Association between parity and the risk for urinary incontinence in women
A meta-analysis of case–control and cohort studies

Hai-Hong Zhou, PhD\textsuperscript{a}, Bo Shu, PhD\textsuperscript{a}, Tong-Zu Liu, PhD\textsuperscript{a}, Xing-Huan Wang, PhD\textsuperscript{b}, Zhong-Hua Yang, PhD\textsuperscript{b}, Yong-Lian Guo, PhD\textsuperscript{a,\textast}

Abstract
Urinary incontinence (UI) is a common complaint for adult female. Cross-sectional studies suggested parity may link with UI, but the association between them was not well-established. We conducted a meta-analysis to investigate the association between parity and UI.

Medline and Embase were searched for eligible case–control and cohort studies about parity and UI. Two authors screened the literature and extracted the data independently. Odds ratio (OR) was used as the measure of the effect of parity on UI. We pooled the ORs of different number of parity by a random-effect model. Subgroup analysis was conducted by a subtype of UI. Sensitivity analysis was conducted to see whether the results were stable.

Thirteen studies (8 cohorts and 5 case–controls) were included in our meta-analysis, with a total of 74,883 adult females. Our meta-analysis showed that compared with nulliparity, ORs of women with 1, 2, and ≥3 parity were 1.43 [95% confidence interval (95% CI): 0.90–2.28; \( I^2 = 81.4\% \); \( n = 4 \)], 1.50 (95% CI: 1.02–2.20; \( I^2 = 82.5\% \); \( n = 4 \)), and 1.58 (95% CI: 1.22–2.03; \( I^2 = 70.1\% \); \( n = 7 \)) compared with nulliparity. The OR for any multiparity to nulliparity was 1.68 (95% CI: 1.39–2.03; \( I^2 = 0\% \); \( n = 4 \)). Subgroup analysis showed that parity was associated with an increased risk of stress UI (OR = 2.32, 95% CI: 1.41–3.81; \( I^2 = 0\% \); \( n = 2 \); 1 compared with null parity) but not urgency UI; However, the definition of parity varies across studies and studies defined parity as delivery times showed higher pooled OR than those not. Sensitivity analysis showed our results were stable.

Current evidence suggested that parity was associated with an increased risk of overall and stress UI but not urgency UI, though the definition of parity may differ. Higher parity may have a more significant effect on overall UI. Standardized definition of parity is needed.

Abbreviations: CI = confidence interval, OR = odds ratio, UI = urinary incontinence.

Keywords: meta-analysis, parity, urinary incontinence

1. Introduction
Urinary incontinence (UI) is a common complaint, particularly in postpartum and aging women.\textsuperscript{[1]} The prevalence of UI in women varies across regions and populations, ranging from 10.8% to 79% among adults.\textsuperscript{[2]} According to the International Continence Society, UI is defined as any involuntary leakage of urine.\textsuperscript{[3]} There are 3 types of UI: stress UI, which is due to effort, physical exertion, or sneezing or coughing; urgency UI, which is associated with urgency; and mixed UI, which is a combination of both.\textsuperscript{[4]}

Demographic characteristics (e.g., age), lifestyle habits (e.g., smoking), and baseline medical conditions (e.g., depression), obstetric characteristics (e.g., pregnancy) may be considered as important risk factors for UI.\textsuperscript{[5–8]} Large cross-sectional surveys have suggested that multiparity was associated with a higher prevalence of UI.\textsuperscript{[5–8,12]} Pregnancy and childbirth were also considered as risk factors for stress UI in some review articles.\textsuperscript{[8,13]} However, due to the limitation of such type of studies (cross-sectional), current evidence can only support the potential association between parity and UI but not their causal relationship.\textsuperscript{[14]} Moreover, the results of the cross-sectional study may be at risk for selective bias.\textsuperscript{[15]} Whether parity causes UI or UI is an effect of parity is unclear.

On the basis of a literature search, we found no comprehensive evidence on the relationship between parity and UI. To establish the potential causation between parity and UI, a meta-analysis was conducted based on case–control and cohort studies of the adult population. Moreover, whether higher parity has significantly affected UI was validated.

