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Additive interaction of disability with chronic conditions on mortality risk in middle-aged and older adults in Spain

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ABSTRACT

Background: Disability and chronic diseases are prevalent conditions associated with mortality, but little information is available on their potential synergistic effects.
Objective: This study aimed to describe additive interactions between disability and chronic diseases on mortality risk in middle-aged and older adults.
Methods: A representative cohort of 22,800 community-dwelling Spanish people aged 50 years or older were interviewed for disability with the Global Activity Limitation Indicator and specific chronic diseases in the 2011–12 and 2014 National Health Surveys and subsequently followed up for mortality. Five-year all-cause mortality risks were standardized in each disability-by-comorbidity category through inverse probability weighting. We computed interaction contrasts as the departure of the standardized risk difference for people with both conditions from the sum of the standardized risk differences for those with any single condition.
Results: The baseline prevalence of disability was 35.1 % (95 % confidence interval [CI] 34.4 %, 35.9 %). There was compelling evidence of synergistic effects of disability with chronic liver disease, heart diseases other than myocardial infarction, cancer, and cerebrovascular disease, with large positive interaction contrasts (95 % CIs) of 106.7 (−16.4, 229.9), 45.7 (6.9, 84.5), 45.1 (−15.0, 105.2), and 42.9 (−41.0, 126.9) excess deaths per 1000 persons. Less clear synergistic responses were observed for other comorbidities. We found some evidence of antagonism for osteoporosis, with a negative interaction contrast of −18.0 (95 % CI −82.2, 46.2) deaths per 1000 persons.
Conclusion: Given the high mortality risk in people with disability, the study of its synergistic effects with target comorbidities can provide relevant information regarding preventive measures.

Introduction

Disability is a complex construct considered as the outcome of multiple interactions between health conditions and features of an individual's physical, social, and attitudinal environment that hinder their full and effective participation in society.[1] The International Classification of Functioning, Disability, and Health goes beyond the purely medical model of disability and integrates the psychosocial perspective, proposing a comprehensive tool for measuring functioning in society, regardless of the reason for the impairments.[2]

The association of disability with a higher risk of mortality is consistent,[3–5] not only due to diseases that cause both disability and mortality, but also because personal, social, and environmental barriers hinder people with disabilities from adopting healthier lifestyles and improving their health status,[6] which in turn increases the risk of mortality.[7,8] Furthermore, there is limited evidence on the effectiveness of interventions to reduce dependency in activities of daily living among community-dwelling people with disability.[9] Thus, appropriate management of chronic diseases in this group can improve their health and quality of life, and reduce the risk of death.

The Global Activity Limitation Indicator (GALI) is a global survey instrument measuring participation restriction. It is a one-question instrument that reflects levels of function and disability[10] and has proven to be a valid and reliable measure of disability to be used in population health surveys.[11]

The main objective of this study is to identify additive interactions

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between disability, as measured with the GALI, and chronic diseases on the risk of all-cause mortality in middle-aged and older adults, thus allowing the detection of synergisms or antagonisms in which the effect on mortality when both conditions coexist is greater or smaller than the sum of their separate effects. This will allow progress in the knowledge of the disability-by-comorbidity interplay, with its eventual preventive derivatives.

Methods

Study population

This study is based on the 5-year mortality follow-up of participants aged 50 years or older in two health surveys in Spain, the 2011–12 National Health Survey and the 2014 European Health Survey for Spain. Both surveys used the same sample design and standardized questionnaires.[12,13] Briefly, the target populations comprised individuals aged 15 years or older who resided in family households throughout the entire Spanish territory. Survey participants were selected through a three-stage random sampling stratified by 19 autonomous communities and 7 municipality sizes (from less than 10,000 to more than 500,000 inhabitants). A total of 2000–2500 census tracts were initially selected across strata with probability proportional to their size, 12–15 households were then sampled within each selected census tract, and a single resident in the household aged 15 years or older was randomly selected for a personal interview. The response rate was 71.1–71.3 % among all eligible subjects. The sample for this study comprised 22,800 participants aged 50 years or older with complete information on baseline characteristics and mortality follow-up (10,755 and 12,045 participants from the 2011–12 and 2014 surveys, respectively). Sampling weights were assigned to study participants to account for the different selection probabilities by autonomous community and the distinct response rates by age, sex, and nationality. The study was approved by the Institute of Health Carlos III Ethics Committee (report number CEI PI 28_2019).

