

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Risk factors for fear of falling in stroke patients: A systematic review and meta-analysis
<b>AUTHORS</b>	Xie, Qi; Pei, Ju-Hong; Gou, Ling; ZHANG, Yabin; Zhong, Juan-Ping; Su, Yu-Jie; Wang, Xing-Lei; Ma, Li; Dou, Xin-Man

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Han, Dug Yeo Auckland District Health Board, Starship Child Health
<b>REVIEW RETURNED</b>	03-Sep-2021

<b>GENERAL COMMENTS</b>	No suggestion made for statistical analysis.
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<b>REVIEWER</b>	Biondi-Zoccai, Giuseppe Sapienza University of Rome
<b>REVIEW RETURNED</b>	08-Sep-2021

<b>GENERAL COMMENTS</b>	<p>The authors report an interesting meta-analysis of risk factors for falling in stroke patients.</p> <p>Despite the work strengths, I recommend addressing the following concerns:</p> <p>Methods and Results: Explore the risk of small study effects with inspection of funnel plots and regression tests.</p> <p>Methods and Results: Explore the presence of potential effect modifiers with meta-regression.</p> <p>Methods and Results: Explore the presence of potential correlation between risk factors and outcomes with multivariate meta-analysis.</p> <p>Methods and Results: Explore the potential prognostic role at short and long term with additional analyses.</p> <p>Methods and Results:</p>
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<b>REVIEWER</b>	Nath, Mintu University of Aberdeen, Medical Statistics Team
<b>REVIEW RETURNED</b>	13-Sep-2021

<b>GENERAL COMMENTS</b>	<p>The study conducts a systematic review to identify risk factors for fear of falling during a stroke. The authors conducted an extensive database covering PubMed, Embase, Cochrane Library database, Web of Science, CINAHL, PsycINFO and other sources.</p> <p>However, the manuscript does not provide the methodological details expected in a manuscript presenting the systematic review and meta-analysis. For example, it is not clear from the text and supplementary materials regarding the estimation of effect size and corresponding 95% CI for categorical and numerical risk</p>
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	<p>factors. The choice of fixed and random effects models are not well-explained. The manuscript does not elaborate on different types of biases and the nature of statistical heterogeneity. The authors did not attempt to address the issue of potential confounders.</p> <p>The manuscript included 2-3 studies to estimate the effect size for most risk factors, while for others, the manuscript presents a narrative based on a single study. Hence the current systematic review has limited scope regarding the objectives, modelling options for meta-analyses and conclusions relevant for the scientific community. The availability of few studies also means the estimate of heterogeneity will be biased or non-estimable. The sensitivity analysis using the leave-one-out approach will also be insufficient in most scenarios.</p> <p>Figures in the manuscript reproduce the forest plots verbatim from RevMan software with no clarifications of statistics presented. The statements on effect sizes and syntheses of the results are repetitive, inadequate and sometimes incorrect.</p> <p>Unless this outcome variable is very rare in nature, the current systematic review does not contribute significantly to the existing knowledge.</p>
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## VERSION 1 – AUTHOR RESPONSE

Replies to Review #1 :

No suggestion made for statistical analysis.

Answer: Thank you very much for your suggestions.

Replies to Review #2 :

1. Methods and Results: Explore the risk of small study effects with inspection of funnel plots and regression tests.

Answer: Thank you for pointing out this important question. We are sorry that we missed this information in the previous manuscript. Actually, funnel plots, plots of the trials' effect estimate against sample size, may be useful to assess the validity of meta-analyses<sup>1 2</sup>. Therefore, for the number of pooled studies more than two studies, drawing funnel plots to detect publication bias. For details, please see the texts marked red in the section of 'statistical analysis', 'results of the meta-analysis' and 'supplementary file'.

2. Methods and Results: Explore the presence of potential effect modifiers with meta-regression.

Answer: Thank you very much for your suggestions. We agree that it is necessary to explore the study of heterogeneity. However, Oxman AD et al.<sup>3</sup> pointed that unless there is a sufficient number of studies, heterogeneity analysis is difficult to produce useful results. We referred to the research of Koji et al.<sup>4</sup> and explored covariates affecting heterogeneity of ORs among included three studies of mobility. Univariate meta-regression analysis identified year of publication, sample size and number of women as a significant source of heterogeneity. For details, please see the texts marked red in the section of 'abstract', 'statistical analysis' and 'results of the meta-analysis'.

