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Prognostic accuracy of antenatal Doppler ultrasound for adverse perinatal outcomes in low- and middle-income countries: a systematic review

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Complete List of Authors:	<p>ALI, SAM; Utrecht University, Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht; Ernest Cook Ultrasound Research and Education Institute Heuving, Simelina; Utrecht University, Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht</p> <p>Kawooya, Michael; Ernest Cook Ultrasound Research and Education Institute</p> <p>Byamugisha , Josaphat; Makerere University, Department of Obstetrics and Gynecology</p> <p>Grobbee, Diederick; Utrecht University, Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht</p> <p>Papageorghiou, Aris; University of Oxford, Nuffield Department of Women's & Reproductive Health</p> <p>Klipstein-Grobusch, Kerstin; Utrecht University, Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht; University of the Witwatersrand, Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences</p> <p>Rijken, Marcus; Utrecht University, Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht; Universitair Medisch Centrum Utrecht, Department of Obstetrics and Gynecology</p>
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4 **Prognostic accuracy of antenatal Doppler ultrasound for**
5 **adverse perinatal outcomes in low- and middle-income**
6 **countries: a systematic review**
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11 Sam Ali^{1,2*}, Simelina Heuving¹, Michael G. Kawooya², Josaphat
12 Byamugisha³, Diederick E. Grobbee¹, Aris T. Papageorghiou⁴,
13 Kerstin Klipstein-Grobusch^{1,5}, Marcus J. Rijken^{1,6}
14
15
16

17
18 ¹Julius Global Health, Julius Center for Health Sciences
19 and Primary Care, University Medical Center Utrecht,
20 Utrecht University, Utrecht, The Netherlands.
21
22

23 ²Ernest Cook Ultrasound Research and Education Institute
24 (ECUREI), Mengo Hospital, Kampala, Uganda.
25

26 ³Department of Obstetrics and Gynecology, Makerere
27 University College of Health Sciences, Kampala, Uganda.
28

29 ⁴Nuffield Department of Women's and Reproductive Health,
30 John Radcliffe Hospital, University of Oxford, Oxford,
31 United Kingdom.
32
33

34 ⁵Division of Epidemiology and Biostatistics, School of
35 Public Health, Faculty of Health Sciences, University of
36 the Witwatersrand, Johannesburg, South Africa.
37
38

39 ⁶Department of Obstetrics and Gynecology, University
40 Medical Center Utrecht, Utrecht University, Utrecht,
41 Netherlands.
42
43
44

45
46
47 **Corresponding author:**

48 Sam Ali

49
50 Department of research, Ernest Cook Ultrasound Research and
51 Education Institute (ECUREI), Mengo Hospital. Sir Albert
52 Cook Road. P.O. Box 7161, Kampala, Uganda.
53

54 **Email:** S.Ali-2@umcutrecht.nl or alisambecker@gmail.com
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ABSTRACT

Objectives This systematic review examined available literature on the prognostic accuracy of Doppler ultrasound for adverse perinatal outcomes in LMIC.

Design We searched PubMed, Embase, Cochrane Library and Scopus from inception to April 2020.

Setting Observational or interventional studies from low- and middle-income countries

Participants Singleton pregnancies of any risk profile.

Interventions Umbilical artery (UA), middle cerebral artery (MCA), cerebroplacental ratio (CPR), uterine artery (UtA), fetal descending aorta (FDA), ductus venosus, umbilical vein, and inferior vena cava.

Primary and secondary outcome measures. Perinatal death, stillbirth, neonatal death, expedited delivery for fetal distress, meconium-stained liquor, low birth weight, fetal growth restriction (FGR), admission to neonatal intensive care unit, neonatal acidosis, Apgar scores, preterm birth, fetal anemia, respiratory distress syndrome, length of hospital stay, birth asphyxia and composite adverse perinatal outcomes.

Results We identified 2825 records, and 30 (including 4977 women) from Africa (40.0%, n= 12), Asia (56.7%, n= 17) and South America (3.3%, n= 01) were included. UA Doppler had good predictive values for perinatal death (Odds ratio 9.8, 95% confidence interval 2.1- 46.4) and FGR (positive predictive value (PPV) of 77.40 to 88.5). UA, MCA, CPR and UtA Dopplers had moderate to high predictive values for

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4 composite adverse perinatal outcomes. MCA and FDA were
5 potent predictors of fetal anemia (sensitivity: 86.0% -
6 98.4% and PPV: 86.0 - 100%). No randomized clinical trial
7 was found. Most studies were of sub-optimal quality, poorly
8 powered and characterized by wide variations in outcome
9 classifications, timing for the Doppler tests and study
10 populations.

11 **Conclusion** Local evidence to guide how antenatal Doppler
12 ultrasound should be used in LMIC is lacking. Well-designed
13 studies, preferably randomized clinical trials, are
14 required. Standardization of practice and classification of
15 perinatal outcomes across countries, in accordance with
16 international standards, is imperative.

