following per under the legal and ethical guidelines of Colombia (Resolutions 8430 of 1993 and 2378 of 2008 of the Ministry of Health of Colombia). Individual informed consent was waived by the approving research and ethics committee of *"Fundacion Universitaria Sanitas"*, based on the same resolutions: 8430 of 1993 and 2378 of 2008 of the Ministry of Health of Colombia. The identification and location information was processed using the codes pre-established by the NRCKD database anonymously.

Consent for publication
none applicable.

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Publisher's Note

ERC, HTA Y DM

MDRD is the eGFR equation most strongly associated with 4-year mortality among patients with diabetes in Colombia

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Trabajo colaborativo con la academia (Universidad de los Andes) como actores de interés.

Objetivo: evaluar la asociación entre la tasa de filtración glomerular (TFGe) y la mortalidad por todas las causas mediante cuatro ecuaciones diferentes basadas en la creatinina, aplicadas en pacientes con DM y enfermedad renal crónica ERC.

Principales hallazgos:

- La fórmula CKD-EPI clasificó 10 veces más individuos en el estadio 5 de ERC en comparación con MDRD o Cockcroft Gault. Por otro lado, MDRD fue la ecuación que menos pacientes clasificó en estadios avanzados (4 o 5).
- Para todas las ecuaciones, cada ml/min adicional de TFGe se asoció con una probabilidad de muerte significativamente menor. Esta magnitud fue diferente al aplicar distintas ecuaciones. Estar clasificado en los estadios 3 o 4 de ERC según MDRD o CKD-EPI-NR se asoció con mayores probabilidades de muerte que estar categorizado en los mismos grupos según otras fórmulas.
- La fórmula de MDRD mostró una asociación mayor con la muerte entre los pacientes de raza negra. Para los pacientes de las demás razas, MDRD y CKD-EPI (sin tener en cuenta la raza) tuvieron un rendimiento muy similar.
- La fórmula de MDRD discrimina mucho mejor el estado vital del paciente con DM y ERC, comparado con las fórmulas de CKD-EPI y Cockcroft Gault (diferencia absoluta de AUC frente a MDRD de 1,6% a 6,4%, $p< 0,001$ para todas las diferencias por pares).

Relevancia de los hallazgos:

- Estos resultados tienen implicaciones clínicas para los profesionales que están en contacto con pacientes con DM en Colombia y otros países de demografía similar, destacando la importancia de realizar siempre una evaluación exhaustiva de la función renal desde su diagnóstico.

Comentario del autor experto:

Dr. Carlos Olimpo Mendivil

Existen varias ecuaciones para tratar de estimar la tasa de filtración glomerular a partir de una medición única de creatinina plasmática, obviando la recolección de orina en 24 horas y facilitando el seguimiento, la prevención y el manejo de la enfermedad renal por diabetes. Las más empleadas son las ecuaciones de Cockroft y Gault, la MDRD y la CKD-EPI, esta última en sus versiones con y sin inclusión de la raza. En este estudio comparamos el grado de asociación de la tasa de filtración estimada por cada uno de estos métodos, con el riesgo de morir por cualquier causa en poco más de 750.000 pacientes con diabetes en Colombia. Las ecuaciones MDRD y CKD-EPI con raza tuvieron una fuerza de asociación con una mortalidad muy similar en la muestra completa, sin embargo, la MDRD tuvo un mucho mejor poder predictivo en los pacientes afrodescendientes, por lo cual en nuestra población con un alto grado de mestizaje es recomendable utilizar la ecuación MDRD para detectar y hacer seguimiento a la función renal en los pacientes con diabetes.

Open access Original research

BMJ Open Diabetes Research & Care

MDRD is the eGFR equation most strongly associated with 4-year mortality among patients with diabetes in Colombia

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ABSTRACT

Introduction We compared the association of glomerular filtration rate (GFR) estimated with the Cockcroft-Gault, Modification of Diet in Renal Disease study (MDRD), Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), or the new CKD-EPI without race (CKD-EPI-NR) equations, with 4-year all-cause mortality in patients with diabetes.

Research design and methods We analyzed a nationwide, centralized database of all adults diagnosed with diabetes assisted by the Colombian Health System between July 1, 2015, and June 30, 2019. Plasma creatinine was used to calculate baseline estimated glomerular filtration rate (eGFR) and classify each patient in a chronic kidney disease (CKD) stage, by each of the four equations. We used multivariate logistic regression to compare the association between CKD stage and mortality, and receiver operating characteristic (ROC) analyses to assess the overall association of eGFR by each equation and mortality.

Results The study included 758,219 patients (58% female, 7.2% black race, mean age 62.3, Glycated hemoglobin A1c [HbA1c] 7.4%). There were 35,296 deaths over the study follow-up. Considering eGFR by each equation as a continuous variable, the odds of death decreased by 1.1%–1.5% for each additional mL/min. Compared with CKD stage 1 of each equation, being placed in CKD stages 3a, 3b, or 4 by MDRD or CKD-EPI-NR was associated with greater odds of death than being categorized in the same stages by CKD-EPI. Among patients of black race, the adjusted OR of mortality for CKD stage 4 relative to stage 1 was 4.63 (95% CI 3.39 to 6.35) for MDRD, 3.66 (2.85 to 4.69) for CKD-EPI-NR, 3.01 (2.38 to 3.81) for CKD-EPI, and 2.82 (2.29 to 3.49) for Cockcroft-Gault. The area under the ROC curve to discriminate by survival status was greatest for MDRD, followed by CKD-EPI-NR, CKD-EPI, and Cockcroft-Gault, in that order ($p<0.001$ for all differences).

Conclusions Compared with other eGFR equations, MDRD showed the strongest association with all-cause mortality in a sample of Latin-American patients with diabetes. This difference was most pronounced among patients of black race.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The association of estimated glomerular filtration rate (eGFR) equations with death and other clinical outcomes in patients with diabetes may differ across populations.

WHAT THIS STUDY ADDS

⇒ In a nationwide study of patients with diabetes in Colombia, Modification of Diet in Renal Disease study (MDRD) showed the strongest association with 4-year mortality, especially among patients of black race.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Regular and universal assessment of eGFR with the MDRD equation may help improve clinical outcomes for patients with diabetes in Latin America.

INTRODUCTION

Diabetes is associated with an increased risk of death,[1] and the coexistence of diabetes and reduced renal glomerular filtration rate further increases such mortality.[2] Also, decreases in estimated glomerular filtration rate (eGFR) over time are associated with higher risk for all-cause mortality independent of initial eGFR and other mortality risk factors at baseline.[3] The association between eGFR loss and mortality is independent of the appearance of the urinary albumin excretion rate, as recently reported in an 8-year community-based study.[4]

Over time, several equations have been developed to estimate glomerular filtration rate (GFR), usually in large studies in which GFR is directly measured by a reference method and regression techniques are employed to predict GFR from plasma biomarkers and demographic factors. Due to its widespread availability and low cost, the most extensively used biomarker is serum creatinine, although adoption of cystatin C is increasing rapidly due to its more accurate performance.[5] Historically, the main focus in the development of these equations has been to minimize the bias of the estimates. Nonetheless, the ability of each eGFR equation

to predict adverse clinical outcomes among patients with diabetes is not necessarily an exact parallel of their GFR-estimating accuracy and may vary substantially across populations. For example, despite better performance in terms of estimating GFR, equations based on both cystatin C and creatinine do not predict mortality as well as equations based on cystatin C alone.[6] Also, the accuracy of each equation is influenced by glomerular function, for example, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) has improved accuracy over the Modification of Diet in Renal Disease study (MDRD) equation at higher eGFR values and in individuals without diabetes.[7]

A very large meta-analysis published a decade ago found that the CKD-EPI equation more accurately categorized the risk for mortality than the MDRD equation across a broad range of populations.[8] However, later studies have found that the performance of eGFR equations on predicting mortality can very much depend on the specific population: A direct comparison of five eGFR equations among patients with diabetes in China found that the 'CKD-EPI Chinese T2DM equation' provided better discrimination in terms of all-cause mortality compared with the standard CKD-EPI equation.[9]

There is very little information on the comparative performance of GFR-estimating equations to identify mortality risk among Latin-American patients with diabetes. For this reason, we undertook a nationwide study of the association between GFR estimated by four different creatinine-based eGFR equations and all-cause mortality among patients diagnosed with diabetes in Colombia.

METHODS

Data sources

For this study, we analyzed data from the Colombian National Registry of Chronic Kidney Disease (NRCKD), a curated, administrative database of all individuals who have been diagnosed with diabetes, hypertension, or chronic kidney disease (CKD) in the Colombian Health System.[10] The NRCKD is administered by the Colombian Fund for High-Cost Diseases ('Fondo Colombiano de Enfermedades de Alto Costo'—in Spanish). This registry was established after a law emitted by the Colombian Ministry of Health in 2008 mandated public and private insurers to report to a centralized database, the NRCKD, a series of pre-established variables in a standardized format, for all eligible patients. Data must be reported by June 30 of each year; hence, each observation period begins on July 1 of the preceding year. Each data point recorded in the database corresponds to the final measurement taken during the observation period for a particular individual. The Colombian Health System has a coverage above 99% of the total population; therefore, the NRCKD has a nationwide scope. The quality and completeness of the data is ensured through a multistep process that includes an initial algorithm designed to identify any errors in the reporting process.[11] Afterwards, a team of experienced professionals conducts a rigorous data monitoring process comparing the reported information with clinical records in a representative sample of cases stratified by hypertension, diabetes, and CKD status. If any inconsistencies are detected, the correct data are retrieved from the clinical records.

Variables

This study uses data from the NRCKD in the period comprised between July 1, 2015, and June 30, 2019. Only adult patients (age >=18 at the start of each observation year) were included. Diagnosis of diabetes or hypertension was analyzed as reported to the NRCKD by the treating physician (Y/N).

Data on date of birth, sex, ethnicity, insurance type, weight, height, and laboratory results were obtained from the NRCKD. Body mass index (BMI) was categorized according to the guidelines established by the WHO.[12] Plasma creatinine values were used to calculate the eGFR using the Cockcroft-Gault,[13] Modification of Diet for Renal Disease (MDRD),[14] Chronic Kidney Disease Epidemiology (CKD-EPI)[15] and the new CKD-EPI without race (CKD-EPI-NR)[16] equations. The NRCKD collects data from multiple hospitals and health centers, but the National Health of Ministry Guidelines for the Management of Chronic Kidney Disease indicates that all commercially available assays in the country should be traceable to the isotope dilution mass spectrometry (IDMS) standard.[17]

From the baseline GFR estimated using the different methods, each patient was classified in a CKD stage according to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.[18] Thus, CKD stages were defined as stage 1: eGFR ≥90 mL/min/1.73 m^2; stage 2: eGFR ≥60 and <90 mL/min/1.73 m^2; stage 3a: eGFR ≥45 and <60 mL/min/1.73 m^2; stage 3b: eGFR ≥30 and <45 mL/min/1.73 m^2; stage 4: eGFR ≥15 and <30 mL/min/1.73 m^2; and stage 5: eGFR <15 mL/min/1.73 m^2. Each patient could be classified in different stages by different equations. Insurance type was classified into three categories (third-party payer, state insurance and special/exceptional health insurance -security forces and employees of some public universities-).[19] The NRCKD self-reported race categories 'Raizal', 'Palenquero', and 'Black, Mulatto, Afro-Colombian, or of African descent' were combined into a single category referred to as 'Black', we analyzed race as Black versus all other categories. This was decided because the number of individuals belonging to other race categories, such as indigenous or Roma, accounted for <1% in any given year.[20]

Data analysis

For baseline clinical and demographic characteristics, quantitative variables are presented as means and SDs, whereas categorical variables are presented as absolute and relative frequencies. The primary outcome for all analyses was death from any cause, inferred from the

variable 'date of death' in the NRCKD. This variable was reported by insurers as the date listed on the death certificate if the patient died during the registry cycle or year, or as missing if the patient was still alive. The accuracy of this information was cross-checked against the data warehouse of The Social Protection Integrated Information System (SISPRO) of the Colombian Ministry of Health and Social Protection. If there were any discrepancies, the official national database of death certificates was consulted.

The association between CKD stage as determined by each equation, and death from any cause, was evaluated using multivariable binomial logistic regression models. eGFR was introduced in models either as a continuous predictor in its original units, or as an ordinal variable with indicator variables corresponding to the KDIGO stages. The reference category was always KDIGO stage 1. All models were adjusted for age, type of health insurance, and baseline BMI. We also conducted stratified analyses to explore how CKD stage was related to mortality in subgroups defined by race (black vs all other) for each eGFR equation. All associations are expressed as ORs with 95% CIs. In the last set of analyses, we compared the overall capacity to predict death between eGFR equations using receiver operating characteristic (ROC) analyses, with the eGFR value as continuous classifier and death status as dichotomous outcome. We calculated the area under the curve (AUC) and determined the significance of the differences seen in AUC between each equation and the Cockcroft-Gault equation as reference. As with logistic regressions, we performed ROC analyses stratified by race. All statistical analyses were carried out in Stata V.17 (StataCorp LP). All hypotheses were tested at a two-tailed significance level of 5% (0.05).

Ethical considerations

This study involved only anonymized secondary data sources which did not allow disclosure of any private information that could lead to the identification of individuals. To maintain privacy, a database-specific individual identification system was used to anonymize data. The confidentiality of the information was maintained throughout the data processing (reporting, managing and analysis) to ensure the privacy of the patients. According to Colombian legislation (resolution 8430 of 1993 by the Colombian Ministry of Health), this study classifies as investigation without risk, and no informed consent was necessary. Because the study involved only secondary retrospective analyses of an anonymized database, it did not qualify as human subjects research as was exempted from Internal Review Board (IRB) review.

RESULTS

We studied a total of 758,219 adults with diabetes. Fifty-eight per cent of the participants were female, baseline mean age was 62.3 years (table 1). Close to three-fourths of the study participants had third-party insurance and one-fourth had state insurance. Patients of black race represented 7.2% of the study sample, and about one-third of patients had a BMI in the obesity range. Remarkably, the prevalence of obesity was 7.9 percentage points higher among women than men. The mean glycated hemoglobin A1c (HbA1c) was 7.44% (57 mmol/mol). Participants in CKD stages 1 or 2 added up to 85% of the sample. About a quarter of participants had a urinary albumin excretion rate (UAER) above 30 mg/g of creatinine or 20 mg/L of urine. Additionally, 75.3% of the patients had a prior diagnosis of hypertension.

Distribution of patients in CKD stages by different equations

In general, CKD-EPI tended to classify a larger proportion of patients in more advanced CKD stages (figure 1). This difference was most accentuated for stage 5: CKD-EPI with or without race classified 10 times more individuals in this category compared with MDRD or Cockcroft-Gault. On the other hand, MDRD was the equation that classified the least patients in advanced CKD stages (4 or 5).

Association between eGFR by different equations and mortality

During the four observational years of the study, 35,296 participants died (cumulative total mortality 4.66%). For all equations, each additional mL/min of eGFR was associated with significantly lower odds of death (1.1%–1.5% lower). Nonetheless, the extent of the increase in mortality as CKD stage progressed was different among equations. Being placed in CKD stages 3a, 3b, or 4 by MDRD or CKD-EPI-NR was associated with greater odds of death than being categorized in the same stages by CKD-EPI (figure 2).

