Supplementary material

Gu Z, Yuanyuan Y, Lingyu Z, Cong C. Assessment of the risk of incident heart failure in patients with osteoporosis: a systematic review and meta-analysis of eligible cohort studies. Pol Arch Intern Med. 2020; 130: 934-941. doi:10.20452/pamw.15598

Supplementary Table S1. The PRISMA for abstract checklist

TITLE	**CHECKLIST ITEM**	REPORTED ON PAGE #
1. Title:	Identify the report as a systematic review, meta-analysis, or both.	1
BACKGROUND		
2. Objectives:	The research question including components such as participants, interventions, comparators, and outcomes.	3
METHODS		
3. Eligibility criteria:	Study and report characteristics used as criteria for inclusion.	3
4. Information sources:	Key databases searched and search dates.	3
5. Risk of bias:	Methods of assessing risk of bias.	/
RESULTS		
6. Included studies:	Number and type of included studies and participants and relevant characteristics of studies.	3
7. Synthesis of results:	Results for main outcomes (benefits and harms), preferably indicating the number of studies and participants for each. If meta-analysis was done, include summary measures and confidence	3

	intervals.	
8. Description of the effect:	Direction of the effect (i.e. which group is favoured) and size of the effect in terms meaningful to clinicians and patients.	3
DISCUSSION		
9. Strengths and Limitations of evidence:	Brief summary of strengths and limitations of evidence (e.g. inconsistency, imprecision, indirectness, or risk of bias, other supporting or conflicting evidence)	3
10. Interpretation:	General interpretation of the results and important implications	3
OTHER		
11. Funding:	Primary source of funding for the review.	1
12. Registration:	Registration number and registry name.	/

Supplementary Table S2. The PRISMA checklist for systematic review

Section/topic	**#**	**Checklist item**	**Reported on page #**
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			

Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	/
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5

Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supporting Tables 3-7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5,6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary	1	State the principal summary measures (e.g., risk ratio,	6

measures	3	difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

Section/topic	**#**	**Checklist item**	**Reported on page #**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS,	8, 9

		follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	/
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10, 11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11-14
Limitations	25	Discuss limitations at study and outcome level (e.g.,	14

		risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14, 15
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	15

Supplementary tables for search strategies of each of the databases

Supplementary Table S3. Pubmed

("Bone Density"[Mesh] OR "Osteoporosis"[Mesh] OR Bone Densit*[Title/Abstract] OR Bone Content*[Title/Abstract] OR Osteoporos*[Title/Abstract] OR Osteopenia[Title/Abstract] OR Bone loss*[Title/Abstract]) AND ("Heart Failure"[Mesh] OR Heart Failure[Title/Abstract] OR Cardia* Failure[Title/Abstract] OR Myocardi* Failure[Title/Abstract])

Supplementary Table S4. Embase

('heart failure'/exp OR 'heart failure' OR 'heart insufficiency':ab,ti OR 'cardiac insufficiency':ab,ti OR 'myocardial insufficiency':ab,ti OR 'myocardi* failure':ab,ti

OR 'cardia* failure':ab,ti OR 'heart decompensation':ab,ti OR 'cardiac decompensation':ab,ti OR 'myocardial decompensation':ab,ti) AND ('bone density'/exp OR 'bone density' OR ((bone NEAR/2 densit*):ab,ti) OR ((bone NEAR/2 conten*):ab,ti) OR 'osteoporos*':ab,ti OR 'osteopenia':ab,ti OR ((Bone NEAR/2 loss*):ab,ti) OR 'osteoporosis'/exp OR 'osteoporosis')

Supplementary Table S5. Web of Science

(TS= (Heart NEAR/1 Failure) OR TS= (Cardia* NEAR/1 Failure) OR TS=(Myocardi* NEAR/1 Failure) OR TS= (Heart NEAR/1 Decompensation) OR TS= (cardia* NEAR/1 Decompensation) OR TS= (myocardi* NEAR/1 Decompensation) OR TS=(heart NEAR/1 insufficiency) OR TS=(cardia* NEAR/1 insufficiency) OR TS=(myocardi* NEAR/1 insufficiency)) AND (TS= (Bone NEAR/1 Densit*) OR TS=(Bone NEAR/1 Content*) OR TS=(Osteoporos*) OR TS=(Osteopenia) OR TS=(Bone NEAR/1 loss*))