17 **Keywords** Pregnancy, ultrasound, prenatal diagnosis,
18 prenatal care, developing countries, and systematic review.
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26 **Article Summary**

27 **Strengths and limitations of this study**

- 28 • This systematic review used the most optimal database
29 combinations and snowballing technique with no time
30 restrictions to identify the records.
- 31 • We comprehensively examined available literature on
32 the prognostic accuracy of antenatal Doppler
33 ultrasound in low and middle-income countries.
- 34 • Although only English language articles were included,
35 it is unlikely that high impact papers were not
36 identified.
- 37 • Pooling and interpreting the data for wider clinical
38 application was difficult due to the large
39 heterogeneity across studies.

40 **INTRODUCTION**

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4 Stillbirths remain a major global challenge,[1] with nearly
5 three million cases reported annually.[2] The vast majority
6 of the cases (98%) are contributed by low- and middle-
7 income countries (LMIC).[3] These deaths have profound
8 effects on the families and communities involved, and
9 strategies for reduction are of high societal importance.
10 The risk of adverse perinatal outcomes is higher in
11 compromised fetuses than in normally growing babies, and is
12 distinguishable using antenatal Doppler ultrasound.[4,5]
13 Prenatal diagnosis of fetuses at risk provides a window for
14 close monitoring and/or expedited delivery of well-
15 developed babies with the prospect of improving survival
16 and long-term wellbeing.[4]

17
18 The predictive performance of Doppler ultrasound for
19 adverse perinatal outcomes has been demonstrated in primary
20 studies, systematic reviews and meta-analysis from high-
21 income countries (HIC), guiding the development HIC
22 practice guidelines.[6] We believe the use of HIC
23 guidelines for clinical guidance in LMIC is inappropriate
24 given the differences in the prevalence of adverse
25 pregnancy outcomes in the two settings. For instance, the
26 stillbirth rates per 1000 total births (95% confidence
27 interval) in HIC is 3.4 (3.4-3.5), Southern Asia 25.5
28 (22.5-29.1) and 28.7 (25.1-34.2) in sub-Saharan Africa.[2]
29 Since the prevalence and severity of disease influences the
30 diagnostic or prognostic test performance, context specific
31 guidance is necessary.[7] However, there are still
32 knowledge gaps about the predictive ability of antenatal
33 Doppler for adverse pregnancy outcomes in LMIC.

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35 This systematic review examined existing literature on
36 the prognostic accuracy of Doppler ultrasound for adverse
37 perinatal outcomes in LMIC. The implications for clinical
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4 utility of the available local evidence to guide practice
5 in LMIC are highlighted.
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9 **MATERIAL AND METHODS**

10 **Protocol and registration**

11 This systematic review protocol was registered in the
12 PROSPERO database: CRD42019128546, and reported in
13 accordance with the Preferred Reporting Items for a
14 Systematic Review and Meta-analysis of Diagnostic Test
15 Accuracy Studies: The PRISMA-DTA Statement.[8]
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18 **Eligibility criteria**

19 We included observational (cohort or case control) studies
20 and randomized clinical trials (RCTs) from LMIC (as per the
21 World Bank country classifications in the year 2020)
22 reporting the prognostic value of Doppler ultrasound for
23 adverse perinatal outcomes in singleton pregnancies of any
24 risk profile. Doppler measurements of interest included
25 umbilical artery (UA), middle cerebral artery (MCA),
26 cerebroplacental ratio (CPR), uterine artery (UtA), fetal
27 descending aorta (FDA), ductus venosus (DV), umbilical vein
28 (UV) and inferior vena cava (IVC). Adverse perinatal
29 outcomes (as defined in the included studies) were
30 perinatal death, stillbirth, neonatal death, expedited
31 delivery for fetal distress, meconium-stained liquor, low
32 birth weight, fetal growth restriction (FGR), admission to
33 neonatal intensive care unit (NICU), neonatal acidosis,
34 Apgar scores, preterm birth, fetal anemia, respiratory
35 distress syndrome (RDS), length of hospital stay, birth
36 asphyxia, and composite adverse perinatal outcomes (CAPO).
37 Conference proceedings/posters that did not appear as full
38 text papers, case reports and review articles without
39 original data were excluded.
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58 **Information sources and search**

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4 We conducted comprehensive literature search in PubMed
5 (Medline), Embase, Cochrane Library and Scopus for articles
6 published from inception to April 07, 2020. The search
7 strategies (online supplementary appendix S1) were
8 developed with the support of a librarian at University
9 Medical Center Utrecht. When applicable, pre-defined search
10 (Title/Abstract) and MeSH/Emtree terms were used. No limits
11 were applied to the searches.
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14 **Study selection**

15 The records retrieved from the databases were exported to
16 Endnote to eliminate duplicates and then transferred to
17 Rayyan for review and selection. Two reviewers (SA and SH)
18 independently assessed all studies for inclusion based on
19 title and abstract. Studies reporting any Doppler parameter
20 and adverse pregnancy outcome of interest in the title or
21 abstract were further retrieved in full text and assessed
22 by the same two reviewers against full eligibility
23 criteria. Disagreements were resolved by discussion or, if
24 required, we consulted the third review author (MJR).
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27 **Data extraction**

