Response to: 'Associations of regular glucosamine use with all-cause and cause-specific mortality: causality assumptions need to be checked' by Safiri and Mansournia

We appreciated Safiri and Mansournia for their interest and comment on our recent study.^{1,2} Safiri *et al*¹ mentioned that we did not explain the steps for the selection of confounders that have been included in our fully adjusted models. We acknowledged that due to the limited number of the words for the manuscript required by the journal, the content for the explanation for selection of confounders was not included. Actually, all confounders in our study were selected according to the published literature,^{3–5} and these were the most important risk factors for mortality. In total, 27 confounders were included in our fully adjusted models, and the adjustment for confounding was sufficient.

As suggested by Safiri and Mansournia,¹ we examined the balance of confounding variables between the glucosamine users and non-users by using standardised mean difference. The most of confounding variables were considered balanced between the two groups (table 1), suggesting that the application of propensity scores was appropriate. We evaluated the proportional hazard assumptions for propensity scores and the outcomes, and no evidence of a violation of the assumption was observed. When we put propensity scores into the models as a covariate to adjust for baseline differences, the results were not substantially changed.

The proportional hazard assumptions for glucosamine use and outcomes were evaluated for all models, and no violation of the assumption was found. Due to 10 models for five outcomes used in our study, we did not provide the hazard curves and p values in the article.² However, we stated clearly that no violation of the assumption was found in the section of statistical analysis in the article.²

We did not provide p values for the differences in the baseline characteristics of the participants between the two groups due to a very large sample size. Even if there was a minor difference, the test also showed statistically significant results. All the p values for the differences in the baseline characteristics were less than 0.001 in this study, and all the baseline variables were included in the fully adjusted models.

Finally, in this study, we excluded participants who withdrew from the study (1299) and those with missing data on the use of glucosamine (6160). We do agree that differential reasons for

loss to follow-up could lead to selection bias. However, the baseline characteristics of the participants excluded and included in this study were generally similar, and no differential reason for loss to follow-up was found.

Zhi-Hao Li, Qing-Mei Huang, Chen Mao

Correspondence to Professor Chen Mao, Department of Epidemiology, School of Public Health, Southern Medical University, Guangzhou, China; maochen9@smu.edu.cn

Contributors All authors critically reviewed the manuscript for important intellectual content.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

© Author(s) (or their employer(s)) 2020. No commercial re-use. See rights and permissions. Published by BMJ.

To cite Li Z-H, Huang Q-M, Mao C. *Ann Rheum Dis* Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2020-217896

Received 6 May 2020

Accepted 7 May 2020

► <http://dx.doi.org/10.1136/annrheumdis-2020-217732>

Ann Rheum Dis 2020;0:1–2. doi:10.1136/annrheumdis-2020-217896

ORCID iD

Chen Mao <http://orcid.org/0000-0002-6537-6215>

REFERENCES

- 1 Safiri S, Mansournia AM. Associations of regular glucosamine use with all-cause and cause-specific mortality: causality assumptions need to be checked. *Ann Rheum Dis* 2020. 10.1136/annrheumdis-2020-217732
- 2 Li Z-H, Gao X, Chung VC, *et al*. Associations of regular glucosamine use with all-cause and cause-specific mortality: a large prospective cohort study. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-217176. [Epub ahead of print: 06 Apr 2020].
- 3 Kantor ED, Lampe JW, Navarro SL, *et al*. Associations between glucosamine and chondroitin supplement use and biomarkers of systemic inflammation. *J Altern Complement Med* 2014;20:479–85.
- 4 Ma H, Li X, Sun D, *et al*. Association of habitual glucosamine use with risk of cardiovascular disease: prospective study in UK Biobank. *BMJ* 2019;365:l1628.
- 5 Bell GA, Kantor ED, Lampe JW, *et al*. Use of glucosamine and chondroitin in relation to mortality. *Eur J Epidemiol* 2012;27:593–603.

