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Association between delivery mode and pelvic organ prolapse: A meta-analysis of observational studies

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A B S T R A C T

Pelvic organ prolapse (POP) is a common disease in aged women with negative physical and psychological influences. The long-term impact of delivery mode on POP remains uncertain. To evaluate the relationship between delivery mode and POP, a meta-analysis was carried out in this study. PubMed, Web of Science and CENTRAL were combined to search for relevant studies. Data were extracted by two investigators independently. Odd ratios (ORs) and 95% confidence intervals (95% CIs) were calculated by a random-effects model. Sensitivity analysis was performed to explore the potential source of heterogeneity. Moreover, Begg's and Egger's tests were conducted to assess the publication bias of included studies. In total, 13 eligible studies were included in our meta-analysis. Among them, six studies using objective standards for POP definition were included in Group 1, 5 studies addressing the women's own perception of POP were included Group 2, and the remaining 2 studies with both objective and subjective measures for POP assessment were included in both group 1 and group 2. Pooled estimates in our study demonstrated increased risk of POP after any vaginal delivery vs. cesarean section (**Group 1**: OR = 7.69; 95% CI = 4.89, 12.07; heterogeneity: P = 0.00, I^2 = 85.8%. **Group 2**: OR = 2.22; 95% CI = 1.72, 2.87; heterogeneity: P = 0.10, I^2 = 43.5%). Similar results were found in the comparison of spontaneous vaginal births only vs. cesarean sections (**Group 1**: OR = 7.76; 95% CI = 4.43, 13.60; **Group 2**: OR = 2.08; 95% CI = 1.50, 2.89). There was no significant difference in POP between assisted vaginal delivery (including vacuum and forceps) and spontaneous vaginal births. Compared with cesarean sections, vaginal delivery (including women delivering only by spontaneous vaginal births and women with both vaginal and cesarean deliveries) is associated with an increased risk of long-term POP.

Introduction

Pelvic organ prolapse (POP) is defined as the descent of female pelvic organs, which may result in protrusion of the vagina, uterus, or both [1]. In addition to negatively affecting daily life activities, sexual function and ability to perform exercise in many women, it brings high economic costs for individuals and society [2]. POP is one of the most common reasons for gynaecological surgery [3] and 12–20% of women in western countries will undergo surgery for pelvic organ prolapse during their life time [4].

The prevalence of POP is influenced by many factors such as age, smoking, body mass index, abdominal hernia, connective tissue diseases, family history, occupation, gynecologic surgery, and lung disease [5–7]. Moreover, childbirth mode has been widely considered as a primary risk factor for it. Vaginal childbirth may induce functional disorders of pelvic floor as a consequence of delivery trauma to pelvic organ neuromuscular function and morphology [8]. Cesarean delivery, particularly cesarean before labor, is believed to offer substantial protection against such trauma; conversely, instrumental vaginal delivery is considered to be accompanied with increased risks of birth defects. The ideal cesarean section rate recommended by the World Health Organization statement is between 10% and 15% [9]. However, the observed rate varies greatly from country to country. In 2011, the rates were 24% in the UK, 33% in America, and 54% in Brazil [10,11]. The increasing use of cesarean section brings many negative public health consequences, including peripartum infection, bleeding, and negative influence on future pregnancies [9].

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Any positive consequences from the increased use of cesarean have not been well quantified.

An extensive body of evidence from epidemiologic studies suggest that cesarean delivery significantly decreases the risk of postpartum urinary incontinence [11], however, little is known about the effects of cesarean delivery on POP. Although pelvic organ prolapse is a rare condition in nulliparous women and in women after one or several caesarean sections [12], the prevention of disorders later in life by cesarean delivery is controversial. Therefore, in order to reach a better understanding of the association between delivery mode and the risk of POP, a meta-analysis was conducted in this study.

