CUENTA DE ALTO COSTO
Fondo Colombiano de Enfermedades de Alto Costo

Producción de **investigación**

2021

PRODUCCIÓN DE INVESTIGACIÓN 2021

CUENTA DE ALTO COSTO

Fondo Colombiano de Enfermedades de Alto Costo

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CUENTA DE ALTO COSTO

Fondo Colombiano de Enfermedades de Alto Costo

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Introducción

En la actualidad, la medicina basada en la evidencia ha tomado especial importancia en la determinación de los mejores estándares de la atención en salud tanto a nivel individual como poblacional. Con ella, se busca la toma de decisiones asertivas, bien fundamentadas, establecidas de manera metódica y sistemática (1). La investigación científica en salud recopila la información relevante respecto a los comportamientos, los factores de riesgo, las tendencias de la enfermedad, el desarrollo y la evaluación de intervenciones, planes y políticas en esta materia (2). Los resultados obtenidos a través de la investigación pueden aprovecharse para la implementación de políticas e intervenciones en salud pública.

En el caso de las enfermedades de alto costo (EAC), la comprensión de las tendencias a nivel clínico y epidemiológico, así como la gestión de estas en los territorios y el acceso a los servicios de salud, permiten planificar la disponibilidad y la oferta de las redes de atención con base en las necesidades identificadas. En ese sentido, y de acuerdo con el compromiso en la promoción de la gestión del riesgo, la mejora de los resultados en salud y la gestión de conocimiento de las EAC, la Cuenta de Alto Costo (CAC) se ha posicionado como referente en el análisis de la información del mundo real en las EAC en el marco del aseguramiento colombiano, disponiendo de un trabajo interdisciplinario y metodológicamente robusto para el abordaje de este fenómeno de gran impacto en el país en asociación con los actores del sistema de salud.

En este documento encontrará los productos de investigación publicados, pósters y ponencias realizadas durante el año 2021 en cabeza del equipo de investigación de la CAC. Finalmente, realizamos una mención especial a los expertos clínicos, a las asociaciones científicas y a las instituciones académicas, entre otros actores del sistema que han contribuido en la concepción, construcción y publicación de estos resultados que enriquecen el conocimiento de las dinámicas en salud de la población colombiana con EAC.

CUENTA DE ALTO COSTO
Fondo Colombiano de Enfermedades de Alto Costo

Enfermedad renal crónica

ERC, HTA Y DM

The effect of comorbidities on glycemic control among Colombian adults with diabetes mellitus: A longitudinal approach with real-world data

Autores: Manuel Alejandro Urina Jassir, Lina Johana Herrera Parra, Juliana Alexandra Hernández Vargas, Ana María Valbuena García, Lizbeth Acuña Merchán, Miguel Alberto Urina Triana.

Revista: BMC Endocrine Disorders.

Alcance: Internacional.

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 el efecto longitudinal sobre las comorbilidades relacionadas con la diabetes mellitus (DM) (hipertensión arterial, enfermedad renal crónica y obesidad) en el control glucémico entre los adultos colombianos diagnosticados con DM entre 2014 y 2019.

Principales hallazgos:

- El 85% de las personas con diabetes tuvieron al menos una de las comorbilidades de interés.
- En las personas con DM y enfermedad renal crónica (ERC), la probabilidad de no alcanzar el adecuado control de la glicemia fue 78% mayor a la de los diabéticos sin afectación renal.
- De igual forma, en los diabéticos con obesidad, la probabilidad de un inadecuado control glicémico fue 52% superior a la de los no obesos.

Relevancia de los hallazgos:

- Se resalta la importancia de la DM de inicio temprano como un grupo de alto riesgo para el desarrollo de complicaciones.
- Estos resultados son fundamentales para el establecimiento de programas de identificación y seguimiento de las personas con DM en un mayor riesgo de inadecuado control glicémico, previniendo la aparición de complicaciones en esta población.
- La evidencia del mundo real es vital para la planeación de los servicios de atención cardiovascular y nefroprotección.

Comentario de los autores expertos:

Dres. Miguel Urina Triana y Manuel Urina-Jassir

Uno de los pilares en la práctica clínica para el tratamiento de la Diabetes Mellitus es mantener un adecuado control glicémico. Este ha sido asociado a la disminución de algunas de las complicaciones asociadas a esta enfermedad. En el estudio *"The effect of comorbidities on glycemic control among Colombian adults with diabetes mellitus: A longitudinal approach with real-world data"* publicado en *BMC Endocrine Disorders,* se evaluó, con los datos obtenidos y auditados por la CAC, el efecto que la hipertensión arterial sistémica, la obesidad y la enfermedad renal crónica tenían sobre el control glicémico encontrando que la presencia de alguna de las dos últimas aumentaba la probabilidad de un peor control glicémico.

Estos hallazgos son útiles e importantes en múltiples ámbitos, pero especialmente en dos, la práctica clínica y en la toma de decisiones por parte de las entidades de salud. Para el clínico, el poder identificar tempranamente a aquellos pacientes que pueden por sus características tener un pobre control glicémico sirve como un sustrato para predecir y establecer que pacientes podrán requerir un mayor o más cercano seguimiento, así como un tratamiento más estricto. Por otra parte, para las entidades tomadoras de decisión en los sistemas de salud, estos hallazgos nutren las posibles estrategias que se puedan generar como por ejemplo mejorar el acceso, estimular un seguimiento más frecuente y definir la necesidad de mejorar la calidad en el manejo de la enfermedad y las comorbilidades que contribuyen a un peor control.

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The effect of comorbidities on glycemic control among Colombian adults with diabetes mellitus: a longitudinal approach with real-world data

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Abstract

Background: Achieving an optimal glycemic control has been described to reduce the incidence of diabetes mellitus (DM) related complications. The association between comorbidities and glycemic control remains unclear. Our aim is to evaluate the effect of comorbidities on glycemic control in people living with DM.

Methods: A retrospective longitudinal study on data from the National Registry of Chronic Kidney Disease from 2014 to 2019 in Colombia. The outcome was poor glycemic control (PGC = HbA1c ≥7.0%). The association between each comorbidity (hypertension (HTN), chronic kidney disease (CKD) or obesity) and PGC was evaluated through multivariate mixed effects logistic regression models. The measures of effect were odds ratios (OR) and their 95% confidence intervals (CI). We also evaluated the main associations stratified by gender, insurance, and early onset diabetes as well as statistical interaction between each comorbidity and ethnicity.

Results: From 969,531 people at baseline, 85% had at least one comorbidity; they were older and mostly female. In people living with DM and CKD, the odds of having a PGC were 78% (OR: 1.78, CI 95%: 1.55-2.05) higher than those without CKD. Same pattern was observed in obese for whom the odds were 52% (OR: 1.52, CI 95%: 1.31-1.75) higher than in non-obese. Non-significant association was found between HTN and PGC. We found statistical interaction between comorbidities and ethnicity (afro descendant) as well as effect modification by health insurance and early onset DM.

Conclusions: Prevalence of comorbidities was high in adults living with DM. Patients with concomitant CKD or obesity had significantly higher odds of having a PGC.

Keywords: Glycated hemoglobin A1c, Diabetes mellitus, Comorbidity, Hypertension, Chronic kidney Disease, Obesity

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Background

Diabetes Mellitus (DM) prevalence is increasing worldwide [1]. The International Diabetes Federation estimated that 9.3% (463 million people) of the global adult population had DM in 2019; with an unsettling projection of 10.2% (578 million people) and 10.9% (700 million people) for 2030 and 2045, respectively [1]. The same phenomena was projected for the South and Central American region; with a prevalence up to 8.5% (31.6 million people) and a prediction up to 9.9% (49.1 million people) in 2045 [1]. The aforementioned region includes Colombia, a country where DM prevalence ranges from 1.8-11.2% depending on the report consulted [2]. This is alarming given the effects DM has on morbidity and the sustainability of health systems [3].

Achieving an optimal glycemic control has been described to decrease the incidence of DM related complications [4–7]. As for microvascular complications, in a recent meta-analysis a more rigorous control was found to reduce the relative risk by 20 and 13% for kidney and eye outcomes, respectively [5]. On the other hand, an effect on macrovascular complications was also described with a reduction in cardiovascular events when intensive glycemic control is employed [6, 7]. In spite of this, only few patients reach the established target; a meta-analysis described that approximately 36% of patients in randomized control trials and 34% in cross-sectional studies achieved the hemoglobin A1c (HbA1c) target (≤7.0% or < 7.0%, respectively) [8].

Different sociodemographic and clinical factors appear to be associated with glycemic control. Regarding age and gender, female and younger patients were more commonly associated with poor control [9]. Taking into account race and ethnicity, studies have demonstrated significant differences between ethnic groups in achieving glycemic target [10, 11]. An additional determinant of inadequate glycemic control is a longer time since the diagnosis of DM [9, 12].

Comorbid conditions, mainly hypertension (HTN), obesity, hyperlipidemia, chronic kidney disease (CKD) and cardiovascular disease, are common in patients living with DM [13]. Studies evaluating the relationship between the presence of comorbidities and glycemic control have showed contradictory findings depending on the analysis. When the total number of comorbidities was used, studies have found no relationship [14] or an inverse relationship [15] between comorbidities and HbA1c. Research using comorbidity scores also established no relationship with HbA1c levels [16]. Whereas in a study evaluating specific comorbidities, subjects with HTN and dyslipidemia were found to have lower odds of achieving glycemic target while no significant association was observed with CKD [17]. Lastly, patients living with DM and overweight or obesity were more commonly associated with poor glycemic levels [18].

Considering the detrimental effects of suboptimal glycemic control, the identification of patients at an increased risk of PGC is crucial for health systems and policy makers as an aid to develop strategies to capture at-risk individuals. Therefore, we aimed to assess the longitudinal effect that common DM-related comorbidities (HTN, CKD, and obesity) have on glycemic control among Colombian adults diagnosed with DM from 2014 to 2019.

Methods

Data sources

We conducted a retrospective longitudinal analysis on data of people diagnosed with DM who were reported by health insurers and providers to the National Registry of Chronic Kidney Disease (NRCKD) from July 1st, 2013 to June 30th, 2019 in Colombia. The NRCKD is managed by the High-Cost Diseases Fund ("Cuenta de Alto Costo" in Spanish). It has been operating since 2008 by a resolution from the Ministry of Health of Colombia [19]. The NRCKD aims to evaluate the burden of CKD and its most common precursors (HTN and DM) as well as the effective 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 approximately 98% of the population is affiliated to the national healthcare system [20], and their insurers are required to report patients living with HTN, DM or CKD to the registry [19]. A unique identification number is assigned to each individual protecting their personal information and allowing future follow up. When a new case enters the NRCKD, a complete registration is done; for old cases, data are updated every year.

The NRCKD undergoes a data auditing process to ensure the veracity 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 health clinical records by a well-stablished data monitoring process in a representative stratified sample of cases with HTN and/or DM, with or without CKD. In case of any inconsistency is identified, the real data on clinical records is captured.

Eligibility of participants

A total of 1,081,863 people aged 18 years or more, diagnosed with DM were reported to the NRCKD from 2014 to 2019. 112,332 were excluded because they had no information available on the measurement of HbA1c. Indeed, 969,531 people met the inclusion criteria and were

analyzed. Figure 1 shows the eligibility flow of the population studied.

Exposure and outcome variables

The presence of comorbidities (HTN, CKD, obesity), reported by health insurers to the NRCKD was considered as the exposure of interest. HTN diagnosis was reported to the NRCKD as its presence or absence. This diagnosis is defined by the treating physician based on his/her clinical judgement [21, 22]. CKD diagnosis was defined by the patients' treating physician and reported to the NRCKD by their insurers as follows: yes/no/undetermined/not studied for CKD during the reporting period. CKD diagnosis was verified by a data monitoring process following an algorithm based on the Colombian CKD guideline that defines the presence of CKD as abnormalities in the structure or function (GFR < 60 ml/min/1.73 m^2) for more than 3 months [23]. People classified as undetermined were those with early kidney impairment that require evidence of functional or structural injury for more than 3 months. Lastly, obesity was determined using the World Health Organization definition (body mass index [BMI] ≥30 kg/m2) [24]. Exhaustiveness and accuracy of exposures were verified in clinical records by a well-established data monitoring process.

A poor glycemic control (PGC) was the dependent variable. It was defined by the measurement of HbA1c, reported during the last 6 months of each follow up period. PGC was treated as a dichotomous variable for each point in time using the cutoff of HbA1c ≥ 7.0%, according to the standard defined by the American Diabetes Association [25].

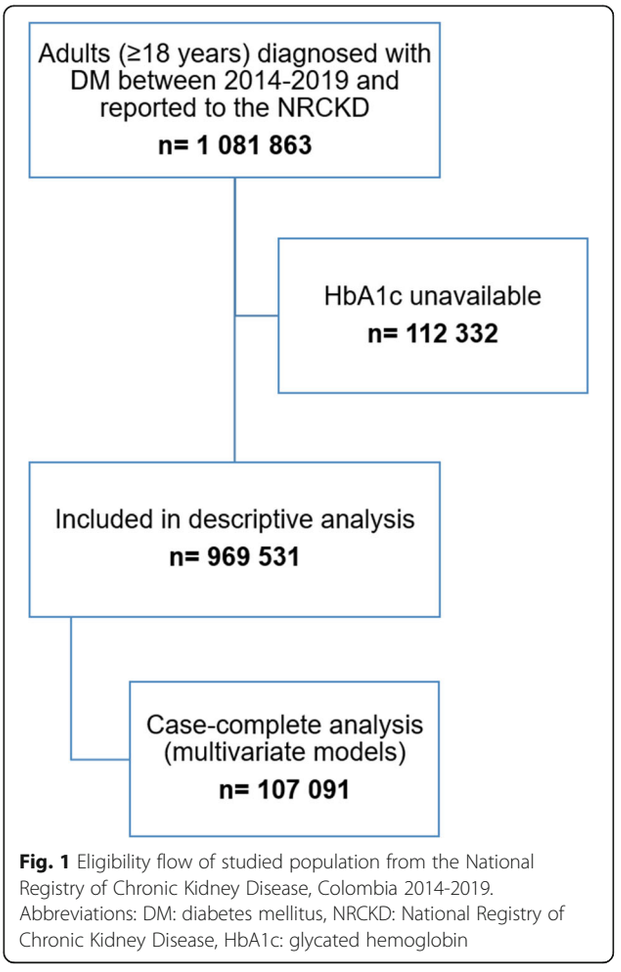

Fig. 1 Eligibility flow of studied population from the National Registry of Chronic Kidney Disease, Colombia 2014-2019. Abbreviations: DM: diabetes mellitus, NRCKD: National Registry of Chronic Kidney Disease, HbA1c: glycated hemoglobin

Covariates

Demographic information included age, gender, health insurance (third payer, state insurance, special insurance, exception insurance or uninsured), and region of residence following the Administrative Department for National Statistics ("Departamento Administrativo Nacional de Estadística" in Spanish) classification (Bogotá, D.C., Central, Eastern, Pacific, Caribbean and Amazonian) [26] (Additional File 1: Table S1). Ethnicity was self-reported and classified in indigenous, afro descendant and other (white, mestizo, gypsy or not classified). In respect of clinical data, age at diagnosis of DM and comorbidities were included. Reported information on weight (kg) and height (meters) was used to calculate BMI (kg/m^2). Otherwise, glomerular filtration rate (GFR) was estimated using the CKD-EPI method and expressed as $mL/min/1.73m^2$ [27]. On the other hand, CKD stages were defined based on the GFR as follows: 1: GFR > 90 with clinical evidence of kidney damage; 2: GFR: 60-90 with clinical evidence of kidney damage; 3: GFR: 30-60, 4: GFR 15-30, 5: GFR: < 15 [28]. Lastly, DM duration was calculated using the date of last contact (last HbA1C test) and the date of diagnosis and informed in years.

Statistical analysis

Descriptive analysis

Baseline demographic and clinical characteristics of the cohort are presented as means or medians and their standard deviation (SD) or interquartile range (IQR), according to their distribution, evaluated by statistical and graphical methods. Otherwise, qualitative data is informed as absolute values (proportions). Baseline characteristics were compared across comorbidities (HTN, CKD and obesity) by using a X^2 test for categorical data and Wilcoxon test was used for numeric variables. We also calculated absolute standardized differences (ASD) between groups of comorbidities to avoid limitations of hypothesis tests taking into account the effect of the sample size. In the case of continuous variables with skewed distribution, rank statistics were used instead the mean [29]. ASD > 10% were considered significant.

Assessment of HbA1c trend

Furthermore, the trend of variation on HbA1c levels during the follow-up for patients with different baseline comorbidity profiles was evaluated by estimating generalized linear mixed models assuming random intercepts for each participant. An interaction term between HbA1c levels and time was included to take into account variations over time, adjusting by each comorbidity. From each model, the predicted Hb1Ac values were plotted over time.

Evaluation of the association between comorbidities and poor glycemic control

The association of interest was estimated using a mixed effects logistic regression model with aleatory intercept, which modelates the odds of PGC for each point in time, taking into account the effect of repeated measures and considering the parameters related to the intercept differentially between each participant, but with a constant slope. The final model for each comorbidity was adjusted by age, gender, ethnicity, health insurance, duration of diabetes. In case of HTN and CKD we also included the BMI (time variant) as a confounder in the final models. Effect measures were the odds ratios and their 95% confidence intervals. We also repeated the final models stratifying by gender, health insurance, and early onset DM (diagnosis < 45 years old [30]) to evaluate a potential effect modification.

Estimation of interaction models

Furthermore, the interaction between each comorbidity and intermediate variables such us ethnicity was explored by the inclusion of a multiplicative term in the final models. p values < 0.05 (two-tailed) were considered statistically significant, except for the effect modification model (p-value < 0.20).

General considerations

Trend and association models were estimated using a case complete approach including people with 6-year HbA1c measurement (n = 107,091). All statistical analyses were performed in Stata version 13 (StataCorp LP, College Station, Texas, USA) and graphs were created in R version 4.0.2.

Sensitivity analysis

We performed sensitivity analysis including a BMI ≥25 kg/m^2 instead of ≥30 kg/m^2 as the exposition to verify the consistency of the association obtained in the main model. Furthermore, we evaluated the association in people with CKD by using a different cut off to define the outcome (HbA1c ≥ 8.0%). Taking into account the potential effect of early onset on PGC, it was tested as a covariate in the final models.

Results

Demographic and clinical characteristics at baseline

969,531 people were analyzed. Mean age at baseline was 61.4 years (SD 13.2), 58.1% were female and 75.7% had third payer insurance. Most people (29.5%) lived in the Central region, followed by Bogotá, D.C. (20.3%). Around 96.0% were self-recognized as "other" ethnicity and 3.5% were afro descendant. Mean age at DM diagnosis was 59.2 years (SD 13.0), median of DM duration was 2.76 years (IQR 1.0-6.0), 56.8% had DM evolution < 5 years and 9.9% had early onset DM. Prevalence of HTN, CKD and obesity were 71.5, 30.6 and 35.2%, respectively. Majority of the people with CKD were classified in stages 2 (43.9%) and 3 (28.9%).

Table 1 shows a characterization by comorbidities. Only 14.9% did not have an associated comorbidity at baseline. Prevalence of comorbidities was higher in women. People with comorbidities were older, except for those with obesity. Age at DM diagnosis was also higher in people with comorbidities. ASD were significant for DM duration in all groups, except for the obese. When comparing the prevalence of obesity by comorbidities, it was also higher in people with HTN and CKD.

Trends of longitudinal variation on HbA1c by comorbidities

After a 6-year follow up, people living with DM and HTN or CKD had a better glycemic control (lower HbA1c levels) than those with obesity. In both DM subjects with HTN or CKD, HbA1c levels were lower in those who had the condition. These findings were contrary to the obese/not obese subjects, where we found higher HbA1c levels when obesity was present. A higher gap in the HbA1c levels between the presence or not of comorbidities was observed in people living with DM and HTN/no HTN than in the other groups. When estimating the longitudinal variation on HbA1c when changing the cut-off from BMI ≥ 30 kg/m^2 to 25 kg/m^2, the trend was opposite to the observed in obese, with a better glycemic control in those with a BMI ≥ 25 kg/m^2 (Fig. 2).

Longitudinal association between comorbidities and glycemic control

The mean number of HbA1c measurements was 3.18 (SD 1.7). Only 11.0% of the patients had 6-year HbA1c measurements and were included in the final models. Global prevalence of PGC was 52.7% (95% CI: 52.6 a 52.8). When analyzing the effect of comorbidities on PGC (HbA1c ≥7.0), we observed no significant association between HTN and PGC. Nevertheless, CKD and obesity were significant and directly associated with PGC in all models. In subjects living with DM and CKD, the odds of having a PGC were 78.0% (OR: 1.78, CI 95%: 1.55-2.05) higher than those without CKD. We also

Table 1 Baseline characteristics of the population studied according to comorbidities in Colombia 2014-2019

Variables[a]	Total (*n* = 969,531)	Comorbidities[d]											
		DM only			HTN			CKD			Obesity		
		Yes (*n* = 144,910)	No (*n* = 824,621)	ASD[e] (%)	Yes (*n* = 693,015)	No (*n* = 276,516)	ASD[e] (%)	Yes (*n* = 297,198)	No (*n* = 672,333)	ASD[e] (%)	Yes (*n* = 341,592)	No (*n* = 627,435)	ASD[e] (%)
Age (y)	61.4 (13.2)	55.0 (13.0)	62.5 (13.0)	58.5	64.0 (12.4)	55.0 (13.0)	71.5	65.1 (14.0)	60.0 (12.6)	40.1	59.4 (12.7)	62.4 (13.4)	23.0
Female	563,687 (58.1)	70,424 (48.6)	493,263 (60.0)	22.6	420,943 (60.7)	142,744 (51.6)	18.4	420,943 (57.6)	142,744 (59.2)	3.1	346,158 (55.7)	217,094 (63.5)	17.1
Health insurance													
Third payer	734,398 (75.7)	108,856 (75.1)	625,542 (76.0)	3.1	528,788 (76.3)	20,561 (74.3)	5.4	217,168 (73.0)	517,230 (77.0)	9.2	271,457 (79.4)	462,723 (73.7)	13.6
State	230,448 (23.8)	35,529 (24.5)	194,919 (23.6)		160,578 (23.1)	69,870 (25.2)		78,500 (26.4)	151,948 (22.6)		68,564 (20.0)	161,600 (25.7)	
Special	1946 (0.2)	319 (0.2)	2312 (0.3)		1576 (0.2)	370 (0.1)		486 (0.1)	1460 (0.2)		687 (0.2)	1258 (0.2)	
Exception	2631 (0.2)	202 (0.1)	1744 (0.2)		1988 (0.2)	643 (0.2)		982 (0.3)	1649 (0.2)		853 (0.2)	1777 (0.3)	
Uninsured	108 (0.1)	4 (0.0)	104 (0.01)		85 (0.1)	23 (0.1)		62 (0.2)	46 (0.1)		31 (0.1)	77 (0.1)	
Region of residence													
Bogotá, D.C.	196,815 (20.3)	32,666 (22.5)	164,149 (20.0)	17.1	134,398 (19.4)	62,417 (22.5)	16.5	55,182 (18.5)	141,633 (21.0)	20.2	72,354 (21.1)	124,389 (20.0)	8.2
Caribbean	168,465 (17.4)	29,317 (20.2)	139,148 (17.0)		117,582 (17.0)	50,883 (18.4)		44,985 (15.1)	123,480 (18.3)		53,045 (15.5)	115,317 (18.3)	
Eastern	131,918 (13.6)	21,638 (15.0)	110,280 (13.3)		89,233 (13.0)	42,685 (15.4)		40,145 (13.5)	91,773 (13.6)		48,960 (14.3)	82,882 (13.2)	
Central	286,454 (29.5)	38,127 (26.3)	248,327 (30.1)		215,779 (31.1)	70,675 (25.5)		84,402 (28.4)	202,052 (30.0)		102,160 (30.0)	184,124 (29.3)	
Pacific	178,174 (18.4)	21,415 (14.8)	156,759 (19.0)		131,532 (19.0)	46,642 (17.0)		70,492 (23.7)	107,682 (16.0)		62,450 (18.2)	115,652 (18.4)	
Amazonian	7705 (0.8)	1747 (1.21)	5958 (0.7)		4491 (0.6)	3214 (1.1)		1992 (0.6)	5713 (0.8)		2623 (0.7)	5071 (0.8)	
Ethnicity[b]													
Indigenous	5078 (0.5)	1275 (1.0)	3803 (0.4)	5.6	2883 (0.4)	2195 (0.8)	6.9	1427 (0.5)	3651 (0.5)	16.1	1174 (0.3)	3892 (0.6)	5.3
Afro descendant	34,514 (3.5)	4608 (3.2)	29,906 (3.6)		22,852 (3.3)	11,662 (4.2)		17,220 (5.8)	17,294 (2.5)		10,765 (3.2)	23,730 (3.8)	
Other	929,939 (96.0)	139,027 (96.0)	790,912 (96.0)		667,280 (96.2)	262,659 (95.0)		278,551 (93.7)	651,388 (97.0)		329,653 (96.5)	599,813 (95.6)	
Age at DM diagnosis (y)	59.2 (13.0)	53.2 (13.0)	60.3 (12.7)	55.3	61.7 (12.1)	53.1 (13.0)	68.3	62.2 (13.5)	58.0 (12.4)	33.1	63.5 (17.1)	57.4 (12.3)	22.0
DM duration (y)[c]	2.76 (1.0-6.0)	1.8 (0.5-4.3)	3.0 (0.9-6.0)	25.5	3.1 (1.0-6.3)	2.0 (0.5-4.3)	37.7	3.2 (1.1-6.6)	2.5 (0.7-5.4)	21.3	2.7 (1.0-5.6)	3.0 (1.0-6.1)	4.3
BMI (kg/m^2)[c]	28.1 (25.3-31.5)	26.0 (24.0-28.0)	28.7 (25.7-32.2)	83.3	28.4 (25.5-32.6)	27.4 (25.1-30.7)	19.6	27.3 (24.5-30.6)	28.5 (25.7-32.3)	25.2	33.1 (31.2-35.7)	26.2 (24.1-28.1)	32.2
HTN diagnosis	693,015 (71.5)	NA	693,015 (84.0)	NA	NA	NA	NA	229,972 (33.1)	67,226 (24.3)	19.2	259,533 (76.0)	433,196 (69.0)	15.5
Glomerular filtration rate (mL/min/1.73 m) [c,f]	79.1 (21.5)	77.1 (21.2)	NA	NA	75.4 (20.8)	87.3 (20.0)	57.3	70.3 (23.8)	NA	NA	77.3 (24.8)	77.4 (21.5)	12.4
CKD diagnosis	297,198 (30.6)	NA	297,198 (36.0)	NA	229,972 (33.1)	67,226 (24.3)	19.6	NA	NA	NA	86,599 (25.3)	210,361 (33.5)	18.0
CKD stages [c]													
1	65,644 (22.4)	NA	65,644 (22.3)	NA	38,594 (17.0)	27,050 (41.2)	67.0	65,644 (22.4)	NA	NA	24,404 (28.5)	41,181 (20.0)	21.3
2	128,930 (43.9)		128,930 (44.0)		100,570 (44.1)	28,360 (43.1)		128,930 (44.0)			35,281 (41.2)	93,544 (45.0)	

Table 1 Baseline characteristics of the population studied according to comorbidities in Colombia 2014-2019 *(Continued)*

Variables[a]	Total (n = 969,531)	Comorbidities[d]											
		DM only			HTN			CKD			Obesity		
		Yes (n = 144,910)	No (n = 824,621)	ASD[e] (%)	Yes (n = 693,015)	No (n = 276,516)	ASD[e] (%)	Yes (n = 297,198)	No (n = 672,333)	ASD[e] (%)	Yes (n = 341,592)	No (n = 627,435)	ASD[e] (%)
3	84,639 (28.9)		84,639 (29.0)		75,879 (33.3)	8760 (13.4)		84,639 (28.8)			22,326 (26.1)	62,263 (30.0)	
4	7522 (2.6)		7522 (2.5)		6907 (3.1)	615 (1.0)		7522 (2.6)			2212 (2.5)	5307 (2.5)	
5	6571 (2.2)		6571 (2.2)		5683 (2.5)	888 (1.3)		6571 (2.2)			1304 (1.5)	5258 (2.5)	
Obesity (BMI > 30 kg/m^2) [c]	341,592 (35.2)	NA	341,592 (41.4)	259,533 (37.4)	82,059 (29.7)	16.4	254,993 (38.4)	86,599 (29.1)	18.6	NA	NA	NA	

Abbreviations: *DM* diabetes mellitus, *HTN* hypertension, *CKD* chronic kidney disease, *BMI* body mass index
[a] Values are absolute values (percentages) for categorical variables. In case of numeric variables, they correspond to mean (SDs) or median (IQRs)
[b] Other category includes people self-recognized as white, mestizo, gypsy or not classified
[c] Less than 5% missing values, except for DM duration in which missing data ranged from 14 to 25%
[d] Differences between groups were evaluated by using X^2 and Wilcoxon tests for categorical and numeric data, respectively. All p-values were < 0.001
[e] Absolute standardized difference (ASD), values > 10% were considered significant
[f] Glomerular filtration rates reported are from patients with CKD diagnosis

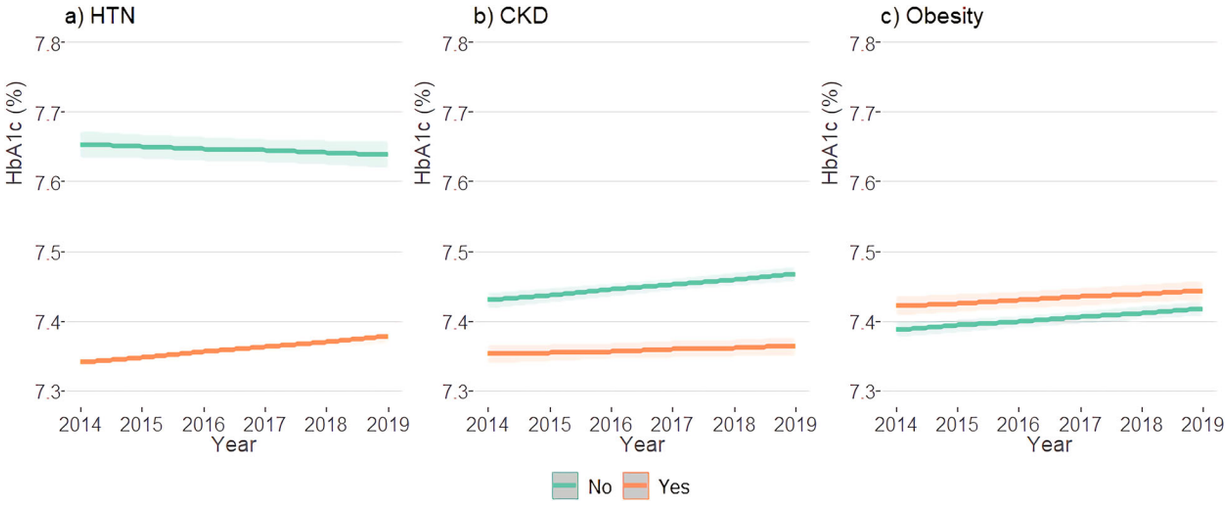

Fig. 2 Longitudinal trend of glycated hemoglobin by comorbidities. Colombia 2014-2019. Figure 2 shows the variation on HbA1c over time by comorbidities. In general, there was a pattern on HbA1c levels in people with diabetes and HTN (**a**) or CKD (**b**), characterized by higher HbA1c in those without the comorbidities. However, an inverse trend was observed in obese (**c**). Abbreviations: HTN: hypertension, CKD: chronic kidney disease, HbA1c: glycated hemoglobin

observed a strong direct association among people living with DM and obesity, in whom the odds were 52.0% (OR: 1.52, CI 95%: 1.31-1.75) higher than in non-obese (Table 2).

In stratified models we did not observe a significant difference by gender. Regarding health insurance, people cover by the state were more likely to achieve a better glycemic control compared with those insured to the third payer, but this effect was only significantly different in CKD. People with obesity and early onset DM had higher odds of having PGC and this effect was significantly different than observed in those diagnosed ≥45 years (Table 2).