28 Using a pre-piloted data extraction sheet, two reviewers
29 (SA and SH) independently extracted data on authors, study
30 title, year of publication, study period, number of women
31 recruited, gestational age at Doppler ultrasound exam,
32 method of pregnancy dating, pregnancy risk profile, blood
33 vessels studied, pregnancy outcomes, and key results. If
34 any relevant information was missing, the corresponding
35 authors were contacted once by e-mail.
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38 **Risk of bias assessment**

39 Two raters (SA and SH) independently evaluated the risk of
40 bias for each study using the quality in prognostic studies
41 (QUIPS) tool.[9] The risk of bias domains included study
42 population, attrition, prognostic factor measurement,
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4 outcome measurement, confounding and statistical analysis.
5 All the domains were separately judged by two raters as
6 having low, moderate or high risk of bias. Any disagreement
7 during this process was resolved by contacting the third
8 rater (MJR).
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12 **Prognostic test accuracy measures**

13 Doppler test prognostic performance measures, as reported
14 in the selected studies, are presented in table S1. These
15 included diagnostic test accuracy measures such as
16 sensitivity, specificity, positive predictive values (PPV)
17 and negative predictive values (NPV); measures of
18 association; proportions; and correlations.
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25 **Data synthesis and analysis**

26 The results were narratively summarized. The large
27 heterogeneity in the study populations, timing for Doppler
28 tests, outcome definitions and prognostic performance
29 measures in the included studies did not allow for a meta-
30 analysis. If a study reported multiple Doppler indices, the
31 most commonly used (pulsatility index) was selected.
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36 **RESULTS**

37 **Study selection**

38 The 2825 records we identified through electronic searches
39 reduced to 2210 after removal of duplicates, and 2162 were
40 further excluded based on title and abstract screening,
41 retaining 48 records. After full-text assessment for
42 eligibility, 23 studies were excluded with reasons, and 25
43 remained (online supplementary appendix S2). Five
44 additional records were identified through snowballing
45 (Figure 1). Thirty studies, involving a total count of 4977
46 women and median (interquartile range) sample size of 100
47 (30, 181) were included in the analysis (table 1).
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57 **Study characteristics**

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4 The selected studies were from Africa (40.0%, n = 12), Asia
5 17 (56.7%, n = 17) and South America (3.3%, n = 01). Twenty
6 studies (67%) recruited high-risk pregnancies, six (16.7%)
7 both high and low-risk populations, while five (16.7%)
8 studied the low-risk group (online supplementary appendix
9 S3). Thirteen (43.3%) studies did not specify a method of
10 pregnancy dating, 13 (43.3%) assessed gestational age using
11 last menstrual period (LMP) combined with ultrasound, three
12 (10.0%) used ultrasound alone, and one (3.3%) study used
13 LMP. No RCTs was identified, and no study provided data on
14 the UV and IVC Doppler (table 1).
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23 **Methodological quality of included studies**

24 The results of the QUIPS assessment are provided in Figure
25 2 and online supplementary appendix S4. Overall, the risk
26 of bias was low in 15 (50%), moderate in 10 (33.3%), and
27 high in five (16.7%) studies. In the study population
28 domain, the risk of bias was low in 73.3%, moderate in
29 23.3%, and high in 3.3% of the studies. Selective reporting
30 remarkably resulted in moderate to high-risk of bias for
31 analysis and reporting in 20 (66.7%) studies. We found
32 moderate to high-risk of bias for outcome measurement in 17
33 (56.7%) studies, mostly due to inconsistencies in outcome
34 classifications (online supplementary table S2).
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43 **Prognostic accuracy of antenatal Doppler ultrasound for** 44 **adverse perinatal outcomes**

45 Twenty studies evaluated the umbilical
46 artery, [10,11,20-29,12-19] and seven reported its
47 predictive values for FGR. The positive predictive values
48 for FGR were between 77.40 and 88.5, [11,16,21,24] while
49 area under the receiver operating characteristic (AU ROC)
50 curve was 0.63, [17] mostly in high-risk pregnancies. The
51 NPV ranged from 55.4 - 95.65. [11,16,21,24] FGR was defined
52 as birth weight or abdominal circumference below the 10th
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4 percentile in two studies, [11,17] ponderal index less than
5 10 in one study, [21] and was not defined in the remaining
6 studies. [16,24,26] Increased flow impedance in the UA had
7 positive predictive values for composite adverse outcome
8 between 66.60 and 96.6 in high-risk
9 pregnancies. [11,13,19,23] All studies provided individual
10 components of the CAPO except only one. [11] Absent or
11 reversed end-diastolic flow (AREDF) in the UA was
12 associated with poor pregnancy outcomes (perinatal death:
13 odds ratio (OR) 9.8, 95% confidence interval (CI) 2.1 to
14 46.4; CAPO: OR 2.4, 95% CI 1.1 to 5.0; and RDS: OR 8.4, 95%
15 CI 2.3 to 30.5). [14,22,26]

