

The authors reply: Letter on: " Sarcopenia and its association with falls and fractures in older adults: A systematic review and meta-analysis" by Zhang et al.

Thank you for the comments to our recent article "Sarcopenia and its association with falls and fractures in older adults: A systematic review and meta-analysis".¹

Firstly, as mentioned in our article, studies were excluded from the meta-analysis if an odds ratio (OR) could not be calculated because of insufficient data, or confidence intervals were not presented. Therefore, we were not able to include the studies of Cawthon,² Schaap,³ and Henwood,⁴ as hazard ratios^{2,3} or risk ratios⁴ were reported. These measures are not

interchangeable with ORs^{5,6} but can be converted if information about the baseline risk is available.⁷ We agree that the above-mentioned studies are valuable; therefore, we contacted the authors to obtain the data needed to compute ORs. Two authors of the three studies responded, which allowed us to include those studies in the meta-analysis.^{2,3} Both were prospective studies examining the association between sarcopenia with falls and fractures. ORs reported in our original article¹ did not change significantly after inclusion

First author, year	N	OR (95% CI)
<u>Cross-sectional design</u>		
Bae, 2017	3827	2.05 (1.12-3.75)
Benjumea, 2018	512	0.88 (0.60-1.30)
Chalhoub, 2015	6658	1.79 (1.43-2.23)
Clynes, 2015	298	1.62 (0.41-6.36)
Dietzel, 2015	288	0.95 (0.35-2.61)
Gadelha, 2018	196	1.81 (0.87-3.78)
Lera, 2017	1006	1.83 (1.07-3.14)
Martinez, 2015	110	2.10 (0.79-5.56)
Meng, 2015	771	1.32 (0.66-2.62)
Sjoblom, 2013	590	2.50 (1.26-4.95)
Tanimoto, 2014	1110	2.01 (1.38-2.93)
Trajanoska, 2018	2301	1.22 (0.90-1.66)
Woo, 2014	2848	1.59 (1.02-2.48)
Yamada, 2013	1882	1.81 (1.43-2.30)
Subgroup ($I^2=33.9\%$)		1.60 (1.37-1.86)
<u>Prospective design</u>		
Bischoff-Ferrari, 2015	445	2.07 (0.95-4.51)
Buckinx, 2018	247	1.35 (0.78-2.35)
Cawthon, 2015	5828	2.38 (1.75-3.23)
Landi, 2012	260	3.45 (1.68-7.09)
Matsumoto, 2017	162	7.68 (1.41-41.8)
Menant, 2017	419	1.67 (1.04-2.69)
Schaap, 2017	489	1.56 (1.03-2.37)
Van Puyenbroeck, 2012	276	1.39 (0.75-2.57)
Subgroup ($I^2=35.8\%$)		1.91 (1.52-2.40)

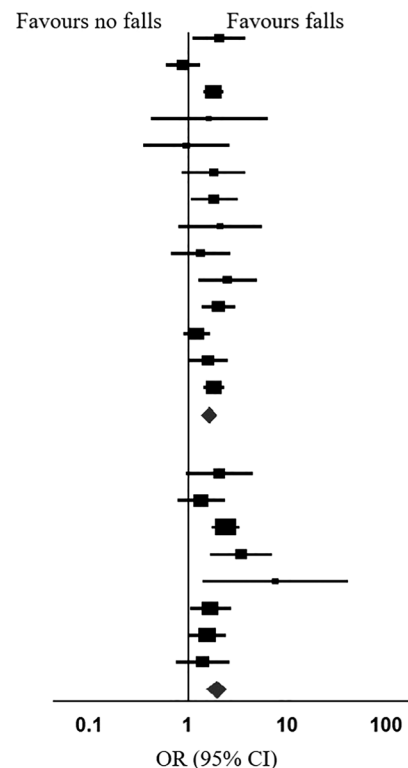


Figure 1 Forest plot of odds ratio for falls in sarcopenic individuals vs. non-sarcopenic individuals

