

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Socioeconomic inequalities in health status and survival: a cohort study in Rome
AUTHORS	Dei Bardi, Luca; Calandrini, Enrico; Bargagli, Anna Maria; Egidi, Viviana; Davoli, Marina; Agabiti, Nera; Cesaroni, Giulia

VERSION 1 – REVIEW

REVIEWER	Daoud, Nihaya Ben-Gurion University of the Negev, Department of Public Health, Faculty of Health Sciences
REVIEW RETURNED	26-Sep-2021

GENERAL COMMENTS	<p>Abstract: Can be more clear to international readers. Please add a definition for the variable 'Disease-Related Co-payment Exemption (DRCE).</p> <p>Introduction: please specify what do you mean by heterogeneity. There are all kinds of heterogeneity. This is a very universal term to use in a study about inequalities. Just use direct term. What do you mean by differences? do you mean inequalities? Age class means age group?</p> <p>Methods: Please add the definition of the variable disease related co-payment exemption. What was the % of the missing cases for different variables in the study? How was the missing treated?</p> <p>Data analysis: Some of the variables might have strong correlations? Was this examined before the multivariable analysis? There might be interactions or confounding effect for different independent variable? Please clarify how this was examined and what decisions were made following this analysis. How the neighborhood SES homogeneity was considered in the multivariable analysis? Would GEE be considered?</p> <p>Survival analysis: please explain how the repeated measure was considered in the analysis. How lost for follow up was considered?</p> <p>Table should be independent and include all the information needed to understand the content. Table 1: include N for the P-value for significance level. Table 2: add the total N for each of the models. Table 3: Add foot not for the Table to define TR</p>
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REVIEWER	Yu, Xue Qin Cancer Council New South Wales, Cancer Research Division
REVIEW RETURNED	12-Oct-2021

GENERAL COMMENTS	<p>This study examines the association between socioeconomic position (SEP) and health status for a large cohort of residents in Rome and to investigate the role of SEPs on their survival. The authors found that there is a significant association between SEP and a proxy of comorbidity (DRCE) and people's survival are associated with both individual SEP and contextual SEP measures, with those having high education level or living in wealthy areas having higher survival.</p> <p>I have some suggestions for the approach of statistical modelling and think that modelling SEPs (individual and contextual) separately first and then combined together may provide more insights about the impact of these SEP measures on survival.</p> <p>I also think it is better to use the term survival (as in the title) consistently throughout the paper, rather than the mixed use of 'mortality' and 'survival'. For example, in the conclusion of "The association between SEP and mortality was independent of baseline health status" would be more accurate "The association between SEP and overall survival was independent of baseline health status".</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Nihaya Daoud, Ben-Gurion University of the Negev

Comments to the Author:

C1: Abstract: Can be more clear to international readers. Please add a definition for the variable 'Disease-Related Co-payment Exemption (DRCE).

A: To facilitate international readers, we rephrased the abstract and the manuscript using "chronic or rare conditions" / "chronicity" instead of "Disease-Related Co-Payment Exemption" or "DRCE".

We think it is now clearer.

C2: Introduction: please specify what do you mean by heterogeneity. There are all kinds of heterogeneity. This is a very universal term to use in a study about inequalities. Just use direct term.

A: Thank you. We changed the beginning of the introduction, deleting the sentence "Heterogeneity in the population is often reflected in heterogeneity in health". We also rephrased the sentence "Among all the factors of heterogeneity, socioeconomic position (SEP) is often used to tackle avoidable disparities in health." in "Among the characteristics of a population, socioeconomic position (SEP) is often used to tackle avoidable disparities in health."

C3: What do you mean by differences? do you mean inequalities?

A: We consider "inequality" as a dimensional concept that expresses differences, variation, or disparity in health without any political comment or moral commitment for which we would have used the word "inequity". In this sense, "difference" or "inequality" can be considered synonyms.

C4: Age class means age group?

A: Yes, it does. To avoid misunderstandings, we agreed to substitute all the "age class" with "age group", modifying the text, the graphs, and Table 1.

Methods:

C5: Please add the definition of the variable disease related co-payment exemption.