Table 2 Multivariate-adjusted odds of poor glycemic control by comorbidities in Colombian adults with diabetes mellitus, 2014-2019

Model	Hypertension			Chronic kidney disease			Obesity		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age adjusted	1.08	0.91 - 1.28	0.36	1.76	1.54 - 2.02	< 0.01	1.49	1.30 - 1.71	< 0.01
Multivariable 1 [a] (Fixed BMI)	1.08	0.91 - 1.28	0.36	1.75	1.53 - 2.00	< 0.01	1.46	1.27 - 1.68	< 0.01
Multivariable 1 [b] (Time variant BMI)	0.98	0.83 - 1.16	0.84	1.87	1.64 - 2.14	< 0.01	NA	NA	NA
Multivariable 2 [c] (Fixed BMI)	1.04	0.87 - 1.24	0.66	1.67	1.45 - 1.93	< 0.01	1.52	1.31 - 1.75	< 0.01
Multivariable 2 [d] (Time variant BMI)	0.94	0.78 - 1.13	0.53	1.78	1.55 - 2.05	< 0.01	NA	NA	NA
Stratified [c]									
Gender									
Men	1.03	0.80-1.33	0.82	1.55	1.25-1.92	< 0.01	1.47	1.17-1.85	< 0.01
Women	1.07	0.83-1.37	0.61	1.78	1.47-2.14	< 0.01	1.59	1.32-1.91	< 0.01
Health insurance									
Third payer	1.10	0.91-1.32	0.32	1.84	1.59-2.12	< 0.01	1.64	1.41-1.90	< 0.01
State insurance	0.83	0.39-1.77	0.63	0.16	0.1-0.30	< 0.01	0.68	0.34-1.37	0.28
Early onset DM									
Diagnosis < 45 y	0.95	0.48-1.84	0.87	2.01	0.93-4.36	0.08	1.72	1.48-1.99	< 0.01
Diagnosis ≥45 y	0.75	0.62-0.90	< 0.01	1.34	1.16-1.54	< 0.01	0.60	0.30-1.20	0.15

Abbreviations: *OR* odds ratio, *CI* confidence interval, *BMI* body mass index
[a] Adjusted for age (continuous), gender (men vs women) and body mass index (continuous and fixed)
[b] Adjusted for age (continuous), gender (men vs women) and body mass index (continuous and time variant)
[c] Adjusted for age (continuous), gender (men vs women), body mass index (continuous and fixed), ethnicity (indigenous or afro descendant vs. other), health insurance (state insurance or uninsured vs. third payer) and diabetes duration (continuous)
[d] Adjusted for age (continuous), gender (men vs women), body mass index (continuous and time variant), ethnicity (indigenous or afro descendant vs. other), health insurance (state insurance or uninsured vs. third payer) and diabetes duration (continuous)

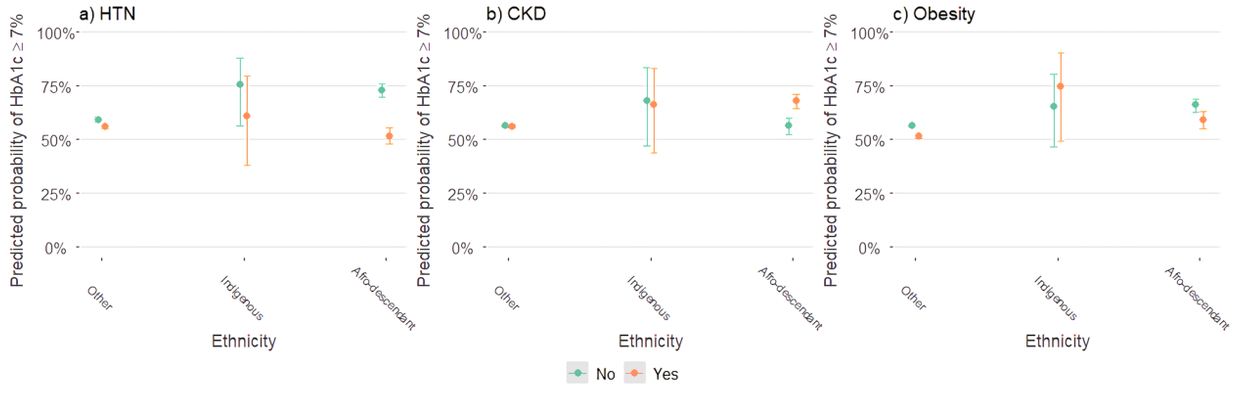

Fig. 3 Predicted probabilities of poor glycemic control according to comorbidities and ethnicity, Colombia 2014-2019. Figure 3 shows the predicted probabilities of poor glycemic control according to the presence of comorbidities and ethnicity estimated in a multivariate model adjusted by for age, gender, BMI (only for HTN and CKD), health insurance and diabetes duration. Predicted probabilities of poor glycemic control were significantly lower in afro descendant with HTN (**a**). An opposite association was found in afro descendant with CKD (**b**). In afro descendant with obesity, the association was similar to those with HTN although it was not statistically significant (**c**). Abbreviations: HTN: hypertension, CKD: chronic kidney disease, HbA1c: glycated hemoglobin, BMI: body mass index

When evaluating the interaction between comorbidity and ethnicity, we only identified a statistically significant interaction between each comorbidity and afro-descendants (all *p*-values were < 0.01). Predictive probabilities of having a PGC were significantly lower in afro-descendant with HTN compared with afro descendant without HTN. Otherwise, an inverse effect was found in afro descendant with CKD who had a significantly higher probability of a PGC. Afro descendant with obesity, had a lower probability of a PGC, following the same pattern observed with HTN, however, the effect was not significant (Fig. 3).

Sensitivity analysis

The associations of interest were consistent with the main models (Additional File 2: Table S2). When analyzing the effect of a BMI ≥ 25 kg/m^2 on the outcome, we observed the same direction and significance but a lower magnitude in respect of the final model including obesity (OR: 1.26, CI 95%: 1.06-1.49). Similarly, direction and statistical significance remained, although the magnitude decreased when the cut-off point of HbA1c was slightly higher to define the PGC (OR: 1.30, CI 95%: 1.11-1.52). Final models adjusted by early onset DM did not show substantial changes, except for HTN in which direction of the association was inverse although it remained non-significant. Therefore, we hypothesized a potential modifying effect and estimated stratified models as previously described.

Discussion

This study evaluated the effect that common diabetes associated comorbidities (CKD, HTN and obesity) have on glycemic control among a Colombian adult population living with DM. Longitudinal, non-adjusted trend of HbA1c over time showed a better glycemic control in people with HTN, CKD and non-obese. However, when estimating multivariate models, an inverse effect was found, and people living with diabetes and CKD or obesity had significantly higher odds of having a PGC compared to those without the comorbidities. Whereas a non-significant association was found between HTN and a PGC.

Our study showed that CKD was associated with 78% increased odds of having a PGC. Taking into account that a less strict goal may be recommended in patients living with DM and advanced comorbid diseases [25, 31], we conducted a sensitivity analysis with a less strict threshold (PGC as HbA1c ≥8.0%). Even with this flexible target, the findings were consistent. Patients living with DM and CKD had an increase likelihood of PGC when compared to those without CKD even with a less stringent goal.

Interestingly, we found statistical heterogeneity in the effect of CKD on PGC by health insurance with 84% decreased odds of PGC in people under state insurance whereas third payer affiliates maintained the same trend of the general findings. Previous studies have evaluated the effect of health insurance on glycemic control [32, 33]. A cross-sectional study in Mexico showed that public health affiliates were more likely to have a better glycemic control than uninsured subjects [32]. Similar findings were described by Zhang et al. in the USA where uninsured subjects were more likely to have HbA1c > 9% [33]. In Colombia, both types of insurance have similar access to healthcare services and medications [34], complicating comparisons with other health systems. A possible explanation to our findings could be

a higher proportion of stage 5 CKD in the state insurance compared with third payer affiliates (10% versus 1.81%) since the precision of HbA1c reduces with advanced CKD stages and this can lead to underestimation of glycemic levels [31, 35]. Furthermore, when evaluating the interaction between CKD and ethnicity, we found that afro descendants living with DM and CKD also had an increased probability of PGC compared to those without CKD.

Our overall findings are consistent to those found by De Cosmo et al. where CKD (defined as low GFR, high albuminuria or both) was associated with a lower probability of achieving the HbA1c target established in a large Italian population living with DM [36]. However, others have reported that people living with DM and CKD had lower odds of having suboptimal glycemic control [37]. It is important to note that despite the previously described limitations, HbA1c is still considered the standard for glycemic follow-up in patients with CKD [31, 38] thus giving relevance to our results. These findings should increase the concern of clinicians taking care of patients with kidney dysfunction given the consequences of a PGC have on DM patients with CKD. A meta-analysis of patients living with DM treated with hemodialysis described an increased risk of mortality in people with HbA1c ≥8.5% when compared to lower levels (6.5-7.4%) [39]. Also, Kuo et al. observed that HbA1c levels > 9% were associated with an increased risk of end stage renal disease and mortality in patients living with diabetes and CKD stages 3-4 [40].

Similar to the CKD effect on PGC, we observed that obese people were 52% more likely to have a PGC than those without obesity. When a lower threshold was used (≥25 kg/m^2), the results followed a similar trend, but magnitude decreased to 26%. Together, these results indicate that an elevated BMI increases the risk of PGC in patients living with DM. Similar conclusions have been described in previous studies [37, 41]. A cross sectional study in Iranian population living with diabetes found an association between obesity and poor glycemic control [41]. Furthermore, Bae et al. describe an increased probability of suboptimal glycemic control when overweight or obesity was present in patients living with DM in the USA [37]. Nevertheless, Chetoui et al. did not found an association between overweight/obesity and poor glycemic control in a Moroccan population living with type 2 DM [12]. In a therapeutically point of view, Gummesson et al. stated that weight reduction in overweight and obese patients living with type 2 DM is consistently followed by a reduction on HbA1c levels [42].

Moreover, when evaluating the effect of comorbidities on PGC stratified by age of diagnosis (< 45 years and ≥ 45 years), we found that people with obesity and early onset DM had higher odds of having PGC. These findings are of interest since previous studies have identified a high prevalence of obesity in patients with early onset DM [43, 44]. Additionally, Gopalan et al. described that patients with a diagnosis at 21-44 years had higher initial HbA1c levels and lower odds of achieving glycemic control after a 1 year follow up compared with those diagnosed at 45-64 years [45]. Therefore, these findings support the importance of early-onset DM to further implement specific cost-benefit strategies within this high-risk group to avoid the long-term deleterious complications of PGC.

Some authors have described the presence of HTN as a predictor of poor glycemic control [17, 41]. However, we did not find a significant association between HTN and PGC. Our results are consistent with those of Badedi et al. describing no association between HTN and HbA1c [46]. Though, this was different when evaluating the interaction between ethnicity and HTN. We found that afro descendants living with DM and HTN had a lower predictive probability of PGC than those without HTN; other ethnicities did not have a significant association. Various authors have described an association between ethnicity and glycemic control [10, 11]. A cross sectional study in the USA, found that non-Hispanic blacks and Mexican Americans when compared to non-Hispanic whites had lower odds of adequate glycemic control [11]. Additionally, the same study described that the proportion of patients with three comorbidities (HTN, Hyperlipidemia and obesity) achieving glycemic control (HbA1c < 7.0%) changed according to their ethnicity: 22.8, 11.4 and 0% of non-Hispanic whites, non-Hispanic blacks and Mexican Americans, respectively [11].

High prevalence of PGC could negatively impact health systems. In people living with DM, higher HbA1c levels were associated with an increase in the rate of DM-related hospital admissions [47]. Following a similar trend, Gil et al. evaluated the effect of uncontrolled DM (HbA1c ≥ 7.5%) on health care utilization and found an increase in the number of general practitioner and specialist visits as well as hospital length of stay among male patients living with DM [48]. Furthermore, a cross-sectional study in Spain described that people with PGC had a higher total health-related costs including medication and hospitalization costs when compared to those controlled [49]. The above suggests that a higher proportion of people with PGC may significantly increase the burden on healthcare systems, with a worse impact in low-and-middle-income countries. Thus, our results should encourage public health decision-making for early identification, increased access to health care, and surveillance in subjects living with DM at a higher risk of PGC due to the coexistence of obesity or CKD.

This study has important strengths. First of all, this report reflects a national scope since data come from the largest registry of people with CKD in the country. By including people with different comorbidities, our results are representative of the Colombian population living with DM who receive services within the framework of the health system. Furthermore, a longitudinal approach was used and the effect of repeated measures during the follow up was considered in the final models. This differs from the commonly used cross sectional analysis in studies evaluating factors influencing glycemic control. On the other hand, the use of HbA1c has been well described to evaluate long term glycemic control and because we only studied people with a new DM diagnosis, changes in glycemic control over time are meaningful for decision making process at a clinical and organizational level.

Some limitations should be considered when interpreting our findings. There is a clear effect of medication and non-pharmacological treatment on prospective glycemic control. Nonetheless, we were unable to adjust for treatment because these data were unavailable so residual confusion cannot be ruled out. Following the same line, although some sociodemographic factors such as educational level, income and urban/rural areas have been associated with PGC, we did not evaluate their effects because these variables are not available in the NRCKD. Moreover, the NRCKD is a passive registry and reporting process is performed by health care insurers; this can lead to underreporting and despite it is minimal, it must be declared. Linked to the above, data on variables are likely subjected to measurement error. Nevertheless, its impact was limited through the data monitoring process. In any case this error would be non-differential and effect estimations tend to the null.

Conclusions

In this adult population living with DM, patients with concomitant CKD or obesity had an increased likelihood of PGC. This supports the importance of weight reduction in diabetes treatment; as well as the increased surveillance and treatment needed in the CKD population. Our findings are based on data from real-world clinical practice thus they should be helpful for public health entities in decision making process. The strategies should be directed in improving access to healthcare, surveillance and treatment in these patients given the detrimental effects of PGC. Whether the presence of HTN modifies the probability of developing a PGC could not be clarified in this study; this effect was only modified in afro descendant ethnicity where HTN decreased the odds of a PGC. Further studies evaluating the effect of pharmacological and lifestyle interventions as well as sociodemographic factors such as educational level, socioeconomic status, or living area (rural versus urban) on the association of interest are needed. The effect of early-onset DM on the increased likelihood of having PGC is noteworthy; hence, further research that evaluates the long-term effect of optimal glycemic levels on the risk of DM-associated complications and mortality is needed.

Abbreviations

ASD: Absolute Standard Differences; BMI: Body Mass Index; CKD: Chronic Kidney Disease; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; DM: Diabetes Mellitus; GFR: Glomerular Filtration Rate; HbA1c: Hemoglobin A1c; HTN: Hypertension; IQR: Interquartile range; NRCKD: National Registry of Chronic Kidney Disease; PGC: Poor Glycemic Control SD: Standard deviation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-021-00791-w.

Additional file 1. Table S1. Distribution of Colombian departments by region*.

Additional file 2. Table S2. Multivariate-adjusted odds of poor glycemic control according to sensitivity analysis criteria, Colombia 2014-2019.

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Authors' contributions

MUJ, LJHP, JAHV, AMVG, LAM, MUT were involved in the conception and design of the study. LJHP and JAHV conducted the statistical analyses and tables/figures. AMVG supervised the statistical analyses. MUJ, LJHP, JAHV, AMVG, LAM, MUT contributed to the interpretation of the analyses. MUJ and JAHV wrote the initial draft of the paper. MUJ, LJHP, JAHV, AMVG, LAM, MUT contributed to the revision of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to that they are owned by the Colombian health system but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All the methods were carried out following national (Resolution 8430 of 1993, stated by The Colombian Health Ministry) and international (The Declaration of Helsinki) standards. Approval by the Ethics Committee of Fundación del Caribe para la Investigación Biomédica (Record 0211 from October 17th, 2020) was obtained. According to the national regulations for conducting human research (Resolution 8430 of 1993, stated by The Colombian Health Ministry), this investigation has no risk for participants. Our research was based on secondary data sources which was anonymized and did not include any private information that could make any subject identifiable. Taking into account the above and the retrospective nature of our research, the Ethics Committee of Fundación del Caribe para la Investigación Biomédica waived the need for informed consent.

Consent for publication

Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Publisher's Note

CUENTA DE ALTO COSTO

Fondo Colombiano de Enfermedades de Alto Costo

VIH/sida

VIH

Supervivencia en las personas que viven con VIH en el marco del sistema de salud colombiano 2011 – 2018

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Trabajo colaborativo con expertos clínicos y miembros de la Organización Panamericana de Salud.

Objetivo:

Describir la supervivencia a siete años y sus principales factores asociados en las personas que viven con VIH (PVV) que fueron atendidas en el sistema de salud colombiano y reportadas a la CAC entre el 1 de febrero de 2011 al 31 de enero de 2018.

Principales hallazgos:

- La estimación de la supervivencia global a los 7 años fue de 94,80% (IC 95%: 94,50 - 95,20).
- El diagnóstico temprano de VIH (linfocitos T CD4+ ≥500 células/μL) mejora la supervivencia en las PVV.
- Las personas en estadio sida (estadio 3) presentaron una menor supervivencia comparada con las PVV en estadio clínico VIH (estadio 1 y 2).

Relevancia de los hallazgos:

- Este estudio es el primer análisis publicado que describe la supervivencia de las PVV que han sido reportadas a la CAC y son atendidas en el sistema de salud colombiano; así como los factores de riesgo que están relacionados con una mayor mortalidad.
- Los hallazgos proponen el abordaje de acciones que minimicen las barreras para el diagnóstico temprano, así como la optimización de las herramientas para aumentar el acceso a los servicios de salud primarios.
- La identificación de los factores asociados a una mejor supervivencia en las PVV que reciben atención en el marco del aseguramiento en Colombia aporta a la planeación de intervenciones enfocadas en estos aspectos que permiten el logro de mejores resultados en salud con un uso más eficiente de los recursos.

Comentario del autor experto:

Dras. Ana María Valbuena y Nathaly Ramírez

Los hallazgos de este estudio evidencian con datos de la vida real, de las PVV atendidas en el marco del sistema de salud colombiano, la importancia del diagnóstico temprano y el tratamiento oportuno para mejorar la supervivencia. Este estudio es producto de la alta rigurosidad metodológica que se lleva a cabo en la CAC y del trabajo colaborativo con expertos clínicos, para brindar información confiable que permita a los actores del sistema de salud en Colombia planear intervenciones enfocadas en estos hallazgos y así disminuir la mortalidad de las PVV.

En este sentido, la búsqueda activa juega un papel importante en el logro de mejores resultados en salud; las entidades y la red de prestadores deben planear y ejecutar estrategias que permitan detectar a esta población tempranamente, así como de indagar y superar las barreras por las cuales la población masculina tiene una supervivencia menor que la femenina. Cabe resaltar también la necesidad del fortalecimiento de los programas de atención integral y de calidad en pro del seguimiento adecuado y oportuno del recuento de linfocitos T CD4+ y la carga viral.

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ARTÍCULO ORIGINAL

Supervivencia en las personas que viven con VIH en el marco del sistema de salud colombiano 2011-2018

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Resumen

Objetivo: Describir la supervivencia a siete años y los principales factores asociados a esta, en las personas con VIH que fueron atendidas en el sistema de salud colombiano entre 2011 a 2018.

Métodos: Análisis de supervivencia de una cohorte de 64 039 personas diagnosticadas con VIH en Colombia. Se aplicó el método de Kaplan-Meier para estimar la probabilidad de supervivencia a partir de la fecha del diagnóstico. Se ajustó un modelo de supervivencia paramétrico flexible de Royston Parmar.

Resultados: La estimación de la supervivencia global a 7 años fue de 94,8% (IC 95%: 94,5-95,2). El mayor riesgo de muerte se presentó en los hombres (HR: 1,2; IC 95%: 1,1-1,4; *p*: 0,010); en personas ≥50 años de edad (HR: 3,1; IC 95%: 1,6-6,3; *p*: 0,002); en el régimen subsidiado (HR: 2,2; IC 95%: 1,9-2,5; *p*: <0,001); en la etapa sida (HR: 2,8; IC 95%: 2,1-3,7; *p*: <0,001); en quienes presentaron la última carga viral detectable (HR: 7,1; IC 95%: 6,0-8,3; *p*: <0,001); y en quienes mostraron conteo de linfocitos T CD4+ <350 células/µL (HR: 1,9; IC 95%: 1,4-2,4; *p*: <0,001).

Conclusión: La probabilidad de la supervivencia de las personas que viven con VIH aumenta al ser diagnosticados en edades jóvenes, en quienes presenten un recuento de linfocitos T CD4+ ≥350 células/µL, una carga viral indetectable (< 50 copias/mL) y no se encuentren en etapa sida.

Palabras clave: Análisis de supervivencia, VIH, Linfocitos T CD4-Positivos, Carga viral (fuente: DeCS).

Survival in people living with HIV in the framework the Colombian health system: 2011-2018

Summary

Objective: to describe the seven-year survival and predictors of mortality among people with HIV who were treated in the Colombian health system between 2011 and 2018.

Methods: 64 039 people diagnosed with HIV in Colombia were included. Kaplan-Meier analysis estimated the probability of survival from the date of diagnosis. A Royston Parmar flexible parametric survival model was fitted.

Results: The overall survival at 7 years was 94.8% (95% CI: 94.5-95.2). Survival was related to sex (men, HR: 1.2; 95% CI: 1.1-1.4; p: 0.010); people ≥50 years of age (HR: 3.1; 95% CI: 1.6-6.3; p: 0.002); subsidized regime (HR: 2.2; 95% CI: 1.9-2.5; p: <0.001); AIDS stage (HR: 2.8; 95% CI: 2.1-3.7; p: <0.001); a detectable viral load (HR: 7.1; 95% CI: 6.0-8.3; p: <0.001); and a CD4+ Lymphocyte count <350 cells/µL (HR: 1.9; 95% CI: 1.4-2.4; p: <0.001).

Conclusion: The probability of survival of people living with HIV increases when they are diagnosed at a young age, in those with a CD4+ T Lymphocyte count ≥350 cells/µL, an undetectable viral load (<50 copies/mL) and are not in the AIDS stage.

Keywords: Survival Analysis, HIV, CD4 Lymphocyte Count , Viral load (MeSH).

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Introducción

Los avances tecnológicos en salud han logrado el aumento de la supervivencia de las personas que viven con el virus de la inmunodeficiencia humana (VIH) (PVV). Tanto es así que estudios recientes han encontrado una probabilidad de supervivencia en PVV con tratamiento antirretroviral (TAR) del 96% durante el primer año después del diagnóstico y hasta del 88% a los 15 años[1]. De hecho, algunos estudios exploran los riesgos de morir por enfermedades cardiovasculares, la enfermedad pulmonar obstructiva crónica y los cánceres, dado los largos tiempos de supervivencia de esta población[2]. Diferente a lo que ocurría hacia finales de 1985 en EE. UU., cuando se reportó que el 83% falleció durante el primer año y la tasa estimada de supervivencia al tercer año era del 11%[3].

Estudios más recientes, realizados en China encontraron un tiempo medio de supervivencia de los casos de VIH/sida mayor de 16 años entre 1997 y 2018[4] con un mayor riesgo de muerte al aumentar la edad, al detectar la enfermedad durante el ingreso hospitalario en fase sida y no recibir TAR[3]. En relación con las personas con el síndrome de inmunodeficiencia adquirida (sida), se ha estimado que la probabilidad de supervivencia a ocho años desde el inicio del sida es del 78% en quienes reciben TAR. En contraste, la supervivencia a 6 años en pacientes con sida sin TAR es del 26%; concluyendo así que más de la mitad de las PVV que reciben TAR sobrevivieron más de 10 años desde el inicio del sida y más de la mitad de las PVV que no reciben tratamiento mueren dentro de los dos años posteriores al inicio del sida[1].

Entre los factores descritos en la literatura que afectan la supervivencia de las PVV están: sexo masculino, edad > 40 años, estadio clínico avanzado[5], bajo índice de masa corporal[6], el no uso temprano de la TAR[7], el diagnóstico tardío de la enfermedad[8] y la presencia de enfermedades oportunistas como la tuberculosis[9]. En cuanto a los resultados de laboratorio también se han descrito variables pronóstico para mortalidad como: el bajo recuento de células T CD4+, la baja albúmina sérica, el recuento alto de glóbulos blancos, el porcentaje elevado de neutrófilos y la anemia[10].

En Colombia, la Cuenta de Alto Costo (CAC) (organismo técnico no gubernamental que promueve la gestión de riesgos, la generación de resultados en salud y la gestión de conocimiento de las enfermedades de alto costo) ha realizado seguimiento de los pacientes con VIH, gracias a la normatividad vigente del país que obliga a las Empresas Administradoras de Planes de Beneficios de salud (EAPB) al reporte de todos los casos con VIH[11]. Estas entidades son las encargadas de la gestión de riesgo de los afiliados independiente si la afiliación es pagada por el trabajador y empleador (régimen contributivo), si es financiada con otros recursos (subsidiado) o si proviene de entidades que tienen su propio financiamiento (universidades, fuerzas militares, policía nacional, medicina prepagada y direcciones territoriales de salud). En un primer acercamiento a los análisis de supervivencia, la CAC encontró en una cohorte de 60 mil pacientes seguida durante siete años una menor supervivencia en las PVV afiliadas al régimen subsidiado, estar en estadio sida y no recibir TAR[12]. Este artículo tiene como fin describir la supervivencia a siete años y los principales factores asociados a esta en las PVV que fueron atendidas en el sistema de salud colombiano y reportadas a la CAC entre el 1 de febrero de 2011 al 31 de enero de 2018.

Métodos

Población de estudio

Personas atendidas dentro del marco del Sistema General de Seguridad Social en Salud (SGSSS) diagnosticadas con VIH entre el 1 de febrero de 2011 al 31 de enero de 2018 y que fueron reportadas a la CAC en cumplimiento de la obligatoriedad de este reporte[13,14] por parte de las entidades encargadas de la gestión del riesgo.

Diseño del estudio

Estudio observacional, de tipo cohorte retrospectiva.

Variables

La variable principal es el tiempo de supervivencia o de censura de los pacientes, medida en años y estuvo delimitado por un primer evento el cual correspondió a la fecha de diagnóstico de infección por VIH y por un segundo evento definido como la fecha de muerte. La confirmación diagnóstica fue realizada según el algoritmo de la Guía de Práctica Clínica (GPC) basada en la evidencia científica para la atención de la infección por VIH/sida en adolescentes (con 13 años de edad o más)[15] y validada con los soportes de los laboratorios clínicos o el reporte en la historia clínica de la confirmación diagnóstica.

Se definió como censura a la derecha las pérdidas del seguimiento debido al abandono de la atención, muerte por causas externas o por finalización del seguimiento sin la ocurrencia del evento muerte. Los pacientes no censurados fueron quienes presentaron muerte por sida o por otra patología no definitoria de sida.

Covariables

Se seleccionaron de acuerdo con el marco conceptual de la investigación. Estas fueron medidas al momento del diagnóstico de VIH: sexo, edad, régimen de afiliación, región de residencia, conteo de linfocitos T CD4+, diagnóstico temprano (definido como los pacientes diagnosticados con linfocitos T CD4+ ≥500 células/μL) y estadio clínico según el sistema de clasificación de los CDC 2008 (16). También se midieron las variables: ultima carga viral para VIH, tiempo entre la fecha de diagnóstico y fecha de inicio de la primera TAR, presencia de enfermedades oportunistas definitorias de sida y comorbilidades durante el periodo de estudio.

Fuentes de datos

Los datos fueron tomados a partir de historias clínicas de personas con diagnóstico de VIH reportados a la CAC entre el 1 de febrero de 2011 al 31 de enero de 2018. La información contiene datos sobre la población afiliada a cualquiera de los regímenes según la ley 100 de 1993[17] o pacientes no afiliados al sistema de salud pero que son atendidos por las Secretarias de Salud de Colombia. Este proceso de reporte estandarizado de variables es obligatorio y se realiza mediante la Resolución 4725 de 2011[14] y la Resolución 783 del 2012[13], declaradas por el Ministerio de Salud y Protección Social de Colombia. Dicha información fue ingresada a un sistema de validación estandarizada que revisó la coherencia entre variables; posteriormente, los datos fueron auditados contrastándolos con los soportes de historia clínica y resultados de laboratorio remitidos a la CAC. En aquellos casos donde no coincidió lo reportado contra lo soportado, se realizó la corrección en la base de datos según la fuente primaria.

Descripción estadística de la población de estudio

Las variables categorizadas fueron presentadas en valores absolutos y relativos.

Análisis de supervivencia

Se realizó la descripción de la información marginal y por categorías de las variables de la muestra de supervivencia. Se aplicó el método de Kaplan-Meier para estimar la probabilidad de supervivencia para diferentes periodos de tiempo a partir de la fecha de diagnóstico. También se evaluaron las funciones de riesgo, las gráficas de doble logaritmo complementario y se realizó la prueba de hipótesis log-rank para comparar la supervivencia entre las categorías de estudio.

Se ajustó un modelo de supervivencia paramétrico flexible de Royston Parmar, con una distribución de base modelada por una función del log-tiempo restringida por splines cúbicos[18], debido a que, el modelo de Cox no cumplía con el supuesto de riesgos proporcionales, esto fue probado mediante el uso de los residuos de Schoenfeld y de Schoenfeld escalados. Para determinar la complejidad adecuada del número de nodos para caracterizar la función de base se realizaron pruebas de sensibilidad variando el número de nodos internos de 1 a 8 y se evaluó mediante el criterio de información de Akaike (AIC) para determinar el ajuste óptimo[18]. El modelo seleccionado fue un modelo con 3 nodos internos (4 grados de libertad). Se presentaron los resultados en una escala de Hazard ratios (HR) para facilitar la interpretación de los efectos de las covariables.

Se consideró significancia estadística a un valor de *p* menor que 0,05. Se utilizó STATA 13 (Stata Corporation, College Station, TX, USA) para todos los análisis estadísticos.

Consideraciones éticas

En Colombia, la legislación permite a la CAC utilizar datos clínicos sobre enfermedades de alto costo, reportados por las aseguradoras de salud, para auditar y generar información confiable. No se hizo ninguna intervención ni modificación intencionada de variables biológicas, fisiológicas, sicológicas o sociales de los individuos participantes, por lo cual el estudio se clasificó como investigación sin riesgo según lo establecido en la Resolución 8430 de 1993 del Ministerio de Salud de la República de Colombia. Por lo anterior, no se requirió consentimiento informado o aprobación ética. La CAC, tiene la responsabilidad de velar por la protección de los datos personales y clínicos de acuerdo con lo establecido en el artículo 15 de la Constitución Política de Colombia de 1991 desarrollado en la Ley estatutaria 1581 de 2012 "por el cual se dictan disposiciones generales para la protección de datos personales".

Resultados

Descripción estadística

Se obtuvo información en 64 907 PVV. De estos, 76,6% correspondieron al sexo masculino. El grupo de edad con mayor número de casos fue entre los 25 a 49 años (60,6%). La mayor proporción de población pertenecía al régimen contributivo. La región colombiana que reportó mayor número de casos fue la Central con el 27,0% de los casos (tabla 1).

Entre las variables clínicas, solo el 16,7% del total de PVV tuvieron un diagnóstico temprano de la enfermedad. Adicionalmente, se evidenció que, del total de pacientes con una clasificación de estadio al momento del diagnóstico, el 39,2% se encontraron en etapa de sida. Con respecto a la última carga viral (CV), el 55,2% de los pacientes se encontraban con cargas virales indetectables (<50 copias/mL).

Con relación al tiempo entre la fecha de diagnóstico y la fecha de inicio de la primera TAR, se evidenció que el tiempo de mayor frecuencia fue menos de 1 a 3 meses (65,6%). La tabla 1 muestra la distribución de las características sociodemográficas y clínicas en hombres y en mujeres.

Las enfermedades oportunistas definitorias de sida que se presentaron con mayor frecuencia en el total de PVV durante el periodo de estudio fueron la tuberculosis y la caquexia asociada a VIH con el 9,3% y 17,1%, respectivamente. Las comorbilidades más frecuentes fueron: la dislipidemia (14,2%), la anemia (8,5%) y otras enfermedades de transmisión sexual (15,5%) (tabla 2).

Análisis de supervivencia

Aproximadamente, entre las personas incluidas en la cohorte, el tiempo de seguimiento fue de mínimo 1 día y máximo 7 años. El 50% de los individuos tuvo seguimiento hasta por 2,7 años y el promedio (3,0 años) estuvo ligeramente por encima de la mediana. La mortalidad ocurrió en 2 940 casos (4,6%), de los cuales 1 766 fueron muertes por sida (1,9%), 589 casos fallecieron por otra patología no definitoria de sida (0,9%) y 1 174 casos por causa externa (1,8%). La estimación de la supervivencia global (SG) a 7 años fue de 94,8% (IC 95%: 94,5-95,2).