First author, year	N	OR (95% CI)
Cross-sectional design		
Clynes, 2015	298	0.99 (0.20-4.93)
Hida, 2013	2868	1.48 (1.15-1.89)
Hida, 2016	1824	1.96 (1.39-2.77)
Hong, 2015	3077	1.61 (1.35-1.91)
Huo, 2015	680	1.14 (0.83-1.56)
Huo, 2016	680	1.53 (1.12-2.08)
Iolascon, 2015	121	1.25 (0.30-5.19)
Locquet, 2018	288	1.73 (0.90-3.34)
Sjblom, 2013	590	3.30 (1.58-6.90)
Trajanoska, 2018	5911	1.67 (1.24-2.24)
Yoo, 2016	1970	6.91 (5.39-8.87)
Yoshimura, 2018	637	1.34 (0.91-1.98)
Subgroup ($I^2=91.5\%$)		1.84 (1.30-2.62)
Prospective design		
Cawthon, 2015	5934	2.19 (1.33-3.61)
Chalhoub, 2015	6658	1.70 (1.33-2.16)
Hars, 2016	913	2.26 (1.01-5.04)
Schaap, 2017	496	0.99 (0.55-1.77)
Scott, 2017	861	2.13 (1.32-3.44)
Steihaug, 2018	191	2.00 (0.60-7.00)
Yu, 2014	4000	1.49 (1.09-2.02)
Subgroup ($I^2=6.1\%$)		1.73 (1.14-2.64)

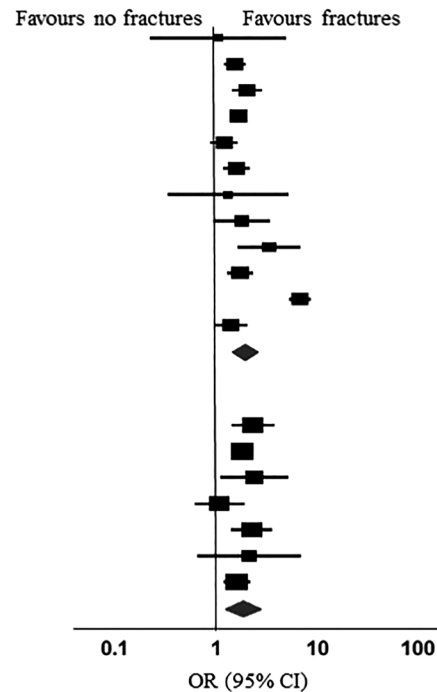


Figure 2 Forest plot of odds ratio for fractures in sarcopenic individuals vs. non-sarcopenic individuals

of these studies (falls prospective studies: pooled OR 1.91, 95% CI 1.52–2.40, $P < 0.001$, $I^2 = 36\%$; fractures prospective studies: pooled OR 1.73, 95% CI 1.14–2.64, $P = 0.011$, $I^2 = 6\%$) (Figures 1 and 2).

Secondly, Zhang *et al.* suggested to take the types of fracture into consideration when conducting the meta-analysis of the association between sarcopenia and fractures. We agree with the authors that fracture sites vary significantly in their risk profiles⁸ and appreciate the subgroup analysis performed by them. However, we have updated the subgroup analysis because (i) some studies reported the association between sarcopenia with more than one type of fracture, and (ii) we obtained additional data from Cawthon² and Schaap³ to compute ORs. Our subgroup analysis showed a significant association between sarcopenia and hip fractures (OR 2.06, 95% CI 1.35–3.14, $P = 0.001$, $I^2 = 94\%$) and incident fractures (OR 1.63, 95% CI 1.13–2.35, $P = 0.009$, $I^2 = 25\%$), but the association was insignificant for non-vertebral fractures (two studies) (OR 1.66, 95% CI 0.78–3.56, $P = 0.190$, $I^2 = 0\%$) and vertebral fractures (two studies) (OR 1.41, 95% CI 0.66–3.01, $P = 0.373$, $I^2 = 82\%$) among older adults (Figure 3).

Finally, Zhang *et al.* raised an important point regarding the number of falls. As each fall is associated with a risk of injury, functional decline, and loss of autonomy, the risk profile of recurrent fallers is not equivalent to that of single fallers.^{9,10} Of the 22 studies included in our meta-analysis, 20 studies reported at least one fall (≥ 1) as outcome, and two studies reported recurrent falls (≥ 2) as outcome.^{2,3} We acknowledge the limitation

of our article that a subgroup analysis regarding the number of falls cannot be performed owing to insufficient data.