Baseline data and mortality follow-up

Trained staff collected baseline information using computer-assisted personal interviews at each resident's home between July 2011 and June 2012, and between January 2014 and January 2015. Age, sex, and attained educational level were obtained by interview. The GALI was obtained by asking subjects the following question: "During at least the last 6 months, to what extent have you been limited due to a health problem in performing activities that people usually do?" The response options were: not limited, limited, but not severely, and severely limited. The GALI has been developed to monitor disability and can be interpreted as both individual functioning (activity) and social functioning (participation).[14] Following the widespread approach in major European health surveys,[11] subjects with mild or severe activity limitations were considered to have a disability. We included answers by family proxies for 1029 of 22,800 participants (4.5 %), as next of kin can provide an adequate assessment of the level of limitation of study participants and their exclusion would mostly affect people with poorer health.

Subjects were also asked whether they had been diagnosed by their physicians with the following chronic conditions: hypertension, diabetes, acute myocardial infarction, other heart diseases, cerebrovascular disease, cancer, chronic obstructive pulmonary disease (COPD), asthma, chronic liver disease, thyroid disease, urinary incontinence, arthritis or osteoarthritis, osteoporosis, depression, and anxiety. We computed the number of these diseases for each participant.

Mortality data were provided by the Spanish National Institute of Statistics, which collects information from the Medical Death Certificates of all deaths registered in the Spanish Civil Registries.[15] Vital status was ascertained through computerized linkage to death certificate data using the Spanish national identification number. Death ascertainment was virtually complete since all deaths in Spain should be reported to the Civil Registries. Participants contributed follow-up time from their baseline interview until death or being censored at the end of the 5-year follow-up period (2011–16 for participants in the 2011 survey and 2014–2019 for participants in the 2014 survey).

Statistical analysis

The cumulative all-cause mortality risk for subjects with and without disability was standardized to the weighted distribution of baseline characteristics (calendar year, age, sex, educational level, and number of comorbidities) in the entire community-dwelling Spanish population aged 50 years or older with inverse probability of exposure weights.[16] We first fitted a sampling-weighted logistic model to estimate each participant's probability of being in its observed disability category given its baseline characteristics. We calculated standardization weights as the inverse of these conditional probabilities, further rescaled by the sampling-weighted marginal proportions in each disability category to stabilize weights.[16] We then assigned combined weights to participants as the product of sampling and standardization weights, thus correcting for sample selection bias and confounding by baseline characteristics.[17] After truncating 0.1 % of lower and upper extreme weights, the mean (range) combined weight was 1.00 (0.03–11.34) (Supplementary Fig. S1). These combined weights provided an effective standardization, since the fully-weighted distribution of baseline characteristics was virtually identical among disability groups (Supplementary Table S1).

We used Kaplan-Meier methods and spline-based survival models[18] weighted by the above combined weights and stratified by disability to obtain nonparametric and smooth estimates of the standardized cumulative all-cause mortality curves in people with and without disability. Spline-based survival models parameterized stratum-specific log cumulative hazards as distinct natural cubic splines of log time with a single internal knot at the 50th percentile,[18] which resulted in similar but more parsimonious cumulative mortality curves than nonparametric methods.

To evaluate departures from risk additivity in the combined effect of disability and specific comorbidities, we first estimated the standardized 5-year risks of all-cause mortality in the four combinations of disability status and presence of comorbidity by fitting spline-based survival models weighted by combined weights and stratified by disability and comorbidity. Combined weights for disability-by-comorbidity analyses were again calculated as the product of sampling and standardization weights, the latter now being the inverse of the probabilities of each participant's disability-by-comorbidity combination conditional on its baseline characteristics as estimated from multinomial logistic models (Supplementary Fig. S2). We estimated the standardized 5-year risk differences in all-cause mortality for each disability-by-comorbidity category compared with people without disability or comorbidity, with 95 % confidence intervals (CIs) derived by applying delta methods to robust standard errors of spline coefficients. The interaction contrast was then calculated as the departure of the standardized risk difference for people with both disability and comorbidity from the sum of the standardized risk differences for those with disability but no comorbidity and those with comorbidity but no disability. Under the assumption that neither disability nor comorbidity are ever preventive, a positive interaction contrast (superadditivity) implies the presence of synergistic responses, whereas a negative interaction contrast (subadditivity) indicates the presence of antagonistic responses.[19]