3. Methods and Results: Explore the presence of potential correlation between risk factors and outcomes with multivariate meta-analysis.

Answer: Thank you for your helpful suggestions. Regarding "explore the presence of potential correlation between risk factors and outcomes with multivariate meta-analysis", we agree that it is

necessary to explore the potential correlation. Due to the limited number of studies, it is not possible to stratify by baseline characteristics and adjust the covariates, so multivariate regression couldn't be performed<sup>5</sup>. However, we think it is necessary to make further explanations in the text, we have added corresponding explanations in the revised version. For details, please see the texts marked red in the section of 'mobility' and 'discussion'.

4. Methods and Results: Explore the potential prognostic role at short and long term with additional analyses.

Answer: Thank you for your helpful suggestions. Due to the limitation of the number of documents included, it is impossible to conduct the potential prognostic role at short and long term with additional meta-analysis, but this issue is of great significance for later clinical research. Therefore, we have extended our discussion with this point in the revised version. Please see the texts marked red in the section of 'discussion'.

Replies to Review #3 :

1. However, the manuscript does not provide the methodological details expected in a manuscript presenting the systematic review and meta-analysis. For example, it is not clear from the text and supplementary materials regarding the estimation of effect size and corresponding 95% CI for categorical and numerical risk factors. The choice of fixed and random effects models are not well-explained. The manuscript does not elaborate on different types of biases and the nature of statistical heterogeneity. The authors did not attempt to address the issue of potential confounders.

Answer: Thank you for pointing out this important question. We are sorry that we did not elaborate on this information in the previous manuscript. In fact, our study directly extracted the OR/RR value or 95%CI from the included research data and merged the OR value through RevMan 5.3 software without going through the data conversion process. We have added and corrected these incorrect statements in 'data extraction and quality assessment', 'statistical analysis' and 'supplementary file 3'. In addition, in the revised version of the manuscript we have added information about choosing fixed and random effects. See the text marked in red in the 'Age' and 'Balance' section for details. Finally, meta-regression was used to analyze the sources of heterogeneity between studies, and the funnel plots were used to indicate whether the included studies had publication bias. Carry out sensitivity analysis and subgroup analysis for studies with large heterogeneity to analyze the source of heterogeneity between studies. For details, please refer to the red marked texts in the 'statistical analysis', 'balance ability', 'mobility' and 'supplementary file 5-7'.

2. The manuscript included 2-3 studies to estimate the effect size for most risk factors, while for others, the manuscript presents a narrative based on a single study. Hence the current systematic review has limited scope regarding the objectives, modelling options for meta-analyses and conclusions relevant for the scientific community. The availability of few studies also means the estimate of heterogeneity will be biased or non-estimable. The sensitivity analysis using the leave-one-out approach will also be insufficient in most scenarios.

Answer: Thank you for your helpful suggestions. We believe that it is necessary. By explaining the research on the association between the fear of falling and the risk factors in stroke patients, as well as the research on the risk factors, it will help to deepen the discussion and provide more enlightenment for future research. However, due to the limitation of the number of studies, it is not possible to perform data consolidation analysis on other risk factors, and only descriptive analysis can be performed in the results section. Therefore, we have expanded the discussion on this point in the revised edition. In addition, in order to understand the source of heterogeneity, we conducted meta-regression analysis and further discussed heterogeneity in the revised edition. For details, please refer to the red marked texts in the 'statistical analysis' and 'discussion'.

3. Figures in the manuscript reproduce the forest plots verbatim from RevMan software with no clarifications of statistics presented. The statements on effect sizes and syntheses of the results are

repetitive, inadequate and sometimes incorrect.

Answer: Thank you for pointing out this important question. We are sorry that we are not elaborate on this information in the previous manuscript. In the updated version, we have reinterpreted the results of statistical analysis, modified the expression, and checked some incorrect information. For details, please see the texts marked red in the section of 'statistical analysis' and 'results of the meta-analysis'.