Acknowledgement

The authors certify that they comply with the ethical guidelines for authorship and publishing of the *Journal of Cachexia, Sarcopenia and Muscle*.¹¹ This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie-Sklodowska-Curie (H2020 Marie Skłodowska-Curie Actions) grant agreement no. 675003 (PANINI programme) and no. 689238 (PreventIT). We are grateful to Cawthon P. M. and Schaap L. A. for providing information on their studies. The Osteoporotic Fractures in Men (MrOS) Study is supported by the National Institutes of Health funding. The following institutes provide support: the National Institute on Aging (NIA), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Center for Advancing Translational Sciences (NCATS), and National Institutes of Health (NIH) Roadmap for Medical Research under the following grant numbers: U01 AG027810, U01 AG042124, U01 AG042139, U01 AG042140, U01 AG042143, U01 AG042145, U01 AG042168, U01 AR066160, and UL1 TR000128. The funders had no role in the design and conduct of the study, data collection and analysis,

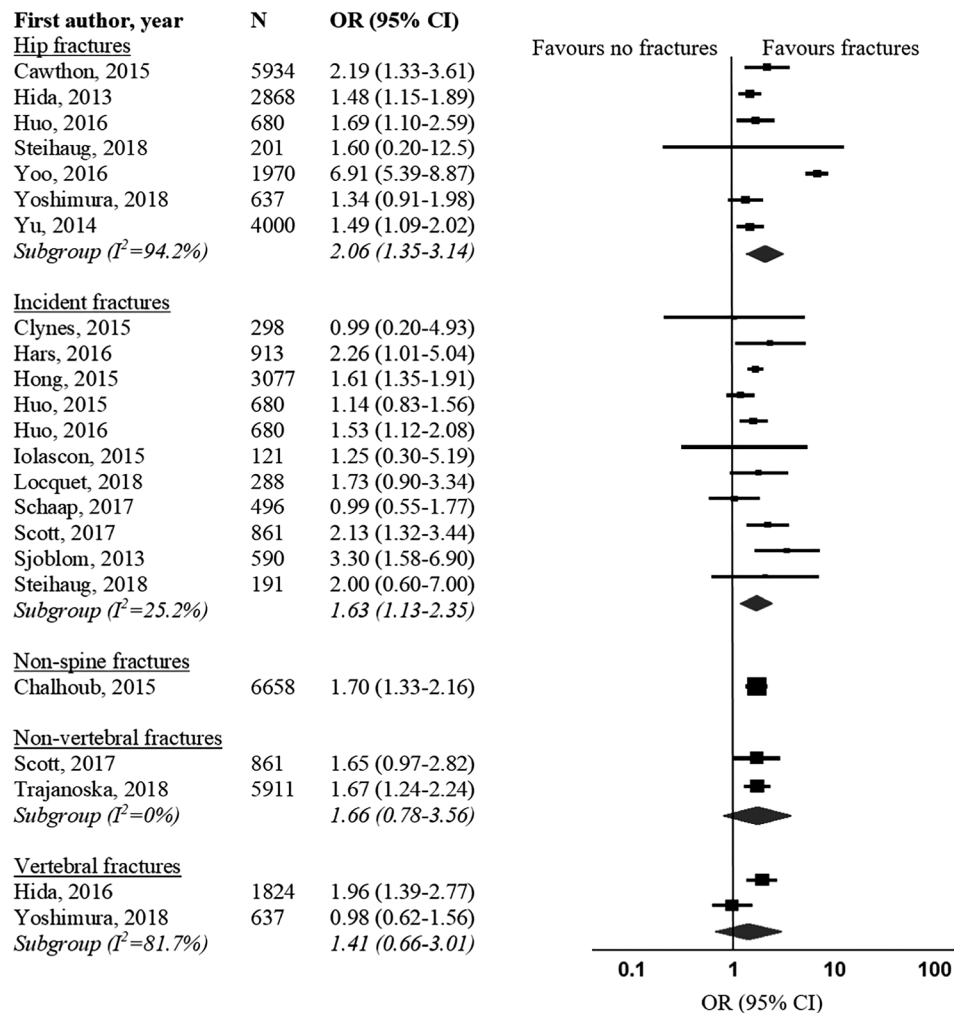


Figure 3 Forest plot of odds ratio for fractures in sarcopenic individuals vs. non-sarcopenic individuals, stratified by fracture types

interpretation of data, or preparation of the manuscript.

