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Beatriz Novak

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Multimorbidity and the combination of chronic non-communicable diseases and their relationship to all-cause mortality among Costa Rican older adults

Multimorbilidad y la combinación de enfermedades crónicas no comunicables y su relación con la mortalidad por todas las causas en adultos mayores de Costa Rica

Beatriz Novak [1]

Abstract: Objective: To estimate the prevalence of multimorbidity due to chronic non-communicable diseases, the prevalence of pairs and triads of these diseases and the respective associated mortality risks in older adults in Costa Rica. **Methods:** The data used belong to the study Costa Rica: Longevity and Healthy Aging Study. Gompertz models (adjusted for sociodemographic factors, health-related behaviors, and functional status) were estimated to assess the association of multimorbidity with all-cause mortality between 2005 and 2009. The study population comprised 2,565 individuals who provided data on all covariates at baseline. **Results:** The prevalence of multimorbidity was 42.6%. The five most frequent disease pairs combine hypertension with diabetes, coronary heart disease, respiratory conditions, arthritis, and osteoporosis (around 14%, 10%, 9%, 7%, and 6%, respectively). The most frequent disease triads were diabetes-hypertension-respiratory conditions and diabetes-hypertension-coronary heart disease (about 3% in both cases). Multimorbidity was associated with 64% increased mortality risk, not adjusting for functional limitations, and 37% when adjusting for functional limitations. The following disease pairs at baseline increased the mortality risk, compared to persons without these combinations at baseline: diabetes-hypertension (49%); cancer-respiratory disease, diabetes-coronary heart disease, and diabetes-stroke (around two times); and cancer-hypertension and cancer-diabetes (around three times). The mortality risk among those with diabetes-hypertension-coronary heart disease and diabetes-hypertension-osteoporosis was twice that of persons without these diseases at baseline. **Conclusion:** There is a need to develop strategies to address the burdens that multimorbidity, particularly cardiometabolic multimorbidity, impose on individuals as well as on the healthcare system.

Palabras clave: Multimorbidity, Noncommunicable chronic diseases, Mortality.

Resumen: Objetivo: Estimar la prevalencia de multimorbilidad por enfermedades crónicas no transmisibles, la prevalencia de pares y tríadas de estas enfermedades y el respectivo riesgo de mortalidad asociado en adultos mayores de Costa Rica. **Métodos:** Los datos pertenecen al estudio Costa Rica: Estudio de Longevidad y Envejecimiento Saludable, un estudio longitudinal representativo a nivel nacional de 2,831 costarricenses de 60 años o más en 2005. Se estimaron modelos de Gompertz (ajustados por factores sociodemográficos, comportamientos relacionados con la salud y estatus funcional) para analizar la asociación de la multimorbilidad con la mortalidad por todas las causas entre 2005 y 2009. La población estudiada consiste en 2,565 personas con información en todas las variables de interés en la línea basal. **Resultados:** La prevalencia de multimorbilidad fue 42,6%. Los pares de enfermedades crónicas más frecuentes combinan hipertensión con diabetes, cardiopatía coronaria, enfermedades respiratorias, artritis y osteoporosis (14%, 10%, 9%, 7% y 6%, respectivamente). Las tríadas más frecuentes son diabetes-hipertensión-enfermedades respiratorias (3%) y diabetes-hipertensión-cardiopatía coronaria (3%). La multimorbilidad incrementa 64% el riesgo de muerte, si no se ajusta por limitaciones funcionales, y 37% ajustando por ellas. Las siguientes combinaciones incrementan el riesgo de muerte, comparando con personas sin estas combinaciones de enfermedades al inicio del estudio: diabetes-hipertensión (49%); cáncer-enfermedades respiratorias, diabetes-cardiopatía coronaria, y diabetes-apoplejía (100%); cáncer-hipertensión y cáncer-diabetes (200%); diabetes-hipertensión-cardiopatía coronaria y diabetes-hipertensión-osteoporosis (100%). **Conclusión:** Es necesario desarrollar estrategias para hacer frente a la carga que la multimorbilidad, especialmente a multimorbilidad cardiometabólica, impone a los individuos y al sistema de salud.

[1] El Colegio de México, MÉXICO. bnovak@colmex.mx

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Keywords: Multimorbilidad, Enfermedades crónicas no transmisibles, Mortalidad.

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1. Introduction

An increase in the relative weight of non-communicable chronic diseases (NCDs) in the morbidity patterns followed the aging process, not only in the populations of high-income countries, but also in those of low- and middle-income countries (World Health Organization - WHO, 2015). Consequently, the prevalence of multimorbidity, the coexistence of two or more NCDs (Ording & Sørensen, 2013), is increasing (Vancampfort et al., 2017), and the number of individuals with multimorbidity is escalating. People with multiple NCDs, compared to those with only one NCD, are at a greater risk of disability, hospitalization, reduced quality of life, development of various mental disorders and depression, and ultimately death (Onder et al., 2015). The evidence indicates that the presence of multiple NCDs is associated with 44.0% increased risk of mortality and that for each chronic disease under consideration, there is 20% increase in the risk of death (Nunes et al., 2016). Life expectancy at age 67 decreases by 1.8 years for each additional disease, with the decrease in life expectancy ranging from 0.4 years for the first chronic condition to 2.6 years for the sixth (DuGoff et al., 2014).