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17 The MCA was reported in 12
18 studies. [11,12,31,32,13,15,19,21,23,26,28,30] The positive
19 predictive values for fetal anemia in Rhesus (Rh)
20 isoimmunized pregnancies requiring transfusion were between
21 83.0 - 90.9 and the AU ROC curve was 0.7. [12,32] Fetal
22 anemia was consistently defined as hemoglobin (Hb) \leq 0.64
23 g/dl in the two studies, though they recruited low numbers
24 of women. [12,32] MCA Doppler had a sensitivity of 87.5%,
25 PPV of 74.0% and AU ROC curve of 0.82 for neonatal
26 acidosis. [30] The positive predictive values for CAPO
27 ranged from 80.0-100% in high-risk
28 pregnancies, [11,13,19,23,31] but two studies did not
29 provide details of the individual components of the
30 CAPO. [11,31]

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32 Nine studies reported the prognostic value of
33 CPR. [11,13,15,19,20,23,26,33,34] CPR showed promising
34 predictive value for adverse perinatal outcomes in
35 unselected pregnancies in the third trimester. One study
36 reported sensitivity 85.10, specificity 89.72, PPV 80.70
37 and NPV 92.30 for FGR. [26] Two studies found sensitivity
38 between 80.90 and 90.91%, and specificity between 50.0 and
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4 78.04% for emergency caesarean section for fetal distress
5 though the tests had poor positive predictive
6 values.[26,34] Abnormal CPR had positive predictive values
7 for CAPO between 81.80 and 100% in high-risk
8 pregnancies.[11,13,15,23]
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13 Eight studies reported the prognostic value of UtA
14 Doppler,[14,23,25,35-39] and two showed positive predictive
15 values of over 91.8% for CAPO in high-risk
16 pregnancies.[23,36] The remaining studies had poor
17 predictive values for adverse perinatal outcomes.
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21 Three studies evaluated the prognostic accuracy of FDA
22 Doppler.[12,13,32] The FDA sensitivity for fetal anemia in
23 Rh isoimmunized pregnancies ranged from 87.0% to 95.7% when
24 used in isolation.[12,32] The sensitivity varied between
25 86.0% and 98.4% and positive predictive values ranged from
26 86.0- 100% when combined with the MCA.[12,32]
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31 The DV was sampled in two studies undertaken in high-
32 risk pregnancies.[20,30] Abnormal DV had a sensitivity of
33 100, PPV of 72.0 and AU ROC curve of 0.88 for the
34 prediction of neonatal acidosis, though this study included
35 only 30 women between 36-41 weeks of gestation.[30] It had
36 borderline significance (OR 0.379, 95% CI 0.03 to 4.63),
37 and a positive predictive value of 92.0% for the prediction
38 of composite adverse perinatal outcomes at 24-34 weeks of
39 gestation.[20]
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48 **DISCUSSION**