Tabla 1. Características sociodemográficas y clínicas de la población de estudio

Variables	Sexo femenino (n=15 221) n (%)	Sexo masculino (n=49 686) n (%)
Características sociodemográficas*		
Edad (años)		
Menores de 15	429 (2,8)	394 (0,8)
15 a 49	12 846 (84,4)	43 795 (88,1)
50 o más	1 817 (11,9)	5 294 (10,7)
Régimen de afiliación		
Contributivo	4 784 (31,4)	29 324 (59,0)
Subsidiado	10 129 (66,6)	18 983 (38,2)
Otros[a]	235 (1,5)	1 300 (2,6)
Sin dato	73 (0,4)	79 (0,2)
Región de residencia[b]		
Bogotá D.C.	1 617 (10,7)	12 304 (24,8)
Caribe	5 081 (33,4)	9 733 (19,6)
Central	3 575 (23,5)	13 969 (28,1)
Oriental	1 945 (12,8)	5 605 (11,3)
Pacífica	2 587 (17,0)	7 321 (14,7)
Otros departamentos	343 (2,3)	675 (1,4)
Sin dato	73 (0,5)	79 (0,2)
Características clínicas		
Conteo de linfocitos T CD4+ (Células/µL)*		
<200	3 746 (24,6)	13 973 (28,1)
200-349	2 277 (15,0)	8 182 (16,5)
≥350	4 644 (30,5)	14 842 (29,9)
Sin dato	4 554 (29,9)	12 689 (25,5)
Diagnóstico temprano de VIH (linfocitos T CD4+ ≥500 Células/µL)*		
Sí	2 724 (17,9)	8 084 (16,3)
No	7 943 (52,2)	28 913 (58,2)
Sin dato	4 554 (29,9)	12 689 (25,5)
Estadio clínico de VIH[c]*		
VIH (estadio 1 y 2)	8 978 (59,0)	27 819 (56,0)
Sida (estadio 3)	5 100 (33,5)	18 643 (37,5)
Sin dato	1 143 (7,5)	3 224 (6,5)
Última carga viral		
Indetectable (<50 copias/mL)	8 090 (53,2)	27 729 (55,8)
Detectable	6 505 (42,7)	19 683 (39,6)
Sin dato	626 (4,11)	2 274 (4,58)
Tiempo entre la fecha de diagnóstico y la fecha de inicio de la primera TAR (meses)		
< 1	4 895 (32,2)	12 034 (24,2)
1 a 3	5 355 (35,2)	20 274 (40,8)
4 a 6	1 025 (6,7)	3 949 (8,0)
7 a 12	797 (5,2)	3 100 (6,2)
> 12	1 154 (7,6)	4 237 (8,5)
Sin dato	1 995 (13,1)	6 092 (12,3)

a. Incluye: régimen especial, régimen de excepción y no asegurado.

b. División acorde al producto interno bruto definido por el Departamento Administrativo Nacional de Estadística para el año 2017(19). Las divisiones son: Región Caribe: Atlántico, Bolívar, Cesar, Córdoba, Sucre, Magdalena, La Guajira. Región Central: Caldas, Risaralda, Quindío, Tolima, Huila, Caquetá, Antioquia. Región Oriental: Norte de Santander, Santander, Boyacá, Cundinamarca, Meta. Región Pacífica: Chocó, Cauca, Nariño, Valle. Otros departamentos: Amazonas, Arauca, Casanare, Guainía, Guaviare, Putumayo, San Andrés, Vaupés, Vichada.
c. Clasificación estadio de VIH CDC 2008
* Estas variables fueron medidas al momento del diagnóstico.

Al analizar las curvas de Kaplan-Meier por categorías de las variables, la supervivencia a lo largo del tiempo de seguimiento fue mayor en los menores de 15 años, pero fue disminuyendo a medida que aumentaban los rangos en los grupos de edad. El régimen subsidiado tuvo menor supervivencia (91,8%; IC 95%: 91,0-92,5), al igual que las personas que fueron diagnosticadas en etapa sida (91,2%; IC 95%: 90,5-91,9) (figura 1).

Las PVV con conteo de linfocitos T CD4+ mayor de 350 células/µL tuvieron una supervivencia de 98,6% (IC 95%: 98,1–98,9) mientras que en los de menos de 200 células/µL fue de 92,2% (IC 95%: 91,4–93,0). La supervivencia fue mayor en los pacientes con conteo de linfocitos T CD4+ mayores o iguales a 350 células/µL, pero fue menor a medida que disminuyeron los valores del conteo (figura 1).

El grupo que presentó la última carga viral indetectable tuvo una probabilidad de supervivencia a los 7 años de 98,3% (IC 95%: 98,0-98,6) mientras que en los detectable fue menor (90,4%; IC 95%: 89,4– 91,3).

La prueba de hipótesis de log-rank realizada a las características sociodemográficas y clínicas (listadas en la tabla 1), evidenció diferencias estadísticamente significativas entre las categorías de las variables excepto entre hombres y mujeres (p=0,1). En la figura 1 se presentan las curvas de supervivencia de Kaplan-Meier, junto con los resultados de la prueba de hipótesis de log-rank para las variables sociodemográficas y clínicas incluidas en el modelo de supervivencia realizado.

Modelo de supervivencia paramétrico flexible

Los resultados en la tabla 3 reflejan el modelo final ajustado por las variables detectadas como estadísticamente significativas mediante la prueba Log-rank y las variables clínicamente relevantes encontradas en la literatura. Al ajustar por las variables incluidas en el modelo, el riesgo de muerte fue mayor en las personas de sexo masculino comparadas con las de sexo femenino (Valor p=0,010). También se observaron diferencias estadísticamente significativas en la supervivencia en las personas de 50 años o más a comparación de los menores de 15 años. El riesgo de muerte también se presentó mayor en las personas con un régimen de afiliación al sistema de salud subsidiado con respecto al contributivo. Igualmente, en pacientes con diagnóstico de sida a comparación con VIH. Llama la atención el alto riesgo que representa la última medición de carga viral detectable a comparación con las personas que presentan una carga viral indetectable (valor p<0,001). Finalmente, en los pacientes con conteo de linfocitos T CD4+ menores a 200 y entre 200 a 349 células/µL, se presentó un mayor riesgo de muerte a comparación de los pacientes con un conteo mayor o igual a 350 células/µL (valor p<0,001).

Tabla 2. Enfermedades oportunistas definitorias de sida y comorbilidades en la población de estudio

Variables	Sexo femenino (n=15 221) n (%)	Sexo masculino (n=49 686) n (%)
Presencia de enfermedades oportunistas definitorias de sida durante el periodo de estudio		
Tuberculosis en cualquier localización		
Sí	1 157 (7,6)	4 878 (9,8)
No	580 (3,8)	1 545 (3,1)
Sin dato	13 484 (88,6)	43 263 (87,1)
Infección por citomegalovirus		
Sí	202 (1,3)	972 (2,0)
No	637 (4,2)	1 739 (3,5)
Sin dato	14 382 (94,5)	46 975 (94,5)
Histomasplosis diseminada o extra pulmonar		
Sí	146 (1,0)	668 (1,3)
No	638 (4,2)	1 758 (3,5)
Sin dato	14 437 (94,9)	47 260 (95,1)
Neumonía por *Pneumocystis jiroveci*		
Sí	501 (3,3)	1 878 (3,8)
No	608 (4,0)	1 705 (3,4)
Sin dato	14 112 (92,7)	46 103 (92,8)
Septicemia por salmonella recurrente		
Sí	31 (0,2)	88 (0,2)
No	644 (4,2)	1 788 (3,6)
Sin dato	14 546 (95,6)	47 810 (96,2)
Sarcoma de Kaposi		
Sí	91 (0,6)	1 067 (2,2)
No	643 (4,2)	1 740 (3,5)
Sin dato	14 487 (95,2)	46 879 (94,4)
Síndrome de desgaste o caquexia asociada a VIH		
Sí	2 368 (15,6)	8 749 (17,7)
No	508 (3,3)	1 299 (2,6)
Sin dato	12 345 (81,1)	39 638 (79,8)
Toxoplasmosis cerebral en mayores de un mes de edad		
Sí	797 (5,2)	2 389 (4,8)
No	599 (3,9)	1 668 (3,4)
Sin dato	13 825 (90,8)	45 629 (91,8)
Presencia de comorbilidades en el periodo de estudio		
Dislipidemia		
Sí	2 251 (14,8)	6 992 (14,1)
No	442 (2,9)	1 165 (2,3)
Sin dato	12 528 (82,3)	41 529 (83,6)
Coinfección con Hepatitis B crónica (VHB)		
Sí	259 (1,7)	2 989 (6,0)
No	648 (4,3)	1 607 (3,2)
Sin dato	14 314 (94,0)	45 090 (90,8)
Coinfección con Hepatitis C crónica (VHC)		
Sí	64 (0,4)	422 (0,9)
No	655 (4,3)	1 795 (3,6)
Sin dato	14 502 (95,3)	47 469 (95,5)
Anemia		
Sí	2 439 (16,0)	3 056 (6,2)
No	494 (3,3)	1 634 (3,3)
Sin dato	12 288 (80,7)	44 996 (90,6)
Cirrosis hepática		
Sí	20 (0,1)	68 (0,1)
No	667 (4,4)	1 820 (3,7)
Sin dato	14 534 (95,5)	47 798 (96,2)
Enfermedad renal crónica		
Sí	213 (1,4)	1.039 (2,1)
No	652 (4,3)	1 740 (3,5)
Sin dato	14 356 (94,3)	46 907 (94,4)
Otras enfermedades de transmisión sexual		
Sí	1 131 (7,4)	8 916 (17,9)
No	589 (3,9)	1 375 (2,8)
Sin dato	13 501 (88,7)	39 395 (79,3)

Discusión

El VIH es una enfermedad que según la literatura, menos del 7% de las PVV se pueden comportar como no progresores a largo plazo y controladores de élite, manteniendo un recuento alto de células CD4 (≥500 células/mm^3) y una carga viral baja o indetectable por un largo tiempo[20]. Por lo tanto, un gran porcentaje de PVV tienen un deterioro de su sistema inmunológico facilitando la aparición de enfermedades definitorias de sida y por ende un mayor riesgo de mortalidad. Este estudio es el primer análisis publicado que describe la probabilidad de supervivencia de las personas que viven con VIH que han sido reportadas a la Cuenta de Alto Costo y son atendidos en el sistema de salud colombiano; así como los factores de riesgo que están relacionados con una mayor mortalidad.

En el presente estudio, el sexo no tuvo un efecto significativo sobre el riesgo de muerte en el modelo sin ajustar; no obstante, al ajustarse se encontró que el sexo masculino presenta un mayor riesgo de mortalidad. En países como Brasil[7] e Irán[21] se ha demostrado que las PVV de sexo masculino tienen un mayor riesgo de muerte, lo cual puede estar explicado por diferencias genéticas[22] y condiciones socioculturales como una mayor percepción de cuidado y adherencia de las mujeres a los programas de salud; y una búsqueda más temprana de los servicios de salud en las mujeres, especialmente por la oferta de la prueba diagnóstica durante el embarazo[23]. Por otro lado, el régimen subsidiado mostró un HR dos veces mayor que el contributivo, lo que podría ser una aproximación de las brechas de desigualdad en las poblaciones, así también lo muestra un estudio en Reino Unido el cual describe que las desventajas socioeconómicas están fuertemente asociadas con peores resultados en salud aún en un entorno con atención médica universal[24].

En cuanto a la edad, nuestros resultados también son consistentes con la literatura que muestra una menor probabilidad de sobrevivir a edades más avanzadas (25). Por ejemplo, un metanálisis[26] realizado con PVV antes del TAR, identificaron la edad ≥45 años como un factor explicativo de la mortalidad tanto en pacientes con VIH-1 y VIH-2, concluyendo que la edad avanzada está asociada con la progresión clínica especialmente en aquellos que no han recibido TAR, por lo cual es importante el diagnóstico temprano y el inicio del tratamiento[27]. Otro estudio[4] realizado a través de un modelo de regresión de riesgos proporcionales de Cox mostró que los pacientes con más de 51 años tienen un HR de 1,90 (1,35-2,68) comparado con las PVV ≤25 años.

El diagnóstico de la infección por el VIH es prioritario, pues es la entrada de los pacientes a la cascada del continuo de la atención para VIH y un indicador clave para el monitoreo de las estrategias en salud pública[28] es así que nuestro estudio mostró que el diagnóstico temprano de VIH (linfocitos T CD4+ ≥500 células/µL) mejora la supervivencia, información similar a otros estudios[20,34]. Este hallazgo debe permitir el fortalecimiento de acciones que minimicen las barreras para

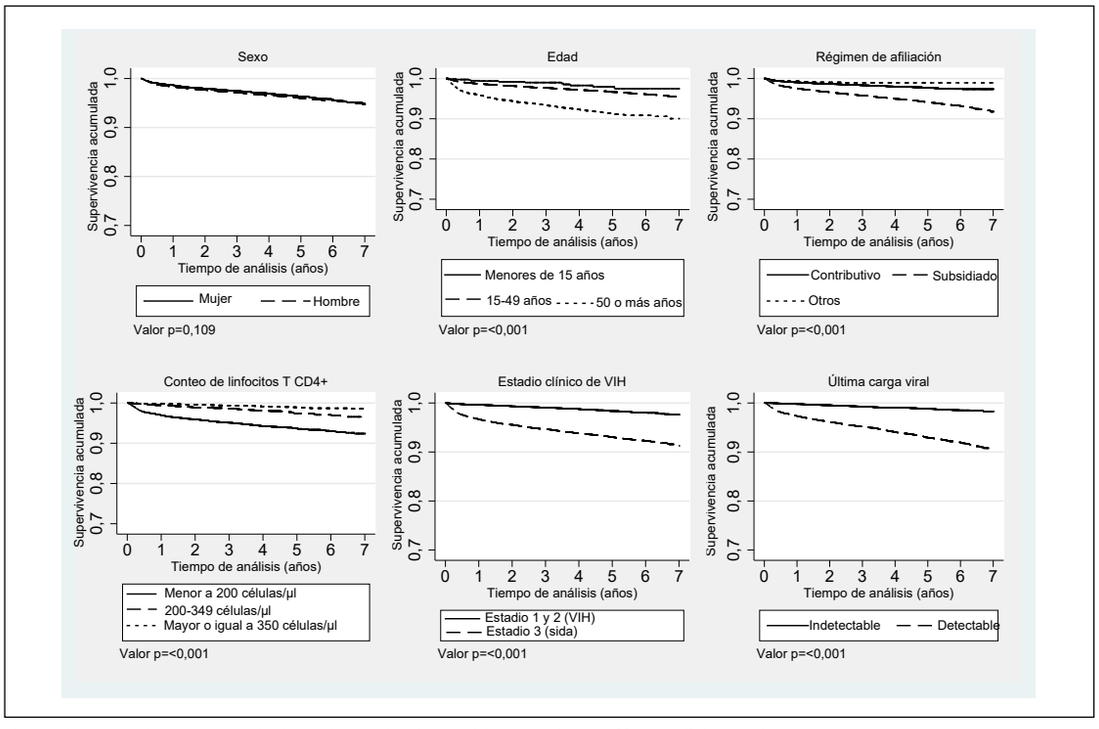

Figura 1. Curvas de supervivencia de Kaplan-Meier de variables sociodemográficas y clínicas en las PVV

Tabla 3. Modelo de supervivencia paramétrico flexible, ajustado con 3 nodos internos y 4 grados de libertad

Variable	HR	95% IC		Valor *p*
		Inferior	Superior	
Sexo				
Femenino*				
Masculino	1,2	1,1	1,4	0,010
Edad				
< de 15 años*				
15 a 49 años	1,2	0,6	2,4	0,637
50 o más años	3,1	1,5	6,3	0,002
Régimen de afiliación al sistema de salud				
Contributivo*				
Subsidiado	2,2	1,9	2,5	<0,001
Otros	0,3	0,1	1	0,050
Conteo de linfocitos T CD4+ (células/µL)				
≥350*				
<200	2,3	1,7	3,2	<0,001
200-349	1,9	1,4	2,4	<0,001
Estadio clínico				
VIH (estadio1 y 2)*				
Sida (estadio 3)	2,8	2,1	3,7	<0,001
Última carga viral				
Indetectable*				
Detectable	7,1	6	8,3	<0,001

HR: Hazard ratio. IC: intervalo de confianza. *Categoría de referencia.
A excepción de la última carga viral, las variables incluidas en el modelo fueron medidas al momento del diagnóstico de VIH.

el diagnóstico temprano como la optimización del uso de diversas herramientas de diagnóstico aumentando el acceso a la prueba[28].

El conteo bajo de linfocitos T CD4+ también ha documentado una relación inversamente proporcional entre el estado inmunológico y la mortalidad; un estudio en España mostró que por cada incremento de 50 linfocitos T CD4+ en el momento del diagnóstico, el riesgo de muerte disminuyó en un 83% (IC 95%: 82,0-84,0)[29]. Resultados recientes también evidencian que las PVV con recuentos de CD4 más bajos se relacionaban con mayor riesgo de mortalidad y morbilidad. Países como Perú, por ejemplo, mostraron una sobrevida de 68% a 8 años de seguimiento en PVV con menos de 100 células/mL, mostrando que la mortalidad va reduciéndose conforme incrementa el recuento de CD4[21].

Por otra parte, nuestro estudio también mostró que las personas en estadio sida (estadio 3) presentaron una menor supervivencia comparada con las PVV en estadio clínico VIH (estadio 1 y 2); los estudios también respaldan este hallazgo, encontrando por ejemplo que en un estudio en Puerto Rico[30] la probabilidad de supervivencia a 6 años fue menor en el grupo de estadio sida (0,57; IC 95%: 0,55-0,60, p<0,001) en comparación con las personas en estadio de VIH (0,87; IC 95%: 0,09-0,72). Un metanálisis que incluyo 57 estudios también concluyó que la mayoría de los pacientes que reciben TAR sobrevivirán más de 10 años después de la aparición del sida, mientras que la mayoría de los pacientes que no reciben TAR mueren dentro de los 2 años siguientes a la etapa final de la enfermedad[1].

La detectabilidad de la carga viral, en el transcurso del seguimiento también evidenció mayor riesgo de mortalidad, información congruente con un estudio[31] que mostró que tener una alta carga viral alcanzaba un HR de 1,17 (IC 95%: 1,07-1,48) para mortalidad. El seguimiento de la carga viral ha sido considerado un mejor predictor de muerte en PVV comparado con el recuento de linfocitos T CD4+, pues los pacientes tardan más en alcanzar un recuento de células CD4 normal y menos tiempo en alcanzar una carga viral indetectable.

Fortalezas y debilidades

Las fortalezas de nuestro estudio se traducen en la veracidad de la información, pues son datos que provienen de un registro nacional que surten un proceso de auditoría estandarizado para garantizar la validez de los datos, así como la obligatoriedad en el registro, que hace que un gran porcentaje de las PVV sean reportadas, por ser atendidos en el sistema de salud (Alrededor del 96% de la población colombiana se encuentra afiliada al SGSSS[32]) mejorando la validez externa de los hallazgos y limitando el sesgo de selección. Por otro lado, al ser un registro anual se pudo hacer la trazabilidad histórica del seguimiento del paciente. No obstante, es un registro pasivo que cuenta con sus propias limitaciones.

Existieron limitaciones que están relacionadas con el alto porcentaje de registros faltantes especialmente en las variables de enfermedades oportunistas definitorias de sida y comorbilidad, pues en el proceso de auditoria no pudieron ser verificables, lo que condiciona la descripción estadística (tabla 2) solo a la población con la información reportada y verificada. Este dato no reportado pudo ser por omisión, por sesgo de recuerdo o falta de soportes en el momento de validar el dato. Tampoco pudo ser incluida la variable relacionada con el tipo de esquema usado al inicio de la TAR, dado que en un gran porcentaje de casos solo se validó uno o dos medicamentos cuando los esquemas están conformados con más de dos medicamentos. Por lo anterior, el análisis múltiple realizado está sujeto al sesgo de confusión residual dado por la imposibilidad de ajustar por estas variables. Además, no se pudieron describir los diagnósticos específicos de muerte de la población dado que el registro solo captura la causa de muerte agrupada como: muerte por VIH/sida, por otra patología no definitoria de Sida y muerte por causa externa, lo cual impide realizar un análisis por causa específica de muerte.

Conclusiones

Nuestro estudio describió que un diagnóstico temprano y un tratamiento oportuno puede cambiar el curso de la enfermedad en términos de supervivencia. Además estimó que la probabilidad de la supervivencia de las PVV aumenta en quienes al ser diagnosticados se encuentran en edades jóvenes, presenten un recuento mayor o igual a 350 células/µL de linfocitos T CD4+, mantengan una carga viral indetectable y no se encuentren en etapa sida. Estos hallazgos pueden orientar las acciones en el fortalecimiento de estrategias y reorientación de los recursos en actividades dirigidas a la detección oportuna de los casos, a la tamización del VIH especialmente en menores de 50 años y a la integración inmediata de las PVV a los programas de VIH para garantizar el manejo adecuado de la enfermedad y el inicio temprano de la terapia antirretroviral. Por otro lado, se sugiere evaluar las debilidades en la gestión de la población masculina y en el régimen de salud subsidiado que limitan la supervivencia de estas subpoblaciones. Futuros estudios pueden ir encaminados a la exploración de posibles interacciones entre las variables de estudio, así como el análisis de nuevas variables que puedan determinar la supervivencia en las PVV.

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Responsabilidades éticas

Protección de personas y animales: Los autores declaran que en este artículo no se hicieron experimentos con humanos o 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.

Conflictos de interés: Los autores declaran no tener conflictos de interés.

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VIH

Healthcare-related expenditures among immigrants and non-immigrants living with HIV in Colombia

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Alcance: Internacional.

Trabajo colaborativo con la academia (institución internacional) y el Ministerio de Salud y Protección Social como actores de interés.

Objetivo:

Comparar los gastos relacionados con la atención médica entre inmigrantes y no inmigrantes que viven con VIH en Colombia, según el régimen de aseguramiento en salud.

Principales hallazgos:

- Los gastos relacionados con la asistencia sanitaria de los inmigrantes venezolanos en el sistema de salud de Colombia fueron sustancialmente menores en términos absolutos que los de la población general.
- Además de los gastos totales, los gastos per cápita también fueron menores para los inmigrantes en comparación con la población general.

Relevancia de los hallazgos:

- Este trabajo amplía el conocimiento sobre los gastos de los inmigrantes con VIH en los sistemas sanitarios nacionales.
- Este estudio visibiliza la necesidad de ampliar el conocimiento para entender si el menor gasto sanitario de esta población es el resultado de las limitaciones en el acceso a la asistencia sanitaria o de las características clínicas propias de esta población.
- Los estudios que evalúan el impacto económico de la atención en la población migrante son fundamentales para cuantificar el acceso a los servicios de salud, la carga económica y social, y determinar las acciones prioritarias requeridas por esta población.

Comentario del autor experto:

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Uno de los temas de mayor importancia para los sistemas de salud es el del monitoreo del gasto asociado a la atención. Este es un insumo esencial para la planeación, así como para la evaluación de la eficiencia de la administración de los recursos de un sistema.

La migración de Venezuela a Colombia en los últimos años ha requerido del sistema de salud colombiano la capacidad de diseñar e implementar estrategias para proporcionar atención a los casi dos millones de personas que se han establecido en el país. El gobierno colombiano ha hecho un importante esfuerzo de inclusión de estas personas en los mecanismos de aseguramiento en salud, lo que ha facilitado a los migrantes venezolanos el acceso a servicios. En esta circunstancia, contar con información sobre el gasto en salud requerido por esta población es de vital importancia.

En este artículo, se comparó el gasto por atención del VIH entre migrantes venezolanos y personas no migrantes, usando datos de la Cuenta de Alto Costo entre 2018 y 2019, y se encontró que el gasto era mayor cuando la atención se daba a personas no migrantes. Estos resultados tienen dos implicaciones relevantes. En primer lugar, aporta evidencia en el sentido de que los migrantes no representan un componente mayoritario del gasto en salud del país, por lo que atender sus necesidades es posible. En segundo, parece mostrar que los migrantes, aun cuando están afiliados a los esquemas contributivos o no contributivos, hacen un uso limitado de estos servicios, por lo que sería importante identificar las barreras que impiden su acceso a ellos.

Aunque aún hace falta más evidencia sobre las implicaciones para el sistema de salud de la atención a los migrantes, este artículo aporta al conocimiento de este fenómeno, y puede contribuir a orientar la política pública en este sentido.

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Healthcare-related expenditures among immigrants and non-immigrants living with HIV in colombia

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Abstract

The perception that immigrants represent a burden to national health systems can hinder the development of policies for their inclusion in health coverage. In order to inform the development of such policies, data on the healthcare needs and healthcare spending for immigrants is required. The objective of this article is to compare the clinical characteristics and healthcare-related expenditures of Venezuelan immigrants and non-migrants living with HIV in Colombia. We analysed data from the Colombian High-cost Diseases Fund from February 1, 2018 to January 31, 2019, identifying the hospital and non-hospital expenditures per patient for Venezuelan immigrants and non-migrant patients, in both the state-subsidised and the contributory coverage schemes. We employed binomial negative regression models to compare expenditures between the two groups. In the contributory scheme, the average annual per-capita expenditure for immigrants was USD $ 859.07 (*SD*: ± $793.37) for non-hospital care. For non-migrants, the average costs were 1,796.53. In the state-subsidised scheme expenditures were higher on average, but still lower for immigrants than for non-migrants. After adjusting by clinical and sociodemographic characteristics, non-hospital per capita expenditures were lower for immigrants as compared with non-migrants (25,37% lower in the state-subsidised scheme, and 33,75% lower in the contributory scheme). Hospital expenditures were also lower, but the small sample size limited analysis. To conclude, Venezuelan immigrants living with HIV do not represent a major economic burden to the health system in Colombia. Further studies are required in order to understand if the lower healthcare expenditures of this population are the result of limitations in healthcare access, of clinical characteristics that were not assessed in this study, or of other unmeasured aspects.

KEYWORDS

Colombia, emigration and immigration, health care expenditures, HIV, public health systems research, universal health care, Venezuela

1 | INTRODUCTION

In order to achieve the goal of universal health coverage, immigrants should be included in the healthcare systems of their host countries (Abubakar et al., 2018). However, the perception that immigrants can overwhelm health systems could stop decision-makers from promoting policies aimed to achieve this inclusion. In order to inform this discussion, data on the healthcare costs associated with

providing care to immigrants are essential. Studies in the United States and some European countries have consistently shown that both public and private health expenditures, as well as the use of healthcare services, are lower for immigrants as compared to non-migrants (Gimeno-Feliu et al., 2016; Stimpson et al., 2010). The expenditures associated with providing care to people living with HIV/AIDS (PLWH) are generally high (Jansà & Borrell, 2002), but studies of human immunodeficiency virus (HIV)-related expenditures in Canada and Spain have found no differences between immigrants and non-migrants (Krentz & Gill, 2011; Velasco et al., 2012). Much less is known about the situation in low- and middle-income countries, in which health systems are relatively weaker and have less resources.

Since 2018, a major migration flow has occurred between Venezuela and Colombia, with an estimated more than one million and a half immigrants of Venezuelan origin living in Colombia in 2019 (Nacional and para la Gestión del Riesgo de desastres, 2018). The Colombian Ministry of Health's response plan granted access to some healthcare, public health and preventive interventions for all Venezuelan immigrants. Besides, the government promoted the regularisation of immigrants, and the affiliation of regular immigrants to the national health insurance systems (Ministerio de Salud y Protección Social, 2018). Irregular immigrants remain without full access to health services (Bojorquez-Chapela et al., 2020), and can only receive emergency care and collective public health actions (such as vaccination).

The Colombian health system is organised in such a way that people with the ability to pay, among them formal workers and pensioners, are affiliated to an insurance system based on contributions of individuals and their employers (contributory insurance), while people without the ability to pay are affiliated to a state-funded scheme (subsidised insurance; Ley 100 del 1993, 1993). PLWH who are insured under one of these schemes (including insured immigrants) are entitled to medical care and medications, while the uninsured can only receive emergency care. The two schemes cover the same healthcare interventions, however, each has its own network of providers, resulting in some differences in both quality and expenses between the schemes.

While immigrants and non-migrants who are affiliated to a coverage scheme are entitled to the same care, some differences could still exist between them in utilisation, driven by barriers to access such as time or trust in the healthcare systems, communication barriers and stigma (Resolución 0273 de 2019, 2019) . There could also be differences in their health status, as immigrants are generally more vulnerable in terms of income, living conditions, social networks and others. These differences could include complications due to previous unmet needs for care, and an increase in sexual risk behaviours after migration. All of these could result in differences between immigrants and non-migrants in expenditures for the provision of services. This study aims to compare the expenditures related to medical care between immigrants and non-migrants living with HIV in Colombia, in both the subsidised and the contributory coverage schemes in the country.

What is known about this topic

- Irregular immigrants, those who are undocumented, remain without full access to health services.
- The expenditures associated with providing care to people living with HIV are generally high.
- Since 2018, a major migration flow has occurred between Venezuela and Colombia, with an estimated more than one million and a half immigrants of Venezuelan origin living in Colombia in 2019.

What this paper adds

- Expenditures related with HIV treatment in people living with HIV in Venezuelan immigrants are lower than those for Colombian nationals.
- Future studies collecting more detailed data are required, in order to understand if the lower healthcare expenditures of this population are the result of limitations in healthcare access or of clinical characteristics.

2 | METHODS

2.1 | Study design

Cross-sectional study using secondary data from February 1, 2018 to January 31, 2019.

2.2 | Source of data

Data for this study were taken from the database of the High Cost Diseases Fund (CAC in Spanish), a fund that pools and oversees the public and private resources of the different insurance schemes. CAC is a non-governmental technical agency of the Colombian General System of Social Security in Health, created by the Ministry of Health and the Ministry of Finance. All insurers and health providers are mandated to report annually the data of all pathologies defined as a high cost disease to the CAC (Resolución 0247 de 2014, 2014; Resolución 1393 de 2015, 2015; Resolución 123 de 2015, 2015; Resolución 2463 de 2014, 2014; Resolución 4700 del 2014, 2014), making it an ideal source to explore expenditures for high-cost diseases such as HIV in Colombia (Decreto 2699 de 2007, 2007). CAC has a HIV administrative registry since 2012 (Resolución 4725 de 2011, 2011), to which all insurers send a mandatory annual report about sociodemographic, clinical, administrative and expenditure data of all PLWH, the resolution includes structure of the variables to report. All the information of the new and prevalent cases is audited against medical records, the diagnosis must be confirmed with the Western blot test or detectable viral load, the cases without a laboratory-confirmed diagnosis of HIV are excluded.

2.3 | Populations of interest and variables

2.3.1 | Outcomes

The main outcome variables were non-hospital and hospital expenditures. Hospital expenditures were defined as the total expenditures per patient reported in all those with one or more hospitalisations during the period when the hospitalisation was related to HIV. Non-hospital expenditures were defined as the total expenditures per patient corresponding to non-hospital care during the period and related to HIV. All hospital and non-hospital expenditures <1,000 Colombian pesos (0.33 USD) and not supported during the audit with valid invoices were eliminated. The expenditures were collected in Colombian pesos (COP), for this analysis it was converted into dollars, using the annual average Exchange Rates for Colombian Peso to US Dollar. During 2018, 1 USD was equivalent to 2,955.60 COP.

2.3.2 | Immigration

Immigrant can be defined as foreign-born person who has moved to another country for the purpose of reside and settlement (Richard & Jillyanne, 2011). Irregular immigrants are those undocumented, without the relevant permit for residence or employment and regular immigrants refers to migration that occurs in compliance with the laws of the country of origin, transit and destination (IOM, 2020). Our study involves a comparison of non-migrants with Venezuelan immigrants with regular migratory status. For this study, non-migrants refer to people with Colombian nationality (by birth or naturalisation).

The CAC database does not include a variable identifying nationality or place of birth. Therefore, we identified Venezuelan immigrants in the database in two ways. First, the report has a variable called "novelty" that has within its categories the option of identifying the person as Venezuelan. Second, in the variable indicating the type of personal identification presented by the patient, one of the options is the special residence permit (PEP in Spanish), a type of permit that has been granted by the Colombian migration department only to Venezuelan immigrants. Patients fulfilling either one of these conditions were classified as Venezuelan immigrants. As this analysis is limited to people with health insurance, those with irregular migration status are not included.

2.3.3 | Type of health insurance

We distinguished between those insured under the subsidised scheme, which covers lower-income population without the ability to pay through state funding, and those insured under the contributory scheme based on workers' and employers' contributions.

2.3.4 | Sociodemographic covariates

These included age, gender (male, female and intersex), region of residence (Bogota D.C, Caribbean, Central, Oriental, Pacific and others) and being part of a key population (sex workers, transgender people, men who have sex with men, people using o injecting psychoactive substances, homeless and prisoners or incarcerated people).

2.3.5 | Clinical covariates

We adjusted for HIV stage (1, 2 or 3), use of antiretroviral treatment, current viral load (copies/ml), number of HIV-related hospitalisations in the past year and number of months with antiretroviral therapy (ART) dispensing.

