

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Factors predicting successful vaginal birth after caesarean section: protocol for evidence-based consensus recommendations using a Delphi survey

| | |
|-------------------------------|--|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2020-047433 |
| Article Type: | Protocol |
| Date Submitted by the Author: | 28-Nov-2020 |
| Complete List of Authors: | Zhu, Weiyang ; Jiaying University, Obstetric Department of Jiaying Maternity and Children Health Care Hospital Ai, Ling ; Jiaying University, Obstetric Department of Jiaying Maternity and Children Health Care Hospital Feng, Ying ; Jiaying University, Obstetric Department of Jiaying Maternity and Children Health Care Hospital Yuan, Haiyan ; Jiaying University, Obstetric Department of Jiaying Maternity and Children Health Care Hospital Wang, Yu ; Jiaying University, Science and Education Division of Jiaying Maternity and Children Health Care Hospital Wang, Meitang ; Changhai Hospital, Emergency Department Mei, Zubing; Shuguang Hospital, Department of Anorectal Surgery |
| Keywords: | OBSTETRICS, PREVENTIVE MEDICINE, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT |
| | |

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 **Factors predicting successful vaginal birth after caesarean section: protocol for**
5 **evidence-based consensus recommendations using a Delphi survey**
6
7

8
9 Weiyong Zhu¹, Ling Ai^{1#}, Ying Feng¹, Haiyan Yuan¹, Yu Wang², Meitang Wang^{3#},
10 Zubing Mei^{4, 5#}
11
12
13

- 14
15 1. Obstetric Department of Jiaying Maternity and Children Health Care Hospital,
16 Jiaying University, Wenzhou Medical University Affiliated Hospital of
17 Women and Children, Jiaying, 314000, China
18
19 2. Science and Education Division of Jiaying Maternity and Children Health
20 Care Hospital, Jiaying University, Wenzhou Medical University Affiliated
21 Hospital of Women and Children, Jiaying, 314000, China
22
23 3. Emergency Department, Changhai Hospital, Navy Medical University,
24 Shanghai, 200433, China.
25
26 4. Department of Anorectal Surgery, Shuguang Hospital, Shanghai University of
27 Traditional Chinese Medicine, Shanghai, 201203, China;
28
29 5. Anorectal Disease Institute of Shuguang Hospital, Shanghai, 201203, China.
30
31
32
33

34 **Correspondence to:**

35
36 Dr. Ling Ai

37
38
39 Obstetric Department of Jiaying Maternity and Children Health Care Hospital,
40
41 Jiaying University, Wenzhou Medical University Affiliated Hospital of Women and
42
43 Children
44

45
46 No.2468 East Central Road, South lake district, Jiaying, 314000, China
47

48
49 Tel: 086 13736836830
50

51
52 E-mail:13736836830@163.com
53
54
55

56
57 Dr. Meitang Wang,

58
59 Emergency Department, Changhai Hospital, Navy Medical University, Shanghai,
60

1
2
3
4 168 Changhai Road, Shanghai 200433, China.
5

6
7 Tel: 86- 189 3010 3301;
8

9 E-mail: wmt88@sina.com
10
11
12
13

14 Dr. Zubing Mei, MD, PhD
15

16 Department of Anorectal Surgery, Shuguang Hospital, Shanghai University of
17 Traditional Chinese Medicine; Anorectal Disease Institute of Shuguang Hospital
18
19 528 Zhangheng Road, Shanghai 201203, China
20

21
22 Tel: 086-2120256187
23

24 E-mail: herrmayor@126.com
25
26
27
28
29
30

31 **Running head:** Delphi survey of factors predicting successful VBAC
32

33 **Abstract Word Count:** 297
34

35 **Word Count (excluding abstract):** 2050
36
37

38 **References:** 53
39

40 **Figure:** 1
41
42

43 **Table:** 1
44
45
46
47
48

49 **Key words:** vaginal birth after caesarean section (VBAC), predictive factors,
50 systematic review, Delphi survey, evidence-based consensus
51
52
53
54
55
56

57 **Funding statement:** This work was supported by Minsheng Special Project of
58 Scientific and Technological Innovation of Jiaxing City (grant no. 2019AD32061), the
59
60

1
2
3
4 National Natural Science Foundation of China (grant no. 81774112), a grant from
5
6 Siming Scholars from Shuguang Hospital (grant no. SGXZ-201913).
7
8
9
10
11
12

13 **Author contributions:**

14
15 Dr. Weiyong Zhu had full access to all of the data in the study and takes responsibility
16
17 for the integrity of the data and the accuracy of the data analysis.
18

19
20 Study concept and design: Ling Ai, Weiyong Zhu and Zubing Mei.
21

22
23 Acquisition, analysis, or interpretation of data: Weiyong Zhu, Ling Ai, Ying Feng,
24
25 Haiyan Yuan, Yu Wang, and Meitang Wang.
26

27
28 Drafting of the manuscript: Weiyong Zhu, Zubing Mei.
29

30
31 Critical revision of the manuscript for important intellectual content: All authors.
32

33
34 Statistical analysis: Zubing Mei, Ling Ai
35

36
37 Administrative, technical, or material support: All authors.
38

39
40 Study supervision: Zubing Mei.
41
42
43

44 **Competing interests statement:**

45
46 The authors declare that they have no conflict of interest.
47
48
49
50

51 **Role of the Funder/Sponsor:**

52
53 The funder of the study had no role in the study design, data collection, data analysis,
54
55 data interpretation or writing of the manuscript. The corresponding author had full
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

access to all the data in the study and has final responsibility for the decision to
submit for publication.

For peer review only

Abstract

Introduction

With the wide adoption of the two-child policy in China since 2016, a large percentage of women with a history of caesarean delivery plan to have a second child. Accordingly, the rate of Vaginal Birth after Cesarean Delivery (VBAC) is increasing. Women attempting repeat VBAC may experience multiple morbidities, which is also one of the leading causes of maternal and perinatal mortality. However, it remains far below expectations how to evaluate successful VBAC. This study aims to use a novel approach to identify a set of predictive factors for successful VBAC to be included in prediction models. We plan to validate these predicting factors collected through a comprehensive literature review combined with a two-round international Delphi survey.

Methods and analysis

This study will apply a methodology through an evidence-based approach. A long list of potential prediction factors for successful VBAC will be extracted and identified through the following stages: First, a systematic review of the published literature will be conducted to extract candidate factors that contribute to the successful VBAC. The online questionnaires will be developed in the field of patient, maternal and fetal-related factors. A two-round international Delphi survey will be distributed to the expert panel in the field of perinatal medicine using Google Forms. Experts will be asked to score each factor using the 9-point Likert rating scale to establish core

1
2
3
4 predictive factors for the successful VBAC. The expert panel will determine on
5
6 whether to include, potentially include, or exclude predictive factors, based on the
7
8
9 GRADE approach and the Delphi method.
10
11
12
13

14 **Ethics and dissemination**

15
16
17 The study was approved by the Institutional Review Board of the Jiaying Maternity
18
19 and Children Health Care Hospital (approval number: 2019-79). The results of this
20
21 study will be submitted to international peer-reviewed journals or conferences in
22
23 perinatal medicine or obstetrics.
24
25
26
27
28
29

30 **Trial registration number**

31
32 Open Science Framework (OSF): DOI 10.17605/OSF.IO/8D6XY.
33
34
35
36
37

38 **Key words**

39
40 Vaginal birth after caesarean section (VBAC), predictive factors, systematic review,
41
42
43 Delphi survey, evidence-based consensus
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Strengths and limitations of this study

- This is the first novel mixed methods used to select predictive factors for successful vaginal birth after cesarean delivery (VBAC) for obstetric patients.
- Predictive factors for successful VBAC will be identified through the combination of a systematic review and Delphi process.
- The consensus on determination of predictive factors for successful VBAC will be based on a two-round Delphi survey among international obstetric experts.
- A Delphi survey-based expert judgment will be made to include or exclude predictive factors for successful VBAC.

Introduction

The overall cesarean delivery (CD) rates have accelerated significantly globally in recent years.¹ It has been reported that successful vaginal birth after cesarean delivery (VBAC) reduces morbidity or complications compared to an elective repeat CD.²

In China, with the wide adoption of the two-child policy since 2016, a large percentage of women with a history of CD plan to have a second child.

Therefore, a trial of labor after one cesarean (TOLAC) is encouraged in some countries to reduce CD rates and associated maternal adverse outcomes.³⁻⁵

Studies have shown that CD after an unsuccessful TOLAC may lead to increased bleeding, postoperative infection, endometritis and increased health care expenditure.⁶⁻⁹

It is crucial to determine the protective and risk factors for an obstetrician to decide on a woman's chance for successful VBAC based on the patients baseline characteristics.

Several studies have reported that patient- related demographic characteristics (patient race and ethnicity, education level and gestational week),^{10 11} maternal factors (maternal age, body mass index and bishop score)^{12 13} and fetal factors (estimated birth weight)¹⁴ that may be associated with a woman's chance for successful VBAC. Some predictive models for successful VBAC have also been published in recent years.^{2 12 15} However, the quality of these models varied considerably in terms of study design, enrolled patients, model internal and external validity, which make the applicability domain of the model rather dubious.

1
2
3
4
5
6
7 The aim of this study is to use a novel approach to identify a set of predictive factors
8
9 for success of VBAC to be included in prediction models. We plan to validate these
10
11 predicting variables collected through a comprehensive literature review combined
12
13 with an international two-round Delphi survey.
14
15
16
17
18

19 **Ethics**

20
21
22 The study was approved by the Institutional Review Board of the Jiaying Maternity
23
24 and Children Health Care Hospital.
25
26
27
28
29

30 **Study design**

31
32 We will carry out a study that combines a comprehensive systematic review and an
33
34 evaluation of the certainty of the evidence based on Grading of Recommendations
35
36 Assessment, Development, and Evaluation (GRADE) approach.¹⁶ As demonstrated in
37
38 the flowchart (Figure 1), a structured Delphi survey-based expert judgment will be
39
40 made to include or exclude predictive factors for successful VBAC.
41
42
43
44
45
46
47

48 **Systematic literature review**

49
50 The systematic review will be performed based on the Preferred Reporting Items for
51
52 Systematic Reviews and Meta-analyses (PRISMA) guidelines,¹⁷ and aims to update
53
54 all potential predictive factors for successful VBAC in hospitalised obstetric patients,
55
56 the search strategy of which is described in detail in Table 1. In summary, we will
57
58
59
60

1
2
3
4 search Pubmed, EMBASE, Cochrane Library and SinoMed from inception to
5
6 November, 2020. Predictive factors and prediction model studies will be selected that
7
8 report potential predictive factors for successful VBAC in hospitalised obstetric
9
10 patients. We define successful VBAC as a successful vaginal delivery after a previous
11
12 cesarean section. Two independent reviewers will screen the articles for eligibility and
13
14 extract the data after duplicated citations are removed. Then the GRADE approach
15
16 will be applied to assess and rate the certainty of the evidence independently.¹⁶
17
18
19
20
21
22 The results of the systematic review will provide the basis to develop a framework for
23
24 voting in the two-round international Delphi survey.
25
26
27
28
29

30
31 When the systematic review is finished, we will hold a face-to-face meeting among
32
33 the research team to discuss the main findings of the systematic review. Through the
34
35 discussion, we will judge which predictive factors should be included in the Delphi
36
37 process. The results will be presented with forest plots for each meta-analysis
38
39 combined with the effect estimates and their confidence intervals. We will also
40
41 evaluate the evidence of the observational studies which will be graded into
42
43 high-quality, moderate-quality and low-quality evidence according to Egger's P value,
44
45 total sample size and between-study heterogeneity as recommended by Mei et al.¹⁸
46
47
48
49
50 After grading the evidence, the research team members will discuss the feasibility and
51
52 acceptability of the potential predictive factors included in the Delphi survey, which
53
54 will be categorised into 3 groups: included, potentially included, and excluded
55
56 predictive factors, the method of which was recommended by Darzi, et al.¹⁹ The
57
58
59
60

1
2
3
4 included predictive factors are defined as those that should be included in the future
5
6 prediction model. The potentially included predictive factors are defined as candidates
7
8 that will potentially be included in the future prediction model. The excluded
9
10 predictive factors are those that will not be considered to be included in the prediction
11
12
13
14 model.
15
16