To explore specific synergisms and antagonisms of disability with comorbidities in older people, we performed subgroup analyses in adults aged 65 years or older. The low mortality risk and low prevalence of several comorbidities in adults aged 50–64 years resulted in fewer than 10 deaths in some disability-by-comorbidity categories for 8 of the 15 studied comorbidities, which precluded accurate analyses of additive interactions between disability and comorbidities in middle-aged adults. Statistical analyses were performed in Stata, version 17 (Stata Corp.,

College Station, Texas) and graphics were produced in R, version 4 (R Foundation for Statistical Computing, Vienna, Austria).

Results

The prevalence of disability (95 % CI) as measured by GALI was 35.1 % (34.4 %–35.9 %) in this non-institutionalized population aged 50 years or older, including 26.8 % (26.1 %–27.5 %) with mild and 8.3 % (7.9 %–8.7 %) with severe activity limitations. Disability prevalence (95 % CI) was 25.1 % (24.1 %–26.1 %) in adults aged 50–64 years and 45.8 % (44.7 %–46.8 %) in adults aged 65 years or older, and it increased from 30.4 % (29.4 %–31.5 %) in 2011 to 39.6 % (38.5 %–40.6 %) in 2014. Compared with people without disability, people with disability were more likely to be older, women, and to have lower educational levels and more comorbidities at baseline (Table 1).

After 5 years of follow-up, there were 825 all-cause deaths among 14,411 participants with no disability and 1672 deaths among 8389 participants with disability. The standardized 5-year risk of all-cause mortality (95 % CI) was 68.8 (62.6–75.6) deaths per 1000 in people with no disability and notably increased to 130.5 (121.2–140.5) deaths per 1000 in people with disability (Fig. 1).

Table 2 shows the standardized 5-year mortality risks by combinations of disability with specific comorbidities, together with the corresponding interaction contrasts. Some comorbidities, such as hypertension, thyroid disease, arthritis, and anxiety, showed negative associations with mortality among people without disability. Hence, their interaction contrasts were inconclusive regarding the net presence of synergistic or antagonistic responses with disability. Among the remaining comorbidities, there was compelling evidence of synergistic effects of disability with chronic liver disease (interaction contrast 106.7 [95 % CI −16.4 to 229.9] deaths per 1000), heart diseases other than myocardial infarction (45.7 [6.9 to 84.5] deaths per 1000), cancer (45.1 [−15.0 to 105.2] deaths per 1000), and cerebrovascular disease (42.9 [−41.0 to 126.9] deaths per 1000). Synergistic responses were also observed to a lesser extent for diabetes (interaction contrast 26.9 [95 % CI −6.3 to 60.2] deaths per 1000), COPD (25.1 [−23.0 to 73.2] deaths per 1000), depression (20.2 [−21.3 to 61.7] deaths per 1000), urinary incontinence (19.2 [−35.8 to 74.1] deaths per 1000), and acute myocardial infarction (16.7 [−56.9 to 90.4] deaths per 1000). On the other hand, there was some evidence of an antagonistic response between disability and osteoporosis, with a negative interaction contrast of −18.0 (95 % CI −82.2 to 46.2) deaths per 1000. The combined effect of disability with asthma was approximately additive (Table 2 and Fig. 2).

In analyses restricted to adults aged 65 years or older, results were quite similar to those obtained in the entire population aged 50 years or older, except that the synergistic effect of disability with cerebrovascular disease was exacerbated and those with acute myocardial infarction, cancer, and COPD were diluted or even reversed (Supplementary Table S2). Among older adults, synergistic responses on 5-year mortality risk were observed between disability and cerebrovascular disease (interaction contrast 97.8 [95 % CI −22.3 to 217.9] deaths per 1000), chronic liver disease (66.9 [−160.4 to 294.1] deaths per 1000), diabetes (35.6 [−16.1 to 87.3] deaths per 1000), depression (33.7 [−32.9 to 100.2] deaths per 1000), and heart diseases other than myocardial infarction (30.6 [−22.7 to 83.8] deaths per 1000). In contrast, there was an antagonistic response between disability and acute myocardial infarction, with a negative interaction contrast of −34.5 (95 % CI −136.6 to 67.7) deaths per 1000 (Supplementary Table S2).