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50 Our results indicate that abnormal UA Doppler is associated
51 with poor perinatal outcomes, mostly in high-risk
52 pregnancies. Abnormal UA, MCA, CPR and UtA Dopplers had
53 moderate to high predictive values for composite adverse
54 perinatal outcomes. Abnormal MCA Doppler had high
55 individual predictive value for fetal anemia, but performed
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4 better when combined with the FDA. However, the majority of
5 the available evidence were of sub-optimal quality, based
6 on a few poorly powered studies and had no RCTs. Further,
7 wide variations in the populations studied, definitions of
8 adverse perinatal outcomes and prognostic accuracy measures
9 across studies was present. Thus, pooling and interpreting
10 the evidence for wider clinical application was difficult.
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16 A strength of this systematic review is that it was
17 conducted according to a registered protocol, using the
18 most optimal database combinations and snowballing with no
19 time restrictions. Although we only included English
20 language articles, it is unlikely that high impact papers
21 were not identified. About half of the studies included in
22 the analysis were of poor quality, and 20 (66.7%) studies
23 selectively reported results potentially raising the risk
24 of reporting bias. A meta-analysis was not possible due to
25 large heterogeneity in the study populations, definition of
26 adverse perinatal outcomes and prognostic accuracy measures
27 across studies.
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36 Evidence from HIC suggest that adding Doppler studies
37 into clinical diagnostic or prognostic rules improves
38 pregnancy risk assessment,[6] and are increasingly becoming
39 integrated into their pregnancy management guidelines.[4,6]
40 The use of guidance based entirely on HIC data in daily
41 practice in LMIC could be misleading considering the
42 differences in the adverse outcome rates in the two
43 settings. The stillbirth rates in LMIC is approximately 10
44 times that of HIC,[2] a large variation likely to influence
45 the predictive performance of diagnostic or prognostic
46 tests.[7] Thus, a proper understanding of existing
47 literature from LMIC is important. This paper reports the
48 findings of a systematic review of primary evidence on the
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4 prognostic value of antenatal Doppler ultrasound for
5 adverse perinatal outcomes in LMIC.
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8 Abnormal blood flow patterns in the UA had moderate to
9 high predictive values for FGR and was associated with poor
10 outcomes in high-risk pregnancies. Similarly, a recent
11 Cochrane review of RCTs from HIC suggests that using UA
12 Doppler in high-risk pregnancies could reduce perinatal
13 deaths by 30% (risk ratio 0.71, 95% CI 0.52 to 0.98), and
14 lead to fewer obstetric interventions.[40] Despite some
15 similarities with our findings, the definitions of adverse
16 outcomes, including FGR were inconsistent (across studies
17 included in this review) with agreed international
18 standards, [4,41] with no clear distinction between early
19 and late FGR. Scanty data from this review indicate that
20 abnormal CPR, UA, MCA and UtA Doppler could be predictive
21 of CAPO. However, in a previous systematic review from HIC,
22 CPR had low predictive accuracy (pooled sensitivity: 57%,
23 specificity: 77%, and summary positive likelihood ratio
24 (LR): 2.5, and negative LR: 0.60) for CAPO in pregnancies
25 with suspected FGR antenatally.[42] In another review, CPR
26 was significantly better than UA and MCA Doppler in
27 predicting CAPO ($P < 0.001$) and emergency delivery for
28 fetal distress in singleton pregnancies of all risk
29 profiles, [43] but the primary studies reviewed had numerous
30 methodological limitations.[43] Further, first trimester
31 UtA Doppler had very low sensitivity 25.8% (95% CI 15.5 to
32 39.7) for CAPO in a systematic review of 18 studies
33 (involving 55974 women).[44] More data from HIC indicate
34 that MCA-PSV reliably predicts fetal anemia in un-
35 transfused fetuses.[45] The area under the hierarchical
36 summary ROC curve for moderate-severe anemia in
37 untransfused fetuses was 87%, pooled sensitivity 86% (95%
38 CI 75 to 93%) and specificity 71% (95% CI 49 to 87%).[45]
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4 Similarly, in our study, MCA alone or when combined with
5 FDA had high predictive values for fetal anemia in Rh
6 isoimmunized pregnancies, but this was based on only three
7 studies. Over all, this review found that high quality
8 studies on the predictive accuracy of Doppler ultrasound
9 for adverse perinatal outcomes in LMIC are scarce. The large
10 heterogeneity across studies precluded a meta-analysis and
11 between study comparisons.
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18 Future studies need to specify the methods and timing
19 for pregnancy dating. Accurate dating is crucial for timing
20 the Doppler tests and interventions to expedite delivery in
21 compromised fetuses. The interpretation and comparison of
22 Doppler studies could be improved by using standard outcome
23 definitions and completeness in reporting.[46] Most primary
24 studies in this review studied the predictive ability of a
25 single variable (Doppler test) for the outcome(s) of
26 interest, without considering existing characteristics of
27 clinical importance to estimate pregnancy risk. The
28 predictive accuracies of new determinants need to be
29 assessed individually and by multivariable analysis to
30 facilitate the clinical applicability of the findings. The
31 clinical applicability of Doppler ultrasound also depends
32 on the clinical judgement of the Doppler measurements and
33 the feasibilities of local healthcare systems to interpret
34 and respond to the results of the Doppler scan. Along the
35 same line, our recently concluded prospective cohort study
36 in a sub-Saharan African setting will soon highlight the
37 prognostic value of Doppler ultrasound in the late third
38 trimester, and the feasibilities of integrating such
39 advanced technologies into routine antenatal care in LMIC.
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54 This review demonstrates that a scientific basis to
55 provide evidence for how antenatal Doppler should be used
56 in LMIC is lacking. Well-designed studies, preferably
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4 randomized clinical trials, testing application models of
5 antenatal Doppler while respecting the local conditions are
6 needed. Moreover, local practice and classification of
7 perinatal outcomes needs to be standardized, utilizing
8 approaches consistent with international consensus.
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15
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26 **Author contributions**

27
28 SA, SH, KKG, and MJR drafted the protocol and conducted the
29 review. MGK, JB, DEG, and ATP critically reviewed the work
30 for important intellectual content. All the authors
31 approved the final manuscript.
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42 ST-POC-1808-17038).
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48 **Competing interests**

49
50 None
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53 **Data sharing statement**

54
55 No additional data are available.
56
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LEGENDS

Online supplementary data legends

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39 **Appendix S1.** Search strings for the databases used to
40 retrieve articles.
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43 **Appendix S2.** List of full-text articles excluded with
44 reasons.
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47 **Appendix S3.** Pregnancy risk profiles in the selected
48 studies
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51 **Appendix S4.** Risk of bias assessment results of the 30
52 studies included in the analysis.

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54 **Table S1.** Statistical measures of prognostic performance of
55 Doppler ultrasound reported in the selected studies.

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57 **Table S2.** Definitions of adverse perinatal outcomes
58 reported in the selected studies
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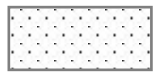
Figures legends

Figure 1. PRIMA flow diagram

Figure 2. Risk of bias assessment results of the 30 included studies

Figure 2 key

Low-risk of bias



Moderate-risk of bias



High-risk of bias

Table legends

Table 1 Summary of studies included in the systematic review of current evidence on the prognostic value of Doppler ultrasound for predicting adverse pregnancy outcomes in LMIC.