2. Methods
This meta-analysis was conducted in accordance with the guidelines of the MOOSE Statement.\textsuperscript{[15]} This study does not involve ethics, as it is based on the analysis of secondary evidence.
2.1. Eligibility criteria

In the present study, we included case-control and cohort studies that investigated the relationship between parity and the risk for UI. The population was limited to adult women. The exposure of interest was multiparity (compared with nulliparity or 1 parity), and the primary outcome was any type of UI. Cross-sectional studies were not included because they are descriptive and mainly used to describe prevalence. Moreover, they are not suitable for cause-and-effect analysis. For cohort studies, only those that reported about the relationship between parity and risk of UI incidence were considered. Parity was defined as the number of offspring a female has borne, according to the MeSH term provided by PubMed. However, as the Child Health Epidemiology Reference Group (CHERG) Small-for-Gestational-Age-Preterm Birth Working Group of Johns Hopkins Bloomberg School of Public Health, parity was defined as number of live births. Both of the terms were treated as parity in current meta-analysis.

2.2. Literature search and screening

We searched MEDLINE (1974 to February 12, 2018) and Embase (1946 to February 08, 2018) for potential publications without any language limitations. MeSH terms and free text words were combined to develop the search strategy. These mainly included “parity” [MeSH], “multiparity,” “urinary incontinence” [MeSH], and “incontinence.” The full search strategy is presented in the Supplementary file, http://links.lww.com/MD/C332.

Two authors (Z.H-H and G.Y-L) searched for eligible studies by reviewing the title and abstract and then the full text. For title and abstract reviewing, studies that were obviously not related were excluded. Conference abstracts, gray literature, and letters to the editor were not considered. Any disagreements were solved via discussion. If consensus is not reached, a third author was asked for judgment (L.T-Z).

2.3. Data extraction

Data were extracted by one author (Z.H-H) and then reviewed by another author (B.S). The following information about each study was collected: author’s first name, year of publication, region, type of study, follow-up year for cohorts, control information for case-control studies, sample size, population characteristics (e.g., mean age), type of UI, number of parity, effect sizes, and variables that were controlled in the statistical analysis. For the effect sizes, we extracted the one controlled for confounding variables. Any disagreements were reviewed by the 2 authors. The corresponding authors of previous studies that did not report any relevant information were contacted for potential data.

2.4. Quality assessment

We assessed the quality of the selected studies using the Newcastle–Ottawa Scale (NOS), which was widely used for quality assessment in the meta-analysis of observational studies. This scale contains 9 items for both case-control and cohort studies. One star was assigned to each item if it met the standards. Otherwise, no star was assigned to the items. A study with more stars indicates higher scientific quality. A study with ≥7 stars was a high-quality study, whereas a study with ≤4 stars was a low-quality study. Quality assessment was performed concurrently by 2 authors (Z.H-H and Y.Z-H).

2.5. Statistical analysis

There were 2 types of studies and some of them used odds ratio (OR). Meanwhile, the others used risk ratio (RR) to measure the effect. Then, we combined them as OR by treating all RRs as OR. This was reasonable because the incidence rate of UI is less than 10%, and the RR was approximately equal to OR.

Most studies presented the results in a categorical manner in which each number of parity corresponds to an OR compared with reference parity. We combined these ORs by category, as it is inappropriate to combine all the ORs with different categories. In detail, we combined the ORs of 1 parity, 2 parity, and ≥3 parity on UI separately from the selected studies. This allows us to detect the different impacts of parity number on the risk for UI. For studies reporting results by the subtype of UI instead of the overall UI, we combined the ORs of each subtype using the fixed-effect model as the overall OR for UI. The random- or fixed-effect model was used in the meta-analysis according to the amount of heterogeneity. P that is higher than 30% indicated moderate to substantial heterogeneity. Thus, the random-effect model was used. Otherwise, the fixed-effect model was utilized.

We also conducted a robust meta-regression analysis to assess the potential dose-response effect of parity on UI. Sensitivity analysis was conducted by excluding low-quality studies and those that only included crude OR. Subgroup analysis was conducted according to the subtype of UI when the number of studies is sufficient. Considering the different definition of parity, subgroup analysis was also conducted according to the definition. Publication bias was identified using the funnel plot. All statistical analyses were performed using stata version 12.0 (STATA, College Station, TX), and P value <.05 was considered statistically significant.

3. Results

We initially searched 2269 publications from the 2 databases, of which 341 were duplicates. Of the remaining publications, 1622 did not meet the criteria of the title and abstract. We further excluded 293 articles based on full-text reading. Finally, 13 eligible studies were included. Figure 1 presents the screening details.

Among the 13 studies, 8 and 5 were cohort and case-control studies, respectively. For cohort studies, the follow-up period ranged from 3 to 18 years, and the median time was 9.5 (interquartile range: 4.75–11.25) years. For the 5 case-control studies, 4 used hospital-based control and 1 utilized community-based control. Seven studies were conducted in European countries, 3 in North America, 2 in South America, and 1 in Australia.