Reference

1. Light RJ, Pillemer DB. Summing up. The science of reviewing research. Cambridge, MA: Harvard University Press, 1984.
2. Egger M, Davey Smith G. Misleading meta-analysis. Lessons from “an effective, safe, simple” intervention that wasn’t. BMJ 1995;310:752-4.
3. Oxman AD, Guyatt GH. A consumer's guide to subgroup analyses. Annals of internal medicine 1992;116(1):78-84. doi: 10.7326/0003-4819-116-1-78 [published Online First: 1992/01/01]
4. Okabayashi K, Ashrafian H, Hasegawa H, et al. Body mass index category as a risk factor for colorectal adenomas: a systematic review and meta-analysis. The American journal of gastroenterology 2012;107(8):1175-85; quiz 86. doi: 10.1038/ajg.2012.180 [published Online First: 2012/06/27]
5. Jackson D, Riley R, White IR. Multivariate meta-analysis: potential and promise. Stat Med 2011;30(20):2481-98. doi: 10.1002/sim.4172 [published Online First: 2011/01/27]

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Han, Dug Yeo Auckland District Health Board, Starship Child Health
<b>REVIEW RETURNED</b>	06-Nov-2021
<b>GENERAL COMMENTS</b>	No suggestion made for statistical analysis.
<b>REVIEWER</b>	Nath, Mintu University of Aberdeen, Medical Statistics Team
<b>REVIEW RETURNED</b>	01-Feb-2022
<b>GENERAL COMMENTS</b>	<p>Choice of fixed and random effects models to conduct the meta-analysis should be based on the distribution of effect sizes and accounting for the relevant sources of errors. The revised text provides inadequate or incorrect justification for selecting the model. The authors suggested that they first employed a fixed-effect model and subsequently considered a random-effects model when the test of heterogeneity was statistically significant. This is not a correct approach to selecting a model for meta-analysis. Some literature on meta-analysis incorrectly suggests such strategies.</p> <p>As presented in the current manuscript, authors should recognise that the random-effects model with very few studies will not accurately estimate between-studies variance. Therefore, the magnitude and precision of the overall effect size will not be correctly estimable from a random-effects model.</p> <p>Meta-regression employing appropriate moderator variables to explain between-studies variation is useful. However, the authors did not justify the selection of moderator variables considered in this manuscript. For example, variables like sample size and the number of females are already considered by the model as the</p>

	weighting factor. Meta-regression models incorporating the above variables as moderator variables are unreasonable.
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## VERSION 2 – AUTHOR RESPONSE

Replies to Review #1 :

No suggestion made for statistical analysis.

Answer: Thank you very much for your approval of the work.

Replies to Review #2 :

1. Methods and Results: Explore the risk of small study effects with inspection of funnel plots and regression tests.

Answer: Thank you for pointing out this important question. We are sorry that we missed this information in the previous manuscript. Indeed, funnel plots, plots of the trials' effect estimate against sample size, may be useful to assess the validity of meta-analyses<sup>1 2</sup>. Therefore, funnel plots and Egger's linear regression test were performed to detect publication bias when the number of studies was >2. For details, please see the texts marked red in the section of 'Statistical analysis (page 6)', 'Physical factors (page 11)' and 'History of falls (page 12)'.

2. Methods and Results: Explore the presence of potential effect modifiers with meta-regression.

Answer: Thank you very much for your suggestions. We agree that it is necessary to explore the study of heterogeneity. However, Oxman AD et al.<sup>3</sup> pointed that unless there is a sufficient number of studies, heterogeneity analysis is difficult to produce useful results. We referred to the research of Koji et al.<sup>4</sup> and explored covariates affecting ORs heterogeneity.

In the 'Statistical analysis' section, We have changed 'To help understand the sources of heterogeneity, meta-regression analysis was performed using study characteristics as moderator variables, including year of publication, sample size, and the number of females' to 'When the number of included studies was >2, subgroup and meta-regression analyses were performed to explore the sources of heterogeneity based on the following factors: SwePASS score, age, sample size and the number of females. Subgroup analysis and meta-regression were performed after post hoc adjustment'.

In the 'mobility' section, we have revised this section, reported as follows: Meta-regression was performed to explore potential sources of heterogeneity based on an a priori list of factors related to clinical prognosis<sup>38</sup>. Univariate meta-regression analysis identified age ( $p=0.017$ ) as a significant source of heterogeneity. However, due to the limited number of studies, it was impractical to eliminate the sources of heterogeneity and adjust covariates; therefore, multivariate meta-regression could not be performed. Please see the texts marked red in the section of 'Statistical analysis (page 6)' and 'mobility (page 12)'.