2.4 | Statistical analysis

A descriptive analysis of the main characteristics of HIV cases was performed, stratified by type of health insurance. Quantitative variables were described with mean and standard deviation, qualitative variables, with frequencies and proportions. For the bivariate analysis, the crude percentage difference stratified by type of health insurance was calculated to assess the association between hospital and non-hospital expenditures and being a Venezuelan immigrant. Continuous variables were compared using the Mann–Whitney *U* test, categorical variables were compared using the Pearson´s Chi-square or Fisher´s Exact test. $p < .05$ (two-tailed) were considered statistically significant. For the multivariable analysis, as the expenditure outcome is a count variable with over dispersion, a binomial negative regression model was employed to obtain the estimation of adjusted percentage difference between Venezuelan immigrants and non-migrants. As the number of immigrants with hospital care expenditures was extremely low (2 and 4 cases in the contributory and subsidised schemes, respectively), no multivariate analysis was conducted. All analyses were run in STATA 12.

3 | RESULTS

Data from 105,264 PLWH were analysed, 370 of whom were Venezuelan immigrants. Table 1 summarises their main sociodemographic characteristics, by migration and insurance scheme, and Table 2 their main clinical characteristics. In both insurance schemes, immigrants and non-migrants, the majority were male, and most were young adults (25–49 years). Slightly over half (59.73%) were affiliated to the contributory insurance scheme. About one-fifth of immigrants were in stages 0–1 of the infection, while only about one-tenth of non-migrants were in those stages.

TABLE 1 Sociodemographic characteristics of people living with HIV by type of health insurance and migration status, Colombia 2018–2019

	Contributory			Subsidized			Total		
	Immigrants (*n* = 265)	Non-migrants (*n* = 62,609)	*p*	Immigrants (*n* = 105)	Non-migrants (*n* = 42,285)	*p*	Immigrants (*n* = 370)	Non-migrants (*n* = 104,894)	*p*
Characteristics	*n*(%)	*n*(%)	value	*n*(%)	*n*(%)	value	*n*(%)	*n*(%)	value
Gender[b]									
Men	253 (95.47)	52,453 (83.78)	.000	79 (75.24)	26,756 (63.28)	0.038	332 (89.73)	79,209 (75.51)	0.000
Intersex	0 (0.0)	0 (0.0)		0 (0.0)	11 (0.03)		0 (0.0)	11 (0.01)	
Women	12 (4.53)	10,156 (16.22)		26 (24.76)	15,518 (36.70)		38 (10.27)	25,674 (24.48)	
Age[c](years)									
Median (IQR)	29 (26–34)	38 (30 – 49)	.000	32 (27–40)	38 (29–49)	0.000	30 (26 – 36)	38 (30 – 49)	0.000
Categories[a]									
≤14	0 (0.0)	169 (0.27)	.000	1 (0.95)	690 (1.63)	0.037	1 (0.27)	859 (0.82)	0.000
15–24	31 (11.70)	5,420 (8.66)		15 (14.29)	4,528 (10.71)		46 (12.43)	9,948 (9.48)	
25–49	222 (83.77)	42,415 (67.75)		76 (72.38)	27,014 (63.89)		298 (80.54)	69,429 (66.19)	
≥50	12 (4.53)	14,605 (23.33)		13 (12.38)	10,053 (23.77)		25 (6.76)	24,658 (23.51)	
Region[a,†]									
Bogota D.C	148 (55.85)	20,403 (32.59)	.000	17 (16.19)	3,320 (7.85)	0.001	165 (44.59)	23,723 (22.62)	0.000
Caribbean	10 (3.77)	6,401 (10.22)		32 (30.48)	16,777 (39.68)		42 (11.35)	23,178 (22.10)	
Central	67 (25.28)	19,482 (31.12)		18 (17.14)	9,656 (22.84)		85 (22.97)	29,138 (27.78)	
Oriental	17 (6.42)	6,525 (10.42)		20 (19.05)	4,696 (11.11)		37 (10.00)	11,221 (10.70)	
Pacific and Others	23 (8.68)	9,798 (16,65)		18 (17.14)	7,836 (18.53)		41 (11.08)	17,634 (16.81)	
Key population									
Sex workers (yes)[b]	0 (0.0)	10 (0.02)	1.000	1 (0.95)	110 (0.26)	0.241	1 (0.27)	120 (0.11)	0.347
Transgender woman (yes)[b]	0 (0.0)	16 (0.03)	1.000	0 (0.0)	81 (0.19)	1.000	0 (0.0)	97 (0.09)	1.000
Transgender man (yes)[b]	1 (0.38)	73 (0.12)	.269	0 (0.0)	184 (0.44)	1.000	1 (0.27)	257 (0.25)	0.597
Men who have sex with men (yes)[a]	217 (81.89)	27,747 (44.32)	.000	46 (43.81)	7,734 (18.29)	0.000	263 (71.08)	35,481 (33.83)	0.000
People using psychoactive substances (non inject) (yes)[b]	4 (1.51)	845 (1.35)	.785	0 (0.0)	1,442 (3.41)	0.053	4 (1.08)	2,287 (2.18)	0.207
People who inject drugs (yes)[b]	0 (0.0)	19 (0.03)	1.000	0 (0.0)	22 (0.05)	1.000	0 (0.0)	41 (0.04)	1.000
Homeless (yes)[b]	0 (0.0)	18 (0.03)	1.000	0 (0.0)	210 (0.50)	1.000	0 (0.0)	228 (0.22)	1.000
Prisoners (yes)[b]	0 (0.0)	272 (0.43)	.634	0 (0.0)	337 (0.80)	1.000	0 (0.0)	609 (0.58)	0.285
None[a]	47 (17.74)	34,200 (54.62)	1.000	58 (55.24)	32,718 (77.37)	1.000	105 (28.38)	66,918 (63.80)	0.000

Abbreviations: IQR, interquartile range.

[a]Chi square test.

[b]Fisher test.

[c]Mann–Whitney *U* test.

[†]Regions defined by the Departamento Administrativo Nacional de Estadística for 2018. according to departmental gross domestic product. Information available at https://www.dane.gov.co/files/investigaciones/pib/departamentales/B_2015/Bol_dptal_2018preliminar.pdf.

TABLE 2 Clinical characteristics of people living with HIV by type of health insurance and migration status. Colombia 2018–2019

	Contributory			Subsidized			Total		
	Immigrants (*n* = 265)	Non-migrants (*n* = 62,609)		Immigrants (*n* = 105)	Non-migrants (*n* = 42,285)		Immigrants (*n* = 370)	Non-migrants (*n* = 104,894)	
Characteristics	*n*(%)	*n*(%)	*p* value	*n*(%)	*n*(%)	*p* value	*n*(%)	*n*(%)	*p* value
Stage[a,b]									
Stage 0	0 (0.0)	16 (0.03)	.000	0 (0.0)	5 (0.01)	.000	0 (0.0)	21 (0.02)	.000
Stage 1	60 (22.64)	7,569 (12.09)		20 (19.05)	4,118 (9.74)		80 (21.62)	11,687 (11.14)	
Stage 2	126 (47.55)	21,412 (34.20)		34 (32.38)	11,646 (27.54)		160 (43.24)	33,058 (31.52)	
Stage 3	77 (29.06)	33,255 (53.12)		44 (41.90)	26,249 (62.08)		121 (32.70)	59,504 (56.73)	
Stage 4	2 (0.75)	274 (0.44)		6 (5.71)	209 (0.49)		8 (2.16)	483 (0.46)	
Unknown	0 (0.0)	83 (0.13)		1 (0.95)	58 (0.14)		1 (0.27)	141 (0.13)	
Use of antiretroviral treatment (yes)[a]	233 (87.92)	53,752 (85.85)	.330	92 (87.62)	35,594 (84.18)	.330	325 (87.84)	89,346 (85.18)	.150
Current viral load (copies/ml)[a]									
<50	134 (50.57)	42,644 (68.11)	.000	41 (39.05)	24,747 (58.52)	.000	175 (47.30)	67,391 (64.25)	.000
50–<1.000	39 (14.72)	6,386 (10.20)		12 (11.43)	5,139 (12.15)		51 (13.78)	11,525 (10.99)	
≥1.000	79 (29.81)	6,799 (10.86)		42 (40.00)	6,930 (16.39)		121 (32.70)	13,729 (13.09)	
Unknown	13 (4.91)	6,780 (10.83)		10 (9.52)	5,469 (12.93)		23 (6.22)	12,249 (11.68)	
Number of hospitalizations in the HIV-related period per year[b]									
0	262 (98.87)	61,036 (97.49)	.278	101 (96.19)	40,314 (95.34)	1.000	363 (98.11)	101,350 (96.62)	.521
1	2 (0.75)	609 (0.97)		2 (1.90)	794 (1.88)		4 (1.08)	1,403 (1.34)	
2	1 (0.38)	136 (0.22)		0 (0.0)	162 (0.38)		1 (0.27)	298 (0.28)	
≥3	0 (0.0)	69 (0.11)		0 (0.0)	96 (0.23)		0 (0.0)	165 (0.16)	
Unknown	0 (0.0)	759 (1.21)		2 (1.90)	919 (2.17)		2 (0.54)	1,678 (1.60)	
Number of months with antiretroviral treatment dispensing per year[a,b]									
0	11 (4.15)	1,947 (3.11)	.000	3 (2.86)	1,454 (3.44)	.000	14 (3.78)	3,401 (3.24)	.000
1–3	82 (30.94)	7,493 (11.97)		46 (43.81)	5,856 (13.85)		128 (34.59)	13,349 (12.73)	
4–6	75 (28.30)	11,262 (17.99)		22 (20.95)	10,211 (24.15)		97 (26.22)	21,473 (20.47)	
7–11	55 (20.75)	24,092 (38.48)		20 (19.05)	9,619 (22.75)		75 (20.27)	33,711 (32.14)	
12	7 (2.64)	9,405 (15.02)		0 (0.0)	8,679 (20.53)		7 (1.89)	18,084 (17.24)	
Unknown	35 (13.21)	8,410 (13.43)		14 (13.33)	6,466 (15.29)		49 (13.24)	14,876 (14.18)	

[a]Chi square test.
[b]Fisher test.

The total expenditure for non-hospital care in the observed period was $ 705,858,266 for Venezuelan immigrants, amounting to 0.2% of the total expenditure of Venezuelan immigrants and non-migrants. The median annual per capita expenditure for non-hospital care was 610.34 for immigrants and 1,725.54 for non-migrants (Table 3). As for hospital care, 1,871 (1.78%) of the cases received hospital care related to HIV during the period, and only five of them were immigrants. Information about hospital expenditures was available in 80% (4/5) of immigrants and 59.38% of non-migrants (1,108/1,866). The mean of annual expenditure of hospital care was $37,317.7 (*SD*: ± $6,379.0) per patient.

Table 4 shows the results of the binomial regression models for non-hospital expenditures, stratified by type of insurance, crude and adjusting for sex, age, stage, current ART and current viral load. In the subsidised scheme, the expenditures of Venezuelan immigrants were on average 25.37% lower than those of non-migrants after adjusting by demographic and clinical covariates, and in the contributive scheme expenditures were 33.75% lower (Table 4).

As previously mentioned, only four immigrants were hospitalised, so the number of observations in this group was very small and did not allow for the estimation of differences by migratory status of the PLWH.

4 | DISCUSSION

According to our results, healthcare-related expenditures for Venezuelan immigrants in Colombia's health system are substantially

TABLE 3 Description of expenditures for people living with HIV by type of health insurance and migration status. Colombia 2018–2019

	Contributory		Subsidized		Total	
Costs types	**Immigrants**	**Non-migrants**	**Immigrants**	**Non-migrants**	**Immigrants**	**Non-migrants**
Non-hospital care	**(*n* = 206)**	**(*n* = 30,299)**	**(*n* = 72)**	**(*n* = 30,876)**	**(*n* = 278)**	**(*n* = 61,175)**
Minimum cost	$ 20.18	$ 0.79	$ 84.25	$ 8.00	$ 20.18	$ 0.79
Maximum cost	$ 4,584.68	$ 52,832.20	$ 3,451.08	$ 40,600.89	$ 4,584.68	$ 52,832.20
Median	$ 506.31	$ 1,300.39	$ 776.49	$ 2,199.22	$ 610.34	$ 1,725.54
IQR	$230.14–$1,024.66	$666.72–$2,141.98	$430.70–$1,915.65	$1,302.61–$2,639.06	$250.37–$1.203,87	$913.52–$2,581.54
Mean	$ 749.13	$ 1,565.40	$ 1,173.60	$ 2,023.35	$ 859.07	$ 1,796.53
SD	$ 717.57	$ 1,379.70	$ 913.01	$ 1,239.46	$ 793.37	$ 1,330.63
Total	$ 154,321.78	$ 47,429,998.52	$ 84,498.85	$ 62,472,978.37	$ 238,820.63	$ 109,902,976.89
Hospital care	**(*n* = 2)**	**(*n* = 431)**	**(*n* = 2)**	**(*n* = 677)**	**(*n* = 4)**	**(*n* = 1,108)**
Minimum cost	$ 978.29	$ 7.80	$ 169.54	$ 1.64	$ 169.54	$ 1.64
Maximum cost	$ 13,972.77	$ 62,566.85	$ 60,706.42	$ 1,510.09	$ 13,972.77	$ 62,566.85
Median	$ 7,475.53	$ 883.26	$ 839.81	$ 1,337.07	$ 1,244.19	$ 1,637.97
IQR	$978.29–$13,972.77	$2,191.91–$4,311.02	$169.54–$1,510.09	$335.60–$3,648.16	$573.91–$7,741.43	$549.07–$3,896.20
Mean	$ 7,475.53	$ 4,341.71	$ 839.81	$ 3,345.04	$ 4,157.67	$ 3,732.73
SD	$ 9,188.48	$ 7,206.34	$ 947.91	$ 5,766.47	$ 6,566.57	$ 6,380.76
Total	$ 14,951.05	$ 1,871,275.34	$ 1,679.63	$ 2,264,591.86	$ 4,135,867.20	$ 16,630.68

Abbreviations: IQR, interquartile range; *SD*, standard deviation.

TABLE 4 Binomial negative regression models for non-hospital expenditures stratified by type of health insurance. Colombia 2018–2019

	Non-hospital expenditures							
	Subsidized (n = 28,040)				Contributory (n = 27,989)			
	Crude		Adjusted		Crude		Adjusted	
Variables	Diff %	95% CI	Diff %	95% CI	Diff %	95% CI	Diff %	95% CI
Immigrant (Ref: Non-Migrant)	−42.00%	(−49.49% to −33.40%)	−25.37%	(−34.07% to −15.51%)	−52.44%	(−57.04% to −46.69%)	−33.75%	(−39.93% to −26.89%)
Sociodemographic								
Age (years)			0.09%	(0.04% to 0.13%)			0.34%	(0.27% to 0.41%)
Gender (Ref: Women)								
Men			−5.78%	(−6.88% to −4.66%)			−7.22%	(−9.36% to −5.03%)
Intersexual			12.61%	(−15.27% to 49.66%)			-	
Clinical								
Stage (Ref: Stage 1)								
2			−0.46%	(−2.64% to 3.67%)			−3.24%	(−5.79% to −0.63%)
3			2.09%	(−0.32% to 1.76%)			10.28%	(7.38% to 13.26%)
Current antiretroviral treatment (Ref: Not)								
1–3 months			1.71%	(−4.51% to 8.34%)			5.48%	(−3.48% to 15.28%)
4–6 months			108.67%	(96.07% to 122.08%)			159.91%	(138.72% to 183.63%)
7–11 months			55.43%	(46.05% to 65.41%)			49.88%	(37.30% to 63.62%)
12 months			78.91%	(68.13% to 90.37%)			121.39%	(103.06% to 141.37%)
Current viral load (Ref: <50 copies/ml)								
50–999			−6.51%	(−8.06% to −4.94%)			2.96%	(0.26% to 5.73%)
≥1.000			−19.80%	(−21.05% to −18.52%)			−24.14%	(−26.28% to −21.94%)

Abbreviations: CI: confidence interval; Diff %: percentage difference; Ref: reference.

lower in absolute terms than those of the general population. This is to be expected, as the number of cases is also lower, and shows that at present Venezuelan immigrants living with HIV are not a major burden for the Colombian health system, as they represent only a small fraction of cases.

Besides the total expenditures, it is interesting to notice that, the per capita expenditures were also lower for immigrants as compared to non-migrants. Other studies have shown that healthcare expenses are lower for immigrants than native populations, and two main sets of explanations have been proposed. The first has to do with the healthy migrant phenomenon, in which immigrants (especially those that migrate for economic or employment reasons) are a self-selected group of relatively healthy people, both in comparison to their population of origin and to the general native population of the host country (Markides & Rote, 2019; Okrainec et al., 2015; Shor et al., 2017; Vang et al., 2017). The second explanation has to do with access to healthcare, explaining the lower utilisation and expenditures for immigrant healthcare as the results of barriers to access (Sarría-Santamera et al., 2016).

In this study, the latter explanation is less likely to apply, as data came from a healthcare insurance database, and therefore the analysis sample is already conditioned on healthcare access as defined by contact with a medical facility and subsequent treatment. At the same time, immigrants in the CAC database were younger on average than non-migrants, and maybe because of that they were mainly at the first stages of HIV. A younger, healthier population is compatible with the healthy migrant phenomenon (Castelli, 2018), however, as the difference in expenditures persisted after adjusting by age and clinical characteristics, further explanations must be sought. Similar to our results, a study (Ruiz-Azarola et al., 2020) that compared immigrants and nationals in the healthcare system of Andalucía, Spain, found that even in a system offering universal coverage that included immigrants, prescription drug costs per patient were higher for nationals, which the authors suggested might be due to a difference in healthcare provision even after contact with a medical facility. If this explanation applies to our case, it would constitute an unfair difference or health inequity to be addressed. However, it is also possible that the clinical status variables we employed provided an imperfect adjustment, so that some health-related differences between immigrants and non-migrants were unaccounted for in our analysis.

As for the difference in expenditures between the subsidised and contributive scheme, as noticed above the former mainly covers a socially vulnerable population with lower income and irregular or no employment.

On the other hand, it is relevant to notice that immigrants who are not affiliated to an insurance scheme would not appear in the CAC database, and probably would not be receiving treatment, as the out-of-pocket expenditure would make it prohibitive. All irregular Venezuelan immigrants in Colombia (over half a million people in 2019) would potentially be in this situation. The number of PLWH among irregular Venezuelan immigrants in Colombia is difficult to estimate, but in 2016 UNAIDS estimated the prevalence of HIV infection in Venezuela at 0.56% (Ministerio del poder popular para la salud, 2016). Applying this proportion to the estimated number of irregular immigrants in Colombia would render a total of 6,397 PLWH, however, the demographic composition of the immigrant population could make a difference in the prevalence among them. Still, the lack of coverage for HIV and other health problems among irregular immigrant is a major issue requiring addressing.

It is also worth noticing that, since most regular Venezuelan immigrants are of lower income and have irregular jobs, and their affiliation to the subsidised health insurance scheme has been promoted by the government as part of its response plan to migration, it would be expected that most PLWH of Venezuelan origin were affiliated to that scheme. Still, in the CAC database most Venezuelan immigrants were reported by the contributive scheme. Two possible explanations for this, both of them implying a barrier to access, are, one, that even after obtaining the PEP immigrants face difficulties registering to the subsidised system; and two, that the subsidised scheme is not detecting or treating PLWH as efficiently as the contributive scheme. A third option is that immigrants who live with HIV are more likely to be of higher socioeconomic status, and therefore to access healthcare through the contributive scheme, than other Venezuelan immigrants.

Among the limitations of this study is the lack of information on individual characteristics such as socioeconomic level, other health conditions, and migration-related variables such as time living in Colombia. Without this, we can only speculate about the reasons for the observed difference in expenditures between immigrants and non-migrants. We also lacked information on the place of birth of PLWH, so we had to infer it from other characteristics. While our identification of Venezuelan immigrants was probably accurate, it's still possible that some of those classified as non-migrants were of Venezuelan origin, but holding an identification document other than the PEP. Still, as the main flow of Venezuelans to Colombia happened recently, and most of those who migrated as part of the recent flow acquired regular status through the PEP, we are confident that our variable is a good enough proxy. Future studies collecting more detailed data are required, in order to understand if the lower healthcare expenditures of this population are the result of limitations in healthcare access, of clinical characteristics that were not assessed in this study, or of other unmeasured aspects.

To conclude, expenditures associated with HIV treatment of PLWH of Venezuelan origin in Colombia are lower than those for the non-migrant population. While guaranteeing healthcare coverage to all people independently of their migration status is part of the international commitments signed by many countries, it is worth noticing that Venezuelan immigrants living with HIV in Colombia are not a burden to the healthcare system, and instead can contribute to economic growth and society's well-being.

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CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

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VIH

Burden and magnitude of risk in HIV/AIDS in the Colombian health system: a real-world data approach

Autores: Silvia Juliana Trujillo Cáceres, Julieth Carolina Castillo, Ana María Valbuena, Lizbeth Acuña Merchán.

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Alcance: Nacional.

Objetivo:

Evaluar la situación epidemiológica de las personas que viven con VIH y sida en los municipios y regiones de Colombia, en el marco del aseguramiento, entre febrero de 2018 y enero de 2019.

Principales hallazgos:

- En 2018, hubo un ligero aumento cercano al 7% en el número de nuevos casos de VIH detectados en comparación con 2017.
- La incidencia y la prevalencia estandarizadas por la edad más altas se registraron en Florencia (Cauca) (354,28 por 100.000 y 3,32 por 100 personas, respectivamente).
- Se evidenció una elevada proporción de personas que no recibieron terapia antiretroviral (TAR) (20,96%; 16,24% y 42,79% en los casos incidentes, prevalentes y fallecidos, respectivamente).

Relevancia de los hallazgos:

- Estos resultados permiten identificar las características geográficas y clínicas de las PVV, así como la situación epidemiológica (incidencia, prevalencia y mortalidad) en el marco del aseguramiento colombiano.
- Lo anterior es vital para la planeación estratégica de los servicios, basada en las necesidades de los territorios. De igual forma, es un insumo valioso para la orientación y evaluación de las políticas públicas en términos de magnitud de esta condición.

Comentario del autor experto:

Dra. Ana María Valbuena

La correcta planeación de los programas de atención, la contratación de la red de prestadores y la oferta de servicios debe basarse en la carga de enfermedad de cada región, perfil clínico y sociodemográficas de cada población. Este artículo permite identificar aquellas áreas con mayor concentración de casos nuevos y prevalentes con un nivel de desagregación geográfica hasta el municipio, como también logró identificar que en el 14% de los municipios del país no tienen casos identificados y reportados de VIH, por lo que deben enfocarse en metodologías orientadas a la búsqueda activa de casos.

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ARTÍCULO ORIGINAL

Burden and magnitude of risk in HIV/AIDS in the Colombian health system: a real-world data approach

Silvia Juliana Trujillo-Cáceres[1,2,*], Julieth Castillo[1,3], Carlos Alvarez-Moreno[4], Ana Valbuena[1,5], Lizbeth Acuña[1,6]

Abstract

Aim: To assess the epidemiological situation of people living with HIV and AIDS (PLWHA) in the municipalities and regions of Colombia in 2018.
Materials and methods: A cross-sectional study was conducted with secondary data from the High-Cost Diseases Fund from February 1st, 2018 to January 31st, 2019. We included sociodemographic, clinical variables, and related to geographic location. We calculated incidence, prevalence, and mortality according to the Colombian geographical regions, department and municipality of residence. Crude and age-standardized rates were estimated.
Results: By 2018, 10,930 new cases of PLWHA were reported, being more frequent in males, aged between 25 to 49 years. 39.32% were reported with AIDS and 35.27% had undetectable HIV viral load. During 2018, there are 109,056 PLWHA in Colombia. The highest age-standardized incidence and prevalence were reported in Florencia (Cauca) (354.28 per 100,000 and 3.32 per 100people, respectively). The age-standardized incidence rate was 22.12 per 100,000 population (95% CI 21.71-22.54). Age-standardized prevalence and mortality were 0.23 per 100 population (95% CI 0.22-0.23) and 3.78 per 100,000 population (95% CI 3.61-3.96), respectively.
Conclusion: Different strategies should be implemented to improve the identification of risk factors in the population, especially in some regions of Colombia and prevent transmission.

Keywords: epidemiology, AIDS, HIV, prevalence, mortality, Colombia.

Carga y magnitud del riesgo en VIH/SIDA en el sistema de salud colombiano: enfoque de datos del mundo real

Resumen

Objetivo: Evaluar la situación epidemiológica de las personas que viven con el VIH y el SIDA (PVVS) en los municipios y regiones de Colombia en 2018.
Materiales y métodos: Se realizó un estudio transversal con datos secundarios del Fondo Colombiano de Enfermedades de Alto Costo entre febrero 1 de 2018 al 31 de enero de 2019. Incluimos variables sociodemográficas, clínicas y relacionadas con la ubicación geográfica. Calculamos la incidencia, prevalencia y mortalidad según la región geográfica colombiana, el departamento de residencia y el municipio. Se estimaron tasas crudas y estandarizadas por edad.
Resultados: Para el 2018, 10.930 nuevos casos de PVVS fueron reportados, siendo más frecuentes en hombres, en edades entre 25 a 49 años. 39.32% fueron reportados con SIDA y 35.27% tuvieron una carga viral de VIH indetectable. 109,056 PVVS en Colombia. Las incidencia y prevalencia ajustadas por edad más altas se informaron en Florencia (Cauca) (354.28 por 100,000 y 3.32 por 100 personas, respectivamente). La tasa de incidencia estandarizada por edad fue de 22.12 por 100,000 habitantes (IC 95% 21.71-22.54). La prevalencia y mortalidad ajustadas por edad fueron 0.23 por 100 habitantes (IC 95% 0.22-0.23) y 3.78 por 100.000 habitantes (IC 95% 3.61-3.96), respectivamente. Se deben implementar diferentes estrategias para mejorar la identificación de los factores de riesgo en la población, especialmente en algunas regiones geográficas de Colombia y prevenir la transmisión.

Palabras clave: epidemiología, SIDA, VIH, prevalencia, mortalidad, Colombia.

Introduction

Colombia is located in the north of South America, is the third-largest in the Latin America region, with 48 million inhabitants[1], of which 77.1% live in the capital cities. As of June 28, 2019, the country's political and administrative division is: 32 departments, 1,101 municipalities, and island (San Andrés, Providence and Santa Catalina) and 20 non-municipal areas. Additionally, departments are grouped into six geographical regions: Caribbean, Central, Pacific, Eastern, and Bogotá C.D. defined by the National Administrative Department of Statistics (DANE, by its acronym in Spanish)[2].

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According to the latest data related with the 90-90-90 targets in Latin America the 80% (62 - >95%) of people living with HIV and AIDS (PLWHA) knew their status, 62% of PLWHA accessed to antiretroviral therapy (ART), and 55% were virally suppressed[3], which may translate that the region has additional challenges.

By 2018, in Latin America there were an estimated of 100,000 (79,000 – 130,000) people with acquired HIV, a 7% increase compared with 2010. The highest increases were observed in Chile (34%) and Bolivia (22%) and the lowest in El Salvador (-48%). In Colombia there are 160,000 (130,000 – 180,000) PLWHA and ranks the third among countries with the lowest rates of HIV infection (incidence per 1,000 population: 0.14 (95% CI 0.10-0.19)). The region's incidence-prevalence ratio continues to decrease, reaching 5.4% (95% CI 4.1-6.8%), but many efforts are needed to reach the 3.0% epidemic transition benchmark[3].

In Colombia, the health system is funding by public and private sources, and its coverage is closer to 96% of the total population, the remaining 4% is grouped under individual insurance. There are two insurance regimes, and both of them include the same services, procedures, medicines, and interventions. However, different health payers are responsible for managing resources and paying to healthcare providers[4].

Since the implementation of the national registry of HIV/AIDS managed by the High-Cost Diseases Fund (CAC, by its acronym in Spanish) in 2011-2012 and actualized within the framework of the national resolution 0273 (2019), 109,056 prevalent cases and 10,930 new cases of HIV have been reported until 2019[5]. We aim to assess the epidemiological situation (incidence, prevalence, and mortality) of PLWHA in the municipalities and geographical regions of Colombia during 2018.

Materials and methods

We performed a cross-sectional study with secondary data sources, including the information of PLWHA reported to the CAC from February 1st, 2018 to January 31st, 2019, by their health payers and providers.

Health providers must collect annual data from their affiliates to update the information on a web platform, which was designed to validate the structure, coherence and consistency of the data. Once the information is reported, a cross-checking with other official sources of vital statistics and the affiliation of PLWHA to the health system with the "Unique Affiliate Database" (BDUA, by its acronym in Spanish) is performed.

A data monitoring process is used to validated that the information uploaded to the platform corresponds to the electronic/printed medical records. This ensures that the information reported corresponds to described in the supports. We included all confirmed cases with HIV, classified according to the clinical practice guidelines for the care of HIV of the Ministry of Health and Social Protection (MSPS, by its acronym in Spanish)[6,7].

If the information reported is different from the observed, the data available in the supports were captured and corrected in the database; otherwise, when the data cannot be found in medical records was considered as missing. To ensure the anonymization of the PLWHA, a unique number was assigned, which also made it possible to include unique registries to estimate the epidemiological indicators. People who died before of the beginning of the period and those without a confirmed diagnosis of HIV/AIDS were excluded from the analysis (Figure 1).

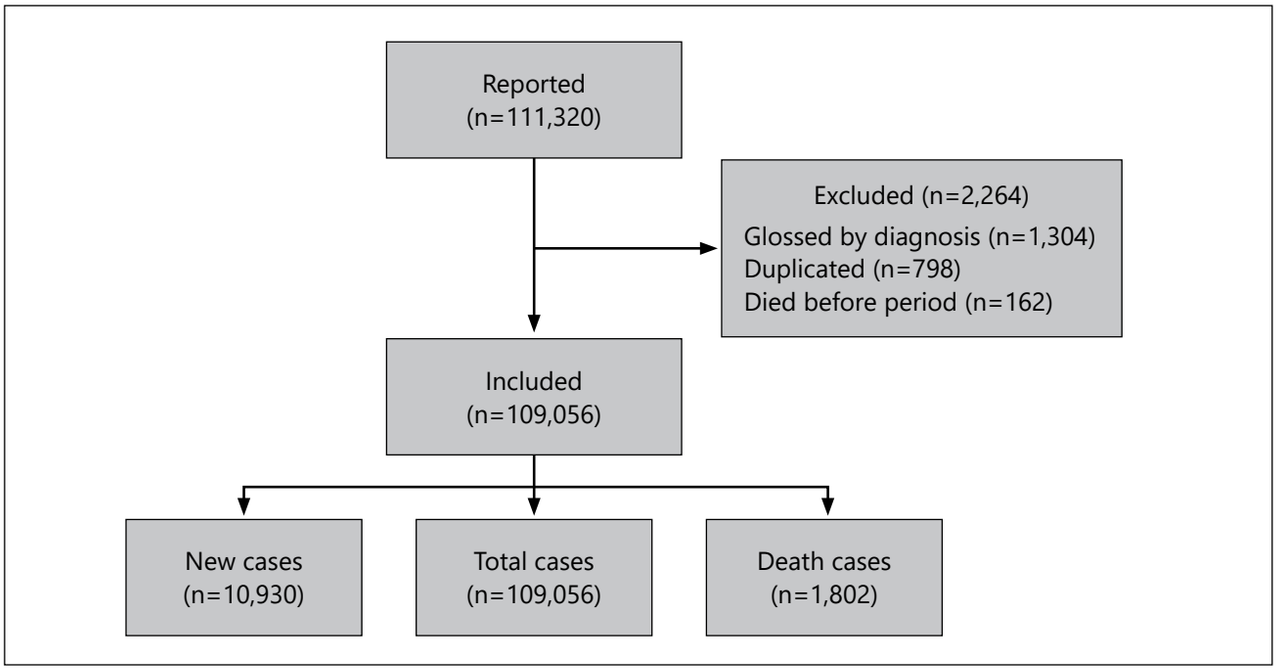


Figure 1. Flow chart of cases included in the analysis

We included sociodemographic variables, e.g., age and sex, and related to location: geographical region (classification given by DANE) according to the gross domestic product of the departments (Figure 2), as well as department and municipality of residence; variables related to the clinical condition were the current clinical status of the disease, CD4 T cells counts- and HIV viral load. Variables were analyzed with measures of central tendency according to their marginal distribution. Categorical data were presented as absolute values and proportions.

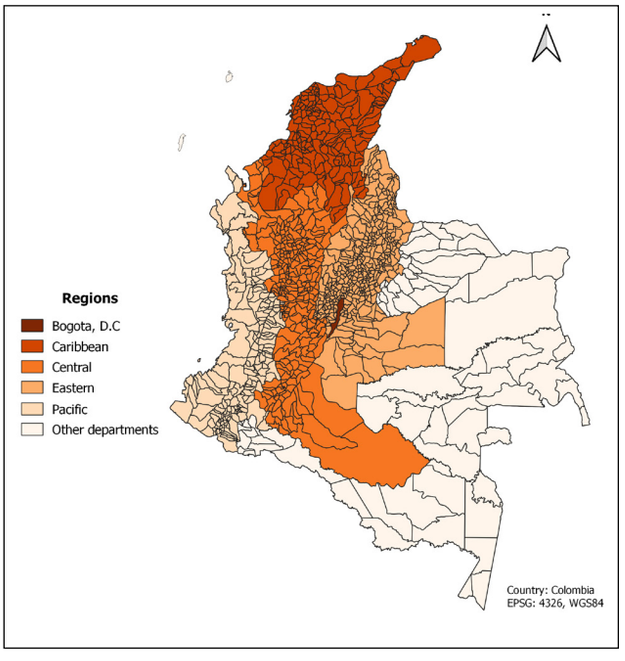


Figure 2. Distribution of geographical regions of Colombia according to DANE, 2018.

