

Demographics and clinical characteristics of a new population of centenarians in Colombia. The COOLCEN cohort

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ABSTRACT

Aim: Centenarians represent a successful model of biological aging that is becoming increasingly common but still largely unknown. Data about centenarians in Colombia is scarce. The aim of this study was to provide a description of the demographic and clinical characteristics of a new cohort of centenarians in Colombia.

Methods: A retrospective, population-based cohort study was undertaken, employing a nationally validated registry provided by a health insurance company. Demographic information and prevalence rates of significant chronic diseases were evaluated. The geographical distribution of centenarians at the national level was mapped. Data were then compared with other age groups (>18-59 and 60-99 years-old), and with previous descriptions of centenarians.

Results: Among the 2,362,436 persons included in the study, a prevalence of 0.12% centenarians was observed, of which 50.7% were female and the majority resides in urban areas (64.9%). Chronic diseases were observed in 275 (9.27%) centenarians, of whom 113 (3.81%) disclosed one chronic disease and 162 (5.46%) disclosed multimorbidity. The most prevalent chronic diseases were essential hypertension (8.6%), and chronic kidney disease (4.4%), which were significantly lower compared to others age groups. Centenarians were free of hematological, inflammatory arthritis, tuberculosis and human immunodeficiency virus infections. COVID-19 was observed in 2% of cases. Significant differences in health outcomes assessed were seen when comparing our results with centenarians from previously described blue zones.

Conclusions: The COOLCEN cohort discloses a low prevalence of age-related chronic diseases, low economic status and no difference in gender distribution. The study will provide valuable insights into healthy aging, disease prevention, and improving the well-being of older adults.

1. Introduction

The contemporary world is confronted with unparalleled social and economic issues due to the rise in life expectancy at birth and the worldwide demographic transition towards an aging population. The significance of this subject lies in the association between the growth in life expectancy and the following rise in the duration of time persons spend in a condition of poor health (Menassa et al., 2023). Notably, human life expectancy has experienced rapid growth over the past four

decades, accompanied by a transformation in the demographic structure (Vollset et al., 2020; World Health Organization, n.d.-a). In 2020, the World Health Organization (WHO) announced that the number of individuals aged 60 and over exceeded the number of those aged below five years, and projections suggest that by 2030, one out of every six individuals will have crossed the threshold of 60 years. By 2050, the number of older adults is anticipated to double, rising from 1 billion to 2.1 billion, with 80% of them residing in low and middle-income countries (Pan American Health Organization, n.d.; World Health

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Organization, n.d.-a). These regions currently lack strategies and plans to address the burden of geriatric diseases, given the existing unmet limitations and needs.

Considering that aging frequently leads to the onset of various chronic conditions, known as aging-associated chronic diseases, including essential hypertension, type 2 diabetes mellitus, obesity, inflammatory and non-inflammatory joint diseases, chronic obstructive pulmonary disease, Parkinson's disease, and cancer, among others (Guo et al., 2022; Jaul & Barron, 2017), a substantial global increase in the elderly population would result in a worldwide healthcare provision crisis and escalating costs. In response to this challenge, the United Nations (UN) has designated the period between 2021 and 2030 as the Decade of Healthy Aging (United Nations, n.d.), urging the development of collaborative and relevant programs, strategies, and research focused on enhancing the well-being of older individuals, their families, and the communities in which they reside (World Health Organization, n.d.-b).

Based on the UN's definition of healthy aging as "the process of developing and maintaining the functional ability that enables well-being in old age", there is a promising model of healthy aging that remains underexplored but holds the potential to address numerous questions on this subject: centenarians (Borras et al., 2020; Marcos-Pérez et al., 2021). A centenarian is an individual who has surpassed 100 years of chronological age since birth (Borras et al., 2020). Centenarians disclose a higher prevalence in the blue zones, which are certain geographical locations characterized by a considerably larger number of age-validated oldest individuals compared to their surrounding regions. The name "Blue Zone" was given to these regions because the maps that show them were shaded blue (Poulain et al., 2020). To date some well-established blue zones have been defined, including Barbagia in Italy, the Nicoya Peninsula in Costa Rica, Loma Linda in California, the Island of Icaria in Greece, and Okinawa in Japan (Buettner & Skemp, 2016). Nevertheless, this phenomenon progressively varies in prevalence, albeit with limited research.

Centenarians exhibit a distinct physiological and morbidity profile compared to octogenarians or even nonagenarians, with most maintaining a pattern of healthy longevity, experiencing only a slight neurocognitive decline or even remission of comorbidities from previous years (Aliberti, De Caro, et al., 2022; Aliberti, Funk, et al., 2022; Fastame, 2022; Tedone et al., 2014). Environmental factors and genetics play pivotal roles in this outcome (Cheng et al., 2022; Zhang et al., 2023). These characteristics render the centenarian a subject of high regard in research, with the potential for discovering of biomarkers and prognostic factors associated with exceptional healthy longevity through exploratory and analytical methodologies. Nonetheless, results over time have been reported by only a limited number of longitudinal cohorts in recent years (Aiello, Accardi, Ali, et al., 2021; Aiello, Accardi, Aprile, et al., 2021; Akema et al., 2023). In Latin America, robust studies on centenarians are scarce (Table 1), primarily focusing on the isolated description of clinical characteristics (Madrigal-Leer et al., 2020; Pedro et al., 2017), with a notable absence of long-term follow-ups. Specifically, in Colombia, research groups dedicated to centenarians are absent, despite an informal recognition of the potential existence of a blue zone (Gutiérrez et al., 2014; Rosselli et al., 2017).

Taking into consideration the existing gap in the evidence regarding centenarians in Colombia and Latin America, which supports the future development of exploratory and analytical studies on protective factors and longevity prognosis, in addition to meeting the goals of global health research on healthy longevity, the aim of this study is to provide a novel and pioneering description of the demographic and clinical characteristics of a cohort of centenarians in Colombia.