Suey S.Y. Yeung

Department of Human Movement Sciences, @AgeAmsterdam, Faculty of Behavioural and Movement Sciences, Amsterdam Movement Sciences, Vrije Universiteit, Amsterdam, The Netherlands

Department of Medicine and Aged Care, @AgeMelbourne, The Royal Melbourne Hospital, The University of Melbourne, City Campus, Level 6 North, 300 Grattan Street, Parkville, Victoria 3050, Australia

Martijn W. Heymans

Department of Epidemiology and Biostatistics, Amsterdam Public Health Research Institute, VU University Medical Center, Amsterdam, The Netherlands

Andrea B. Maier 

Department of Human Movement Sciences, @AgeAmsterdam, Faculty of Behavioural and Movement Sciences, Amsterdam Movement Sciences, Vrije Universiteit, Amsterdam, The Netherlands

Department of Medicine and Aged Care, @AgeMelbourne, The Royal Melbourne Hospital, The University of Melbourne, City Campus, Level 6 North, 300 Grattan Street, Parkville, Victoria 3050, Australia
andrea.maier@unimelb.edu.au

References

- Yeung SSY, Reijnierse EM, Pham VK, Trappenburg MC, Lim WK, Meskers CGM, et al. Sarcopenia and its association with falls and fractures in older adults: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle*. 2019;**10**:485–500.
- Cawthon PM, Blackwell TL, Cauley J, Kado DM, Barrett-Connor E, Lee CG, et al. Evaluation of the usefulness of consensus

- definitions of sarcopenia in older men: results from the observational osteoporotic fractures in men cohort study. *J Am Geriatr Soc.* 2015;**63**:2247–2259.
3. Schaap LA, van Schoor NM, Lips P, Visser M. Associations of sarcopenia definitions, and their components, with the incidence of recurrent falling and fractures; the Longitudinal Aging Study Amsterdam. *J Gerontol A Biol Sci Med Sci.* 2018;**73**:1199–1204.
 4. Henwood T, Hassan B, Swinton P, Senior H, Keogh J. Consequences of sarcopenia among nursing home residents at long-term follow-up. *Geriatr Nurs.* 2017;**38**:406–411.
 5. Stare J, Maucort-Boulch D. *Odds ratio, hazard ratio and relative risk.* 2016;**13**:59–67.
 6. Scott I. Interpreting risks and ratios in therapy trials. *Australian Prescriber.* 2008;**31**:12–16.
 7. Grant RL. Converting an odds ratio to a range of plausible relative risks for better communication of research findings. *BMJ.* 2014;**348**:f7450.
 8. FitzGerald G, Boonen S, Compston JE, Pfeilschifter J, LaCroix AZ, Hosmer DW Jr, et al. Differing risk profiles for individual fracture sites: evidence from the Global Longitudinal Study of Osteoporosis in Women (GLOW). *J Bone Miner Res.* 2012;**27**:1907–1915.
 9. Vassallo M, Sharma JC, Allen SC. Characteristics of single fallers and recurrent fallers among hospital in-patients. *Gerontology.* 2002;**48**:147–150.
 10. Bischoff-Ferrari HA, Orav JE, Kanis JA, Rizzoli R, Schlogl M, Staehelin HB, et al. Comparative performance of current definitions of sarcopenia against the prospective incidence of falls among community-dwelling seniors age 65 and older. *Osteoporos Int.* 2015;**26**:2793–2802.
 11. von Haehling S, Morley JE, Coats AJS, Anker SD. Ethical guidelines for publishing in the journal of cachexia, sarcopenia and muscle: update 2017. *J Cachexia Sarcopenia Muscle.* 2017;**8**:1081–1083.