We calculated the three main epidemiological indicators: incidence, prevalence and mortality. HIV incidence was defined as PLWHA, whose infection diagnosis date occurred within the reporting period, and prevalence was defined as people diagnosed with HIV and reported during the period. Finally, to estimate the mortality, deaths were identified by using the administrative information reported by the providers, and verified in the single register of affiliates from the MSPS. All of these indicators were estimated according to the Colombian geographical regions, department and municipality of residence, highlighting the places with the highest rates.

Crude and age-standardized rates were calculated by using the direct method, taking the Colombian population projected by DANE (n= 49,834,240) until July 2018 as the reference. National estimations were standardized using the world population projected by the United Nations for Latin America and the Caribbean for 2020(8). Morbidity and mortality indicators were plotted using QGis 3.12 (Open Source Geospatial Foundation). STATA version 13.0 (STATA Corp, College Station, Texas, USA) was used to the statistical analysis. According to resolution 8430 of 1993 of the MSPS of Colombia, this investigation has no risk, and not intervention was carried out. However, the confidentiality and anonymization of the information was guaranteed.

Results

HIV incidence in 2018

In 2018, 10,930 new cases of PLWHA were reported. A summary of the characteristics of the study population is provided in Table 1. PLWHA frequency was higher in males, aged between 25 to 49 years. The median age was 30 years (IQR 24 – 40). Regarding the clinical status, 39.32% (n=4,298) cases were reported with AIDS (stage 3) and 35.27% (n=3,855) had undetectable HIV viral load.

The national age-standardized incidence rate was 22.12 per 100,000 population (95% CI 21.71-22.54). The highest incidence rates were estimated in Bogotá, C.D. and Central regions, which were even higher than the national (Table 2). The five municipalities in Colombia that reported the highest incidence were: Florencia (Cauca) 354.28 per 100,000 (95% CI 106.1-766.89), Barranca de Upía (Meta) 251.10 (95% CI 49.03-852.66), Magangué (Bolívar) 228.53 (95% CI 195.24-266.02), Armenia (Antioquia) 161.41 (95% CI 63.78-340.37) and Aguada (Santander) 128.96 (95% CI 3.26-662.27). Figure 3A shows the municipalities with a higher incidence. In contrast, the lowest incidences were observed in Madrid (Cundinamarca), Cimitarra (Santander), and Potosí (Nariño). The supplementary table 1 describes the data for the 1,122 municipalities in Colombia.

HIV prevalence in 2018

The total number of cases reported in 2018 was 109,056 PLWHA, being more frequent in males, aged between 25 to 49 years. The median age was 38 years (IQR 30 – 49). The geographical region with the highest prevalence was the Central. Regarding the clinical status, 56.4% (n=61,505) cases had AIDS (stage 3). Nevertheless, the highest proportion of PLWHA (63.9%; n=69,682) had undetectable HIV viral load (Table 1).

The age-standardized prevalence was 0.23 per 100 people (95% CI 0.22-0.23), with an increase of 13% in the number of cases compared to 2017. The highest prevalence were estimated in Bogotá, C.D., and Central regions and, were even higher than the national (Table 2). The five municipalities in Colombia that reported the highest prevalence were: Florencia (Cauca) 3.32 (95% CI 2.79-3.91), Magangué (Bolívar) 2.14 (95% CI 2.04-2.24), Armenia (Antioquia) 1.73 (95% CI 0.91-2.82), Santiago (Norte de Santander) 0.93 (95% CI 0.12-2.64) and Armenia (Quindío) 0.92 (95% CI 0.85-0.98). Figure 3B shows the municipalities with a higher prevalence. 14.17% of municipalities did not report cases with HIV (supplementary material, table 1).

Table 1. Clinical and sociodemographic characteristics of people living with HIV in Colombia, 2018

Characteristics	Incident cases		Prevalent cases		Deaths	
	n	%	n	%	n	%
Sex						
Female	2,020	18.48	26,348	24.16	456	25.29
Male	8,910	81.52	82,697	75.83	1,346	74.65
Intersexual	0	0.00	11	0.01	1	0.06
Age group (years)						
Less than 2	10	0.09	24	0.02	0	0.00
2 - 14	42	0.38	860	0.79	7	0.39
15 - 24	2,830	25.89	10,250	9.40	82	4.55
25 - 49	6,726	61.54	72,352	66.34	1,069	59.29
≥ 50	1,322	12.10	25,570	23.45	645	35.77
Region[a]						
Bogota, D.C.	2,278	20.84	24,994	22.92	247	13.70
Caribbean	2,463	22.53	23,889	21.91	529	29.34
Central	3,000	27.45	30,154	27.65	478	26.51
Eastern	1,215	11.12	11,875	10.89	196	10.87
Pacific	1,794	16.41	16,622	15.24	312	17.30
Other departments	180	1.65	1,522	1.40	41	2.27
Current clinical status at diagnosis						
Stage 0	71	0.65	214	0.20	2	0.11
Stage 1	2,198	20.11	30,422	27.90	264	14.65
Stage 2	4,101	37.52	33,889	31.07	328	18.20
Stage 3	3,807	34.83	39,435	36.16	1,029	57.10
Not date	753	6.89	5,096	4.67	179	9.93
Current viral load (patient with ART and viral load in the last six months)						
< 50 copies	3,352	42.35	55,727	75.28	112	37.84
≥50 copies to ≤200 copies	1,038	13.11	5,896	7.96	24	8.11
>200 to <=1000 copies	639	8.07	3,185	4.30	17	5.74
> 1000 copies	2,886	36.46	9,220	12.45	143	48.31
On ART						
Yes	8,639	79.04	91,344	83.76	1,031	57.21
Not	2,291	20.96	17,712	16.24	771	42.79

[a] The regions in Colombia are made up of departments. Departments are formed by a grouping of municipalities. The grouping of regions depends on the department's gross domestic product (GDP) and is available in annual reports from the DANE (Departamento Admistrativo Nacional de Estadística) (2). Geographical regions are: Bogotá, D.C.; Caribbean: Atlántico, Bolívar, Cesar, Córdoba, La Guajira, Magdalena and Sucre; Central: Antioquia, Caldas, Caquetá, Huila, Quindío, Risaralda and Tolima; Eastern: Boyacá, Cundinamarca, Meta, Norte de Santander and Santander; Pacific: Cauca, Chocó, Nariño and Valle del Cauca; Other departments: Amazonas, Arauca, Casanare, Guainía, Guaviare, Putumayo, San Andrés, Vaupés and Vichada.

HIV mortality in 2018

In 2018, 1,802 deaths were reported in PLWHA. The characteristics of people who died during the period are provided in Table 1. Mortality was higher in males, aged between 25 to 49 years. The median age was 43 years (IQR 34 – 55). Regarding the clinical status, 84.35% (n=1,520) had AIDS. The majority of cases had no measurement of the last viral load (42.01%; n=757) and 42.51% (n=766) did not received ART.

The age-standardized mortality rate was 3.78 per 100,000 population (95% CI 3.61-3.96), with an increase of 56.4 % in the number of deaths compared to 2017. The highest mortality rates were estimated in the Caribbean and Central regions, which were even higher than the national (Table 2). The five municipalities in Colombia that reported the highest mortality were: Armenia (Antioquia) 283.08 (95% CI 8.07-1,067.90), Saladoblanco (Huila) 141.13 (95% CI 3.57-542.00), Morales (Bolívar) 113.94 (95% CI 13.80-324.36), Vigia del Fuerte (Antioquia) 94.22 (95% CI 3.54-347.12) and Calamar (Guaviare) 78.97 (95% CI 9.56-260.47). Figure 4 shows the municipalities with the highest mortality. Moreover, the municipalities with the lowest mortality were Patía (Cauca), Santa Rosa del Sur (Bolívar), and Piendamó (Cauca) (supplementary material, table 1).

Discussion

In 2018, there was a slight increase of almost 7% in the number of newly detected HIV infections compared with 2017[3]. The estimated prevalent cases of HIV in 2019, reported by the MSPS through the Spectrum tool, was 157,702 from those, only 69.15% (n=109,056) were reported to the CAC. The final number of PLWHA may be higher. Regarding incident cases, around 10.000 new cases were reported to the CAC and were attended by the health system, while, the Institute of National Health-INH estimated 15,908 new HIV cases by 2019[9].

The observed gap could be explained because while the CAC records the information provided by the health insurers, the INH performs the epidemiological surveillance of the newly diagnosed cases. This difference can be given by under-registration or the inability of the health system to linkage to care and retain the newly diagnosed HIV population. It is important to highlight that Colombia has a registry of all PLWHA treated within the framework of the health system, established by a resolution from the MSPS and all health insurers in cooperation with their healthcare providers must report all cases to the CAC; for this reason, our approach does not incorporate methodologies such as UNAIDS, which are based on estimates or mathematical models[10,11].

The HIV infection was more frequent in municipalities located in four of six regions of Colombia. The highest age-standardized incidence and prevalence were reported in Florencia (Cauca) (354.28 per 100,000 and 3.32 per 100 persons, res-

Table 2. Epidemiological indicators of HIV/AIDS in Colombia, 2019

Indicator	Geographical region	Crude	Age-standardized rate	95% CI
Incidence*	**Bogota, D.C.**	**27.84**	**27.17**	**(26.06-28.31)**
	Caribbean	**22.83**	**23.61**	**(22.68-24.56)**
	Central	**24.31**	**24.29**	**(23.43-25.18)**
	Eastern	14.15	14.24	(13.45-15.06)
	Pacific	21.12	20.96	(20.00-21.95)
	Other departments	12.47	12.85	(11.02-14.90)
Prevalence**	**Bogota, D.C.**	**0.31**	**0.28**	**(0.28-0.29)**
	Caribbean	0.22	0.23	(0.23-0.24)
	Central	**0.24**	**0.24**	**(0.23-0.24)**
	Eastern	0.14	0.14	(0.13-0.14)
	Pacific	0.20	0.19	(0.19-0.20)
	Other departments	0.11	0.12	(0.11-0.12)
Mortality*	Bogota, D.C.	3.01	2.75	(2.41-3.11)
	Caribbean	**4.90**	**5.28**	**(4.84-5.75)**
	Central	**3.87**	**3.80**	**(3.45-4.16)**
	Eastern	2.28	2.29	(1.98-2.63)
	Pacific	3.67	3.65	(3.25-4.09)
	Other departments	2.84	3.37	(2.41-4.59)

*Per 100,000 population
** Per 100 population

pectively). Among those municipalities, we found that almost 60% of cases had AIDS (stage 3); the above indicates delays in linkage-to-care of people with HIV for early detection as well as the continued risk of onward transmission. If the goals of 90-90-90 are considered, it is evident that Colombia has a limitation in achieving especially the first 90 related to diagnose at least 90% of the infected population. Also, the fact of detecting people when they are already in an advanced stage (34% of incident cases and 54% of people who died) should be an alert to establish early detection programs that include new test and treatment strategies.

According to mortality data, municipalities in the Central region had the highest mortality rates: Armenia (Antioquia) 283.08, Saladoblanco (Huila) 141.13, and Vigia del Fuerte (Antioquia) 94.22 per 100,000. These results may be explained because most cases were diagnosed in stage 3 (84.35%) and had a viral load ≥ 1000 copies/ml. It is important to note that in general, PLWHA, once they are admitted in HIV care programs, maintain a high rate of virological success (viral load <200 copies / ml) (83%).

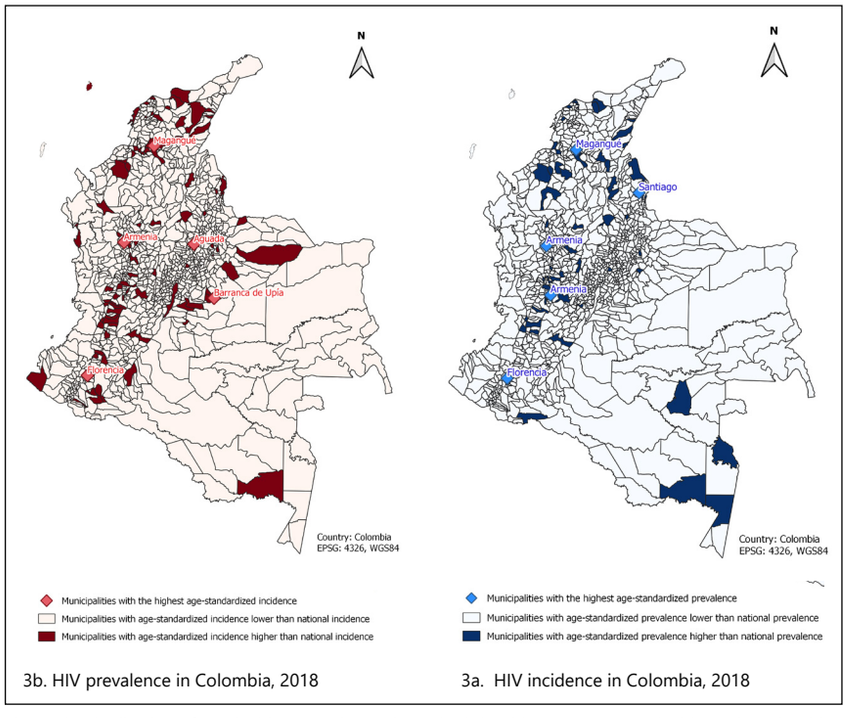
Regarding the geographical location of PLWHA in Colombia, previous studies have described the HIV epidemic as a disease affecting the entire country[12]. In our study, the trends in all the indicators are consistent in the three major regions, and geographical differences may be explained by ethnic and cultural factors and their relationship with sexual behavior[13].

On the other hand, there is a high proportion of people who did not receive ART (20.96%; 16.24% and 42.79% in incident, prevalent and death population, respectively). Therefore, emphasis should be placed on the initiation and retention of highly active antiretroviral therapy (HAART). Reasons to explain that patients have no HAART are various, from lack of adherence, administrative purposes, and not offered by practitioners. The last reason is due to the current clinical practice guideline is outdate and requires and update including the best evidence available[6,7].

Some strengths of the study will be discussed. Taking into account that HIV/AIDS is considered a high-cost disease of public health interest in Colombia, PLWHA must be reported by their health care insurers and providers to the administrative registry managed by the CAC and, that ensures the completeness of the data. The mandatory nature of the reporting process also allows an epidemiological and clinical follow-up based on real-world information. In addition, there is a competitive compensation mechanism within the health system that obliges insurers to report the variables requested by regulation and allows the characterization of the population with HIV. Among other strengths, data is verified by a data monitoring process against clinical records. Further, information reported to the CAC is one of the sources that MSPS provides to international initiatives such as GAM (Global AIDS Monitoring 2020 – Indicators for monitoring the 2016 United Nations Political Declaration on Ending AIDS)[14].

Our estimations could be limited due to under-reporting effect. In fact, we only have the information reported for people enrolled with an authorized public or private insurance agency of the national healthcare system.

Our results allow identifying the geographical and clinical characteristics of PLWHA as well as the epidemiological situation (incidence, prevalence, and mortality) in Colombia. While there are 14% of the municipalities without HIV cases, it is necessary to keep the infection under control and to strengthen the reporting process to the CAC in order to



3a. HIV incidence in Colombia, 2018 3b. HIV prevalence in Colombia, 2018

Figure 3. Distribution of HIV incidence and prevalence in Colombia, 2018; 3a. HIV incidence in Colombia, 2018; 3b. HIV prevalence in Colombia, 2018

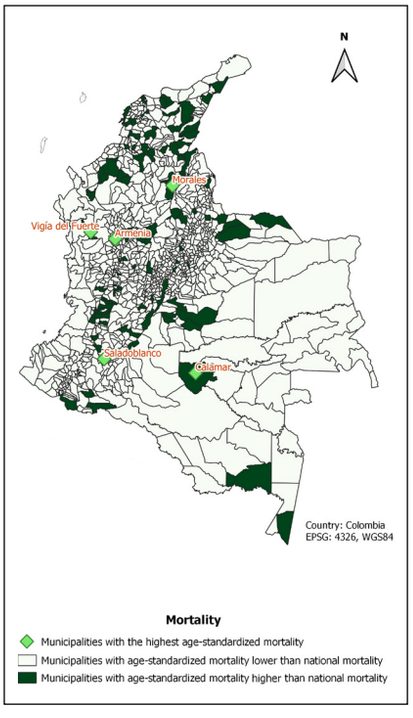


Figure 4. HIV mortality in Colombia, 2018

avoid the under-reporting. Furthermore, future work is needed to integrate data from different sources and follow-up programs within the primary care[15].

Finally, different strategies should be implemented to improve early detection of risk factors and prevent transmission, emphasizing on specific protection activities and monitoring other sexually transmitted infections. Also early detection strategies guarantee a timely linkage-to-care programs and avoid delays in ART initiation(16).

Ethical disclosure

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Protection of human and animal subjects. This research do not use animal nor human material or data.

Confidentiality of data. The confidentiality and anonymization of the information was guaranteed.

Conflicts of interest. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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VIH

Colombian HIV/AIDS registry and health risk management

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Revista: Infectio.

Alcance: Nacional.

Trabajo colaborativo con el Ministerio de Salud y Protección Social.

Objetivo:

Describir el proceso de gestión de datos del registro colombiano de VIH/sida, sus resultados epidemiológicos y sus contribuciones a la investigación y a la gestión del riesgo en salud.

Principales hallazgos:

El registro nacional de VIH/sida permite obtener:

- Información epidemiológica para el seguimiento de las tendencias del VIH/sida en el marco del aseguramiento en Colombia.
- Medición periódica de los indicadores de gestión del riesgo, sus tendencias e identificación de las brechas existentes en función de aspectos demográficos y del aseguramiento.
- Evidencia basada en información del mundo real para orientar la toma de mejores decisiones en salud.
- Información para fortalecer la gestión del riego a través de un mecanismo de distribución de incentivos en función de los resultados.

Relevancia de los hallazgos:

- El registro permite seguir la tendencia de la magnitud del VIH/sida en el país y de los principales indicadores de gestión del riesgo. Lo anterior permite monitorear la carga de esta enfermedad y ofrece un insumo valioso a los tomadores de decisiones para orientar la política pública.
- El registro colombiano de VIH/sida complementa otras fuentes de información nacional como el Sistema de Vigilancia en Salud Pública (SIVIGILA), ya que permite el seguimiento a la vinculación a la atención, al inicio de la TAR y la continuidad en la atención.

Comentario del autor experto:

Dra. Cielo Ríos Hincapié

El artículo *"Colombian HIV/AIDS registry and health risk management"* publicado en inglés en el año 2021 en la revista Infectio, nos dio la oportunidad de presentar de manera concisa y clara el proceso que la Cuenta de Alto Costo sigue en el manejo y uso de la información, en este caso, en VIH/Sida. A través del artículo es posible evidenciar los momentos críticos del proceso, los cuales incluyen la recolección, validación, auditoría, análisis, diseminación y uso de la información. Esta última etapa se ve reflejada en cuatro productos clave para el país:

1. La disponibilidad de información epidemiológica sobre el VIH/Sida en Colombia, la cual se utiliza para reportes nacionales e internacionales, especialmente a ONUSIDA para el informe Global del sida;
2. El seguimiento anual de indicadores de gestión del riesgo por parte de las EPS, permitiendo monitorear los avances en la prestación de servicios en VIH desde el tamizaje hasta la indetectabilidad del virus en las personas que viven con VIH, que es el objetivo final del tratamiento;
3. Artículos científicos, resultado de los subanálisis que se hacen de los datos y que permiten contribuir a la gestión del conocimiento; y
4. La posibilidad de llevar a cabo una distribución de incentivos a las buenas prácticas, basados en el desempeño alcanzado por parte de las aseguradoras.

De esta manera, la Cuenta de Alto Costo ha permitido al país hacer el seguimiento de la respuesta al VIH en Colombia desde el año 2012 y direccionar los esfuerzos de los integrantes del sistema general de seguridad social en salud hacia las metas de eliminación al año 2030.

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Colombian HIV/AIDS registry and health risk management

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Abstract

HIV/AIDS information systems are a critical tool for keeping track of the HIV pandemic in any country, leading to the AIDS elimination to 2030 and achievement of the 95-95-95 goals set by 2025. In this article, we describe the data management process of the Colombian National HIV/AIDS registry, its epidemiological results and contributions to research and health risk management. This registry is a longitudinal database. Variables and periodicity are defined by The Ministry of Health and Social Protection. Reporting is done by health insurers and their healthcare providers on annual bases. The information is uploaded through a web platform run by the High-Cost Diseases Fund, in charge of the validation, auditing process, consolidation, analysis and publication of the data. Security and confidentiality of the information is also taken care of by the High-Cost Disease Fund. Main results include epidemiological follow up of the epidemic, periodic evaluation of 25 risk management indicators, publication of research studies and the calculation of an economic incentive for insurers to improve health risk management. The registry has shown to be useful not only for the management of clinical information but also for administrative purposes.

Keywords: Health information systems, Registries, HIV, Risk Management, Information Management.

Registro colombiano de VIH/SIDA y gestión del riesgo en salud

Resumen

Los sistemas de información sobre el VIH/SIDA son una herramienta fundamental para realizar el seguimiento de la pandemia del VIH en cualquier país, con miras a la eliminación del SIDA hasta el 2030 y al logro de las metas 95-95-95 establecidas para el 2025. En este artículo se describe el proceso de gestión de datos del Registro Nacional de VIH/SIDA de Colombia, sus resultados epidemiológicos, sus aportes a la investigación y a la gestión del riesgo en salud. Este registro es una base de datos longitudinal. Las variables y la periodicidad son definidas por el Ministerio de Salud y Protección Social. Los reportes son realizados por las aseguradoras de salud y sus prestadores de servicios de salud sobre bases anuales. La información se carga a través de una plataforma web gestionada por el Fondo de Enfermedades de Alto Costo, encargado del proceso de validación, auditoría, consolidación, análisis y publicación de los datos. El Fondo de Enfermedades de Alto Coste también se encarga de la seguridad y la confidencialidad de la información. Los principales resultados son el seguimiento epidemiológico de la epidemia, la evaluación periódica de 25 indicadores de gestión del riesgo, la publicación de estudios de investigación y el cálculo de un incentivo económico para que las aseguradoras mejoren la gestión del riesgo sanitario. El registro ha demostrado ser útil no sólo para la gestión de la información clínica, sino también para fines administrativos.

Palabras clave: Sistemas de información en salud, Registros, VIH, Gestión de riesgos, Gestión de la información.

Introduction

Monitoring HIV results is a critical step for countries to achieve the Sustainable Development Goals to 2030 and to end inequalities as stated in the 2021 Political Declaration on HIV and AIDS agreed at the High-Level Meeting on AIDS of the United Nations General Assembly[1].

Epidemiological surveillance systems and disease-specific registries provide tools that allow this monitoring, however, the data and its results will always rely on the quality of the information reported by the healthcare providers or institutions performing the care and reporting of the data[2]. Awareness of the importance of HIV registries as platforms for research is growing and contributes to knowledge generation. Many reports are the result of government policies, public organizations such as academia or medical research associations[3]. Health-information systems offer the potential to improve quality of care and population health by informing clinical decision-making and policy formulation, sector surveillance, health risk management and resource allocation. However, to achieve these goals, key features need to be in place: popula-

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tion definition, temporal elements of data reporting, core data, appropriate terminology, quality and safety in data analysis, and governance, as stated in the framework for high-quality data collection developed by the European Medical Agency[4].

A review by Craig et al. aimed to assess the elements that make up a registry and whether they contain research data. This identified 13 HIV registries that include specific-registry information, collaboration processes and research data[5]. Examples of these registries or observational cohorts were EMBRACE (USA)[6], CFAR Registry (USA)[7], CCR/HIV of the VA Department (USA)[8], San Francisco HIV/AIDS Surveillance Registry[9], New York City HIV/AIDS Surveillance Registry[10], Stiching HIV Monitoring in Netherlands[11], HARS in Missouri[12], Australian National HIV Registry[13], InfCare HIV (Sweden)[14], Minnesota HIV Surveillance Registry[15], IeDEA (Rwanda)[16] and others[5,17,18].

Colombia has a solidarity-based health insurance system, regulated by the Ministry of Health and Social Protection (MHSP) with two main regimens (Contributive and Subsidized, according to payment capacity of their affiliates) that covers nearly 97.64% of the population[19], but include the same services, procedures, medicines, and interventions for their users. Insurers are responsible for managing resources, paying to healthcare providers[20] and data reporting to most of health information systems.

The MHSP delegated to the High-Cost Diseases Fund (CAC, in Spanish), a technical organization of the health system, the monitoring of this disease through the National HIV/AIDS registry. We aimed to describe the data management process of the Colombian registry, its epidemiological results and contributions to research and health risk management.

Methods

1. Background and national policies

The MHSP established the legal framework of the national HIV/AIDS registry (resolutions 4725 of 2011, 0783 of 2012 and 0273 of 2019)[21–23]. These norms include the periodicity, form and content of the information to be reported by all insurance companies and healthcare providers. The annual report covers the cases enrolled and cared for by the insurance companies along a year that starts February 1st of any reporting year to January 31st of the following year. The variables are adjusted periodically according to new clinical guidelines, country information needs, and lessons learned from the implementation.

2. Contents of the registry

2.1. Patients included in the HIV/AIDS registry

The national HIV/AIDS registry is a longitudinal database containing data of two types of populations: 1. pregnant women, children born to mothers living with HIV/AIDS and people reported with active tuberculosis (TB) that were negative to the HIV test or do not have HIV test results at the time of reporting, and 2. People diagnosed with HIV/AIDS including pregnant women, children born to mothers living with HIV/AIDS and TB patients already diagnosed with HIV. The reason for these two types of reporting is to follow the adherence of the health insurers and healthcare providers to the national HIV/AIDS guidelines and national strategies. The HIV diagnosis is based on the algorithm defined by the national clinical guidelines[24,25].

2.2. Registry files

Health insurers and healthcare providers collect and summarize the data from the two types of populations in two different files, one for people living with HIV/AIDS (PLWHA) and the other one for the non-HIV or unknown HIV status patients that are followed. Sociodemographic, clinical, and administrative variables are collected for the reporting period. The CAC provides all entities with reporting instructions and an auditing manual as recommended by the MHSP.

2.3. Structure of the database

Registry structure includes 193 variables, grouped in subsections like: identification data, demographics, and administrative updates for all patients; clinical information, current ART, AIDS-defining clinical conditions, current clinical status, prevention interventions and prophylaxis for the HIV/AIDS patients; pregnant women, children born to mothers living with HIV/AIDS and people with active TB with unknown HIV diagnosis or negative HIV test have their own registry files, that cover only 43 variables.

The sociodemographic data (personal identification, date of birth, sex, etc.) are crucial for cross-checking with other official sources of information like the "Unique Affiliated Database" (BDUA, in Spanish) to verify the reliability of the patient's status as vital statistics are updated on the last date of the period.

The clinical section includes variables related with the diagnosis (date of diagnosis, transmission mechanism, reason for testing, clinical stage, CD4 T-cell count and viral load at diagnosis); treatment (initial and current treatment, substitution therapies, reasons for switching ART, among others) and follow up (success of ART therapy determined by suppression of viral load, most recent CD4 T-cell count, AIDS-related diseases, opportunistic infections and presence of coinfections developed along the care) are also requested. Administrative variables updates refer to PLWHA status in the health system (insured, disaffiliated, change of healthcare provider, i.e.) and the cost of HIV/AIDS care services (total costs of hospital care and total costs of non-hospital care). In addition, if the patient has died, the cause and date of death are recorded.

3. Software: Interconnection System and Health Information Exchange (SISCAC, in Spanish)

SISCAC is the platform set up by the CAC for healthcare insurers and their providers to upload their reports. It is implemented on SharePoint; storage is done in Structured Query Language and MongoDB databases as well as cognitive ser-

vices for artificial intelligence and Power BI are in the Azure cloud, which are Microsoft® services. This platform has a simple interface and can be adapted to the technological characteristics of each healthcare provider in the country. The portal offers notifications, system, and web services and two main menus: apps and microservices.

4. Data management

4.1. Data collection

Data from clinical records of the reporting populations (described above) is extracted by health care providers to the standardized registry files once a year and reported to the health insurers. These ones collect the data from different providers, review the data and fill the gaps according to the services supplied along the year. On the reporting dates, when data is considered complete, they upload the information into the SISCAC platform established by the CAC and run an automated validation mesh prior to sending the data.

4.2. Data validation

The platform contains an automatic validator mesh to check security, structure, consistency, and confidentiality of registered data. This validation is done at the time of reporting. Consolidated data is cross-checked by the CAC professionals with an official database of persons affiliated in the health system to verify the insurer and vital status of the reported patients. After this step, the data management coordinator approves the dataset to be audited.

4.3. Data auditing

As reporting is done based on medical records, this information is sent later to an auditing process, conducted by health professionals with experience in clinical auditing. They compared the database information against the clinical records. If the information reported is different from the available registers, an adjustment is requested based on the registers.

According to the findings, the information is classified in three groups: conforming data (CD) when reported information was the same found in medical records; non-conforming data (NCD) when reported information was different from the one registered on medical records, but adjustments can be done; and original data not available (ODNA), when the information is not found on clinical records. In the last case, the information is not taken into account for the analysis. This classification is considered in the rating process for health insurers.

4.4. Data analysis

After the auditing process, a single database is consolidated. Sometimes a patient could be reported by two insurers that had the patient at different times along the year or that provided different services. In those cases, the patient is counted only once for epidemiological indicators. Cases that died outside the period are excluded from analysis. Crude and standardized measures are estimated for the epidemiological indicators defined below. Numeric data are presented as medians and interquartile ranges (IQR) or media and standard deviation (SD) according with distributions. Category data sets are presented as frequencies and proportions.

HIV prevalent cases are all the ones reported in the period; HIV Incident cases are the ones that were diagnosed within the reporting period; and mortality cases are those reported by health insurers within the period and verified with external sources from the MHSP. Finally, 25 HIV risk management indicators are estimated to evaluate the quality of care provided by insurers and health care institutions. These indicators were chosen after a literature review and agreed by expert´s consensus[26].

4.5. Data dissemination and use

When information is ready, an annual report is prepared and published through the CAC´s website. Information is also presented through technical documents, research publications and conferences to HIV/AIDS partners in the country that can use it for knowledge management and decision-making at the local and national levels and for international reporting.

5. Distribution mechanism

With the results of the indicators, the CAC calculates an ex-post incentive mechanism for the contributive and subsidized insurers following the provisions of current regulations (Resolution 1912 of 2015 - MHSP[27]). This mechanism seeks to improve risk management of this disease and is based on four indicators: screening for HIV in pregnant women, early detection of PLWHA, undetectable viral load and HIV prevalence. Those healthcare insurers that achieve the highest results receive the resources established for the mechanism, while those that get the lowest results are the ones that deliver those resources.

6. Security and confidentiality

All records in the database are numbered with a unique identifier number to ensure data anonymization and the follow-up across the years. This database is stored on the SISCAC platform, which has strict controls for each user to ensure that only those who have authorization can access the information.

Figure 1 illustrates the complete process of building the national registry from data collection to data dissemination

Results

1. Epidemiological situation of the HIV/AIDS in Colombia, 2012-2019

From 2012 to 2019, the country has seen a 300% increase in the reported cases to the registry, going from 37,325 to 109,056. Prevalence increased from 0.09% to 0.22%. Mortality went up from 1.1 per 100,000 population to 3.6 per 100,000 population, and the incidence increased from 13.8 per 100,000 population to 21.9 per 100,000 population (Figure 2).