A: We agree that the term “DRCE” does not help the readers and can be unclear, so we choose to use the term “chronic or rare conditions” / “chronicity” throughout the manuscript. We defined the variable in the section “Variables of interest” (page 4) in the following way:

“The number of chronic or rare conditions was derived from the Disease-Related Co-payment Exemptions Registry from 01 Jan 2008 to 09 Oct 2011. To characterize the baseline health status of the population, a binary variable indicating the presence of chronic or rare conditions was used.”

C6: What was the % of the missing cases for different variables in the study? How was the missing treated?

A: We used the 2011 Census population, which was complete of educational attainment, age, sex, and census block of residence. We selected only those with an identifier in the Regional Health Information System. Moreover, selecting those living in residential areas, for each subject an average neighborhood real estate price was available. For these reasons, we have a dataset without missing information on any of the variables.

Data analysis:

C7: Some of the variables might have strong correlations? Was this examined before the multivariable analysis?

A: Associations between variables were not analyzed before multivariable analyses but they were during the modeling through the estimation of Variance Inflation Factors (VIF) not reported in the draft. The complete models had low VIF (lower than 2.5), but we are not reporting those results since we ran new models (please, refer to point C8). We ran VIFs for the new models and they were always lower than commonly used thresholds of 10, 5, and 2.5, hence, multicollinearity is not likely to affect estimates or confidence intervals. We described these measures either in the method section and in the results section.

C8: There might be interactions or confounding effect for different independent variable? Please clarify how this was examined and what decisions were made following this analysis.

A: In the first analysis we considered all covariates as confounders, using them to adjust the estimations of SEP. After your insightful consideration, we ran backward elimination stepwise models starting from a model with all considered variables and all possible first-level interactions. The logistic model with the highest AIC conserved all variables and all interactions. The best AIC-wise AFT model removed, in order:

- the interaction between individual and contextual SEP,
- gender and contextual SEP,
- citizenship and contextual SEP,
- citizenship and contextual SEP,
- citizenship and gender.

Looking at these results, we choose to:

- stratify all models and analyses by sex,
- remove foreign citizens from the analyses,
- analyze the interactions further.

Therefore, to analyze the interactions further, we ran explorative analyses stratifying for education first and price quintiles then, we found that all relationships in all strata have the same directions although slightly different strengths. As the main interest of this study was to find the presence (or absence) of inequalities at individual and/or contextual level, but not to analyze how the different socioeconomic indicators interact with the other variables, we choose to show the overall effect only.

It is worth noting that, with a huge dataset like ours of almost two million individuals, every interaction can result as statistically significant.

The new results are now in the manuscript pages 7 and 8, Table 2 and Table 3, Supplemental Material, Table S1, and Table S2.

C9: How the neighborhood SES homogeneity was considered in the multivariable analysis? Would GEE be considered?

A: neighborhood SEP homogeneity was not considered in the multivariable analyses. Interpreting your comment as a suggestion, we chose to run a null Random Intercept Model clustering at the neighborhood level for both logistic and survival models (that is: overall intercept plus one intercept per every neighborhood).

For the logistic models, the resulting Intraclass Correlation Coefficient (ICC) was ICC = 0.017 for females and ICC = 0.014 for males, meaning that less than 2% of the whole variance was captured by clustering at the neighborhood level. Looking at these results, we chose not to go further in the multilevel analysis for the logistic models.

In the survival models, we tried to replicate the analysis made for the logistics using nested frailty models, but several runs of the models never reached convergence. This could be due to very low intraclass correlation. Moreover, considering that only a low percentage of individuals experienced death in our 5-year follow-up (6.7% females and 7.2% males), it is unlikely to find strong correlations between time at death and neighborhood. Hence, we chose not to consider further multilevel analysis for AFT models either.

C10: Survival analysis: please explain how the repeated measure was considered in the analysis. How lost for follow up was considered?

A: Data has no repeated measure: it consists of baseline observation, date of death (when/if occurred), and date of emigration outside the municipality of Rome (when/if occurred). The status "lost to follow up" hence refers to people who emigrated outside the municipality of Rome and was considered as "no event", i.e. right-censored, as in usual survival analysis. As discussed in the main document, we also considered people reaching their 100th birthday and living people at 31/12/2006 as right censored ("no event"). We ran a logistic model to analyze baseline differences between stayers and leavers, as discussed in the "strength and weakness" section of the draft on pages 9-10. We ran these analyses again for the new models (please refer to previous answers) and the results were similar.

C11: Table should be independent and include all the information needed to understand the content.

A: Thank you. We checked all the tables and changed them accordingly.