Method

Search strategy

Databases including PubMed, Web of Science, and CENTRAL were searched. We searched all of the included databases up to March 1, 2018, without language restrictions. Both the medical subject heading (MeSH) and text-word were combined to search relevant studies using the following search strategy: ("Pelvic Organ Prolapse"[Mesh] OR pelvic floor dysfunction OR cystocele OR rectocele OR urinary incontinence OR urge incontinence OR mixed incontinence OR stress urinary incontinence OR enterocele) OR (uterus OR uterine OR vaginal OR vault OR urogenital OR bladder OR pelvic organ OR genitourinary) AND prolapse) AND ("Cesarean Section"[Mesh] OR uterine-incision delivery OR delivery mode OR childbirth OR vaginal birth OR spontaneous vaginal birth OR instrumental vaginal delivery) The reference lists of retrieved full-text publications were also carefully screened to identify any further studies

Inclusion and exclusion criteria

Studies meeting the following criteria were included. 1) Any cross-sectional, or case control, or cohort studies, or randomised controlled trials(RCT) on the delivery modes and POP outcomes among primi- and multiparous women. 2) Studies presenting an analysis of at least two delivery modes with POP. 3) Studies with an analysis that is relevant to at least one of the following: age, BMI, or parity. 4) Studies beyond 1 year after delivery because a higher proportion of advanced stage pelvic organ support might have been observed earlier in the first year after delivery.

Studies were excluded for the following reasons. 1) All animal studies, reviews, case reports, abstracts, conference proceedings, editorials and reports with incomplete data. 2) Studies with confounding or missing data. 3) Studies which fail to report numerical values for the outcomes of interest. 4) Report of outcomes for only one mode of delivery.

Data extraction

Data screening and extraction were performed by 2 well-trained and qualified reviewers independently based on the inclusion and exclusion criteria. Information regarding the literature was extracted by the reviewers using a standardized form in the selection process. The baseline characteristics from the eligible literature, including the authors' names, publication year, research types, years of data collected, the number of analyzed participants, diagnostic criterion, follow-up time, and assessment of exposure and outcome were evaluated. Any disagreement was initially resolved via discussion; if a consensus could not be reached, then a third reviewer was consulted. If two or more reports included the same participants, then only the most recent report was included in the meta-analysis.