3. Methods and Results: Explore the presence of potential correlation between risk factors and outcomes with multivariate meta-analysis.

Answer: Thank you for your helpful suggestions. Regarding "explore the presence of potential correlation between risk factors and outcomes with multivariate meta-analysis", we agree that it is necessary to explore the potential correlation. Due to the limited number of studies, it is not possible to stratify by baseline characteristics and adjust the covariates, so multivariate regression couldn't be performed<sup>5</sup>. However, we think it is necessary to make further explanations in the text, we have added corresponding explanations in the revised version, reported as follows:

In the 'mobility' section, we have revised this section, reported as follows: Meta-regression was performed to explore potential sources of heterogeneity based on an a priori list of factors related to clinical prognosis<sup>38</sup>. Univariate meta-regression analysis identified age ( $p=0.017$ ) as a significant source of heterogeneity. However, due to the limited number of studies, it was impractical to eliminate

the sources of heterogeneity and adjust covariates; therefore, multivariate meta-regression could not be performed.

In 'Discussion' section, we have added the following: (2) All the included studies were observational studies, and therefore the role of confounding factors should be considered. However, due to the limited number of studies, a multivariate meta-analysis could not be performed to assess the robustness of our findings and analyze the effect size of multiple risk factors at the same time<sup>60</sup>. For details, please see the texts marked red in the section of 'mobility (page 12)' and 'study limitations in the discussion (page 17)'.

4. Methods and Results: Explore the potential prognostic role at short and long term with additional analyses.

Answer: Thank you for your helpful suggestions. This issue is of great significance for later clinical research. Therefore, we have extended our discussion with this point in the revised version. Please see the texts marked red in the section of 'discussion (page 15-16)'.

Replies to Review #3 :

1. However, the manuscript does not provide the methodological details expected in a manuscript presenting the systematic review and meta-analysis. For example, it is not clear from the text and supplementary materials regarding the estimation of effect size and corresponding 95% CI for categorical and numerical risk factors. The choice of fixed and random effects models are not well-explained. The manuscript does not elaborate on different types of biases and the nature of statistical heterogeneity. The authors did not attempt to address the issue of potential confounders.

Answer: Thank you for pointing out this important question. We are sorry that we did not elaborate on this information in the previous manuscript. In fact, our study directly extracted the OR/RR value or 95%CI from the included research data and merged the OR value through RevMan 5.3 software. In 'data extraction and quality assessment', we have added the following: The OR/RR or 95% CI was directly extracted from the included studies. In 'statistical analysis', we have revised it to 'To assess the risk factors of FoF, the OR/RR and associated 95% CI were extracted from included studies, and then RevMan 5.3 software was used to merge the OR/RR value.'

In addition, in the revised version of the manuscript we have added information about choosing fixed and random effects. In the 'Statistical analysis' section, we changed '95% CI for FoF was calculated using a fixed-effects model, however a random-effects model was used whenever Cochrane's Q-statistic detected significant heterogeneity' to 'Statistical heterogeneity between studies was quantified by the I<sup>2</sup> statistics and formally tested by Cochran's Q statistic. A random-effects model for meta-analysis was an obvious conservative choice based on the heterogeneity of geographic settings and the variability of screening and diagnostic tools. However, when the number of studies was small (n<5), a fixed-effects model was used<sup>27-29</sup>. The findings were illustrated in the form of forest plots.' In the 'Results' section, according to the re-selection of the effect model, the data of some risk factors were re-analyzed, reported as follows: Age (OR=1.00, 95% CI, 0.98 to 1.03); improved balance ability (OR=5.54; 95% CI, 3.48 to 8.81.) lower mobility (OR=1.12; 95%CI, 1.05 to 1.19), and walking aid (OR= 1.98; 95% CI, 1.37 to 2.88). For details, please see the texts marked red in the section of 'Statistical analysis (page 6)', 'Age (page 11)', 'balance ability (page 11)', 'mobility (page 12)' and 'use of walking aid (page 12)'.