17 18 19 **Expert panel participants**

20
21
22 The expert panel will be selected from all over the world including obstetricians and
23
24 senior researchers with expertise in management of obstetric or perinatal
25
26 complications in hospitalised obstetric patients, and in the development, validation,
27
28 and application of predictive models for clinical practice. Panel experts will
29
30 participate in a web-based panel conference, complete surveys and questionnaires, if
31
32 necessary, will also provide feedback on reports. They will disclose that they do not
33
34 have any conflicts of interest and then complete the declaration-of-interest forms to
35
36 avoid any potentially existing conflicts regarding the existing predictive models and
37
38 other factors. We anticipate that at least 20 representatives from the expert panel with
39
40 at least five representatives from each of international association will be included.
41
42
43
44
45
46
47
48
49

50 We will select members of the expert panel by using the following predesigned
51
52 criteria:
53

- 54
55
56 1) First or corresponding authors of a journal article on predictive factors for
57
58 successful VBAC in hospitalised obstetric patients.
59
60

- 1
- 2
- 3
- 4 2) Representative members from International Federation of Gynaecologists and
- 5
- 6 Obstetricians (FIGO), the American College of Obstetricians and Gynecologists
- 7
- 8 (ACOG), the Royal College of Obstetricians and Gynaecologists (RCOG), and
- 9
- 10 Chinese Obstetricians and Gynecologists Association (COGA).
- 11
- 12
- 13
- 14 3) Guideline authors of the above mentioned associations of obstetricians and
- 15
- 16 gynecologists.
- 17
- 18
- 19

20 The research team is composed of one senior obstetrician, 2 to 3 resident physicians
21
22 working in gynecology and obstetrics, a senior researcher, who will work together to
23
24 compile the evidence for presentation, draft the questionnaire for the two-round
25
26 Delphi survey, analyse the responses, and summarise the results.
27
28
29
30

31 32 33 **Two-round Delphi survey**

34
35
36 A list of predictive factors will be delivered to the expert panel by e-mail in the form
37
38 of google form questionnaire, which we summarise based on the results of the
39
40 systematic review and identify them finally by group discussion among the research
41
42 team members. Each member of expert panel will provide his or her response
43
44 independently. Discussions are not allowed among expert panel members. During the
45
46 first-round survey, the initial list of predictive factors yielded by the systematic
47
48 review will be supplemented with other relevant factors which might be suggested by
49
50 the expert panel members. These will constitute all the item list of the first-round
51
52 Delphi survey. We initially classify the predictive factors into three categories
53
54 according to the literature reports and general knowledge, including patient-related
55
56
57
58
59
60

1
2
3
4 factors (race/ethnicity, level of education, delivery interval and gestational week),
5
6 maternal-related factors (maternal age, body mass index, previous vaginal delivery
7
8 history and trial of labor after a caesarean delivery history) and fetal-related factors
9
10 (estimated fetal weight).
11
12
13
14
15
16

17 The second-round Delphi survey will be designed for the experts to make final
18
19 clinical or methodological judgements regarding the predictive factors for successful
20
21 VBAC based on the reports of the first-round survey.
22
23
24
25
26

27 The expert panel members will be asked to rate the importance of each candidate item
28
29 using a 9-point Likert scale, where 1 to 3 means “low importance”, 4 to 6 means “not
30
31 critically important” and 7 to 9 means “critical importance”.²⁰⁻²³ An “unable to rate”
32
33 option will also be set. The expert panel members will be instructed to choose “unable
34
35 to rate” if they think they do not have adequate knowledge or expertise on a particular
36
37 list of statement.^{24 25} During the first round, panel members can suggest some more
38
39 related items to be incorporated into the second round of survey after discussion by
40
41 the research team. Only panel members who have finished the first-round survey can
42
43 move to the second-round survey. During the second round, they will be reminded of
44
45 what they rated during the first round and will be shown the distribution of responses
46
47 across the 1 to 9 scale for each question in the questionnaire. The expert panel
48
49 members have the right to retain their first-round scores or rescored for some specific
50
51 statements. Both rounds of online voting are anonymous to minimise bias.
52
53
54
55
56
57
58
59
60

Consensus definition and analysis plan

We will consider consensus to be reached and the predictive factors will be included if more than 70% of panel members score the statement within 7 to 9 (critical importance) or less than 15% of panel members score the statement within 1 to 3 (low importance); or in contrast, the predictive factors will be excluded if more than 70% of panel members score the statement within 1 to 3 (low importance) or less than 15% of panel members score the statement within 7 to 9 (critical importance).

This framework is recommended by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) group used to assess the importance of evidence. At the end of the questionnaire, we will encourage experts who participate in the survey to add some other potential predictive factors that they think are relevant, and it is better to provide some reasons.

Finally, the panel members' agreement on the factors' importance will be assessed using the Disagreement Index (DI), as described in the RAND/UCLA approach.²⁶ The DI generally reflects the distribution and symmetry of the scores (ranging from 1 to 9), with a higher DI representing wider spread across the 9-point scale, while lower DI representing increasing consensus. If the DI exceeds 1.0, the distribution is regarded as extreme variation in rated scores, while the DI is less than 1.0, we consider no extreme variation existence, which means that a consensus is reached.

Ethics and dissemination

Information from patients and the public has informed the conception and requirement for this Delphi study as part of an existing programme of research that is centred on lumbar spinal surgery for LBLP and patient outcome.

Ethics and dissemination

Results of this evidence-based international Delphi survey to provide recommended predictive factors will be presented at relevant international conferences, and will be published in peer-reviewed journals. It will provide both obstetricians and researchers with valid and consensus predictors which can be used both in clinical practice and in quality improvement initiatives.

Patient and public involvement

Details from patients and the public have provided the conception and requirement for this Delphi process as one part of the study protocol that is focused on predictive factors of successful VBAC.

Discussion

In this work, we will apply a novel evidence-based approach to systematically identify and assess predictive factors of successful VBAC in hospitalised obstetric patients. We will first conduct an extensive systematic literature review to identify a

1
2
3
4 number of potentially relevant patient, maternal and fetal-related predictive factors
5
6 through GRADE approach. We will next develop an international two-round Delphi
7
8 survey to reach a consensus among international obstetric experts from 4 international
9
10 obstetricians and gynecologists associations of the world (FIGO, ACOG, RCOG and
11
12 COGA) on the importance of the selected factors. Our ultimate purpose of this study
13
14 is to reach evidence-based consensus on the predictive factors of successful VBAC
15
16 used for future international prediction model development for successful VBAC. At
17
18 the moment, there are no validated prediction models for successful VBAC based on
19
20 large prospective cohort studies.
21
22
23
24
25
26
27
28
29

30 **Strengths and limitations**

31
32 Our study has several strengths due to its rigorous methods that are robust and
33
34 reproducible for several reasons. First, our systematic review will be conducted based
35
36 on the PRISMA guidelines.¹⁷ The search strategy is most comprehensive compared
37
38 with the previously ones.^{11 27} Secondly, we will apply the GRADE approach to assess
39
40 the certainty of evidence, which is a most solid method for decision making in several
41
42 aspects, including for the development of future clinical guidelines.¹⁶ Thirdly, our
43
44 research team will provide objective suggestions to identify all potential predictive
45
46 factors for successful VBAC. Fourthly, the consensus regarding the issue will be
47
48 based on a two-round Delphi survey among international obstetric experts from
49
50 multiple international obstetrician and gynecologist associations of the world, making
51
52 the results more convincing. Moreover, the two-round Delphi survey will be
53
54
55
56
57
58
59
60

1
2
3
4 completely anonymous to reduce bias to the greatest extent. These set of methods will
5
6 guarantee the internal and external validity of the study results.
7
8
9

10
11 There are limitations to this study as well. Firstly, the quality of the included studies
12
13 varied considerably because most of the studies are observational cohort studies, and
14
15 some are retrospective in study design. Secondly, the statements of Delphi survey to
16
17 be developed are generally brief in nature. Some unknown domains related to the
18
19 predictive factors may not be involved and addressed adequately. Thirdly, some of the
20
21 experts involved in the Delphi survey will be clinical researchers instead of
22
23 obstetricians, and they might lack knowledge regarding certain aspects of factors for
24
25 successful of VBAC. Fourthly, though representative participants will be enrolled as
26
27 expert panel in the Delphi survey mainly from Europe, USA and China, the experts do
28
29 not cover the whole global regions, which may lead to a selection bias, and the results
30
31 could not be applicable to regions outside Europe, USA and China.
32
33
34
35
36
37
38
39
40
41
42

43 In summary, this study protocol summarises the design of validation of studies
44
45 predicting factors collected through a comprehensive literature review combined with
46
47 a two-round international Delphi survey . The results from this study will be
48
49 interpreted for the purpose of clinical decision making for obstetricians to determine
50
51 the suitable patients for VBAC.
52
53
54
55
56
57
58
59
60

References

1. Denham SH, Humphrey T, deLabrusse C, et al. Mode of birth after caesarean section: individual prediction scores using Scottish population data. *BMC pregnancy and childbirth* 2019;19(1):84.
2. Baranov A, Salvesen K, Vikhareva O. Validation of prediction model for successful vaginal birth after Cesarean delivery based on sonographic assessment of hysterotomy scar. *Ultrasound in Obstetrics & Gynecology* 2018;51(2):189-93.
3. Obstetricians ACo, Gynecologists. Vaginal birth after cesarean delivery. ACOG Practice Bulletin No. 184. *Obstetrics and Gynecology* 2017;130(5):e217-e33.
4. No RRG-tG. 45: Birth After Previous Caesarean Birth. *Royal College of Obstetrician and Gynaecologists* 2015
5. Vaginal birth after cesarean: New insights. In National Institutes of Health Consensus Development Conference; 2010.
6. El-Sayed YY, Watkins MM, Fix M, et al. Perinatal outcomes after successful and failed trials of labor after cesarean delivery. *American journal of obstetrics and gynecology* 2007;196(6):583. e1-83. e5.
7. Guise J-M, Denman MA, Emeis C, et al. Vaginal birth after cesarean: new insights on maternal and neonatal outcomes. *Obstetrics & Gynecology* 2010;115(6):1267-78.
8. McMahon MJ, Luther ER, Bowes Jr WA, et al. Comparison of a trial of labor with an elective second cesarean section. *New England journal of medicine* 1996;335(10):689-95.
9. Suarez-Easton S, Zafran N, Garmi G, et al. Postcesarean wound infection: prevalence, impact, prevention, and management challenges. *International journal of women's health* 2017;9:81.
10. Lehmann S, Baghestan E, Børdahl PE, et al. Low risk pregnancies after a cesarean section: Determinants of trial of labor and its failure. *PloS one* 2020;15(1):e0226894.
11. Wu Y, Kataria Y, Wang Z, et al. Factors associated with successful vaginal birth after a cesarean section: a systematic review and meta-analysis. *BMC pregnancy and childbirth* 2019;19(1):1-12.
12. Manzanares S, Ruiz-Duran S, Pinto A, et al. An integrated model with classification criteria to predict vaginal delivery success after cesarean section. *The Journal of Maternal-Fetal & Neonatal Medicine* 2020;33(2):236-42.
13. Minsart A-F, Liu H, Moffett S, et al. Vaginal birth after caesarean delivery in Chinese women and Western immigrants in Shanghai. *Journal of Obstetrics and Gynaecology* 2017;37(4):446-49.
14. Smithies M, Woolcott CG, Brock J-AK, et al. Factors associated with trial of labour and mode of delivery in Robson Group 5: A select group of women with previous caesarean section. *Journal of Obstetrics and Gynaecology Canada* 2018;40(6):704-11.