Discussion

In this large follow-up study, we observed a substantially increased risk of all-cause mortality in people with mild or severe disability compared to their non-disabled counterparts, even after controlling for differences in sociodemographic and clinical factors. We also found compelling evidence of synergistic effects on mortality between

Table 1
Baseline characteristics by disability among participants aged 50 years or older in the 2011–12 and 2014 Spanish National Health Surveys.[a]

Characteristic		Disability[b]		
	Overall	No	Yes	*P* value[c]
No. of participants	22,800	14,411 (64.9)	8389 (35.1)	
Survey year				<0.001
2011–12	10,755 (48.8)	7311 (52.3)	3444 (42.3)	
2014	12,045 (51.2)	7100 (47.7)	4945 (57.7)	
Age (years)				<0.001
50–54	3653 (19.7)	2851 (24.1)	802 (11.6)	
55–59	3468 (17.1)	2531 (19.4)	937 (12.8)	
60–64	3269 (14.7)	2320 (16.0)	949 (12.4)	
65–69	3174 (13.7)	2147 (14.2)	1027 (12.9)	
70–74	2680 (11.0)	1640 (10.3)	1040 (12.3)	
75–79	2547 (9.5)	1404 (8.0)	1143 (12.2)	
80–84	2226 (8.0)	971 (5.2)	1255 (13.1)	
≥85	1783 (6.3)	547 (2.8)	1236 (12.7)	
Sex				<0.001
Women	12,989 (53.6)	7516 (49.2)	5473 (61.6)	
Men	9811 (46.4)	6895 (50.8)	2916 (38.4)	
Educational level				<0.001
Less than primary	5485 (22.4)	2593 (16.5)	2892 (33.4)	
Primary	6292 (25.3)	3711 (23.2)	2581 (29.1)	
First-stage secondary	4834 (23.0)	3396 (25.5)	1438 (18.3)	
Second-stage secondary	3681 (17.4)	2742 (20.3)	939 (12.0)	
University	2508 (12.0)	1969 (14.6)	539 (7.2)	
No. of comorbidities[d]				<0.001
0	5548 (26.8)	4921 (36.9)	627 (8.3)	
1	5661 (25.3)	4331 (29.9)	1330 (16.8)	
2	4691 (19.7)	2774 (18.1)	1917 (22.7)	
3	3022 (12.5)	1385 (8.8)	1637 (19.3)	
≥4	3878 (15.6)	1000 (6.3)	2878 (32.9)	
Comorbidity				
Hypertension	9740 (40.8)	5322 (35.3)	4418 (51.1)	<0.001
Diabetes	3457 (14.8)	1604 (11.1)	1853 (21.7)	<0.001
Acute myocardial infarction	937 (4.3)	331 (2.4)	606 (7.9)	<0.001
Other heart diseases	2571 (10.3)	980 (6.3)	1591 (17.8)	<0.001
Cerebrovascular disease	727 (3.2)	188 (1.3)	539 (6.7)	<0.001
Cancer	1446 (6.1)	598 (4.0)	848 (10.1)	<0.001
COPD	1780 (7.7)	658 (4.4)	1122 (13.8)	<0.001
Asthma	1235 (5.1)	517 (3.4)	718 (8.2)	<0.001
Chronic liver disease	393 (1.7)	130 (0.9)	263 (3.2)	<0.001
Thyroid disease	1954 (8.2)	1006 (6.8)	948 (10.9)	<0.001
Urinary incontinence	2052 (8.2)	580 (3.5)	1472 (16.9)	<0.001
Arthritis or osteoarthritis	9049 (37.1)	3848 (24.6)	5201 (60.3)	<0.001

(*continued on next page*)

Table 1 (*continued*)

Characteristic		Disability[b]		
	Overall	No	Yes	*P* value[c]
Osteoporosis	2304 (9.3)	843 (5.3)	1461 (16.7)	<0.001
Depression	3331 (13.3)	1139 (6.9)	2192 (25.2)	<0.001
Anxiety	2570 (10.8)	892 (5.9)	1678 (20.0)	<0.001

COPD, chronic obstructive pulmonary disease.
[a] Unweighted counts (sampling-weighted percentages).
[b] Mild or severe activity limitation in the Global Activity Limitation Indicator.
[c] *P* value for homogeneity of sampling-weighted percentages between people with and without disability.
[d] Number of comorbidities computed from those listed in the table.

