SUPPLEMENTARY DATA

SUPPLEMENTARY METHODS AND RESULTS

External adjustment for baseline cardiovascular disease

Baseline cardiovascular disease (CVD) is a potential confounder for the association between disability and CVD mortality, since it relates to disability at baseline and is an independent risk factor for subsequent CVD mortality. Given that baseline chronic conditions were not measured in participants without disability, we performed bias analyses to assess the magnitude of confounding that could be expected in the disability-CVD mortality association by failing to adjust for baseline CVD.

We used the 10-year risk ratio for CVD mortality between people with and without disability as an effect measure and initially ignored the control of measured sociodemographic characteristics. To quantify confounding, we divided the crude risk ratio RR_c by the risk ratio standardized to the baseline CVD distribution among people with disability RR_s, which can be shown to be

$$\frac{RR_c}{RR_s} = \frac{RR_0P_1 + 1 - P_1}{RR_0P_0 + 1 - P_0},$$

where RR_0 is 10-year risk ratio for CVD mortality associated with baseline CVD among people without disability and P_1 and P_0 are the baseline prevalences of CVD among people with and without disability, respectively.[1,2] This equation shows that the stronger the associations between baseline CVD and disability and mortality, the greater the bias. Assuming no multiplicative interaction between disability and baseline CVD (risk ratio homogeneity), RR_0 was estimated from the study data as the sampling-weighted 10-year risk ratio for CVD mortality between people with disability with and without baseline CVD. The study data were also used to estimate P_1 as the sampling-weighted prevalence of baseline CVD among people with disability. In addition, since baseline CVD was not measured in study participants without disability, we used external data to estimate the baseline CVD prevalence among people without disability as

$$P_0 = \frac{P - P_{\text{dis}}P_1}{1 - P_{\text{dis}}},$$

where P_{dis} was the sampling-weighted prevalence of disability estimated from the study data and P was the overall prevalence of CVD in the community-dwelling Spanish population aged 40 years or older, which was obtained using external clinical data for 2013 from a representative sample of 4.8 million primary healthcare users in the *Base de Datos Clínicos de Atención Primaria* (BDCAP).[3] The estimated bias parameters P_1, P_0, and RR_0 are shown in table 2 of the supplementary data. The ratio of crude to CVD-standardized risk ratios was then $RR_c/RR_s = (2.39 \cdot 0.230 + 0.770)/(2.39 \cdot 0.059 + 0.941) = 1.220$; that is, assuming no other confounder, the 10-year risk ratio for CVD mortality between people with and without disability would be overestimated by 22.0% due to failure to adjust for baseline CVD.

The preceding bias analysis ignores the adjustment for measured sociodemographic characteristics in the present study, such as age and sex, which are major risk factors for CVD mortality. Age and sex strongly affect the development of CVD and disability, so that controlling for these demographic factors could partially adjust for confounding by baseline CVD. To measure the residual confounding by baseline CVD in the association between disability and CVD mortality after age and sex adjustment, we divided the risk ratio standardized for sex and age $RR_{s\text{-partial}}$ by the risk ratio further standardized for baseline CVD $RR_{s\text{-full}}$, which resulted in the expression

$$\frac{RR_{s\text{-partial}}}{RR_{s\text{-full}}} = \frac{\sum_{i=1}^{I} E_i \dfrac{RR_{i0}P_{i1} + 1 - P_{i1}}{RR_{i0}P_{i0} + 1 - P_{i0}}}{\sum_{i=1}^{I} E_i},$$

where E_i is the expected number of CVD deaths among participants with disability in stratum $i = 1, \ldots, I$ of sex by age group (40-54, 55-64, 65-74, 75-84, or ≥ 85 years) and RR_{i0}, P_{i1}, and P_{i0} are the stratum-specific bias parameters defined above.[2] Thus, the residual confounding by baseline CVD is a weighted average of the stratum-specific magnitudes of confounding, with weights proportional to the expected number of CVD deaths in each stratum. The expected CVD deaths E_i were estimated from the study data by multiplying the sampling-weighted number of participants with disability in each sex-by-age stratum by the sampling-weighted 10-year risk of CVD mortality among people without disability in that stratum, whereas RR_{i0}, P_{i1}, and P_{i0} were estimated using the same procedure described above within each sex-by-age stratum. Estimates of sex- and age-specific bias parameters E_i, P_{i1}, P_{i0}, and RR_{i0}