Association between eGFR and mortality, by race

As seen in figure 3, classification in more advanced CKD stages by MDRD showed a clearly stronger association with death among patients of black race. The difference was specially marked for stage 4, but was also evident for stages 3a and 3b. Relative to patients in CKD stage 1, the OR of mortality for those in stage 4 was 4.63 (95% CI 3.39 to 6.35) for MDRD, 3.66 (2.85 to 4.69) for CKD-EPI-NR, 3.01 (2.38 to 3.81) for CKD-EPI, and 2.82 (2.29 to 3.49) for Cockcroft-Gault. For patients of all other races, MDRD and CKD-EPI-NR had a very similar performance, while CKD-EPI exhibited a weaker association with mortality.

Comparison of the equations' ability to predict death using ROC analysis

For the complete study sample, the area under the ROC curve to discriminate by survival status was greatest for MDRD, followed by CKD-EPI-NR, CKD-EPI, and Cockcroft-Gault, in that order ($p<0.001$ for all differences, table 2). Among patients of black race only, ROC analyses also indicated superiority of MDRD, followed by CKD-EPI, CKD-EPI-NR, and again in the last place Cockcroft-Gault (absolute AUC difference vs MDRD 1.6% to 6.4%, $p<0.001$ for all pairwise differences). For

Table 1 Baseline characteristics of study participants

	Men (n=312,647)	Women (n=445,572)	Total (n=758,219)
Age (years)	61.5 (12.6)	62.9 (12.5)	62.3 (12.6)
Age group (%)			
<40	4.8	3.8	4.2
40–49	11.7	9.6	10.4
50–59	25.6	23.4	25.5
60–69	30.8	30.4	30.6
70–79	20.0	21.6	21.0
>=80	7.1	9.3	8.4
Health insurance (%)			
Third party	78.8	68.6	72.8
State	20.4	30.8	26.5
Special/exceptional	0.9	0.6	0.7
Race (%)			
Black	7.0	7.3	7.2
Other	93.0	92.7	92.9
n for body mass index	312 621	445 514	758 135
BMI (kg/m^2)	27.7 (4.6)	28.6 (5.6)	28.2 (5.2)
BMI category (%)			
Normal weight	27.3	26.5	26.8
Overweight	44.8	37.7	40.6
Obesity	27.9	35.8	32.6
n for blood pressure	312 066	445 043	757 109
SBP (mm Hg)	124.0 (13.7)	124.3 (13.9)	124.2 (13.8)
DBP (mm Hg)	76.6 (8.6)	76.5 (8.5)	76.6 (8.5)
n for HbA1c	284 260	394 391	678 651
HbA1c (%)	7.46 (2.0)	7.42 (2.0)	7.44 (2.0)
HbA1c (mmol/mol)	58	57	57
n for blood lipids	293 103	419 567	712 670
Non-HDLc (mg/dL)	137.1 (45.1)	144.8 (46.3)	141.6 (46.0)
LDLc (mg/dL)	103.3 (37.7)	110.9 (39.6)	107.8 (39.0)
CKD stage (%)*			
1	47.3	41.7	44.0
2	39.6	42.0	41.0
3a	8.0	11.2	9.9
3b	2.9	3.5	3.2
4	0.9	0.9	0.9
5	1.3	0.7	1.3
Urinary albumin excretion (%)			
<30 mg/g or <20 mg/L	71.1	78.7	75.5
30–299 mg/g or 20–199 mg/L	23.4	17.8	20.2
>=300 mg/g or >=200 mg/L	5.5	3.6	3.4
Hypertension (%)	71.3	78.1	75.3

Data are means (SD) unless indicated otherwise.
*As reported by the treating physician to the NRCKD.
CKD, stages were defined according to the KDIGO classification; DBP, diastolic blood pressure; KDIGO, Kidney Disease: Improving Global Outcomes; LDLc, low-density lipoproteins cholesterol; non-HDLc, non-high density lipoproteins cholesterol; NRCKD, Colombian National Registry of Chronic Kidney Disease; SBP, systolic blood pressure.

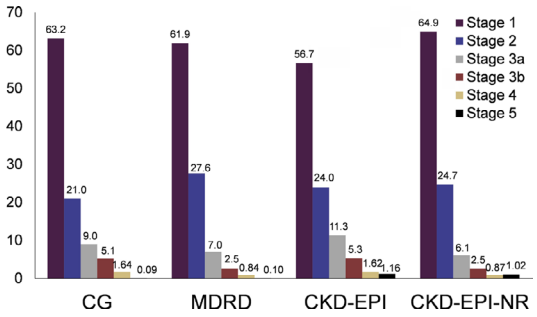

Figure 1 Distribution of study participants in chronic kidney disease (CKD) stages, according to each estimated glomerular filtration rate equation. CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CKD-EPI-NR, Chronic Kidney Disease Epidemiology Collaboration without race; MDRD, Modification of Diet in Renal Disease study.

patients of other races, MDRD also performed significantly better than any of the other equations by a smaller, yet significant margin (AUC 1.0% to 3.2% higher for MDRD, p<0.001 for all differences).

Sensitivity analyses

In order to confirm that our results would not be modified by other confounding variables, we performed sensitivity analyses in which all logistic models were additionally adjusted by baseline HbA1c, non-high-density lipoproteins cholesterol, urinary albumin excretion rate and systolic blood pressure. The results continued to show that being placed in CKD stages 3a, 3b, or 4 by MDRD or CKD-EPI-NR was associated with greater odds of death than being categorized in the same stages by CKD-EPI. Among patients of black race, classification in more advanced CKD stages by MDRD continued to show a stronger association with death, with a more marked difference for stage 4 (OR vs stage 1 for MDRD: 4.27 (2.75 to 6.62), for Cockcroft-Gault: 2.67 (1.98 to 3.59), for CKD-EPI: 3.13 (2.31 to 4.24), for CKD-EPI-NR: 3.40 (2.42 to 4.78)).

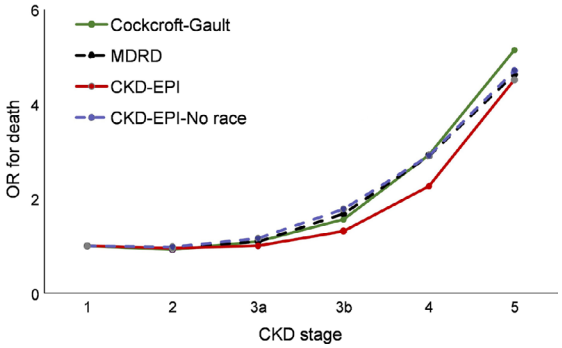

Figure 2 Association between chronic kidney disease (CKD) stage, according to each estimated glomerular filtration rate equation, and all-cause mortality. Data are ORs compared with participants classified in CKD stage 1 by each equation, adjusted for age, insurance type and baseline body mass index. CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; MDRD, Modification of Diet in Renal Disease study.

DISCUSSION

In this nationwide study of patients diagnosed with diabetes, we compared the magnitude of the association of eGFR estimated with four different equations (Cockcroft-Gault, MDRD, CKD-EPI or CKD-EPI-NR) with 4-year all-cause mortality. We found that overall, MDRD had the strongest association with death, either when patients were classified in KDIGO stages based on MDRD eGFR, or when the overall discriminative capacity of the four equations was compared using ROC analysis.

These are clinically relevant results because they may influence the decision about which equation to use when caring for Latin-American patients with diabetes. In addition to the use of different biomarkers or their combinations for the estimation of GFR, the mathematical expression employed may have a relevant influence on the performance of eGFR to predict not just advanced CKD, but also death and other serious adverse clinical outcomes in patients with diabetes. For example, an analysis of data from the US National Health and Nutrition Survey (NHANES) found the CKD-EPI-based calculation of eGFR to better predict the risk of death, as compared with the MDRD-based calculation, or to serum creatinine concentrations.[21] Similarly, a study in Italy found the CKD-EPI eGFR to better stratify patients with diabetes according to their total and cardiovascular mortality risk.[22] The contrast between these results and ours highlights the different performance of eGFR equations when applied to different populations.

The finding that in our sample more advanced CKD stages according to CKD-EPI showed a relatively weaker association with death may be related to the fact that this equation classified a much larger proportion of patients as having advanced CKD. Hence, many lower risk subjects could have been classified in these stages, which resulted in a lower OR. Other studies have found large discrepancies in the proportion of individuals being classified as having advanced CKD depending on the eGFR equation employed.[23]

The difference between MDRD and the other equations in terms of association with death was much larger among patients of black race, providing support for the use of this equation in black Latin-American patients. Unexpectedly, even in black patients, the CKD-EPI equation that does not include race had a stronger association with mortality than the original version with race. One prior study in Brazil had found the use of CKD-EPI equations without race/ethnicity adjustment to be more appropriate for the Brazilian population.[24] This finding may have major implications, as patients of African descent tend to have a lower overall prevalence of CKD,[25] but a higher incidence of end-stage renal disease[26]

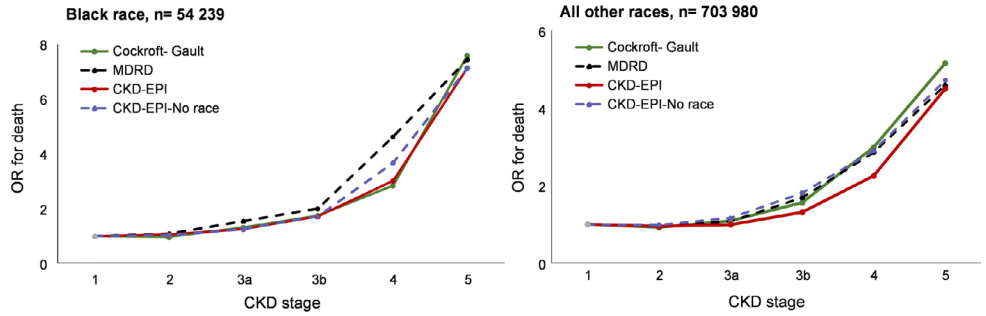

Figure 3 Association between chronic kidney disease (CKD) stage, according to each estimated glomerular filtration rate equation, and all-cause mortality, by race. Data are ORs compared with participants classified in CKD stage 1 by each equation, adjusted for age, insurance type and baseline body-mass index. CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; MDRD, Modification of Diet in Renal Disease study.

compared with other races. Many biological and social factors have been postulated to explain this apparent paradox, but imprecision in GFR estimation with race adaptation could be one contributor. Recent evidence suggests that the use of cystatin C for eGFR estimation in black patients may provide an even better prediction of the end-stage renal failure and mortality risk associated with low eGFR.[27]

Implications

Our results have clinical implications for professionals treating patients with diabetes in Colombia and other countries of similar demographics, especially countries with a sizeable population of African origin. First, they highlight the importance of always performing a thorough evaluation of renal function since diabetes diagnosis, including but not restricted to eGFR. Second, they suggest that in such context the estimation of GFR with MDRD may provide a more accurate estimation of mortality risk, so that even if less patients are classified in more advanced CKD stages, the limited resources available in our countries will be better focalized to those patients who really are at increased risk.

It is also important to highlight that eGFR is only one of a portfolio of CKD risk assessment tools that frequently must include other markers such as urinary albumin/creatinine ratio, cystatin C, 24-hour urinary albumin excretion and others. Thus, it is not possible to expect a single marker to perform well in all patients.

In terms of directions for future research, our results can be expanded and complemented by longer follow-up of the Colombian population, by the replication of our analyses in other Latin-American countries and/or by the incorporation of new and emerging CKD markers. Nonetheless, they do encourage the routine assessment of renal function and inform the choice of the tool to do so.

Strengths and limitations

Our study involved a nationwide sample, and laboratory and demographic variables were obtained from a centralized, curated database of all patients diagnosed with diabetes in Colombia. The primary endpoint of all-cause death is unequivocal, and the survival status of each participant was ascertained against official sources. Despite the potential limitations of self-reported race, previous studies have demonstrated a consistent association between

Table 2 ROC analyses, comparison versus Cockcroft-Gault equation, by race

	Race					
	Black		Other		All participants	
eGFR equation	AUC	P value vs Cockcroft-Gault	AUC	P value vs Cockcroft-Gault	AUC	P value vs Cockcroft-Gault
Cockcroft-Gault	0.327	–	0.395	–	0.392	–
MDRD	0.391	<0.001	0.427	<0.001	0.423	<0.001
CKD-EPI	0.375	<0.001	0.417	<0.001	0.414	<0.001
CKD-EPI-NR	0.371	<0.001	0.420	<0.001	0.418	<0.001

AUC, area under the ROC curve; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CKD-EPI-NR, Chronic Kidney Disease Epidemiology Collaboration without race; eGFR, estimated glomerular filtration rate ; MDRD, Modification of Diet in Renal Disease study; ROC, receiver operating characteristic.

self-reported race and health outcomes in Colombia.[28] Even though a 4-year follow-up might be insufficient to evaluate association between exposures like eGFR and mortality, the sample size was large enough to allow us to reveal existing differences in the association of the different eGFR equations with mortality. One relevant limitation is the absence of cystatin C measurements to perform a comparison of the equations using this newer biomarker. However, the penetration of this test in the Colombian system is still very low and did not permit us to undertake such analyses. Finally, our study is subject to the limitations of all routinely collected data studies, in which the data were not initially collected to answer the specific research question.

In summary, our results suggest that GFR estimated with the MDRD equation may have a stronger association with all-cause mortality in Latin-American patients with diabetes, especially if they are of black race.

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Contributors COM acts as guarantor of the article's content, conceived the study, performed data analyses, supervised project activities and participated in the writing and critical assessment of the manuscript. SG-G performed data analyses and participated in the writing and critical assessment of the manuscript. LJH-P performed data analyses and participated in the writing and critical assessment of the manuscript. JAHV performed data analyses and participated in the writing and critical assessment of the manuscript. NR-G performed data analyses and participated in the writing and critical assessment of the manuscript. LA-M performed data analyses and participated in the writing and critical assessment of the manuscript.

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VIH/sida

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Cuenta de Alto Costo

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Enfermedades de Alto Costo

VIH

Factors associated with coronary artery disease among people living with human immunodeficiency virus: Results from the Colombian HIV/AIDS registry

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Trabajo colaborativo con la academia (Fundación del Caribe para la Investigación Biomédica) y las sociedades científicas (Sociedad Colombiana de Cardiología) como actores de interés.

Objetivo: evaluar los factores asociados a la presencia de enfermedad coronaria en las personas que contrajeron la infección por el VIH en el marco del aseguramiento colombiano entre 2018 y 2021.

Principales hallazgos:

- Entre las 36.483 personas viviendo con el VIH, 196 presentaron enfermedad coronaria, lo que corresponde a una prevalencia del 0,53%.
- Se observó una alta frecuencia de factores de riesgo cardiovascular clásicos en las personas que viven con el VIH en Colombia. Entre ellos se destacan la elevación del LDL-c (87%), la hipertrigliceridemia (74%) y el sobrepeso u obesidad (28%).
- La edad mayor a 50 años, el sexo masculino, la obesidad, la diabetes, la disfunción renal y la presencia de condiciones definitorias de sida se asociaron con una mayor posibilidad de tener enfermedad coronaria en las personas que viven con el VIH.
- En las personas mayores a 50 años que viven con el VIH, factores de riesgo cardiovascular clásicos como el sexo masculino o las comorbilidades se asociaron con una mayor frecuencia de enfermedad coronaria. Mientras que, en los menores de 50 años, aquellos con historia de condiciones definitorias del sida tuvieron una mayor posibilidad de presentarla.

Relevancia de los hallazgos:

- Estos resultados contribuyen a la identificación y seguimiento oportunos de los factores de riesgo en las personas que viven con el VIH y son un punto de partida para desarrollar intervenciones integrales en los que tienen mayor riesgo de presentar enfermedad coronaria.