Funnel plots and Egger's linear regression test were used to indicate whether the included studies had publication bias. The meta-regression and subgroup analysis were used to analyze the sources of heterogeneity between studies. The statistics section that has been modified is as follows:

'Publication bias was identified using a funnel plot and Egger's linear regression test<sup>30</sup>. When the number of included studies was >2, subgroup and meta-regression analyses were performed to explore the sources of heterogeneity based on the following factors: SwePASS score, age, sample size and the number of females. Subgroup analysis and meta-regression were performed after post hoc adjustment'. For details, please refer to the red marked texts in the 'statistical analysis', 'balance ability', 'mobility' and 'supplementary file 4-5'.

For potential confounders, we attempted to explore whether there was a potential correlation between risk factors and outcomes using multivariate meta-analysis. However, the limited number of studies did not make it possible to stratify by baseline characteristics and adjust for covariates, so multivariate regressions could not be performed<sup>5</sup>. We thought it necessary to provide further explanation in the text, and we have added the corresponding explanation in the revised version. In the 'mobility' section, we have revised this section, reported as follows: Meta-regression was performed to explore potential sources of heterogeneity based on an a priori list of factors related to clinical prognosis<sup>38</sup>. Univariate meta-regression analysis identified age ( $p=0.017$ ) as a significant source of heterogeneity. However, due to the limited number of studies, it was impractical to eliminate the sources of heterogeneity and adjust covariates; therefore, multivariate meta-regression could not be performed. In 'Discussion' section, we have added the following: (2) All the included studies were observational studies, and therefore the role of confounding factors should be considered. However, due to the limited number of studies, a multivariate meta-analysis could not be performed to assess the robustness of our findings and analyze the effect size of multiple risk factors at the same time<sup>60</sup>. For details, please see the texts marked red in the section of 'mobility' and 'study limitations in the discussion (page 17)'.

2. The manuscript included 2-3 studies to estimate the effect size for most risk factors, while for others, the manuscript presents a narrative based on a single study. Hence the current systematic review has limited scope regarding the objectives, modelling options for meta-analyses and conclusions relevant for the scientific community. The availability of few studies also means the estimate of heterogeneity will be biased or non-estimable. The sensitivity analysis using the leave-one-out approach will also be insufficient in most scenarios.

Answer: Thank you for your helpful suggestions. According to your comments, we have revisited the article and acknowledged that some inadequacies in the paper. However, based on the universality and serious consequences of the fear of falling in stroke patients, we think that this work has important clinical implications. After careful analysis based on your comments, the present study shows that female patients, poor balance ability, lower mobility, use of walking aid, and history of falls are major risk factors for fear of falling. These results provide useful insights into the mechanism of fear of falling, and guide the development of risk stratification tools, which is useful to promote active rehabilitation exercise behaviors and reduce the risk of falls. In addition, we also point out directions for future research in this area.

However, due to the limitation of the number of studies, it is not possible to perform data consolidation analysis on other risk factors, and only descriptive analysis can be performed in the results section. Therefore, we have revised introduction section and expanded the discussion about these factors in the revised edition. In addition, in order to understand the source of heterogeneity, we conducted meta-regression and subgroup analysis in the revised edition. For details, please refer to the red marked texts in the 'introduction', 'statistical analysis', and 'discussion'.

3. Figures in the manuscript reproduce the forest plots verbatim from RevMan software with no clarifications of statistics presented. The statements on effect sizes and syntheses of the results are repetitive, inadequate and sometimes incorrect.

Answer: Thank you for pointing out this important question. We are sorry that we are not elaborate on this information in the previous manuscript. In the updated version, we have reinterpreted the results of statistical analysis, modified the expression, and checked some incorrect information. For details, please see the texts marked red in the section of 'statistical analysis' and 'results of the meta-analysis'.

#### Reference

1. Light RJ, Pillemer DB. Summing up. The science of reviewing research. Cambridge, MA: Harvard University Press, 1984.
2. Egger M, Davey Smith G. Misleading meta-analysis. Lessons from "an effective, safe, simple"

intervention that wasn't. BMJ 1995;310:752-4.