Costa Rica, like other Latin American countries, is witnessing the aging of its population at an accelerated speed. From 2010 to 2019, the proportion of Costa Rican citizens aged 65 and above increased by 2.9% (Ministry of Health, 2019). In 2008, adults aged 65 years and over constituted 6.2% of the total population. By 2019, this figure had risen to 8.5%. It is estimated that by the year 2050, this proportion would reach 20.7% (University of Costa Rica et al., 2020). At the same time the prevalence of type 2 diabetes mellitus, hypertension, and cardiovascular disease (CVD) increased over time (Santamaría-Ulloa et al., 2019; University of Costa Rica et al., 2020). In 2019, NCDs accounted for 80.7% of all deaths (31.7% for CVDs, 26.5% for cancer, 6.9% for chronic obstructive pulmonary disease, 4.7% for diabetes, and 30.1% for other chronic diseases) (Ministry of Health, 2021). Although the death rate for adults aged 65 and older decreased by 14% between 2000 and 2018, primarily due to a decrease in cardiovascular deaths, it remains the leading cause of death for people in this age group, followed by cancer.

Both, type 2 diabetes and hypertension are important risk factors for CVD, which, as mentioned earlier, is the leading cause of death in Costa Rica, especially among people over 60 years of age (Navarro-Ureña et al., 2019). Results from the 2011 Costa Rican National Survey of Cardiovascular Risk Factors showed that the group with the highest prevalence of hypertension was composed of individuals aged 65 years and older. In 2015, this age group also had the highest prevalence of diagnosed hypertension, at 65.3% among men and at 74.8% among women (Ministry of Health, 2021). In 2010, the prevalence of type 2 diabetes among individuals aged 65 years and over was 26.5%, 19.5% among men, and 32.7% among women (Wong-McClure, 2016). In 2018, the prevalence of diabetes among individuals in the same age group was 28.0%, 26% among men, and 30% among

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women (University of Costa Rica et al., 2020). Mortality rate for diabetes mellitus increased between 2000 and 2018 (University of Costa Rica et al., 2020). It is estimated that the effect of diabetes on life expectancy at age 60 in the year 2035 will result in a reduction of approximately seven months (Santamaría-Ulloa & Montero-López, 2020).

In recent decades, malignant tumor related conditions have increased in Costa Rica (Ministry of Health, 2019). In 2020, Costa Rica exhibited the highest cancer mortality rate in Central America. The highest rates among men were observed for gastric and prostate cancer, while for women, the most significant cancer-related mortality was attributed to breast cancer (Calderón et al., 2023). Although, compared with other Latin American countries, stroke-related mortality rates are low in Costa Rica, stroke is still a public health problem due to its consequences, particularly as a cause of disability (Pabón-Páramo, 2020). Costa Rica's 2018 National Disability Survey revealed that 24% of people aged 60 years and older with multimorbidity were in a situation of dependency for the performance of basic activities of daily living. This figure was 38% among those over 80 years of age (Medellín et al., 2019). In addition, it was estimated that life expectancy in Costa Rica at age 60 was 23.3 years (95% CI [22.9-25.8]), while multimorbid life-expectancy was 11.5 years (95% CI [9.3-13.8]) and disabling multimorbidity was 5.5 years (95% CI [4.2-6.9]). For females, these figures were 25.1 years (95% CI [23.3-26.9]), 15.2 years (95% CI [12.9-17.4]), and 8.6 years (95% CI [7.2-10.0]) for life expectancy, multimorbid life expectancy, and disabling multimorbidity (Lam et al., 2024).

The presence of multiple NCDs requiring the use of drugs can result in the development of polypharmacy. The practice of polypharmacy has the potential to exert adverse effects on the patient's health. These effects may arise from a variety of sources, including interactions between the medications themselves or between the medications and the patient's underlying disease or other medications that the patient is taking (Salive, 2013). In low- and middle-income countries, particularly in Latin America, the structure of health systems is not designed to address the complexities of multimorbidity (Miranda et al., 2019). Prior research indicates that the prevalence of polypharmacy among older adults in Costa Rica is already considerable, with approximately 60% of individuals taking at least four medications and approximately 50% of diabetic patients taking more than five medications simultaneously (Jiménez Herrera & Fernández Rojas, 2008).

Furthermore, the economic impact of NCDs represents a significant concern. For individuals and households seeking care, as well as for the health system, NCDs impose significant financial costs (WHO, 2018). Per capita estimates (in 2015 dollars) indicate that gross domestic product (GDP) losses in Costa Rica between 2015 and 2030 would be in the order of 961, 1514, 3238, and 1275, due to diabetes, cardiovascular diseases, respiratory diseases, and cancer, respectively (Bloom et al., 2018).

Despite the high prevalence of NCDs among Costa Rican older adults, the existing research on the impacts, including mortality, of multimorbidity and different combinations of NCDs is limited. New strategies can be developed to address the needs of people with multimorbidity by knowing which diseases are combined in the same individual. For all of the above, the objective of this study was to estimate the prevalence of multimorbidity due to NCDs (defined as having two or more NCDs), the

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prevalence of pairs and triads of these diseases and their associated risk of all-cause mortality between 2005 and 2009 in individuals aged 60 years or older living in Costa Rica at baseline.

2. Methods

2.1 Data source

The data utilized in this study were derived from the 2005, 2007, and 2009 Costa Rican Study on Longevity and Healthy Aging (CRELES), a nationally representative longitudinal survey of the health and life experiences of 2,831 Costa Ricans aged 60 years and over in 2005. The main objective of the study was to examine the relationship between the exceptionally high longevity of older adults in Costa Rica and a number of factors, including their health, nutritional status, socioeconomic status, life-course behaviors, family support and life conditions, as well as their access to, use of, and expenditures on healthcare. The sample design for the CRELES study was based on the 2000 Costa Rican Population Census. To account for the complex sample design and non-response rates, the sampling weights were calculated as the inverse of selection probabilities. The Science and Ethics Committee of the University of Costa Rica approved the CRELES study (session reference VI-763-CEC-23-04) (National Archive of Computerized Data on Aging, 2013).