C12: Table 1: include N for the P-value for significance level.

A: after your comment, we discussed the utility of showing unadjusted chi-squared tests at this stage of analysis. We came up to the conclusion of showing neither chi tests nor minimum N.

We don't find useful to show minimum N that gives significance level in the table as it could be misleading and could make the table difficult to read. Moreover, we discussed the utility of the chi-tests in this table as it is meant to describe the study population. We don't find these tests informative at this point of the analysis, as we model and test for associations later in the draft. In addition, they could be misleading as it is not straightforward if they refer to Females-Males differences or inter-category differences.

C13: Table 2: add the total N for each of the models.

A: Although the total N is the same for every gender-strata model we ran, we agreed to show the Ns in both Table 2 and Table 3.

C14: Table 3: Add foot not for the Table to define TR.

A: We welcomed the suggestion and added a definition of TR in Table 3.

Reviewer: 2

Dr. Xue Qin Yu, Cancer Council New South Wales, The University of Sydney

Comments to the Author:

This study examines the association between socioeconomic position (SEP) and health status for a large cohort of residents in Rome and to investigate the role of SEPs on their survival. The authors found that there is a significant association between SEP and a proxy of comorbidity (DRCE) and people's survival are associated with both individual SEP and contextual SEP measures, with those having high education level or living in wealthy areas having higher survival.

C1: I have some suggestions for the approach of statistical modelling and think that modelling SEPs (individual and contextual) separately first and then combined together may provide more insights about the impact of these SEP measures on survival.

A: We show the complete models as part of the supplemental material, with each indicator adjusted for every other variable in the analysis. Following your suggestion, we summarized the two measures of SEP into one, defining as "High" overall SEP all individuals with the highest individual or contextual SEP and the highest or second-highest other measure. Similarly, we defined as "Low" overall SEP all people with the lowest individual or contextual SEP and the lowest or second-lowest other measure. All those outside these definitions were categorized as "Medium" overall SEP. In Table C1 is represented the categorization, the outcoming numerosity, and the resulting percentages.

Table C1: Categorization of Overall SEP variable, numerosity, and percentages by sex.

		real estates price quintiles					overall SEP	N	%
	education	1 (high)	2	3	4	5 (low)			
Males	High	71,461	48,623	35,421	26,373	20,553	High	182,728	22.4
	Medium	62,644	81,148	84,215	81,687	81,215	Medium	424,821	52.1
	Low	19,294	30,218	45,912	54,413	72,782	Low	208,410	25.5
Females	High	75,550	53,129	39,188	30,034	24,663	High	216,197	22.4
	Medium	87,518	96,323	93,430	84,750	79,883	Medium	511,237	53.0
	Low	31,425	45,936	65,488	73,981	82,986	Low	236,850	24.6

With this new variable, we ran new logistic and survival models. Results are reported respectively in Table C2 and C3 where a comparison between the three types of SEP measure can be made.

Table C2: Association between indicators of socioeconomic position and having 1+ Chronic or Rare Disease

		FEMALES (N=964,284)		MALES (N=815,959)	
		OR	95%CI	OR	95%CI

age		1.03	1.03	1.03	1.06	1.06	1.06
education	High	1	-	-	1	-	-
	Medium	1.42	1.40	1.44	1.58	1.55	1.60
	Low	1.62	1.59	1.64	1.62	1.59	1.65
real estate	1 (higher)	1	-	-	1	-	-
price quintiles	2	1.24	1.22	1.26	1.27	1.25	1.30
	3	1.52	1.50	1.54	1.54	1.52	1.57
	4	1.62	1.59	1.64	1.61	1.58	1.64
	5 (lower)	1.89	1.86	1.92	1.89	1.85	1.92
overall SEP	High	1	-	-	1	-	-
	Medium	1.46	1.44	1.48	1.53	1.50	1.55
	Low	1.88	1.85	1.90	1.86	1.83	1.89

Odds Ratios (OR) Adjusted for age.