15. Mooney SS, Hiscock R, Clarke IDA, et al. Estimating success of vaginal birth after caesarean section in a regional Australian population: Validation of a prediction model. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2019;59(1):66-70.
16. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *Journal of clinical epidemiology* 2011;64(4):401-06.
17. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine* 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097 [published Online First: 2009/07/22]
18. Mei Z, Wang Q, Zhang Y, et al. Risk factors for recurrence after anal fistula surgery: a meta-analysis. *International Journal of Surgery* 2019;69:153-64.
19. Darzi AJ, Karam SG, Spencer FA, et al. Risk models for VTE and bleeding in medical inpatients: systematic identification and expert assessment. *Blood advances* 2020;4(12):2557-66. doi: 10.1182/bloodadvances.2020001937 [published Online First: 2020/06/17]
20. Xu Q, Huang Y, Chen B. Comprehensive assessment of health education and health promotion in five non-communicable disease demonstration districts in China: a cross-sectional study. *BMJ open* 2017;7(12):e015943. doi: 10.1136/bmjopen-2017-015943 [published Online First: 2017/12/29]
21. Mrowietz U, de Jong EM, Kragballe K, et al. A consensus report on appropriate treatment optimization and transitioning in the management of moderate-to-severe plaque psoriasis. *Journal of the European Academy of Dermatology and Venereology : JEADV* 2014;28(4):438-53. doi: 10.1111/jdv.12118 [published Online First: 2013/02/27]
22. Suzuki Y, Fukasawa M, Nakajima S, et al. Development of disaster mental health guidelines through the Delphi process in Japan. *International journal of mental health systems* 2012;6(1):7. doi: 10.1186/1752-4458-6-7 [published Online First: 2012/07/04]
23. Konstantinou K, Hider SL, Vogel S, et al. Development of an assessment schedule for patients with low back-associated leg pain in primary care: a Delphi consensus study. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2012;21(7):1241-9. doi: 10.1007/s00586-011-2057-2 [published Online First: 2011/11/05]
24. Williamson PR, Altman DG, Blazeby JM, et al. Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012;13:132. doi: 10.1186/1745-6215-13-132 [published Online First: 2012/08/08]
25. Teoh JY, MacLennan S, Chan VW, et al. An International Collaborative Consensus Statement on En Bloc Resection of Bladder Tumour Incorporating Two Systematic Reviews, a Two-round Delphi Survey, and a Consensus Meeting. *European urology* 2020;78(4):546-69. doi: 10.1016/j.eururo.2020.04.059 [published Online First: 2020/05/12]

- 1
2
3 26. Danese S, Bonovas S, Lopez A, et al. Identification of Endpoints for Development
4 of Antifibrosis Drugs for Treatment of Crohn's Disease. *Gastroenterology*
5 2018;155(1):76-87. doi: 10.1053/j.gastro.2018.03.032 [published Online First:
6 2018/03/31]
7
8 27. Wingert A, Hartling L, Sebastiani M, et al. Clinical interventions that influence
9 vaginal birth after cesarean delivery rates: Systematic Review &
10 Meta-Analysis. *BMC pregnancy and childbirth* 2019;19(1):529. doi:
11 10.1186/s12884-019-2689-5 [published Online First: 2020/01/01]
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Table 1. Search strategy for Pubmed.

| |
|--|
| 1. "Vaginal Birth after Cesarean"[Mesh] |
| 2. "Trial of Labor"[Mesh] |
| 3. "Cesarean Section, Repeat"[Mesh] |
| 4. "Cesarean Section"[Mesh] |
| 5. 1-4/OR |
| 6. 'Vaginal Birth after Cesarean' OR VBAC OR 'trial of labor' OR 'cesarean section' OR TOLAC OR 'vaginal birth*' OR 'vaginal deliver*' OR 'trial of labour' OR 'active labor' OR 'active labour' |
| 7. 5 OR 6 |

Figure legend**Figure 1.** Flowchart of the study design.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

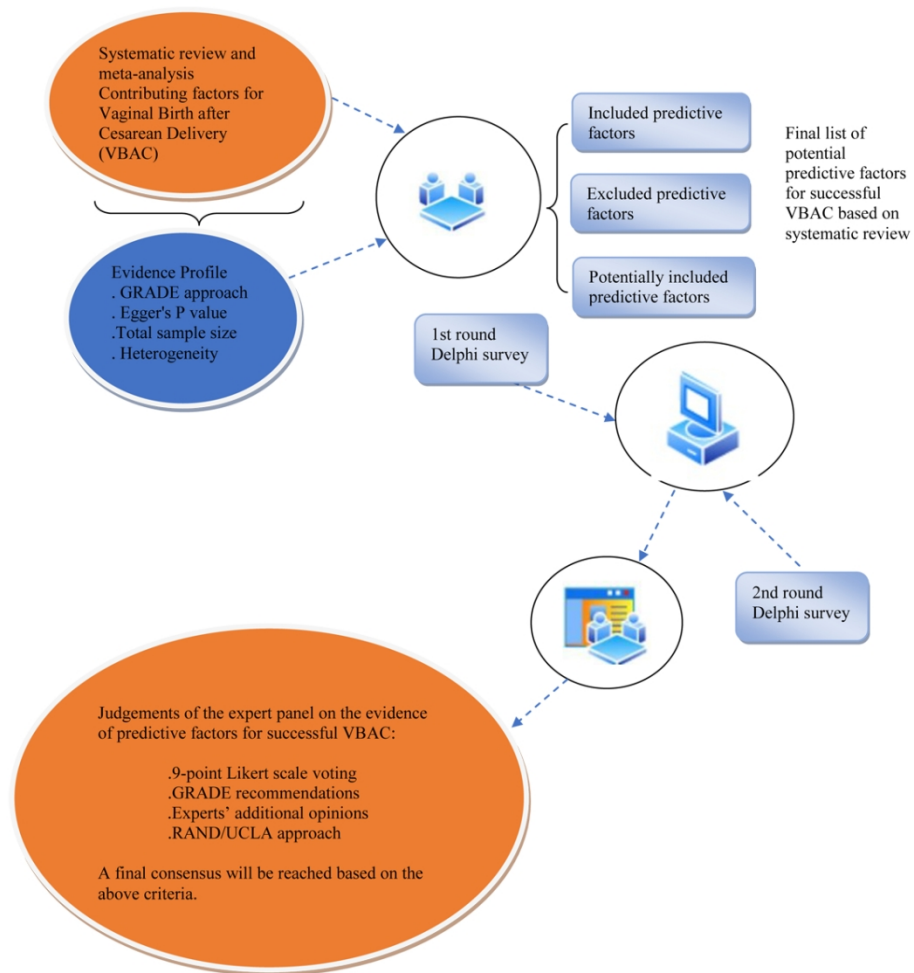


Figure 1. Flowchart of the study design.

BMJ Open

Factors predicting successful vaginal birth after caesarean section: protocol for evidence-based consensus recommendations using a Delphi survey

| | |
|---------------------------------|--|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2020-047433.R1 |
| Article Type: | Protocol |
| Date Submitted by the Author: | 04-Mar-2021 |
| Complete List of Authors: | Zhu, Weiyang ; Jiaxing University, Obstetric Department of Jiaxing Maternity and Children Health Care Hospital Ai, Ling ; Jiaxing University, Obstetric Department of Jiaxing Maternity and Children Health Care Hospital Feng, Ying ; Jiaxing University, Obstetric Department of Jiaxing Maternity and Children Health Care Hospital Yuan, Haiyan ; Jiaxing University, Obstetric Department of Jiaxing Maternity and Children Health Care Hospital Wang, Yu ; Jiaxing University, Science and Education Division of Jiaxing Maternity and Children Health Care Hospital Wang, Meitang ; Changhai Hospital, Emergency Department Mei, Zubing; Shuguang Hospital, Department of Anorectal Surgery |
| Primary Subject Heading: | Obstetrics and gynaecology |
| Secondary Subject Heading: | Evidence based practice |
| Keywords: | OBSTETRICS, PREVENTIVE MEDICINE, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT |
| | |

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 **Factors predicting successful vaginal birth after caesarean section: protocol for**
5 **evidence-based consensus recommendations using a Delphi survey**
6
7

8
9 Weiyong Zhu¹, Ling Ai^{1#}, Ying Feng¹, Haiyan Yuan¹, Yu Wang², Meitang Wang³,
10 Zubing Mei^{4, 5#}
11
12

- 13
14
15 1. Obstetric Department of Jiaying Maternity and Children Health Care Hospital,
16 Jiaying University, Wenzhou Medical University Affiliated Hospital of
17 Women and Children, Jiaying, 314000, China
18
19 2. Science and Education Division of Jiaying Maternity and Children Health
20 Care Hospital, Jiaying University, Wenzhou Medical University Affiliated
21 Hospital of Women and Children, Jiaying, 314000, China
22
23 3. Emergency Department, Changhai Hospital, Navy Medical University,
24 Shanghai, 200433, China.
25
26 4. Department of Anorectal Surgery, Shuguang Hospital, Shanghai University of
27 Traditional Chinese Medicine, Shanghai, 201203, China;
28
29 5. Anorectal Disease Institute of Shuguang Hospital, Shanghai, 201203, China.
30
31
32
33

34 **Correspondence to:**

35
36 Dr. Ling Ai

37
38
39 Obstetric Department of Jiaying Maternity and Children Health Care Hospital,
40
41 Jiaying University, Wenzhou Medical University Affiliated Hospital of Women and
42
43 Children
44

45
46 No.2468 East Central Road, South lake district, Jiaying, 314000, China
47

48
49 Tel: 086 13736836830
50

51
52 E-mail:13736836830@163.com
53
54

55
56 Dr. Zubing Mei, MD, PhD
57
58
59
60

1
2
3
4 Department of Anorectal Surgery, Shuguang Hospital, Shanghai University of
5 Traditional Chinese Medicine; Anorectal Disease Institute of Shuguang Hospital
6
7 528 Zhangheng Road, Shanghai 201203, China
8
9 Tel: 086-2120256187
10
11 E-mail: herrmayor@126.com
12
13
14
15
16
17
18

19 **Running head:** Delphi survey of factors predicting successful VBAC
20
21
22

23
24 **Count**

25
26 **Abstract Word Count:** 297
27

28
29 **Word Count (excluding abstract):** 2566
30

31
32 **References:** 34
33

34
35 **Figure:** 1
36

37
38 **Table:** 1
39
40
41

42 **Key words:**

43
44
45 vaginal birth after caesarean section (VBAC), predictive factors, systematic review,
46
47 Delphi survey, evidence-based consensus
48
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Introduction

With the wide adoption of the two-child policy in China since 2016, a large percentage of women with a history of caesarean delivery (CD) plan to have a second child. Accordingly, the rate of vaginal birth after caesarean delivery (VBAC) is increasing. Women attempting repeat VBAC may experience multiple morbidities, which is also one of the leading causes of maternal and perinatal mortality. However, it remains to be addressed how we evaluate factors for successful VBAC. This study aims to use a novel approach to identify a set of potential predictive factors for successful VBAC, especially for Chinese women, to be included in prediction models which can be most applicable to pregnant women in China. We plan to assess all potential predictive factors collected through a comprehensive literature review. Then the certainty of the evidence for the identified potential predictive factors will be assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process. Finally, a two-round international Delphi survey will be conducted to determine the level of consensus.

Methods and analysis

This study will apply a methodology through an evidence-based approach. A long list of potential predictive factors for successful VBAC will be extracted and identified through the following stages: First, an up-to-date systematic review of the published literature will be conducted to extract identified potential predictive factors for

1
2
3
4 successful VBAC. Second, an online Delphi survey will be performed to achieve
5
6 expert consensus on which factors should be included in future prediction models.
7
8
9 The online questionnaires will be developed in the field of patient, maternal and
10
11 fetal-related factors. A two-round international Delphi survey will be distributed to
12
13 the expert panel in the field of perinatal medicine using Google Forms. Experts will
14
15 be asked to score each factor using the 9-point Likert rating scale to establish potential
16
17 predictive factors for the successful VBAC. The expert panel will determine on
18
19 whether to include, potentially include, or exclude predictive factors, based on a
20
21 systematic review of clinical evidence and the Delphi method.
22
23
24
25

26 27 **Ethics and dissemination**

28
29 The study was approved by the Institutional Review Board of the Jiaying Maternity
30
31 and Children Health Care Hospital (approval number: 2019-79). The results of this
32
33 study will be submitted to international peer-reviewed journals or conferences in
34
35 perinatal medicine or obstetrics.
36
37
38
39
40
41
42

43 **Trial registration number**

44
45 Open Science Framework (OSF): DOI 10.17605/OSF.IO/8D6XY.
46
47
48
49

50 **Key words**

51
52 Vaginal birth after caesarean section (VBAC), predictive factors, systematic review,
53
54 Delphi survey, evidence-based consensus
55
56
57
58
59
60

Strengths and limitations of this study

- This study aims to use a mixed methods approach to select potential predictive factors for successful vaginal birth after caesarean section (VBAC) for obstetric patients.
- Potential predictive factors for successful VBAC will be identified through a combination of a systematic literature review and a modified Delphi process.
- The consensus on the potential predictive factors for successful VBAC will be achieved based on a two-round Delphi survey among international experts in the field of obstetrics.
- The expert panel will determine whether to include, potentially include, or exclude the candidate predictive factors, based on the GRADE approach and the Delphi method.