Table 1

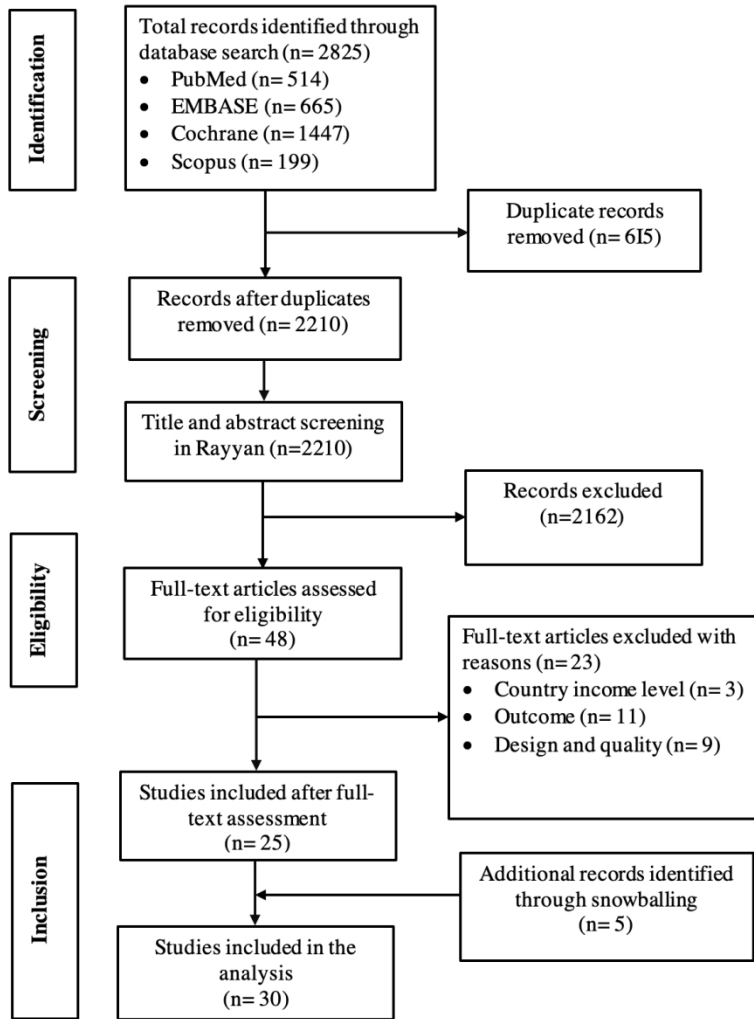
Author, Year	Country	Study Period	Women	Weeks	Study Design	Dating method	Vessels	Abnormal Doppler Thresholds
Abdallah, 2019. [10]	Egypt	2015-2017	92	>= 37	Cohort	LMP or first trimester ultrasound	UA	UA (RI, PI and S/D ratio) > 95 th centile
Agbaje, 2018. [17]	Nigeria	2014-2015	120	26	Cohort	LMP and/or early dating sonograms	UA	S/D ratio > 95 th percentile, RI > 95 th percentile, and AREFD.
Alanwar, 2018. [33]	Egypt	2017	100	30 - 40	Cohort	Not specified	CPR	CPR PI < 1 or CPR PI < 5 th percentile.
Allam, 2013. [30]	Egypt	2007-2010	30	36 - 41	Cohort	Not specified	MCA, DV	MCA S/D ratio < 4.37, DV RI > 0.29, or Decrease in a-, v- and d- waves, or reversed flow in both a- and v-waves.
Anshul, 2010. [18]	India	2005-2007	100	>= 28	Cohort	LMP and first trimester dating scan	UA	S/D ratio >= 3 or AREFD.
Bano, 2010. [11]	India	Not stated	90	30 - 41	Cohort	Not specified	UA, MCA, CPR	MCA < 2SD; UA > 2SD or CPR PI < 1.08
Dhand, 2011. [31]	India	2005-2006	121	28 - 41	Cohort	LMP and fetal biometry < 22 weeks	MCA	Not specified
Dorman, 2002. [35]	Kenya	1996-1997	854	24 - 31	Cohort	LMP and fetal biometry	UtA	Early diastolic notch or mean/ipsilateral UtA RI >= 0.58
Ebrashy, 2005. [19]	Egypt	2002-2003	80	>= 28	Case-control	Fetal biometry (BPD, AC and FL)	UA, MCA, CPR	UA RI > 0.72, MCA RI < 0.69, CPR RI < 1.0