3. Oxman AD, Guyatt GH. A consumer's guide to subgroup analyses. Annals of internal medicine 1992;116(1):78-84. doi: 10.7326/0003-4819-116-1-78 [published Online First: 1992/01/01]

4. Okabayashi K, Ashrafian H, Hasegawa H, et al. Body mass index category as a risk factor for colorectal adenomas: a systematic review and meta-analysis. The American journal of gastroenterology 2012;107(8):1175-85; quiz 86. doi: 10.1038/ajg.2012.180 [published Online First: 2012/06/27]

5. Jackson D, Riley R, White IR. Multivariate meta-analysis: potential and promise. Stat Med 2011;30(20):2481-98. doi: 10.1002/sim.4172 [published Online First: 2011/01/27]

### VERSION 3 – REVIEW

<b>REVIEWER</b>	Nath, Mintu University of Aberdeen, Medical Statistics Team
<b>REVIEW RETURNED</b>	02-May-2022

<b>GENERAL COMMENTS</b>	<p>I noted authors incorporated a major revision in the statistical methodologies from the last version. In the earlier version, I enquired about the reasoning behind the choice of sample size and the number of females as covariates of meta-regression. The revised version still suggests the inclusion of these variables without any justification. Further clarifications are required to explain the context of subgroup analysis and post-hoc adjustment as presented in the Methods section.</p> <p>The manuscript includes numerous instances of ambiguous, verbose or incorrect statistical statements and terminologies. I recommend that authors check the full manuscript with a statistician to enhance the clarity of presentation and interpretation. I have noted a few instances below.</p> <p>-----</p> <p>Subgroup analysis and meta-regression were performed after post hoc adjustment.</p> <p>However, no significant statistically association was observed when entered into a meta-analysis using a fixed-effects model.</p> <p>Univariate meta-regression analysis identified age (<math>p=0.017</math>) as a significant source of heterogeneity.</p> <p>However, due to the limited number of studies, it was impractical to eliminate the sources of heterogeneity and adjust covariates; therefore, multivariate meta-regression could not be performed.</p> <p>Due to this meta-analysis's relatively large sample size, the sensitivity analysis (leave-one-out method) showed that none of the studies had a significant impact on the final pooled results.</p> <p>No publication bias was shown by Egger's linear regression test (<math>p=0.205</math>) the funnel plot.</p> <p>-----</p>
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## VERSION 3 – AUTHOR RESPONSE

Replies to Review #3 :

1. I noted authors incorporated a major revision in the statistical methodologies from the last version. In the earlier version, I enquired about the reasoning behind the choice of sample size and the number of females as covariates of meta-regression. The revised version still suggests the inclusion of these variables without any justification. Further clarifications are required to explain the context of subgroup analysis and post-hoc adjustment as presented in the Methods section.

Answer: Thanks very much for the suggestions and for your patience. We pre-specified the proportion of females as a covariate. Primarily, the higher risk of women developing affective disorders has been linked to sex differences in the biological susceptibility, genetic and hormonal factors, and sex differences in physiological stress responsivity or the exposure to environmental risk factors, including higher exposure to (sociocultural) stressors<sup>1</sup>. Second, women are more susceptible to mood swings than men and are more likely to experience negative emotions, such as anxiety and irritability, because of an illness<sup>2,3</sup>. All these factors may exacerbate the risk for fear of falling (FoF) in women. In addition, previous studies have shown that older women are associated with a higher incidence of FoF<sup>4</sup>. The sample size was chosen as a covariate because we believed that the smaller sample size of single studies could have an impact on the reliability of FoF outcomes. For example, the smaller the sample size, the greater the sampling error, resulting in a more difficult representation of the overall parameters. Finally, previous studies have shown that baseline characteristics (e.g., gender, sample size) are associated with heterogeneity in meta-analysis<sup>5-7</sup>. Therefore, we presuppose that these two variables could lead to a larger impact on FoF.

Later, we studied the relevant literature again based on your valuable suggestions and reviewed these variables again. Previous studies have demonstrated that older populations and smaller SwePASS scores were more likely to have a larger impact on FoF<sup>4,8-11</sup>, so we performed the post-hoc subgroups and meta-regression analyses on these two variables. Thank you again for your suggestions, which helped us to have a more comprehensive understanding and provided more inspiration for future research. Therefore, we have revised the methods section and added the relevant instructions in the discussion section.