Introduction

The overall cesarean delivery (CD) rates have accelerated significantly globally in recent years.¹ Though successful vaginal birth after cesarean delivery (VBAC) has been reported to reduce morbidity or complications compared to an elective repeat CD,² recent evidence has continued to highlight the risks of VBAC.³ In China, with the wide adoption of the two-child policy since 2016, a large percentage of women with a history of CD plan to have a second child and an elective repeat CD can be a suitable choice. However, a trial of labor after one cesarean (TOLAC) is encouraged in some countries which has been reported to reduce maternal adverse outcomes.⁴⁻⁶ Studies have also shown that CD after an unsuccessful TOLAC may lead to increased bleeding, postoperative infection, endometritis and increased health care expenditure.⁷⁻¹⁰

Therefore, for obstetricians, it is crucial to identify the potential protective and risk factors influencing a woman's successful VBAC based on the patients' baseline characteristics. Several studies have reported that patient demographic characteristics (patient race and ethnicity, education level and gestational week),^{11 12} maternal factors (maternal age, body mass index, bishop score, diabetes, hypertensive disorders complicating pregnancy and previous vaginal deliver)¹²⁻¹⁵, fetal factors (estimated birth weight)¹⁶ and other related factors (oxytocin implementation)¹⁵ that may be associated with a woman's chance for successful VBAC. Some predictive models for successful VBAC have also been published in recent years.^{13 17 18} However, the

1
2
3
4 quality of these models varied considerably in terms of study design, enrolled patients,
5
6 internal and external validity of the models, which make the models' applicability
7
8 domain rather dubious.
9
10

11
12
13
14 This study aims to use a novel approach to identify a set of potential predictive factors
15
16 for successful VBAC, especially for Chinese women, to be included in future
17
18 prediction models which can be most applicable to pregnant women in China. We
19
20 plan to assess all potential predictive factors collected through a comprehensive
21
22 literature review. Then the certainty of the evidence for the identified potential
23
24 predictive factors will be assessed using the Grading of Recommendations
25
26 Assessment, Development, and Evaluation (GRADE) process. Finally, a two-round
27
28 international Delphi survey will be conducted to determine the level of consensus.
29
30
31
32
33
34
35
36
37

38 **Ethics**

39
40 The study was approved by the Institutional Review Board of the Jiaying Maternity
41
42 and Children Health Care Hospital.
43
44
45
46
47

48 **Study design**

49
50 We will carry out a study that combines a comprehensive systematic review and an
51
52 evaluation of the certainty of the evidence based on GRADE approach.¹⁹ As
53
54 demonstrated in the flowchart (**Figure 1**), a structured Delphi survey-based expert
55
56
57
58
59
60

1
2
3
4 judgment will be made to include or exclude potential predictive factors for successful
5
6 VBAC.
7
8
9

11 **Systematic literature review**

12
13
14 The systematic review will be performed based on the Preferred Reporting Items for
15
16 Systematic Reviews and Meta-analyses (PRISMA) guidelines,²⁰ and aims to update
17
18 all potential predictive factors for successful VBAC among women with a previous
19
20 CD history, the search strategy of which is described in detail in Table 1. In summary,
21
22 we will search Pubmed, EMBASE, Cochrane Library and SinoMed from inception to
23
24 November, 2020. Predictive factors and prediction model studies will be selected that
25
26 report potential predictive factors for successful VBAC among women with a
27
28 previous history of CD. We define successful VBAC as a successful vaginal delivery
29
30 after a previous cesarean section. Two independent reviewers will screen the articles
31
32 for eligibility and extract the data after duplicated citations are removed.
33
34
35
36
37
38
39
40
41
42

43 For a given potential predictive factor, we will pool the summary relative risks (RRs)
44
45 or odds ratios (ORs) with 95% CIs for predictive factors reported ≥ 2 studies using
46
47 random-effects models.²¹ Cochran Q and the I^2 statistics will be applied to investigate
48
49 sources of heterogeneity, with an I^2 statistic $>50\%$ referring to substantial
50
51 heterogeneity.²² Publication bias will be tested using Egger's test, with a P value < 0.1
52
53 indicating significant difference.²³ Then the GRADE approach will be applied to
54
55 assess and rate the certainty of the evidence independently.¹⁹ The results of the
56
57
58
59
60

1
2
3
4 systematic review will provide the basis to develop a framework for voting in the
5
6 two-round international Delphi survey.
7
8
9

10
11 When the systematic review is finished, we will hold a face-to-face meeting among
12
13 the research team to discuss the main findings of the systematic review. Through the
14
15 discussion, we will judge which potential predictive factors should be included in the
16
17 Delphi process. The results will be presented with forest plots for each meta-analysis
18
19 combined with the effect estimates and their confidence intervals. We will also
20
21 evaluate the evidence of the observational studies which will be graded into
22
23 high-quality, moderate-quality and low-quality evidence according to Egger's P value,
24
25 total sample size and between-study heterogeneity as recommended by Mei et al.²⁴
26
27 After grading the evidence, the research team members will discuss the feasibility and
28
29 acceptability of the potential predictive factors included in the Delphi survey, which
30
31 will be categorised into 3 groups: included, potentially included, and excluded
32
33 predictive factors, the method of which was recommended by Darzi, et al.²⁵ The
34
35 included potential predictive factors are defined as those that should be included in
36
37 the future prediction model. The potentially included predictive factors are defined as
38
39 candidates that will potentially be included in the future prediction model. The
40
41 excluded predictive factors are those that will not be considered to be included in the
42
43 prediction model.
44
45
46
47
48
49
50
51
52
53
54
55
56
57

58 **Expert panel participants**

59
60

1
2
3
4 The expert panel will be selected from all over the world including obstetricians and
5
6 senior researchers with expertise in management of obstetric or perinatal
7
8 complications for pregnant women with a previous history of CD, and in the
9
10 development, validation, and application of predictive models for clinical practice.
11
12

13
14 Panel experts will participate in a web-based panel conference, complete surveys and
15
16 questionnaires, if necessary, will also provide feedback on reports. They will disclose
17
18 that they do not have any conflicts of interest and then complete the
19
20 declaration-of-interest forms to avoid any potentially existing conflicts regarding the
21
22 existing predictive models and other factors.
23
24
25
26
27
28
29

30 We will select members of the expert panel by using the following predesigned
31
32 criteria:
33

- 34
35 1) First or corresponding authors of a journal article on potential predictive factors
36
37 for successful VBAC in hospitalised obstetric patients.
38
39
- 40
41 2) Representative members from International Federation of Gynaecologists and
42
43 Obstetricians (FIGO), the American College of Obstetricians and Gynecologists
44
45 (ACOG), the Royal College of Obstetricians and Gynaecologists (RCOG), and
46
47 Chinese Obstetricians and Gynecologists Association (COGA).
48
49
- 50
51 3) Guideline authors of the above mentioned associations of obstetricians and
52
53 gynecologists.
54
55

56 The research team is composed of one senior obstetrician, 2 to 3 resident physicians
57
58 working in gynecology and obstetrics, a senior researcher, who will work together to
59
60

1
2
3
4 compile the evidence for presentation, draft the questionnaire for the two-round
5
6 Delphi survey, analyse the responses, and summarise the results.
7
8
9

10 11 **Two-round Delphi survey** 12

13
14 The expert panel will answer questions on three categories of the potential predictive
15
16 factors for successful VBAC: patient-related, maternal-related and fetal-related
17
18 predictive factors. The results of the systematic review will be presented to the experts
19
20 and they will be asked to rate their agreement with these three aspects of potential
21
22 predictive factor proposals. For example, they will rate their agreements with the
23
24 following statements: (1) that maternal age is a predictive factor of limited / critical
25
26 importance to successful VBAC; (2) that level of education is a predictive factor of
27
28 limited / critical importance to successful VBAC; or (3) that estimated fetal weight is
29
30 a predictive factor of limited / critical importance to successful VBAC.
31
32
33
34
35
36
37
38
39

40 A list of potential predictive factors will be delivered to the expert panel by e-mail in
41
42 the form of google form questionnaire, which we summarise based on the results of
43
44 the systematic review and identify them finally by group discussion among the
45
46 research team members. Each member of expert panel will provide his or her
47
48 response independently. Discussions are not allowed among expert panel
49
50 members. During the first-round survey, the initial list of potential predictive factors
51
52 yielded by the systematic review will be supplemented with other relevant factors
53
54 which might be suggested by the expert panel members. These will constitute all the
55
56
57
58
59
60

1
2
3
4 item list of the first-round Delphi survey. We initially classify the potential predictive
5
6 factors into three categories according to the literature reports and general knowledge,
7
8 including patient-related factors (race/ethnicity, level of education, delivery interval
9
10 and gestational week), maternal-related factors (maternal age, body mass index,
11
12 previous vaginal delivery history and trial of labor after a CD history) and
13
14 fetal-related factors (estimated fetal weight).
15
16
17
18
19
20
21

22 The second-round Delphi survey will be designed for the experts to make final
23
24 clinical or methodological judgements regarding the potential predictive factors for
25
26 successful VBAC based on the reports of the first-round survey.
27
28
29
30
31

32 The expert panel members will be asked to rate the importance of each candidate item
33
34 using a 9-point Likert scale, where 1 to 3 means “low importance”, 4 to 6 means “not
35
36 critically important” and 7 to 9 means “critical importance”.²⁶⁻²⁹
37
38
39

40 An “unable to rate” option will also be set. The expert panel members will be
41
42 instructed to choose “unable to rate” if they think they do not have adequate
43
44 knowledge or expertise on a particular list of statement.^{30 31} During the first round,
45
46 panel members can suggest some more related items to be incorporated into the
47
48 second round of survey after discussion by the research team. Only panel members
49
50 who have finished the first-round survey can move to the second-round survey.
51
52
53 During the second round, they will be reminded of what they rated during the first
54
55 round and will be shown the distribution of responses across the 1 to 9 scale for
56
57
58
59
60

1
2
3
4 each question in the questionnaire. The expert panel members have the right to retain
5
6 their first-round scores or rescored for some specific statements. Both rounds of
7
8 online voting are anonymous to minimise bias.
9
10

11 12 13 14 **Consensus definition and analysis plan**

15
16 We will consider consensus to be reached and the potential predictive factors will be
17
18 included if more than 70% of panel members score the statement within 7 to 9
19
20 (critical importance) or less than 15% of panel members score the statement within 1
21
22 to 3 (low importance); or in contrast, the potential predictive factors will be excluded
23
24 if more than 70% of panel members score the statement within 1 to 3 (low importance)
25
26 or less than 15% of panel members score the statement within 7 to 9 (critical
27
28 importance).³²
29
30
31
32
33
34
35
36
37

38 This framework is recommended by the GRADE (Grading of Recommendations
39
40 Assessment, Development, and Evaluation) group used to assess the importance of
41
42 evidence. At the end of the questionnaire, we will encourage experts who participate
43
44 in the survey to add some other potential predictive factors that they think are relevant,
45
46 and it is better to provide some reasons.
47
48
49
50
51
52

53 Finally, the panel members' agreement on the factors' importance will be assessed
54
55 using the Disagreement Index (DI), as described in the RAND/UCLA approach.³³ The
56
57 DI generally reflects the distribution and symmetry of the scores (ranging from 1 to 9),
58
59
60

1
2
3
4 with a higher DI representing wider spread across the 9-point scale, while lower DI
5
6 representing increasing consensus. If the DI exceeds 1.0, the distribution is regarded
7
8 as extreme variation in rated scores, while the DI is less than 1.0, we consider no
9
10 extreme variation existence, which means that a consensus is reached.
11
12
13
14
15
16

17 **Patient and public involvement**

18
19 This protocol will be carried out without patient or public involvement.
20
21
22

23 **Discussion**

24
25 In this work, we will apply a novel evidence-based approach to systematically
26
27 identify a set of potential predictive factors for successful VBAC in pregnant women
28
29 with a history of CD. We will first conduct an extensive systematic literature review
30
31 to identify a number of potentially relevant patient, maternal and fetal-related
32
33 predictive factors through systematic review and assess the level of evidence of their
34
35 predictive value using the GRADE approach. We will next develop an international
36
37 two-round Delphi survey to reach a consensus among international obstetric experts
38
39 from 4 international obstetricians and gynecologists associations of the world (FIGO,
40
41 ACOG, RCOG and COGA) on the importance of the selected factors. Our ultimate
42
43 purpose of this study is to reach evidence-based consensus on the potential predictive
44
45 factors of successful VBAC used for future prediction model development. At the
46
47 moment, there are no validated prediction models for successful VBAC based on
48
49 large prospective cohort studies.
50
51
52
53
54
55
56
57
58
59
60

Strengths and limitations

Our study has several strengths due to its rigorous methods that are robust and reproducible for several reasons. First, our systematic review will be conducted based on the PRISMA guidelines.²⁰ The search strategy is most comprehensive compared with the previously ones.^{12 34} Secondly, we will apply the GRADE approach to assess the certainty of evidence, which is a most solid method for decision making in several aspects, including for the development of future clinical guidelines.¹⁹ Thirdly, our research team will provide objective suggestions to identify all potential predictive factors for successful VBAC. Fourthly, the consensus regarding the issue will be based on a two-round Delphi survey among international obstetric experts from multiple international obstetricians and gynecologists associations of the world, making the results more convincing. Moreover, the two-round Delphi survey will be completely anonymous to reduce bias to the greatest extent. These set of methods will guarantee the internal and external validity of the study results.