Geerts, 2007.[20]	South Africa	Not stated	113	24 - 34	Cohort	LMP and fetal biometry	UA, CPR, DV	UA PI >95 th centile; UA/MCA > 1; DV PI > 95 th centile.
Khanduri, 2013.[21]	India	2009-2011	60	23 - 37	Cohort	LMP and first or second trimester ultrasound	UA, MCA	UA PI > 1.42 or UA RI > 0.72, MCA PI <1.5, MCA RI < 0.59
Kumari, 2019.[12]	India	2015-2016	30		Cohort	Not specified	UA, MCA, FDA	MCA PSV > 1.50 MoM, FDA PSV delta > 70.50. Not specified for UA
Lakhkar, 2006.[13]	India	2001-2002	58	> 30	Cohort	LMP, clinical gestational age, 1 st or 2 nd trimester biometry	UA, MCA, CPR, FDA	S/D ratio, RI or PI of UA > 2SD; MCA < 5 th centile; FDA > 2SD; CPR PI or S/D ratio < 1.0
Lakshmi, 2013.[22]	India	2007-2008	238	< 35	Cohort	LMP or first trimester ultrasound	UA	Absent and/or reversed end-diastolic flow (AREDF)
Malik, 2013.[23]	India	2010-2011	100	31 - 41	Cohort	LMP	UA, MCA, CPR, UtA	Not specified
Masihi, 2019.[34]	Iran	2016-2017	181	38 - 40	Cohort	First trimester ultrasound	CPR	CPR PI <1.94
Mullick, 1993.[24]	India	Not stated	73	22 - 26, 30 - 32, > 37	Cohort	Not specified	UA	S/D ratio >= 4 (26 weeks), 3.5 (30-32 weeks) and 3 (37-40 weeks)
Nagar, 2015.[25]	India	2009 - 2011	500	26 - 30	Cohort	LMP and ultrasound before 21 weeks	UA, UtA	UA (S/D ratio or RI) > 95 th centile or AREDF. UtA S/D ratio > 95 th centile
Najam, 2016.[26]	India	Not stated	150	28 - 40	Cohort	Not specified	UA, MCA, CPR	UA S/D ratio > 2SD, or AREDF, MCA SD ratio < 5 th percentile,

								MCA/UA SD ratio of < 1.0
Nouh, 2011.[36]	Egypt	2009-2011	80	8 - 12, 26	Case-control	LMP and first trimester ultrasound	UtA	UtA PI > 95th percentile, and/or Unilateral or bilateral notch
Pares, 2008.[32]	Brasil	1997-2005	46	20 - 34	Cohort	Sonographic exam at <= 20 weeks	MCA, FDA	FDA-MV >= 2SD MCA-PSV >= 1.5 MoM
Pattinson, 1991.[14]	South Africa	1987-1989	53	16 - 28	Cohort	LMP and biometry: 16-20 weeks	UA, UtA	UA RI > 95 th centile UtA RI > 0.58
Pattinson, 1993.[27]	South Africa	1990	496	16 - 24	Cohort	Not specified	UA	UA RI > 95 th centile
Phupong, 2003.[37]	Thailand	2000-2001	322	22 - 28	Cohort	LMP and first trimester ultrasound	UtA	Unilateral or bilateral early diastolic notch
Rani, 2016.[15]	India	2012-2014	223	30 - 36	Cohort	Not specified	UA, MCA, CPR	UA PI > 1.03, UA RI > 0.695; MCA PI < 1.2, MCA RI < 0.75; CPR PI < 1.08 or CPR RI < 1.05.
Rocca, 1995.[16]	Egypt	Not stated	113	>= 28	Cohort	Not specified	UA	UA S/D ratio >= 3
Verma, 2016.[38]	India	Not stated	165	22 - 24	Cohort	Not specified	UtA	Bilateral diastolic notches or mean UtA PI > 1.45 (UtA PI > 95 th centile).
Waa, 2010.[28]	Kenya	2007	100	>= 28	Cohort	Not specified	MCA, UA	MCA RI < 0.71, and UA > 0.71.
Yelikar, 2013.[29]	India	Not stated	189	> 32	Cohort	Not specified	UA	UA S/D ratio > 90 th centile or AREDF
Zarean, 2018.[39]	Iran	2015-2016	100	30 - 34	Cohort	Not specified	UtA	UtA PI > 95 th centile

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4 ^aLMP: last menstrual period; UA: umbilical artery; MCA: middle cerebral artery; CPR: cerebroplacental ratio;
5 UtA: uterine artery; FDA: fetal descending aorta; DV: ductus venosus; RI: resistive index; PI: pulsatility
6 index; S/D ratio: systolic diastolic ratio; PSV: peak systolic velocity; MV: mean velocity; AREDF: absent
7 and/or reversed end diastolic flow.
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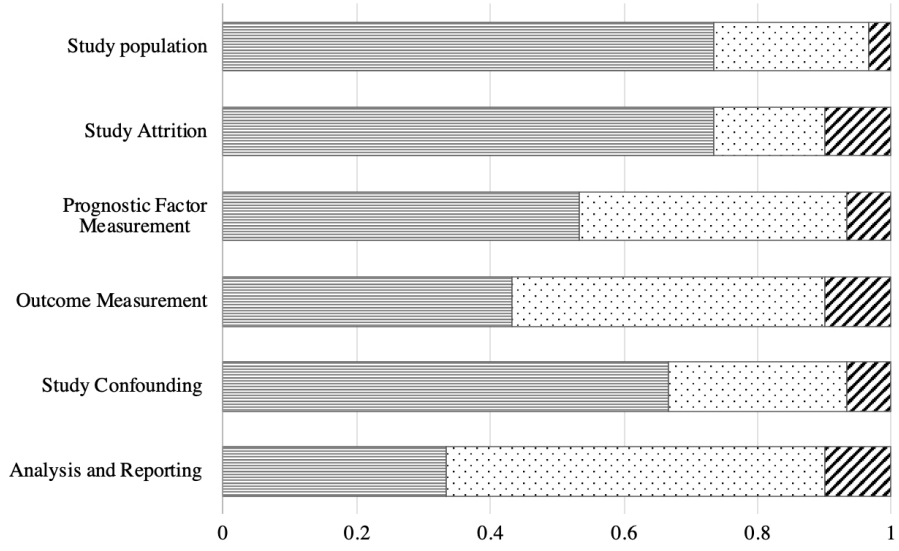
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PRISMA flow diagram