2. Material and methods

2.1. Study population

Data analysis for this retrospective, population-based cohort study

Table 1

Research on centenarians in Colombia, Latin America and around the world.

Database	Publications		
	Colombia	Latin America	All (N)
	n (%)		
PubMed	1 (0.04)	38 (1.48)	2554
Scopus	2 (0.06)	76 (2.34)	3247
Scielo	0	14 (2.14)	654
LILACS/BVS	1 (0.3)	291 (100)	291
Imbiomed	1 (6.66)	7 (46.6)	15
Grey literature	2	ND	ND

Number of results obtained by searching for (Centenaria* [using English and Spanish languages]) on PubMed, Scopus, and Latin American health sciences databases (retrieved 22 Dec 2023). In the case of PubMed and Scopus, the 'Affiliation' tag was adjusted to identify the country/region of origin of the publications. Book chapters and conference papers were excluded. The accuracy of the results was not confirmed. BVS: Biblioteca Virtual en Salud; LILACS: Literatura Latinoamericana y del Caribe en Ciencias de la Salud. ND: No accurate data available.

was carried out using the COOSALUD EPS registry. COOSALUD EPS is a Colombian health insurance company, responsible for promoting and undertaking insurance, as well as organizing and guaranteeing the delivery of health services. The data regarding the prevalence of significant chronic diseases were accurately collected at the individual level by capturing confirmed diagnoses from experienced medical practitioners within an extensive health provider network. Simultaneously, demographic information, such as basic demographics and residential locations of the members, was extracted from the COOSALUD's basic demographics registry, utilizing the most recent available data. The registry includes demographic and epidemiological data diagnoses carried out during admission and defined by the International Classification of Diseases (ICD-10).

Based on these datasets, the distributions of chronic disease prevalence and demographic characteristics were computed, including gender, regime, and zone, conditioned on specific age groups: 18-59 years old, 60-99 years old, and 100 or more years old. The co-occurrence of multiple diseases and medical conditions within centenarians without any reference to an index condition (i.e., multimorbidity) (Bayliss et al., 2008) was also investigated as well as differences in sex, living areas, and individual chronic diseases within the centenarian population. To ensure data quality, the study excluded populations belonging to indigenous communities due to unreliable birthdate records. Additionally, member addresses facilitated georeferencing, enabling us to calculate centenarian prevalence at the municipal level and visualize the results on a map.

2.2. Statistical analyses

Data are presented as frequency and percentages. Chi-squared tests were applied to assess the hypothesis of independence among the variables mentioned above within the defined age groups. The statistical analysis was conducted using the R software (Version 4.3.1) (<https://www.r-project.org/>), while georeferencing analysis utilized ArcGIS Pro 3.1. (<https://www.esri.com/en-us/arcgis/products/arcgis-pro/>).

2.3. Ethical statements

This was an observational study based on anonymized secondary data, performed in compliance with Act 008430/1993 of the Ministry of Health of the Republic of Colombia, which classified it as minimal-risk research. The institutional review board of COOSALUD EPS approved the study design.

3. Results

A total of 2,362,436 individuals aged 18 and above were identified, with 0.12% (n=2964) being centenarians. Data concerning centenarians and other age groups are disclosed in Table 2. Among this group, 50.7% (n=1502) were women, 98.7% (n=2924) were covered by subsidized health insurance, and the majority currently resides in urban areas (64.9%; n=1925). Georeferentiation of the entire population of the COOLCEN cohort is shown in Fig. 1.

The most prevalent age-related chronic diseases among centenarians were essential hypertension (8.6%), chronic kidney disease (4.4%), and type 2 diabetes mellitus (2.1%). A similar trend emerged within the age group spanning from 60 to 99 years, where essential hypertension and type 2 diabetes mellitus stood out as the most common conditions (Table 2). However, it is worth noting that the prevalence of these conditions in centenarians was significantly lower, even in comparison to the 18 to 59-year-old group, where essential hypertension was also the most prevalent condition (Table 2). There was no evidence registered of hematological disorders and infectious diseases such as human immunodeficiency virus (HIV) and tuberculosis. COVID-19 (by polymerase chain reaction or antigen tests) was observed in 2% of cases. These findings contrast with the two other age groups, where the

Table 2
Demographics and clinical characteristics of centenarians compared with adults (18-59 years-old) and longeval (60-99 years-old).

Variable	Age Range			p-value
	18 – 59 years-old	60 – 99 years-old	>100 years-old	
	n (%)			
Population (N=2,362,436)	1,841,914	517,558	2964	-
Female	983,881 (53.4)	267,914 (51.8)	1502 (50.7)	< 0.001
Male	858,033 (46.6)	249,644 (48.2)	1462 (49.3)	
Health insurance, contributive	270,235 (14.7)	36,766 (7.1)	39 (1.3)	< 0.001
Health insurance, subsidized	1,571,356 (85.3)	480,784 (92.9)	2924 (98.7)	
Rural area	613,453 (33.3)	153,691 (29.7)	1039 (35.1)	< 0.001
Urban area	1,228,461 (66.7)	363,867 (70.3)	1925 (64.9)	
Diabetes	31,741 (1.7)	59,924 (11.6)	63 (2.1)	< 0.001
Hypertension	77,778 (4.2)	160,380 (31)	256 (8.6)	< 0.001
Cerebrovascular disease	3211 (0.2)	5088 (1)	8 (0.3)	< 0.001
Heart disease	2255 (0.1)	3943 (0.8)	7 (0.2)	< 0.001
Chronic kidney disease	7033 (0.4)	42,955 (8.3)	129 (4.4)	< 0.001
Cancer	8455 (0.5)	12,400 (2.4)	8 (0.3)	< 0.001
Arthropathy*	1981 (0.1)	1832 (0.4)	0	< 0.001
Hemophilia	337 (0.01)	62 (0.01)	0	0.006
Orphan and rare disease	508 (0.02)	165 (0.03)	0	0.176
Human immunodeficiency virus	7842 (0.4)	888 (0.2)	0	< 0.001
Asthma	992 (0.1)	530 (0.1)	0	< 0.001
Chronic obstructive pulmonary disease	1834 (0.1)	7478 (1.4)	22 (0.7)	< 0.001
Transplant	250 (0.02)	88 (0.01)	0	0.153
Tuberculosis (past or present history)	574 (0.03)	203 (0.04)	0	0.011
COVID-19	75,518 (4.1)	28,465 (5.5)	59 (2)	< 0.001

*Includes inflammatory arthritis

prevalence was significantly higher compared to centenarians.