2.2 Study population

The study population was restricted to respondents who provided data on all covariates. During the mortality observation period, between 2005 and 2009, 565 deaths were recorded. Of the 2,831 original respondents, 266 were excluded due to lack of information on the variables of interest, bringing the final sample size to 2,565 (90.6% of the original sample) and 473 registered deaths (83.7% of the total registered deaths).

2.3 Sampling weights

The CRELES study includes a variable containing sample weights to correct for the oversampling of individuals aged 95 years or older and the higher rate of nonresponse among younger men of higher socioeconomic status residing in urban settings (National Archive of Computerized Data on Aging, 2013).

2.4 Multimorbidity

There are different approaches to measuring multimorbidity. However, counting the number of chronic diseases from a list of individual diseases is the most used measure for assessing multimorbidity because of its simplicity (Lefèvre et al., 2014). The CRELES study employs self-report data on eight NCDs. Accordingly, multimorbidity was defined as the number of the following diseases: arthritis, cancer, diabetes, hypertension, osteoporosis, respiratory conditions, stroke, and coronary heart disease (CHD).

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2.5 Control variables

Evidence from older adult literature suggests that a number of factors are related to the risk of all-cause and specific mortality, such as education, marital status, health behaviors, and functional impairment (Carr et al., 2023; Fukushima et al., 2024; IHME-CHAIN Collaborators, 2024; Klopack et al., 2022; Sánchez-Sánchez et al., 2024; Wang & Yi, 2023).

The set of covariates is composed of the following variables: age (continuous); educational level (0= Elementary school incomplete, 1= No formal education, 1= Elementary complete, 2= More than elementary education); marital status (0= Married/cohabiting, 1= Single/separated/divorced/widowed); current smoker (0= No, 1= Yes); and physical activities (0= No, 1= Yes); physical activities (0= No, 1= Yes) , and body mass index (BMI). BMI was calculated using body weight (in kg) and body height (in meters) as kg/m2 (0= Normal weight, 18.5≤BMI<25, 1= Underweight, BMI<18.5, 2= Overweight, 25≤BMI<30, 3= Obese, BMI≥30). Body height and weight were measured by trained professionals.

In addition, two indexes were included to consider functional status: the Activities of Daily Living (ADL) index, which considers functional ability in four basic categories, personal hygiene, continence, eating, and mobility (0= No limitations; 1= One limitation; 2= 2 to 9 limitations); and, the Instrumental Activities of Daily Living (IADL) index, which considers the ability to prepare food, buy food or clothing, manage money and medicines (0= No limitations; 1= One limitation; 2= 2 to 4 limitations).

2.6 Methods

Gompertz models were used to estimate the effect of multimorbidity on the risk of death controlling for other predictors of mortality and lifestyle factors. The Gompertz function has been shown to provide an effective description of all-cause mortality (Juckett & Rosenberg, 1993). In this model, the mortality rate associated with age exhibits an exponential growth pattern, whereby the initial mortality rate is multiplied by a factor that increases exponentially with age. From a biological perspective, the Gompertz model suggests that the observed increase in mortality rates with age reflects an increased vulnerability to mortality causes experienced by young adults (Ricklefs & Scheuerlein, 2002).

The longitudinal design of the CRELES study allows for the application of survival analysis techniques. The CRELES study provides information on the exact date of entry into the study and the date of exit from the study, which is either the date of death or the date of completion of the follow-up period. The vital status of the respondents was retrieved from the information provided by the 2007 and 2009 waves. Follow-up time for individuals included in the analytical sample was 4.79 years (mean 3.02 years and median 3.57 years). Survival duration was measured in days, from the day of study entry to the day of death or lost to follow-up.

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The Gompertz model, expressed in the proportional hazard metric, can be formulated as follows:

$$\mu(t/x_j) = \mu_0(t)\exp(x_j\beta_j)$$

Where, μ_0, the baseline hazard, is:

$$\mu_0(t) = \exp(\gamma t)\exp(\beta_0)$$

Therefore,

$$\mu(t\ /\ x_j) = exp\ (\gamma t) exp\ (\beta_0 + x_j\beta_j)$$

Here, Y is the shape parameter and $exp(\beta_0)$ Is the scale parameter. If $\gamma > 0$, $\mu(t)$ is a monotonically increasing function. If $\gamma > 0$, $\mu(t)$ is a monotonically decreasing function. When $\gamma > 0$, $\mu(t)$ is constant. X is a vector of variables containing information on each individual j. In addition to multimorbidity, vector x incorporates the control variables previously outlined. These variables were evaluated at baseline.

2.6.1 *Analytical strategy*

First, the prevalence of individual NCDs, of multimorbidity, and of all possible pairs and triads of NCDs were estimated. Secondly, Gompertz models were employed to evaluate the effect of each NCD individually and of multimorbidity on all-cause mortality, as well as for all pairs and triads of NCDs with a prevalence exceeding 1.0%. This limitation was imposed to circumvent any spurious associations (Guisado-Clavero et al., 2018).

In all cases, two models were estimated. The initial model (Model a) was adjusted for age, sex, demographic and socioeconomic variables (educational attainment and marital status), and health-related behavioral variables (smoking status, BMI, and physical activity). The second model (Model b) incorporated functional status into Model a. The mortality risk of individuals with multimorbidity was compared to the mortality risk of those with zero or one chronic disease (Nunes et al., 2016). A comparison was made between individuals with a specific combination of NCDs and those without such a combination, including those without any NCDs.

P-values < 0.05 were considered statistically significant. All statistical analyses were performed using Stata, version 17 (StataCorp LLC, College Station, Texas).