are given in table 2 of the supplementary data. Substituting these estimates into the previous equation, we obtained a ratio of partially- to fully-standardized risk ratios of $RR_{s\text{-partial}}/RR_{s\text{-full}} = 1.059$, so that the positive confounding by baseline CVD would be substantially reduced from 22.0% to 5.9% upon sex and age adjustment. Thus, little residual confounding by baseline CVD could be expected in the association between disability and CVD mortality after adjusting for these and other sociodemographic characteristics in the present study.

For self-reported data in this study and clinical data from BDCAP, prevalent CVD included heart disease (ischemic heart disease, heart failure, or atrial fibrillation for BDCAP) and cerebrovascular disease. Disaggregating both comorbidities, we also evaluated the magnitude of confounding in the association of disability with ischemic heart disease mortality (and, respectively, cerebrovascular disease mortality) by failing to adjust for baseline heart disease (and, respectively, baseline cerebrovascular disease). Bias parameters for these associations were estimated following the same methods described above and are provided in table 2 of the supplementary data. As occurred for CVD, failure to adjust for baseline heart disease would result in a 27.7% upward bias in the 10-year risk ratio for ischemic heart disease mortality associated with disability, which would drop to 3.6% after controlling for sex and age. However, baseline cerebrovascular disease would introduce similar upward biases of 19.3% and 12.5% in the association between disability and cerebrovascular mortality without and with control for sex and age, respectively. The larger residual confounding by baseline cerebrovascular disease after sex and age adjustment was due to the stronger sex- and age-specific associations between cerebrovascular disease and disability, particularly in the oldest age groups.

Table 1 of the supplementary data. Distribution of baseline sociodemographic characteristics by disability category after standardization to the overall community-dwelling Spanish population aged 40 years or older, 2007-2008

Characteristic	Overall[a]	Disability[b]				*P*[c]
		No	Mild	Moderate	Severe/ complete	
Sex						0.48
Women	52.7	52.7	53.1	55.9	53.2	
Men	47.3	47.3	46.9	44.1	46.8	
Age, y						0.85
40-54	44.1	44.1	44.2	45.5	44.9	
55-64	22.3	22.3	21.6	20.6	19.8	
65-74	17.4	17.4	17.7	17.5	19.2	
75-84	12.6	12.6	12.9	12.8	12.6	
≥ 85	3.6	3.7	3.6	3.7	3.5	
Living with a partner						0.58
No	25.3	25.4	25.7	24.8	22.6	
Yes	74.7	74.6	74.3	75.2	77.4	
Educational level						0.58
Less than primary	23.7	23.9	24.1	23.7	23.6	
Primary	31.1	31.0	31.3	30.0	38.5	
Secondary	28.5	28.5	28.3	31.0	24.5	
University	16.6	16.6	16.3	15.2	13.4	
Monthly household income, €						0.03
< 1000	28.4	28.6	28.8	30.9	37.9	
1000-1500	24.3	24.3	24.4	24.5	30.0	
1500-2000	17.5	17.4	17.6	20.5	14.4	
2000-2500	11.6	11.5	11.3	10.6	8.0	
≥ 2500	18.3	18.2	17.9	13.5	9.8	
Municipality size (inhabitants)						0.18
<10 000	22.6	22.6	22.2	22.6	28.2	
10 000-20 000	10.1	10.1	10.4	8.8	14.2	
20 000-50 000	13.8	13.9	14.5	16.7	9.5	
50 000-100 000	9.6	9.6	9.0	8.9	5.8	
≥ 100 000	43.9	43.9	43.9	42.9	42.3	
Geographical region						0.48
Northwest	10.7	10.7	10.5	12.7	11.0	
Northeast	11.0	11.0	11.4	10.8	8.5	
Madrid	13.7	13.7	13.0	10.2	10.8	
Central	13.2	13.2	12.6	13.8	17.7	

East	28.6	28.7	30.0	30.6	29.4
South	19.1	19.1	19.0	19.1	19.3
Canary Islands	3.6	3.6	3.4	2.9	3.4

[a] Sampling-weighted percentages.
[b] Fully-weighted percentages taking into account both sampling and standardization weights.
[c] *P* value for homogeneity of fully-weighted percentages among disability categories.