Centenarian characteristics by living areas, sex and chronic disease status are disclosed in Table 3, and the prevalence of multimorbidity is shown in Table 4. Chronic diseases were observed in 275 (9.27%) centenarians, of whom 113 (3.81%) disclosed one chronic disease and 162 (5.46%) disclosed multimorbidity. The two most common multimorbidity combinations were hypertension-chronic kidney disease (2.6%) and hypertension-diabetes mellitus-chronic kidney disease (1.1%) (Table 4).

Upon analyzing the geographical distribution of centenarians, it was observed that the highest prevalence of centenarians per 10,000 inhabitants is in the Colombian Caribbean region, with potential blue zones identified in the territorial areas of Sucre and Bolívar (two areas with a prevalence of centenarians ranging from 60 to 92 centenarians per 10,000 inhabitants) (Fig. 1). Additionally, there are areas with a high prevalence (between 33 and 59 centenarians per 10,000 inhabitants) in the territorial areas of Córdoba and Magdalena, which are also coastal regions.

4. Discussion

In this study, a cohort of Colombian centenarians is described. In Colombia, aging is one of the most significant demographics changes the country is facing in terms of healthcare, social security and pension system. Analyzing data obtained through Colombian national surveys, a sustained increase in the rate of centenarians per 10,000 inhabitants since 1950, with a peak in the 1990s and over the last 10 years is observed. Thus, for the year 2019 (latest official data), Colombia had a global centenarian rate of 4.5 per 10,000 inhabitants, with a higher rate among centenarian women (5.66 per 10,000 Colombian women) (Fig. 2). Despite this trend, there are not enough studies providing robust data on morbidity profiles, factors associated with healthy aging, functional capacity, quality of life, causes of death, or outcomes of interventions specifically in the centenarian population.

Up to date, four descriptive studies concerning centenarian populations have been carried out in Colombia (Table 5) (Gutiérrez et al., 2014; Ibarra Chacón & Parra Hernández, 2019; López Rippe & Zapata Bravo, 2021; Rosselli et al., 2017). These were descriptive studies with a primary objective of evaluating the clinical characteristics (Gutiérrez et al., 2014; Ibarra Chacón & Parra Hernández, 2019). Geriatric syndromes, like delirium, dementia, and falls were the most prevalent, along with mortality rates reaching up to 50% in emergency rooms (Gutiérrez et al., 2014). It was reported in a small study (N =77) that most of the centenarians had multimorbidity, with less than 10% maintaining independence (Ibarra Chacón & Parra Hernández, 2019). Nevertheless, comparison of these results with the description of our cohort is not achievable due to the lack of clarity in scale use and specialist assessment. In contrast to previous investigations with fewer than 100 centenarians (Gutiérrez et al., 2014; Ibarra Chacón & Parra Hernández, 2019), our cohort characterizes almost 3000 centenarians with a relatively healthy morbidity profile, underscored by a markedly low prevalence of age-related chronic diseases.

Biological aging is quantified as a representation of the processes of organic aging, life expectancy, and the state of an individual's health (Nakamura & Miyao, 2003). In contrast to chronological age, which merely tallies the years a person has lived, biological aging pertains to functional capacity, susceptibility to the development of age-related diseases, and quality of life (Fraser et al., 2022; Klemera & Doubal, 2006). Consequently, centenarians, despite having achieved a century of life, may experience successful biological aging, enabling their independence, daily activity engagement, free from age-related chronic diseases, and continued pursuit of life objectives (Mitnitski et al., 2002). Conversely, individuals who are chronologically 80 years old may exhibit accelerated biological aging, resulting in the emergence of chronic comorbidities that impact their quality of life, compromise their autonomy, and culminate in a "premature" dead compared to