3. Resultados

The mean age of the participants in the analytical sample was 70 years (SE = 0.17, range = 60-109 years). The sample was composed of 52% female and 61% married or cohabiting individuals. Moreover, 49% of the respondents had completed at least the primary level of education. Most respondents (90%) were not current smokers. Approximately 69% of respondents were overweight or obese, while approximately 68% did not engage in regular exercise. Forty-two percent of

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respondents had two or more limitations in ADLs, and approximately 14% had two or more limitations in IADLs. The prevalence of multimorbidity among individuals in this population was found to be nearly 43% (Table 1). The results of statistical tests conducted to verify the equality of proportions between individuals with and without multimorbidity (Table 2) revealed that those with multimorbidity were more likely to be older, female, and to have received only some elementary education than those without multimorbidity. In addition, they were more likely to be obese and to have two or more limitations in both activities of daily living (ADLs) and instrumental activities of daily living (IADLs).

When considered individually, Table 3 shows that hypertension was the most prevalent NCD, affecting 48% of the population, followed by diabetes, which affected approximately 21% of the population. The prevalence of respiratory conditions, CHD, and arthritis was observed to be between 14% and 17%. Table 3 indicates that the prevalence of cancer and stroke was approximately 6% and 4%, respectively.

In total, there were 23 combinations of two NCDs and 12 combinations of three NCDs. The five most frequently occurring disease pairs were hypertension in conjunction with diabetes, CHD, respiratory conditions, arthritis, and osteoporosis, with a prevalence of 14%, 10%, 9%, 7%, and 6%, respectively. In all but one instance, hypertension formed part of a triad of NCDs. The two most prevalent triads were diabetes-hypertension-respiratory conditions (3.2%) and diabetes-hypertension-CDH (3.1%) (Table 3).

3.1.1 *Mortality risk*

The all-cause mortality risk of individuals with arthritis, hypertension, osteoporosis, and respiratory conditions was found to be comparable to that of individuals without these diseases. However, individuals with cardiometabolic diseases or cancer exhibit an elevated risk of mortality from all causes in comparison to those who are not affected by these diseases. The highest risk of mortality is observed among individuals with CHD, at 55%. In comparison, individuals with a history of stroke have a mortality risk that is more than double that of people without stroke at baseline (Figure 1, panel a). Including functional limitations, the all-cause mortality risk in individuals with a history of stroke at baseline was no longer statistically significant. (Figure 1, panel b). In comparison to individuals without multimorbidity, the risk of mortality was found to be 64% higher when the model was not adjusted for functional limitations (Relative Risk (RR) = 1.64, 95% Confidence Interval (95% CI) [1.28; 2.10], $p < 0.001$) (Figure 1, panel a). Furthermore, when functional limitations were considered, the risk of mortality was found to be 37% higher (RR=1.37, 95% CI [1.07; 1.75], $p<0.010$) (Figure 1, panel b).

The mortality risk associated with specific NCD pairs was similar to that observed in their respective reference groups (Figure 2, panels a and b). In contrast, the all-cause mortality risk of respondents with cancer-diabetes, cancer-hypertension, cancer-respiratory conditions, CHD-diabetes, CHD-

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hypertension, CHD-stroke, diabetes-hypertension, diabetes-stroke, hypertension-osteoporosis, and hypertension-stroke at baseline, was higher than the mortality risk of the respective reference groups. These combinations increased the all-cause mortality risks between 52%,, among respondents with CHD-hypertension, to 3.7 times, among those with cancer-diabetes, compared to those in their respective reference groups (Figure 2, panel a).

Table 1

Baseline characteristics of the weighted analytical sample (CRELES, 2005)

Variable	% in sample (N = 2,565)
Sex	
Males	47.80
Females	52.20
Educational level	
No formal education	13.09
Elementary incomplete	37.55
Elementary complete	27.78
More than elementary	21.58
Marital status	
Married/cohabiting	60.89
Single/separated/divorced/widowed	39.11
Current smoker	
Yes	9.79
No	90.21
Body mass index (BMI)	
Underweight	3.11
Normal	28.13
Overweight	42.14

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Obese	26.61
Activities of daily living (ADL)	
0 Limitations	39.18
1 Limitation	19.10
2+ Limitations	41.72
Instrumental activities of daily living (IADL)	
0 Limitations	77.91
1 Limitation	7.65
2+ Limitations	14.44
Physical activity	
Yes	32.07
No	67.93
Multimorbidity	
Yes (2+ Chronic diseases)	42.57
No (0/1 Chronic diseases)	57.43

N = Analytical sample size.

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Table 2

Baseline characteristics of the weighted analytical sample, by multimorbidity status at baseline (CRELES, 2005)

Variable	0/1 NCD (N = 1,473)	2+ NCD (N = 1,092)	*p* value[a]
Age (Mean, SE)	69.76 (0.22)	71.03 (0.28)	< 0.001
Sex (%)			
Female	44.61	62.43	< 0.001
Male	55.39	37.57	< 0.001
Educational level (%)			
No formal education	12.39	14.03	0.223
Elementary incomplete	35.75	39.98	0.029
Elementary complete	29.42	25.57	0.031
More than elementary	22.44	20.42	0.219
Marital status (%)			
Married/Cohabiting	62.67	58.48	0.031
Single/Separated/Divorced/Widowed	37.33	41.52	0.031
Current smoker (%)			
Yes	12.60	6.01	< 0.001
No	87.40	93.99	< 0.001
Body Mass Index BMI (%)			
Underweight	3.41	2.71	0.313
Normal	31.85	23.12	< 0.001
Overweight	43.52	40.28	0.100
Obese	21.22	33.89	< 0.001
Activities of daily living (ADL) (%)			
0 Limitations	48.92	26.04	< 0.001
1 Limitation	19.25	18.89	0.819
2+ Limitations	31.83	55.07	< 0.001
Instrumental activities of daily living (IADL) (%)			
0 Limitations	83.15	70.84	< 0.001
1 Limitation	5.20	10.96	< 0.001
2+ Limitations	11.65	18.20	< 0.001
Physical activity (%)			
Yes	38.26	23.73	< 0.001
No	61.74	76.27	< 0.001

N = Analytical sample size; NCD = Non-communicable chronic disease; SE = Standard error.