Table 2 of the supplementary data. Bias parameters for external adjustment of the disability-cardiovascular mortality association for baseline cardiovascular disease in the Survey on Disability, Personal Autonomy, and Dependency, Spain, 2007-2008 to 2017.

	Cardiovascular disease				Ischemic heart disease				Cerebrovascular disease			
Stratum	E^a	P_1[b]	P_0[c]	RR_0[d]	E^a	P_1[b]	P_0[c]	RR_0[d]	E^a	P_1[b]	P_0[c]	RR_0[d]
Overall		0.230	0.059	2.39		0.171	0.049	3.55		0.092	0.012	3.49
Age, y												
Women												
40-54	2.8	0.082	0.004	7.87	0.8	0.049	0.002	4.59||	1.0	0.038	0.003	4.00[e]
55-64	9.7	0.144	0.016	2.91	2.7	0.108	0.008	4.59||	1.6	0.054	0.006	4.00[e]
65-74	64.0	0.223	0.048	3.22	16.8	0.175	0.033	2.36	19.0	0.080	0.012	3.44
75-84	415.5	0.259	0.155	1.82	84.5	0.201	0.127	2.03	102.2	0.098	0.029	2.96
≥ 85	556.0	0.270	0.269	1.55	105.1	0.200	0.252	3.17	130.0	0.106	0.035	2.19
Men												
40-54	9.5	0.128	0.015	6.08	5.4	0.076	0.013	7.07	1.7	0.065	0.002	8.26[e]
55-64	23.8	0.217	0.071	2.55	10.7	0.147	0.061	3.66	5.2	0.096	0.011	8.26[e]
65-74	76.6	0.293	0.150	2.22	30.8	0.206	0.128	3.44	16.1	0.126	0.027	5.00
75-84	250.7	0.356	0.248	1.63	84.8	0.274	0.212	2.52	52.5	0.141	0.050	1.74
≥ 85	215.8	0.328	0.315	1.67	64.3	0.253	0.277	3.37	31.5	0.127	0.053	3.47

[a] Sampling-weighted expected number of cardiovascular disease deaths (and, respectively, ischemic heart disease and cerebrovascular disease deaths) among participants with disability in each sex-by-age stratum estimated from study data.

[b] Sampling-weighted prevalence of baseline cardiovascular disease (and, respectively, heart disease and cerebrovascular disease) among people with disability in each sex-by-age stratum estimated from study data.

[c] Prevalence of baseline cardiovascular disease (and, respectively, heart disease and cerebrovascular disease) among people without disability in each sex-by-age stratum derived by combining study data with external information on sex- and age-specific prevalences of cardiovascular disease (resp., heart disease and cerebrovascular disease) in the entire community-dwelling Spanish population from the *Base de Datos Clínicos de Atención Primaria* (BDCAP) 2013.

[d] Sampling-weighted 10-year risk ratio for cardiovascular disease mortality (and, respectively, ischemic heart disease and cerebrovascular disease mortality) between people with disability with and without baseline cardiovascular disease (and, respectively, heart disease and cerebrovascular disease) in each sex-by-age stratum estimated from study data.
[e] Risk ratio combining adjacent age strata due to sparse data.