In the 'Methods' section, we have changed 'When the number of included studies was >2, subgroup and meta-regression analyses were performed to explore the sources of heterogeneity based on the following factors: SwePASS score, age, sample size and the number of females. Subgroup analysis and meta-regression were performed after post hoc adjustment.' to 'We planned to conduct subgroup and meta-regression analyses based on sample size and proportion of female<sup>31</sup>. As previous studies have shown that SwePASS score and age were influencing factors, we performed the post-hoc subgroup and meta-regression analyses on these two factors when the number of studies >2<sup>31-33</sup>.' For details, please see the texts marked red in the section of 'Statistical analysis (page 6)'.

In the 'Discussion' section, we have added the relevant information, reported as follows: We also explored the sources of heterogeneity using meta-regression if the analysis included more than two studies. We pre-specified sample size and the proportion of females as the meta-regression variables because we considered that studies with smaller sample sizes and a larger proportion of females could have a larger impact on FoF<sup>31</sup>. In the post-hoc analyses, we also added age and SwePASS score as potential regressors because previous studies showed that older populations and smaller SwePASS scores could lead to a larger impact on FoF<sup>31-33</sup>. For details, please see the texts marked red in the section of 'Discussion (page 16)'.

2. The manuscript includes numerous instances of ambiguous, verbose or incorrect statistical statements and terminologies. I recommend that authors check the full manuscript with a statistician to enhance the clarity of presentation and interpretation. I have noted a few instances below.

Subgroup analysis and meta-regression were performed after post hoc adjustment.

However, no significant statistically association was observed when entered into a meta-analysis using a fixed-effects model.

Univariate meta-regression analysis identified age ( $p=0.017$ ) as a significant source of heterogeneity.

However, due to the limited number of studies, it was impractical to eliminate the sources of heterogeneity and adjust covariates; therefore, multivariate meta-regression could not be performed.

Due to this meta-analysis's relatively large sample size, the sensitivity analysis (leave-one-out method) showed that none of the studies had a significant impact on the final pooled results.

No publication bias was shown by Egger's linear regression test ( $p=0.205$ ) the funnel plot.

Answer: Thank you for pointing out this important question. Based on your valuable suggestions, we have revised the relevant information.

In the 'Abstract' section, we have revised 'The leave-one-out analysis showed that no single study significantly affected the final pooled results.' to 'Sensitivity analysis (leave-one-out method) showed that the pooled estimate was stable.' Please see the texts marked in the section of 'Abstract (page 2)'.

In the 'Statistical analysis' section, we have changed 'The Stata 15 performed meta-regression and Egger's linear regression test' to 'Meta-regression and Egger's test were performed by the Stata V.15.1'. We have changed 'To assess the risk factors of FoF, the OR/RR and associated 95%CI were extracted from included studies, and then RevMan 5.3 software was used to merge the OR/RR value.' to 'To assess the risk factors of FoF, we conducted a meta-analysis by the RevMan V.5.3 software to pool the OR/RR value with 95% CI.' We have changed 'When the number of included studies was >2, subgroup and meta-regression analyses were performed to explore the sources of heterogeneity based on the following factors: SwePASS score, age, sample size and the number of females. Subgroup analysis and meta-regression were performed after post hoc adjustment.' to 'We planned to conduct subgroup and meta-regression analyses based on sample size and proportion of female<sup>31</sup>. As previous studies have shown that SwePASS scores and age were influencing factors, we performed the post-hoc subgroup and meta-regression analyses on these two factors when the number of studies >2<sup>31-33</sup>.' We have revised 'A p-value of ( $p < 0.05$ ) was the threshold for statistical significance' to 'Statistical significance was set at  $P$  value < 0.05.' For details, please see the texts marked red in the section of 'Statistical analysis (page 6)'.

In the 'Age' section, we have revised 'Two studies reported the relationship between age and FoF in stroke patients (2 studies, 500 participants). However, no significant statistically association was observed when entered into a meta-analysis using a fixed-effects model.' to 'Two studies with 500 participants reported the relationship between age and FoF in stroke patients. Meta-analysis using a fixed-effects model showed that there was no statistically significant association.' Please see the texts marked red in the section of 'Age (page 10)'.

In the 'Female' section, we have revised 'Two studies reported the correlation between females and FoF in stroke patients (2 studies, 741 participants). The analysis revealed the risk of FoF in women with stroke was 2.13 times higher than in men.' to 'Two studies 741 participants reported the correlation between females and FoF in stroke patients. A pooled analysis using a fixed-effects model demonstrated that women experienced a significantly higher incidence of FoF than men.' Please see the texts marked red in the section of 'Female (page 10)'.