[a] p-value for the difference between individuals with 0/1 and 2+ chronic diseases multimorbidity).

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Table 3

Weighted prevalence of one chronic disease and all possible combinations of two and three non-communicable chronic diseases with prevalence >1.0% at baseline

One NCD	%	Two NCDs	%	Three NCDs	%
HYP	48.50	HYP-DIA	14.22	HYP-DIA-RES	3.18
DIA	20.82	HYP-CHD	10.52	HYP-DIA-CHD	3.10
RES	16.58	HYP-RES	8.85	HYP-CHD-RES	2.00
CHD	15.20	HYP-ART	7.13	HYP-ART-DIA	1.69
ART	14.19	HYP-OST	5.65	HYP-ART-OST	1.68
OST	9.80	DIA-CHD	4.29	HYP-ART-CHD	1.65
CAN	5.91	DIA-RES	4.21	HYP-ART-RES	1.55
STR	3.63	CHD-RES	3.27	HYP-OST-CHD	1.50
		ART-OST	2.83	HYP-OST-DIA	1.45
		ART-RES	2.80	HYP-OST-RES	1.31
		ART-DIA	2.74	DIA-CHD-RES	1.19
		ART-CHD	2.59	HYP-STR-DIA	1.02
		HYP-CAN	2.59		
		HYP-STR	2.56		
		OST-RES	2.32		
		OST-CHD	2.18		
		OST-DIA	2.13		
		CAN-DIA	1.66		
		CAN-CHD	1.24		
		STR-CHD	1.23		
		STR-DIA	1.21		
		CAN-ART	1.14		
		CAN-RES	1.06		

ART = Arthritis; CAN = Cancer; CHD = Coronary heart disease; DIA = Diabetes; HYP = Hypertension; OST = Osteoporosis; RES = Respiratory conditions; STR = Stroke.

After adding functional limitations to the model, the all-cause mortality risk among individuals with CHD-hypertension, CHD-stroke, and hypertension-osteoporosis at baseline was comparable to the mortality risk observed in their respective reference groups. The remaining NCD pairs remained statistically significant, increasing the risk of all-cause mortality from 49%, for CHD-hypertension, to 3.50 times, for cancer-diabetes (Figure 2, panel b). The presence of cancer in conjunction with other health conditions has been demonstrated to exert a synergistic effect, thereby increasing the risk of mortality (Ferrer et al., 2017). Therefore, the coexistence of cancer with diabetes, hypertension, and respiratory conditions increased the mortality risks associated with these diseases.

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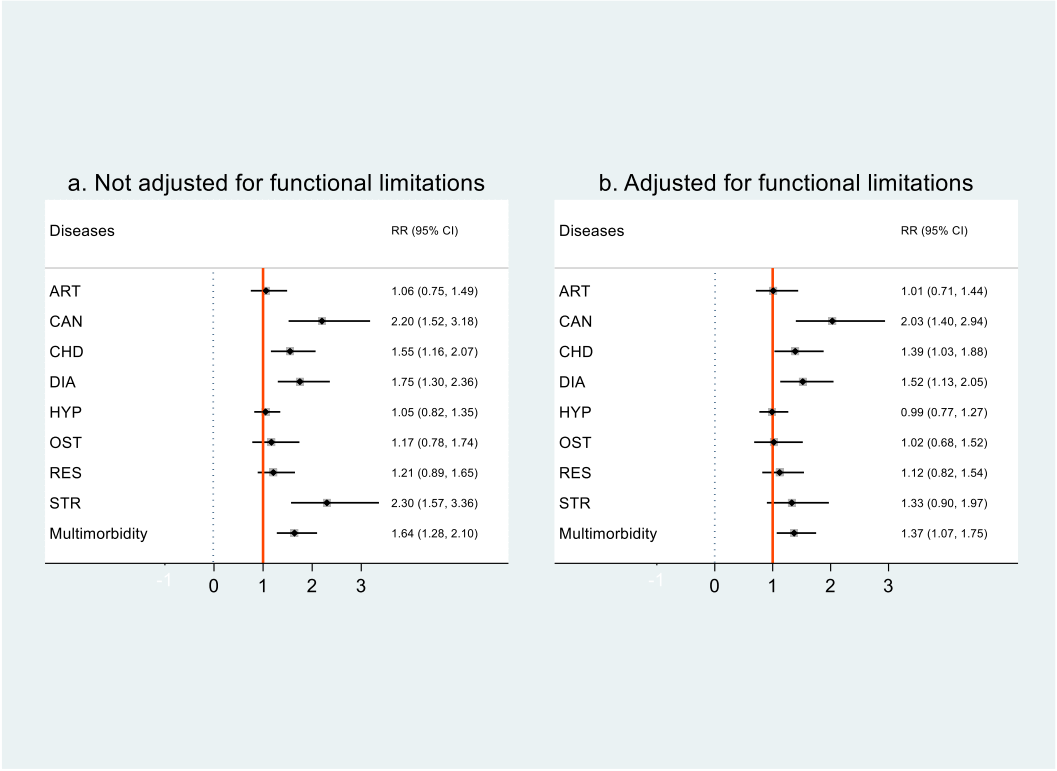
Figure 1

All-cause mortality risks of individual non-communicable chronic diseases and multimorbidity at baseline (CRELES, 2005-2009). Gompertz models



Note. RR = Relative risk; 95% CI = Confidence interval at 95. ART = Arthritis; CAN = Cancer; CHD = Coronary heart disease; DIA = Diabetes; HYP = Hypertension; OST = Osteoporosis; RES = Respiratory conditions; STR = Stroke. All models were adjusted for age, sex, educational attainment, marital status, smoking status, body mass index, and physical activity.