Comentario del autor experto:

Dr. Manuel Urina Jassir

La enfermedad cardiovascular (ECV) es una de las principales causas de morbilidad y mortalidad en las personas que viven con el virus de la inmunodeficiencia humana (VIH). En el artículo "*Factors associated with coronary artery disease among people living with human immunodeficiency virus: Results from the Colombian HIV/AIDS registry*" publicado en la revista International *Journal of Cardiology Cardiovascular Risk and Prevention*, se analizaron los factores asociados a la enfermedad coronaria de las personas que viven con VIH con los datos de la Cuenta de Alto Costo. En este artículo, se describe que factores como el género, la edad, la obesidad, la diabetes mellitus y la enfermedad renal crónica aumentaban la probabilidad de tener enfermedad coronaria. Estos hallazgos son claves para una identificación temprana de aquellos que están en un mayor riesgo de ECV por lo que sirven como base para desarrollar estrategias preventivas y de seguimiento, tanto a nivel individual como de salud pública, predicción, prevención y tratamiento, incluyendo el trasplante anticipado a la diálisis y el ingreso programado TRR. Más detalles en el documento completo.

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Factors associated with coronary artery disease among people living with human immunodeficiency virus: Results from the Colombian HIV/AIDS registry

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ABSTRACT

Background: People living with HIV (PLWHIV) are at a higher risk of developing coronary artery disease (CAD). We aimed to assess the factors associated with CAD among PLWHIV in Colombia.
Methods: We conducted a retrospective cohort study based on adults newly diagnosed with HIV, reported to the Colombian HIV/AIDS registry from 2018 to 2021. Baseline demographic and clinical characteristics were compared by age (<50 and ≥ 50 years). Our main outcome was the presence of CAD. Logistic regression models were used to assess the association between traditional and HIV-related factors with CAD. These associations were also evaluated in stratified models by age. Effect measures were odds ratios (OR) and their 95% confidence intervals.
Results: Among 36,483 PLWHIV, the frequency of CAD was 0.53% (n = 196). There was a high prevalence of impaired fasting glucose/diabetes mellitus (12.62%), overweight/obesity (27.79%), elevated LDL-c (86.69%), and hypertriglyceridemia (72.76%). Factors associated with CAD included male gender (OR: 2.01, 95% CI: 1.12–3.58), age ≥50 years (OR: 4.96, 95% CI: 3.29–7.45), lipoatrophy or lipodystrophy (OR 5.12, 95% CI: 1.12–23.33), AIDS-defining conditions (OR: 1.83, 95% CI: 1.07–3.12), obesity (OR: 2.95, 95% CI: 1.69–5.10), diabetes mellitus (OR: 2.50, 95% CI: 1.25–4.97), and renal impairment (OR: 3.15, 95% CI: 1.83–5.42).
Conclusions: Traditional CAD risk factors are common in PLWHIV. There were traditional and disease-specific factors associated with increased odds of CAD. These findings may aid clinicians and decision-makers in reducing the impact of CAD in PLWHIV.

1. Introduction

People living with HIV (PLWHIV) have improved their life expectancy due to effective antiretroviral therapy (ART), shifting to a chronic course with an increased risk of non-communicable conditions such as cardiovascular diseases (CVDs) [1,2]. PLWHIV are at a higher risk of developing coronary artery disease (CAD) [2,3]. A meta-analysis including 80 studies and 793,635 subjects estimated a crude incidence of CVD of 61.8 (95% CI, 45.8–83.4) per 10,000 person-years among PLWHIV. Additionally, these authors identified a 2-fold increase in the risk of developing CVD when compared to people without HIV [4]. Furthermore, there has been an increased burden due to CVDs among PLWHIV throughout the last decades [4,5]. Despite falling overall mortality rates, an analysis of a nationwide database in the United States

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[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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found a significant increase in CVD-related mortality from 1999 to 2013 [5].

Multiple factors may increase the risk of CAD and CVD in this population. These can be classified as HIV-related and ART-related factors in addition to the traditional CVD risk factors [3]. Within the first group, lower CD4 cell counts were described as a predictive factor in a Brazilian cohort study [6]. Additionally, a combination of ART including abacavir (e.g., abacavir-lamivudine-darunavir) has been associated with a higher risk of acute myocardial infarction [7]. Moreover, known atherogenic risk factors, including increased low-density lipoprotein cholesterol (LDL-c), diabetes mellitus (DM), and obesity are also highly prevalent in PLWHIV [8,9].

Recognizing the predictors associated with an even higher risk of CAD is crucial. This will be useful for the early identification of PLWHIV which requires clinicians and healthcare systems to develop tailored preventive and surveillance strategies to reduce CAD-related morbidity and mortality. Thus, our study sought to assess the factors associated with CAD among incident cases of HIV/AIDS in a large, nationwide, and real-world database in Colombia.

2. Methods

2.1. Study design and population

A retrospective cohort study based on data obtained from the Colombian Registry of HIV/AIDS was conducted. The information, structure, and management of the registry have been published elsewhere [10]. In short, this is an administrative registry managed by the High-Cost Diseases Fund (CAC, in Spanish) since 2012 by a resolution of the Colombian Ministry of Health and Social Protection [11]. In this registry, all health insurers and providers throughout Colombia are required to report the data of PLWHIV and those at risk (e.g., pregnant women, and people with active tuberculosis [TB]) within the framework of the health system [10,11]. Importantly, the registry has a national scope as 97–99% of Colombian citizens are affiliated with the health system [12].

The data collected are extracted from medical records by the insurers and providers and subsequently, uploaded to a health interoperability platform. These data include demographic, clinical (e.g., AIDS-defining conditions), ART-related, prevention interventions (e.g., prophylaxis, STD prevention), and administrative variables. Moreover, the registry undergoes a strict data-monitoring process to validate the reported data with the clinical records and correct them in case of inconsistencies. Lastly, confidentiality is assured by anonymization of the records from each subject with a unique identifier number and by limiting access to the database to authorized people only [10].

2.2. Eligibility criteria

We included adults (≥18 years old) that were reported to the registry as incident cases of HIV (at any stage) from February 1st, 2018, to January 31st, 2021. Those with unclear HIV diagnosis (ruled out infection, under evaluation, or without HIV testing) and pregnant women were excluded from the analysis.

2.3. Study variables and definitions

Demographic variables included age, sex, self-reported ethnicity, health insurance, and region of residence. We classified our variables into three main categories: HIV-related, ART-related, and traditional CVD risk factors. From the former, we assessed the following, viral load, and CDC 2014 clinical stage at diagnosis [13]. Also, we evaluated the presence of hepatitis C, hepatitis B, TB coinfection (including treatment), AIDS-defining infections or malignancies, lipoatrophy/lipodystrophy, and initial ART divided by class (nucleoside analog reverse transcriptase inhibitors [NRTIs], non-nucleoside analog reverse transcriptase inhibitors [NNRTIs], protease inhibitors [PIs], integrase inhibitors, fusion inhibitors, or coreceptor antagonist).

Regarding CVD risk factors, data on fasting plasma glucose (FPG), LDL-c, triglycerides (TG), and weight/height were obtained from the registry. FPG levels were classified as normal (<100 mg/dL), impaired fasting glucose (IFG; 100–125 mg/dL), and DM (≥126 mg/dL) [14]. LDL-c levels were divided into normal (<130 mg/dL) and abnormal or elevated (≥130 mg/dL), based on the Colombian Association of Infectious Diseases (ACIN, its acronym in Spanish) consensus on CVD risk where 130–159 mg/dL is considered "borderline high" [15]. Hypertriglyceridemia was defined as TG levels ≥175 mg/dL [16]. Body mass index (BMI) was calculated based on weight and height and classified according to the World Health Organization (WHO) as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obesity (≥30 kg/m^2) [17].

The Framingham Risk Score (FRS) adjusted to the Colombian population (i.e., FRS times a factor of 0.75) [15,18] was calculated by their treating physician and its result (in percentage) was reported to the registry. We classified the CVD risk into three categories, low (<10%), intermediate (10–20%), and high-risk (≥20%) [19]. Lastly, other laboratories available were hemoglobin (gr/dL), alanine aminotransferase (ALT; UI/L), and glomerular filtration rate (GFR) based on creatinine levels using the CKD-EPI formula (mL/min/1.73 m^2) [20].

2.4. Outcome

The main outcome was CAD, reported to the registry as its presence or absence at the cohort entry, or its development during the follow-up, according to the clinical records. This information is commonly sent to the registry as a diagnosis of "coronary artery disease", "cardiovascular disease", "ischemic cardiomyopathy", "previous infarction", or "myocardial infarction". It is then grouped as "coronary artery disease" and validated/audited by the registry team.

2.5. Statistical analysis

Descriptive statistics were used for baseline demographic and clinical characteristics. According to the data distribution, continuous variables are presented as medians and interquartile ranges (IQR). Categorical variables are described with frequencies and percentages. Baseline characteristics were compared across age (<50 years and ≥50 years) using X^2 and Mann-Whitney U tests for qualitative and quantitative variables, respectively. To avoid the effect of group sizes on hypothesis tests, we also estimated absolute standardized differences (ASD), and values ≥ 10% were considered significant [21].

To identify the characteristics associated with CAD, we used a logistic regression model. Variables retrieved in the final model were selected following a combination of the statistical criterion and their clinical relevance. We also repeated the final model by age (<50 years and ≥50 years) as a sensitivity analysis to evaluate a potential effect modification. Effect measures were odds ratios (OR) and their 95% confidence intervals. A complete-case approach was used. Hosmer and Lemeshow's test evaluated the goodness of fit in this model. Statistical significance was set at a p-value ≤0.05. R version 4.2.0 [22] and RStudio [23] were used for statistical analyses.

2.6. Ethics declaration

This study was approved by Fundación del Caribe para la Investigación Biomédica's Ethics Committee (Record 0250 - May 24, 2022). We followed the Colombian Health Ministry (Resolution 8430 of 1993) and the Declaration of Helsinki research standards. The need for informed consent was waived considering the retrospective design which is based on secondary data sources (administrative registry). The Ministry of Health, as custodian of the information, authorizes the use of the information for research purposes on relevant topics for decision-

making in the country.

3. Results

3.1. Baseline characteristics

We analyzed 36,483 incident cases with CAD being reported in 196

Table 1
Baseline characteristics of the population studied by age groups in Colombia, 2018–2021.

Characteristic[a]	Total	≥50 years	<50 years	ASD[b](%)
	n = 36,483	n = 4395	n = 32,088	
Sex, male	31,379 (86.01)	3270 (74.40)	28,109 (87.60)	34.1
Self-reported ethnicity				6.7
Afro descendant	1975 (5.41)	299 (6.80)	1676 (5.22)	
Other	34,508 (94.59)	4096 (93.20)	30,412 (94.78)	
Health insurance				28.1
Third payer	21,328 (58.46)	2034 (46.28)	19,294 (60.13)	
State	13,570 (37.20)	2134 (48.56)	11,436 (35.64)	
Other	1585 (4.34)	227 (5.16)	1358 (4.23)	
Region of residence				24.0
Central	10,373 (28.43)	1359 (30.92)	9014 (28.09)	
Bogotá D.C.	8384 (22.98)	671 (15.27)	7713 (24.04)	
Caribbean	7099 (19.46)	1002 (22.80)	6097 (19.00)	
Pacific	5578 (15.29)	800 (18.20)	4778 (14.89)	
Eastern	4470 (12.25)	507 (11.54)	3963 (12.35)	
Amazonian	579 (1.59)	56 (1.27)	523 (1.63)	
Viral load at diagnosis[d]				2.7
Suppressed (<1000 copies/mL)	2298 (7.03)	251 (6.43)	2047 (7.11)	
Unsuppressed (>1000 copies/mL)	30,390 (92.97)	3650 (93.57)	26,740 (92.89)	
Clinical stage at diagnosis[d]				65.0
Stage 1	6352 (19.65)	322 (8.09)	6030 (21.27)	
Stage 2	12,749 (39.44)	972 (24.43)	11,777 (41.55)	
Stage 3	13,223 (40.91)	2684 (67.47)	10,539 (37.18)	
ART at diagnosis	32,187 (91.13)	3920 (92.08)	28,267 (91.00)	3.9
Current ART groups[d]				
NRTIs	32,035 (99.28)	3878 (98.90)	28,157 (99.34)	4.6
NNRTIS	20,033 (62.09)	2118 (54.02)	17,915 (63.20)	18.7
PIs	8949 (27.74)	1080 (27.54)	7869 (27.76)	0.5
Fusion inhibitors	3 (0.01)	0 (0.00)	3 (0.01)	1.5
Integrase inhibitors	3192 (9.89)	712 (18.16)	2480 (8.75)	27.8
CCR5 antagonist	2 (0.01)	0 (0.00)	2 (0.01)	1.2
HIV-related conditions[c]				
Lipoatrophy or lipodystrophy	74 (0.20)	17 (0.39)	57 (0.18)	4.0
Coinfection with chronic HBV or HCV	695 (1.91)	91 (2.07)	604 (1.88)	1.4
Previous TB	1423 (3.90)	313 (7.12)	1110 (3.46)	16.4
Anti-TB treatment,	1352 (5.10)	305 (9.60)	1047 (4.49)	20.1
AIDS-defining conditions	6758 (18.66)	1551 (35.66)	5207 (16.34)	45.2
Comorbidities[c]				
Cirrhosis	14 (0.04)	8 (0.18)	6 (0.02)	5.2
Chronic kidney disease	165 (0.45)	82 (1.87)	83 (0.26)	15.7
Cancer	180 (0.49)	49 (1.12)	131 (0.41)	8.1
Fasting plasma glucose[d]				39.8
Normal (<100 mg/dL)	27,350 (87.38)	2738 (74.28)	24,612 (89.13)	
Impaired fasting glucose (100–125 mg/dL)	3371 (10.77)	754 (20.46)	2617 (9.48)	
Diabetes (≥126 mg/dL)	580 (1.85)	194 (5.26)	386 (1.40)	
Hypertrigliceridemia[d]	23,772 (72.76)	2454 (63.51)	21,318 (74.00)	22.8
Abnormal LDL-c[d]	24,849 (86.69)	2802 (81.17)	22,047 (87.45)	17.3
Cardiovascular risk[e]				62.0
Low (<10%)	12,456 (96.06)	2049 (82.22)	10,407 (99.35)	
Intermediate (10–20%)	310 (2.39)	266 (10.67)	44 (0.42)	
High (>20%)	201 (1.55)	177 (7.10)	24 (0.23)	
Body mass index[c]				16.5
Underweight	3022 (8.54)	437 (10.32)	2585 (8.30)	
Normal	22,538 (63.67)	2398 (56.65)	20,140 (64.63)	
Overweight	8038 (22.71)	1128 (26.65)	6910 (22.17)	
Obesity	1798 (5.08)	270 (6.38)	1528 (4.90)	
Hemoglobin (gr/dL)[c]	15 (13.30–16.00)	13 (11.90–15.00)	15 (13.60–16.00)	66.7
ALT(IU/L)[c]	26 (18.00–40.00)	25 (18.00–38.00)	26 (18.00–41.00)	6.4
Glomerular Filtration Rate (ml/min/1.73m)[c]	109 (93.46–121.00)	86 (72.07–99.00)	113 (97.76–122.00)	122.0

Abbreviations: ALT: alanine transaminase, ART: antiretroviral therapy, HBV: hepatitis B virus, HCV: hepatitis C virus, LDL-c: low-density lipoprotein cholesterol, NNRTIs: non-nucleoside analog reverse transcriptase inhibitors, NRTIs: nucleoside analog reverse transcriptase inhibitors, PIs: protease inhibitors, TB: tuberculosis.
[a] Values are absolute values (percentages) for categorical variables. In the case of numeric variables, they correspond to the median (IQRs).
[b] Absolute standardized difference (ASD). Values higher than 10% were considered significant.
[c] Less than 10% missing values.
[d] 10–20% missing values.
[e] More than 20% missing values.

cases (0.53%). Overall, most were <50 years old (87.95%), male (86.01%), had third-payer insurance (58.46%), and lived between the Central region (28.43%) and Bogotá, D.C (22.98%). Viral load at diagnosis was unsuppressed (>1000 copies/mL) in 92.97% and slightly higher in people over 50 years. Stage 3 at diagnosis was seen in 40.91% of patients and was higher (67.47%) in ≥50 years old. The majority started ART after being diagnosed (91.13%) and the most common ART was NRTIs in 99.28%.