Correspondence response

Table 1 Baseline characteristics of study participants by glucosamine use

Characteristics	Overall (N=495 077)	Glucosamine non-users (n=400 731)	Glucosamine users (n=94 346)	SMD
Age, mean (SD), years	56.55 (8.09)	55.95 (8.20)	59.08 (7.07)	0.409
Women	269 549 (54.4)	210 497 (52.5)	59 052 (62.6)	0.205
TDI, mean (SD)	-1.31 (3.09)	-1.20 (3.14)	-1.79 (2.79)	0.201
Education				0.017
Degree	160 288 (32.4)	129 146 (32.2)	31 142 (33.0)	
No degree	334 789 (67.6)	271 585 (67.8)	63 204 (67.0)	
Ethnicity				0.085
White	455 861 (92.1)	367 313 (91.7)	88 548 (93.9)	
Others	39 216 (7.9)	33 418 (8.3)	5798 (6.1)	
Household income (£)				
<18 000	116 815 (23.6)	95 680 (23.9)	21 135 (22.4)	0.094
18 000–30 999	127 517 (25.8)	100 419 (25.1)	27 098 (28.7)	
31 000–51 999	127 427 (25.7)	102 879 (25.7)	24 548 (26.0)	
52 000–100 000	97 565 (19.7)	80 314 (20.0)	17 251 (18.3)	
>100 000	25 753 (5.2)	21 439 (5.3)	4314 (4.6)	
BMI, mean (SD), kg/m ²	27.43 (4.80)	27.45 (4.84)	27.36 (4.65)	0.02
Smoking status				0.184
Never	271 144 (54.8)	219 107 (54.7)	52 037 (55.2)	
Former	171 668 (34.7)	135 486 (33.8)	36 182 (38.4)	
Current	52 265 (10.6)	46 138 (11.5)	6127 (6.5)	
Alcohol consumption				0.081
Never	21 931 (4.4)	18 688 (4.7)	3243 (3.4)	
Former	17 858 (3.6)	15 136 (3.8)	2722 (2.9)	
Current	455 288 (92.0)	366 907 (91.6)	88 381 (93.7)	
Physical activity (min/week)				0.137
<150	228 019 (46.1)	189 753 (47.4)	38 266 (40.6)	
≥150	267 058 (53.9)	210 978 (52.6)	56 080 (59.4)	
Vegetable consumption (servings/day)				0.167
<2.0	97 853 (19.8)	83 776 (20.9)	14 077 (14.9)	
2.0–3.9	222 743 (45.0)	179 783 (44.9)	42 960 (45.5)	
≥4.0	174 481 (35.2)	137 172 (34.2)	37 309 (39.5)	
Fruit consumption (servings/day)				0.286
<2.0	136 458 (27.6)	118 612 (29.6)	17 846 (18.9)	
2.0–3.9	201 446 (40.7)	163 136 (40.7)	38 310 (40.6)	
≥4.0	157 173 (31.7)	118 983 (29.7)	38 190 (40.5)	
Supplement or drug use				
Vitamin	157 133 (31.7)	104 719 (26.1)	52 414 (55.6)	0.627
Minerals and other dietary supplements	184 377 (37.2)	118 971 (29.7)	65 406 (69.3)	0.864
Aspirin	66 052 (13.3)	53 402 (13.3)	12 650 (13.4)	0.002
Statin	56 544 (11.4)	46 186 (11.5)	10 358 (11.0)	0.017
Non-aspirin NSAIDs	71 109 (14.4)	53 152 (13.3)	17 957 (19.0)	0.157
Chondroitin	7813 (1.6)	1581 (0.4)	6232 (6.6)	0.343
Health conditions				
Cardiovascular disease	28 709 (5.8)	24 621 (6.1)	4088 (4.3)	0.081
Cancer	39 659 (8.0)	31 506 (7.9)	8153 (8.6)	0.028
Diabetes	25 968 (5.2)	22 517 (5.6)	3451 (3.7)	0.093
Hypertension	279 956 (56.5)	225 247 (56.2)	54 709 (58.0)	0.036
Respiratory diseases	1957 (0.4)	1555 (0.4)	402 (0.4)	0.006
Digestive diseases	1417 (0.3)	1259 (0.3)	158 (0.2)	0.030
High cholesterol	86 406 (17.5)	70 408 (17.6)	15 998 (17.0)	0.016
Arthritis	23 217 (4.7)	15 440 (3.9)	7777 (8.2)	0.185
Dementia	219 (0.0)	184 (0.0)	35 (0.0)	0.004
Depression	76 642 (15.5)	53 848 (13.4)	15 133 (16.0)	0.073
Long-standing illness	162 123 (32.7)	131 024 (32.7)	31 099 (33.0)	0.006

Values are numbers (%) unless stated otherwise.

BMI, body mass index; NSAID, non-steroidal anti-inflammatory drug; SMD, standardised mean difference; TDI, Townsend Deprivation Index.