Table C3. Association between indicators of socioeconomic position and survival

		FEMALES (N=964,284)			MALES (N=815,959)		
		TR	95%CI		TR	95%CI	
age		0.90	0.90	0.90	0.91	0.91	0.91
education	High	1	-	-	1	-	-
	Medium	0.90	0.87	0.92	0.82	0.80	0.84
	Low	0.82	0.80	0.84	0.70	0.68	0.71
real estate	1 (higher)	1	-	-	1	-	-
price quintiles	2	0.95	0.93	0.96	0.94	0.92	0.96
	3	0.92	0.90	0.94	0.88	0.86	0.90
	4	0.91	0.89	0.93	0.86	0.84	0.88
	5 (lower)	0.86	0.85	0.88	0.82	0.80	0.84
chronicity	none	1	-	-	1	-	-
	one or more	0.73	0.72	0.74	0.70	0.69	0.71
Overall SEP	High	1	-	-	1	-	-
	Medium	0.89	0.88	0.91	0.85	0.83	0.87
	Low	0.84	0.82	0.86	0.76	0.74	0.78

Times Ratios (TR) Adjusted for age.

As the estimates of Overall SEP reflect the estimates obtained with the single SEP indicators, we decided not to show these results in the paper.

C2: I also think it is better to use the term survival (as in the title) consistently throughout the paper, rather than the mixed use of 'mortality' and 'survival'. For example, in the conclusion of "The

association between SEP and mortality was independent of baseline health status" would be more accurate "The association between SEP and overall survival was independent of baseline health status".

R: We welcomed this suggestion and changed the text accordingly when possible.

VERSION 2 – REVIEW

REVIEWER	Cursio, John The University of Chicago, Public Health Sciences
REVIEW RETURNED	10-May-2022

GENERAL COMMENTS	<p>Thank you for this well-written and informative manuscript. I have a few comments regarding the research presented here:</p> <p>1) The authors' Table 1 shows age categories such as 25-34, 35-44, 45-54, and so on. However, the information in Table 2 and Table 3 treats age as a continuous variable. Did the authors' consider using the age categories in the logistic and accelerated failure time models? That would make the tables and models more descriptive, and reveal if age groups adjusted for education and real estate (SEPs) show different effects on comorbid conditions and survival.</p> <p>2) The authors might consider an ordinal model for the presence of chronic or rare diseases, instead of a logistic model. The categories could be 0,1,2,3 or more chronic conditions based on the distribution found in the data set. In addition, a non-proportional odds model may reveal interesting patterns and effects of SEP across different levels of the ordinal outcome.</p> <p>3) Table 3 shows chronicity of none versus one or more. Breaking out one or more with multiple categories 1, 2, 3 or more may reveal interesting patterns and could be useful in the accelerated failure time model.</p> <p>The main idea in 2 and 3 is that someone with only one comorbid condition can be very different than someone with 2, 3 or more comorbid conditions. Here the effect is treated equally for everyone with one or more comorbid condition.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 3 Dr. John Cursio, The University of Chicago.

Comments to the Author:

Comment 0 (C0): Thank you for this well-written and informative manuscript. I have a few comments regarding the research presented here:

Reply 0 (R0): We kindly thank Reviewer 3, Dr. John Cursio, for his work and comments. We proceed to reply with a point-by-point response.

C1: The authors' Table 1 shows age categories such as 25-34, 35-44, 45-54, and so on. However, the information in Table 2 and Table 3 treats age as a continuous variable. Did the authors' consider using the age categories in the logistic and accelerated failure time

models? That would make the tables and models more descriptive, and reveal if age groups adjusted for education and real estate (SEPs) show different effects on comorbid conditions and survival.

R1: We agree with the Reviewer's suggestion, and we ran new models using the 10-years age groups in all analyses. Following this choice, we modified tables 2, 3, S1, and S2, all the figures and text in the manuscript, referencing all of them accordingly.

C2: The authors might consider an ordinal model for the presence of chronic or rare diseases, instead of a logistic model. The categories could be 0,1,2,3 or more chronic conditions based on the distribution found in the data set. In addition, a non-proportional odds model may reveal interesting patterns and effects of SEP across different levels of the ordinal outcome.

R2: Unfortunately, because of the nature of the data, we do not think analyses with more than two categories (0, 1+) would be appropriate due to the definition of the measure and the low numerosity in specific categories of the variables (age group, SEP, sex).