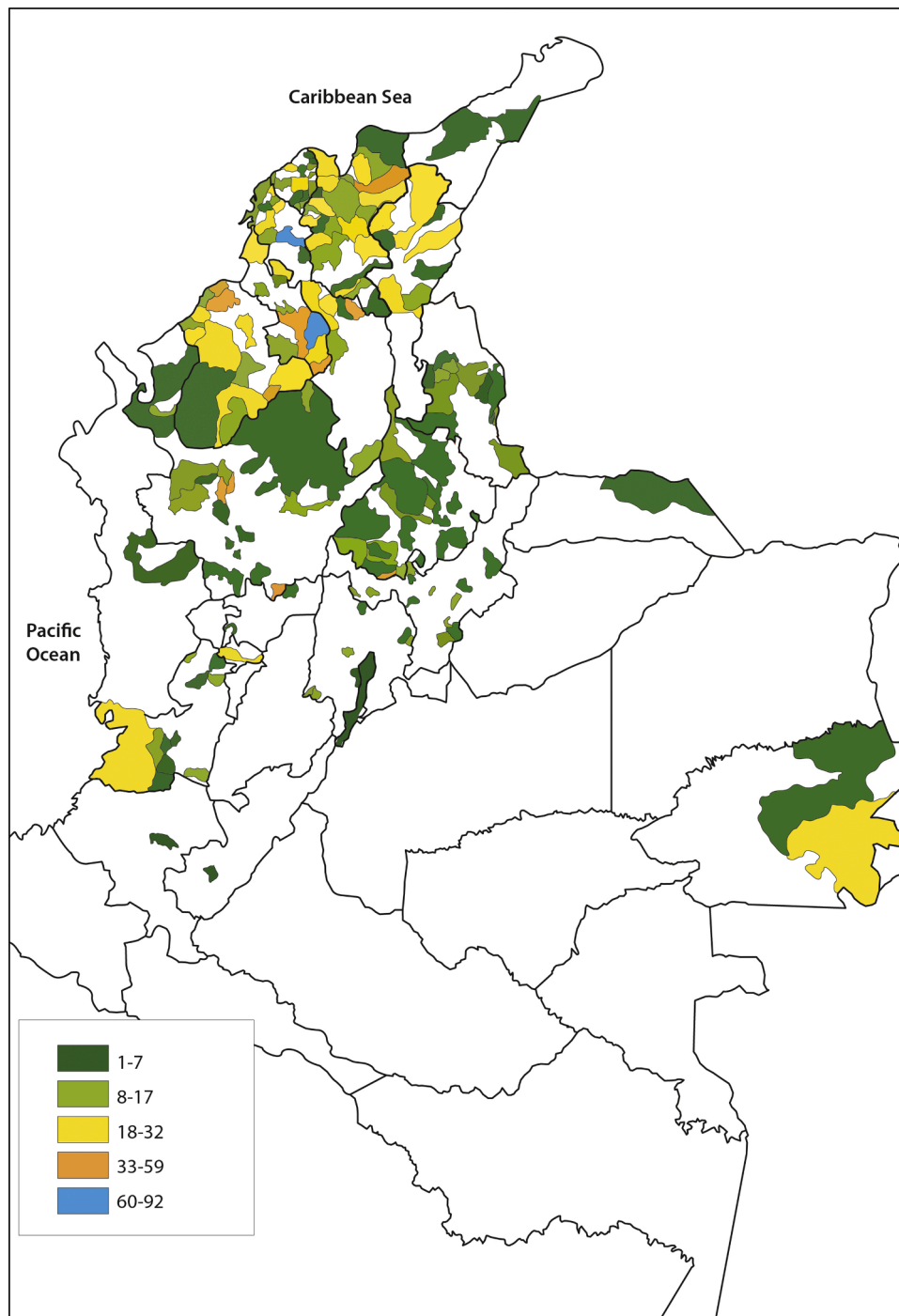


Fig. 1. Prevalence of Colombian centenarians according to the COOSALUD EPS registry (x10,000).

centenarian longevity (Chen et al., 2022; Klemra & Doubal, 2006; Mitnitski et al., 2002).

Although the precise variables influencing biological aging outcomes (both retardation and acceleration) are not completely understood, existing literature suggests that heredity, lifestyle, and the external environment in which the human life cycle unfolds exert significant influence (Jee & Park, 2017; Xu et al., 2022). Heritability (i.e., the proportion of phenotypic variation in a population that is attributable to genetic variation among individuals) seems to be low (15–30%) (Ruby et al., 2018), thereby presenting a valuable avenue for research. This extends not only to life expectancy extension but also to enhancing healthy aging. However, this does not imply that genetic variants and

factors associated with aging, aging characteristics, longevity, and life expectancy have not been identified. To date, three polymorphic genes have been consistently found to influence longevity: *APOE*, *FOXO3A* and *CHRNA3* (Murphy CT, 2023).

In the present study, an analysis was conducted utilizing an original national database encompassing 2,362,436 individuals, of whom 2964 centenarians were identified, with a gender distribution mirroring one another (50.7% vs. 49.3%). On a global scale, 98.7% of these centenarians were recipients of subsidies, indicating their reliance on state assistance due to inadequate economic means for household sustenance. Additionally, 64.9% of them were situated in urban area. No significant gender-based discrepancy was noted; however, disparities in the

Table 3
Centenarian characteristics by living areas, sex and chronic disease status.

State	Centenarians (N)	Prevalence (x 10,000 inhabitants)*	Males (%)*	Rural (%)*	Absence of chronic disease (%)*	One chronic disease (%)*	Two or more chronic diseases (%)*
Bolívar	476	12.34	47.06	30.88	90.55	2.73	6.72
Valle del Cauca	405	8.37	45.93	20.74	84.94	4.69	10.37
Magdalena	388	12.54	54.38	42.53	95.10	2.84	2.06
Atlántico	308	8.97	49.68	18.83	88.96	5.84	5.19
Sucre	256	22.34	51.95	60.16	97.27	2.34	0.39
Córdoba	252	20.77	48.41	48.02	96.03	3.57	0.40
Antioquia	207	4.65	55.56	40.58	79.71	7.73	12.56
Cesar	203	16.63	54.68	30.05	96.06	2.96	0.99
Norte de Santander	200	5.78	39	28.50	94.50	2.50	3
Santander	144	4.21	49.31	51.39	80.56	3.47	15.97
Risaralda	48	18.60	70.83	0	100	0	0
Boyacá	29	3.08	34.48	79.31	86.21	6.90	6.90
Cundinamarca	24	4.05	20.83	25	91.67	8.33	0
Bogotá	6	1.82	50	0	66.67	0	33.33
Guainía	5	2.15	60	20	80	0	20
Cauca	3	6.79	0	33.33	100	0	0
Chocó	3	3.43	33.33	0	100	0	0
Guajira	3	2.34	33.33	33.33	66.67	33.33	0
Caldas	2	2.23	0	50	100	0	0
Huila	1	1.08	0	0	100	0	0
Arauca	1	0.28	100	100	100	0	0
TOTAL	2964	8.88	49.33	35.05	90.72	3.81	5.47

* The differences in the prevalence of centenarians as well as the distribution of centenarians by sex, zone (rural or urban), and multimorbidity, were statistically significant at the 0.05 level among Colombian territories. No centenarians were registered in the following states: Meta, Tolima, Casanare, Nariño, Quindío, San Andres, Vichada, Caquetá and Putumayo.