There are limitations to this study as well. Firstly, the quality of the included studies varied considerably because most of the studies are observational cohort studies, and some are retrospective in study design. Secondly, the statements of Delphi survey to be developed are generally brief in nature. Some unknown domains related to the potential predictive factors may not be involved and addressed adequately. Thirdly, some of the experts involved in the Delphi survey will be clinical researchers instead

1
2
3
4 of obstetricians, and they might lack knowledge regarding certain aspects of factors
5
6 for successful VBAC. However, clinical researchers will be trained in advance and
7
8 may have a more evidence-based perspective of predictive factors, thus they may be
9
10 more aware of the evidence and how factors appear to interact. Fourthly, though
11
12 representative participants will be enrolled as expert panel in the Delphi survey
13
14 mainly from Europe, USA and China, the experts do not cover the whole global
15
16 regions, which may lead to a selection bias, and the results could not be applicable to
17
18 regions outside Europe, USA and China.
19
20
21
22
23
24
25
26

Implications for clinical practice and further research

27
28
29 This study will present a group of agreed predictors that the expert panel can use to
30
31 predict successful VBAC more accurately. First of all, the evaluated predictors may
32
33 help obstetricians assess the risk of the individual patient. Based on the findings of
34
35 this study, further investigations are warranted to provide some more possible
36
37 predictors.
38
39
40
41
42
43
44
45

46 In a related study to be conducted by our research team, we will involve these
47
48 variables that predict successful VBAC found in this consensus study. This will
49
50 enable us to make adjustment for these factors in terms of the level of evidence based
51
52 on the results of the study, which will improve the prediction accuracy. Further
53
54 research should focus on evaluating the importance of these predictors. In addition,
55
56 this study could provide the direction of future research on the evaluation of risk
57
58
59
60

1
2
3
4 factors for successful VBAC, which will ultimately be incorporated in the
5
6 development and validation of prediction models of successful VBAC.
7
8
9

10 11 **Conclusion**

12
13
14 In summary, this study protocol summarises the design of the assessment of potential
15
16 predictive factors collected through a comprehensive literature review combined with
17
18 a two-round international Delphi survey . The results from this study will be
19
20 interpreted for the purpose of clinical decision making for obstetricians to determine
21
22 the suitable patients for VBAC, which will be most applicable to pregnant women in
23
24
25
26
27 China.
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Contributorship statement:

Ling Ai and Zubing Mei contributed equally as co-corresponding author.

Dr. Weiyong Zhu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Weiyong Zhu and Zubing Mei.

Acquisition, analysis, or interpretation of data: Weiyong Zhu, Ling Ai, Ying Feng, Haiyan Yuan, Yu Wang, and Meitang Wang.

Drafting of the manuscript: Weiyong Zhu, Zubing Mei.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Zubing Mei, Ling Ai

Administrative, technical, or material support: All authors.

Study supervision: Zubing Mei.

Competing interests:

The authors declare that they have no conflict of interest.

Funding:

This work was supported by Minsheng Special Project of Scientific and Technological Innovation of Jiaxing City (grant no. 2019AD32061), the National Natural Science Foundation of China (grant no. 81774112), a grant from Siming Scholars from Shuguang Hospital (grant no. SGXZ-201913).

References

1. Denham SH, Humphrey T, deLabrusse C, et al. Mode of birth after caesarean section: individual prediction scores using Scottish population data. *BMC pregnancy and childbirth* 2019;19(1):84.
2. Obstetricians ACo, Gynecologists. ACOG Practice Bulletin No. 205: Vaginal birth after cesarean delivery. *Obstetrics and gynecology* 2019;133(2):e110-e27.
3. Hidalgo-Lopezosa P, Hidalgo-Maestre M. Risk of uterine rupture in vaginal birth after cesarean: Systematic review. *Enfermería Clínica (English Edition)* 2017;27(1):28-39. doi: <https://doi.org/10.1016/j.enfcle.2016.08.002>
4. Obstetricians ACo, Gynecologists. Vaginal birth after cesarean delivery. ACOG Practice Bulletin No. 184. *Obstetrics and Gynecology* 2017;130(5):e217-e33.
5. No RRG-tG. 45: Birth After Previous Caesarean Birth. Royal College of Obstetrician and Gynaecologists 2015
6. Vaginal birth after cesarean: New insights. In National Institutes of Health Consensus Development Conference; 2010.
7. El-Sayed YY, Watkins MM, Fix M, et al. Perinatal outcomes after successful and failed trials of labor after cesarean delivery. *American journal of obstetrics and gynecology* 2007;196(6):583. e1-83. e5.
8. Guise J-M, Denman MA, Emeis C, et al. Vaginal birth after cesarean: new insights on maternal and neonatal outcomes. *Obstetrics & Gynecology* 2010;115(6):1267-78.
9. McMahon MJ, Luther ER, Bowes Jr WA, et al. Comparison of a trial of labor with an elective second cesarean section. *New England journal of medicine* 1996;335(10):689-95.
10. Suarez-Easton S, Zafran N, Garmi G, et al. Postcesarean wound infection: prevalence, impact, prevention, and management challenges. *International journal of women's health* 2017;9:81.
11. Lehmann S, Baghestan E, Børdahl PE, et al. Low risk pregnancies after a cesarean section: Determinants of trial of labor and its failure. *Plos one* 2020;15(1):e0226894.
12. Wu Y, Kataria Y, Wang Z, et al. Factors associated with successful vaginal birth after a cesarean section: a systematic review and meta-analysis. *BMC pregnancy and childbirth* 2019;19(1):1-12.
13. Manzanares S, Ruiz-Duran S, Pinto A, et al. An integrated model with classification criteria to predict vaginal delivery success after cesarean section. *The Journal of Maternal-Fetal & Neonatal Medicine* 2020;33(2):236-42.
14. Minsart A-F, Liu H, Moffett S, et al. Vaginal birth after caesarean delivery in Chinese women and Western immigrants in Shanghai. *Journal of Obstetrics and Gynaecology* 2017;37(4):446-49.
15. Familiari A, Neri C, Caruso A, et al. Vaginal birth after caesarean section: a multicentre study on prognostic factors and feasibility. *Archives of gynecology and obstetrics* 2020;301(2):509-15. doi: 10.1007/s00404-020-05454-0 [published Online First: 2020/02/13]

16. Smithies M, Woolcott CG, Brock J-AK, et al. Factors associated with trial of labour and mode of delivery in Robson Group 5: A select group of women with previous caesarean section. *Journal of Obstetrics and Gynaecology Canada* 2018;40(6):704-11.
17. Baranov A, Salvesen K, Vikhareva O. Validation of prediction model for successful vaginal birth after Cesarean delivery based on sonographic assessment of hysterotomy scar. *Ultrasound in Obstetrics & Gynecology* 2018;51(2):189-93.
18. Mooney SS, Hiscock R, Clarke IDA, et al. Estimating success of vaginal birth after caesarean section in a regional Australian population: Validation of a prediction model. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2019;59(1):66-70.
19. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *Journal of clinical epidemiology* 2011;64(4):401-06.
20. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine* 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097 [published Online First: 2009/07/22]
21. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled clinical trials* 1986;7(3):177-88.
22. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *Bmj* 2003;327(7414):557-60.
23. Egger M, Smith GD, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *Bmj* 1997;315(7109):629-34.
24. Mei Z, Wang Q, Zhang Y, et al. Risk factors for recurrence after anal fistula surgery: a meta-analysis. *International Journal of Surgery* 2019;69:153-64.
25. Darzi AJ, Karam SG, Spencer FA, et al. Risk models for VTE and bleeding in medical inpatients: systematic identification and expert assessment. *Blood advances* 2020;4(12):2557-66. doi: 10.1182/bloodadvances.2020001937 [published Online First: 2020/06/17]
26. Xu Q, Huang Y, Chen B. Comprehensive assessment of health education and health promotion in five non-communicable disease demonstration districts in China: a cross-sectional study. *BMJ open* 2017;7(12):e015943. doi: 10.1136/bmjopen-2017-015943 [published Online First: 2017/12/29]
27. Mrowietz U, de Jong EM, Kragballe K, et al. A consensus report on appropriate treatment optimization and transitioning in the management of moderate-to-severe plaque psoriasis. *Journal of the European Academy of Dermatology and Venereology : JEADV* 2014;28(4):438-53. doi: 10.1111/jdv.12118 [published Online First: 2013/02/27]
28. Suzuki Y, Fukasawa M, Nakajima S, et al. Development of disaster mental health guidelines through the Delphi process in Japan. *International journal of mental health systems* 2012;6(1):7. doi: 10.1186/1752-4458-6-7 [published Online First: 2012/07/04]

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
29. Konstantinou K, Hider SL, Vogel S, et al. Development of an assessment schedule for patients with low back-associated leg pain in primary care: a Delphi consensus study. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2012;21(7):1241-9. doi: 10.1007/s00586-011-2057-2 [published Online First: 2011/11/05]
30. Williamson PR, Altman DG, Blazeby JM, et al. Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012;13:132. doi: 10.1186/1745-6215-13-132 [published Online First: 2012/08/08]
31. Teoh JY, MacLennan S, Chan VW, et al. An International Collaborative Consensus Statement on En Bloc Resection of Bladder Tumour Incorporating Two Systematic Reviews, a Two-round Delphi Survey, and a Consensus Meeting. *European urology* 2020;78(4):546-69. doi: 10.1016/j.eururo.2020.04.059 [published Online First: 2020/05/12]
32. Bilbro NA, Hirst A, Paez A, et al. The IDEAL Reporting Guidelines: A Delphi Consensus Statement Stage specific recommendations for reporting the evaluation of surgical innovation. *Annals of surgery* 2020 doi: 10.1053/j.ajkd.2020.03.014
10.1097/sla.0000000000004180 [published Online First: 2020/07/14
2020/07/11]
33. Danese S, Bonovas S, Lopez A, et al. Identification of Endpoints for Development of Antifibrosis Drugs for Treatment of Crohn's Disease. *Gastroenterology* 2018;155(1):76-87. doi: 10.1053/j.gastro.2018.03.032 [published Online First: 2018/03/31]
34. Wingert A, Hartling L, Sebastianski M, et al. Clinical interventions that influence vaginal birth after cesarean delivery rates: Systematic Review & Meta-Analysis. *BMC Pregnancy Childbirth* 2019;19(1):529. doi: 10.1186/s12884-019-2689-5 [published Online First: 2020/01/01]

Table 1. Search strategy for Pubmed.

| |
|--|
| 1. "Vaginal Birth after Cesarean"[Mesh] |
| 2. "Trial of Labor"[Mesh] |
| 3. "Cesarean Section, Repeat"[Mesh] |
| 4. "Cesarean Section"[Mesh] |
| 5. 1-4/OR |
| 6. 'Vaginal Birth after Cesarean' OR VBAC OR 'trial of labor' OR 'cesarean section' OR TOLAC OR 'vaginal birth*' OR 'vaginal deliver*' OR 'trial of labour' OR 'active labor' OR 'active labour' |
| 7. 5 OR 6 |

Figure legend**Figure 1.** Flowchart of the study design.