Globally, 18.66% had AIDS-defining conditions and a low percentage (<1%) had lipoatrophy/lipodystrophy; both were higher in subjects ≥50 years. The prevalence of comorbidities such as cirrhosis, chronic kidney disease (CKD), and cancer was less than 1%. Regarding the cardiometabolic profile, IFG/DM, overweight/obesity, and intermediate and high cardiovascular risk were more common in patients ≥50 years. On the contrary, a worse lipid profile was more frequent in younger patients.

Table 1 shows the characterization by age group. Significant differences were found in gender, health insurance, and region of residence. Clinical stage at diagnosis, AIDS-defining conditions, cardiovascular risk as well as LDL-c, TG, FPG, BMI, and GFR values were the main clinical variables with significant differences across groups.

3.2. Multivariable analysis to identify factors associated with CAD

A total of 22,125 (60.64%) patients had complete information and were included in multivariable analysis. The prevalence of CAD was 0.55%. Being male, age ≥50 years, lipoatrophy or lipodystrophy, the presence of AIDS-defining conditions, obesity, DM, and renal impairment (GFR ≤60 ml/min/1.73 m^2) were significantly associated with higher odds of CAD. Unexpectedly, patients with a viral load >1000 copies/mL at diagnosis had a significantly lower chance of CAD (Table 2).

In stratified models, among people aged ≥50 years, being male or having DM and renal impairment were significantly associated with increased odds of CAD, whereas in individuals <50 years, those with AIDS-defining conditions were more likely to develop CAD (Table S1).

4. Discussion

In this retrospective cohort study from the largest database of PLWHIV in Colombia, we identified a high prevalence of traditional CVD risk factors. Age ≥50 years, male gender, comorbidities such as obesity, DM and renal dysfunction, and AIDS-defining conditions were associated with higher odds of CAD in newly diagnosed cases.

Table 2
Multivariable-adjusted logistic model of coronary artery disease in Colombian adults newly diagnosed with HIV, 2018–2022.

Characteristic	OR	95% CI	*p*-value
Male versus female	2.01	1.12–3.58	0.018
Age ≥50 years versus <50	4.96	3.29–7.45	<0.001
Health insurance			
State versus third-payer	0.91	0.61–1.32	0.607
Other versus third-payer	0.65	0.19–2.08	0.465
Viral load at diagnosis unsuppressed (>1000 copies/mL) versus suppressed (<1000 copies/mL)	0.49	0.28–0.86	0.014
Clinical stage at diagnosis			
Stage 2 versus 1	0.88	0.51–1.50	0.645
Stage 3 versus 1	0.69	0.36–1.28	0.242
HIV-related conditions			
Lipoatrophy or lipodystrophy	5.12	1.12–23.33	0.035
AIDS-defining conditions	1.83	1.07–3.12	0.026
Obesity (BMI ≥30 kg/m^2)	2.95	1.69–5.10	<0.001
Diabetes Mellitus	2.50	1.25–4.97	0.009
Hypertrigliceridemia	1.32	0.87–1.98	0.189
Abnormal LDL-c, No	0.79	0.45–1.36	0.397
GFR ≤60 ml/min/1.73m^2 versus >60 ml/min/1.73m^2	3.15	1.83–5.42	<0.001

Abbreviations: BMI: body mass index, CI: confidence interval, GFR: glomerular filtration rate, OR: odds ratio, LDL-c: low-density lipoprotein cholesterol.

As described by other authors, regardless of the definitions and criteria used, we identified a high frequency of CAD risk factors in PLWHIV [8,24,25]. The Copenhagen Comorbidity Study described that PLWHIV had a higher risk of abdominal obesity, elevated LDL-c, and hypertriglyceridemia [8]. Consistent with this, we identified a high frequency of elevated LDL-c (87%), hypertriglyceridemia (73%), and overweight/obesity (28%). To an extent, these findings are aligned with those described by Cahn et al. in a cohort study among Latin American individuals where 80% out of 4010 PLWHIV had dyslipidemia [25]. Identifying the cardio-metabolic risk profile of PLWHIV in Colombia will raise awareness and support the lifestyle and pharmacological strategies needed to reduce the burden of disease associated with these risk factors, including CAD.

Moreover, the prevalence of these risk factors varied by age group. For instance, we identified that hypertriglyceridemia and elevated LDL-c were more frequent in those under 50 years. In the mentioned study by Cahn et al., where a high dyslipidemia rate was reported, most subjects were in the 28–47-year age group [25]. In contrast, other authors have described increased rates of dyslipidemia in older people [26]. These findings should alarm clinicians and public health institutions to tailor strategies specifically to young populations for the prevention of premature cardiovascular morbidity and mortality.

Regarding the outcome, we identified a relatively low frequency of CAD in incident cases of HIV. Others have described CVD prevalence as ranging from 1.7% to 8.4% [6,27,28]. In the HIV-Brazil Cohort Study, 1.7% of their population developed a cardiovascular event at a rate of 3.5 per 1000 person-years [6]. On the other hand, Delabays et al. utilizing data from the Swiss HIV Cohort Study, informed that 8.4% of 6373 PLWHIV developed atherosclerotic cardiovascular disease (ASCVD) [28]. Our results may differ due to methodological aspects such as a lack of data on other ASCVD events (e.g., stroke or cardiovascular death) and by having a relatively short follow-up period. Our research intends to be a starting point for new studies among Colombian and Latin American populations with prolonged follow-up periods and strict cardiovascular events definitions.

Our main aim was to identify accessible predictors or factors associated with CAD in PLWHIV to be used by clinicians in their daily practice. In that regard, demographical, traditional, and HIV-related factors were associated with a higher chance of having CAD in this population. As expected, and as described by other authors [6,28,29], age (≥50 years) and being a male increased the odds of CAD. Regarding traditional risk factors, the three variables that reached statistical significance were obesity, DM, and renal dysfunction, which are well-known CAD risk factors [30–32]. This is a worrisome finding considering the high frequency of these conditions among PLWHIV in this study and reported by other authors [8,33] which places a considerable number of PLWHIV at an even higher risk of developing CAD. In our analysis, we did not identify a significant effect of lipid profile abnormalities on CAD. However, other authors have described that, as in the population without HIV, dyslipidemia increases the risk of CAD [6,29]. Considering this, clinicians must actively screen, prevent, and treat these risk factors (DM, dyslipidemia, obesity, and chronic kidney disease) to lower the risk of developing CAD and further complications in this population.

Prior research has identified that HIV as a sole entity increases the risk of CVD [4], and some studies point out specific HIV-related variables associated with even higher risk [6,29,34]. In this cohort, AIDS-defining conditions were associated with a higher likelihood of CAD. Similarly, Mesquita et al. described an association between severe infections (bacterial, viral, fungal, or parasites) and CVD among PLWHIV in a hospital setting [35]. This may represent a clinical surrogate of inflammation, which has been one of the pathophysiological hypotheses related to developing CAD in this population [2,36].

Furthermore, an additional clinical factor associated with CAD was lipoatrophy/lipodystrophy, which is considered an HIV-related CVD risk-enhancing factor by recent guidelines [2].

Unexpectedly, an unsuppressed viral load at diagnosis was associated with lower odds of CAD. Delabays et al. reported that patients with ASCVD had lower viral load than those without an ASCVD [28]. This differs from other studies that have found no association between viral load and CAD/CVD [6,29]. More recently, a study utilizing longitudinal coronary computed tomography angiography identified that individuals with inadequate viral suppression were at a higher risk of progression of coronary artery stenosis [37]. In this analysis, the authors utilized multiple viral loads over time to assess viral suppression, while in our study we used a single measurement taken at diagnosis [37]. Overall, our findings suggest that identifying patients with advanced stages of HIV (AIDS-defining conditions) to provide closer follow-up and aiming for HIV/AIDS control/suppression is crucial for reducing the impact of CAD.

4.1. Strengths and limitations

Our study analyzed a large sample from a well-established nationwide administrative registry that allows us to perform statistical analysis with sufficient power and improves the generalizability of our results. In addition, all records were under a standardized data-monitoring process to ensure data quality and completeness.

This study is not without limitations. First, the registry includes the information reported by the providers and health insurers which could lead to possible underreporting or errors in the reporting of the study variables, including our outcome (CAD). However, as mentioned before, a strict data monitoring and auditing process aims to reduce this to the minimum. Second, even though the model had an adequate fit, the low frequency of CAD may affect the distribution of predictors across outcome groups. Moreover, patients with advanced disease at diagnosis might have had a shorter follow-up time, preventing the development or detection of CAD. Third, despite the clear evidence of lifestyle habits on the development of CAD, we could not evaluate the effect of smoking, diet, or physical activity as these are not collected in the registry. Further studies evaluating the longitudinal effect of these key factors are needed. Fourth, information on other known risk factors (e.g., hypertension, abdominal obesity) which could have an impact on CAD was lacking in the registry. Fifth, non-HIV-related-pharmacotherapy is not included in the registry, thus the effect of possible preventive medications such as lipid-lowering therapy was not assessed. Studies evaluating this relationship are also welcomed.

5. Conclusions

There is a high frequency of cardiovascular risk factors among incident PLWHIV in Colombia. CAD poses a major risk for morbidity in this population. We identified both traditional and non-traditional risk factors that are associated with CAD including age, gender, comorbidities such as obesity, DM, and renal dysfunction as well as lipoatrophy/lipodystrophy and AIDS-defining conditions. These results may serve as a starting point in developing strategies and interventions targeting those at a higher risk to develop CAD among PLWHIV and highlights the importance of early identification of comorbidities and risk classification in this population. Further studies with longer follow-ups that include other atherosclerotic cardiovascular outcomes are needed to further clarify the prevalence and incidence of ASCVD in PLWHIV.

Credit author statement

Manuel Urina-Jassir: Conceptualization, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Andrés Felipe Patiño-Aldana:** Conceptualization, Methodology, Formal analysis, Visualization, Writing – review & editing. **Lina Johana Herrera-Parra**: Conceptualization, Methodology, Formal analysis, Visualization, Validation, Writing – review & editing. **Juliana Alexandra Hernández Vargas**: Conceptualization, Methodology, Formal analysis, Visualization, Writing – review & editing. **Silvia Juliana Trujillo-Cáceres**: Conceptualization, Methodology, Formal analysis, Visualization, Writing – review & editing. **Ana María Valbuena-García**: Conceptualization, Methodology, Formal analysis, Visualization, Writing – review & editing, Supervision. **Lizbeth Acuña-Merchán**: Conceptualization, Methodology, Formal analysis, Visualization, Writing – review & editing, Supervision. **Daniela Urina-Jassir**: Conceptualization, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Miguel Urina-Triana**: Conceptualization, Methodology, Visualization, Writing – review & editing, Supervision.

Competing interests

The authors report no relationships that could be construed as a conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcrp.2023.200205.

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Cáncer

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Cáncer

Survival in stomach cancer: analysis of a national cancer information system and a population-based cancer registry in Colombia

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Trabajo colaborativo con el registro poblacional de cáncer de Cali.

Objetivo: evaluar la supervivencia del cáncer gástrico en Colombia (2014 - 2019) utilizando los datos del registro nacional de cáncer de la Cuenta de Alto Costo, y en Cali utilizando los datos del registro poblacional de cáncer de Cali (1998 - 2017).

Principales hallazgos:

- La supervivencia neta a 3 años de las personas con cáncer gástrico fue del 36,8% (IC 95%: 35,5 - 38,1). Esta fue mayor en personas del régimen especial (61,7%; IC 95%: 44,8 - 74,8) o contributivo (40,5%; IC 95%: 38,7 - 42,3).
- En el análisis multivariado se identificó un mayor riesgo de muerte en hombres, personas afiliadas al régimen subsidiado y diagnosticados en estadios avanzados.
- En Cali, la supervivencia neta a 5 años se mantuvo estable en los hombres durante los últimos 20 años. En las mujeres, tuvo un incremento del 50% comparado con el periodo 1998 - 2002.

Relevancia de los hallazgos:

- El análisis permite identificar poblaciones con mayor riesgo y permiten diseñar estrategias que permitan cerrar brechas en virtud del régimen de aseguramiento y el sexo para mejorar la equidad del sistema de salud colombiano.
- El monitoreo continuo de indicadores de supervivencia contribuye a la evaluación del impacto de los planes de atención del cáncer implementados en el país y guiar futuras intervenciones.

Comentario del autor experto:

Dr. Luis Eduardo Bravo

Stomach cancer is the leading cause of specific mortality in Colombia and Andean low-middle income countries in Latin America. In the paper "Survival in stomach cancer: analysis of a national cancer information system and a population-based cancer registry in Colombia" published in the Colombia Médica *Journal, stomach cancer survival was explored from two different but complementary data sources. Population survival estimates from the RPCC were lower than those observed in the NCIS. Gastric cancer survival in Colombia has a gap of at least 40 percentage points compared to countries that perform population-based screening. Gastric Cancer Net survival was higher in people with special insurance or third payer than state insurance, GC survival was higher in women and people diagnosed at early stages. Despite declining incidence and mortality, gastric cancer continues to present a significant clinical challenge because most cases are diagnosed in advanced stages with poor prognosis and limited treatment options. The Colombian government can use these survival indicators to monitor the gastric cancer control plan.*

Colombia Médica

ORIGINAL ARTICLE

Survival in stomach cancer: analysis of a national cancer information system and a population-based cancer registry in Colombia

Supervivencia del cáncer de estómago: análisis de un sistema de información nacional sobre el cáncer y de un registro de cáncer de base poblacional en Colombia

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Registros de cáncer, cáncer de estómago, análisis de supervivencia, epidemiología, Detección temprana de cáncer, Incidencia, Neoplasias de Estómago, Helicobacter pylori, Pronóstico.

Abstract

Background:

Stomach cancer is among the most frequent, is a leading cause of mortality in low- and middle-income countries. Assessing its survival is important to guide evidence-based health policies.

Aims:

To estimate stomach cancer survival in Colombia (2014-2019) with data from the National Cancer Information System (NCIS) and in Cali with data from the Cali Population Cancer Registry (RPCC) (1998-2017).

Methods:

NCIS estimated the overall 3-year net survival for 8,549 people, while RPCC estimated 5-year net survival for 6,776 people.