In the 'Balance ability' section, we have changed 'Three studies mentioned balance ability as an independent risk factor' to 'Three studies reported the correlation between balance ability and FoF'. We have revised 'Subgroup analysis of the SwePASS score showed that the risk of FoF was 2.30-5.54 times higher in low balance than with high balance.' to 'Subgroup analysis of the SwePASS score showed that stroke patients with lower balance levels were significantly more susceptible to

FoF than higher balance levels.’ We have changed ‘The difference between this subgroup was statistically significant ( $p=0.007$ ).’ to ‘This subgroup difference was statistically significant ( $p=0.007$ ).’ Please see the texts marked red in the section of ‘Balance ability (page 10)’.

In the ‘Mobility’ section, we have revised ‘Univariate meta-regression analysis identified age ( $p=0.017$ ) as a significant source of heterogeneity. However, due to the limited number of studies, it was impractical to eliminate the sources of heterogeneity and adjust covariates; therefore, multivariate meta-regression could not be performed. Due to this meta-analysis’s relatively large sample size, the sensitivity analysis (leave-one-out method) showed that none of the studies had a significant impact on the final pooled results. In addition, no publication bias was shown by Egger’s linear regression test ( $p=0.619$ ) and the funnel plot (Supplementary file 4).’ to ‘Meta-regression analysis showed subgroup effects for age ( $P_{interaction}=0.017$ ), sample size ( $P_{interaction}=0.019$ ) and proportion of female ( $P_{interaction}=0.019$ ). Sensitivity analysis (leave-one-out method) showed that the pooled estimate was stable. In addition, there was no evidence of publication bias according to a funnel plot (Supplementary file 4) and the Egger’s test ( $P=0.619$ ).’ Please see the texts marked red in the section of ‘Mobility (page 11)’.

In the ‘History of falls’ section, we have changed ‘Experience of falls was listed as an independent risk factor for FoF in 4 studies’ to ‘Four studies reported the correlation between experience of falls and FoF’. We have revised ‘No publication bias was shown by Egger’s linear regression test ( $p=0.205$ ) the funnel plot (Supplementary file 5).’ to ‘There was no evidence of publication bias according to a funnel plot (Supplementary file 5) and the Egger’s test ( $p=0.205$ ).’ Please see the texts marked red in the section of ‘History of falls (page 11)’.

In the ‘Use of walking aid’ section, we have revised ‘Two studies listed influencing factors between the walking aid for stroke patients and FoF’ to ‘Two studies listed the relationship between the walking aid for stroke patients and FoF’. We have revised ‘The results further confirmed that...’ to ‘A meta-analysis using a fixed-effects model that included two studies revealed that...’ Please see the texts marked red in the section of ‘Use of walking aid (page 11)’.

In the ‘Other risk factors’ section, we have revised ‘The significant risk factors of FoF were anxiety ( $OR=2.29$ ; 95%CI, 1.43 to 3.67), depression ( $OR=1.80$ ; 95%CI, 1.22 to 2.67), poor lower limb motor function ( $OR= 1.14$ ; 95%CI, 1.00 to 1.29), and physically inactiveness ( $OR=2.04$ ; 95%CI, 1.01 to 4.12)’ to ‘Among them, anxiety ( $OR=2.29$ ; 95%CI, 1.43 to 3.67), depression ( $OR=1.80$ ; 95%CI, 1.22 to 2.67), poor lower limb motor function ( $OR= 1.14$ ; 95%CI, 1.00 to 1.29), and physically inactiveness ( $OR=2.04$ ; 95%CI, 1.01 to 4.12) increased the risk of FoF in patients with stroke.’ Please see the texts marked red in the section of ‘Other risk factors (page 12)’.

In the ‘Discussion’ section, we have revised ‘who showed that the FoF and they were moderately correlated.’ to ‘who showed that the FoF and they were positively correlated.’ We have revised ‘Pearson correlation coefficients’ to ‘Pearson’s correlation coefficients’ We have revised ‘A significant, moderate, and positive correlation’ to ‘A significantly positive correlation’ Please see the texts marked red in the section of ‘Discussion (page 13-14)’.

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