In total, 74,883 adult women were included in this meta-analysis. The mean age of the participants was 47.40 years, and the median age was 50 (interquartile range: 36.25–55.25) years. The total number of cases was not identified because some cohort studies did not report the information. The parity number ranged from 0 to ≥4. In terms of outcome, all types of UI, stress UI, and urgency UI were reported in 8, 5, and 2 studies, respectively. Table 1 depicts the basic characteristics of these studies.

The total quality of the selected studies ranged from 3 to 8. Of these studies, 6 were identified as high quality, 6 as moderate quality, and 1 as low quality (Table 2). The corresponding authors of the 2 potential studies were contacted. However, they did not provide any relevant data.
3.1. Multiparity versus nulliparity for the overall UI

Of the 13 studies, 11 reported nulliparity as the reference parity. Moreover, 4 studies have shown the ORs of 1 parity compared to nulliparity, 4 on 2 parity, 6 on ≥3 parity, and 4 on any multiparity.

Our meta-analysis showed that the ORs of women with 1, 2, and ≥3 parity were 1.43 [95% confidence interval (95% CI): 0.90–2.28; I² = 81.4%; n = 4], 1.50 (95% CI: 1.02–2.20; I² = 82.5%; n = 4), and 1.58 (95% CI: 1.22–2.03; I² = 70.1%; n = 7) compared with nulliparity. The OR for any multiparity to nulliparity was 1.68 (95% CI: 0.99–2.85; I² = 60.42%; n = 2). Our results suggested that ≥2 parity may increase the risk of the overall UI for women compared with nulliparity. Figure 2 presents the forest plot of the results.

3.2. Meta-regression analysis

Thirteen studies can be used in the meta-regression analysis. These include another 2 studies with 1 parity as the reference. On the basis of the above-mentioned results, we centered all the reference parity to 0 to further explore the potential dose–response effect of parity on UI. Figure 3 presents the dose–response relationship. Our meta-regression analysis showed that, compared with nulliparity, each parity increase was associated with the increased risk of overall UI in women with ≥2 parity (OR = 1.13, 95% CI: 1.05–1.22).

3.3. Sensitivity analysis, subgroup analysis, and publication bias

We excluded studies with low quality[21] and those that only provided crude OR[24] Results showed significant decrease in heterogeneity, whereas the pooled ORs (random-effect) did not change (Figure S1, http://links.lww.com/MD/C332). Compared with nulliparity, the ORs of women with 1, 2, and ≥3 parity were 1.68 (95% CI: 0.99–2.85; I² = 60.42%; n = 2), 1.39 (95% CI: 1.08–1.78; I² = 23.4%; n = 2), and 1.55 (95% CI: 1.33–1.81; I² = 0%; n = 5), respectively.

A subgroup analysis was conducted considering the type of UI. There were 5 studies that focused on stress UI and 2 studies reported about urgency UI. We only combined the ORs of stress UI but not those of urgency UI because of the heterogeneous parity number. Our subgroup analysis showed that parity was significantly associated with the increased risk of stress UI, regardless of the parity numbers (OR = 2.32; 95% CI: 1.41–3.81; I² = 0%; n = 2; 1 parity compared with null parity), as shown in Fig. 2. However, none of the 2 studies reported an association between urgency UI and parity (Fig. 4).

Of the 13 studies, 6 did not clarify the definition of parity, 5 defined parity as delivery times, 1 defined parity as number of babies, and 1 defined parity as number of term pregnancies. Subgroup analysis showed that, for studies defined parity as delivery times, the ORs were larger than those without definition or with other definitions, but there were no substantial changes of
Table 1

Basic characteristics of included studies.