Results:

The 3-year net survival was 36.8% (95% CI: 35.5-38.1). Net survival was higher in people with special insurance (61.7%; 95% CI: 44.8-74.8) or third payer (40.5%; 95% CI: 38.7-42.3) than state insurance (30.7%; 95% CI: 28.7-32.8). It was also higher in women and people diagnosed at early stages. Multivariable analysis showed consistency with survival estimations with a higher risk of death in men, people with state insurance, and diagnosed at advanced stages. In Cali, the 5-year net survival remained stable in men during the last 20 years. In women the 5-year net survival in women increased 8.60 percentage points, equivalent to a 50% increase compared to the 1998-2002 period. For 2013-17, it was 19.1% (95%CI: 16.2-22.2) in men, and 24.8% (95% CI: 20.4-29.3) in women.

Conclusions:

Population survival estimates from the RPCC were lower than those observed in the NCIS. The differences in their methods and scope can explain variability. Nevertheless, our findings could be complementary to improve cancer control planning in the country.

Conflicts of interest:
The authors declare that they have no conflict of interest.

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Resumen

Antecedentes:

El cáncer de estómago se encuentra entre los más frecuentes y es una de las principales causas de mortalidad en los países de ingresos bajos y medianos. Evaluar su supervivencia es importante para orientar las políticas de salud basadas en la evidencia.

Objetivo:

Estimar la supervivencia del cáncer de estómago en Colombia (2014-2019) con datos del Sistema Nacional de Información del Cáncer (NCIS) y en Cali con datos del Registro Poblacional de Cáncer de Cali (RPCC) (1998-2017).

Métodos:

El NCIS estimó la supervivencia neta a tres años para 8,549 personas y el RPCC la calculó a 5 años para 6,776 personas registradas en sus bases de datos.

Resultados:

La supervivencia neta a tres años en Colombia fue del 36.8% (IC 95%: 35.5-38.1). La supervivencia neta fue mayor en personas con seguro especial (61.7%; IC 95%: 44.8-74.8) o tercer pagador (40.5%; IC 95%: 38.7-42.3) que el seguro estatal (30.7%; IC 95%: 28.7-32.8). También fue mayor en mujeres y personas diagnosticadas en etapas tempranas. El análisis multivariable mostró consistencia con la estimación de supervivencia con mayor riesgo de muerte en hombres, personas con seguro estatal y diagnosticados en estadios avanzados. En Cali, la supervivencia neta a 5 años se mantuvo estable en los hombres durante los últimos 20 años. En las mujeres aumentó 8.60 puntos porcentuales, equivalente a un aumento del 50% en comparación con el período 1998-2002. Para el período 2013-17 fue 19.1% (IC 95%: 16.2-22.2) en los hombres y 24.8% (IC 95%: 20.4-29.3) en las mujeres.

Conclusiones:

Las estimaciones de supervivencia del RPCC fueron más bajas que las obtenidas por el NCIS. Las diferencias en sus métodos y alcance pueden explicar la variabilidad. Sin embargo, nuestros hallazgos pueden ser complementarios para mejorar la planificación del control del cáncer en el país.

Remark

1) Why was this study conducted?

To estimate gastric cancer survival in the Colombian population notified to the National Cancer Information System (NCIS) that received health services within the framework of the national health system. To compare these results with those obtained by a population-based cancer registry.

2) What were the most relevant results of the study?

People with insurance paid by the government have lower gastric cancer survival than those affiliated with the third payer and the special insurance. The Colombian National Cancer Information System (NCIS) obtained gastric cancer survival estimates higher than those of the population-based cancer registry. Gastric cancer survival in Colombia has a gap of at least 40 percentage points compared to countries that perform population-based screening.

3) What do these results contribute?

The Colombian government can use survival indicators to monitor the gastric cancer control plan.

Introduction

Stomach cancer is among the most frequent and lethal types of cancer worldwide. By 2020, it was the fifth type in terms of incidence, and every year accounts for more than 1.1 million and 0.8 million new cases and deaths, respectively [1,2].

Stomach cancer is the leading cause of specific mortality in Colombia and Andean low-middle income countries in Latin America, where gastric cancer incidence rates are higher than those observed in high-income countries [3]. Although the stomach cancer burden of morbidity and mortality has steadily decreased in the last decades, its survival remains the lowest compared with other solid tumors such as breast, prostate, or cervical [4].

Survival is one of the most interesting indicators for cancer surveillance and control because it reflects the effectiveness of prevention and treatment. Associated factors with stomach cancer survival are diverse; and could be related to the individual, the disease itself, and the health system [5]. However, the key prognostic factor is staging at diagnosis, and it depends on a well-organized screening population program. Japan and Korea have significantly improved stomach cancer control through nationwide screening programs that can detect up to 70% of new cases in the early stages [6-8]. In Latin America, the screening coverage is poor, with low cost-effectiveness of the implemented programs [5,9-11]; and about 90% of people are diagnosed in advanced stages.

Colombia has a situation comparable to Latin America, lacking a nationwide stomach cancer screening program despite its epidemiologic and economic burden; as well as a high prevalence of *Helicobacter pylori* infection, which represents a major risk factor for stomach cancer [12]. According to the High-Cost Diseases Fund (CAC in Spanish), 73% of the new cases that received care within the framework of the national health system in 2019 were diagnosed in advanced stages [13].

The National Cancer Information System (NCIS) managed by the CAC collects and analyzes demographic, clinical, and administrative information on people with cancer in Colombia through the annual report of 134 variables. The NCIS methodology and scope have been published elsewhere [14].

The NCIS survival estimates are a metric of the effectiveness of cancer care providers and insurers in the Colombian health system that report cancer cases to the NCIS. On the other

hand, the Population-based cancer survival provides an indicator of the overall effectiveness of the health care system to deliver screening, early diagnosis, and evidenced-based treatment services and follow-up care to all individuals in the population. The survival estimates of both information systems are complementary, so they could serve as a mutual verification method [15,16].

Therefore, we aimed to estimate 3-year net survival at the national level in people treated within the framework of the national health system during the period 2015-2019, with data from NCIS managed by the CAC; and 5-year net survival in Cali from the Population-based Cancer Registry of Cali (RPCC in Spanish) during the period 1998-2017.

Materials and Methods

Setting

Colombia, a middle-income country, has a population of 50.6 million and a gross national income per capita of U.S. $6,510 [17]. In 1994, it was established the current health insurance system, which is considered public-private [18]. It is a universal and mandatory system that covers almost 96% of the total population. There are two insurance sources; the first is funded by the third payer, and groups the country's workforce; in the remaining cases, the state resources support the second, including the unemployed. The third payer and state insurance cover approximately 45% and 49% of the insured population. The remaining population is under private insurance, in addition to the third payer or government insurance (police, military forces, or government employees) [19].

Cali is the third-largest city in Colombia and the most densely populated in the country's southwest, with 20% of the Colombian population. According to the 2018 census, Cali had 2.2 million inhabitants, 53.2% of which were women, and 26.2% were self-reported as afro-descendants [20]. The average life expectancy at birth was 74.4 years [20]. Cali has more than 165 enabled oncology services in urban areas [21], but only five centers have integrative oncology services. More than 9.5 thousand new cancer cases were diagnosed in 2019, 55% of whom lived outside Cali.

Data sources

NCIS. The NCIS, administered by the CAC, performed survival analysis on real-world and nationwide data. The NCIS is a passive and non-public registry created by the Colombian Ministry of Health in 2014 [22]. Its goal is to collect and analyze demographic and clinical information on people who receive health services within the national health system through the annual report of 134 variables. The national health system insures 98% of the Colombian population, and health insurers and providers must report all cancer cases to the NCIS [19]. This information system can provide reliable information on real-life trends in access to health care for common types of cancer in Colombia, including identifying barriers to adequate access to treatment. To identify and protect the personal information of the participants, they have created unique identifiers. Data is updated for prevalent cases yearly, while new cancer cases are fully registered. A well-established data monitoring process guarantees information quality, which is carried out in two steps: a prior identification of mistakes in the reporting process through a systematized algorithm. Then, the reported information is audited and compared with clinical health records to ensure accuracy for all new cases. The NCIS methods and scope have been previously described [14]. In 2019, the proportion of data quality was up to 83%, and it has increased throughout the years, consolidating the NCIS as a reliable data source.

The Population-based Cancer Registry of Cali (RPCC). The RPCC has operated continuously since 1962. The official censuses carried out by the National Department of Statistics (DANE) in 1964, 1973, 1983, 1993, and 2005 provide information on the population of Cali [19,23].

The RPCC includes the new cases of stomach cancer throughout notification and active searching in primary data sources, including hospitals, clinics, pathology laboratories, and

cancer centers. General mortality by age, sex, and calendar year is periodically obtained from death certificates from the Secretary of Health in Cali. The RPCC integrates the data into the database following the international standards of good practice [24,25]. The RPCC is a certified member of the International Association of Cancer Registries and meets the international standards of quality recommended by the International Agency for Research on Cancer (IARC) [24,25]. Elsewhere is a complete review of history, goals, logistics, coverage, procedures, and methods for incidence, mortality, and survival estimations [21,26].

Patient selection

NCIS

Case definition. The NCIS included all the new cases of a primary stomach cancer in people aged ≥15 years and reported between January 2nd, 2014, and January 1st, 2019. Health providers confirmed the diagnosis on medical records through a data monitoring process. The International Classification of Diseases 10th edition (ICD-10) [27] defined the location (C160-C169) of the tumor. For net survival analysis, NCIS applied additional exclusion criteria. Cases with a time from diagnosis to death or last contact of unknown length or "0" years, as well as a follow-up time higher than the maximum (3 years), were excluded. Patients with tumors classified as *in-situ* were also excluded. Information regarding death was reported to the CAC by health insurers. In addition, the deaths were verified by external sources from the Ministry of Health and the National Registry of Civil Status.

RPCC

Case definition. Men and women aged 15-99 years old, residing in the urban area of Cali, with a diagnosis of primary malignant neoplasm of the stomach, codified as C16 according to the Classification of Diseases for Oncology 3rd edition (ICD-O-3)[28], no matter if it was confirmed or partially or fully treated; and registered in the RPCC from 1998 to 2017. The basis for the diagnosis can be microscopic (fluid cytology, bone marrow, histology of a primary tumor and autopsy); and non-microscopic (clinical, surgical, and imaging diagnosis). Cases that have come to the city for treatment or diagnosis are not considered as residing in Cali [15].

The RPCC updated the vital status and date of the last contact by crossing with external sources: the mortality database of the Secretary of Public Health in Cali, the registry of hospital discharges from medium and high complexity healthcare institutions, pathology reports, and insurance databases (public and private).

Full follow-up. People who die before or on the same follow-up closing date, o people who die after the follow-up closing date; or people who are alive and the date of the last contact is greater than the closing date of the follow-up.

Incomplete follow-up. People who are alive, and the date of the last contact is less than the closing date of the follow-up.

Cases with the following conditions were excluded from the analysis: i) cancer diagnosis only based on death certificates, showing the same date for both diagnosis and death, and ii) other causes: unknown age or sex and benign tumors. In the supplementary Table, S1 has summarized the quality indicators for cases.

Statistical Analyses

NCIS. We performed a descriptive analysis of demographic and clinical variables at baseline, including age at diagnosis, sex, health insurance, region of residence, and clinical stage. According to their distribution, continuous variables were reported as medians and interquartile ranges (IQR), while categorical data were summarized as absolute variables and proportions.

In all analyses, the dependent variable was the time between diagnosis and death for any cause or being censored. It was set to a maximum of 3 years. People who did not have the event or were lost to follow-up were censored. 3-year overall survival was estimated using the Kaplan-Meier method, while net survival was calculated through the Pohar-Perme estimator [29]. Life tables for all-cause mortality in the general Colombian population were built to estimate expected net survival. The period approach was used because the established follow-up was unavailable for all patients. We also analyzed overall survival and net survival by sex, health insurance, region of residence, and stage at diagnosis, comparing the curves with the log-rank test and the method developed by Pavlič and Perme (log-rank type test) [30], respectively. Net survival was age-standardized using a traditional direct method with an internal standard.

We also estimated a flexible parametric model with restricted cubic spline functions for modeling non-linear and time-dependent effects on the log excess hazard scale proposed by Royston-Parmar [30-33]. A generalized linear model using a Poisson assumption with smoothing splines was selected because it violated the proportional hazards principle. To determine the model's complexity and goodness of fit, the Akaike information criterion was evaluated [33].

The final model had 4 knots and 5 degrees of freedom. It was adjusted by age and stage at diagnosis, sex, health insurance, and region of residence, and the results are presented as hazard ratios (H.R.s) and their 95% confidence interval.

RPCC. The dependent variable was the time of follow-up between cancer diagnosis and the event of interest (death by any cause) or being censored. The maximum observation time until the occurrence of the event was five years. Censoring was defined as loss of follow-up and cases without the event at the end of the study period (December 31st, 2018).

The 20-year survival was estimated by combining the cohort analysis approach for the periods 1998-2002, 2003-2007, and 2008-2012, and the period analysis for the interval 2013-2017 due to the lack of complete five-year follow-up information for all subjects [34,35]. 5-year net survival was calculated by using the Pohar-Perme estimator [29]. Life tables for all-cause mortality in the general population in Cali were built from the number of deaths and population by age, sex and calendar year [35,36]. Survival estimations were age-standardized using the international cancer survival standard weights (group 1) [37].

Ethical considerations

NCIS. This study has no risk for participants. Information was collected and analyzed following international standards (The Declaration of Helsinki, The Belmont Report, and The International Guidelines prepared by the Council for International Organizations of Medical Sciences (CIOMS)), as well as national regulations (Resolution 8430 of 1993, stated by The Colombian Health Ministry) for conducting human research. Confidentiality was guaranteed throughout the information processing (reporting, managing, analysis, and publication). All records were anonymized before the analysis. Furthermore, access to data was restricted to the research team and the results only can be used for approved research or academic purposes.

RPCC. The RPCC follows the European Network of Cancer Registries (ENCR) guidelines [38]. The director of the RPCC is responsible for security data and confidentiality. Team members of the RPCC sign an agreement for maintaining data confidentiality and privacy of personal information. Access to the RPCC installations is restricted only for authorized personal. Confidential information is accessed by security passwords, closed files, and the destruction of supports with personal identification when they are no longer useful. Only the manager of the RPCC is authorized to perform the initial matching for detecting new cases and updating vital status and last contact information. Each case is identified with an internal I.D. assigned by the RPCC and all datasets are anonymized for statistical analysis.

This research study was approved by the institutional ethics committee of the Universidad del Valle as stated in the approval certificate number 001-020 dated January 2020.

Results

NCIS

Demographic and clinical characteristics at baseline. A total of 8,549 people reported from 2015 to 2019 met the inclusion criteria and were analyzed. Demographic and clinical characteristics of new cases of stomach cancer at baseline are shown in Table 1. Most cases occurred in men above 50 years, affiliated with the third payer insurance, living in the Central Region, and diagnosed in advanced stages.

Survival analysis. All participants contributed a total of 9,317 years, and 4,478 deaths were observed. The Median follow-up time was 0.8 years (min: 0.2 years, max: 3.0 years). 3-year net survival was 36.8% (95% CI: 35.5-38.1). Net survival at 1 and 2 years was 55.8% (95% CI: 54.7-56.9) and 41.2% (95% CI: 39.9-42.4), respectively.