Table 4
Prevalence of multimorbidity among centenarians.

Combination of Chronic Diseases	Number of chronic diseases	Centenarians (N)	Percentage
None	0	2689	90.72
AH	1	101	3.40
AH-CKD	2	78	2.63
AH-DM-CKD	3	32	1.08
AH-DM	2	18	0.61
POCD	1	5	0.17
AH-POCD	2	5	0.17
CVD	1	4	0.13
DM-CKD	2	4	0.13
AH-CKD-POCD	3	4	0.13
AH-DM-CKD-POCD	4	4	0.13
AH-HD	2	3	0.10
CA	1	2	0.07
AH-CKD-CA	3	2	0.07
DM	1	1	0.001
HD-POCD	2	1	0.001
CVD-HD	2	1	0.001
CKD-POCD	2	1	0.001
AH-CA	2	1	0.001
AH-CVD	2	1	0.001
AH-DM-POCD	3	1	0.001
AH-DM-CA	3	1	0.001
AH-CKD-CVD	3	1	0.001
AH-CKD-HD	3	1	0.001
AH-CKD-CVD-HD	4	1	0.001
AH-DM-CKD-CA	4	1	0.001
AH-DM-POCD-CA	4	1	0.001

Abbreviations: AH: Arterial Hypertension, POCD: Pulmonary Obstructive Chronic Disease, CVD: Cerebrovascular Disease, CA: Cancer, DM: Diabetes Mellitus, CKD: Chronic Kidney Disease, HD: Heart Disease.

socioeconomic status of centenarians were evident. These disparities reflect broader regional socio-economic and healthcare contexts such as inadequate support from both social and governmental networks during the aging process; migration from rural areas, where agricultural activities fail to yield sufficient income to meet urban living costs; and the lack of state-sponsored retirement savings mechanisms (pensions),

thereby depriving centenarians of autonomous income for sustenance (Barrientos, 2021). Bolívar, Valle del Cauca, Magdalena and Atlántico were the geographical zones (states) where the majority of COOSALUD EPS centenarians were located, with significant differences in sex, zone (rural or urban), and multimorbidity among them (Table 3). These differences may be attributed both to distinct environmental factors as well as the great genetic diversity of the Colombian population (Rojas et al., 2010).

Three centenarians' categories are defined according to Evert et al (Evert et al., 2003): 1) Escapers (individuals who reach and continue beyond the age of 100 without age-related chronic diseases); 2) Delayers (those who develop these diseases late in life after becoming centenarians), and 3) Survivors (those who reach and continue beyond 100 years while living with age-related chronic diseases). Among these, the Escaper phenotype stands out as the most prevalent (Brandão et al., 2017; Gessert et al., 2002), as in our study, accounting for 90.72%. However, and as mentioned, some chronic diseases were not included in this analysis given the retrospective design of the study and the lack of a systematic evaluation of them. From this, it can be inferred that mechanisms of protection or adaptation to stressors operate throughout the lifespans of centenarians.

In our centenarian cohort, low rates of morbidity and multimorbidity were confirmed (Table 4) (Ioakeim-Skoufa et al., 2022; von Berenberg et al., 2017). The highest prevalence of age-related chronic disease was observed in essential hypertension, with a prevalence of 8.6%. This was followed by chronic kidney disease at 4.4% and type 2 diabetes mellitus at 2.1%. Notably, there is a significant disparity in the prevalence of these diseases when compared to other age groups (Table 2) as well as with centenarians from other populations (e.g., Spain and Germany) (Ioakeim-Skoufa et al., 2022; von Berenberg et al., 2017). Differences in the prevalence of chronic diseases and multimorbidity among centenarian populations may be due to different study designs and methods, but also to diverse environment and genetic background. Certain population-related factors such as heritability may affect our cohort. Research in this area is ongoing, and new insights may emerge as our understanding of longevity and the factors contributing to it continues to evolve.

In our sample, the absence of Tuberculosis and HIV was observed,

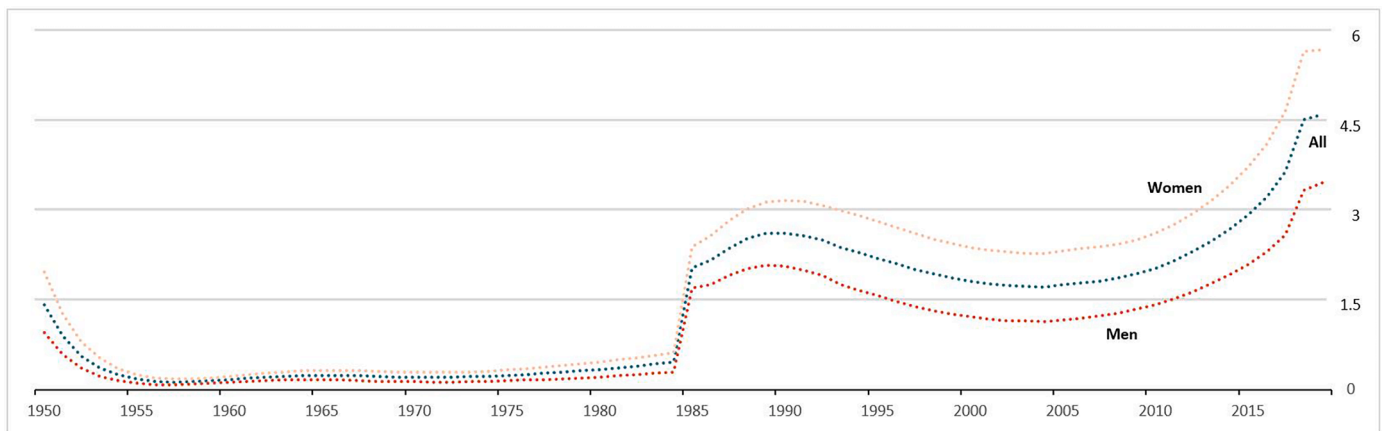


Fig. 2. Global and gender-specific rates of centenarians per 10,000 Colombian inhabitants from 1950 to 2019. Data analyzed from Colombia's state demographic surveys conducted between 1950 and 2019 (<https://www.dane.gov.co/index.php/estadisticas-por-tema/demografia-y-poblacion/censo-nacional-de-poblacion-y-vivenda-2018>).