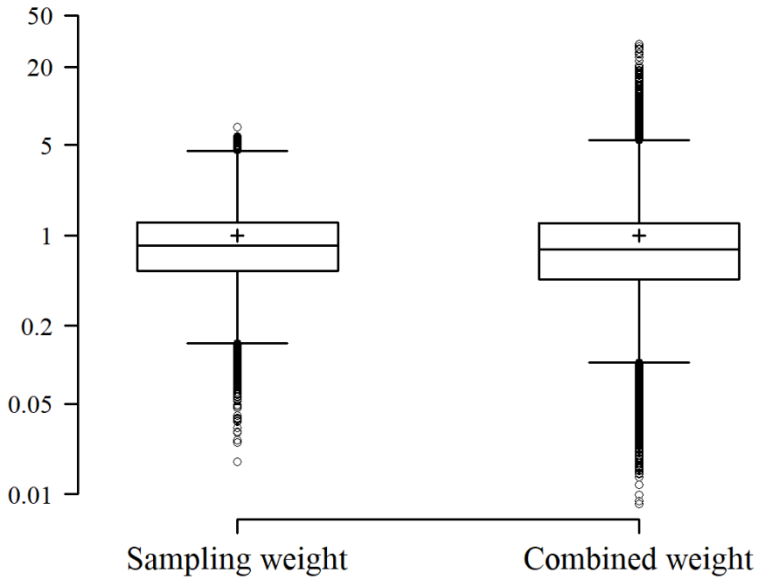

Figure 1 of the supplementary data. Distribution of sampling weights and combined weights, taking into account sampling and standardization of disability categories by sociodemographic characteristics in the Survey on Disability, Personal Autonomy, and Dependency, Spain, 2007–2008.

Boxes represent the mean (+), median (middle horizontal line), quartiles (border horizontal lines), and individual outlying weights (circles).