Table 1. Age-standardized baseline demographic and clinical characteristics of people with stomach cancer within the Colombian health system, 2015-2019

Variable ‡	New cases (n=8,549)
Age at diagnosis (years)	65 (54-74)
Age groups	
15-19	6 (0.1)
20-24	36 (0.4)
25-29	95 (1.1)
30-34	184 (2.1)
35-39	264 (3.1)
40-44	374 (4.4)
45-49	619 (7.2)
50-54	868 (10.2)
55-59	969 (11.3)
60-64	1,061 (12.4)
65-69	1,111 (13.0)
70-74	1,044 (12.2)
75-79	930 (10.9)
80 and more	986 (11.6)
Sex	
Males	5,226 (61.1)
Females	3,323 (38.9)
Stage at diagnosis †	
Early	1,442 (16.9)
Advanced	4,709 (55.1)
Unknown	2,398 (28.0)
Health insurance	
Third payer	4,844 (56.6)
Paid by the state	3,459 (40.5)
Exception	79 (0.9)
Private	57 (0.7)
Uninsured	110 (1.3)
Geographical region of residence §	
Bogotá, D.C.	2,111 (24.7)
Caribbean	450 (5.3)
Central	2,852 (33.3)
Eastern	1,371 (16.0)
Pacific	1,649 (19.3)
Other provinces	116 (1.4)

‡ Values are absolute numbers (%). Age is reported as median (interquartile range).
† Stages IA, I.B., IIA and IIB were grouped as early. Advanced stage includes IIIA, IIIB, IIIC and IV.
§ Colombian provinces are grouped in six regions, according to their gross domestic product by the Department of National Statistics (DANE in Spanish) as follows: 1) Bogotá, D.C (country's capital); 2) Caribbean (Atlántico, Bolívar, Cesar, Córdoba, La Guajira, Magdalena and Sucre); 3) Central (Antioquia, Caldas, Caquetá, Huila, Quindío, Risaralda and Tolima); 4) Eastern (Boyacá, Cundinamarca, Meta, Norte de Santander and Santander); 5) Pacific (Cauca, Chocó, Nariño and Valle del Cauca); 6) Other provinces (Amazonas, Arauca, Casanare, Guainía, Guaviare, Putumayo, San Andrés, Vaupés and Vichada).

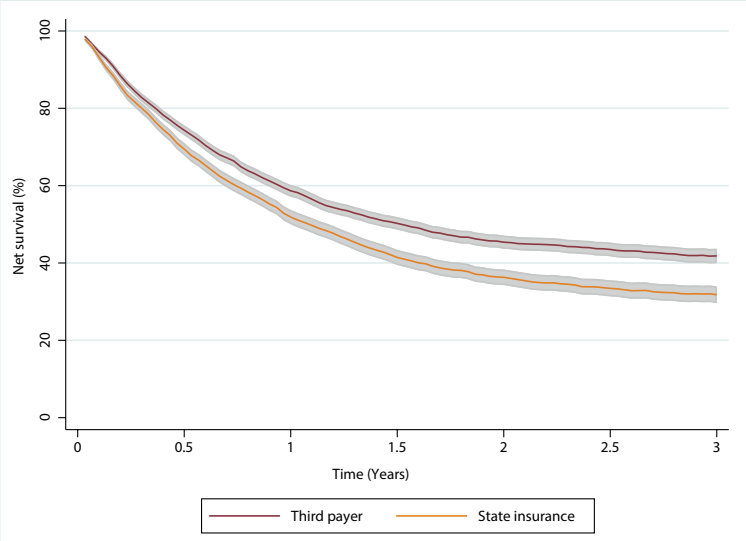

Figure 1. Colombia. Three-year net survival standardized by age according to health insurance in people diagnosed and treated with stomach cancer.

We also estimated net survival by sex, age, health insurance, stage and region of residence at diagnosis. Regarding health insurance (Figure 1), net survival was significantly higher in people affiliated to special insurance (61.7%; 95% CI: 44.8-74.8) or to the third payer (40.5%; 95% CI: 38.7-42.3) in those affiliated to state insurance (30.7%; 95% CI: 28.7-32.8) (log-rank type $p < 0.001$). Figure 2 shows that net survival was significantly higher in women (42.6%; 95% CI: 40.2-44.9) than men (34.8%; 95% CI: 33.1-36.5) (log-rank type $p < 0.001$).

On the other hand, net survival was significantly higher in people diagnosed at early stages (IA, IB, IIA, IIB) (58.1%; 95% CI: 54.5-61.5), compared with those at advanced stages (25.1%; 95% CI: 23.4-26.9) (log-rank type $p < 0.001$) (supplementary Figure S1). Net survival was also significantly higher in people aged <60 years (33.9%; 95% CI: 31.9-36.0), compared with those aged ≥60 years (38.4%; 95% CI: 36.7-40.1) (log-rank type $p < 0.001$).

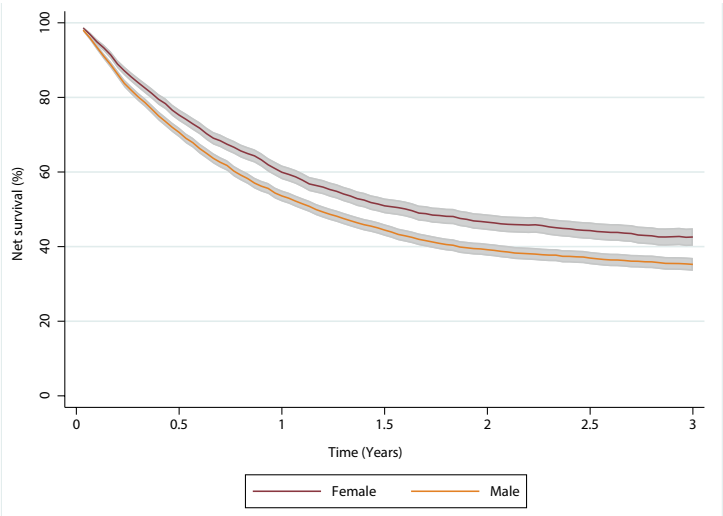

Figure 2. Colombia. Three-year net survival standardized by age according to sex in people diagnosed and treated for stomach cancer.

Table 2. Multivariable-adjusted hazard ratios in people with stomach cancer treated within the Colombian health system

Variables §	Aged <60 years (n= 3,212)			Aged ≥60 years (n=5,335)		
	HR-adjusted	95% CI	p-value	HR-adjusted	95% CI	p-value
Sex						
Females (reference)	1.0	-	-	1.0	-	-
Males	1.1	0.9-1.2	0.209	1.2	1.1-1.3	<0.001
Health insurance						
Third payer (reference)	1.0	-	-	1.0	-	-
Paid by the state	1.1	0.9-1.2	0.335	1.3	1.2-1.4	<0.001
Exception	0.7	0.4-1.2	0.187	0.9	0.6-1.3	0.646
Special	0.5	0.2-0.9	0.036	0.7	0.4-1.3	0.220
Uninsured	1.0	0.7-1.5	0.915	0.9	0.6-1.4	0.660
Stage at diagnosis						
Unknown (reference)	1.0	-	-	1.0	-	-
Early	0.6	0.5-0.7	<0.001	0.6	0.5-0.7	<0.001
Advanced	1.5	1.4-1.7	<0.001	1.4	1.3-1.5	<0.001
Geographical region of residence						
Bogotá, D.C. (reference)	1.0	-	-	1.0	-	-
Caribbean	1.2	0.9-1.5	0.061	0.9	0.8-1.1	0.616
Central	0.9	0.8-1.1	0.742	0.8	0.7-0.9	<0.001
Eastern	0.9	0.8-1.1	0.388	0.9	0.8-1.1	0.747
Pacific	1.1	0.9-1.2	0.866	0.9	0.8-0.9	0.027
Other provinces	0.6	0.4-0.9	0.048	0.6	0.4-0.9	0.024

§ All variables were measured at diagnosis.
H.R.: hazard ratio, CI: confidence interval.

Supplementary Figure S2 shows net survival by region of residence at diagnosis. There were no statistically significant differences, except for people living in the Caribbean region (29.4%; 95% CI: 24.0-35.0), who had a significantly lower net survival than those in the Central region (38.5%; 95% CI: 36.2-40.8).

Flexible parametric model results. Overall, people under state insurance were at a higher risk of death those affiliated to the third payer (adjusted HR=1.2, 95% CI: 1.1-1.3; p <0.001). Otherwise, people with special insurance had a significantly lower risk (adjusted HR=0.6, 95% CI: 0.4-0.9; p= 0.022). Regarding sex, men had a significantly higher risk of death than women (adjusted HR=1.2, 95% CI: 1.1-1.2; p <0.001). Furthermore, people diagnosed at early stages had a lower risk of death than those with unknown staging (adjusted HR=0.6, 95% CI: 0.5-0.7; p <0.001). The age-stratified model showed a higher risk in men aged ≥60 years. Furthermore, older people with state insurance risk was also higher than younger people. The effect of early detection remained the same despite age (Table 2).

RPCC

Six thousand seven hundred seventy-six people diagnosed with stomach cancer, living in Cali, and registered in the RPCC database between 1998 and 2019, aged between 15 and 99 years, were included in survival analysis (42.4% were women). Otherwise, 687 cases (9.2%) were excluded (25,26). During the period 2013-2017, 83.3% of cases were morphologically verified, and 2.7% had a death certificate as the only evidence for cancer diagnosis.

Table 3 shows 1, 3, and 5-year net survival for both sexes of people with stomach cancer between 1998 and 2019. In the last decade (2008-2017), 5-year net survival was close to 21% being, significantly higher than the previous decade (1998-2007). Furthermore, in the last quinquennium, it improved by 4.7 percentage points that representing an increase of 25% compared with the first quinquennium (21.3% (95 CI%: 19.2-23.6) vs. 16.6% (95% CI: 19.2-23.6)).

5-year net survival by sex is described in Table 4. In men, it remained stable during the last 20 years; while in women, it significantly improved in the last decade, showing an increase of 50% (8.6 percentage points) in the previous quinquennium compared with the first one (24.8% (95% CI: 20.4-29.3) vs. 16.2% (95% CI: 13.1-19.7)).

Table 3. Cali, Colombia. Age-standardized net survival at 1, 3 and 5 years in adults (15-99 years) diagnosed with stomach tumors, by calendar period (both genders).

Period of diagnosis	Net Survival §					
	1 year	95% CI	3 years	95% CI	5 years	95% CI
1998-2002	32.1	29.8 - 34.3	18.8	16.7 -21.1	16.6	14.5 -18.9
2003-2007	35.1	33.0 - 37.1	21.0	19.1 - 23.1	18.7	16.7 -20.9
2008-2012	39.4	37.2 - 41.5	22.7	20.7 - 24.8	21.0	18.9 - 23.2
2013-2017	43.8	41.4 - 46.0	23.8	21.7 - 25.9	21.3	19.2 - 23.6

§ Values are percentages.
CI: confidence interval.

Table 4. Cali, Colombia. Age-standardized net survival at 5 years in adults (15-99 years) diagnosed with stomach tumors, by sex and calendar period.

Period of diagnois	Male		Female		Both	
	NS§	95% CI	NS §	95% CI	NS§	95% CI
1998-2002	17.2	14.3 - 20.4	16.2	13.1 -19.7	16.6	14.5 -18.9
2003-2007	18.5	15.8 - 21.5	19.2	16.2 -22.4	18.7	16.7 -20.9
2008-2012	19.1	16.4 - 21.9	24.0	20.4 -27.8	21.0	18.9 - 23.2
2013-2017	19.1	16.2 - 22.2	24.8	20.4 -29.3	21.3	19.2 - 23.6

§ Values are percentages.
NS: net survival; CI: confidence interval.

Supplementary Table S1shows that about 63% of people diagnosed with stomach cancer died during the first year of follow-up.

Discussion

The NCIS provides nationwide stomach cancer data; this survival analysis was performed with Observational Routinely collected health Data (RECORD). In addition, the Cali population-based Cancer Registry, one of the oldest in Latin America, compared these survival estimates at the national level with those calculated by its team for the city of Cali.

Population-based cancer survival reflects the overall effectiveness of the health system for cancer control. It measures the mean survival achieved by all patients with stomach cancer despite their demographic and clinical conditions. Survival is the primary goal in the care of patients with stomach cancer. Early detection of stomach cancer and radical surgery associated with adjuvant treatments are the driving force behind stomach cancer control [39].

Stomach cancer is a multifactorial disease mainly related to *Helicobacter pylori* gastritis, which usually begins early. Environmental, infectious and host-related factors may interact to develop the disease. During the last half-century, stomach cancer incidence and mortality rates have significantly decreased worldwide. It is associated with the lower use of salt in processed food and the greater availability of fresh fruits and vegetables. In many countries, tobacco use and the prevalence of *H. pylori* infection have also decreased [40,41].

Unfortunately, advances in the treatment of stomach cancer are insufficient, there is no vaccine development against *H. pylori*, and early detection programs in Latin America have not been successful due to a lack of continuity and low-cost effectiveness. Chemoprevention remains an option for stomach cancer control as a primary prevention strategy to eradicate *H. pylori* infection [9,10].

Regarding our analysis, the CAC gathers a large volume of RECORD data by an interconnection platform that allows the flow of cancer data in real-time between health insurers and providers [42]. On the other hand, the RPCC was established in 1962; it is a population-based cancer registry that provides continuous information on new cases of all types of cancer in permanent residents of Cali through active search and notification[21,26]. For stomach cancer survival analysis, these two information systems, CAC and RPCC, have comparable variables for the person, tumor, vital status, and date of the last contact. Unfortunately, there is a limitation to obtaining information about staging.

The 3-year net survival was 36.8% (95% CI: 35.5-38.1), according to the NCIS. In the flexible parametric model, we found that people with insurance paid by the state had a significantly higher risk of death than those affiliated to the third payer and the special insurance. The mortality risk was also significantly higher in men than women; and in people diagnosed at advanced stages. When analyzing data from the RPCC, the 5-year net survival during the period 2013-2017 was 21.3%. In addition, we observed it was almost stable in men; while in women, it significantly improved in the last decade and, in the previous quinquennium, it showed an increase of 50% compared with the first one.

Stomach cancer survival from the RPCC was higher than observed in other Latin American countries such as Ecuador and Chile (19.1% and 16.7%, respectively) while were lower than estimated in Costa Rica (40.0%) during the period 2010-2014 [22] (Supplementary Table S2). The above suggests that stomach cancer continues to have a high social burden in Cali and Colombia, being the major cause of cancer deaths [26,43].

In most countries, advances in surgical and multimodality treatments and post-operative care have only modestly improved survival and prognosis. South Korea and Japan have well-established national stomach cancer prevention and screening programs [2,44] with 5-year net survival of 69% and 60% (Supplementary Table S2),respectively, with an average increase between 10% and 20% in the last 20 years according to CONCORD-3 [35]. In those countries, strategies have been focused on eradicating*H. pylori*and the early detection of cancer by population-based endoscopic screening programs.

CONCORD-3 results also highlighted that survival increased up to 5% in five European countries (Denmark, Lithuania, and the United Kingdom in North Europe, Poland in Eastern Europe and Austria in western Europe), with 5-year net survival ranging from 20% to 27%. In the United States and Austria, survival estimations ranged from 30% to 35% during the period 2010-2014 [35].

When comparing survival in Japan or Korea with the estimations reported in the United States, the overall difference is due to earlier diagnosis, fewer proximal and gastroesophageal junction lesions, and histologic or genetic variations in Asian countries [45,46]. Self-selection bias and lead-time bias could overestimate the survival gap between countries. Healthy or health-conscious individuals may overrepresent participants in screening programs, and ever-screened patients may seem to be surviving longer because they are diagnosed earlier, not screening-test effect. It could lead to an overestimation of the effectiveness of the screening program. Western countries such as Colombia have no population-based screening programs for stomach cancer [47].