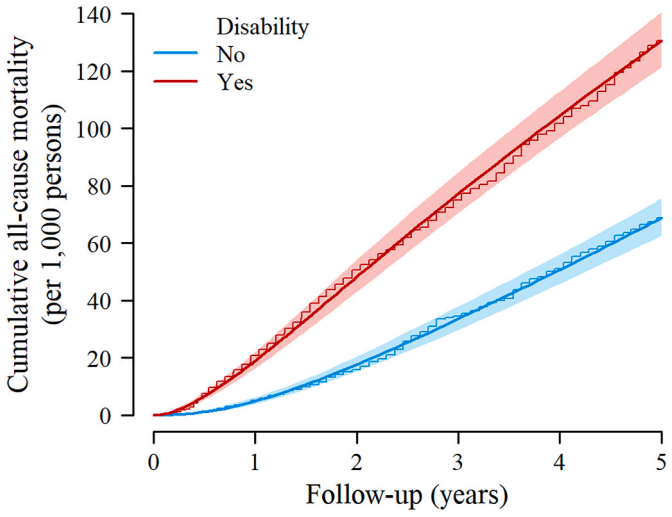

Fig. 1. Standardized cumulative all-cause mortality by disability in the community-dwelling Spanish population aged 50 years or older, Spanish National Health Surveys, 2011–16 and 2014–2019.
Parametric cumulative mortality curves (smooth lines) and their 95 % confidence intervals (shaded regions) were estimated from a spline-based survival model and nonparametric cumulative mortality curves (step functions) were obtained from Kaplan-Meier methods, both weighted by combined weights and stratified by disability. Combined weights were used to standardize cumulative mortality curves in each disability category to the weighted distribution of baseline characteristics in the entire community-dwelling Spanish population aged 50 years or older, including survey year (2011 or 2014), age (50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, or ≥85 years), sex (women or men), educational level (less than primary, primary, first-stage secondary, second-stage secondary, or university), and number of comorbidities (0, 1, 2, 3, or ≥4).

disability and selected comorbidities, including chronic liver disease, cardiovascular diseases, and cancer.

A limited number of works have primarily measured mortality associated with disability in representative samples.[5,20–23] Our study adds to the evidence of an independent association between disability and mortality, even when measured with the single-item GALI instrument on global health-related activity limitations used in European health surveys. However, to our knowledge, this is the first study that focuses on measuring the additive interaction of disability with chronic diseases on mortality risk. We present information on crude and adjusted risks corresponding to all subgroups of disability and comorbidity, which facilitates both the interpretation of relative (not shown) and absolute measures of association. Our measures of risk allow for estimating the absolute impact of the interactions. However, regarding the estimation of additive interactions, the study must be considered as descriptive, since we lack sufficient information to contrast the hypotheses related to the interaction phenomena found.

For those comorbidities showing superadditive interactions with disability, including chronic liver disease, heart diseases other than myocardial infarction, cancer, cerebrovascular disease, diabetes, COPD, depression, urinary incontinence, and acute myocardial infarction, it is conceivable that there are instances of physiological mechanisms that act synergistically to increase the risk of mortality. That is, the risk with both conditions (disability and the disease) is greater than would be expected by adding the separate effects of disability in the absence of the disease and the disease in the absence of disability. People with disabilities may also experience unhealthy lifestyles, like limited levels of physical activity, or suffer from mental and social problems, such as emotional distress, social isolation, and lack of community participation, which may worsen the prognosis of concurrent diseases.[24]

The interaction with diabetes is an example of a stable estimate of superadditivity and deserves some comment. If we made a causal interpretation it would be that of every 1000 people with diabetes and disability, 168.8 die at 5 years, with 103.1 of them attributable to both conditions and, of these, 26.9 (26.9/103.1 = 26 % of the absolute effect) are due only to their interaction (Table 2 and Fig. 2). This has interesting preventive implications since adequate control of diabetes could considerably reduce the risk of death in people with disabilities. Similar public health implications apply to other salient comorbidities, such as chronic liver disease, cardiovascular diseases, and cancer, as adequate secondary and tertiary prevention of these chronic conditions in disabled people could also contribute to increasing their life expectancy. The figures found in the case of chronic liver disease are quite impressive since the interaction accounts for 61 % of the absolute effect (106.7/173.6), although this estimate should be interpreted with caution since the confidence intervals are very wide.