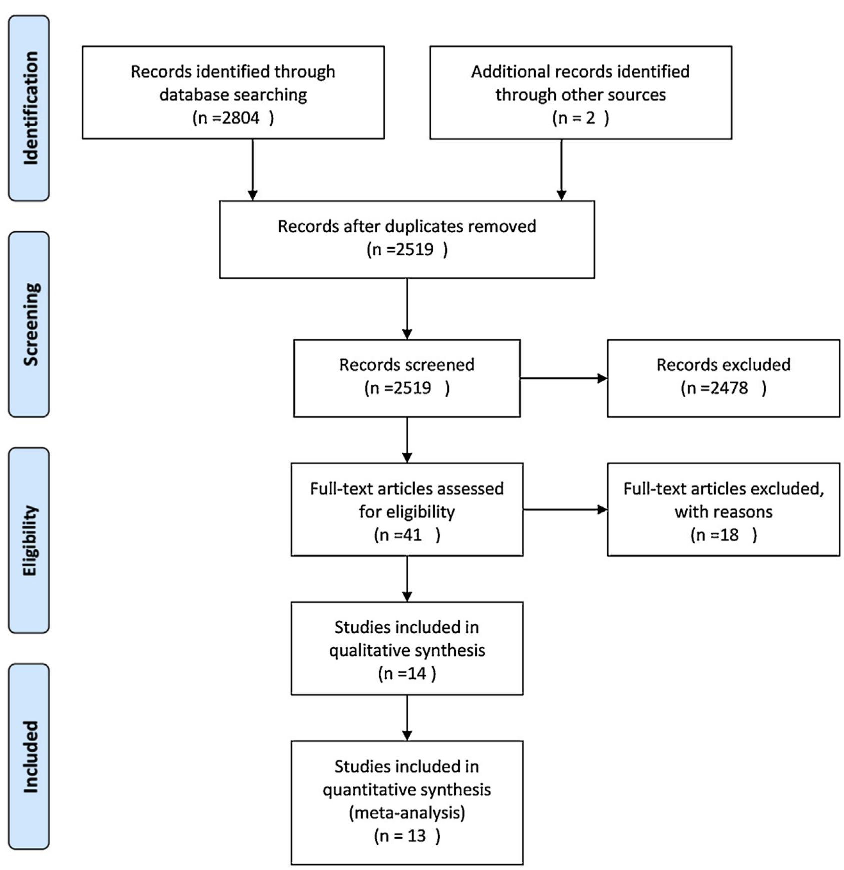

Fig. 1. Flowchart of the literature search and article identification process.

Statistical analysis

We accepted the definition of POP in each research. Considering there would be heterogeneity in definitions, the eligible studies were classified into two groups according to the measures used to assess POP. The Group 1 included studies in which physical examination or objective standard was adopted to evaluate POP, such as pelvic organ prolapse quantification (POP-Q). While Group 2 included studies in which POP was defined according to the women's own perception of POP. For each group, the initial

Table 1
Characteristics of the eligible studies-1(POP-Q).

Study	Publication year	Publication types	Years data collected	Analyzed participants (n)	Diagnostic criterion	Specific inclusion criteria	Follow-up time postpartum (years)
Larsson C	2009	nested case-control study	1973–2004	1444548	ICD9 or ICD10	Case: Women with a prolapsed diagnosis who delivered in 1973-2004 and had their first diagnosis of POP more than 365 days after the last labor. Control: unclear	NR
Leijonhufvud A	2011	cohort study	1973–2004	91002	Women had POP surgery identified by the Swedish Classification of Operations and Major Procedures for 1973-1996 and 1997-2005	Women having their first and all subsequent deliveries by cesarean and an age-matched sample of women only having vaginal deliveries.	cesarean cohort: 26.9 vaginal cohort: 25.9 [a]
Glazener C	2012	Twelve-year longitudinal study	1993–1994	762	POP-Q	A subsample of women who agreed to be examined	12
Trutnovsky G	2015	Retrospective observational study	2012–2014	1258	POP-Q and a four-dimensional translabial ultrasound and physician-led interview	The 'Forceps delivery (FD) group' included women with at least one forceps delivery or a failed trial of forceps. The 'Normal vaginal delivery (NVD) and Vacuum delivery (VD) group' included women with at least one NVD or VD, but no history of forceps. The 'Caesarean section (CS) group included women who had delivered exclusively by CS.	NR
Handa VL	2011	longitudinal cohort study	2008–	1011	POP-Q and Epidemiology of Prolapse and Incontinence Questionnaire	Women with first birth (maternal age between 15 and 50, singleton, nonpremature, without placenta previa, fetal congenital anomaly or prior myomectomy) 5–10 years before enrollment.	5–10
Volløyhaug I	2015	cross-sectional study	1990–1997	608	POP-Q and pelvic floor ultrasound	NVD group: women have had subsequent NVD and CD after the first delivery, but no forceps or vacuum deliveries. CD group: women had only delivered by Cesarean section. The forceps group: women have had forceps, normal or Cesarean delivery after their first child, but no vacuum delivery. The vacuum group: women have had vacuum, normal or Cesarean delivery after their first child, but no forceps delivery.	16–24
Handa VL	2012	cohort study	2008–	449	POP-Q	Participants who had experienced at least one vaginal birth were recruited 5–10 years after delivery of their first child	5–10
Karen Ng	2017	cohort study	2009–2014	506	POP-Q	Exclusion criteria were those who were pregnant at the time of invitation or within 6 months after a delivery, and those who had unrelated pelvic floor injury.	3–5
Gyhagen M	2013	cohort study	2008	5199	postal questionnaire	Singleton primiparae with a birth in 1985–88 and no further births	20
Volløyhaug I	2015	cross-sectional study	2013	1580	Postal questionnaire	Women who delivered their first child between 1990 and 1997.	15–23
Lukacz ES	2006	cross-sectional study	April 2004 to January 2005	4043	Epidemiology of Prolapse and Incontinence Questionnaire	A random sample of women aged 25–84 years	NR
Gyhagen M	2015	cohort study	2008	5127	postal questionnaire	Primiparae who delivered during the period 1985–1988 and had no further deliveries.	20
Martin Huser	2017	prospective observational study	2002–2007	865	Pelvic Organ Prolapse Distress Inventory (POPDI-6)	The inclusion criteria were primiparity, singleton pregnancy, cephalic presentation, and term delivery (38–42 weeks). Women with operative vaginal delivery (vacuum extraction or forceps delivery) were not enrolled	5–10