Results from both the NCIS and the RPCC are consistent regarding better survival in women than men. In contrast, in Japan, women show a small but consistently lower survival associated with more advanced stages among women. It suggests a gender inequity in screening, medical examinations, or treatment for stomach cancer in Japan [48]. Our findings show that gender inequity in Colombia goes in the opposite direction.

One of the most important findings from the NCIS analysis was the statistically significant differences in the risk of death by health insurance, with better outcomes in people affiliated with the third payer or special insurance than those insured by the state. Our results are consistent with a study performed with data from a population-based registry in Manizales, Colombia. People affiliated with the third payer had about 30% lower risk of dying than people with state insurance [49]. In both cases, insurance could be a proxy of access and health care quality. It would also represent the distribution of exogenous sociodemographic factors related to risk awareness and a timely diagnosis and treatment [50]. Despite the increase in coverage from 2010, there is differential access to health care according to the insurance system, and inequities in cancer diagnosis and treatment persist even between types of insurance [49].

Finally, it is worth mentioning that our results are valuable for improving cancer planning and strengthening national information systems on cancer and population registries. Furthermore, results from both approaches allow identifying gaps in the reporting process of cancer cases that receive care within the national health system. Regardless of differences in their methodology and scope, the NCIS and RPCC information may be complementary to identify cancer burden in terms of its frequency, distribution at demographic and insurance levels, as well as barriers for adequate access to health care and outcomes of cancer management performed by insurers and providers such as survival.

Prevention will always be preferable to cure, especially for gastric cancer with high lethality. Unfortunately, there is no vaccine development against *H. pylori*, and early detection programs in Latin America have not been successful. Therefore, chemoprevention remains an option for stomach cancer control as a primary prevention strategy to eradicate *H. pylori* infection.

However, cancer treatment costs are increasing and creating financial hardship in providing high-quality cancer care equally to all citizens. The evidence from this research suggests that there is inequality in gastric cancer care in the current Colombian health system. People with insurance paid by the government have lower survival than those affiliated with the third payer and the special insurance. Decision-makers in the Colombian government, insurance companies, and hospitals that provide cancer care in the Colombian health system must introduce policy changes to reduce existing gaps. It is unacceptable that there is political tolerance of inequality in access to affordable cancer care [16].

Strengths and limitations

Our study's main strength was exploring stomach cancer survival from two different but complementary data sources. Data from the NCIS provides a real-world approach from an insurance perspective at the national level, while the RPCC is population-based. Also, data from the NCIS was fully validated by a well-established and systematic data monitoring process. Regarding deaths, the official source of the Ministry of Health confirms that they are exhaustively validated [14].

On the other hand, population-based survival estimates by the RPCC reflect all patients with stomach cancer in Cali, regardless of socioeconomic status and disease characteristics. In addition, the RPCC follows the CONCORD-3 guidelines for the standardization, cleaning, and construction of quality indicators. This process facilitates a specific exclusion of cases from the study and allows a uniform coding format for the mandatory variables [16,35].

There is a limitation regarding the comparability of survival estimates obtained by the RPCC and the CAC due to their different definition of the stomach cancer case [21,51]. The RPCC includes invasive stomach cancer cases, regardless of whether they have been confirmed or partially, or fully treated. The basis of the diagnosis can be both morphological; as non-morphological. For the 2013-2017 period, 83.3% of stomach cancer cases had morphological verification. In 14%, the diagnosis was clinical, and in 2.7%, the cancer cases were registered from the death certificate only [52].

In contrast, Colombian health insurers notify the CAC of stomach cancer cases with morphological or clinical confirmation treated in the framework of the national health system. Although notification of stomach cancer cases to the CAC is mandatory, it does not guarantee the completeness and could limit the comparability of our findings [14,51].

Due to the above, the NCIS information could underestimate cancer incidence rates and overestimate survival compared to those obtained by the RPCC. In addition, the quality of notification of cancer cases is related to the organization of cancer services, which influences the clinical outcomes of cancer.

The RPCC does not have information on tumor stages in patients with stomach cancer. The RPCC passively follows up to obtain the vital status of the patient and the date of the last

contact. The RPCC periodically updates the vital status with the Secretary of Health in Cali, but the linkage with the national databases is insufficient and depends on death certificates that have inherent inaccuracies and missing data. Furthermore, Cali does not have a census of the migratory flows of the population and lacks life tables by socioeconomic stratum and by the state of insurance to the national health system.

Final comments

The RPCC and CAC regularly conduct cancer situational analyses and are essential to monitor and evaluate national and regional progress in stomach cancer surveillance and control. Collaboration between reporting systems and cancer registries enables these complementary systems to verify survival estimates to identify gaps, implement standards, and develop improvement plans to ensure data quality.

The standardization of the data allows regional and international comparisons and facilitates decision-making. It is a priority to unify the case definition and for the CAC to work with the cancer registries to complement the incidence and survival information and achieve the link with the national databases to improve the passive follow-up process.

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Supplementary material.

Table S1. Quality indicators in people diagnosed with stomach cancer, both sexes, Cali, Colombia (1998-2017)

Year	Patients	ASR	Age <15	MV	DCO	Excluded				Included		Dead	Complete	Observed Survival						Median F-U
	(n)	(W)	(n)	(%)	(%)	No.	%	DCO (n)	Others (n)	No.	%	(n)	F-U (%)	1 year	LFU 0-1y	3 years	LFU 1-3y	5 years	LFU 3-5y	(months)
1998	322	21.99	0	79.2	9.6	42	13.0	31	11	280	87.0	229	82.1	0.35	13.9	0.15	0.0	0.11	0.0	2.7
1999	316	20.32	1	72.5	11.7	54	17.1	37	17	262	82.9	200	77.1	0.39	9.9	0.27	1.5	0.22	0.4	3.5
2000	339	21.14	0	70.8	13.9	57	16.8	46	11	282	83.2	240	85.1	0.31	8.2	0.15	0.4	0.12	0.0	2.6
2001	341	20.80	0	72.4	13.8	51	15.0	47	4	290	85.0	233	81.0	0.38	8.6	0.22	0.0	0.20	0.3	4.4
2002	352	20.43	0	73.3	13.9	73	20.7	43	30	279	79.3	228	82.1	0.33	8.6	0.21	0.7	0.18	0.0	2.9
2003	349	19.11	0	75.9	10.6	45	12.9	37	8	304	87.1	244	80.6	0.42	9.2	0.25	0.3	0.21	0.3	4.9
2004	392	20.16	0	79.6	8.9	45	11.5	35	10	347	88.5	288	83.3	0.38	6.6	0.23	0.0	0.20	0.6	5.1
2005	409	20.48	0	78.7	10.0	57	13.9	41	16	352	86.1	302	85.8	0.34	6.8	0.19	0.3	0.14	0.0	3.8
2006	398	18.63	0	82.7	5.3	30	7.5	20	10	368	92.5	319	87.0	0.32	4.1	0.19	0.0	0.17	0.0	3.7
2007	381	17.42	0	82.7	3.9	20	5.2	15	5	361	94.8	314	87.3	0.40	1.7	0.20	0.0	0.17	0.0	5.4
2008	346	15.27	0	84.1	4.0	17	4.9	10	7	329	95.1	283	86.3	0.33	2.1	0.19	0.0	0.16	0.0	4.1
2009	344	14.54	0	83.7	4.1	17	4.9	11	6	327	95.1	271	83.2	0.37	2.4	0.23	0.0	0.20	0.0	5.6
2010	376	15.37	1	85.4	2.9	13	3.5	10	3	363	96.5	304	84.8	0.40	0.6	0.21	0.0	0.18	0.0	6.6
2011	379	14.78	0	85.2	2.9	11	2.9	10	1	368	97.1	308	84.0	0.42	0.5	0.23	0.3	0.21	0.3	7.2
2012	382	14.66	0	82.7	1.3	9	2.4	5	4	373	97.6	309	87.7	0.39	1.6	0.20	0.0	0.18	0.0	6.0
2013	399	14.77	0	80.2	2.3	24	6.0	6	18	375	94.0	318	97.1	0.37	2.7	0.18	0.0	0.14	0.3	4.5
2014	424	15.02	0	75.2	5.2	35	8.3	21	14	389	91.7	325	97.7	0.36	2.1	0.20	0.0	-	-	5.2
2015	385	13.28	0	70.9	6.0	35	9.1	21	14	350	90.9	281	95.1	0.35	3.4	0.19	1.4	-	-	2.8
2016	395	13.34	0	75.4	6.1	42	10.6	18	24	353	89.4	286	95.8	0.37	4.0	-	-	-	-	4.8
2017	434	14.20	1	84.6	0.9	10	2.3	4	6	424	97.7	323	98.3	0.36	0.9	-	-	-	-	5.4
Total	**7,463**	**16.66**	**3**	**78.9**	**6.7**	**687**	**9.2**	**468**	**219**	**6,776**	**90.8**	**5,605**	**87.6**	**0.37**	**4.5**	**0.20**	**0.3**	**0.16**	**0.1**	**4.5**

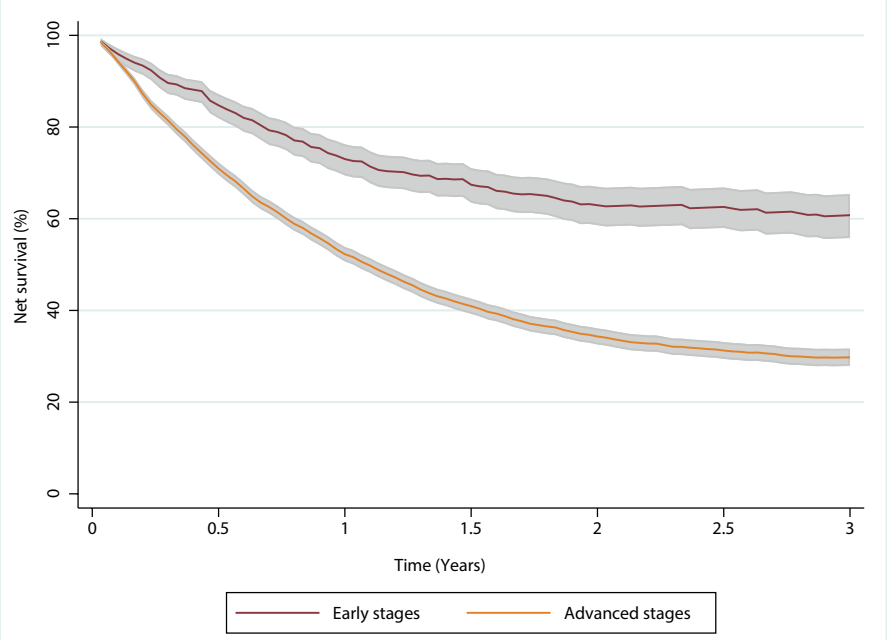
ASR: age-standardized rate; DCO: death certificate only; F-U: follow-up; MV: microscopically verified.

Table S2. Age-standardized five-year net survival in adults (15-99 years) diagnosed with stomach tumors, by country and calendar period of diagnosis (2000-2004, 2005-2009, 2010-2014)

Country		Period of diagnosis					
		2000-2004		2005-2009		2010-2014	
		N.S. (%)	95% CI	NS (%)	95% CI	NS (%)	95% CI
America (Central and South)							
Cali. Colombia		18.4	16.0 - 20.9	18.1	15.9 - 20.2	17.1§	14.7 - 19.4
Colombia	(4 registries)	18.4	16.0 - 20.9	17.7	16.2 - 19.3	17.1§	15.4 - 18.8
Ecuador	(5 registries)	17.8	12.3 - 23.3	17.4	12.0 - 22.7	19.1	13.1 - 25.1
Chile	(4 registries)	14.5	11.7 - 17.4	16.3	14.7 - 18.0	16.7	14.2 - 19.3
Costa Rica *		48.4	45.5 - 51.2	38.4	36.3 - 40.5	40.6	38.5 - 42.7
America (North)							
United States	(48 registries)	26.2	25.8 - 26.5	30.1	29.7 - 30.4	33.1	32.7 - 33.4
Asia							
Japan	(16 registries)	50.5	50.0 - 50.9	57.6	57.3 - 57.9	60.3	59.9 - 60.7
Korea*		48.6	48.2 - 48.9	61.1	60.8 - 61.5	68.9	68.6 - 69.2
Northern Europe							
Denmark *		14.7	13.2 - 16.3	15.4	13.9 - 16.9	19.9	18.1 - 21.6
Lithuania*		22.0	20.7 - 23.3	24.9	23.4 - 26.4	27.0	24.9 - 29.0
United Kingdom*	(4 registries)	16.2	15.7 - 16.6	19.2	18.7 - 19.7	20.7	20.1 - 21.2
Eastern Europe							
Poland *	(16 registries)	15.9	15.2 - 16.5	19.9	19.3 - 20.4	20.9	20.3 - 21.4
Western Europe							
Austria *		30.0	28.7 - 31.3	34.2	32.9 - 35.6	35.4	34.0 - 36.9
Netherlands *		19.7	18.8 - 20.6	22.9	22.0 - 23.9	25.0	24.0 - 26.0

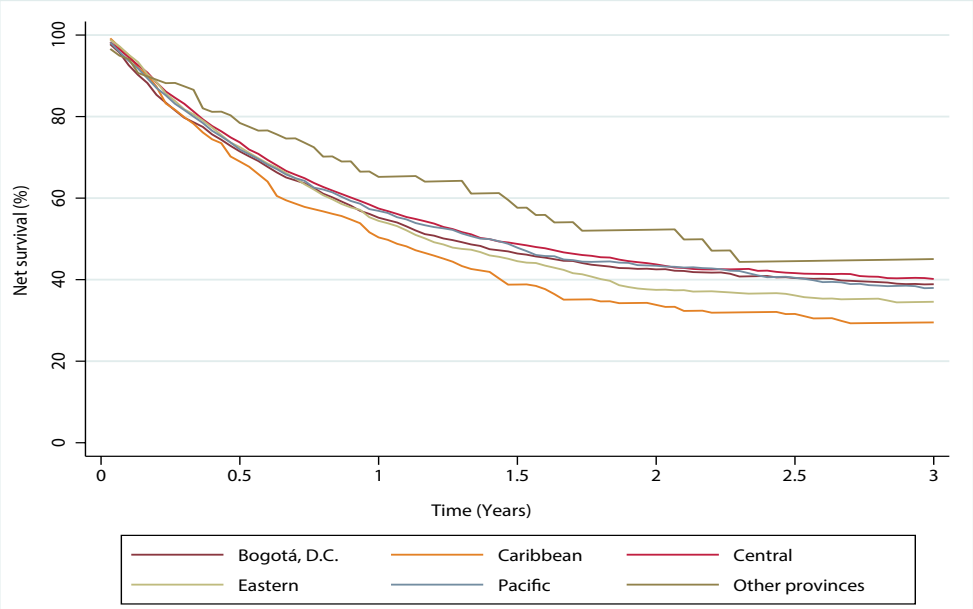
N.S. (%): Age-standardized five-year net survival
§: Survival estimate considered less reliable because 15% or more of patients were (a) lost to follow-up or censored alive within five years of diagnosis or. if diagnosed in 2010 or later. before December 31st 2014; or (b) registered only from a death certificate or at autopsy; or (c) registered with incomplete dates. i.e.. unknown year of birth. unknown month and/or year of diagnosis. or unknown year of last vital status.
* Data with 100% coverage of the national population.
Source: CONCORD-3. Lancet 2018;391 (10125).

Figure S1



Age-standardized net survival at 3 years in people diagnosed with stomach cancer in Colombia, by stage at diagnosis. Comparison of net survival by stage at diagnosis in people with stomach cancer diagnosed and treated in the framework of the Colombian health system. Stages IA and IB were grouped as early. Advanced stages include IIA, IIB, IIIA, IIIB, IIIC, y IV.