We observed some instance of subadditive interactions. The excess risk of mortality attributable to osteoporosis was lower among people with disabilities than among their non-disabled counterparts. Of every 1000 people with osteoporosis and disability, 142.2 die at 5 years, with 74.5 of them attributable to both conditions and, of these, −18.0 are due only to their interaction. This means that their interaction prevented 18.0 deaths per 1000 that would have occurred in the absence of interaction. Apart from random variability and residual confounding, we can only conjecture the possible reasons for this finding. One hypothesis is that care, treatment, and preventive measures for this condition in patients with disability protect them from risk to a greater extent than those without this particular disease. People with osteoporosis are recommended healthy diets, with calcium, Vitamin D, a healthy body mass index, and regular physical activity.[25]

The study has limitations that deserve comment. First, despite the large sample size, some estimates were imprecise and thus compatible with a wide range of effects. However, it should be pointed out that not all values within a confidence interval represent hypotheses with the same likelihood. The hypothesis represented by the point estimate is the most compatible with the study data.[26] Second, unmeasured confounding may have affected some estimates. However, we included important determinants of the association of disability and diseases with mortality in the set of adjusting variables, so we expect residual confounding to be modest. Third, the reduced number of deaths and the low prevalence of most chronic conditions among survey participants aged 15–49 years precluded analyses of additive interactions between disability and comorbidity in young adults. We therefore restricted analyses to adults aged 50 years or older, which may be prone to survivor bias due to the selective survival of disabled people with better prognosis. Nevertheless, we expect this selection bias to be low, as the estimated risk of disabled participants dying between ages of 15 and 49 was below 10 %. Finally, chronic health conditions may be responsible for the disability, particularly among people with mild activity limitations, which may partially explain the synergistic effects between disability and comorbidities. We combined mild with severe disability since

Table 2
Standardized 5-year risks of all-cause mortality (per 1000 persons) by disability and specific comorbidities in the community-dwelling Spanish population aged 50 years or older, Spanish National Health Surveys, 2011–16 and 2014–2019.