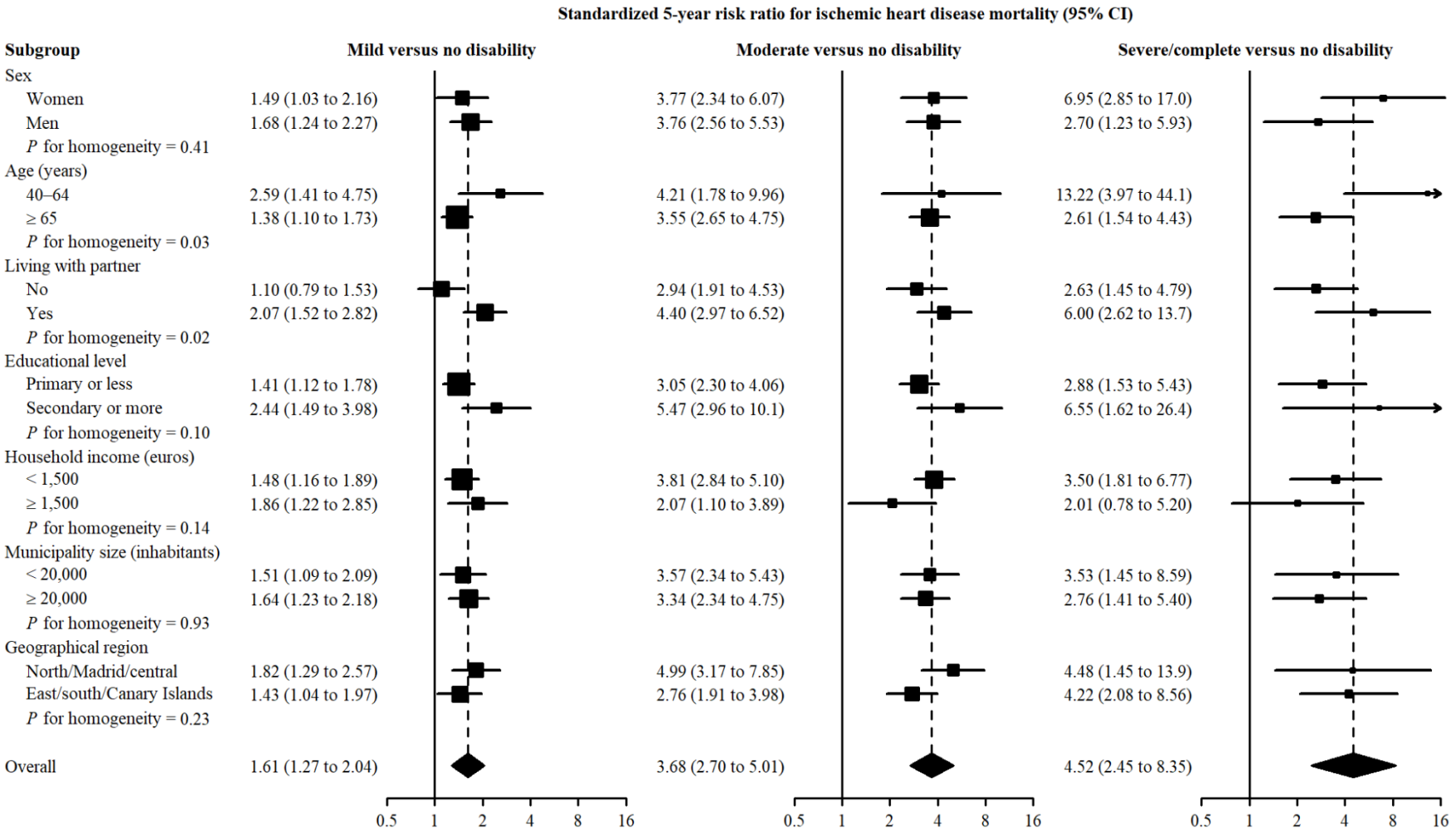

Figure 2 of the supplementary data. Standardized 5-year risk ratios for ischemic heart disease mortality across disability categories by subgroup in the community-dwelling Spanish population aged 40 years or older, 2007-2008 to 2017.

Subgroup-specific risk ratios (squares with area inversely proportional to the variance) and 95% confidence intervals (CIs, horizontal lines) were obtained from spline-based survival models stratified by disability category and sociodemographic subgroup, weighted by combined weights, and accounting for competing deaths from other causes. Combined weights were used to standardize ischemic heart disease mortality in each disability category to the

distribution of baseline sociodemographic characteristics in the entire community-dwelling Spanish population aged 40 years or older, including sex, age, living with partner, educational level, household income, municipality size, and geographical region.

Correcciones a la figura 2

Cambiar “versus” a “vs”

Cambiar “Age (years)” a “Age, y”

Cambiar guión largo a guión, “40-64”

Cambiar “with partner” a “with a partner”

Cambiar “income (euros” a “income, €”

Cambiar “1,500” a “1500”

Cambiar coma por espacio fine en “20,000”

En las columnas con cifras, cambiar “to” a guión y cerrar espacios, p ej.

1.49 (1.03-2.16)

Cerrar “95%CI”

Quitar el zero antes del punto decimal en los valores de “P for homogeneity”