ICD9: *International Classification of Diseases*, the 9th revision; ICD10: *International Classification of Diseases*, the 10th revision.
POP-Q: pelvic organ prolapse quantification.
NR: not reported.
NVD: normal vaginal delivery; CD: Cesarean delivery.
[a] Mean follow-up time.

unstratified analyses were performed using data from all the selected studies to compare the occurrence of POP between cesarean sections (CS) only (included women who had delivered exclusively by cesarean section) and vaginal deliveries (VD) (at least one spontaneous vaginal birth or instrumental vaginal delivery). Studies that permitted stratification were then pooled, and sub-analysis based on these strata was carried out. The strata included cesarean sections (CS) only versus spontaneous vaginal deliveries (SVD) only, any instrumental vaginal deliveries (IVD) (included any forceps births and any vacuum births) versus spontaneous vaginal births (SVD) only.

In this meta-analysis, OR and 95% confidence intervals (CIs) with a level of $\alpha = 0.05$ were used as the effective value to evaluate the outcomes. Q test and I^2 statistic were used as indices of heterogeneity [13]. For the Q statistic, the level of significance was set at $P < 0.05$. For the I^2, a value of <25%, 25–75% and >75% represents little/no, moderate, and considerable heterogeneity, respectively. When the included studies had substantial heterogeneity, a random-effects model or a fixed-effects model was used. Sensibility analyses were conducted to determine the cause of the heterogeneity. Potential publication bias was investigated by both Begg's correlation test and Egger's regression test. All of the statistical analyses were performed using STATA software, version 12.0 (STATA Corp., College Station, TX, USA).

Result

Literature search and study characteristics

In all, 2806 records were identified through databases searching, including 681 from Web of Science, 1999 from PubMed, 124 from CENTRAL, and 2 from the reference lists of retrieved full-text publications. After removing 287 duplicates records, 2519 studies were left for screening. By screening titles and abstracts, we retrieved 41 reports for full-text screening, of which 14 were included. One of the 14 studies reported conflicting data and therefore was excluded [14]. Finally, 13 eligible studies were included in this meta-analysis [15–23] (Fig. 1). Of the 13 included studies, 6 adopted objective standards for POP definition [15–17,20,21,23], 5 addressed the women's own perception of POP [22,24–27], and the remaining 2 employed both objective and subjective measures to conduct POP assessment [18,19]. The 2 studies that employed questionnaires and clinical examination as diagnostic criteria provided complete data for each measurement and the data collected by different diagnostic criteria was included in different group separately. The baseline characteristics of the 13 eligible studies are shown in Table 1. In group 1, there are eight studies reporting the association between delivery mode and POP. Of the 8 studies, a Swedish study contained the most samples, and POP were identified from 2 Swedish health registries [15]. Another Swedish study reported POP by identifying women who had POP surgery according to the national inpatient register [16]. Other studies in this group employed POP-Q as diagnostic criteria [17–21,23]. Seven studies examined the association between POP and vaginal birth as well as the association between POP and cesarean sections [15–20,23]. Four studies compared the risk of POP between spontaneous vaginal delivery and cesarean sections [15–17,19]. There studies researched the association between POP and SVD as well as the association between POP and IVD [17,19,21]. While in group 2, seven studies were included [18,19,22,24–27]. Most studies adopted questionnaires to identify POP and an Austria study [18] conducted a physician-led interview to assess the symptoms of women. There were totally 13 studies examining the association between POP and different delivery mode, including 7 for any VD vs. CS only [18,19,22,24–27], 5 for SVD only vs. CS only [18,19,22,24,27], and 1 for SVD only vs. IVD [19].