Regarding the first aspect, we used an administrative database aimed at helping people with chronic or rare diseases to receive appropriate and free-of-charge assistance. The database was not intended for medical or statistical purposes. Hence, our definition of chronicity is quite rough, and we possibly observe only the more severe cases of illnesses. This can be noticed in Table 1, where approximately only one-third of the population of 65-74 years have one (or more) certified chronicity. Moreover, people with multiple chronic conditions may not be interested to have multiple certificates as the expenses for specialist visits or diagnostic tests could be already covered, totally or partially, by the first. Hence, there could be a big difference between who owns a chronicity certificate and who does not, and less marked differences between who has one certification and who owns more.

Then, there is an issue of numerosity because the number of people steeply decreases when considering more than one certificate by sex, age group, or other variables. As an example, looking at Table 1 in the manuscript, we notice that only 4.1% of males (N≈4,500) in the 25-34 age category have at least one certified chronic condition, and only ≈500 individuals (0.5% of the 25-34 male population) have two or more certificates. In the whole study population, females owning at least one certificate are ≈23% while the percentage drops to ≈8% for females with two or more. In males, the percentages are respectively ≈21% and ≈8%. We addressed the above issues in the Discussion section (strength and weakness, page 10-11).

However, we found the Reviewer's suggestion very interesting, and we decided to implement it, defining a three-category variable indicating the number of conditions (0, 1, 2+). We limited the variable to three categories because of numerosity and ran both ordinal and non-proportional odds models.

The results from ordinal models stratified by sex and adjusted by age are shown in **Table A**, while ordinal models stratified by sex and adjusted for every other variable in the table are reported in **Table B**.

Results from these models, those reported in Table 2, and supplementary material Table S1 appear to be almost identical. For this and the previously stated reasons, we chose to not show the results from ordinal models in the manuscript.

Table A: Association between indicators of socioeconomic position and number of Chronic or Rare Diseases. Residents aged 25-99 years. Rome, 09 Oct 2011.

		FEMALES (N=964,284)			MALES (N=815,959)		
		OR	95%CI		OR	95%CI	
age group	25-34	1	-	-	1	-	-
	35-44	1.62	1.58	1.67	1.69	1.63	1.75
	45-54	2.77	2.70	2.84	3.63	3.51	3.75
	55-64	5.32	5.19	5.45	8.72	8.44	9.00
	65-74	7.22	7.04	7.40	15.34	14.86	15.83
	75-84	7.13	6.95	7.32	18.76	18.15	19.38
	85-99	4.77	4.63	4.92	13.47	12.93	14.02
education	High	1	-	-	1	-	-
	Medium	1.36	1.34	1.38	1.55	1.53	1.58
	Low	1.64	1.62	1.67	1.68	1.65	1.71
real estate	1 (higher)	1	-	-	1	-	-
price quintiles	2	1.23	1.21	1.25	1.25	1.23	1.27
	3	1.51	1.49	1.54	1.52	1.50	1.55
	4	1.60	1.58	1.63	1.58	1.55	1.61
	5 (lower)	1.90	1.87	1.93	1.84	1.81	1.88

Odds Ratios (OR) from ordinal models Adjusted for age with 95% Confidence Intervals (95%CI).

Table B: Association between indicators of socioeconomic position and number of Chronic or Rare Diseases. Residents aged 25-99 years. Rome, 09 Oct 2011.

		FEMALES (N=964,284)			MALES (N=815,959)		
		OR	95%CI		OR	95%CI	
age	25-34	1	-	-	1	-	-
	35-44	1.60	1.56	1.64	1.68	1.62	1.74
	45-54	2.68	2.61	2.75	3.61	3.50	3.73
	55-64	5.19	5.06	5.32	8.81	8.53	9.10
	65-74	6.95	6.77	7.13	15.48	14.99	15.98
	75-84	6.76	6.59	6.95	18.82	18.21	19.46
	85-99	4.65	4.51	4.80	14.05	13.48	14.63
education	High	1	-	-	1	-	-
	Medium	1.24	1.22	1.26	1.41	1.38	1.43
	Low	1.37	1.35	1.39	1.43	1.40	1.45
real estate	1 (higher)	1	-	-	1	-	-
price quintiles	2	1.19	1.17	1.21	1.18	1.15	1.20
	3	1.42	1.40	1.45	1.39	1.37	1.42
	4	1.49	1.46	1.51	1.42	1.39	1.44
	5 (lower)	1.73	1.70	1.76	1.63	1.60	1.66

Odds Ratios (OR) from ordinal models Adjusted for every variable in the table

The results from non-proportional odds models, stratified by sex and adjusted for every other variable in the analysis, are reported in **Table C**. Results do not differ in meaning, trend, and statistical significance from those of logistic models: lower educated people and people living in less expensive neighborhood are more likely to have 1 and/or 2+ certified chronicity than people highly educated or living in more expensive neighborhoods. Due to the same reasons already mentioned before, we chose to show these results to the Reviewer only.