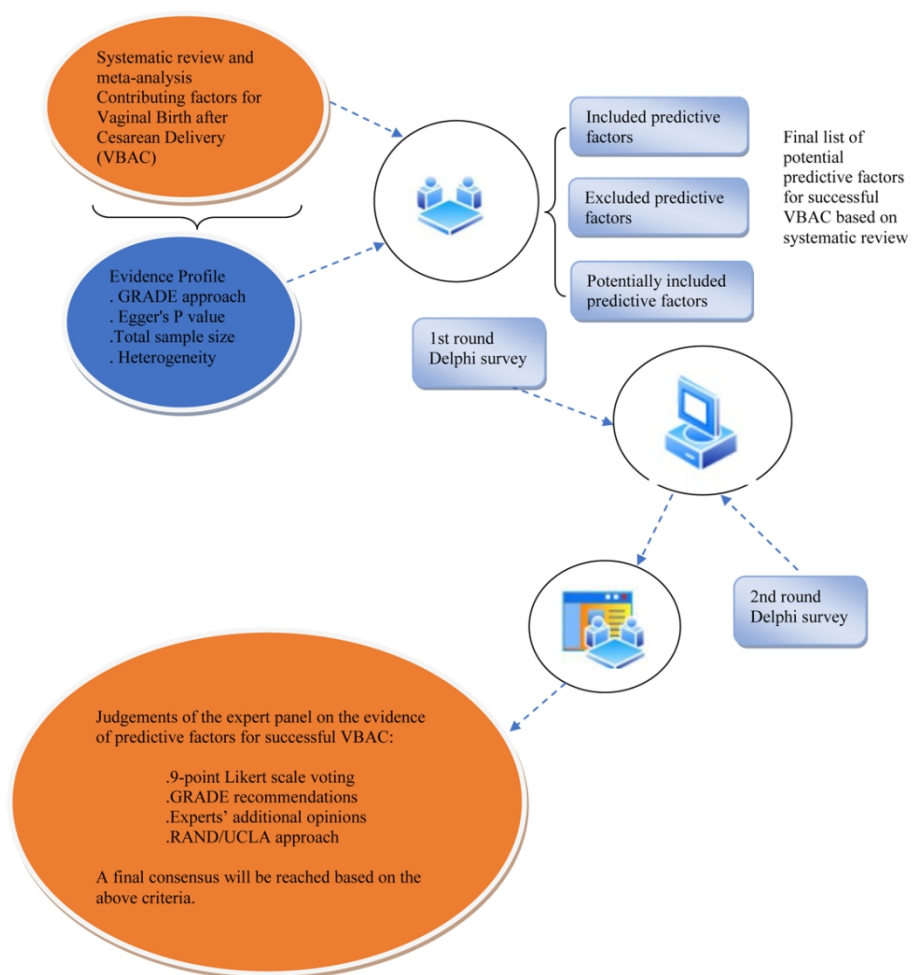


Figure 1. Flowchart of the study design.

BMJ Open

Factors predicting successful vaginal birth after caesarean section: protocol for evidence-based consensus recommendations using a Delphi survey

| | |
|---------------------------------|---|
| Journal: | <i>BMJ Open</i> |
| Manuscript ID | bmjopen-2020-047433.R2 |
| Article Type: | Protocol |
| Date Submitted by the Author: | 31-Mar-2021 |
| Complete List of Authors: | Zhu, Weiyang ; Jiaxing University, Obstetric Department of Jiaxing Maternity and Children Health Care Hospital Ai, Ling ; Jiaxing University, Obstetric Department of Jiaxing Maternity and Children Health Care Hospital Feng, Ying ; Jiaxing University, Obstetric Department of Jiaxing Maternity and Children Health Care Hospital Yuan, Haiyan ; Jiaxing University, Obstetric Department of Jiaxing Maternity and Children Health Care Hospital Wang, Yu ; Jiaxing University, Science and Education Division of Jiaxing Maternity and Children Health Care Hospital Wang, Meitang ; Changhai Hospital, Emergency Department Mei, Zubing; Shuguang Hospital, Department of Anorectal Surgery; Shanghai University of Traditional Chinese Medicine, Anorectal Disease Institute of Shuguang Hospital |
| Primary Subject Heading: | Obstetrics and gynaecology |
| Secondary Subject Heading: | Evidence based practice |
| Keywords: | OBSTETRICS, PREVENTIVE MEDICINE, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT |
| | |

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 **Factors predicting successful vaginal birth after caesarean section: protocol for**
5 **evidence-based consensus recommendations using a Delphi survey**
6
7

8
9 Weiyong Zhu¹, Ling Ai^{1#}, Ying Feng¹, Haiyan Yuan¹, Yu Wang², Meitang Wang³,
10
11 Zubing Mei^{4, 5#}
12
13

- 14
15 1. Obstetric Department of Jiaying Maternity and Children Health Care Hospital,
16 Jiaying University, Wenzhou Medical University Affiliated Hospital of
17 Women and Children, Jiaying, 314000, China
18
19 2. Science and Education Division of Jiaying Maternity and Children Health
20 Care Hospital, Jiaying University, Wenzhou Medical University Affiliated
21 Hospital of Women and Children, Jiaying, 314000, China
22
23 3. Emergency Department, Changhai Hospital, Navy Medical University,
24 Shanghai, 200433, China.
25
26 4. Department of Anorectal Surgery, Shuguang Hospital, Shanghai University of
27 Traditional Chinese Medicine, Shanghai, 201203, China;
28
29 5. Anorectal Disease Institute of Shuguang Hospital, Shanghai, 201203, China.
30
31
32
33

34 **Correspondence to:**

35
36 Dr. Ling Ai

37
38
39 Obstetric Department of Jiaying Maternity and Children Health Care Hospital,
40
41 Jiaying University, Wenzhou Medical University Affiliated Hospital of Women and
42
43 Children
44

45
46 No.2468 East Central Road, South lake district, Jiaying, 314000, China
47

48
49 Tel: 086 13736836830
50

51
52 E-mail:13736836830@163.com
53
54

55
56 Dr. Zubing Mei, MD, PhD
57
58
59
60

1
2
3
4 Department of Anorectal Surgery, Shuguang Hospital, Shanghai University of
5 Traditional Chinese Medicine; Anorectal Disease Institute of Shuguang Hospital
6
7 528 Zhangheng Road, Shanghai 201203, China
8

9
10 Tel: 086-2120256187

11
12 E-mail: herrmayor@126.com or herrmayor@shutcm.edu.cn
13
14
15
16
17
18

19 **Running head:** Delphi survey of factors predicting successful VBAC
20
21
22

23
24 **Count**

25
26 **Abstract Word Count:** 297
27

28
29 **Word Count (excluding abstract):** 2566
30

31
32 **References:** 34
33

34
35 **Figure:** 1
36

37
38 **Table:** 1
39
40
41

42 **Key words:**
43

44
45 vaginal birth after caesarean section (VBAC), predictive factors, systematic review,
46

47
48 Delphi survey, evidence-based consensus
49
50
51
52
53
54
55
56
57
58
59
60

Abstract

Introduction

With the wide adoption of the two-child policy in China since 2016, a large percentage of women with a history of caesarean delivery (CD) plan to have a second child. Accordingly, the rate of vaginal birth after caesarean delivery (VBAC) is increasing. Women attempting repeat VBAC may experience multiple morbidities, which is also one of the leading causes of maternal and perinatal mortality. However, it remains to be addressed how we evaluate factors for successful VBAC. This study aims to use a novel approach to identify a set of potential predictive factors for successful VBAC, especially for Chinese women, to be included in prediction models which can be most applicable to pregnant women in China. We plan to assess all potential predictive factors collected through a comprehensive literature review. Then the certainty of the evidence for the identified potential predictive factors will be assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process. Finally, a two-round international Delphi survey will be conducted to determine the level of consensus.

Methods and analysis

This study will apply a methodology through an evidence-based approach. A long list of potential predictive factors for successful VBAC will be extracted and identified through the following stages: First, an up-to-date systematic review of the published literature will be conducted to extract identified potential predictive factors for

1
2
3
4 successful VBAC. Second, an online Delphi survey will be performed to achieve
5
6 expert consensus on which factors should be included in future prediction models.
7
8
9 The online questionnaires will be developed in the field of patient, maternal and
10
11 fetal-related factors. A two-round international Delphi survey will be distributed to
12
13 the expert panel in the field of perinatal medicine using Google Forms. Experts will
14
15 be asked to score each factor using the 9-point Likert rating scale to establish potential
16
17 predictive factors for the successful VBAC. The expert panel will determine on
18
19 whether to include, potentially include, or exclude predictive factors, based on a
20
21 systematic review of clinical evidence and the Delphi method.
22
23
24
25

26 27 **Ethics and dissemination**

28
29 The study was approved by the Institutional Review Board of the Jiaying Maternity
30
31 and Children Health Care Hospital (approval number: 2019-79). The results of this
32
33 study will be submitted to international peer-reviewed journals or conferences in
34
35 perinatal medicine or obstetrics.
36
37
38
39
40
41
42

43 **Trial registration number**

44
45 Open Science Framework (OSF): DOI 10.17605/OSF.IO/8D6XY.
46
47
48
49

50 **Key words**

51
52 Vaginal birth after caesarean section (VBAC), predictive factors, systematic review,
53
54 Delphi survey, evidence-based consensus
55
56
57
58
59
60

Strengths and limitations of this study

- This study aims to use a mixed methods approach to select potential predictive factors for successful vaginal birth after caesarean section (VBAC) for obstetric patients.
- Potential predictive factors for successful VBAC will be identified through a combination of a systematic literature review and a modified Delphi process.
- The consensus on the potential predictive factors for successful VBAC will be achieved based on a two-round Delphi survey among international experts in the field of obstetrics.
- The expert panel will determine whether to include, potentially include, or exclude the candidate predictive factors, based on the GRADE approach and the Delphi method.

Introduction

The overall cesarean delivery (CD) rates have accelerated significantly globally in recent years.¹ Though successful vaginal birth after cesarean delivery (VBAC) has been reported to reduce morbidity or complications compared to an elective repeat CD,² recent evidence has continued to highlight the risks of VBAC.³ In China, with the wide adoption of the two-child policy since 2016, a large percentage of women with a history of CD plan to have a second child and an elective repeat CD can be a suitable choice. However, a trial of labor after one cesarean (TOLAC) is encouraged in some countries which has been reported to reduce maternal adverse outcomes.⁴⁻⁶ Studies have also shown that CD after an unsuccessful TOLAC may lead to increased bleeding, postoperative infection, endometritis and increased health care expenditure.⁷⁻¹⁰

Therefore, for obstetricians, it is crucial to identify the potential protective and risk factors influencing a woman's successful VBAC based on the patients' baseline characteristics. Several studies have reported that patient demographic characteristics (patient race and ethnicity, education level and gestational week),^{11 12} maternal factors (maternal age, body mass index, bishop score, diabetes, hypertensive disorders complicating pregnancy and previous vaginal deliver)¹²⁻¹⁵, fetal factors (estimated birth weight)¹⁶ and other related factors (oxytocin implementation)¹⁵ that may be associated with a woman's chance for successful VBAC. Some predictive models for successful VBAC have also been published in recent years.^{13 17 18} However, the

1
2
3
4 quality of these models varied considerably in terms of study design, enrolled patients,
5
6 internal and external validity of the models, which make the models' applicability
7
8 domain rather dubious.
9
10

11
12
13
14 This study aims to use a novel approach to identify a set of potential predictive factors
15
16 for successful VBAC, especially for Chinese women, to be included in future
17
18 prediction models which can be most applicable to pregnant women in China. We
19
20 plan to assess all potential predictive factors collected through a comprehensive
21
22 literature review. Then the certainty of the evidence for the identified potential
23
24 predictive factors will be assessed using the Grading of Recommendations
25
26 Assessment, Development, and Evaluation (GRADE) process. Finally, a two-round
27
28 international Delphi survey will be conducted to determine the level of consensus.
29
30
31
32
33
34
35
36
37

38 **Ethics**

39
40 The study was approved by the Institutional Review Board of the Jiaying Maternity
41
42 and Children Health Care Hospital.
43
44
45
46
47

48 **Study design**

49
50 We will carry out a study that combines a comprehensive systematic review and an
51
52 evaluation of the certainty of the evidence based on GRADE approach.¹⁹ As
53
54 demonstrated in the flowchart (**Figure 1**), a structured Delphi survey-based expert
55
56
57
58
59
60