and the prevalence of COVID-19 infection was 2%. Notably, as compared to other age groups and the prevalence of SARS-CoV-2 infection in Colombia (12.5%), this prevalence was significantly lower (<https://tinyurl.com/yc224h32>). Public health policies, intense isolation and loneliness during the lockdown, stemming from the fear of falling ill and a higher risk of experiencing severe complications due to old age (MacLeod et al., 2021), could be some of the reasons why centenarians showed a lower prevalence of SARS-CoV-2 infection. Previously, social and cultural factors have been discussed in which more vulnerable individuals, especially older adults with comorbidities, had a more prolonged and restricted isolation compared to other age groups (Tsinda & Mmbando, 2021). This contrasted with individuals in different age groups who, due to work, academic, or social situations, were more exposed to social contact. Although the virulence of the circulating viral strain, phenotypic variations, and cross-reactivity are also probable reasons (Tsinda & Mmbando, 2021), there is no precise evidence supporting these hypotheses in centenarians.

Comparisons of our findings with those of previous studies conducted on centenarians from blue zones (Aiello, Accardi, Aprile, et al., 2021; Arakawa et al., 2005; Bendjilali et al., 2014; Deiana et al., 1999; Madrigal-Leer et al., 2020; Passarino et al., 2002; Spencer-Hwang et al., 2018; Stathakos et al., 2005; Tigani et al., 2011; Willcox et al., 2017; Willcox et al., 2008), show similar trends in terms of sociodemographic characteristics, particularly in relation to the average age which ranges from 100 to 107 years. However, there are discrepancies in gender distribution, as it is often observed that women constitute most centenarians. Furthermore, significant differences were observed in the health outcomes assessed (Table 6). In our sample, the gender distribution is nearly equal, confirming previous data from the 2018 national population and housing census (López Rippe & Zapata Bravo, 2021). This lack of female predominance in our cohort is not a widely recognized or documented phenomenon. However, considering that the rate of centenarian women in Colombia is higher than that of men, the ratio of centenarian women/men correlates with those described in other blue zones (Madrigal-Leer et al., 2020; Stathakos et al., 2005; Tigani et al., 2011; Willcox et al., 2008), allowing us to affirm that the proportion of centenarian women is greater than that of men in Colombia. Therefore, the gender distribution in our cohort may be due to random error. Centenarians come from diverse backgrounds and populations, making it difficult to draw general conclusions about their physical characteristics. For example, the transition of geriatric care and its evolution have been a differentiating factor described with a relevant impact on the prognosis of centenarians, which can affect individuals differently depending on their gender (Murata et al., 2023).

On the other hand, several hypotheses have been raised to explain

the predominance of women in extreme longevity. First, survival in real cohorts followed from birth differs from survival in late-tracking cohorts subject to specific conditions. This is known as the "tempo effect," and to eliminate this bias, cohort data, not time periods, must be meticulously evaluated, which can overestimate survival (Guillot, 2006). To understand causal factors and extreme life expectancy, one must know the mortality of the entire cohort from birth, not just a population subgroup (Borgan & Keilman, 2019; Guillot, 2006). Second, social conflicts and wars often disproportionately affect men, who are enlisted in military activities, affecting their survival and life expectancy (Jawad et al., 2020). Third, there is a possible biological reason associated with the availability of two X chromosomes, which protects against mutations and epigenetic modifications (Hossin, 2021). Therefore, women may be genetically predisposed to live longer than men (Camus et al., 2012).

When comparing the clinical behavior and prevalence of some diseases among centenarians, it becomes apparent that there are significant differences in the prevalence rates (Table 6). Hence, drawing a definitive conclusion on the uniformity of clinical characteristics among centenarians on a worldwide scale is challenging. In this sense, it was observed from the existing data that cataracts is the most common disease (67%) in the Nicoya Peninsula, followed by essential hypertension (55%) and functional gastrointestinal disorders (44%) (Madrigal-Leer et al., 2020). Conversely, in the cohorts of Sicily (Aiello, Accardi, Aprile, et al., 2021), Sardinia (Deiana et al., 1999; Passarino et al., 2002) and Okinawa (Arakawa et al., 2005; Bendjilali et al., 2014; Willcox et al., 2017; Willcox et al., 2008), where the diet tends to restrict calories naturally and includes a high consumption of lean vegetables, clinical profiles typically exhibit stability, with a relative low prevalence of age-related chronic diseases, assuming that the "Escapers" phenotype predominates. While infectious and neurological diseases have not been frequently reported in these cohorts, the Nicoya Peninsula disclosed a significant percentage of psychiatric manifestations (approximately 25%) (Madrigal-Leer et al., 2020). Interestingly, in Sweden, a country without traditional blue zones and with high income levels, a national analysis of 5882 centenarians revealed that the most common comorbidities among them are congestive heart failure (22.2%), cerebrovascular disease (18.5%), and acute myocardial infarction (13.7%). However, as discussed previously, the morbidity rates were higher in men, except in the case of dementia (6.6% vs. 10.5%) and rheumatic diseases (2.6% vs. 4.1%), where it was more common in women (Murata et al., 2023). These manifestations may be linked to sociodemographic factors and social determinants of health in centenarians that have not undergone extensive scrutiny in these regions. Nevertheless, it becomes evident that centenarians described in these cohorts, as indicated by phenotypic and molecular parameter results, as well as in our

Table 5
Characteristics and results of previous studies on centenarians in Colombia.