Table C: Association between indicators of socioeconomic position and number of Chronic or Rare Diseases. Residents aged 25-99 years. Rome, 09 Oct 2011.

1 vs 0		FEMALES (N=964,284)			MALES (N=815,959)		
		OR	95%CI		OR	95%CI	
age	25-34	1	-	-	1	-	-
	35-44	1.54	1.50	1.59	1.59	1.53	1.65
	45-54	2.41	2.34	2.47	2.97	2.87	3.08
	55-64	3.82	3.71	3.92	5.85	5.65	6.06
	65-74	4.46	4.33	4.58	8.77	8.46	9.08
	75-84	4.13	4.01	4.26	9.85	9.49	10.21
	85-99	2.86	2.76	2.97	7.41	7.06	7.78
education	High	1	-	-	1	-	-
	Medium	1.18	1.16	1.20	1.32	1.29	1.34
	Low	1.26	1.23	1.28	1.37	1.34	1.40
real estate	1 (higher)	1	-	-	1	-	-
price quintiles	2	1.15	1.13	1.17	1.19	1.16	1.22
	3	1.30	1.28	1.33	1.32	1.29	1.35
	4	1.34	1.31	1.37	1.32	1.29	1.35
	5 (lower)	1.52	1.49	1.55	1.51	1.47	1.54
2+ vs 0		FEMALES (N=964,284)			MALES (N=815,959)		
		OR	95%CI		OR	95%CI	
age	25-34	1	-	-	1	-	-
	35-44	2.10	1.95	2.25	2.41	2.19	2.65
	45-54	4.89	4.57	5.23	8.50	7.78	9.30
	55-64	14.42	13.51	15.40	30.07	27.55	32.82

	65-74	22.42	21.00	23.92	61.58	56.45	67.19
	75-84	22.61	21.17	24.15	79.09	72.44	86.35
	85-99	15.59	14.54	16.73	58.49	53.28	64.21
education	High	1	-	-	1	-	-
	Medium	1.44	1.40	1.48	1.56	1.52	1.60
	Low	1.65	1.61	1.70	1.55	1.50	1.59
real estate	1 (higher)	1	-	-	1	-	-
price quintiles	2	1.25	1.22	1.28	1.16	1.13	1.19
	3	1.63	1.59	1.67	1.48	1.43	1.52
	4	1.74	1.69	1.78	1.54	1.49	1.58
	5 (lower)	2.12	2.06	2.18	1.81	1.76	1.86

Odds Ratios (OR) from non-proportional odds models Adjusted for every variable in the table

C3: Table 3 shows chronicity of none versus one or more. Breaking out one or more with multiple categories 1, 2, 3 or more may reveal interesting patterns and could be useful in the accelerated failure time model.

R3: As previously stated in Reply 2, the number of individuals in the category 2+ can be small, and we are afraid of the low numerosity when adjusting for other variables, resulting in estimates based on few individuals. We previously ran accelerated failure time models with more than two categories of chronicity, and we know there is a strong negative association between survival and the number of chronic conditions.

Those analyses are presented in Table D and E. **Table D** shows the estimates stratified by sex and adjusted by age group while **Table E** shows the estimates stratified by sex and adjusted for every other variable in the table. As said, an increasingly negative effect on survival with an increasing number of chronicity is visible, although the biggest difference in effect is between the category “0” and “1” and smaller differences are visible between the category “1” and “2+”. It can also be seen that Odds Ratios of the other variables are stable and totally alike to Table 3 and Table S2. For the reasons previously stated and considering that the biggest difference in survival is between “not having” and “having” chronicity, we chose to not show the tables in the manuscript.

Table D. Association between indicators of socioeconomic position and survival. Italian residents aged 25-99 years. Rome, 2011-2016.