| Ref. | Region      | Study type, follow-up | Sample | Population | Parity (Definition) | Risk of UI | Type of UI | Adjustments                                                                 |
|------|-------------|-----------------------|--------|------------|---------------------|------------|------------|-----------------------------------------------------------------------------|
|      | Sweden      | Cohort study, 10 y    | 229    | Primiparous women, Mean age (SD): 29.9 (4.1) | Null (No definition) | Reference  |           | Age, maternal weight, fetal weight, history of perineal rupture, history of instrumental delivery |
|      |             | Altman et al[20]      |        |            |                     | 1          |            | SUI                                           | Survey time, area, diabetes, dementia, stroke, BMI, fall, visits to general practitioner, physical ability, urine burns or stings, constipation, postpartum, hysterectomy |
|      |             | Australian            |        |            |                     | 2          |            | SUI                                           |                                                     |
|      |             |                         |        |            |                     | 3 to 4     |            | Null (No definition)                                                        |                                                     |
|      |             | Byles et al[21]        |        | Old women, aged from 70 to 75 y | Null (No definition) | Reference  |           | Age, race, BMI, physical activity, postmenopausal hormone use, diuretic use |                                                     |
|      |             | Devore et al[22]       |        |            |                     | 1          |            | Any type                                       |                                                     |
|      |             | Norway                |        |            |                     | 2          |            | Any type                                       |                                                     |
|      |             | Ebbesen et al[23]     |        |            |                     | 3 or more  |           | Null (No definition)                                                        |                                                     |
|      |             | Brazil                |        | Pregnant women beyond 20 weeks, aged from 20 to 50 y | 1 (Delivery times) |           | 1 or more | Age, BMI, weight change, smoking                                                |                                                     |
|      |             | Herrmann et al[24]    |        |            |                     | 2–3        |           | 1       | Any type                                       | Crude                                                |
|      |             | Legendre et al[25]     |        |            |                     | 4 or more  |           | 1       | Any type                                       |                                                     |
|      |             | Leroy et al[26]        |        | Puerperal women up to 90 d, mean age (SD): 25.9 (7.7) | 1 or more  | Reference  | SUI                                           | Age, UI during pregnancy, types of previous birth, newborn’s head circumference, weight, gestational age at birth, smoking, and constipation |
|      |             | America                |        |            |                     | 1 or more  |           | Null (No definition)                                                        |                                                     |
|      |             | Hirsch et al[27]       |        |            |                     | 1 or more  |           | Null (No definition)                                                        |                                                     |
|      | Denmark     | Leroy et al[28]       |        |            |                     | 1 or more  |           | Null (Delivery times)                                                        |                                                     |
|      |             | Zhou et al.           |        | Puerperal women up to 90 d, mean age (SD): 25.9 (7.7) | 1 or more  | Reference  | SUI                                           | Age, BMI, diabetes, and birth history                |

(continued)
| Ref.          | Region       | Study type, follow-up | Sample       | Population                                                                 | Parity (Definition) | Risk of UI   | Type of UI          | Adjustments                                                                 |
|--------------|--------------|-----------------------|--------------|----------------------------------------------------------------------------|---------------------|-------------|---------------------|-----------------------------------------------------------------------------|
| Moeller et al\[28\] | Italy        | Case–control study, hospital-based control | Women in first level gynecological centers aged 40–88 y for cases, and 40–86 y for controls. Results based on vaginal birth | 1–2 Null (Delivery times) | 0.8 (0.4, 1.6) | UUI                  | Null Reference                                                                 |
|              |              |                       |              |                                                                            |                     |             |                     | Age, delivery type, education, BMI, obstetric history and hormonal replacement therapy |
|              |              |                       |              |                                                                            |                     |             |                     |                                                                            |
| Parazzini et al\[29\] | Italy        | Case–control study, hospital-based control | Women aged 40–60 y from and urban and rural county | 1–2 Null (Delivery times) | 0.8 (0.4, 1.7) | UUI                  | Reference                                                                 |
|              |              |                       |              |                                                                            |                     |             |                     |                                                                            |
| Pizzoferrato et al\[30\] | France       | Cohort study, 12 y    | 236          | Nulliparous women at a term of 37–41 wks, mean age was 41.3 y             | 1–2 Null (Delivery times) | 1.63 (0.62, 4.25) | Mixed UI                    | Null (Number of term pregnancies)                                                                 |
|              |              |                       |              |                                                                            |                     |             |                     |                                                                            |
| Skoner et al\[31\] | Poland       | Case–control study, hospital-based control | 94 cases, 46 controls | 2 or more Null (Number of term pregnancies) | 1.63 (0.62, 4.25) | SUI                  | Reference                                                                 |
|              |              |                       |              |                                                                            |                     |             |                     |                                                                            |
| Waetjen et al\[32\] | America      | Cohort study, 5 y     | 2702         | Community-based women at 7 clinical sites, aged 40–55 y                   | 4 or more Null (No definition) | 1.18 (0.46, 3.11) | Any type                    | Null (No definition)                                                                 |
|              |              |                       |              |                                                                            |                     |             |                     |                                                                            |

BMI = body mass index, UI = urinary incontinence.
## Table 2

Risk of bias of included studies.