Meta-analyses and sensibility analyses

The meta-analysis of any VD vs. CS only in two groups indicated that vaginal delivery history was associated with increased incidence of POP compared with cesarean sections (**Group 1**: OR = 7.69; 95% CI = 4.89, 12.07; heterogeneity: P = 0.00, I^2 = 85.8% **Group 2**: OR = 2.22; 95% CI = 1.72, 2.87; heterogeneity: P = 0.10, I^2 = 43.5%; Table 2, Fig. 2A). The sensitivity analysis for Group 1 indicated that no single study significantly changed the pooled ORs, suggesting that the results of our meta-analysis were stable (Fig. 3A).

When comparing spontaneous vaginal births only with cesarean sections, four studies in Group 1 and four studies in Group 2 reported increased risks of POP (**Group 1**: OR = 7.76; 95% CI = 4.43, 13.60; **Group 2**: OR = 2.08; 95% CI = 1.50, 2.89). The heterogeneity of studies in Group 1 was significant too (**Group 1**: P = 0.00, I^2 = 90.0% **Group 2**: P = 0.08, I^2 = 51.6%; Table 2, Fig. 2B). Sensitivity analysis of studies included in Group 1 indicated that the results were not stable. After removing the studies of Larsson C [15] and Leijonhufvud A [16], the estimate turned to be 10.97 (8.63,13.96) and 5.38(4.79,6.04) respectively (Fig. 3B).

The meta-analysis in Group 1 (3 studies) demonstrated no significant difference in POP between assisted vaginal delivery (including vacuum and forceps) and spontaneous vaginal births (OR = 0.84; 95% CI = 0.44, 1.58; heterogeneity: P = 0.03, I^2 = 71.9%). The sensitivity analysis demonstrated omission of any single study did not have considerable impact on the pooled ORs. Only one

Table 2
Data showing risk of pelvic organ prolapse between different delivery modes.

Groups	Events in case n/N[a] (%)	Events in control n/N[a] (%)	OR (95% CI)	*P* value of OR	Test for heterogeneity	
					I^2 (%)	*P*
Group 1						
Any VD vs. CS only	17516/1379945 (1.27)	382/159671 (0.24)	7.69(4.89, 12.07)	0.00	85.8	0.00
SVD only vs. CS only	15391/1268417 (1.21)	353/159450 (0.22)	7.76(4.43, 13.60)	0.00	90.0	0.00
SVD only vs. IVD	160/1023 (15.64)	91/519 (17.53)	0.84(0.44,1.58)	0.58	71.9	0.03
Group 2						
Any VD vs. CS only	1807/14184 (12.74)	171/4060 (4.21)	2.22(1.72, 2.87)	0.00	43.5	0.10
SVD only vs. CS only	783/8701 (9.00)	128/3375 (3.79)	2.08(1.50, 2.89)	0.00	51.6	0.08
SVD only vs. IVD	10/325 (3.08)	9/126 (7.14)	0.41(0.16, 1.04)	0.06	–	–

CS: cesarean sections.
VD: vaginal delivery.
SVD: spontaneous vaginal delivery.
IVD: instrumental vaginal delivery.
Case: Any VD/SVD only; control: CS only/IVD.
[a] Total number of deliveries.