Data showed that in Colombia HIV affects men in a major proportion (75.8%) than women. The male/female ratio was 3.14:1. The mean age of diagnosis for men was 32.6 years (SD

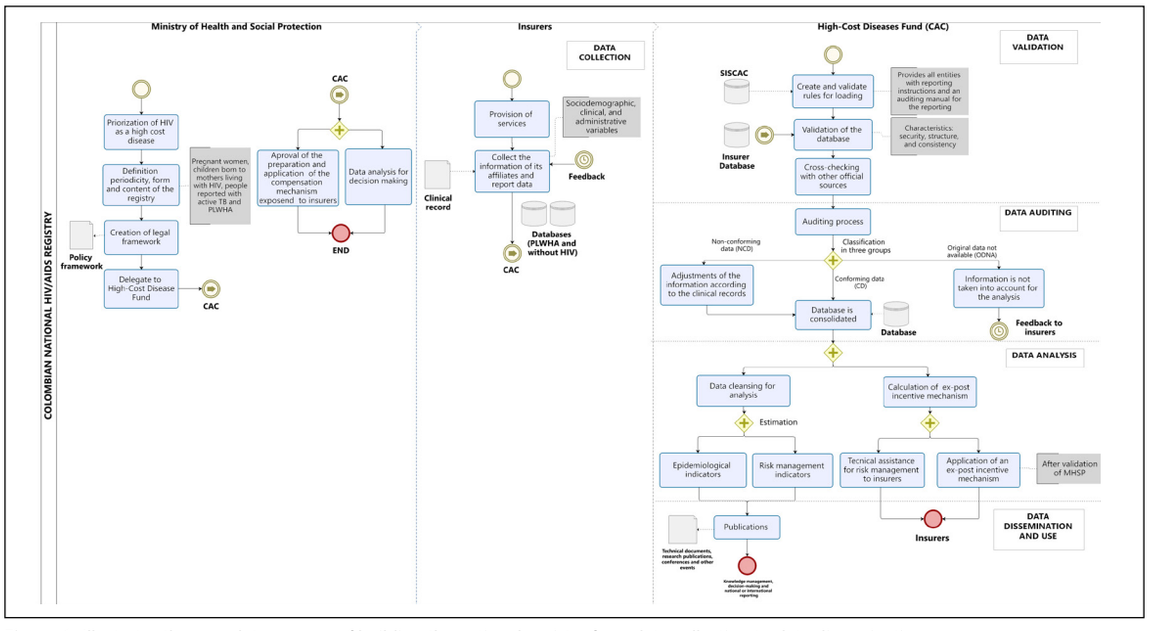

Figure 1. Illustrates the complete process of building the national registry from data collection to data dissemination.
Construction process of the HIV/AIDS national registry from the normativity of the MHSP until the publication of the information and use of data for decision-making. Abbreviations: MHSP: Ministry of Health and Social Protection, PLWHA: People living with HIV/AIDS, SISCAC: Interconnection system and health information exchange, TB: Tuberculosis.

±11.7) while in women was 36.1 years (SD ±13.5). The highest incidence and prevalence by geographical regions were observed in Bogotá, while the highest mortality was seen in the Caribbean and the Central regions (Figure 3). The main way of transmission was sexual (90.3% of cases) and 56.5% of all reported cases were diagnosed on stage 3 (AIDS) 2014 CDC´s classification[28], with AIDS wasting syndrome (13.7%) and TB (7.3%) being the most frequent opportunist infections.

Since 2019, data on key populations is being recorded, finding that 43.1% of new HIV infections in 2019 were diagnosed on men who have sex with men. The median lymphocyte count at diagnosis increased from 249 cells/µl (IQR 106-440) in 2012 to 329 cells/µl. (IQR 309–686) in 2019. The proportion of people with viral suppression (VL < 50 copies/ml) increased from 50.8 % in 2012 to 63.9% in 2019. This data is published annually at https://cuentadealtocosto.org/site/publicaciones/.

2. Risk management indicators

Over the 2012–2019 period, we have measured 25 national level indicators. 18 indicators have shown an increase in performance compared to the baseline (median 16.9%; IQR 1.7% - 26.5%). The biggest difference was seen with the indicators: proportion of HIV exposed children under 6 months tested for HIV (23.5% versus 98.0%), proportion of PLWHA with annual Tuberculin Skin Test (TST) (18.8% versus 61.4%), and proportion of PLWHA in latent tuberculosis therapy (14.6% versus 48.7%). Instead, two indicators saw a poorer perfor-

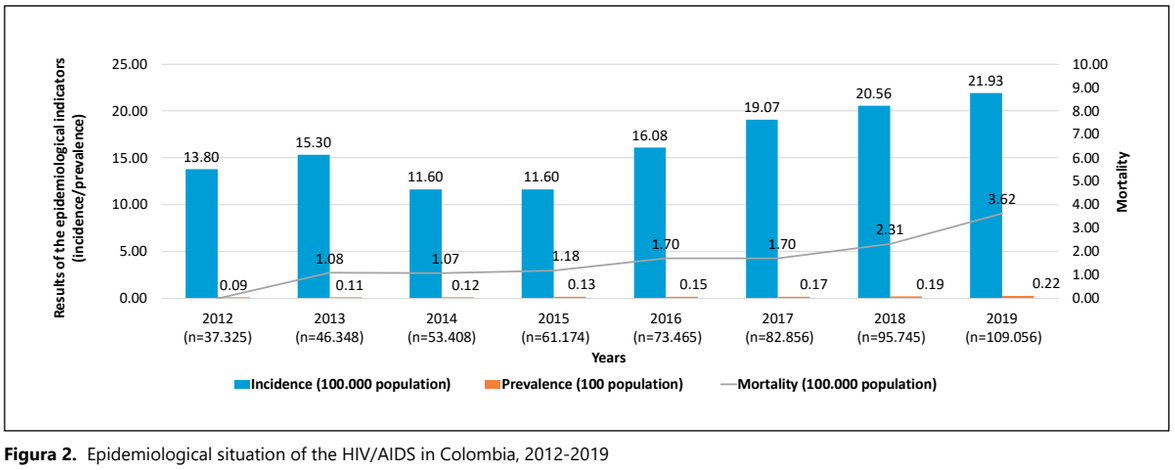

Figura 2. Epidemiological situation of the HIV/AIDS in Colombia, 2012-2019
Epidemiological indicators of the national HIV/AIDS registry in Colombia: incidence, prevalence and mortality from the beginning of the registry in 2012 up to the most recent measurement.

mance: Coverage of antiretroviral therapy in line with National Clinical Guidelines, decreasing 2.4%, and the proportion of PLWHA, not on antiretroviral therapy, with a CD4 count done in the reporting period, decreasing by 17.8%.

In 2019, 3 risk management indicators met the established target: proportion of HIV exposed children under 6 months tested for HIV (>95%), proportion of PLWHA on antiretroviral therapy with a viral load done in the reporting period (≥95) and the proportion of PLWHA with antiretroviral therapy switch (<30). Table 1 shows the results of the indicators since the establishment of the registry and the percentage difference between the baseline in 2012 and the last measurement in 2019.

Likewise, the Colombian registry has made possible to monitor Colombia's progress towards the UNAIDS 90-90-90 targets. Of the estimated 119,000 PLWHA that know their HIV status in 2019 (information given by the MHSP), 84,992 (71.4%) were on ART treatment, and 72,272 of them (85.0%) were virologically suppressed (<1,000 copies/ml).

3. Research

With the HIV/AIDS registry information, three scientific articles have been produced describing the situation of PLWHA in Colombia: "*Burden and magnitude of risk in HIV/AIDS in the Colombian health system: a real-world data approach*"[29], "*Epidemiological and clinical characterization in minors under 13 years living with HIV in Colombia. 2018: a cross-sectional study*"[30], and "*Survival in people living with HIV in the framework the Colombian health system: 2011-2018 in the pediatric population*[31]", which shows the multiples sub-analyses that can be done with the wide range of variables collected.

4. Distribution mechanism

Implementation of the ex-post incentive mechanism for the contributive and subsidized regimes have increased the performance of the insurers. This is reflected on the key four indicators that are evaluated: screening for HIV in pregnant women, which went up from 61.3% to 92.0%; early detection of PLWHA, that increased mildly from 57.4% to 58.0%; undetectable viral load, from 51.4% to 70.0%; and the HIV prevalence that increased from 0.09% to 0.22%. The best they perform the higher the amount they received. Extra resources are expected to be reinvested in strengthening the insurer´s HIV/AIDS programs.

Discussion

The main results of the National HIV/AIDS registry are: 1. Epidemiological information to follow trends of the HIV epidemic in Colombia; 2. Periodic measurement of risk management indicators; 3. Data for operational research; and 4. Information for an incentive distribution mechanism.

The registry shows the increase in reported HIV cases in the country and improvement of the main risk management indicators to reduce the burden of this disease. While, UNAIDS monitoring shows that since 2010, new HIV infections have

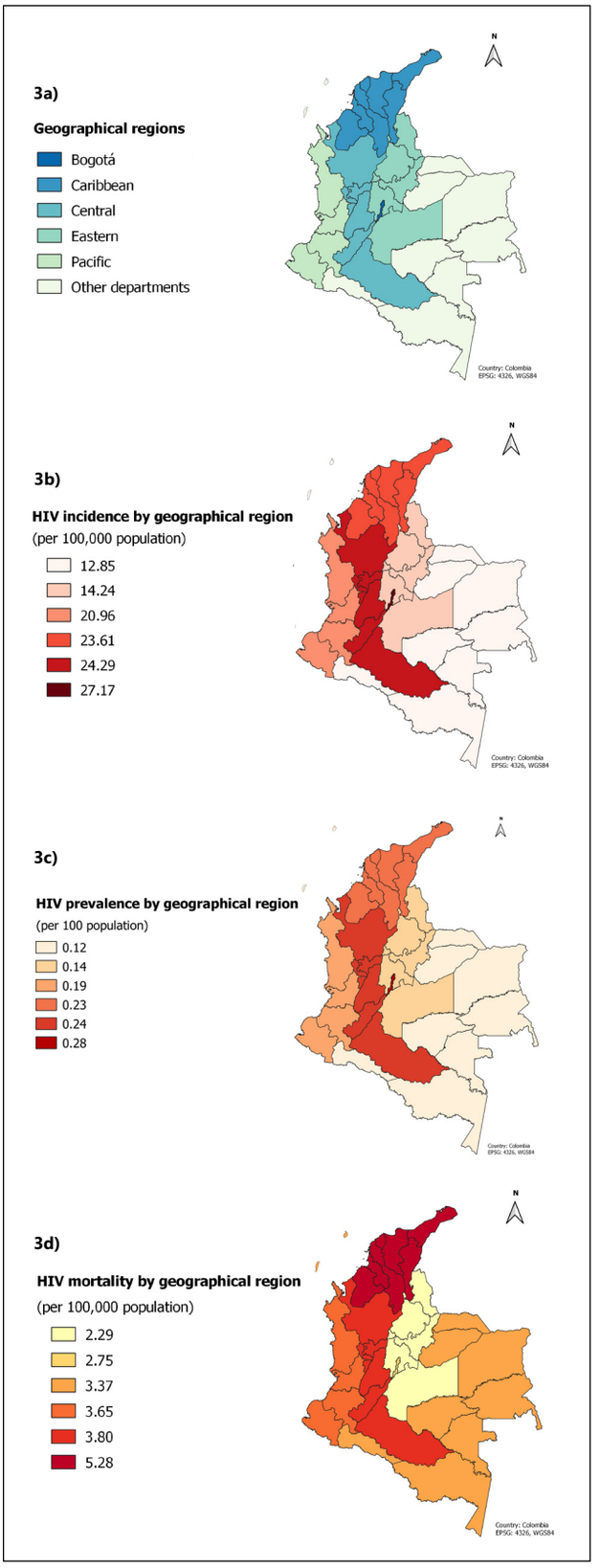

Figure 3. Age-standardized epidemiologic indicators of HIV/AIDS by geographical region.
Geographical region distribution (3a), age-standardized incidence (3b), age-standardized prevalence (3c) and age-standardized mortality (3d).

Table 1. Risk management indicators of Colombian HIV/AIDS Registry, 2012-2019

Indicators	Rank			Year of follow-up (%)								Difference between baseline and last measurement
	High	Medium	Low	2012	2013	2014	2015	2016	2017	2018	2019	
Proportion of pregnant women screened for HIV.	≥95	85 - 94.9	<85	61.3	86.2	70.5	78.9	85.5	89.0	91.0	92.0	30.7
Proportion of children under 6 months with postnatal prophylaxis for HIV.	100	*	<100	77.0	82.8	96.3	96.1	92.8	86.5	91.0	96.0	19.0
Proportion of HIV exposed children under 6 months tested for HIV.	≥95	85 - 94.9	<85	23.5	40.5	47.3	58.3	70.6	75.0	73.0	98.0	74.5
Coverage of antiretroviral therapy in line with National Clinical Guidelines.	≥95	85 - 94.9	<85	98.4	99.9	95.5	95.8	94.2	94.7	84.0	86.0	-12.4
Proportion of PLWHA, not on antiretroviral therapy, with a CD4 count done in the reporting period.	≥95	85 - 94.9	<85	67.8	84.4	55.7	54.1	53.1	44.7	58.0	50.0	-17.8
Proportion of PLWHA on antiretroviral therapy with a viral load done in the reporting period.	≥95	85 - 94.9	<85	*	86.7	63.6	79.3	86.7	85.9	88.0	95.0	8.3
Proportion of PLWHA with antiretroviral therapy and undetectable viral load.	>90	70 - 89.9	<70	*	*	*	51.4	57.5	66.8	68.0	70.0	18.6
Proportion of PLWHA with early diagnosis among incident cases.	≥95	85 - 94.9	<85	*	*	*	57.4	60.0	59.0	59.0	58.0	0.6
Proportion of PLWHA receiving expert medical assistance.	≥95	≥90 - <95	<90	*	*	93.3	94.0	92.9	93.3	92.9	94.3	0.3
Proportion of PLWHA with CD4 + T lymphocyte count at diagnosis.	≥95	≥90 - <95	<90	*	*	63.4	65.7	75.0	78.1	86.9	91.4	25.7
Proportion of PLWHA with a viral load result at diagnosis.	≥95	≥90 - <95	<90	*	*	*	*	*	*	*	87.8	**
Proportion of PLWHA with a total lymphocyte count at diagnosis.	≥95	≥90 - <95	<90	*	*	52.5	52.2	66.5	64.0	76.0	*	*
Proportion of PLWHA with annual Tuberculin Skin Test (TST).	≥80	≥50 - <80	<50	*	*	14.6	22.5	33.9	38.8	46.8	48.7	34.1
Proportion of PLWHA with follow-up of CD4 + T lymphocytes and viral load in the last 6 months.	≥95	≥90 - <95	<90	*	*	69.5	72.8	74.0	73.1	73.9	70.0	0.5
Proportion of PLWHA with annual syphilis screening.	≥95	≥90 - <95	<90	*	*	*	*	*	*	*	79.5	**
Proportion of PLWHA with annual cardiovascular risk assessment.	≥80	≥60 - <80	<60	*	*	*	*	*	*	*	61.6	**
Proportion of ART in pregnant women living with HIV.	100	≥95 - <100	<95	*	*	82.6	93.7	95.1	96.8	82.3	89.0	6.4
Proportion of PLWHA with adequate prescription of antiretroviral therapy.	≥95	≥90 - <95	<90	*	*	68.8	67.0	57.7	69.1	72.0	75.0	6.2
Proportion of PLWHA with active tuberculosis on simultaneous treatment for tuberculosis and HIV.	≥80	≥60 - <80	<60	*	*	54.4	80.6	87.3	76.2	70.2	75.8	21.4
Proportion of PLWHA with undetectable viral load after 48 weeks or more of antiretroviral therapy.	≥80	≥70 - <80	<70	*	*	50.1	55.0	61.2	63.1	64.4	79.0	28.9
Proportion of PLWHA on virological failure with a genotype study.	≥90	≥70 - <90	<70	*	*	*	*	*	*	*	28.1	**
Proportion of PLWHA with antiretroviral therapy switch.	<30	≥30 - <40	≥40	*	*	8.1	9.7	7.2	7.4	5.8	6.0	2.1
Proportion of PLWHA in latent tuberculosis therapy.	≥95	≥90 - <95	<90	*	*	12.8	18.0	27.8	28.6	28.7	61.4	48.6
Proportion of PLWHA with prophylaxis for Pneumocystis jirovecii pneumonia.	≥95	≥90 - <95	<90	*	*	43.2	50.0	56.4	61.7	66.8	68.8	25.6
Proportion of PLWHA with full hepatitis B vaccine schedule (if indicated).	≥95	≥90 - <95	<90	*	*	31.5	39.3	45.1	46.1	54.9	47.1	15.6

Abbreviations: PLWHA: Persons living with HIV/AIDS. * The indicator was not measured. ** It is not possible to calculate the difference.
Management risk indicators measured in Colombia from 2012.

decreased by about 31%[32], Colombia has seen an increase reported cases, probably due to the differences in these estimates[33] a better capture of cases by the health information system or major access the PLWHA to care services.

Our registry complies one of the key definitions set by the Agency for Healthcare Research and Quality (AHRQ)[3] as an organized system that uses observational methods to collect uniform data on a population defined by a particular disease (in this case HIV/AIDS), followed over time. The purpose of this registry is to describe the impact of the disease on patients' health, estimate the burden of the HIV/AIDS epidemic in the country and the trends over time. In a health care system with limited funds, AIDS care represents an important economic burden[34]. Therefore, HIV registries contribute to improving outcomes related to healthcare and managing resources efficiently[35]. This registry periodically publishes information available and accurate, avoiding expensive data collection to assess health system results, as indicated by Cylus J et al[36]. As data infrastructure grows and more suitable data becomes available, the necessity to transform the data into useful information emerges.

Mayer et al[4], in a systematic review of the literature, identified 13 HIV registries, of which 61.5% are the product of a collaboration policy and 53.8% have a management process for requesting data collaboration, although there are shortcomings related to ethical support and research data[5]. In comparison, our registry contains all the key features for data collection like criteria for inclusion of participants (case definitions, data elements collected, etc.) and support for data interoperability between the MHSP, the CAC, health insurers and health care providers.

We have a legal commitment, supported by an epidemiological team, to produce an annual report of the HIV/AIDS situation in the country and to propose ideas for future research. In this way, the information generated allows the monitoring of HIV case management and follow-up of global goals aimed at elimination of the pandemic[37], as demonstrated by Zheng et al[33], who indicates that National HIV registries are the starting point for this follow up as the requested information is available on the national system and easily accessible from the clinical records. Although, it can contain incomplete data, it can also be strengthened by routine record practices.

Our registry, that started with 37,325 cases reported, captured information from 109,056 PLWHA in 2019. This has allowed us to characterize this population and to provide a useful tool for public health making decisions in Colombia. Other registries have a variable number of PLWHA, like the Singapore one[33] with up to 5,000 PLWHA per year; The Swedish National HIV Registry[33] with 7,000 cases; Australia in the Kirby institute[38] reported 28,000 cases and close to 1,000 new cases per year. These registries are usually part of a wider national health information system. Other registries consolidate information from several countries to have a larger volume of information and to analyze the behavior of the disease between regions. This is the case of IeDEA registry[39], which consolidates and analyzes data on almost 2 million PLWHA under care in routine settings from 46 countries around the world, or the Global AIDS Monitoring (GAM) report of UNAIDS[40] which is a worldwide HIV monitoring and evaluation system.

The Colombian HIV/AIDS registry works as a complement to other sources of national information like The Public Health Surveillance System (SIVIGILA in Spanish)[41], which monitors case notification of diseases of public health interest like HIV, but doesn´t do follow up of linking to care, ART initiation or retention on care. In this way, the CAC registry and the SIVIGILA help to show different faces of the epidemic in the country.

Registry's strengths include data collection of priority groups for screening like pregnant women, children born to HIV-positive mothers and TB patients, with disaggregated data by geographic regions and municipalities. Self-reporting of PLWHA within key populations is also important to identify disease burden among smaller groups like MSM, transgender women or people who inject drugs. Other strength of the data collection process is the inclusion of health services planning information like affiliation, insurers, health care providers and costs, which have standardized definitions and labels for all elements of the dataset. This information also undergoes an auditing process and frequent feedback to the reporting entities.

Our estimates and analysis may be limited due to underreporting and missing data (estimated on 5%) not found in the medical records. In fact, we only rely on data reported in the medical records of persons affiliated to public or private health insurance regimes, with a coverage of 97.8% in Colombia[19]. However, as it is a high-cost disease, a low percentage of Colombians would probably look for care with out-of-pocket money. The percentage of PLWHA who are not affiliated to the health system and, therefore, are not reported in this registry, is unknown. This is the case for PLWHA assisted by non-governmental organizations that look after illegal migrants or vulnerable populations. Although the health insurers report all their affiliates, it´s possible that the cases lost to follow up (PLWHA without care in the last year) have outdated information, however this percentage is less than 2.0%. Other limitations are the heterogeneity in medical records among health providers (manual and/or digital) and practices of care in health programs. On the other hand, the process of auditing and analyzing the data highlight the need to continue strengthening the information system and move forward to reporting of HIV data in real time.

In conclusion, the Colombian HIV/AIDS registry has been useful not only for the clinical follow-up of patients but also to evaluate the quality of care provided by insurers and health institutions and for building public health policies based on evidence that aimed at PLWHA. Although different information sources in Colombia track HIV/AIDS at different points of care, the CAC registry consolidates the most significant number of variables that relate to the continuum of care. However, additional work is needed to integrate data from different sources and follow-up programs within the primary care to have a full comprehension of the HIV situation in the country. Finally, this exercise could be useful for other countries in the Latin American region that are interested in the development of specific disease follow-up registries.

Ethical disclosures

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Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this investigation.

Right to privacy and informed consent. The authors declare that no data that enables identification of the patients appears in this article.

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

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Factors associated with delays in time to treatment initiation in Colombian women with cervical cancer: A cross-sectional analysis

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Revista: Gynecologic Oncology Reports.

Alcance: Internacional.

Trabajo colaborativo con la Asociación Colombiana de Hematología y Oncología (ACHO) como actor de interés.

Objetivo:

Describir los factores asociados a las demoras para el inicio del tratamiento (TIT) en las mujeres colombianas con cáncer de cérvix durante el año 2018.

Principales hallazgos:

- Solo el 12% de las mujeres iniciaron el tratamiento en los 30 días posteriores al diagnóstico.
- La mediana global del TIT fue de 71 días, variando de 70 a 76 días en las mujeres tratadas con cirugía o quimioterapia, respectivamente.
- La edad, el aseguramiento, la región de residencia y el diagnóstico tardío se asociaron con una espera promedio para iniciar el tratamiento > 45 días.
- La metástasis en el momento del diagnóstico se asoció con atrasos en el TIT superiores a 45 días en el modelo multinomial.

Relevancia de los hallazgos:

- Para el conocimiento de los autores, este es el primer estudio enfocado en los factores asociados al TIT en los casos nuevos de cáncer de cérvix notificados en el contexto del aseguramiento en Colombia.
- Los hallazgos permiten identificar las brechas para el acceso oportuno al tratamiento del cáncer en el marco del escenario real de los servicios de atención sanitaria colombiana.
- Estos resultados son fundamentales para implementar intervenciones para reducir el impacto de las barreras para el tratamiento oportuno en los resultados en salud de esta población.

Comentario del autor experto:

Dr. Jaime Alberto González Díaz

El cáncer de cérvix continúa siendo una enfermedad prevenible que aún sigue generando alta mortalidad en Colombia, se investigaron los factores asociados a retraso en la terapia, situación que no debería existir una vez se hace un diagnóstico de cáncer y, por tanto, da información importante para diseñar modelos de atención eficientes que permitan disminuir mortalidad y morbilidad producto de dichos retrasos.

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Factors associated with delays in time to treatment initiation in Colombian women with cervical cancer: A cross-sectional analysis

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ABSTRACT

Cervical cancer (CC) is one of the leading causes of morbidity in upper-middle income countries such as Colombia. Several studies have reported poor prognosis when treatment is delayed. We aimed to describe the factors associated with delays in time to treatment initiation (TTI) in Colombian women with CC. Cross-sectional analysis including newly diagnosed cases of CC during 2018 and reported to the National Administrative Cancer Registry. TTI was defined as days from diagnosis to the first treatment (chemotherapy, radiation, or surgery). Linear and multinomial logistic regression models were estimated to analyze the association of interest. 1,249 new cases of CC were analyzed (26.98% *in-situ* and 40.11% locally advanced). The median age was 46 years (IQR: 36–58). Median TTI was 71 days (IQR: 42–105), varying from 70 days (IQR: 43–106) among the surgery group to 76 days (IQR: 41–118) in women under chemotherapy. Only 12.41% were treated within 30 days from diagnosis. TTI was significantly longer in women with state insurance ($\beta = 18.95$ days, 95% CI: 11.77–26.13) compared with those insured by the third payer. Women from the Pacific and Eastern regions also had a significantly longer TTI than those living in the capital of Colombia. Age, health insurance, region of residence, and stage at diagnosis were associated with TTI longer than 45 days in the multinomial model. We concluded that demographic variables (age, region of residence, and health insurance) which are proxies of social disparities and poor access to quality health care services, were associated with delays in TTI.

1. Background

Cervical cancer (CC) is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women worldwide. In 2018, there were an estimated 569,847 new cases of CC and 311,365 deaths from the disease worldwide. WHO has called for action for the elimination of CC as a public health problem especially in low and middle Human Development Index (HDI) countries, where it is the second most common cancer, affecting significantly countries on the African continent, especially in sub-Saharan Africa, South-Eastern Asia, and Latin America and the Caribbean, while in countries with high HDI values, incidence and mortality rates are declining (WHO larc, 2018; Wild et al., 2020). However, even within countries, differences due to socioeconomic or racial disparities in disease burden and mortality have been observed, as in the United States, a country with a high HDI, where CC incidence and mortality among African American women is twice than in white women. These disparities are explained by the presence of inequalities in access to primary prevention, screening, and treatment services. Geographic location can also play a role. Women living in rural areas have the lowest screening rates and the highest incidence rates of CC in both, low and high HDI countries. It is known that women in countries and areas with lower HDIs are currently the least likely to have

Abbreviations: HDI, Human Development Index; GLOBOCAN, The Global Cancer Observatory; NACR, National Administrative Cancer Registry; CAC, Cuenta de Alto Costo (High Cost Diseases Fund); DANE, Departamento Administrativo Nacional de Estadística (Department for National Statistics); IQR, Interquartile range.

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access to or complete doses of HPV vaccine (Wild et al., 2020).

Delays in accessing timely and appropriate treatment are among the various conditions that result in poor prognosis (Ferreira da Silva et al., 2019; Ramey et al., 2018; Perri et al., 2014). Treatment of CC usually consists of chemoradiation or radical hysterectomy/trachelectomy with lymph node dissection in early stages and chemoradiation in advanced stages. Treatment may be adjusted according to the patient's health conditions, age, desire for parity, or comorbidities (Ferreira da Silva et al., 2019). Delays in access to treatment are given for different reasons such as second medical or pathological opinions, or geographical, administrative, economic, or cultural barriers, substantially affect the living conditions of women with this disease because time intervals are important to ensure the effectiveness of treatment (Ferreira da Silva et al., 2019; Chen et al., 2019). Delays of more than three months in therapeutic cancer care could decrease the prognosis and increase morbidity, reduction of survival is a subject of discussion due to differences in the results of several studies (Ferreira da Silva et al., 2019; Ramey et al., 2018; Perri et al., 2014), though, analyses of delay of treatment for women with CC have been more limited in scope (Ramey et al., 2018).

In Colombia, despite the progress made in the country and the high health coverage that exists, it is not unrelated to the situation mentioned above; it is a disease that continues to have a great impact on morbidity and mortality and is also the second most common type of cancer among women in the country. Further, according to The Global Cancer Observatory (GLOBOCAN), by 2018 CC was the sixth cause of cancer-related death in Colombia (GLOBOCAN, 2018).

The High Cost Diseases Fund (CAC, by its acronym in Spanish) is the entity responsible in the country for managing the National Administrative Cancer Registry (NACR), based on the information provided mainly by health insurers, as well as a small proportion of the uninsured population, which annually monitors the situation of CC, including the time that elapses once the diagnosis has been confirmed until treatment for CC begins. Therefore, we aimed to describe the associated factors to delays in time to treatment initiation (TTI) in Colombian women with CC during 2018.

2. Methods

2.1. Data sources

We performed a cross-sectional analysis using data provided by the NACR managed by the CAC. The NACR was established in 2012 by the Ministry of Health of Colombia (Ministry of Health and Social Protection R of C. Resolution 4496, 2012) to evaluate the demographic, clinical, and administrative situation of people with cancer through the annual report of 134 variables. It is an administrative and passive registry with a national scope due to the fact of ~97% of the Colombian population is insured to the national health system (Ministry of Health and Social Protection R of C. Health insurance coverage in Colombia [Internet]., 2020) and must be reported to the NACR by its health insurers (Ministry of Health and Social Protection R of C. Resolution 4496, 2012). Taking into account the above, it provides reliable information about real-life patterns of cancer distribution and risk management across the country.

Since its first measurement in 2015, 279,155 people with cancer have been reported. Each record is identified with a unique code to protect the personal information of the participants and allow the follow-up within the cohort. Data on prevalent cases are updated every year, while for new cases, full registration is completed.

On the other hand, the quality of the information was assured by a well-established data monitoring process, which was carried out in two steps: a prior identification of mistakes in the reporting process through a systematized algorithm, and once the structure and consistency of the variables were approved, the information was audited and compared with the health clinical records. All newly diagnosed and those previously diagnosed who were treated during the period were audited, otherwise, if they did not receive any treatment a random sample was taken.

2.2. Eligibility of participants

All women newly diagnosed with CC (International Classification of Diseases code 10 (ICD-10): C53 to D06) and reported to the NACR from January 2, 2018, to January 1, 2019, were eligible. CC diagnosis could be clinical or histopathological and it was confirmed by the data monitoring process previously described. A total of 1,930 new cases of CC were identified. Of these, 681 (35.28%) were excluded: 619 had no information about treatment (people diagnosed close to the cut-off date or the data was not available on clinical records) and 62 received palliative treatment rather than with curative purposes. Thus, the studied population included 1,249 women with CC.

2.3. Dependent variable

TTI was calculated from the date of diagnosis (clinical or histopathological) to the date of surgery, chemotherapy, or radiation. To establish the diagnosis, the date of the pathology report was considered as the first option, when it was not available, the date in which the physician made the clinical diagnosis and defined the treatment was used. TTI was analyzed both, as a continuous variable and as a categorical variable based on the literature: 30 days or less, 31–45 days and, more than 45 days (Perri et al., 2014).

2.4. Demographic and clinical variables

Demographic information included age, ethnicity, geographical region of residence, and health insurance. Regarding ethnicity, we used a proxy that classified women in indigenous, Romanis, blacks, or whites from the self-designation. Geographical regions were defined by the Department for National Statistics (DANE, by its acronym in Spanish), from Colombia's 32 departments according to the gross domestic product, identifying 6 regions: Bogotá C.D., Central, Eastern, Pacific, Caribbean, and Other departments (Fig. S1 of Supplementary Material). Moreover, health insurance was classified according to the funding source as follows: third payer, state insurance, especial and exception insurance and, a minimum proportion as uninsured. For this analysis, we reclassified the variable as third payer, state insurance, and other.

In respect of clinical data, the stage at diagnosis (0, I, II, III, and IV) was classified based on the revised 2018 International Federation of Gynecology and Obstetrics (FIGO) system (Bhatla et al., 2018) and then were grouped as *in-situ* (0), local early stages/bulky (stages IA1 to IIA2), locally advanced (stages IIB2-IIIA) and metastatic (IIIB-IVB) (Marth et al., 2017). Histology was grouped as squamous carcinoma, adenocarcinoma/adenosquamous carcinoma, and no specified (Ferreira da Silva et al., 2019; Perri et al., 2014). Finally, treatment was grouped as surgery, radiation, or chemotherapy.

2.5. Statistical analysis

We performed a descriptive analysis summarizing continuous variables as medians and interquartile range (IQR) and categorical variables as absolute values and percentages. The differences in demographic and clinical variables according to the wait-time groups were evaluated using the Kruskal-Wallis test and X^2 test for continuous and categorical data, respectively. Associated factors were evaluated through both, bivariate and multivariate linear or multinomial logistic regression models, depending on the outcome (continuous or categorical, respectively). In the case of multinomial models, TTI $\leq$ 30 days was considered the reference category. Variables with less than 0.200 *p*-value, in the bivariate analysis, as well as those we considered important according to the directed acyclic graph method and the literature review were retained in the final models. R squared and Hosmer and Lemeshow tests

were used to verify the goodness of fit of linear and multinomial models, respectively. Adjusted coefficients (β) and odds ratio (OR) and their 95% confidence intervals were reported to determine the magnitude and direction of associations between covariates and the TTI. We also performed a sensitivity analysis excluding women diagnosed as *in-situ* to verify the consistency of our findings. *p*-values <0.05 (two-tailed) were considered statistically significant and all statistical analyses were performed in Stata version 13 (StataCorp LP, College Station, Texas, USA).

3. Results

3.1. Demographic and clinical characteristics of participants

A total of 1,249 women newly diagnosed with CC were analyzed. Demographic and clinical variables for all women as well as comparing by wait-time groups are presented in Table 1. The median age was 46 years (IQR: 36–58). Most women (94.16%) were self-identified as white, 50.04% belonged to the state insurance and 25.62% lived in the Central region followed by Bogotá, C.D. (21.86%). Regards clinical characteristics, 40.11%, and 27.86% were diagnosed in advanced and early stages, respectively. About 27.00% were classified as *in-situ* tumors and 56.20% were squamous cell carcinoma. The most frequent treatment was surgery (47.16%) followed by radiation (42.43%). The median TTI was 71 days (IQR: 42–105), varying from 70 days (IQR: 43–106) among the surgery group to 76 days (IQR: 41–118) in those women under chemotherapy. Only 12.41% were treated within 30 days from diagnosis. The shorter TTI according to the stage at diagnosis was observed in women with metastasis (median: 34 days, IQR: 19–58).