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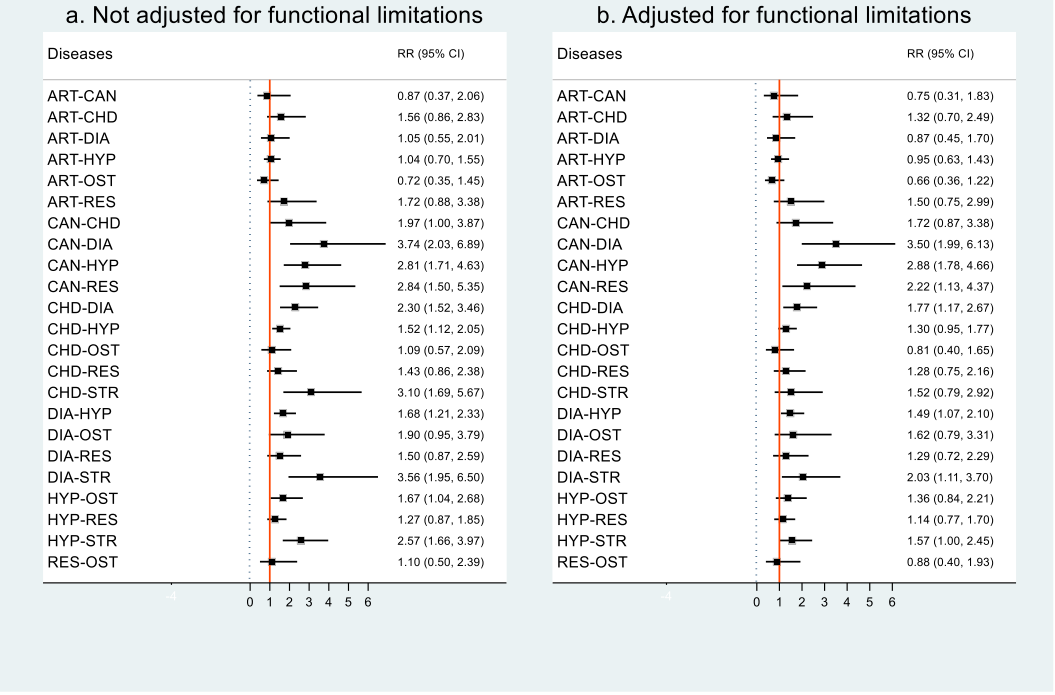
Figure 2

All-cause mortality risk of the combinations of two non-communicable chronic diseases at baseline (CRELES, 2005-2009). Gompertz models



Note. RR = Relative risk; 95% CI = Confidence interval at 95. ART = Arthritis; CAN = Cancer; CHD = Coronary heart disease; DIA = Diabetes; HYP = Hypertension; OST = Osteoporosis; RES = Respiratory conditions; STR = Stroke. All models were adjusted for age, sex, educational attainment, marital status, smoking status, body mass index, and physical activity.

In some cases, the all-cause mortality risk associated with specific NCD triads was comparable to that observed in the respective reference groups. (Figure 3, panels a and b). In comparison, the risk of all-cause mortality among individuals with diabetes- hypertension-respiratory conditions was approximately twice that of individuals without this triad of NCDs. For those with diabetes coexisting with hypertension-CHD, hypertension-respiratory conditions, hypertension-stroke, and hypertension-osteoporosis, the risk of all-cause mortality was between two and four times higher than the mortality risk of the respective reference groups (Figure 3, panel a). After adjusting for functional limitations, the all-cause mortality risk of respondents with diabetes-hypertension-respiratory conditions was comparable to the mortality risk of individuals in the reference group. The mortality risk of the other three triads approximately doubled that of their respective reference groups (Figure 3, panel b).

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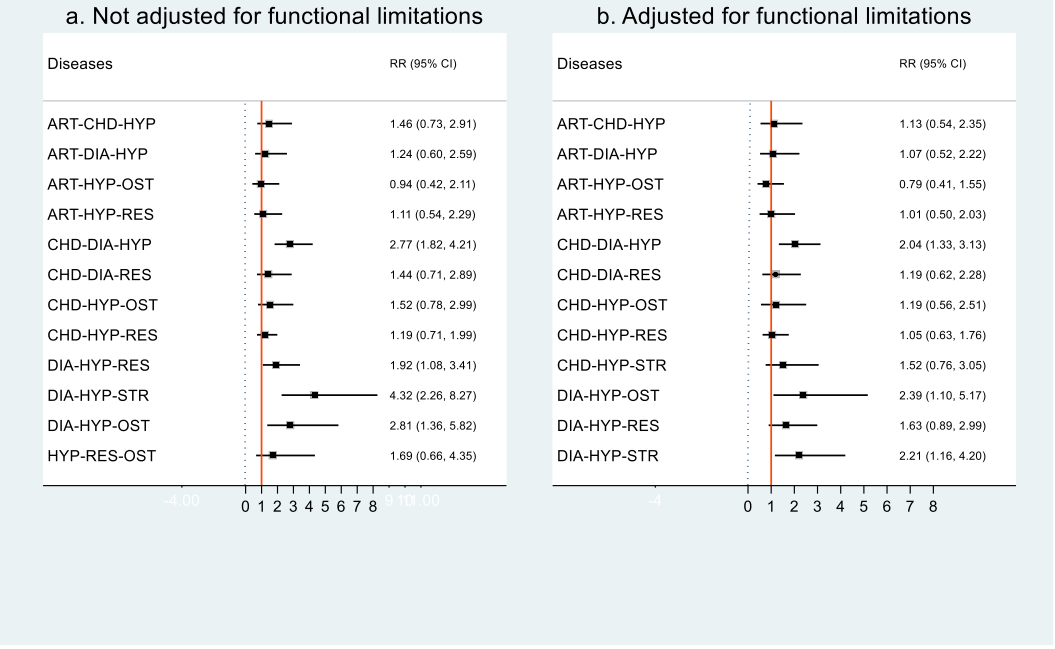
Figure 3