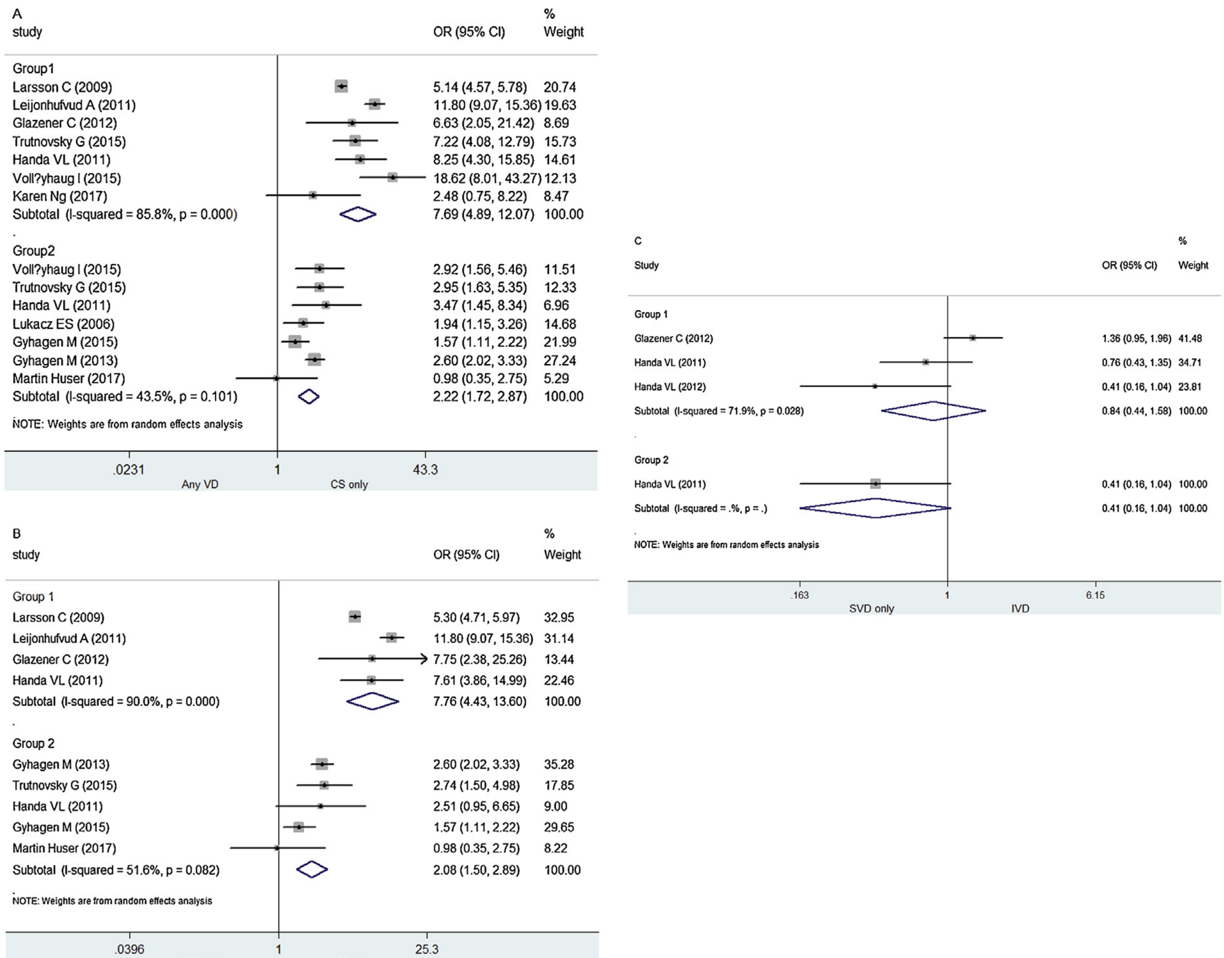

Fig. 2. Forest plot for delivery modes and POP.
A: Any VD vs. CS only; B: SVD only vs. CS only; C: SVD only vs. IVD.
Group 1: studies that used physical examination or objective standard to evaluate POP.
Group 2: studies defined POP according to the women's own perception of POP.
CS: cesarean sections.
VD: vaginal delivery.
SVD: spontaneous vaginal delivery.
IVD: instrumental vaginal delivery.

study in Group 2 compared instrumental delivery with spontaneous vaginal birth, which suggested no significant difference in POP (OR = 0.41, 95%CI = 0.16, 1.04), (Table 2, Fig. 2C)

Publication bias

The results of Begg's correlation test and Egger's regression test did not demonstrate any significant publication bias in the meta-analysis (Table 3).