Figure S2.



Age-standardized net survival at 3 years in people diagnosed with stomach cancer in Colombia, by region of residence. Comparison of net survival by region of residence in people with stomach cancer diagnosed and treated in the framework of the Colombian health system. Colombian provinces are grouped in six regions according to their gross domestic product by the Department of National Statistics (DANE in Spanish) as follows: 1) Bogotá. D.C (' 'country's capital); 2) Caribbean (Atlántico. Bolívar. Cesar. Córdoba. La Guajira. Magdalena and Sucre); 3) Central (Antioquia. Caldas. Caquetá. Huila. Quindío. Risaralda and Tolima); 4) Eastern (Boyacá. Cundinamarca. Meta. Norte de Santander and Santander); 5) Pacific (Cauca. Chocó. Nariño and Valle del Cauca); 6) Other provinces (Amazonas. Arauca. Casanare. Guainía. Guaviare. Putumayo. San Andrés. Vaupés and Vichada).

Participación en eventos científicos

presentación de pósters y ponencias orales

Cuenta de Alto Costo

Fondo Colombiano de Enfermedades de Alto Costo

Hemofilia

CAC
Cuenta de Alto Costo

Fondo Colombiano de
Enfermedades de Alto Costo

Póster

Hemofilia

Título

Quality of life in people with haemophilia: *Preliminary results from a nationwide registry in Colombia.*

Autores

Juliana Alexandra Hernández Vargas, Ginna Paola Fernández Deaza, Adriana Linares, María Helena Solano, Claudia Casas, Lizbeth Acuña Merchán.

Evento

Annual Congress of the European Association for Haemophilia and Allied Disorders 2023.

Ámbito: internacional.

Objetivo

Caracterizar la calidad de vida relacionada con la salud (HRQoL) y sus predictores en las personas con hemofilia en el sistema de salud colombiano.

Principales hallazgos

- La hemartrosis, la artropatía, y el régimen subsidiado modificaron negativamente el HRQoL en niños y adultos.
- La actividad física debe hacer parte del manejo integral en los adultos para mejorar su HRQoL.

Enlace

Enfermedad renal crónica

CAC
Cuenta de Alto Costo

Fondo Colombiano de
Enfermedades de Alto Costo

Ponencias orales

Enfermedad renal crónica

Título

Development of a National Chronic Kidney Disease Registry in Latin America: *Experiences from Colombia.*

Autores

Andrés Mauricio García, Xinliang Liu, Nathaly Ramírez García, Ana María Valbuena García, Lizbeth Acuña Merchán.

Evento

Fall 2022 – Marshall Business Research conference.

Ámbito: internacional.

Objetivo

Describir las características sociodemográficas y clínicas, y los indicadores de gestión del riesgo de los pacientes con ERC.

Principales hallazgos

- En Colombia, en el 2019, se informaron 925.996 pacientes con ERC. La mayoría se encuentra en el estadio 3 (50,94%).
- La morbimortalidad mostró una tendencia decreciente desde 2017 a 2019.
- El control de la presión arterial y la medición de LDL mostró un nivel alto de cumplimiento para todos los estadios de ERC.

Enlace

Título

MDRD is the eGFR equation most strongly associated with four-year mortality among patients with diabetes in Colombia.

Autores

Sofía Gnecco González, Lina J. Herrera Parra, Juliana A. Hernández Vargas, Nathaly Ramírez García, Lizbeth Acuña Merchán, Carlos O. Mendivil.

Evento

IDF Congress 2022.

Ámbito: internacional.

Objetivo

Evaluar las diferencias en la asociación de la TFG y la mortalidad cuando la TFG es estimada por la fórmula de Cockcroft-Gault, MDRD, CKD-EPI, o la nueva CKD-EPI sin raza, entre los pacientes con diabetes.

Principales hallazgos

- La ecuación MDRD mostró una clara superioridad en los pacientes de raza negra.
- Para los pacientes de otras razas, MDRD y CKD-EPI sin raza funciona bien de forma equitativa.

Enlace

Póster

Enfermedad renal crónica

Título

Anticipating chronic kidney disease progression in people with diabetes from a national administrative registry in Colombia: *a machine learning approach.*

Autores

Paul Rodríguez Lesmes, Juliana Alexandra Hernández Vargas, Lina Johana Herrera Parra, Silvia Juliana Trujillo Cáceres, Andrés García Suaza, Juan Pablo Martínez, Santiago Ortiz, Andrés Ramírez, Rubén Cáceres, Ana María Valbuena, Alejandro Bryon Nieto, Lizbeth Acuña Merchán.

Evento

XXV Simposio Colombiano de nefrología, diálisis y trasplante.

Ámbito: nacional.

Objetivo

Desarrollar un modelo predictivo para clasificar la progresión de la ERC en la población colombiana diagnosticada con DM de uno a cuatro años, de acuerdo a su estadio basal y régimen de aseguramiento en salud.

Principales hallazgos

- Aunque la frecuencia basal de personas con estadios indeterminados o no estudiados se duplicó en el régimen subsidiado que, en el contributivo, las estimaciones a 4 años no presentaron diferencias por régimen en la progresión a estadios avanzados, diálisis, trasplante o muerte.
- El abordaje para anticipar los resultados de salud a través del *machine learning* apoyan la toma de decisiones y la planificación de la asistencia sanitaria, proporcionando evidencia del mundo real.

Enlace

VIH/sida

CAC
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Póster

VIH

Título

Impacto de la pandemia de COVID-19 en el acceso a la atención de las personas que viven con VIH en Colombia.

Autores

Luis Alejandro Moreno Ramírez, Andrés Felipe Patiño Aldana, Iván Camilo de la Pava Cortés, Juliana Hernández Vargas, Lina Johana Herrera Parra, Lizbeth Acuña Merchán.

Evento

XIII Encuentro Nacional de Enfermedades infecciosas, ACIN.

Ámbito: nacional.

Objetivo

Identificar los cambios en la incidencia, el acceso a la atención y la mortalidad en las personas viviendo con VIH (PVV).

Principales hallazgos

- En el año 2020 se observó un descenso en el número de casos incidentes comparado con el 2019. Estos casos nuevos tendieron a reportarse en estadios clínicos más tardíos. Así mismo, hubo un incremento en el número de PVV fallecidas en todas las regiones de Colombia con relación a la emergencia sanitaria por la pandemia de COVID-19.

Enlace

Título

Retos de la gestión del riesgo de las personas viviendo con el VIH en el aseguramiento en Colombia.

Autores

Luis Alejandro Moreno Ramírez, Andrés Felipe Patiño Aldana, Ana María Valbuena García, Lizbeth Acuña Merchán.

Evento

Encuentro científico INS: La investigación en salud pública con enfoque integral impacta los territorios.

Ámbito: nacional.

Objetivo

Identificar desigualdades y oportunidades de mejora en los territorios según los resultados de gestión del riesgo de las PVV en el marco del aseguramiento en Colombia.

Principales hallazgos

- Risaralda, Quindío, Valle del Cauca, Bogotá, D. C., Antioquia, Atlántico y Bolívar tuvieron incidencias superiores a las estimadas a nivel nacional (24,78 casos nuevos por 100.000 habitantes).
- En los territorios con mayor incidencia del VIH, con bajos resultados en detección temprana, seguimiento clínico y cobertura de tratamiento, se deben priorizar intervenciones que mitiguen la trasmisión de la enfermedad y mejoren los resultados.

Enlace

Ponencia oral

VIH

Título

Resistencia a los medicamentos antirretrovirales en personas que viven con el VIH en Colombia.

Autores

Luis Alejandro Moreno Ramírez, Luis Alberto Soler, Ana María Valbuena, Lizbeth Acuña Merchán.

Evento

V Congreso Virología Clínica- ACIN.

Ámbito: nacional.

Objetivo

Caracterizar la resistencia a los diferentes medicamentos antirretrovirales en personas viviendo con el VIH en quienes se realizó el estudio de genotipificación en Colombia tanto al inicio del tratamiento antirretroviral (TAR) como al momento de presentar fracaso virológico, desde el año 2000 hasta el 2019.

Principales hallazgos

- La principal familia con resistencia es la de inhibidores de la transcriptasa reversa seguido por inhibidores de la proteasa. La tendencia de resistencia a inhibidores de nucleótidos y a no nucleótidos va en aumento.
- Debemos acelerar la transición a esquemas que contengan inhibidores de la integrasa (mayor eficacia, más fácil de administrar, menos efectos secundarios, barrera genética alta).
- Se deben implementar periódicamente estudios representativos de farmacorresistencia al VIH a nivel nacional o crear un sistema de información que permita conocer la historia de resistencia a los antirretrovirales de cualquier persona que vive con el VIH.

Enlace

Cáncer

CAC
Cuenta de Alto Costo

Fondo Colombiano de
Enfermedades de Alto Costo

Póster

Cáncer

Título

Lung cancer in the Colombian health system: *a review of trends in morbidity and survival.*

Autores

Silvia Trujillo, Juliana Hernández Vargas, Ginna Paola Fernández Deaza, Lizbeth Acuña Merchán.

Evento

World Cancer Congress 2022.

Ámbito: internacional.

Objetivo

Describir la situación epidemiológica y clínica y la supervivencia global en personas con cáncer de pulmón reportadas entre 2015 y 2020.

Principales hallazgos

- La supervivencia global a 6 años fue del 13,9% (IC 95%: 11,7 - 16,3). Esta fue mayor en mujeres (17%), con respecto a los hombres (12%).
- Al final del periodo de seguimiento, la supervivencia global fue significativamente mayor en casos diagnosticados tempranamente (30%), en comparación con los estadios tardíos (8%).

Enlace

Título

Association of breast and cervical cancer screening with early diagnosis and mortality: *an ecological approach.*

Autores

Ginna Fernández Deaza, Juliana Hernández Vargas, Silvia Juliana Trujillo Cáceres, Lizbeth Acuña Merchán.

Evento

World Cancer Congress 2022.

Ámbito: internacional.

Objetivo

Evaluar el efecto del tamizaje de cáncer de mama y cérvix en la mortalidad general, mortalidad temprana, diagnóstico temprano, y estadificación TNM.

Principales hallazgos

- En las EAPB con cobertura de mamografía ≥ 20%, la mortalidad disminuyó significativamente hasta en 31%. Ajustado por el efecto de la edad, la tamización con la mamografía se asoció inversamente con la mortalidad general.
- En cuanto a la mortalidad temprana, en las EAPB con mayor cobertura de mamografía (≥ 20%), la mortalidad temprana fue hasta un 7% mayor, contrario a lo observado con la mortalidad general.
- En las entidades con cobertura de citología cervicouterina ≥ 45%, las tasas de mortalidad disminuyeron 20%, aunque este efecto no fue estadísticamente significativo.
- En las entidades con mayor cobertura de citología, la mortalidad temprana disminuyó hasta en un 17%.

Enlace

Título

Disparities in Multiple Myeloma (MM) Survival in Colombia: *Findings from a National Administrative Registry.*

Autores

Sergio Augusto Cáceres Maldonado, Sandra Milena Puentes Sánchez, Ana María Valbuena García, Lizbeth Alexandra Acuña Merchán.

Evento

SOHO 2023 Annual Meeting.

Ámbito: internacional.

Objetivo

Estimar la supervivencia global a 5 años en los pacientes con mieloma múltiple (MM) en el marco del aseguramiento en salud colombiano.

Principales hallazgos

- La supervivencia global a 5 años es del 46,75% (IC 95% 44,46 - 49,01), con una mediana a los 5,53 años.
- La regresión de Cox muestra que la edad al diagnóstico, el sexo masculino, el estar afiliado al régimen subsidiado, y la residencia en las regiones Caribe, Central o Pacífica son factores de riesgo de muerte en la cohorte.
- Las brechas entre los regímenes del aseguramiento y las regiones geográficas impactan la mortalidad por todas las causas en las personas con MM.

Enlace

Título

Retos y avances en la gestión del cáncer de mama en el marco del aseguramiento en salud en Colombia: un enfoque mixto.

Autores

Ginna Paola Fernández Deaza, Ana María Valbuena García, Lizbeth Alexandra Acuña Merchán.

Evento

Encuentro científico INS: la investigación en salud pública con enfoque integral impacta los territorios.

Ámbito: nacional.

Objetivo

Identificar los retos y avances en la gestión del riesgo de las mujeres con cáncer de mama.

Principales hallazgos

- La proporción de casos detectados en estadios tempranos disminuyó entre el 2017 y 2020, con una marcada brecha entre los regímenes contributivo y subsidiado.
- El desempeño de los indicadores de oportunidad ha sido bajo/medio, pese a la mejora significativa en la oportunidad de la atención y el tratamiento en el 2021.
- En los grupos focales se identificó que la no disponibilidad de la mamografía y determinados factores individuales afectan negativamente el diagnóstico temprano, así como la fragmentación de la atención, además de aspectos administrativos, son barreras para el tratamiento.

Enlace

Hepatitis C crónica

CAC
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Fondo Colombiano de
Enfermedades de Alto Costo

Póster

Hepatitis C crónica

Título

Impact of the COVID-19 pandemic on chronic hepatitis C healthcare in Colombia.

Autores

Luis Alejandro Moreno Ramírez, Lizbeth Alexandra Acuña Merchán, Mauricio Orrego Beltrán, Sandra Milena Vásquez Vasquez.

Evento

World Hepatitis Summit.

Ámbito: internacional.

Objetivo

Describir el impacto de la pandemia por COVID-19 en la provisión de servicios de salud en los pacientes con hepatitis C crónica en Colombia.

Principales hallazgos

- La detección de la hepatitis C crónica se detuvo debido al temor de los pacientes al contagio con el COVID-19, ni los servicios de prevención realizaron el mismo número de cribados, ya que estaban centrados en la atención de la pandemia.
- La proporción de casos que iniciaron tratamiento con antivirales de acción directa disminuyó en un 12,20%.
- Se observó un aumento en las teleconsultas y seguimientos telefónicos, lo cual permitió monitorear la adherencia, el comportamiento de la enfermedad y la cura de la infección.

Enlace

Enfermedad de Gaucher

CAC
Cuenta de Alto Costo

Fondo Colombiano de
Enfermedades de Alto Costo

Póster

Enfermedad de Gaucher

Título

Definición de aspectos claves en la atención de la EG: de la mejor evidencia disponible a la gestión del riesgo.

Autores

Camilo de la Pava Cortés, Juliana Alexandra Hernández Vargas, Lizbeth Alexandra Acuña Merchán.

Evento

2° Simposio Cochrane Colombia: avances en síntesis de evidencia para la toma de decisiones.

Ámbito: nacional.

Objetivo

Identificar los indicadores descritos en la evidencia para evaluar la gestión del riesgo en las personas con EG que son atendidas en el marco del SGSSS colombiano.

Principales hallazgos

- La medida más relevante para el diagnóstico fue la actividad de la enzima β-glucosidasa ácida.
- Para el continuo de la atención en salud las medidas principales fueron el hemograma completo, la volumetría de bazo e hígado y el seguimiento del componente óseo que comprende el dolor y la crisis ósea, junto con el apoyo de imágenes diagnósticas.
- A partir de la frecuencia del reporte de estas mediciones en los artículos, se propusieron 12 IGR que pueden orientar la evaluación de la gestión del riesgo en las personas con EG, agrupados en las etapas de diagnóstico, tratamiento y seguimiento.

Enlace

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