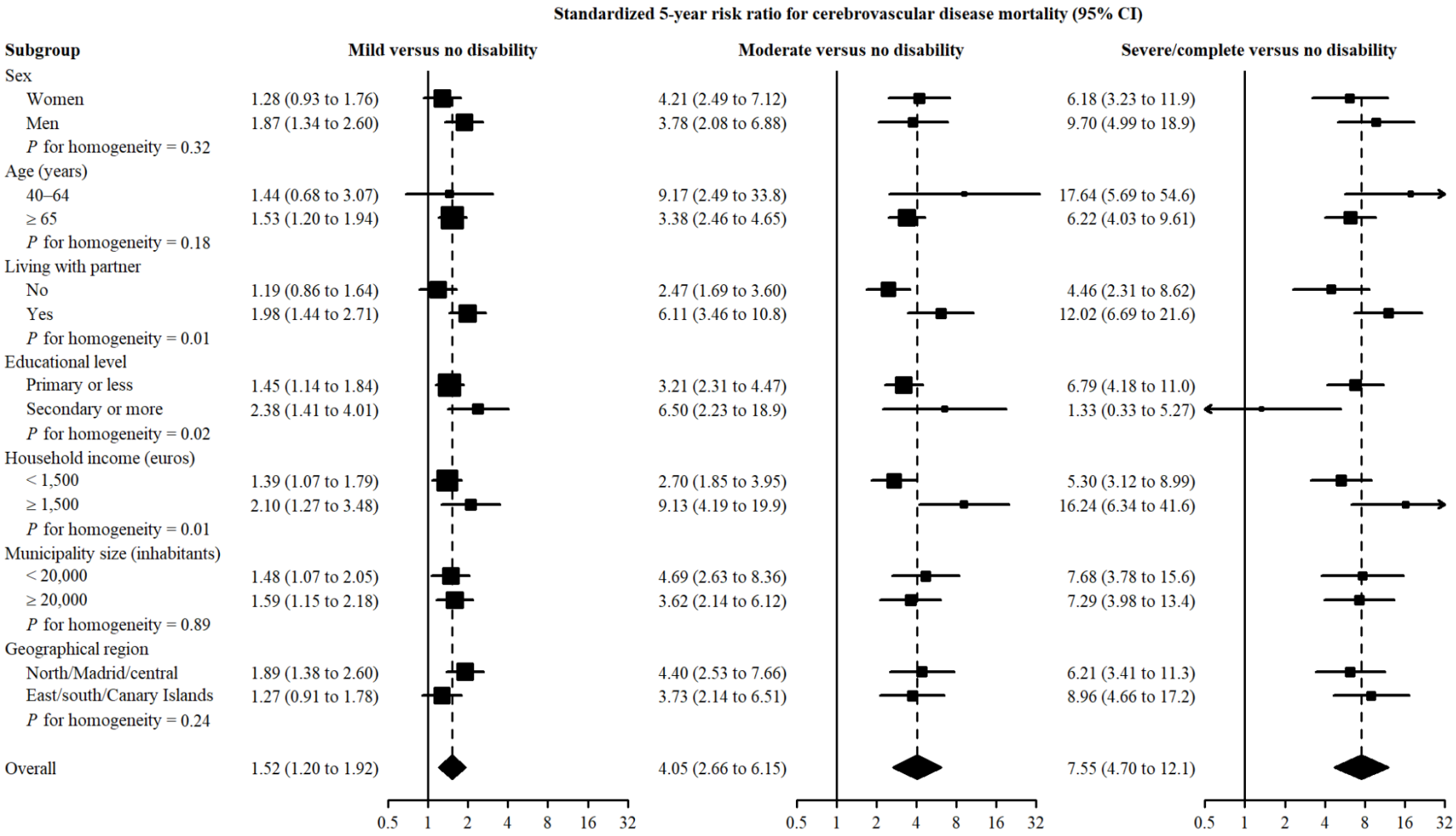

Figure 3 of the supplementary data. Standardized 5-year risk ratios for cerebrovascular disease mortality across disability categories by subgroup in the community-dwelling Spanish population aged 40 years or older, 2007-2008 to 2017.

Subgroup-specific risk ratios (squares with area inversely proportional to the variance) and 95% confidence intervals (CIs, horizontal lines) were obtained from spline-based survival models stratified by disability category and sociodemographic subgroup, weighted by combined weights, and accounting for competing deaths from other causes. Combined weights were used to standardize cerebrovascular disease mortality in each disability category to the

distribution of baseline sociodemographic characteristics in the entire community-dwelling Spanish population aged 40 years or older, including sex, age, living with partner, educational level, household income, municipality size, and geographical region.

Correcciones a la figura 2

Cambiar “versus” a “vs”

Cambiar “Age (years)” a “Age, y”

Cambiar guión largo a guión, “40-64”

Cambiar “with partner” a “with a partner”

Cambiar “income (euros” a “income, €”

Cambiar “1,500” a “1500”

Cambiar coma por espacio fine en “20,000”

En las columnas con cifras, cambiar “to” a guión y cerrar espacios, p ej.

1.49 (1.03-2.16)

Cerrar “95%CI”

Quitar el zero antes del punto decimal en los valores de “P for homogeneity”

REFERENCES OF THE SUPPLEMENTARY DATA

1. Greenland S, Lash TL. Bias analysis. In: Rothman KJ, Greenland S, Lash TL, eds. *Modern Epidemiology, 3rd ed*. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:345–380.
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3. Ministerio de Sanidad, Portal Estadístico del Sistema Nacional de Salud. *Base de Datos Clínicos de Atención Primaria - BDCAP*. https://www.sanidad.gob.es/estadEstudios/estadisticas/estadisticas/estMinisterio/SIAP/home.htm. Accessed 26 Sep 2024.