Comorbidity	Without disability[a]		With disability[a]		Interaction contrast[d] (95 % CI)
	Without comorbidity	With comorbidity	Without comorbidity	With comorbidity	
Overall					
No. of deaths/participants	825/14,411		1672/8389		
Standardized 5-year risk[b] (SE)	68.8 (3.3)		130.5 (4.9)		
Standardized risk difference[c] (95 % CI)	0.0 (reference)		61.8 (50.2–73.4)		
Hypertension					
No. of deaths/participants	448/9057	374/5322	747/3942	916/4418	
Standardized 5-year risk[b] (SE)	71.4 (4.9)	66.0 (4.5)	134.3 (6.7)	122.5 (8.0)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	−5.3 (−18.4 to 7.7)	62.9 (46.7–79.1)	51.1 (32.7–69.6)	−6.4 (−30.7 to 17.8)
Diabetes					
No. of deaths/participants	670/12,797	154/1604	1170/6521	500/1853	
Standardized 5-year risk[b] (SE)	65.6 (3.7)	84.5 (8.7)	122.9 (5.3)	168.8 (13.0)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	18.9 (0.5–37.4)	57.3 (44.6–70.0)	103.1 (76.6–129.7)	26.9 (−6.3 to 60.2)
Acute myocardial infarction					
No. of deaths/participants	768/14,071	56/331	1487/7777	184/606	
Standardized 5-year risk[b] (SE)	66.0 (3.3)	122.7 (27.1)	128.8 (5.0)	202.2 (25.4)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	56.6 (3.2–110.1)	62.8 (50.9–74.6)	136.2 (86.0–186.3)	16.7 (−56.9 to 90.4)
Other heart diseases					
No. of deaths/participants	705/13,420	120/980	1198/6783	469/1591	
Standardized 5-year risk[b] (SE)	68.7 (3.8)	74.4 (8.7)	125.6 (5.3)	177.1 (16.6)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	5.7 (−12.9 to 24.3)	57.0 (44.3–69.7)	108.4 (75.1–141.7)	45.7 (6.9–84.5)
Cerebrovascular disease					
No. of deaths/participants	800/14,219	24/188	1475/7846	195/539	
Standardized 5-year risk[b] (SE)	68.2 (3.3)	121.6 (30.4)	125.8 (5.0)	222.2 (29.6)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	53.5 (−6.4 to 113.3)	57.6 (45.8–69.4)	154.0 (95.6–212.4)	42.9 (−41.0 to 126.9)
Cancer					
No. of deaths/participants	743/13,801	80/598	1438/7519	232/848	
Standardized 5-year risk[b] (SE)	62.9 (3.1)	136.7 (18.9)	122.1 (4.9)	241.0 (23.4)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	73.8 (36.2–111.5)	59.2 (47.8–70.6)	178.2 (131.9–224.4)	45.1 (−15.0 to 105.2)
Chronic obstructive pulmonary disease					
No. of deaths/participants	733/13,745	92/658	1332/7256	337/1122	
Standardized 5-year risk[b] (SE)	66.5 (3.6)	106.1 (14.6)	124.0 (5.1)	188.6 (18.7)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	39.5 (10.1–68.9)	57.5 (45.2–69.7)	122.1 (84.7–159.5)	25.1 (−23.0 to 73.2)
Asthma					
No. of deaths/participants	792/13,889	33/517	1503/7665	166/718	
Standardized 5-year risk[b] (SE)	68.3 (3.4)	95.0 (18.9)	129.1 (5.0)	159.4 (22.9)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	26.7 (−10.9 to 64.3)	60.8 (48.9–72.8)	91.1 (45.7–136.4)	3.5 (−55.8 to 62.9)
Chronic liver disease					
No. of deaths/participants	813/14,274	10/130	1601/8117	69/263	
Standardized 5-year risk[b] (SE)	68.8 (3.4)	76.2 (32.0)	128.4 (4.9)	242.4 (53.8)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	7.3 (−55.7 to 70.4)	59.6 (47.9–71.3)	173.6 (68.0–279.2)	106.7 (−16.4 to 229.9)
Thyroid disease					
No. of deaths/participants	788/13,391	34/1006	1521/7416	143/948	
Standardized 5-year risk[b] (SE)	68.9 (3.4)	58.3 (16.8)	130.7 (5.1)	120.9 (18.2)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	−10.6 (−44.2 to 23.0)	61.8 (49.7–73.9)	52.0 (15.7–88.3)	0.8 (−49.2 to 50.8)
Urinary incontinence					
No. of deaths/participants	737/13,826	87/580	1181/6904	490/1472	
Standardized 5-year risk[b] (SE)	66.1 (3.5)	108.8 (17.5)	124.4 (5.2)	186.2 (21.0)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	42.7 (7.7–77.7)	58.3 (46.0–70.5)	120.1 (78.4–161.9)	19.2 (−35.8 to 74.1)
Arthritis or osteoarthritis					
No. of deaths/participants	580/10,513	245/3848	618/3145	1044/5201	
Standardized 5-year risk[b] (SE)	75.5 (5.1)	61.0 (5.0)	141.9 (7.6)	113.1 (6.5)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	−14.4 (−28.4 to −0.5)	66.5 (48.6–84.3)	37.6 (21.4–53.7)	−14.5 (−38.5 to 9.6)
Osteoporosis					
No. of deaths/participants	776/13,522	46/843	1352/6850	297/1461	
Standardized 5-year risk[b] (SE)	67.7 (3.4)	96.9 (26.5)	131.0 (5.2)	142.2 (18.2)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	29.2 (−23.2 to 81.6)	63.3 (51.1–75.5)	74.5 (38.2–110.8)	−18.0 (−82.2 to 46.2)
Depression					
No. of deaths/participants	768/13,263	56/1139	1292/6179	373/2192	
Standardized 5-year risk[b] (SE)	67.3 (3.5)	74.9 (12.0)	128.2 (5.2)	156.0 (16.3)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	7.6 (−16.8 to 32.0)	60.9 (48.7–73.2)	88.7 (56.1–121.4)	20.2 (−21.3 to 61.7)
Anxiety					
No. of deaths/participants	791/13,513	33/892	1418/6698	246/1678	
Standardized 5-year risk[b] (SE)	68.4 (3.4)	57.6 (19.1)	130.5 (5.2)	131.1 (19.2)	
Standardized risk difference[c] (95 % CI)	0.0 (reference)	−10.8 (−48.9 to 27.4)	62.1 (49.9–74.2)	62.7 (24.4–101.0)	11.4 (−43.1 to 66.0)

CI, confidence interval; SE, standard error.