1
2
3
4 judgment will be made to include or exclude potential predictive factors for successful
5
6 VBAC.
7
8
9

11 **Systematic literature review**

12
13
14 The systematic review will be performed based on the Preferred Reporting Items for
15
16 Systematic Reviews and Meta-analyses (PRISMA) guidelines,²⁰ and aims to update
17
18 all potential predictive factors for successful VBAC among women with a previous
19
20 CD history, the search strategy of which is described in detail in Table 1. In summary,
21
22 we will search Pubmed, EMBASE, Cochrane Library and SinoMed from inception to
23
24 November, 2020. Predictive factors and prediction model studies will be selected that
25
26 report potential predictive factors for successful VBAC among women with a
27
28 previous history of CD. We define successful VBAC as a successful vaginal delivery
29
30 after a previous cesarean section. Two independent reviewers will screen the articles
31
32 for eligibility and extract the data after duplicated citations are removed.
33
34
35
36
37
38
39
40
41
42

43 For a given potential predictive factor, we will pool the summary relative risks (RRs)
44
45 or odds ratios (ORs) with 95% CIs for predictive factors reported ≥ 2 studies using
46
47 random-effects models.²¹ Cochran Q and the I^2 statistics will be applied to investigate
48
49 sources of heterogeneity, with an I^2 statistic $>50\%$ referring to substantial
50
51 heterogeneity.²² Publication bias will be tested using Egger's test, with a P value < 0.1
52
53 indicating significant difference.²³ Then the GRADE approach will be applied to
54
55 assess and rate the certainty of the evidence independently.¹⁹ The results of the
56
57
58
59
60

1
2
3
4 systematic review will provide the basis to develop a framework for voting in the
5
6 two-round international Delphi survey.
7
8
9

10
11 When the systematic review is finished, we will hold a face-to-face meeting among
12
13 the research team to discuss the main findings of the systematic review. Through the
14
15 discussion, we will judge which potential predictive factors should be included in the
16
17 Delphi process. The results will be presented with forest plots for each meta-analysis
18
19 combined with the effect estimates and their confidence intervals. We will also
20
21 evaluate the evidence of the observational studies which will be graded into
22
23 high-quality, moderate-quality and low-quality evidence according to Egger's P value,
24
25 total sample size and between-study heterogeneity as recommended by Mei et al.²⁴
26
27 After grading the evidence, the research team members will discuss the feasibility and
28
29 acceptability of the potential predictive factors included in the Delphi survey, which
30
31 will be categorised into 3 groups: included, potentially included, and excluded
32
33 predictive factors, the method of which was recommended by Darzi, et al.²⁵ The
34
35 included potential predictive factors are defined as those that should be included in
36
37 the future prediction model. The potentially included predictive factors are defined as
38
39 candidates that will potentially be included in the future prediction model. The
40
41 excluded predictive factors are those that will not be considered to be included in the
42
43 prediction model.
44
45
46
47
48
49
50
51
52
53
54
55
56
57

58 **Expert panel participants**

59
60

1
2
3
4 The expert panel will be selected from all over the world including obstetricians and
5
6 senior researchers with expertise in management of obstetric or perinatal
7
8 complications for pregnant women with a previous history of CD, and in the
9
10 development, validation, and application of predictive models for clinical practice.
11
12

13
14 Panel experts will participate in a web-based panel conference, complete surveys and
15
16 questionnaires, if necessary, will also provide feedback on reports. They will disclose
17
18 that they do not have any conflicts of interest and then complete the
19
20 declaration-of-interest forms to avoid any potentially existing conflicts regarding the
21
22 existing predictive models and other factors.
23
24
25
26
27
28
29

30 We will select members of the expert panel by using the following predesigned
31
32 criteria:
33

- 34
35 1) First or corresponding authors of a journal article on potential predictive factors
36
37 for successful VBAC in hospitalised obstetric patients.
38
39
- 40
41 2) Representative members from International Federation of Gynaecologists and
42
43 Obstetricians (FIGO), the American College of Obstetricians and Gynecologists
44
45 (ACOG), the Royal College of Obstetricians and Gynaecologists (RCOG), and
46
47 Chinese Obstetricians and Gynecologists Association (COGA).
48
49
- 50
51 3) Guideline authors of the above mentioned associations of obstetricians and
52
53 gynecologists.
54
55

56
57 The research team is composed of one senior obstetrician, 2 to 3 resident physicians
58
59 working in gynecology and obstetrics, a senior researcher, who will work together to
60

1
2
3
4 compile the evidence for presentation, draft the questionnaire for the two-round
5
6 Delphi survey, analyse the responses, and summarise the results.
7
8
9

10 11 **Two-round Delphi survey** 12

13
14 The expert panel will answer questions on three categories of the potential predictive
15
16 factors for successful VBAC: patient-related, maternal-related and fetal-related
17
18 predictive factors. The results of the systematic review will be presented to the experts
19
20 and they will be asked to rate their agreement with these three aspects of potential
21
22 predictive factor proposals. For example, they will rate their agreements with the
23
24 following statements: (1) that maternal age is a predictive factor of limited / critical
25
26 importance to successful VBAC; (2) that level of education is a predictive factor of
27
28 limited / critical importance to successful VBAC; or (3) that estimated fetal weight is
29
30 a predictive factor of limited / critical importance to successful VBAC.
31
32
33
34
35
36
37
38
39

40 A list of potential predictive factors will be delivered to the expert panel by e-mail in
41
42 the form of google form questionnaire, which we summarise based on the results of
43
44 the systematic review and identify them finally by group discussion among the
45
46 research team members. Each member of expert panel will provide his or her
47
48 response independently. Discussions are not allowed among expert panel
49
50 members. During the first-round survey, the initial list of potential predictive factors
51
52 yielded by the systematic review will be supplemented with other relevant factors
53
54 which might be suggested by the expert panel members. These will constitute all the
55
56
57
58
59
60

1
2
3
4 item list of the first-round Delphi survey. We initially classify the potential predictive
5
6 factors into three categories according to the literature reports and general knowledge,
7
8 including patient-related factors (race/ethnicity, level of education, delivery interval
9
10 and gestational week), maternal-related factors (maternal age, body mass index,
11
12 previous vaginal delivery history and trial of labor after a CD history) and
13
14 fetal-related factors (estimated fetal weight).
15
16
17
18
19
20
21

22 The second-round Delphi survey will be designed for the experts to make final
23
24 clinical or methodological judgements regarding the potential predictive factors for
25
26 successful VBAC based on the reports of the first-round survey.
27
28
29
30
31

32 The expert panel members will be asked to rate the importance of each candidate item
33
34 using a 9-point Likert scale, where 1 to 3 means “low importance”, 4 to 6 means “not
35
36 critically important” and 7 to 9 means “critical importance”.²⁶⁻²⁹
37
38
39

40 An “unable to rate” option will also be set. The expert panel members will be
41
42 instructed to choose “unable to rate” if they think they do not have adequate
43
44 knowledge or expertise on a particular list of statement.^{30 31} During the first round,
45
46 panel members can suggest some more related items to be incorporated into the
47
48 second round of survey after discussion by the research team. Only panel members
49
50 who have finished the first-round survey can move to the second-round survey.
51
52
53 During the second round, they will be reminded of what they rated during the first
54
55 round and will be shown the distribution of responses across the 1 to 9 scale for
56
57
58
59
60

1
2
3
4 each question in the questionnaire. The expert panel members have the right to retain
5
6 their first-round scores or rescored for some specific statements. Both rounds of
7
8 online voting are anonymous to minimise bias.
9
10

11 12 13 14 **Consensus definition and analysis plan**

15
16 We will consider consensus to be reached and the potential predictive factors will be
17
18 included if more than 70% of panel members score the statement within 7 to 9
19
20 (critical importance) or less than 15% of panel members score the statement within 1
21
22 to 3 (low importance); or in contrast, the potential predictive factors will be excluded
23
24 if more than 70% of panel members score the statement within 1 to 3 (low importance)
25
26 or less than 15% of panel members score the statement within 7 to 9 (critical
27
28 importance).³²
29
30
31
32
33
34
35
36
37

38 This framework is recommended by the GRADE (Grading of Recommendations
39
40 Assessment, Development, and Evaluation) group used to assess the importance of
41
42 evidence. At the end of the questionnaire, we will encourage experts who participate
43
44 in the survey to add some other potential predictive factors that they think are relevant,
45
46 and it is better to provide some reasons.
47
48
49
50
51
52

53 Finally, the panel members' agreement on the factors' importance will be assessed
54
55 using the Disagreement Index (DI), as described in the RAND/UCLA approach.³³ The
56
57 DI generally reflects the distribution and symmetry of the scores (ranging from 1 to 9),
58
59
60

1
2
3
4 with a higher DI representing wider spread across the 9-point scale, while lower DI
5
6 representing increasing consensus. If the DI exceeds 1.0, the distribution is regarded
7
8 as extreme variation in rated scores, while the DI is less than 1.0, we consider no
9
10 extreme variation existence, which means that a consensus is reached.
11
12
13
14
15
16

17 **Patient and public involvement**

18
19 This protocol will be carried out without patient or public involvement.
20
21
22

23 **Discussion**

24
25 In this work, we will apply a novel evidence-based approach to systematically
26
27 identify a set of potential predictive factors for successful VBAC in pregnant women
28
29 with a history of CD. We will first conduct an extensive systematic literature review
30
31 to identify a number of potentially relevant patient, maternal and fetal-related
32
33 predictive factors through systematic review and assess the level of evidence of their
34
35 predictive value using the GRADE approach. We will next develop an international
36
37 two-round Delphi survey to reach a consensus among international obstetric experts
38
39 from 4 international obstetricians and gynecologists associations of the world (FIGO,
40
41 ACOG, RCOG and COGA) on the importance of the selected factors. Our ultimate
42
43 purpose of this study is to reach evidence-based consensus on the potential predictive
44
45 factors of successful VBAC used for future prediction model development. At the
46
47 moment, there are no validated prediction models for successful VBAC based on
48
49 large prospective cohort studies.
50
51
52
53
54
55
56
57
58
59
60

Strengths and limitations

Our study has several strengths due to its rigorous methods that are robust and reproducible for several reasons. First, our systematic review will be conducted based on the PRISMA guidelines.²⁰ The search strategy is most comprehensive compared with the previously ones.^{12 34} Secondly, we will apply the GRADE approach to assess the certainty of evidence, which is a most solid method for decision making in several aspects, including for the development of future clinical guidelines.¹⁹ Thirdly, our research team will provide objective suggestions to identify all potential predictive factors for successful VBAC. Fourthly, the consensus regarding the issue will be based on a two-round Delphi survey among international obstetric experts from multiple international obstetricians and gynecologists associations of the world, making the results more convincing. Moreover, the two-round Delphi survey will be completely anonymous to reduce bias to the greatest extent. These set of methods will guarantee the internal and external validity of the study results.

There are limitations to this study as well. Firstly, the quality of the included studies varied considerably because most of the studies are observational cohort studies, and some are retrospective in study design. Secondly, the statements of Delphi survey to be developed are generally brief in nature. Some unknown domains related to the potential predictive factors may not be involved and addressed adequately. Thirdly, some of the experts involved in the Delphi survey will be clinical researchers instead

1
2
3
4 of obstetricians, and they might lack knowledge regarding certain aspects of factors
5
6 for successful VBAC. However, clinical researchers will be trained in advance and
7
8 may have a more evidence-based perspective of predictive factors, thus they may be
9
10 more aware of the evidence and how factors appear to interact. Fourthly, though
11
12 representative participants will be enrolled as expert panel in the Delphi survey
13
14 mainly from Europe, USA and China, the experts do not cover the whole global
15
16 regions, which may lead to a selection bias, and the results could not be applicable to
17
18 regions outside Europe, USA and China.
19
20
21
22
23
24
25
26

Implications for clinical practice and further research

27
28
29 This study will present a group of agreed predictors that the expert panel can use to
30
31 predict successful VBAC more accurately. First of all, the evaluated predictors may
32
33 help obstetricians assess the risk of the individual patient. Based on the findings of
34
35 this study, further investigations are warranted to provide some more possible
36
37 predictors.
38
39
40
41
42
43
44

45 In a related study to be conducted by our research team, we will involve these
46
47 variables that predict successful VBAC found in this consensus study. This will
48
49 enable us to make adjustment for these factors in terms of the level of evidence based
50
51 on the results of the study, which will improve the prediction accuracy. Further
52
53 research should focus on evaluating the importance of these predictors. In addition,
54
55 this study could provide the direction of future research on the evaluation of risk
56
57
58
59
60

1
2
3
4 factors for successful VBAC, which will ultimately be incorporated in the
5
6 development and validation of prediction models of successful VBAC.
7
8
9

10
11 Therefore, this study protocol summarises the design of the assessment of potential
12
13 predictive factors collected through a comprehensive literature review combined with
14
15 a two-round international Delphi survey . The results from this study will be
16
17 interpreted for the purpose of clinical decision making for obstetricians to determine
18
19 the suitable patients for VBAC, which will be most applicable to pregnant women in
20
21
22
23
24
25 China.
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Contributorship statement:

Ling Ai and Zubing Mei contributed equally as co-corresponding author.