When comparing by wait-time groups, we found statistically significant differences in age, health insurance, stage at diagnosis, and type of treatment distribution. Also, by using the suitable hypothesis tests, women in the lowest TTI group, were slightly older, affiliated to the state insurance, diagnosed in advanced stages, and treated with surgery than those with the longest TTI (Table 1).

3.2. Factors associated with TTI (continuous outcome)

Age, health insurance, and region of residence were associated with the TTI in the multivariate linear regression model. TTI was significantly longer in women living in the Pacific region (β = 11.82 days, 95% CI: 1.48–22.16, $p = 0.025$), compared to Bogotá, the capital of Colombia. The same association was observed for women living in the Eastern region (β = 11.72 days, 95% CI: 0.11–23.34, $p = 0.048$). Furthermore, receiving attention under the state insurance was associated with a significantly longer TTI than those insured by the third payer (β = 18.95 days, 95% CI: 11.77–26.13, $p < 0.001$). On the other hand, age was associated with a slight but significant decrease in the TTI (β = 0.25 days, 95% CI: 0.01–0.48, $p < 0.039$) (see Table 2).

3.3. Factors associated with delays in TTI (categorical outcome)

In the final multinomial logistic regression model, age, health insurance, region of residence, and stage at diagnosis were significantly associated with a TTI longer than 45 days. We found that compared to women affiliated to the third payer insurer, those with state insurance had a significantly higher odds of delay in TTI (more than 45 days) relative to women who had a timely treatment (OR = 2.46, 95% CI: 1.59, 3.80, $p < 0.001$). Regarding region of residence, living in the Caribbean region rather than Bogotá was associated with a significant decrease of 59% in odds of having delays in TTI related to those who received a timely treatment (OR = 0.41, 95% CI: 0.23, 0.74, $p = 0.003$). Finally, we found a strong, negative, and significant association between metastasis at diagnosis and delays in TTI, related to women who were treated opportunely (OR = 0.10, 95% CI: 0.01, 0.86, $p = 0.036$) (see Table 3).

Fig. 1 shows the predicted probabilities of receiving treatment for each wait-time group, according to health insurance. As we previously mentioned, women under state insurance were above 80% more likely to receive the first treatment after an average of 45 days, compared with those affiliated to the third payer (~70%).

Finally, we repeated the analysis excluding women diagnosed with *in-situ* tumors, and important differences in the direction, magnitude, and statistical significance of the associations were not observed.

Table 1
Demographic and clinical characteristics of women newly diagnosed with cervical cancer by time to treatment initiation groups, Colombia 2018.

Variable[1]	Total (n = 1,249)	Time to treatment initiation			*p*-value[2]
		≤30 days (n = 155)	31–45 days (n = 140)	>45 days (n = 954)	
Age (years)	46 (36–58)	43 (34–54)	49 (36–63)	46 (37–57)	**0.004**
Ethnicity					0.199
White	1,176 (94.16)	147 (94.84)	130 (92.86)	899 (94.23)	
Indigenous	45 (3.60)	3 (1.93)	4 (2.86)	38 (3.99)	
Black	28 (2.24)	5 (3.23)	6 (4.28)	17 (1.78)	
Health insurance					**0.017**
State insurance	625 (50.04)	59 (38.06)	65 (46.43)	501 (52.52)	
Third payer	593 (47.48)	91 (58.71)	71 (50.71)	431 (45.18)	
Other	31 (2.48)	5 (3.23)	4 (2.86)	22 (2.30)	
Region of residence					0.168
Central	320 (25.62)	36 (23.23)	42 (30.00)	242 (25.37)	
Bogotá, C.D.	273 (21.86)	36 (23.23)	26 (18.57)	211 (22.12)	
Caribbean	245 (19.62)	41 (26.45)	33 (23.57)	171 (17.92)	
Pacific	232 (18.57)	21 (13.55)	20 (14.29)	191 (20.02)	
Eastern	139 (11.13)	18 (11.61)	15 (10.71)	106 (11.11)	
Other	40 (3.20)	3 (1.93)	4 (2.86)	33 (3.46)	
Stage at diagnosis					**0.044**
In-situ	337 (26.98)	34 (21.94)	27 (19.29)	276 (28.93)	
Local early/bulky	348 (27.86)	40 (25.81)	42 (30.00)	266 (27.88)	
Locally advanced	501 (40.11)	69 (44.52)	66 (47.14)	366 (38.36)	
Metastatic	5 (0.41)	2 (1.29)	1 (0.71)	2 (0.22)	
Unknown	58 (4.64)	10 (6.44)	4 (2.86)	44 (4.61)	
Histology					0.604
Squamous cell carcinoma	702 (56.20)	88 (56.77)	86 (61.43)	528 (55.35)	
Adenocarcinoma	204 (16.33)	24 (15.48)	21 (15.00)	159 (16.67)	
Other	330 (26.42)	42 (27.10)	30 (21.43)	258 (27.04)	
Unknown	13 (1.05)	1 (0.65)	3 (2.14)	9 (0.94)	
First treatment					**0.039**
Surgery	589 (47.16)	66 (42.58)	51 (36.43)	472 (49.48)	
Radiation	530 (42.43)	71 (45.81)	70 (50.00)	389 (40.78)	
Chemotherapy	130 (10.41)	18 (11.61)	19 (13.57)	93 (9.74)	

[1] Values are absolute values (percentages) or medians (IQR).
[2] Proportions were compared by a X^2 test and Kruskal-Wallis test was used for continuous variables.

4. Discussion

To the best of our knowledge, this is the first study focused on identifying factors associated with TTI in women newly diagnosed with

Table 2
Crude and multivariate-adjusted average changes in time to treatment initiation in women newly diagnosed with cervical cancer, Colombia 2018.

Variable[1]	Crude β (95% CI)	Adjusted[1] β (95% CI)
Age (years)	0.22 (−0.01, 0.44)	**0.25 (0.01, 0.48)**
Ethnicity		
Indigenous	Ref.	Ref.
White	−19.05 (−34.87, −3.23)	−7.89 (−23.75, 7.95)
Black	−14.04 (38.71, 10.64)	−2.72 (−27.42, 21.97)
Health insurance		
Third payer	Ref.	Ref.
State insurance	18.66 (12.48, 24.84)	**18.95 (11.77, 26.13)**
Other	−11.91 (−33.27, 9.45)	−11.25 (−32.78, 10.29)
Region of residence		
Bogotá, C.D.	Ref.	Ref.
Central	1.06 (−8.19, 10.31)	−1.08 (−10.47, 8.31)
Caribbean	4.74 (−4.89, 14.37)	−6.40 (−16.92, 4.13)
Pacific	19.78 (9.76, 29.78)	**11.82 (1.48, 22.16)**
Eastern	13.04 (1.36, 24.73)	**11.72 (0.11, 23.34)**
Other	25.30 (6.86, 43.74)	16.31 (−2.34, 34.97)
Stage at diagnosis		
In-situ	Ref.	Ref.
Local early/bulky	0.27 (−8.61, 9.15)	4.91 (−4.45, 14.27)
Locally advanced	−0.36 (−8.54, 7.81)	−1.12 (−12.41, 10.17)
Metastatic	−44.43 (−90.45, 1.59)	−39.74 (−85.49, 6.01)
Unknown	2.13 (−13.77, 18.03)	0.65 (−15.99, 17.29)
First treatment		
Chemotherapy	Ref.	Ref.
Surgery	−7.58 (−17.83, 2.66)	−2.41 (−14.81, 9.99)
Radiation	−10.51 (−20.59, −0.43)	−8.46 (−18.49, 1.57)

[1] Final model was adjusted by age (continuous), ethnicity (categorical), health insurance (categorical), region of residence (categorical), stage at diagnosis (categorical) and first treatment (categorical).

Table 3
Multivariate-adjusted odds ratio for wait-time groups in women newly diagnosed with cervical cancer, Colombia 2018.

Variable[1]	Adjusted OR (95% CI) [1]	
	TTI 31–45 days	TTI > 45 days
Age (years)	**1.03 (1.01, 1.05)**	**1.03 (1.01, 1.04)**
Health insurance		
Third payer	Ref.	Ref.
State insurance	1.50 (0.85, 2.64)	**2.46 (1.59, 3.80)**
Other	1.05 (0.26, 4.32)	1.02 (0.35, 2.93)
Region of residence		
Bogotá, C.D.	Ref.	Ref.
Central	1.41 (0.70, 2.84)	0.98 (0.58, 1.66)
Caribbean	0.67 (0.30, 1.49)	**0.41 (0.23, 0.74)**
Pacific	1.01 (0.44, 2.34)	0.99 (0.54, 1.83)
Eastern	1.16 (0.49, 2.76)	0.98 (0.52, 1.84)
Other	1.35 (0.26, 6.84)	1.14 (0.32, 4.09)
Stage at diagnosis		
In-situ	Ref.	Ref.
Local early/bulky	1.06 (0.51, 2.19)	0.87 (0.51, 1.49)
Locally advanced	0.69 (0.28, 1.65)	1.21 (0.62, 2.39)
Metastatic	0.31 (0.02, 4.14)	**0.10 (0.01, 0.86)**
Unknown	0.34 (0.09, 1.32)	0.49 (0.20, 1.15)
First treatment		
Chemotherapy	Ref.	Ref.
Surgery	0.65 (0.25, 1.69)	1.26 (0.60, 2.63)
Radiation	0.83 (0.39, 1.76)	1.07 (0.59, 1.93)

[1] Final model was adjusted by age (continuous), health insurance (categorical), region of residence (categorical), stage at diagnosis (categorical) and first treatment (categorical). Wait-time category of reference was TTI $\leq$ 30 days which is considered timely.

CC conducted in Colombia. The overall median TTI was 71 days, varying from 70 to 76 days in those who were treated with surgery or chemotherapy, respectively. Demographic variables (age, region of residence, and health insurance) which are proxies of social disparities and poor access to quality health care services, were associated with TTI in both linear and multinomial models. Regarding clinical characteristics, metastasis at diagnosis was associated with delays in TTI longer than 45 days in the multinomial model.

Our findings point out that less than 15% of the study population was treated within 30 days from diagnosis. The above represents a concerning scenario due to evidence suggests that delays in TTI have been associated with poor prognosis and worse survival (Chen et al., 2019; Choan et al., 2005; Nascimento and Azevedo e Silva, 2015) and their negative impact could be higher in low-middle income countries where research studies about this topic are also limited.

The median TTI estimated in our study was more than double the goal established in the protocol for public health surveillance and risk control of breast and cervical cancers in Colombia that is less than 30 days (Jimenez Herrera, 2018). This protocol was proposed within the framework of the 10-year cancer control plan to decrease cancer burden through early detection, treatment, rehabilitation, and palliation by reducing health disparities in access and treatment (Sardi et al., 2019). Despite the above, our results suggest that targeted interventions are required to guarantee a timeless treatment and prevent gaps in care from widening over time.

When comparing the median TTI we found, it was lower than the estimated in Brazil (114 days) (Ferreira da Silva et al., 2019) and Taiwan (Chen et al., 2019), but longer than the observed in Israel (Perri et al., 2014). Regards factors associated with delays in TTI, the evidence is limited. We identified demographic variables (age, region of residence, and health insurance) as the main predictors for TTI in Colombian women with CC. A strong direct and statistically significant association was found in women affiliated to state insurance when the outcome was analyzed as a continuous or categorical variable. However, in Taiwanese women with CC, health insurance was not associated with delays in TTI (Shen et al., 2016). In other contexts and types of cancer, such as breast cancer, there have been identified that women with public or no insurance and with low socioeconomic status tend to have longer treatment delay (Ramey et al., 2018; Smith et al., 2013; Ashing-Giwa and Rosales, 2013).

Delays in TTI observed in women with state insurance in Colombia are the result of a fragmented administrative health care system, which exhibits wider gaps in people with insurance subsidized by the government. It has been identified as the most significant barrier for an effective access to cancer diagnosis and treatment in the country (Sardi et al., 2019). Further, health insurance is a proxy of socioeconomic conditions, and it is well known that lower socioeconomic status contributes to and exacerbates healthcare problems and explains the wide variation in cancer access in the Americas and within the countries (Gribble et al., 1993).

Consistent with the above, the linear regression model showed strong, positive, and statistically significant associations between Pacific and Eastern regions with longer treatment delay. Taking into account that Colombian regions are grouped based on the gross domestic product, they are a proxy of social and economic development. In fact, in those regions, there are a limited number of centers and trained personnel and, usually, people have to be transfered to more specialized centers, mainly located in the center or north of the country.

In respect of age, our findings are consistent with the estimated in women with CC from Brazil (Ferreira da Silva et al., 2019) and Taiwan (Shen et al., 2016), where a direct association was observed. Comparable associations have been identified in previous studies concluding that the rate of treatment refusal increases with age (Jassem et al., 2014; Germann et al., 2005; Ward et al., 2013).

Despite we found differences in staging at diagnosis by wait-time groups, they were no longer significant when adjusting for potential

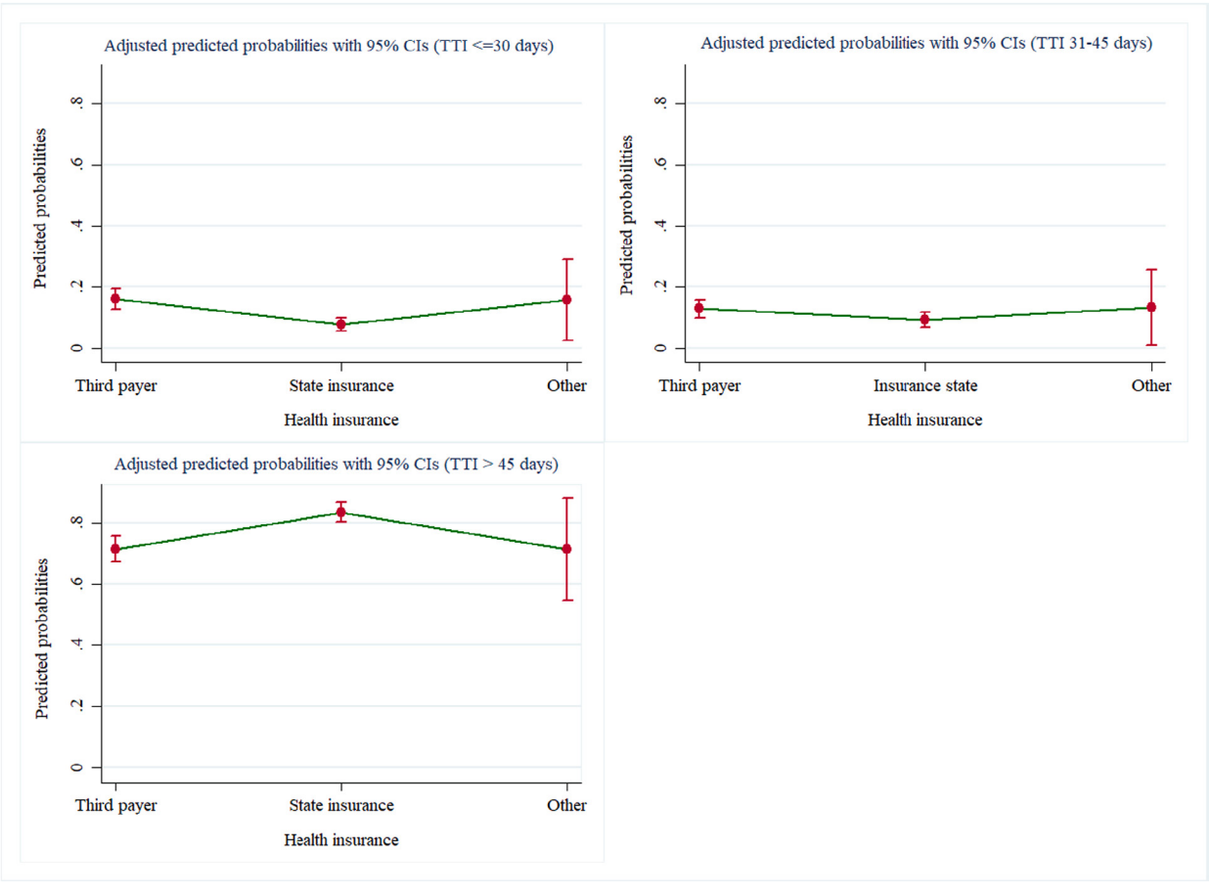

Fig. 1. Predicted probabilities of being in a wait-time group by health insurance in women newly diagnosed with cervical cancer, Colombia 2018. Predicted probabilities were estimated after the final multinomial logistic regression model for each wait-time group, according to health insurance. Predicted probability of having a time to treatment initiation longer than 45 days was higher in those women affiliated to the state insurance compared to those under the third payer o other insurance.

predictors, except for metastasis at diagnosis which was negatively associated with TTI longer than 45 days, related to TTI less than 30 days. Evidence from published studies has highlighted variables such as stage at diagnosis and treatment protocol as predictors for treatment delay (Ferreira da Silva et al., 2019; Shen et al., 2016). Shen et al. (2016) identified that the odds of treatment delay significantly increased with the increasingly advanced cancer stage. Otherwise, the evidence is inconsistent and some studies have found earlier stage was associated with longer TTI (Ramey et al., 2018). According to that, our findings did not show a homogeneous pattern across the stages of diagnosis.

When comparing the different types of treatment contemplated (surgery, chemotherapy, or radiotherapy), none was associated with longer TTIs than the other, taking into account that treatment depends on the stage of the disease. Similar findings are mentioned in the Brazilian publication, in which the median time from diagnosis to treatment initiation presented no significant variation according to the type of first treatment (surgery or radiation), although, the prevalence of treatment delay was greater than 80% in the surgery/radiation group. Likewise, the chemoradiotherapy protocol group had a higher probability of treatment delay than those treated with surgery alone or surgery plus radiation (Ferreira da Silva et al., 2019).

It is important to mention that treatment protocols may include one or more types of therapy and even different technologies which may shorten or lengthen times, an example of this is the study conducted in the United States which found that chemotherapy plus radiotherapy presented shorter times than radiotherapy alone, and in terms of techniques, intensity-modulated radiation therapy (IMRT) was associated with an increase in TTI versus non-IMRT (Ramey et al., 2018).

It is necessary to continue with similar studies that deepen in the different unique treatments or concurrent, as well as the inclusion of the various technologies available.

4.1. Strengths and limitations

The current analysis has important strengths, including the large completeness of the NACR, which guarantees the external validity and utility of our findings in the decision-making process at national and regional levels. This fact provides a unique opportunity to translate our findings directly into practice. Also, to our knowledge, it is the first approach to identify factors related to TTI in women with CC in Colombia using national data provided by health care insurers and providers, which allow the stakeholders to identify the gaps for effective cancer access and treatment within the framework of the real scenario of health care services. Furthermore, the accuracy and quality of the information of all new cases were verified by a data monitoring process.

On the other hand, considering that information was recorded for administrative purposes mainly, some limitations must be addressed. First, the passive case reporting by the health insurers could lead to under-reporting. In any case, it would be a small proportion because the reporting process is mandatory. The above means that the NACR data is

not collected directly from the patient or clinician; instead, it is reported by the insurers and later confirmed in medical records or other administrative sources (pharmacy, billing, and national databases). The cross-sectional nature of the analysis does not allow establishing the causality of the associations. Moreover, we lacked information about the socio-economic profile, lifestyle, comorbidities, as well as installed capacity of health services, instead, we included the best proxies available in the final models. Finally, information bias cannot be ruled out because clinical records are the primary data source and they may be subject to error.

4.2. Conclusions

Among women with a newly confirmed diagnosis of CC, treated within the framework of the Colombian health system we found a median TTI of 71 days and less than 15% had the first treatment within 30 days from diagnosis. Demographic variables (age, living in the Pacific or Eastern regions, and state insurance) which are proxies of social disparities and poor access to quality health care services, were positively associated with delays in TTI in our study population. These findings have public health relevance in providing an initial approach to identify gaps in cancer treatment access and their variability by region and health insurance. Our results should be confirmed by using longitudinal analysis, including variables related to sociodemographic, lifestyle, and healthcare access conditions instead of proxies.

Ethics approval and consent to participate

Because the present analysis was performed with secondary data sources, it has no risk for participants and informed consent or ethics approval was not required. 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 which stated that due the nature of the NACR and its direct regulation by the state, an ethics approval was not necessary. 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.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due they are owned and managed by the Colombian health system but are available from the corresponding author on reasonable request.

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The study had no sources of funding.

Authors contributions

LA and AMV had the research idea. Analyses were performed by JAHV. The first draft of the manuscript was written by JAHV and PXRB. JAG wrote about the clinical aspects to support the discussion. All authors reviewed the final version.

This article is an original research work and all authors have seen and approved the final version of the manuscript. We declare that it hasn't been published before, as well as not being considered for publication in a different journal.

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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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2021.100697.

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CÁNCER

National Cancer Information System Within the Framework of Health Insurance in Colombia: A Real-World Data Approach to Evaluate Access to Cancer Care

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Alcance: Internacional.

Trabajo colaborativo con la Asociación Colombiana de Hematología y Oncología (ACHO) como actor de interés y con la Universidad de Miami, como representante internacional de la academia.

Objetivo:

Describir la metodología y el alcance del Sistema de Información Nacional de Cáncer (SINC), centrándose en los resultados en términos de acceso a la atención en salud a través de la medición de indicadores de gestión del riesgo.

Principales hallazgos:

- Los casos prevalentes de cáncer invasivo notificados en el contexto del aseguramiento colombiano han aumentado de 163.776 en el 2015 a 331.021 en el 2020 (incremento del 102,12%).
- Los indicadores relacionados con el tiempo hasta el diagnóstico y el tratamiento no han alcanzado las metas establecidas en los consensos en el cáncer de mama, de cuello uterino y de próstata.
- En el caso de los tumores de estómago y de colon y recto, el cumplimiento es mayor, aunque sin alcanzar el nivel máximo de cumplimiento.
- El diagnóstico temprano y la oportunidad en el diagnóstico y el tratamiento son factores que siguen representando un reto para las en la atención sanitaria en el marco del aseguramiento colombiano.

Relevancia de los hallazgos:

- El SINC proporciona datos en tiempo real para mejorar la gestión del riesgo y disminuir la carga del cáncer en Colombia a partir de la información reportada en el marco del aseguramiento.
- Permite la identificación de brechas en el acceso a la atención oncológica y contribuye a la generación de intervenciones conjuntas para su mitigación.
- Contribuye a la estabilidad financiera del sistema sanitario a través del mecanismo de redistribución de recursos basado en los resultados en salud.

Comentario del autor experto:

Dr. Jaime Alberto González Díaz

Compartir con la comunidad científica de oncología desde el *Journal Global Oncology* lo que ha logrado en Colombia la Cuenta de Alto Costo en el registro administrativo nacional de cáncer (NCIS) es muy satisfactorio, ya que, para médicos y administradores en salud en países de ingresos medios o bajos, se convierte en un referente y para Colombia se constituye en una fuente de información para la correcta toma de decisiones de política pública en salud.

HEALTH SERVICES RESEARCH

National Cancer Information System Within the Framework of Health Insurance in Colombia: A Real-World Data Approach to Evaluate Access to Cancer Care

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original reports abstract

PURPOSE The National Cancer Information System (NCIS) has been operating since 2014, including information reported by health care insurers and providers on people with cancer diagnosed and treated within the Colombian health system. Its main purpose is to identify barriers to an effective access to cancer diagnosis and treatment across the country. We aimed to describe the methodology, scope and results in terms of access to health services with real-world data provided by the NCIS.

METHODS Reporting of all cases of cancer by insurers and providers is mandatory by law. Data gathered include demographic and clinical information about new and old cases of cancer who receive health services. Over the years, the reporting process has been automated and it is currently performed in real time. Data quality is ensured through a standardized data-monitoring process. Access to health services is monitored by quality measures defined by consensus.

RESULTS Since 2015, prevalent cases of invasive cancer have increased from 163,776 to 331,021 in 2020 (increment of 102.12%). Regarding quality measures, the proportion of people staged at diagnosis has increased over the years, especially in breast cancer. Meanwhile, early diagnosis is still concerning for breast and prostate cancer. Time to diagnosis and treatment have not consistently reached the expected goals in breast, cervical, and prostate cancer, whereas they have shown a better level of compliance for stomach and colon and rectum tumors, still not reaching the highest performance.

CONCLUSION The real-world information approach provided by the NCIS may be complementary for cancer control planning in Colombia, emphasizing better management processes of health insurers and providers by identifying barriers for timely access to health care.

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INTRODUCTION

Cancer is a leading cause of morbidity and mortality worldwide.[1,2] The estimated 18.1 million new cases and 9.6 million cancer deaths in 2018 by the Global Cancer Observatory[3] could rise to more than 22 million new cases and 14 million deaths by 2030, with a major impact in countries with low or medium human development index.[4]

The growing burden of cancer requires national control plans on the basis of high-quality data provided by nationwide information systems.[5] In this context, data from population registries and country-level surveillance systems can be useful to monitor its frequency, find patterns of access to screening and treatment services, and improve cancer survival.[6,7]

On the other hand, the Colombian health system is public-private with universal and mandatory coverage.[8] There are two main regimes of insurance (third payer and state) based on individual financial status. The first one groups the country's workforce, whereas people unable to pay for health care are enrolled under the state program.[9]

Despite universal health coverage and a government-sponsored 10-year cancer control plan, barriers in accessing cancer care persist. They are mainly administrative, social, and economic, which means that the objectives set by the government are not always achieved, with patients being diagnosed at advanced stages, which affects quality of life, survival, and costs of care. Some of them can also be explained by the fragmentation of cancer care because of the lack of comprehensive care medical centers and trained medical personnel, and geographic barriers that finally harm the diagnostic and therapeutic process.[9,10]

Taking into account the need for real-world information with a national scope, the National Cancer

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

How real-world data from the National Cancer Information System is integrated into the decision-making process to improve access to cancer care in Colombia?

Knowledge Generated

The National Cancer Information System may be complementary to other sources such as population-based registries for cancer control planning in Colombia. Barriers to cancer care still persist and depend on the type of cancer and factors related to the health system. Regarding quality measures, early diagnosis and timeliness of diagnosis and treatment are key prognostic factors that are still a challenge for stakeholders in health care.

Relevance

Our findings are relevant to strengthen information-based health services planning in other middle-income countries where similar approaches could be useful to improve cancer control and quality of health care.

Information System (NCIS), managed by the High Cost Diseases Fund (Cuenta de Alto Costo [CAC] in Spanish), was created by the Colombian Health Ministry[11,12] for improving the decision-making process through the evaluation of access to cancer diagnosis and follow-up within the framework of the national health system. Data from the NCIS are translated into information that allows the stakeholders to take action through policies and processes aimed to reduce the burden of disease and improve financial sustainability.

Therefore, we aimed to describe the methodology and scope of the NCIS, focusing on its results in terms of access to health care through quality measures.

METHODS

NCIS Overview

Cancer has been defined by the national government as a high-cost disease and a central public health issue.[13] The Ministry of Health has established a regulatory framework to improve survival and quality of life of people living with cancer, which includes the creation of national surveillance systems.[11] The model of cancer care was defined in the 10-year Plan for Cancer Control in Colombia, 2012-2021,[14] including three strategic aspects: surveillance, situational analysis, and research. In 2014, the reporting of people with cancer was stated as mandatory for health insurers by Resolution 247 and the NCIS was created.[12]

Since then, the NCIS has collected and analyzed demographic, clinical, and health-related quality measures in people with cancer across the country[11,12] (Appendix Fig A1).

Taking into account that the national health system covers about 96% of the total population in Colombia[15] and they must be reported by their health care insurers, the NCIS estimations reflect a real-life pattern of cancer distribution and risk management.

The Ministry of Health[13] defined 11 priority cancers according to their epidemiologic burden, the possibility of prevention, and the associated cost: seven solid tumors (breast, prostate, cervical, stomach, colon and rectum, lung, and melanoma) and four hematologic neoplasms (acute lymphoblastic and myeloid leukemia, and non-Hodgkin and Hodgkin lymphomas). Nonetheless, the NCIS includes information on other types of cancer.

Case Eligibility

All people, regardless of age or insurance situation, diagnosed with cancer, located in any anatomical site, are included. Cancer diagnosis is confirmed by microscopic (histology of fluids or primary tumor tissues) or non-microscopic methods (clinical, imaging, or surgical approaches). All single or multiple primary malignant tumors in any clinical stage are included, whereas benign, intermediate borderline tumors and those whose malignancy cannot be proved are excluded. The frequency of the report is annual, with a cutoff date of January 1st of each year.

Variables

The NCIS yearly collects 132 variables stated by the Ministry of Health through a resolution,[12] defined following a 10-step consensus conference methodology,[16] developed with a panel of clinical experts and the stakeholders from the health system, scientific and patient associations, the academy, and state regulatory authorities.

Variables are classified into three groups. There are 16 sociodemographic variables: sex, occupation, health insurance, ethnic background, municipality of residence, and identification of the health insurer that provided care during the period. Clinical section has 108 variables: diagnosis, staging, and first treatment (25 variables); history of a previous cancer diagnosis (three variables); and specific information about systemic therapy (29 variables), surgery (12 variables), radiation therapy (20 variables), cell transplant (five variables), or complementary treatment (14 variables). The final section has 10 variables to determinate vital status.

Each year, the operational definition of the variables is reviewed and updated with an expert panel.

Clinical Classification and Staging

The anatomic site is coded using the International Classification of Diseases 10th revision (ICD-10).[17] Invasive cancer is defined following the International Agency for Research on Cancer criteria on the basis of ICD-10.[18] Staging is determined with the eighth edition of the American Joint Committee on Cancer tumor-node-metastasis (TNM) classification[19] in solid tumors, except for some types such as cervical cancer, for which the revised 2018 International Federation of Gynecology and Obstetrics system is used.[20]

Non-Hodgkin lymphoma staging in pediatrics is defined with the Murphy's classification,[21] whereas for non-Hodgkin lymphoma in adults and Hodgkin lymphoma in adults and pediatrics, it is based on the Ann Arbor[22] or Lugano[23] systems. In leukemia, risk stratification is used.

Reporting Process

Annually, health care providers must report information on the clinical management of people with cancer to their health insurers. For cases reported in previous periods, clinical data are updated, whereas for new cases, a complete registration is performed. Each patient is identified with a unique ID for linking data sets. Health insurers upload the information into an interconnection system called SISCAC (Sistema de Interconexión e Intercambio de Información en Salud [by the Spanish acronym for System of interconnection and exchange of health information]) that allows the registration process in real time (Fig 1).

Data-Monitoring Process

Once the report is completed, a data-monitoring process is performed to guarantee data quality. It is achieved in two steps. An initial cross-check is done through a systematized validation mesh that identifies loading mistakes according to specified filters and rules, by evaluating variable's structure, coherence, and consistency.

Then, information is compared with clinical records to verify its authenticity in an auditing process performed by a trained health professional staff. All new cases of a prioritized type of cancer and people previously diagnosed with a prioritized cancer who were treated during the period are audited. From nonprioritized cases, a random sample is audited.

During the auditing process, the first step is the verification of vital and affiliation status with external sources provided by the Ministry of Health. Inconsistent data are adjusted according to the information on clinical records. Finally, all observations (audited or not) are reviewed in three essential aspects: people who died before the measurement period, records with administrative inconsistencies or lack of clinical supports for diagnosis confirmation, and duplicates (Fig 1).

Exhaustiveness of Death

It is confirmed with the official source of the Ministry of Health. The annual matching allows determining the vital status and the date of death (Fig 1).

Cases Included in Epidemiologic Analyses

Although the main purpose of the NCIS is not to establish epidemiologic burden of cancer, it estimates an approach of morbidity and mortality measures among insured people. In that sense, cases who died before the measurement period are excluded, as well as some records without confirmed cancer diagnosis or valid supports to prove it. Duplicates are excluded under certain conditions. In multiple primary tumors of different locations or organs, all records are analyzed, but metastases are excluded. When a tumor appears in subsites of the same organ or on opposite sides of the body (for paired organs), it is determined if they are two different primary tumors or a reporting error; thus, cases are included or excluded, respectively (Fig 1).

Cancer Frequency

Counts of new and prevalent cases and deaths are based on the reporting process by health care insurers and providers. Frequency measures are calculated including only invasive cancers, except for cervical cancer, which may include carcinomas in situ (ICD-10: D060, D061, D067, or D069) following the International Agency for Research on Cancer criteria. New cases are those diagnosed by either clinical or pathologic methods during the reporting period. Point prevalence is estimated for each period including all cancer cases, regardless of vital status at the cutoff date. The all-cause mortality rate is also calculated. The estimated population at the national, department, and municipality level by the Department of National Statistics are used as denominators.