		FEMALES (N=964,284)			MALES (N=815,959)		
		TR	95%CI		TR	95%CI	
age group	25-34	1	-	-	1	-	-
	35-44	0.43	0.37	0.51	0.51	0.46	0.58
	45-54	0.18	0.16	0.21	0.22	0.20	0.25
	55-64	0.08	0.07	0.09	0.10	0.09	0.11
	65-74	0.04	0.03	0.04	0.04	0.04	0.05
	75-84	0.01	0.01	0.01	0.02	0.01	0.02
	85-99	0.00	0.00	0.01	0.01	0.01	0.01
education	High	1	-	-	1	-	-
	Medium	0.87	0.85	0.89	0.84	0.82	0.86
	Low	0.79	0.77	0.81	0.71	0.70	0.73
real estate	1 (higher)	1	-	-	1	-	-
price quintiles	2	0.96	0.94	0.98	0.96	0.93	0.98
	3	0.96	0.94	0.98	0.91	0.89	0.94
	4	0.95	0.93	0.97	0.90	0.88	0.92
	5 (lower)	0.94	0.91	0.96	0.88	0.86	0.91
chronicity	none	1	-	-	1	-	-
	one	0.79	0.77	0.80	0.75	0.74	0.77
	two or more	0.66	0.65	0.67	0.62	0.61	0.64

Time Ratios (TR) Adjusted for age and number of chronicity with 95% Confidence Interval (95%CI)

Table E. Association between indicators of socioeconomic position and survival. Italian residents aged 25-99 years. Rome, 2011-2016.

		FEMALES (N=964,284)			MALES (N=815,959)		
		TR	95%CI		TR	95%CI	
age group	25-34	1	-	-	1	-	-
	35-44	0.44	0.38	0.52	0.52	0.47	0.59
	45-54	0.19	0.16	0.22	0.23	0.21	0.26
	55-64	0.08	0.07	0.10	0.10	0.09	0.11
	65-74	0.04	0.03	0.05	0.04	0.04	0.05
	75-84	0.01	0.01	0.02	0.02	0.02	0.02
	85-99	0.00	0.00	0.01	0.01	0.01	0.01
education	High	1	-	-	1	-	-
	Medium	0.87	0.85	0.89	0.84	0.83	0.86
	Low	0.79	0.77	0.81	0.71	0.70	0.73
real estate	1 (higher)	1	-	-	1	-	-
price quintiles	2	0.99	0.97	1.01	1.00	0.98	1.02
	3	1.00	0.98	1.02	0.99	0.96	1.01
	4	1.01	0.98	1.03	0.99	0.97	1.02
	5 (lower)	1.00	0.97	1.02	1.00	0.98	1.03
chronicity	none	1	-	-	1	-	-
	one	0.79	0.78	0.81	0.76	0.75	0.78
	two or more	0.67	0.66	0.68	0.63	0.62	0.64

Time Ratios (TR) Adjusted for every variable in the table

C4: The main idea in 2 and 3 is that someone with only one comorbid condition can be very different than someone with 2, 3 or more comorbid conditions. Here the effect is treated equally for everyone with one or more comorbid condition.

R4: We thank the Reviewer for his insightful comments, with which we agree. However, the main focus of our study was not to analyze comorbid conditions, but the effect of different measures of socioeconomic levels on health and survival.

To summarize Reply 2 and 3, we are aware of the limit in treating people with one certified morbidity and people with more than one condition equally. Unfortunately, the need to treat this variable as dichotomic (0/1+) comes from the intrinsic nature of the data we used to measure morbidity. It should not be intended as a real or substitutive measure, but only as a proxy for chronicity: due to its bureaucratic nature we are likely to underestimate mild forms of chronicity and to not observe multi-chronicity in people who have specialist visits' or diagnostic tests' expenses already covered by previous certificates. This, the low number of individuals with 2+ certified chronicity, and the fact that models' results are totally alike when treating the variable as dichotomic or with multiple categories, lead us to keep the variable as presence/absence of chronicity. In future studies, if better-quality morbidity data would be available, we would not hesitate to use more categories. To better explain our reasons for the dichotomization of the variable to the readers, we chose to report part of the responses to the Reviewer in the discussion section.

VERSION 3 – REVIEW

REVIEWER	Cursio, John The University of Chicago, Public Health Sciences
REVIEW RETURNED	06-Jun-2022
GENERAL COMMENTS	Thank you for responding to my comment accordingly and thoroughly. The authors may want to describe in the methods section that they performed ordinal models as a sensitivity analysis, and the same conclusions were found as from the logistic models due to the nature of their data. This is optional, but important for the reader to see.