Discussion

This meta-analysis examined the association between different delivery modes and the presence of POP > 1 year after delivery. The pooled results from the meta-analysis of 13 observational studies by using the random-effects model indicate that the mode of delivery is associated with the risk of POP.

The 13 eligible studies were divided into two groups according to the diagnostic criteria used for POP definition. Pooled analyses of data from seven studies in Group 1 and seven studies in Group 2 demonstrated significant increases in the risk of POP when comparing any vaginal births with cesarean sections. The results were similar when comparing spontaneous vaginal delivery to cesarean sections in two groups. No significant difference in POP was found between instrumental delivery and spontaneous vaginal delivery in two groups. Heterogeneity in Group 1 was significant, but the sensitivity analysis did not demonstrate that any single study significantly changed the pooled ORs. Age, parity, composition of vaginal delivery group (women delivering only ever by vaginal routes vs. women with both vaginal and cesarean deliveries), and the definition of POP were examined as the potential sources of heterogeneity.

In this meta-analysis, comprehensive search without language restrictions was performed to make sure that all potential eligible studies could be included. Duplicate assessment of eligibility and data extraction were conducted to prevent potential bias in the process of literature screen and data abstraction. We used appropriate statistical methods to generate pooled estimates and explored possible sources of heterogeneity. The relatively large number of participants in our study improved the precision of risk estimates. Most of eligible studies used multivariable-adjusted risk estimates, thereby minimizing confounding factor.