Risk Management Indicators (quality measures)

Conforming to the main goal of the NCIS, a set of indicators to evaluate access and quality of care were established, among other aspects. They were defined using the consensus methodology,[16] and the detailed process has been previously described.[24] Currently, risk management indicators are measured for breast and cervical cancer,[25] stomach and colon and rectum cancer,[26] prostate cancer,[27] lung cancer,[28] and melanoma,[29] as well as hematologic neoplasms in adults, Hodgkin and non-Hodgkin lymphomas[30] and myeloid and lymphoblastic acute leukemia,[31] and leukemia (myeloid and lymphoblastic) in childhood.[32] They are measured annually and their compliance is evaluated through a three-category scale: low, medium, and high performance. The cutoff points for each category vary according to the indicator and were also defined by consensus after a systematic review.

Most quality measures are focused on the process of attention and a few on results of the health care continuum, covering aspects related with diagnosis, staging, treatment,

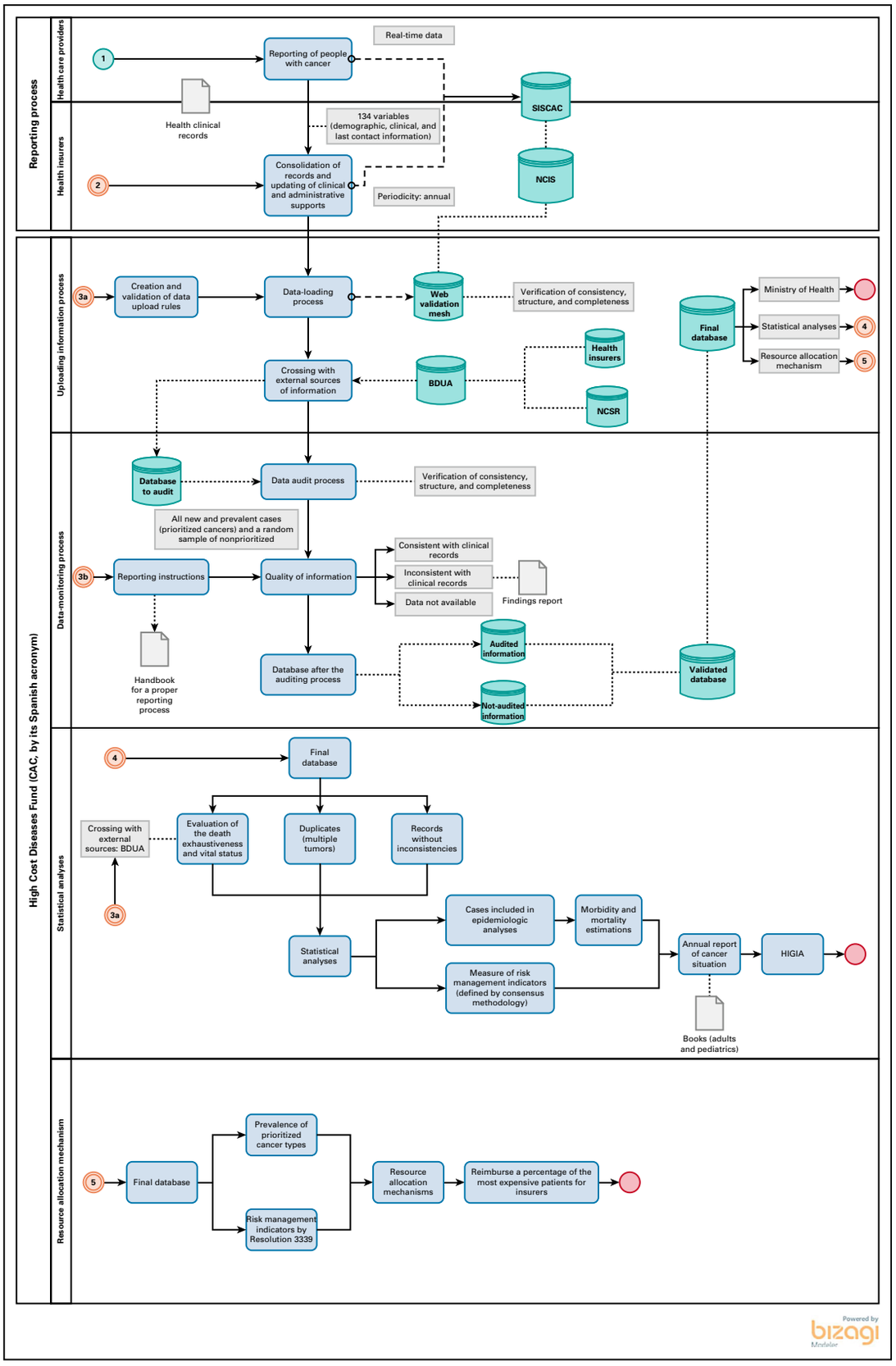

FIG 1. General structure and information flow through the NCIS. First, health insurers and providers must report people with cancer who received care within the national health system. Once data are loaded, their consistency, structure, and completeness are validated according to some reporting rules previously defined. Then, the resulting data set goes to a standardized data-monitoring process where a random sample is taken and information reported is validated with clinical records. Finally, after some additional validation with external sources, a depurated data set is ready to be analyzed. BDUA, Base de Datos Única de Afiliados (National Database of Affiliated People); HIGIA, Hechos, Información, Gestión, Innovación, Acción (Epidemiologic and Quality Measures Dashboard); NCIS, National Cancer Information System; NCSR, Registro Nacional del Estado Civil (National Civil Status Registry); SISCAC, Sistema de Interconexión e Intercambio de Información en Salud (System of interconnection and exchange of health information).

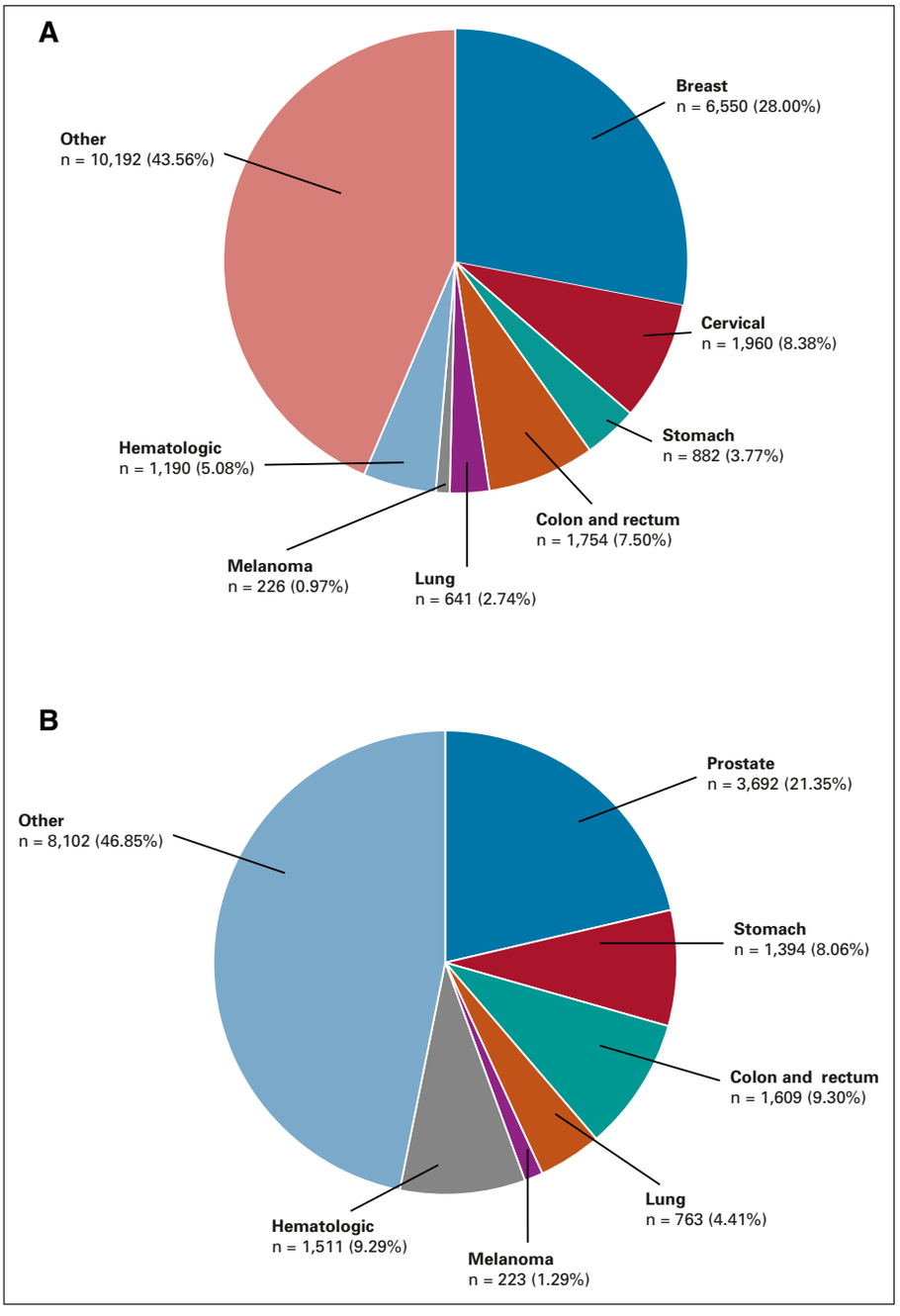

FIG 2. New cases distribution by type of cancer and sex in Colombia, 2020: (A) females of all ages and (B) males of all ages. Includes invasive cases only. Lymphomas (Hodgkin and non-Hodgkin) and leukemia (myeloid and lymphoid) were included in hematologic neoplasms.

waiting times to be diagnosed and treated, access to interdisciplinary attention, palliative care, and end-point outcomes such as 5-year observed survival.

Evaluation and monitoring of risk management indicators is highly valuable to identify gaps in cancer diagnosis and treatment, considering the sources of heterogeneity related to health care services that include type of insurance, availability of trained personnel and facilities, and social and economic disparities between regions.

Ethical Considerations

The NCIS follows international standards by the Council for International Organizations of Medical Sciences and national regulations (Resolution 8430 of 1993, stated by The Colombian Health Ministry) for conducting human research. Confidentiality is guaranteed in compliance with Law 1581 of 2012, which stated conditions for protecting personal data in Colombia. All NCIS members follow a security policy for maintaining confidentiality and privacy of personal information. Access to data is also according to predefined user profiles by security passwords. Furthermore, each case is identified with an internal ID assigned by the NCIS, all data sets are anonymized for statistical analysis, and the results only can be used for approved purposes.

RESULTS

Registry Evolution: Frequency of Cancer Within the Colombian Health System

Since 2015, prevalent cases of invasive cancer reported to the CAC have increased by 102.12%, going from 163,776 to 331,021 in 2020. Furthermore, 40,689 new cases of invasive cancer and 26,305 deaths were reported by 2020 among people who receive health care within the national health system.

By 2020, among new cases of invasive cancer, the most frequent type was breast cancer (16.36%; n = 6,656), followed by prostate (9.07%; n = 3,692) and colon and rectum cancer (8.27%; n = 3,363). Breast cancer was the leading cause of death (11.35%; n = 2,986), followed by colon and rectum (8.83%; n = 2,324) and prostate cancer (8.10%; n = 2,131). Figure 2 shows the distribution of new cases by sex and type of cancer.

Trend of Quality Measures in the NCIS

TNM staging in newly diagnosed cancer cases is described in Figure 3. When comparing the current reporting period with the baseline, the biggest improvement in TNM coverage was observed in breast and prostate cancer, although the high level of compliance (≥ 90%) has not been reached for any type of cancer.

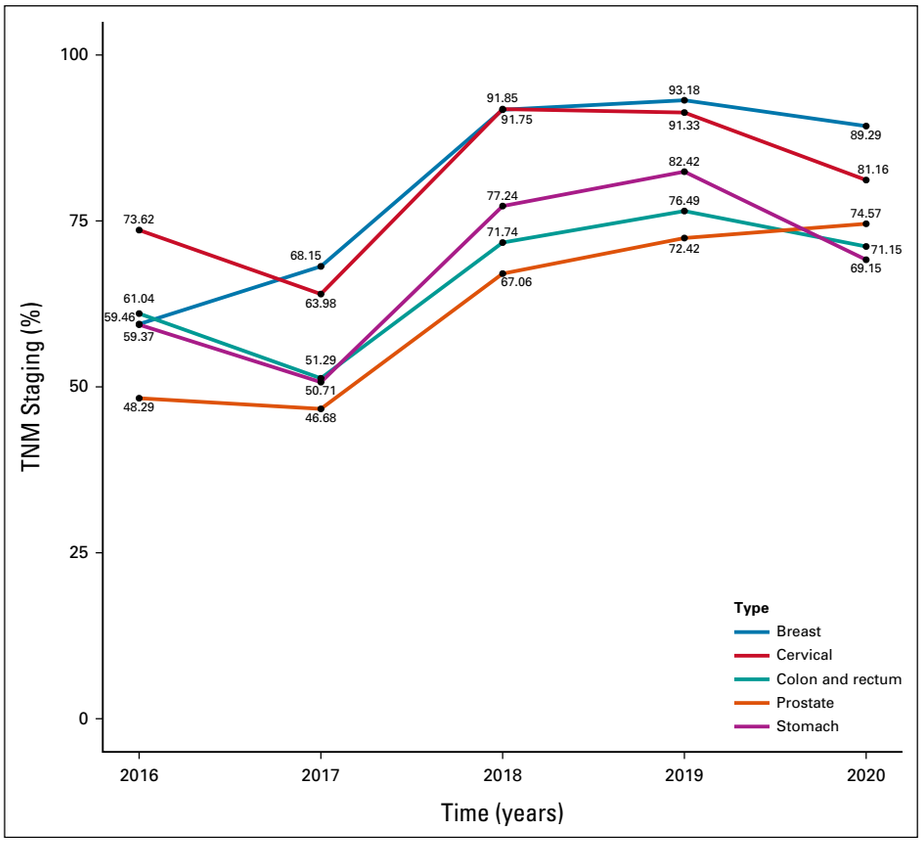

FIG 3. Trend of TNM staging at diagnosis by type of cancer in Colombia, 2015-2020. High level of compliance for TNM staging at diagnosis has been established up to 90%. TNM, tumor-node-metastasis.

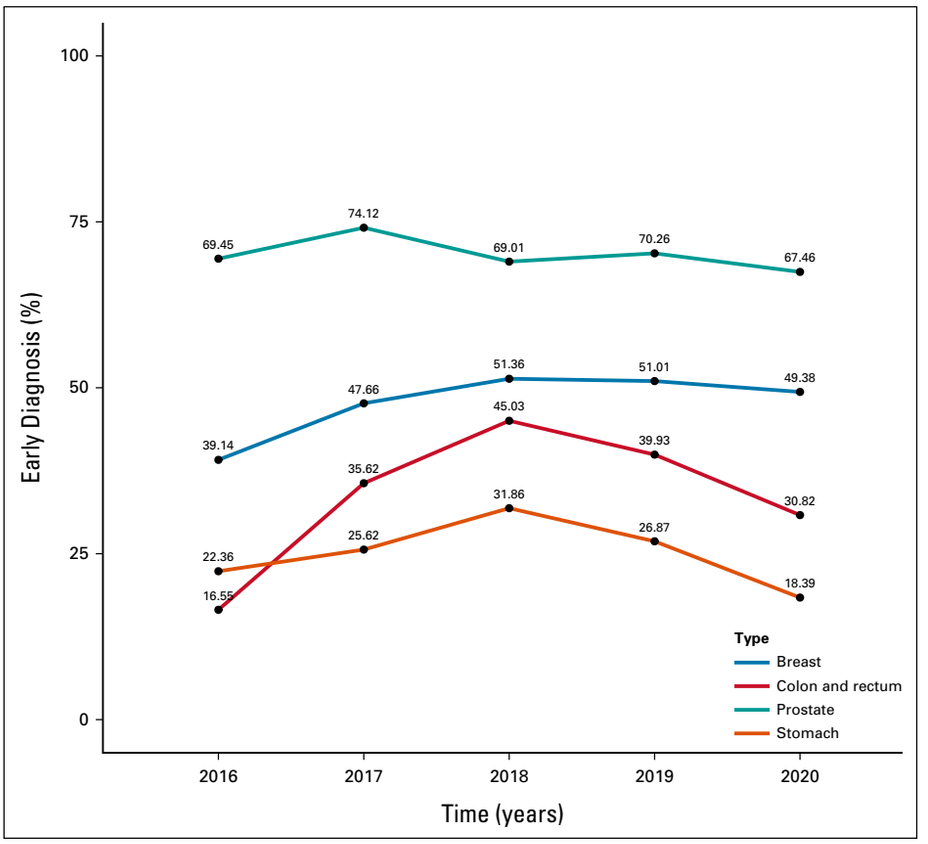

FIG 4. Evolution of early diagnosis as an indicator of access to health care by type of cancer in Colombia, 2015-2020. High level of compliance for early diagnosis has been established as follows: breast (≥ 50%), prostate (≥ 69%), stomach (> 12%), and colon and rectum (> 19%). According to the consensus, there is no indicator to identify the proportion of newly diagnosed women with cervical cancer in early stages. In fact, cervical cancer was not included in the graph.

Figure 4 shows the proportion of new cases diagnosed in early stages by type of cancer. A heterogeneous pattern has been identified over the years, especially for stomach and colon and rectum cancer. By 2020, early diagnosis was higher than the baseline for all types, except prostate and stomach cancer. Despite well-established screening programs for breast and prostate cancer, early diagnosis remains a challenge for insurers and providers.

Access to health care can be assessed with waiting times for diagnosis and treatment initiation. According to the NCIS quality measures, goals have not been consistently achieved during the follow-up (Fig 5). Regarding diagnosis, the longest waiting time was observed in prostate cancer. When comparing with 2019, there was a generalized increase in delays to be diagnosed. Time to treatment initiation (TTI) showed a more stable trend, with the lowest waiting time for breast and cervical cancer. Gaps between time to diagnosis and treatment were broader for stomach and colon and rectum cancer than prostate.

Diffusion of the Results

The results of the current situation of cancer in Colombia are published in different formats. Annually, the epidemiologic trends, clinical characteristics, and risk management of the prioritized types of cancer are described in two electronic books in adult[33] and pediatric population.[34] Data are also available on interactive platforms such us SISCAC (accessed by health insurers and providers) and HIGIA (public access).

DISCUSSION

The NCIS provides real-time data to improve risk management and decrease the burden of cancer in Colombia. It adds value through the identification of gaps in access to cancer care contributing to the generation of interventions for their mitigation. It is also a source of information to evaluate compliance with cancer policies and improve the comprehensive health care routes. On the other hand, it contributes to the financial stability of the health system through the redistributive allocation mechanisms on the basis of results that were stated by law[35] from data analyzed by the NCIS with the objective of improving clinical outcomes, health quality, and timeliness of cancer care.

From the analysis of quality measures trend, a heterogeneous pattern in access to cancer care was identified. It is important to mention that delays in diagnosis and treatment initiation have been associated with worse health outcomes, with negative impact on survival.

A cohort in the United States that evaluated the association between delays in treatment initiation and survival found a median TTI increased from 20 days (interquartile range

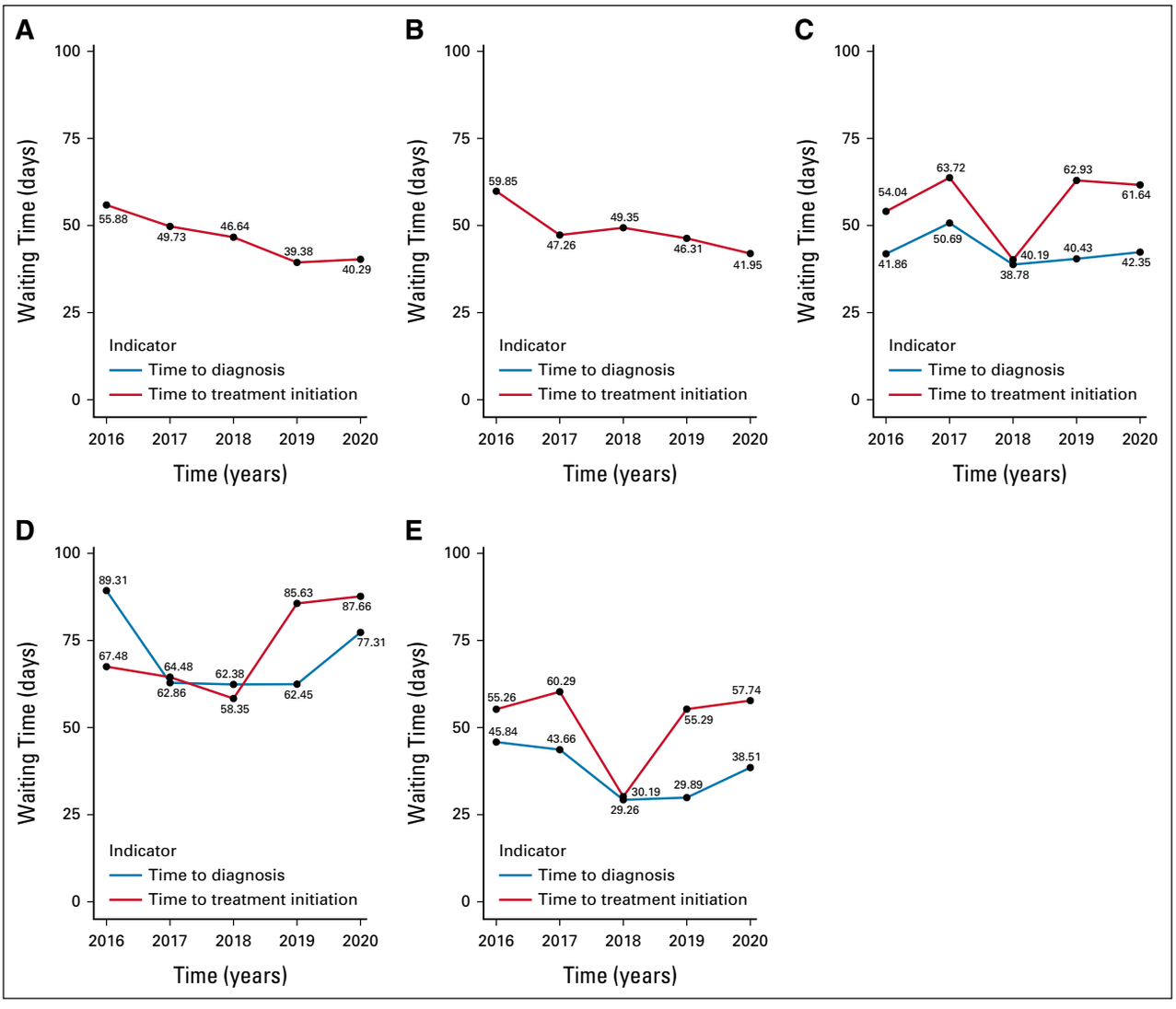

FIG 5. Waiting times to diagnosis and treatment initiation by type of cancer in Colombia, 2015-2020: (A) breast, (B) cervical, (C) colon and rectum, (D) prostate, and (E) stomach. Time to diagnosis was defined as the number of days between the clinical suspicious and the clinical or pathologic diagnosis. Values are means. This quality measure has not been defined for breast and cervical cancer. TTI was defined as the number of days between the clinical or pathologic diagnosis and the first treatment. Values are means. High level of compliance for a timely diagnosis was < 30 days for all types of cancer. Regarding TTI, waiting time should be < 15 days for breast and cervical cancer and < 30 days for other types. TTI, time to treatment initiation.

[IQR]: 0-27) in colorectal cancer to 57 days (IQR: 31-87) in prostate cancer.[36] All waiting times in this study were higher than that estimated in the NCIS and longer delays in prostate cancer are consistent with our results. In this study, delays in TTI were associated with an increased risk of mortality ranging from 1.20% to 3.20% per week in early-stage breast, lung, renal, and pancreatic cancers.[36]

These results are consistent with a prospective cohort that estimated a median TTI of 26 days (IQR: 16-40) for colorectal, 32 days (IQR: 21-48) for breast, and 79 days (IQR: 55-117) for prostate cancer, similar to our population. In addition, shorter TTI was directly associated with a lower mortality. The broader difference was identified in colorectal cancer with an increase of 47.80% in the 5-year predicted mortality when delays for TTI were more than 180 days.[37]

Finally, a systematic review and meta-analysis found that each 4 weeks of surgical delay increased the chance of death by 6%-8% for all types of cancer. In breast cancer particularly, an 8-week delay in surgery would increase the risk of death by 17% and a 12-week delay by 26%.[38] In the NCIS, TTI in Colombian women was higher than 4 weeks, meaning that barriers to an effective access to treatment could be directly increasing the risk of death.

Diagnosis and treatment delays are multifactorial, including among others, system barriers. National quality measures in terms of access to cancer health care are a good strategy to quantify and minimize system delays.[38] Most health systems have implemented this metric, setting that TTI should be < 30 days, being able to increase even to a maximum of 45 days in middle-income contexts.[39] Level of compliance for the NCIS indicators was established following international targets, although they have not been achieved. In this sense, the role of the NCIS is crucial to identify the barriers and patterns of access to cancer care and promote a more integrated, centralized, and multidisciplinary approach from the health system perspective.

Several factors have contributed to the continuity of the NCIS. The most important is the mandatory report by health insurers. Besides, the CAC has established standardized policies to collect, validate, analyze, and disseminate its information. Furthermore, the innovation has been a vital aspect in the NCIS, finishing with the launch of SISCAC, the most ambitious platform in the country to interconnect the health system stakeholders.

Moreover, the CAC has settled continuous training strategies with the health insurers to guarantee an adequate reporting process. Another important strength is the data-monitoring process from which the data quality and reliability are verified.

On the other hand, estimations obtained from the NCIS offer an opportunity to design policies to improve access to high-quality cancer care from a precise real-world source of data.

The NCIS has some limitations. Since the NCIS depends on the reporting process performed by health insurers and although it is mandatory, there is a risk of underreporting, especially in undiagnosed cancers with high mortality, affecting the completeness of the NCIS. In addition, as each health care provider has autonomous and independent procedures to handle the data, information bias cannot be ruled out.

In conclusion, the NCIS is helpful to identify barriers in accessing care from the health system perspective. It also describes the real-life situation of cancer care in the insured population being complementary to other sources of information for cancer planning. Targets in time to diagnosis and treatment have not been achieved and delays could be associated with worsened survival.

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Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/go/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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Travel, Accommodations, Expenses: Boehringer Ingelheim, Pfizer, E.R. Squibb Sons LLC, Janssen, Seattle Genetics, Celgene

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APPENDIX

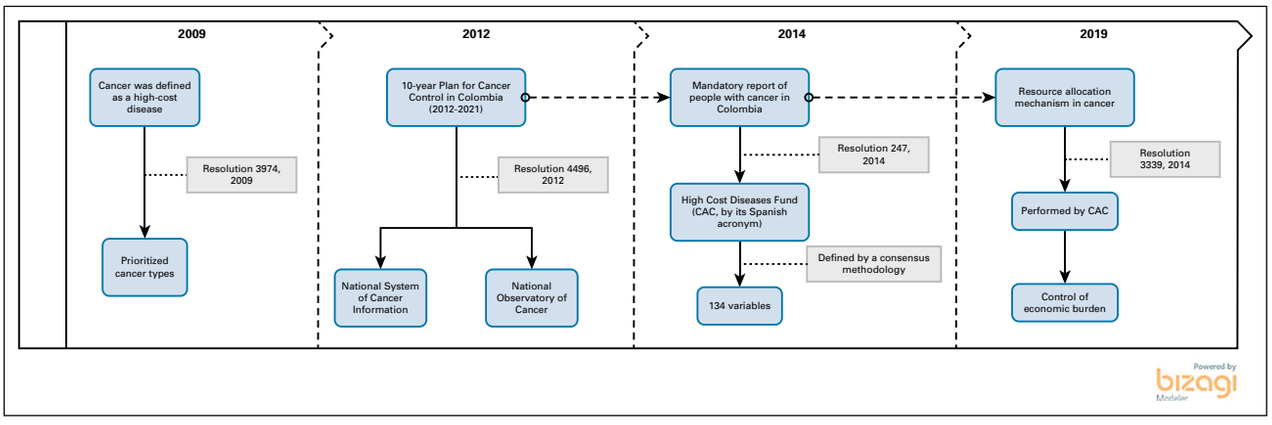

FIG A1. Legal framework of cancer as a high cost disease in Colombia. Since 2009, health policies to improve cancer control have been established in Colombia, including the 10-year national plan in 2012 which stated the basis of national surveillance systems. Then, in 2014 the NCIS was created to collect and analyze access to cancer care among insured population. Finally, in 2019 a resource allocation mechanism based on cancer results in terms of access to health care was stated by the Ministry of Health. It aims to control the economic burden of cancer among insurers.

CUENTA DE ALTO COSTO

Fondo Colombiano de Enfermedades de Alto Costo

Participación en eventos científicos

Presentación de pósters y ponencias orales

CUENTA DE ALTO COSTO

Fondo Colombiano de Enfermedades de Alto Costo

Hemofilia

Presentación oral

Título	Autores	Evento	Ámbito	Objetivo	Principales hallazgos	Enlace para consulta
Presence of inhibitors and all-cause mortality in patients with non-severe hemophilia A	Andrés García, Juliana Hernández, Ana María Valbuena, Lizbeth Acuña	Marshall Business Research Conference 2021	Internacional	Analizar la relación entre la presencia de inhibidores y la mortalidad por todas las causas en pacientes con hemofilia A no severa en Colombia entre 2015 y 2019.	• Se analizaron 3.673 casos con hemofilia A no severa y se identificaron 22 fallecidos a lo largo de los 5 años de seguimiento. • Un total de 350 pacientes de los 3.673 (9,52%) desarrollaron inhibidores durante el periodo de estudio. • Los pacientes con hemofilia A que desarrollaron inhibidores tenían tasas de mortalidad un 5% mayores que las de aquellos sin inhibidores.	Link CAC

CUENTA DE ALTO COSTO
Fondo Colombiano de Enfermedades de Alto Costo

Artritis reumatoide

Póster

Título	Autores	Evento	Ámbito	Objetivo	Principales hallazgos	Enlace para consulta
Evaluación de la artritis reumatoide en tiempos de sindemia	Lizbeth Acuña, Luis Alberto Soler, Ana María Valbuena, Luis Alejandro Moreno, Nathalia Castrillón	Congreso Internacional de Salud Pública de la Universidad de Antioquia	Nacional	Describir la actividad de la artritis reumatoide en la población reportada a la CAC en el periodo 2020, según las clinimetrías aplicadas.	• Se utilizó el DAS28 realizado en consulta presencial en el 45% de los pacientes (n= 40.585). • En el 1,70% de los pacientes (n=1.575) se utilizaron clinimetrías alternas como SDAI (n= 600), CDAI (n= 793) y RAPID3 (n= 182). • Al 53,20% de los pacientes (n= 47.975), no se les registró clinimetría en los últimos 6 meses del periodo evaluado, por lo cual no fue posible conocer el estado de actividad de la enfermedad.	Link CAC

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Fondo Colombiano de Enfermedades de Alto Costo

COVID-19

Póster

Título	Autores	Evento	Ámbito	Objetivo	Principales hallazgos	Enlace para consulta
Chronic exposure to PM2.5 and COVID-19 mortality during the first year of the epidemic in Colombia: an ecological study	Laura A. Rodríguez Villamizar, Luis Carlos Belalcázar Cerón, Julián Alfredo Fernández Niño, Diana Marcela Marín Pineda, Oscar Alberto Rojas Sánchez, Lizbeth Alexandra Acuña Merchán, Nathaly Ramírez García, Sonia Cecilia Mangones Matos, Jorge Mario Vargas, Julián Herrera, Dayana Milena Agudelo Castañeda, Juan Gabriel Piñeros Jiménez, Néstor Y. Rojas Roa, Víctor Mauricio Herrera Galindo	33rd Annual Conference of the Internacional Society for Environmental Epidemiology (ISEE 2021)	Internacional	Determinar la asociación entre la exposición crónica al material particulado fino (PM2.5) y la mortalidad por COVID-19 en Colombia.	• La población mayor a 65 años de edad y la población urbana presentaron mayores tasas de mortalidad por COVID-19 a nivel municipal en Colombia. • La exposición prolongada a PM2.5, el índice de pobreza y la prevalencia de enfermedades crónicas durante los primeros meses de la pandemia, no fueron significativos con la mortalidad por COVID-19 a nivel municipal, pasados 12 meses desde el inicio de la pandemia.	Link CAC

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2. Eyler A. Research methods for Public Health. New York: Springer Publishing; 2021. 276 p.

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