All-cause mortality risk of the combination of three non-communicable diseases at baseline (CRELES, 2005-2009). Gompertz models



Note. RR = Relative risk; 95% CI = Confidence interval at 95. ART = Arthritis; CAN = Cancer; CHD = Coronary heart disease; DIA = Diabetes; HYP = Hypertension; OST = Osteoporosis; RES = Respiratory conditions; STR = Stroke. All models were adjusted for age. sex, educational attainment, marital status, smoking status, body mass index, and physical activity.

3.2 Sensitivity analysis

3.2.1 Changing the multimorbidity reference group

As stated in the Analytical strategy section, the reference groups were defined as those composed of individuals with no multimorbidity, that is, those individuals with zero or only one chronic disease. An alternative methodology defines the reference group as comprising individuals who are free of NCDs (Nunes et al., 2016). Consequently, individuals with a single NCD and those with two or more NCDs are compared with those without NCDs. Using this approach the risk of all-cause mortality among individuals with multimorbidity was 65% higher than the risk of mortality among those without NCDs. This result is like that obtained through the methodology delineated in the Analytical

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strategy section. In addition, no difference was found between the mortality risk among those without NCDs and those with a single NCD at baseline. The latter result lends support to the decision to compare the mortality risk of individuals with multimorbidity with that of those without NCDs or with a single NCD.

3.2.2 *Missing data*

As mentioned in the study population section, the study population consists of 2,565 respondents (90.6% of the original sample); 473 deaths were recorded (83.7% of the total registered deaths). Among individuals who were excluded from the analytical sample, about 35% died during the observation period, while among individuals who remained in the study population only 18% died during the same period. The exclusion of individuals from the study population due to lack of information on the variables of interest resulted in the loss of 92 deaths. This exclusion could have produced biased estimates, probably underestimating the effect of multimorbidity on mortality. A multiple imputation method was used to address missing data. This procedure allows the inclusion of individuals excluded from the analytical sample due to incomplete data. Results after multiple imputation were similar to those presented in the Results section. As expected, some coefficients were slightly higher in magnitude and significance (results are available upon request).

3.2.3 *Mental Health*

When analyzing multimorbidity-mortality relationships, some studies include mental health measures in the multimorbidity index (Roman Lay et al., 2020); others include depression as a control variable. (Jani et al., 2019). Although the CRELES study includes the Geriatric Depression Scale (GDS) short form , the GDS was not administered to proxy respondents, who represent 25% of the original sample, and 23% of the analytic sample. Consequently, the inclusion of a measure of depression symptoms would have resulted in a notable reduction in the study sample, from 2,565 to 1,974 individuals. Of these, 76.8% exhibited no symptoms of depression, 17.1% displayed indications of mild depression, and 6.1% demonstrated symptoms of moderate to severe depression. However, adjustment for depressive symptoms did not substantially change the results (results are available upon request).

4. Discusión

The results show that hypertension was the most common disease (48%), followed by diabetes (21%). Although hypertension treatment and control has improved in Costa Rica in recent decades, surpassing most high-income countries in this regard (NCD Risk Factor Collaboration, 2021), hypertension prevalence remains high in Costa Rica. Regarding diabetes, it continues to be a major public health challenge in Costa Rica, despite a decrease in diabetes-related mortality rates in recent years, largely due to the implementation of public health policies in Costa Rica (Santamaría-Ulloa & Montero-López, 2020).

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In 2005, the prevalence of multimorbidity among Costa Ricans aged 60 years and older was greater than 40%. However, it is difficult to make a direct comparison with previous research. The comparability of prevalence estimates is complicated by several factors related to the study design, including the setting, data source and collection, classification of the diseases involved, and the definition of multimorbidity used (Holzer et al., 2017). For example, Arokiasamy et al. (2015) using data from the WHO´s 2010 Study on Global Ageing and Adult Health (SAGE) revealed that among Mexicans aged 60-69 years the prevalence of multimorbidity was 50.1%, and 60.7% among those aged 70 years and older. Although, the prevalence of multimorbidity among Mexican older adults reported by Arokiasamy et al. (2015) is higher than the prevalence of multimorbidity obtained in the present study (35.4% and 45.4% among individuals aged 60-69 and more than 70, respectively), the comparison is not directly. Even though Arokiasamy and colleagues defined multimorbidity as having two or more chronic diseases that were also selected from a set of eight diseases (angina pectoris, arthritis, asthma, chronic lung disease, diabetes, hypertension, stroke, and vision impairment) this set is different from the set used in the present study. In this study, angina pectoris was included in the category of CHD along with other cardiac conditions, and asthma and chronic lung disease in the category respiratory conditions. Due to the wording of the questions used in the CRELES study, it was not possible to consider the latter two conditions separately. In addition, the present study included cancer and osteoporosis in the index of multimorbidity rather than vision impairment, as did the study by Arokiasamy and colleagues.