Dr. Weiyong Zhu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Weiyong Zhu and Zubing Mei.

Acquisition, analysis, or interpretation of data: Weiyong Zhu, Ling Ai, Ying Feng, Haiyan Yuan, Yu Wang, and Meitang Wang.

Drafting of the manuscript: Weiyong Zhu, Zubing Mei.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Zubing Mei, Ling Ai

Administrative, technical, or material support: All authors.

Study supervision: Zubing Mei.

Competing interests:

The authors declare that they have no conflict of interest.

Funding:

This work was supported by Minsheng Special Project of Scientific and Technological Innovation of Jiaxing City (grant no. 2019AD32061), the National Natural Science Foundation of China (grant no. 81774112), a grant from Siming Scholars from Shuguang Hospital (grant no. SGXZ-201913).

References

1. Denham SH, Humphrey T, deLabrusse C, et al. Mode of birth after caesarean section: individual prediction scores using Scottish population data. *BMC pregnancy and childbirth* 2019;19(1):84.
2. Obstetricians ACo, Gynecologists. ACOG Practice Bulletin No. 205: Vaginal birth after cesarean delivery. *Obstetrics and gynecology* 2019;133(2):e110-e27.
3. Hidalgo-Lopezosa P, Hidalgo-Maestre M. Risk of uterine rupture in vaginal birth after cesarean: Systematic review. *Enfermería Clínica (English Edition)* 2017;27(1):28-39. doi: <https://doi.org/10.1016/j.enfcle.2016.08.002>
4. Obstetricians ACo, Gynecologists. Vaginal birth after cesarean delivery. ACOG Practice Bulletin No. 184. *Obstetrics and Gynecology* 2017;130(5):e217-e33.
5. No RRG-tG. 45: Birth After Previous Caesarean Birth. Royal College of Obstetrician and Gynaecologists 2015
6. Vaginal birth after cesarean: New insights. In National Institutes of Health Consensus Development Conference; 2010.
7. El-Sayed YY, Watkins MM, Fix M, et al. Perinatal outcomes after successful and failed trials of labor after cesarean delivery. *American journal of obstetrics and gynecology* 2007;196(6):583. e1-83. e5.
8. Guise J-M, Denman MA, Emeis C, et al. Vaginal birth after cesarean: new insights on maternal and neonatal outcomes. *Obstetrics & Gynecology* 2010;115(6):1267-78.
9. McMahon MJ, Luther ER, Bowes Jr WA, et al. Comparison of a trial of labor with an elective second cesarean section. *New England journal of medicine* 1996;335(10):689-95.
10. Suarez-Easton S, Zafran N, Garmi G, et al. Postcesarean wound infection: prevalence, impact, prevention, and management challenges. *International journal of women's health* 2017;9:81.
11. Lehmann S, Baghestan E, Børdahl PE, et al. Low risk pregnancies after a cesarean section: Determinants of trial of labor and its failure. *Plos one* 2020;15(1):e0226894.
12. Wu Y, Kataria Y, Wang Z, et al. Factors associated with successful vaginal birth after a cesarean section: a systematic review and meta-analysis. *BMC pregnancy and childbirth* 2019;19(1):1-12.
13. Manzanares S, Ruiz-Duran S, Pinto A, et al. An integrated model with classification criteria to predict vaginal delivery success after cesarean section. *The Journal of Maternal-Fetal & Neonatal Medicine* 2020;33(2):236-42.
14. Minsart A-F, Liu H, Moffett S, et al. Vaginal birth after caesarean delivery in Chinese women and Western immigrants in Shanghai. *Journal of Obstetrics and Gynaecology* 2017;37(4):446-49.
15. Familiari A, Neri C, Caruso A, et al. Vaginal birth after caesarean section: a multicentre study on prognostic factors and feasibility. *Archives of gynecology and obstetrics* 2020;301(2):509-15. doi: 10.1007/s00404-020-05454-0 [published Online First: 2020/02/13]

16. Smithies M, Woolcott CG, Brock J-AK, et al. Factors associated with trial of labour and mode of delivery in Robson Group 5: A select group of women with previous caesarean section. *Journal of Obstetrics and Gynaecology Canada* 2018;40(6):704-11.
17. Baranov A, Salvesen K, Vikhareva O. Validation of prediction model for successful vaginal birth after Cesarean delivery based on sonographic assessment of hysterotomy scar. *Ultrasound in Obstetrics & Gynecology* 2018;51(2):189-93.
18. Mooney SS, Hiscock R, Clarke IDA, et al. Estimating success of vaginal birth after caesarean section in a regional Australian population: Validation of a prediction model. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2019;59(1):66-70.
19. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *Journal of clinical epidemiology* 2011;64(4):401-06.
20. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS medicine* 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097 [published Online First: 2009/07/22]
21. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled clinical trials* 1986;7(3):177-88.
22. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *Bmj* 2003;327(7414):557-60.
23. Egger M, Smith GD, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *Bmj* 1997;315(7109):629-34.
24. Mei Z, Wang Q, Zhang Y, et al. Risk factors for recurrence after anal fistula surgery: a meta-analysis. *International Journal of Surgery* 2019;69:153-64.
25. Darzi AJ, Karam SG, Spencer FA, et al. Risk models for VTE and bleeding in medical inpatients: systematic identification and expert assessment. *Blood advances* 2020;4(12):2557-66. doi: 10.1182/bloodadvances.2020001937 [published Online First: 2020/06/17]
26. Xu Q, Huang Y, Chen B. Comprehensive assessment of health education and health promotion in five non-communicable disease demonstration districts in China: a cross-sectional study. *BMJ open* 2017;7(12):e015943. doi: 10.1136/bmjopen-2017-015943 [published Online First: 2017/12/29]
27. Mrowietz U, de Jong EM, Kragballe K, et al. A consensus report on appropriate treatment optimization and transitioning in the management of moderate-to-severe plaque psoriasis. *Journal of the European Academy of Dermatology and Venereology : JEADV* 2014;28(4):438-53. doi: 10.1111/jdv.12118 [published Online First: 2013/02/27]
28. Suzuki Y, Fukasawa M, Nakajima S, et al. Development of disaster mental health guidelines through the Delphi process in Japan. *International journal of mental health systems* 2012;6(1):7. doi: 10.1186/1752-4458-6-7 [published Online First: 2012/07/04]

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
29. Konstantinou K, Hider SL, Vogel S, et al. Development of an assessment schedule for patients with low back-associated leg pain in primary care: a Delphi consensus study. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society* 2012;21(7):1241-9. doi: 10.1007/s00586-011-2057-2 [published Online First: 2011/11/05]
30. Williamson PR, Altman DG, Blazeby JM, et al. Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012;13:132. doi: 10.1186/1745-6215-13-132 [published Online First: 2012/08/08]
31. Teoh JY, MacLennan S, Chan VW, et al. An International Collaborative Consensus Statement on En Bloc Resection of Bladder Tumour Incorporating Two Systematic Reviews, a Two-round Delphi Survey, and a Consensus Meeting. *European urology* 2020;78(4):546-69. doi: 10.1016/j.eururo.2020.04.059 [published Online First: 2020/05/12]
32. Bilbro NA, Hirst A, Paez A, et al. The IDEAL Reporting Guidelines: A Delphi Consensus Statement Stage specific recommendations for reporting the evaluation of surgical innovation. *Annals of surgery* 2020 doi: 10.1053/j.ajkd.2020.03.014
10.1097/sla.0000000000004180 [published Online First: 2020/07/14
2020/07/11]
33. Danese S, Bonovas S, Lopez A, et al. Identification of Endpoints for Development of Antifibrosis Drugs for Treatment of Crohn's Disease. *Gastroenterology* 2018;155(1):76-87. doi: 10.1053/j.gastro.2018.03.032 [published Online First: 2018/03/31]
34. Wingert A, Hartling L, Sebastianski M, et al. Clinical interventions that influence vaginal birth after cesarean delivery rates: Systematic Review & Meta-Analysis. *BMC Pregnancy Childbirth* 2019;19(1):529. doi: 10.1186/s12884-019-2689-5 [published Online First: 2020/01/01]

Table 1. Search strategy for Pubmed.

| |
|--|
| 1. "Vaginal Birth after Cesarean"[Mesh] |
| 2. "Trial of Labor"[Mesh] |
| 3. "Cesarean Section, Repeat"[Mesh] |
| 4. "Cesarean Section"[Mesh] |
| 5. 1-4/OR |
| 6. 'Vaginal Birth after Cesarean' OR VBAC OR 'trial of labor' OR 'cesarean section' OR TOLAC OR 'vaginal birth*' OR 'vaginal deliver*' OR 'trial of labour' OR 'active labor' OR 'active labour' |
| 7. 5 OR 6 |

Figure legend**Figure 1.** Flowchart of the study design.

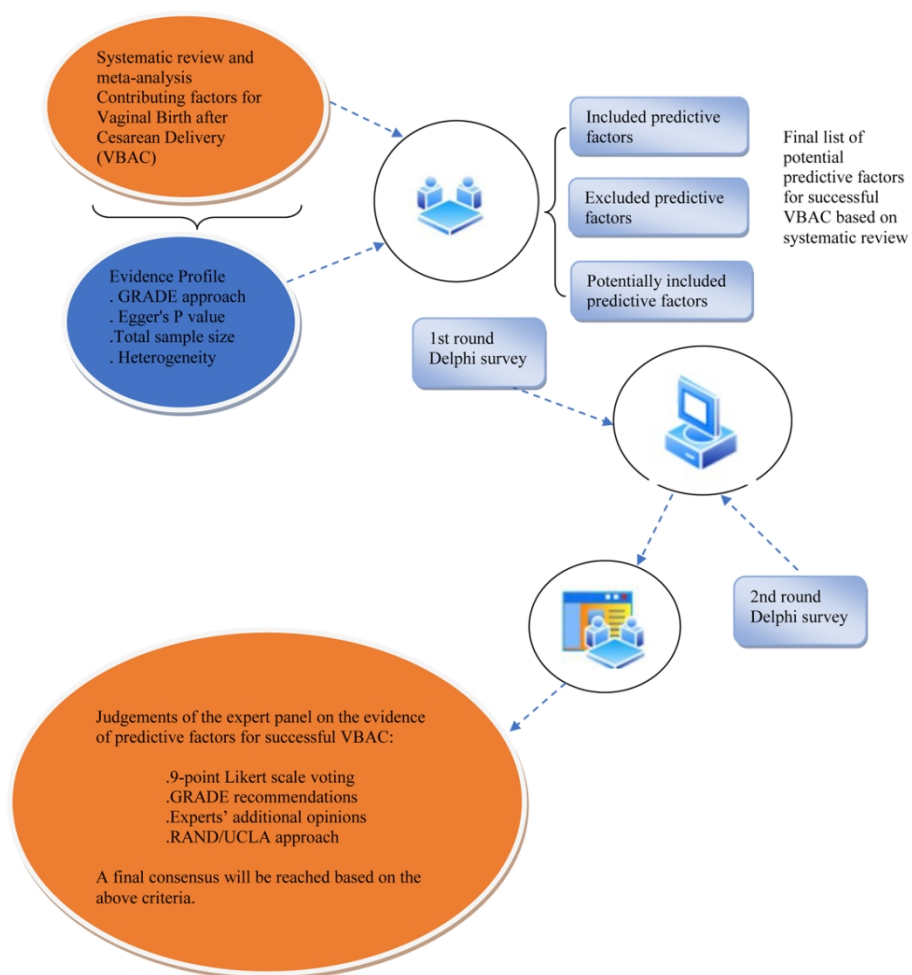


Figure 1. Flowchart of the study design.