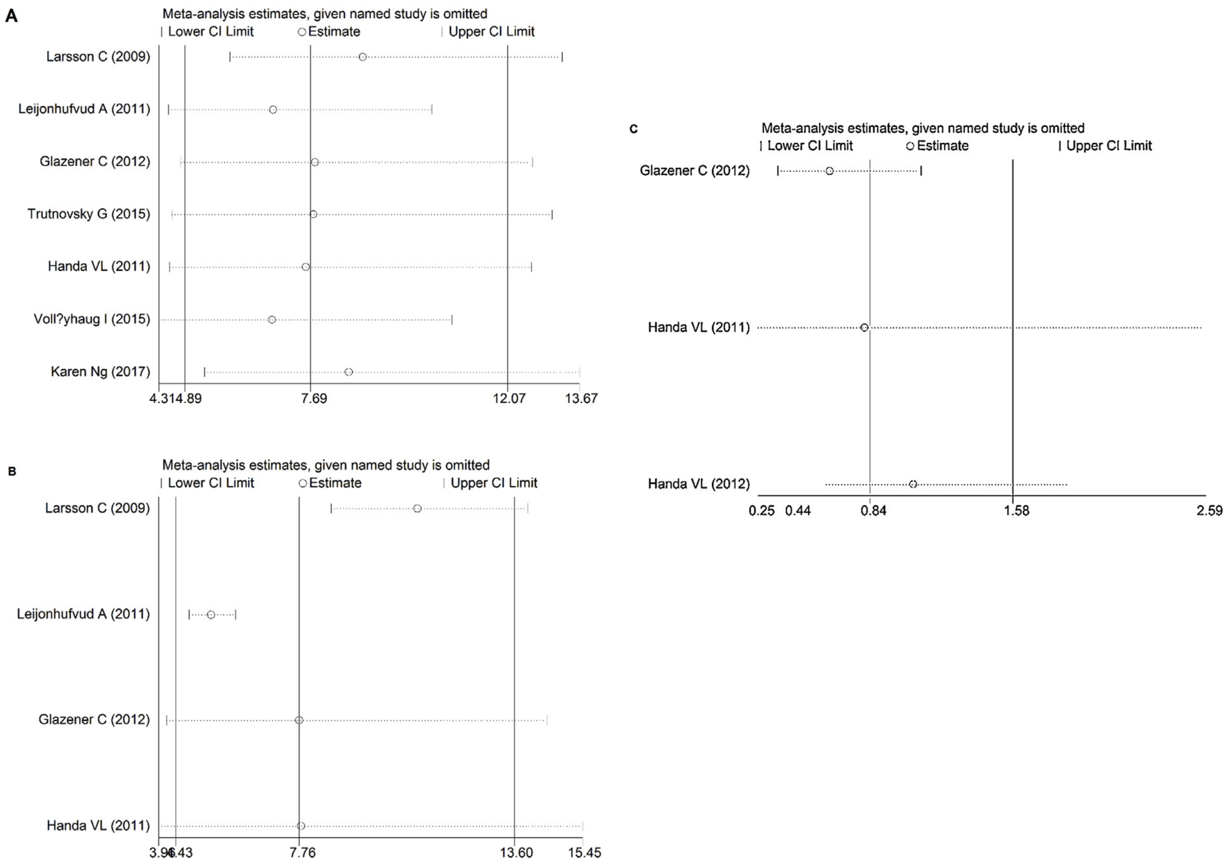

Fig. 3. Sensitivity analysis on the association between delivery mode and POP.
Sensitivity analysis for studies included in Group 1.
A: Any VD vs. CS only; B: SVD only vs. CS only; C: SVD only vs. IVD.

The limitations of this study are largely the weaknesses of eligible studies. Although there were numerous studies assessing the association between delivery mode and POP, it was frequently impossible to compare data quantitatively [28,29]. The components of vaginal delivery group in most primary studies were incontinence. In some studies, vaginal delivery group included women delivering only ever by vaginal routes (including instrumental delivery or not) [23]. While vaginal birth group in some primary studies included multiparous women with both vaginal and cesarean births [25]. Furthermore, studies included in this meta-analysis were heterogeneous and varied in the ability to stratify POP symptoms by parity, severity, and timing of cesarean, thereby contributing to the heterogeneity in the pooled analysis.

Many studies have extensively investigated the association between different delivery modes and POP, but the findings are controversial. Durnea CM et al [30] conducted a cohort study to investigate the impact of the mode of delivery on postnatal pelvic floor dysfunction in primiparas, and they found that instrumental delivery was associated with an increased prolapse score, while CS did not seem to offer protection. While different conclusion were reached by Kurt S et al. [31]. They reported that Vaginal birth increased the risk of POP/SUI surgery 2.33 times ($p = 0.03$). Therefore, potentially increasing use of cesarean section may be beneficial for decreasing the need of SUI and pelvic organ prolapse surgery [16,25]. A meta-analysis of Keag OE et al. [32] shown that cesarean delivery is associated with a reduced rate of urinary incontinence and pelvic organ prolapse when compared with vaginal delivery.

This meta-analysis suggests that patients with vaginal delivery history have increased incidence of POP compared that with cesarean sections. In one of our recent studies, we found that vaginal delivery is an independent risk factor causing the damage of pelvic floor muscle(PFM), and episiotomy may cause injury of PFM [33].

In conclusion, the results provided here may be useful when counseling women about the risk and benefits of different delivery modes. Although we have quantified one benefit of cesarean section, women and their doctors have to take other consequences into consideration. Planned cesarean section contributes an increased risk of neonatal intensive care admission for the baby and many negative public health consequences for the mother. A former cesarean also carries risks in succedent pregnancies, including an increased risk of uterine rupture and abnormal placentation [34]. In general, both the advantages and disadvantages of different delivery modes should be considered by women and their doctors when discussing delivery management options.

Table 3
Publication bias of eligible studies.

Groups	Egger's test		Begg's test	
	t	*P*	z	*P*
Group 1				
Any VD vs. CS only	1.50	0.207	0.00	1.000
SVD only vs. CS only	0.77	0.523	−0.34	1.000
SVD only vs. IVD	−3.16	0.195	1.04	0.296
Group 2				
Any VD vs. CS only	−0.21	0.843	0.00	1.000
SVD only vs. CS only	−0.62	0.578	0.73	0.462
SVD only vs. IVD	–	–	–	–

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