[a] Mild or severe activity limitation in the Global Activity Limitation Indicator.

[b] Standardized 5-year risks of all-cause mortality (per 1000 persons) in non-disabled and disabled people with and without each index comorbidity were estimated from spline-based survival models weighted by combined weights and stratified by disability and comorbidity, with SEs of mortality risks derived by applying delta methods to robust SEs of spline coefficients. Combined weights were used to standardize mortality risks in each disability-by-comorbidity category to the weighted distribution of baseline characteristics in the entire community-dwelling Spanish population aged 50 years or older, including survey year (2011 or 2014), age (50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, or ≥85 years), sex (women or men), educational level (less than primary, primary, first-stage secondary, second-stage secondary, or university), and number of comorbidities other than the index comorbidity (0, 1, 2, 3, or ≥4).

[c] Standardized 5-year risk differences in all-cause mortality (per 1000 persons) and their 95 % CIs comparing each disability-by-comorbidity category with the reference category: people without both disability and the index comorbidity.

[d] Interaction contrasts (per 1000 persons) and their 95 % CIs were calculated as departures of the standardized risk difference for people with both disability and comorbidity from the sum of the standardized risk differences for those with disability but no comorbidity and those with comorbidity but no disability.

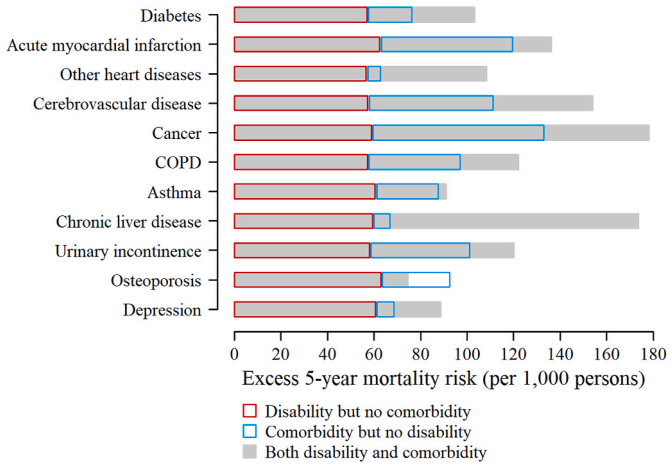

Fig. 2. Standardized excess 5-year risks of all-cause mortality by combinations of disability with specific comorbidities in the community-dwelling Spanish population aged 50 years or older, Spanish National Health Surveys, 2011–16 and 2014–2019. Gray bars exceeding the sum of red and blue bars represent positive interaction contrasts (synergistic responses of disability with comorbidities), whereas gray bars below the sum of red and blue bars represent negative interaction contrasts (antagonistic responses). Excess 5-year mortality risks comparing each disability-by-comorbidity category to people without both disability and the index comorbidity were standardized to the weighted distribution of baseline characteristics in the entire community-dwelling Spanish population aged 50 years or older, including survey year (2011 or 2014), age (50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, or ≥85 years), sex (women or men), educational level (less than primary, primary, first-stage secondary, second-stage secondary, or university), and number of comorbidities other than the index comorbidity (0, 1, 2, 3, or ≥4). Results were restricted to those comorbidities positively associated with all-cause mortality among non-disabled and disabled people. COPD, chronic obstructive pulmonary disease. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

people with mild activity limitations accounted for most cases of disability and public health interventions to better control chronic diseases are likely to be more effective in this subgroup.

Conclusion

The risk of death is markedly higher in people with disabilities as compared to their non-disabled counterparts, even after adjusting for differences in sociodemographic and clinical factors. In absolute terms, the number of deaths attributable to disability might well be very high. The population with disability must receive adequate preventive measures and health promotion initiatives to both improve survival and offer a better quality of life. Taking into account the high mortality observed in the population with disability, the study of interaction phenomena between disability and chronic health conditions can provide relevant information in terms of preventive measures.

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CRediT authorship contribution statement

Roberto Pastor-Barriuso: Writing – original draft, Software, Methodology, Formal analysis, Conceptualization. **Iñaki Galán:** Writing – review & editing, Resources, Project administration, Funding acquisition, Data curation. **Javier Damián:** Writing – original draft, Methodology, Conceptualization.

Declaration of competing interest

Authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dhjo.2024.101672.

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