Authors	Number of participants and study design	Objective	Main results
(Rosselli et al., 2017)	N=3165 Secondary analysis	To estimate the number and geographic distribution of centenarians in Colombia using three databases with information spanning from 2005 to 2014	Three regions exhibiting the highest centenarian rates during the assessed time frame were discerned: La Guajira (with a rate of 2.22 centenarians per 10,000 inhabitants), Chocó (1.90), and Sucre (1.61). Furthermore, the regions boasting the greatest prevalence of centenarians were Sucre (2.17 per 10,000 inhabitants), Chocó (1.29), and Córdoba (1.11). Delirium (31%), dementia (15%), and falls (15%) were identified as the most prevalent geriatric syndromes. Hospital mortality stood at 53%, with community-acquired pneumonia and heart failure ranking as the most diagnosed conditions during hospitalization. Respiratory causes (26%) and falls (19.6%) were determined as the prevailing motives for consultation. Hospital mortality stood at 18.2%, with over 90% manifesting at least one geriatric syndrome. Additionally, 62.4% displayed varying degrees of dependence, ranging from moderate to severe or total. The assessment revealed that the centenarians were predominantly multimorbid. It was determined that there is a ratio of 1.38 women for every centenarian man. It was observed that possessing some level of formal education, being in a partnership, not being affiliated with an ethnic group, and
(Gutiérrez et al., 2014)	N=29 Descriptive study	To describe the clinical characteristics of centenarians treated in the emergency room at a tertiary center between 2005 and 2012	Delirium (31%), dementia (15%), and falls (15%) were identified as the most prevalent geriatric syndromes. Hospital mortality stood at 53%, with community-acquired pneumonia and heart failure ranking as the most diagnosed conditions during hospitalization. Respiratory causes (26%) and falls (19.6%) were determined as the prevailing motives for consultation. Hospital mortality stood at 18.2%, with over 90% manifesting at least one geriatric syndrome. Additionally, 62.4% displayed varying degrees of dependence, ranging from moderate to severe or total. The assessment revealed that the centenarians were predominantly multimorbid. It was determined that there is a ratio of 1.38 women for every centenarian man. It was observed that possessing some level of formal education, being in a partnership, not being affiliated with an ethnic group, and
(Ibarra Chacón & Parra Hernández, 2019)	N=77 Descriptive study	To describe the in-hospital morbidity and mortality among centenarians treated in the emergency room at a tertiary center between 2011 and 2018.	Delirium (31%), dementia (15%), and falls (15%) were identified as the most prevalent geriatric syndromes. Hospital mortality stood at 53%, with community-acquired pneumonia and heart failure ranking as the most diagnosed conditions during hospitalization. Respiratory causes (26%) and falls (19.6%) were determined as the prevailing motives for consultation. Hospital mortality stood at 18.2%, with over 90% manifesting at least one geriatric syndrome. Additionally, 62.4% displayed varying degrees of dependence, ranging from moderate to severe or total. The assessment revealed that the centenarians were predominantly multimorbid. It was determined that there is a ratio of 1.38 women for every centenarian man. It was observed that possessing some level of formal education, being in a partnership, not being affiliated with an ethnic group, and
(López Rippe & Zapata Bravo, 2021)	N=767 (n=485; physicians) Secondary analysis	To explore the sociodemographic characteristics and healthcare satisfaction levels of older adults aged 60 and above (including centenarians), based on the results of a Colombian national census conducted in 2018.	Delirium (31%), dementia (15%), and falls (15%) were identified as the most prevalent geriatric syndromes. Hospital mortality stood at 53%, with community-acquired pneumonia and heart failure ranking as the most diagnosed conditions during hospitalization. Respiratory causes (26%) and falls (19.6%) were determined as the prevailing motives for consultation. Hospital mortality stood at 18.2%, with over 90% manifesting at least one geriatric syndrome. Additionally, 62.4% displayed varying degrees of dependence, ranging from moderate to severe or total. The assessment revealed that the centenarians were predominantly multimorbid. It was determined that there is a ratio of 1.38 women for every centenarian man. It was observed that possessing some level of formal education, being in a partnership, not being affiliated with an ethnic group, and

Table 5 (continued)

Authors	Number of participants and study design	Objective	Main results
			not encountering daily life difficulties could potentially be factors linked to exceptional longevity.

own cohort, generally maintain stability. This observation reflects a successful aging process and a significant delay in biological age compared to the prevalence of chronic diseases in other age groups. However, unlike other blue zones, Colombia is a high mixed-race and multi-ethnic country (Ossa et al., 2016). Authors have previously mentioned that this factor is essential in the stratification of the risk of developing an age-related chronic disease, with a tendency towards a decrease in risk (Martschenko et al., 2023; Razieh et al., 2022). This fits with the low prevalence we observed in our cohort compared to what is known in the blue zones around the world. Moreover, it is also a novel variable that, from a translational perspective, could provide useful and original information about genetic and biological variants specific to this population, with the potential to confer protection against developing chronic diseases (Martschenko et al., 2023). This is a point that is currently under development in the COOLCEN cohort.