Supplementary Table S6. The Cochrane library

#1 MeSH descriptor: [Heart Failure] explode all trees

#2 (Heart Failure):ti,ab,kw (Word variations have been searched)

#3 (Cardia* Failure):ti,ab,kw (Word variations have been searched)

#4 (Myocardi* Failure):ti,ab,kw (Word variations have been searched)

#5 (Heart Decompensation):ti,ab,kw (Word variations have been searched)

#6 (Cardia* Decompensation):ti,ab,kw (Word variations have been searched)

#7 (Myocardi* Decompensation):ti,ab,kw (Word variations have been searched)

#8 (Heart Insufficiency):ti,ab,kw (Word variations have been searched)

#9 (Cardia* Insufficiency):ti,ab,kw (Word variations have been searched)

#10 (Myocardi* Insufficiency):ti,ab,kw (Word variations have been searched)

#11 (Bone Density):ti,ab,kw (Word variations have been searched)

#12 (Bone Densit*):ti,ab,kw (Word variations have been searched)

#13 (Bone Content*):ti,ab,kw (Word variations have been searched)

#14 (Osteoporos*):ti,ab,kw (Word variations have been searched)

#15 (Osteopenia):ti,ab,kw (Word variations have been searched)

#16 (Bone loss*):ti,ab,kw (Word variations have been searched)

#17 (Osteoporosis):ti,ab,kw (Word variations have been searched)

#18 MeSH descriptor: [Bone Density] explode all trees

#19 MeSH descriptor: [Osteoporosis] explode all trees

#20 {OR #1-#10}

#21 {OR #11-#19}

#22 #20 AND #21

Supplementary Table S7. ClinicalTrials

(osteoporosis OR osteopenia OR bone density OR bone loss OR bone content) AND heart failure

Supplementary Table S8. Excluded studies with reasons

Article reference excluded	Reason
Liu, R. and J. Wu, Incidence and risk factors of cardiac complications among patients with osteoporotic hip fractures. Chinese Journal of Trauma, 2018. 34: 357-361.	Case series study
Ni Mhuircheartaigh O, Crowson CS, Gabriel SE, et al., Fragility Fractures Are Associated with an Increased Risk for Cardiovascular Events in Women and Men with Rheumatoid Arthritis: A Population-based Study. J Rheumatol, 2017. 44: 558-564.	Fragility fracture as the exposure
Fohtung RB, Brown DL, Koh WJH, et al., BONE MINERAL DENSITY AND SUBSEQUENT DEVELOPMENT OF HEART FAILURE IN OLDER ADULTS: THE CARDIOVASCULAR HEALTH STUDY. Journal of the American College of Cardiology, 2016. 67: 1323-1323.	Overlapping patients

Pfister R, Michels G, Sharp SJ, et al., Low bone mineral density predicts incident heart failure in men and women in EPIC-Norfolk prospective study. European Heart Journal, 2014. **35**: 527-528.	Overlapping patients
Shen C, Deng J, Zhou R, et al., Relation between bone mineral density, bone loss and the risk of cardiovascular disease in a Chinese cohort. American Journal of Cardiology, 2012. 110: 1138-1142.	Hazard ratio or event statistic for heart failure not provided
Farhat GN, Newman AB, Sutton-Tyrrell K, et al., The association of bone mineral density measures with incident cardiovascular disease in older adults. Osteoporos Int, 2007. 18: 999-1008.	No data concerning heart failure
Pfister R, Michels G, Sharp SJ, et al., Low bone mineral density predicts incident heart failure in men and women: the EPIC (European Prospective Investigation into Cancer and Nutrition)-Norfolk prospective study.	BMD as the only exposure without further classification into osteoporosis or osteopenia

JACC Heart Fail, 2014. 2: 380-389.	

Supplementary Table S9. Sensitivity analyses

Analyses	pooled HR of remained studies	95% Confidence interval	P-value	heterogeneity	
				I^2 statistics	P-value (Chi^2 test)
1	1.18	1.06−1.30	0.002	52.61	0.15
2	1.26	1.11−1.44	<0.001	0.00	0.81
3	1.13	1.06−1.21	<0.001	0.00	0.62

1. Exclusion of the study of Fohtung 2017
2. Exclusion of the study of Chiu 2017
3. Exclusion of the study of Yu 2014

A P-value < 0.05 was considered to be significant.