Regarding the prevalence of pairs and triads of NCDs, the findings of a study that analyzed data from a 16-year longitudinal study of the Brazilian city of São Paulo (Roman Lay et al., 2020) indicated that in 2000, the prevalence of the pairs diabetes-hypertension, diabetes-CHD, and CHD-respiratory conditions was, in all cases, lower than that observed in the present study. However, the prevalence of the triad diabetes-hypertension-CHD was found to be similar. The prevalence of diabetes-hypertension, diabetes-CHD, diabetes-cancer, and CHD-hypertension found in the present study falls within the range observed in a systematic literature review of 19 articles on the subject. However, the prevalence of cancer-hypertension was considerably higher than that observed in this study (Sinnige et al., 2013).

Multimorbidity was found to be associated with an elevated risk of all-cause mortality over a period of approximately five years, even when accounting for functional status at baseline. Comparability of the results may be compromised, as previously mentioned, by differences in the type and number of chronic conditions considered, the severity of these conditions, their effect on functional status, and their prevalence in the population of interest (Lefèvre et al., 2014). However, the results obtained in this study align with the findings of other research (Jani et al., 2019; Sun et al., 2023).

The elevated risk of all-cause mortality among respondents with diabetes-CDH, diabetes-hypertension, and diabetes-stroke at baseline, in comparison with those in the respective reference groups, was to be anticipated considering the established relationship between cardiovascular

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multimorbidity and mortality (Singh-Manoux et al., 2018). The all-cause mortality risk among respondents with stroke-CDH, CHD-hypertension-stroke, and diabetes-hypertension-respiratory conditions at baseline was no longer statistically significant when functional limitations were included in the model. This may reflect the role of functional status as a mediator of the effect of multimorbidity on mortality (Nunes et al., 2016; St John et al., 2014), as multimorbidity can cause disability (Storeng et al., 2020) and disability is a mortality predictor (Yang et al., 2021). Both respiratory conditions and stroke have an impact on physical functioning (Eriksson et al., 2008).

Of the 10 NCDs pairs and triads shown to increase the all-cause mortality risk in models adjusting for functional limitations, seven include diabetes. At the same time, four of these combinations correspond to cardiometabolic multimorbidity, defined as having two of the following diseases: CHD, diabetes, and stroke (Singh-Manoux et al., 2018). Diabetes doubles the risk of several vascular diseases, independently of other common risk factors (Emerging Risk Factors Collaboration et al., 2010). The prevalence of diabetes is high in this population, at 20.8%, as it is the prevalence of hypertension, about 50.0%. It is thus no surprise that six of the ten combinations of two and three NCDs included hypertension, which is one of the most significant preventable cardiometabolic risk factors.

The most important characteristics of the increase in cardiometabolic diseases are high blood pressure and the growing consequences of diabetes and obesity (Palloni et al., 2015). The risk of developing cardiometabolic multimorbidity is twofold for overweight individuals but increases to more than tenfold for those with class II or III obesity (BMI ≥ 35) (Kivimäki et al., 2017). The prevalence of overweight and obesity is high in Costa Rica. In 2014, 31.4% (26.4 to 36.8%) of individuals aged 65 were obese and 31.4 % (26.4 to 36.8%) overweight (Wong-McClure et al., 2016).

4.1 Strengths and limitations

One of the strengths of this study is the use of a nationally representative survey of a Latin American country. This study employed a longitudinal sample that, over a follow-up period of nearly 5 years, estimated the effect of the presence of multiple NCDs on the risk of death. The linkage of the CRELES survey with national mortality registries ensured valid and complete data on deaths. The CRELES survey data allowed controlling for potential confounders at the individual level. This approach is rarely used in studies of the association between multimorbidity and mortality (Nunes et al., 2016). Furthermore, research on the effect of multimorbidity on mortality does not adequately address the role of potential mediators, or confounders, such as disability (Eriksson et al., 2008).

Despite its strengths, the present study has several limitations. Multiple definitions of multimorbidity have emerged in the absence of consensus (Almirall & Fortin, 2013). Here, the assessment of multimorbidity was conducted using the most straightforward measure available, counting the number of NCDs reported by respondents. It should be noted, however, that this number is limited. Therefore, it is possible that important diseases were not considered. In addition, data on disease

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duration, severity, and stage were not included. This information is not available in the CRELES database. Although different studies have shown that self-reports of NCDs can be reliably used to study multimorbidity (Jiang et al., 2015), misreporting of NCDs varies by educational level and may have affected some of our results. Some studies show that the use of self-reported data may underestimate the prevalence of multimorbidity (Fortin et al., 2017). Our results may not only underestimate the prevalence of multimorbidity. They may also underestimate the associated mortality risks. In addition, mortality was assessed based on self-reported NCDs at baseline. This did not allow for analysis of the progression of chronic disease multimorbidity over the five-year follow-up period. Consequently, it would be beneficial to conduct a more comprehensive investigation on this topic in future research.

5. Conclusión

The co-occurrence of multiple NCDs represents a significant challenge to the effective treatment of these conditions, given that health systems, professional training programs, and clinical protocols often address diseases in isolation (Bezzina & Pope, 2023). Currently, the population of older adults with multimorbidity faces fragmented healthcare services. This can lead to potentially inefficient and ineffective care (WHO, 2015). In Costa Rica, as in other settings, the impact of multimorbidity on functioning, healthcare utilization, and healthcare expenditure is typically greater than would be expected for the diseases included in the multimorbidity index when considered separately (Ministry of Health, 2018).

In conclusion, the results of this study highlight the need to develop strategies to address the burden of multimorbidity, especially cardiometabolic multimorbidity, on individuals and health systems. The need to develop and implement effective strategies for the prevention and treatment of multimorbidity among older Costa Ricans is underscored by its increasing prevalence.

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