The phenomena of health stability may be examined from several theoretical frameworks, including the interplay between proteodynamics, longevity, and centenarians (Frankowska et al., 2023). This hypothesis posits that individuals inclined toward longevity, combined with certain environmental protective factors, exhibit exceptional cellular dynamics. This manifests in enhanced regulation of epigenetic and post-translational errors, contributing to a delay in cellular senescence and, consequently, biological aging (Frankowska et al., 2023; Witkowski et al., 2021). Ageing of the immune system, or immunosenescence, also contributes to the morbidity and mortality of the elderly (Yousefzadeh et al., 2021). An aged, senescent immune system has a causal role in driving systemic ageing and therefore represents a key therapeutic target to extend healthy ageing (Yousefzadeh et al., 2021). Immune resilience, defined as the capacity to preserve and/or rapidly restore immune functions that promote disease resistance (immunocompetence) and control inflammation in infectious diseases as well as other causes of inflammatory stress, is a trait observed across the age spectrum aligned with a specific immunocompetence-inflammation balance linked to favorable immunity-dependent health outcomes (Ahuja et al., 2023). Persons with optimal immune resilience have health and survival advantages (Ahuja et al., 2023). This, in turn, may reduce the chance of developing cancer, autoimmune disorders, pulmonary conditions, or cardiometabolic diseases, even when exposed to risk factors throughout life. Concerning chronic infectious diseases, exposure to these microorganisms and the natural progression of these diseases, even in adulthood (between 70 and 80 years), drastically diminish the likelihood of reaching 100 years due to the prognostic implications of these conditions (Lelisho et al., 2022; Wing, 2017). These observations could clarify the figures discerned in the analysis.

There are limitations to our study, including its retrospective design, as well as potential drawbacks associated with registry-based studies. Because data in registries are collected from various centers, there can be substantial variation in the auditing and control measures employed and the quality of the data gathered. The absence of systematic recording or the lack of employment of specialized tools for evaluation might be ascribed to the missing variables. Such was the case with mental, neurological and autoimmune diseases, not included into our analyses. Future longitudinal studies may overcome these shortcomings.

Table 6
Demographics and clinical characteristics of Colombian centenarians compared with centenarians from blue zones.

Variable	Colombia N=2964	Sardinia (Italy) N=222 (Deiana et al., 1999; Fastame et al., 2020; Passarino et al., 2002)	Nicoya (Costa Rica) N=43 (Madrigal-Leer et al., 2020)	Greece N=489 (Stathakos et al., 2005; Tigani et al., 2011)	Okinawa (Japan) N=1644 (Arakawa et al., 2005; Willcox et al., 2008)	p- value
	Frequency (%)					
Age (range)	(100 – 112)	(99 – 110)	(100 – 107)	(99 – 109)	(99 – 112)	-
Female	1502 (50.7)	149 (67)	25 (58)	376 (76.8)	1378 (83.8)	< 0.001
Urban area	1925 (64.9)	ND	ND	107/400 (26.7)	ND	< 0.001
Diabetes	63 (2.1)	ND	5 (11.6)	11 (2.2)	ND	0.002
Hypertension	256 (8.6)	ND	24 (55.8)	66 (13.7)	479 (29.1)	< 0.001
Cerebrovascular disease	8 (0.3)	ND	ND	23 (4.7)	180 (11)	< 0.001
Heart disease	7 (0.2)	ND	4 (9.3)	9 (1.8)	ND	< 0.001
Chronic kidney disease	129 (4.4)	ND	2 (4.6)	ND	ND	NS
Cancer	8 (0.3)	ND	3 (6.9)†	7 (1.45)	ND	< 0.001
Arthropathy*	0	ND	11 (25.5)	74 (15.4)	ND	< 0.001
Hemophilia	0	ND	ND	ND	ND	NA
Orphan and rare disease	0	ND	ND	ND	ND	NA
Human immunodeficiency virus	0	ND	0	ND	ND	NA
Asthma	0	ND	0	ND	ND	NA
Chronic obstructive pulmonary disease	22 (0.7)	ND	9 (20.9)	ND	ND	< 0.001
Transplant	0	ND	ND	ND	ND	NA
Tuberculosis‡	0	ND	ND	4 (0.8)	ND	0.002
History of tobacco consumption	ND	ND	14 (32.59)	37 (9.25)	438 (36.6)	< 0.001
History of alcohol consumption	ND	ND	16 (37.2)	ND	208 (12.7)	< 0.001
Poverty status	ND	ND	43 (100)	ND	ND	NA
No literacy	ND	ND	19 (41.2)	295/480 (61.4)	ND	0.026

No data were evaluated for Loma Linda, due to lack of accurate data.

ND: No data (or lack of accurate data); NS: Not significant, NA: not applicable.

*Includes inflammatory arthritis or osteoarthritis.

‡History of tuberculosis.

†Reported as tumors.

5. Conclusion

The COOLCEN cohort has a low prevalence of age-related chronic diseases, low economic status and no difference in gender distribution. In addition, it was identified that the areas with the highest prevalence of centenarians are the coastal regions. These findings represent a valuable research resource for exploring and contrasting centenarian phenotypes based on clinical, sociodemographic, and biological (e.g., genetics, immune) variables. Studying centenarians provides valuable insights into healthy aging, disease prevention, and improving the well-being of older adults. It has the potential to advance scientific understanding, influence public health strategies, and ultimately enable more people to live longer, healthier lives.

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Ethics statement

The institutional review board of COOSALUD EPS approved the study design.

CRediT authorship contribution statement

Ivan David Lozada-Martinez: Methodology, Data curation, Formal analysis, Visualization, Investigation, Writing – original draft, Writing – review & editing. **Juan Sebastian Marin:** Methodology, Data curation, Formal analysis, Visualization, Investigation, Writing – original draft, Writing – review & editing. **Sandra Milena Castelblanco-Toro:** Methodology, Investigation, Writing – original draft, Writing – review & editing. **Enrique A Mazonett-Granados:** Methodology, Investigation, Writing – review & editing. **John Fredy Suárez:** Methodology, Investigation, Writing – review & editing. **Mauricio Sarmiento:** Methodology, Investigation, Writing – review & editing. **Juan-Manuel Anaya:** Conceptualization, Methodology, Data curation, Project administration, Supervision, Writing – original draft, Writing – review & editing.

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.

Data availability

Data will be made available on request.

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