| Ref.          | Study type      | Selection | Comparability | Exposure/Outcome | Total score |
|---------------|-----------------|-----------|---------------|------------------|-------------|
| Altman et al[20] | Cohort study    | ★★★★ ★★ | ★             | ★                | 7           |
| Byles et al[21]  | Cohort study    | ★★★★     | ★             | ★                | 3           |
| Devore et al[22] | Cohort study    | ★★★       | ★             | ★                | 5           |
| Ebbesen et al[23] | Cohort study   | ★★★★ ★★ | ★             | ★                | 6           |
| Herrmann et al[24] | Cohort study  | ★★★★ ★★ | ★             | ★                | 7           |
| Hirsch et al[25] | Case-control    | ★★★★ ★★ | ★             | ★                | 7           |
| Legendre et al[26] | Cohort study | ★★★★ ★★ | ★             | ★                | 5           |
| Leroy et al[27]    | Case-control    | ★★★★      | ★             | ★                | 5           |
| Moeller et al[28]  | Case-control    | ★★★★ ★★ | ★             | ★                | 8           |
| Parazzini et al[29] | Case-control | ★★★★ ★★ | ★             | ★                | 7           |
| Skoner et al[30]   | Cohort study    | ★★★★     | ★             | ★                | 5           |
| Leroy et al[31]    | Case-control    | ★★★★      | ★             | ★                | 5           |
| Waetjen et al[32]  | Cohort study    | ★★★★ ★★ | ★             | ★                | 8           |

The most important factors that should be controlled were age and BMI; the sufficient follow-up rate (cohort)/response rate (case-control) was defined as 80% or more.

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![Figure 2](image.png)

Figure 2. Relationship between parity number and risk of UI.
the significance. The amount of heterogeneity was decreased (Figure S2, http://links.lww.com/MD/C332).

We used the data of women with $\geq 3$ parity for publication bias. Funnel plot suggested possible publication bias (Figure S3, http://links.lww.com/MD/C332).

4. Discussion

To the best of our knowledge, this is the first meta-analysis that investigated the relationship between parity and the risk of UI. In this meta-analysis, we combined the effect sizes of the cohort and case-control studies for the assessment of a potential causation relationship between parity and UI. For overall UI, women with $\geq 2$ parity had an increased risk for UI, and every increase in parity would increase the ORs for UI to approximately 12%. Meanwhile, for stress UI, women with $\geq 1$ parity also had an increased risk for UI. However, we did not find any association between parity and urgency UI.

In our meta-analysis, 1 parity was associated with the increased risk of stress UI but not overall UI compared with nulliparity. This result may be partly attributed to the overall UI that includes both stress and urgency UI, and the later offsets the impact of parity on stress UI. Another possibility is the limited number of studies and sample size for overall UI with insufficient power to detect the difference.

UI is a disease associated with multiple mechanisms. Bladder overactivity, poor bladder control, and pelvic floor musculature impairment were all the direct causes of UI.\(^{[35]}\) The results are attributed to pelvic floor musculature and connective tissue injury during the process of parturition that influences the normal urinary continence function.\(^{[4]}\) However, this was also highly dependent on the type of delivery. In some studies, caesarean delivery was not associated with risk of UI.\(^{[29,36]}\) In our
Further high-quality cohort studies must be conducted to verify more significance of overall and stress UI but not urgency UI. Higher parity has a suggested association with the increased risk of UI. However, the corresponding authors of previous studies did not provide relevant data. Indeed, there were 2 other
categorical diagnoses of parity may in
fluence the de
nition.

In conclusion, current evidence from case-control and cohort studies suggests that parity was associated with the increased risk of overall and stress UI but not urgency UI. Higher parity has a more significant effect on overall UI in a dose-response manner. However, these results should be interpreted with caution. Further high-quality cohort studies must be conducted to verify our results.

Author contributions
Z.H.H.: project development, search and screen literature, collect data, drafted the manuscript, revise manuscript; B.S: check the data, revise manuscript; G.Y.-L.: project development, screen literature, statistical analysis, and revise manuscript; Y.Z.H.: quality assessment, revise manuscript; L.T.Z. and W.X.H. revise manuscript, provide professional guidance of UI.

Conceptualization: Hai-Hong Zhou.
Data curation: Hai-Hong Zhou, Shu Bo, Zhong-Hua Yang.
Methodology: Hai-Hong Zhou.
Project administration: Hai-Hong Zhou, Tong-Zu Liu, Yong-Lian Guo.
Software: Hai-Hong Zhou.

Supervision: Tong-Zu Liu, Xing-Huan Wang, Yong-Lian Guo.
Writing – original draft: Hai-Hong Zhou.
Writing – review & editing: Bo Shu, Tong-Zu Liu, Xing-Huan Wang, Zhong-Hua Yang, Yong-Lian Guo.

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