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Risk of bias assessment results of the 30 included studies

482x350mm (72 x 72 DPI)

Appendix S1. Search strings for the databases used to retrieve articles

EMBASE

(‘developing countr*’:ti,ab,kw OR ‘developing nation*’:ti,ab,kw OR ‘developing population*’:ti,ab,kw OR ‘developing econom*’:ti,ab,kw OR ‘undeveloped countr*’:ti,ab,kw OR ‘undeveloped nation*’:ti,ab,kw OR ‘undeveloped economy’:ti,ab,kw OR ‘undeveloped economies’:ti,ab,kw OR ‘least developed countr*’:ti,ab,kw OR ‘least developed nation*’:ti,ab,kw OR ‘least developed economy’:ti,ab,kw OR ‘least developed economies’:ti,ab,kw OR ‘less-developed countr*’:ti,ab,kw OR ‘less-developed nation*’:ti,ab,kw OR ‘less-developed population’:ti,ab,kw OR ‘less-developed populations’:ti,ab,kw OR ‘less-developed econom*’:ti,ab,kw OR ‘lesser developed countr*’:ti,ab,kw OR ‘lesser developed nation*’:ti,ab,kw OR ‘lesser developed population’:ti,ab,kw OR ‘lesser developed populations’:ti,ab,kw OR ‘lesser developed economy’:ti,ab,kw OR ‘lesser developed economies’:ti,ab,kw OR ‘under-developed countr*’:ti,ab,kw OR ‘under-developed nation*’:ti,ab,kw OR ‘underdeveloped countr*’:ti,ab,kw OR ‘underdeveloped nation*’:ti,ab,kw OR ‘underdeveloped population*’:ti,ab,kw OR ‘underdeveloped econom*’:ti,ab,kw OR ‘low income countr*’:ti,ab,kw OR ‘middle income countr*’:ti,ab,kw OR ‘low income nation*’:ti,ab,kw OR ‘middle income nation*’:ti,ab,kw OR ‘low income population*’:ti,ab,kw OR ‘middle income population*’:ti,ab,kw OR ‘low income econom*’:ti,ab,kw OR ‘middle income econom*’:ti,ab,kw OR ‘lower income countr*’:ti,ab,kw OR ‘lower income nation*’:ti,ab,kw OR ‘lower income population*’:ti,ab,kw OR ‘lower income economy’:ti,ab,kw OR ‘lower income economies’:ti,ab,kw OR ‘resource limited’:ti,ab,kw OR ‘low resource countr*’:ti,ab,kw OR ‘lower resource countr*’:ti,ab,kw OR ‘low resource nation*’:ti,ab,kw OR ‘low resource population*’:ti,ab,kw OR ‘low resource economy’:ti,ab,kw OR ‘low resource economies’:ti,ab,kw OR ‘underserved countr*’:ti,ab,kw OR ‘underserved nation*’:ti,ab,kw OR ‘underserved population*’:ti,ab,kw OR ‘underserved economy’:ti,ab,kw OR ‘underserved economies’:ti,ab,kw OR ‘under-served country’:ti,ab,kw OR ‘under-served countries’:ti,ab,kw OR ‘under-served nation’:ti,ab,kw OR ‘under-served nations’:ti,ab,kw OR ‘under-served population’:ti,ab,kw OR ‘under-served populations’:ti,ab,kw OR ‘underserved economy’:ti,ab,kw OR ‘underserved economies’:ti,ab,kw OR ‘derived countr*’:ti,ab,kw OR ‘deprived nation’:ti,ab,kw OR ‘deprived nations’:ti,ab,kw OR ‘derived population*’:ti,ab,kw OR ‘deprived economy’:ti,ab,kw OR ‘deprived economies’:ti,ab,kw OR ‘poor countr*’:ti,ab,kw OR ‘poor nation*’:ti,ab,kw OR ‘poor population*’:ti,ab,kw OR ‘poor econom*’:ti,ab,kw OR ‘poorer countr*’:ti,ab,kw OR ‘poorer nation*’:ti,ab,kw OR ‘poorer population*’:ti,ab,kw OR ‘poorer econom*’:ti,ab,kw OR ‘Imic’:ti,ab,kw OR ‘Imics’:ti,ab,kw OR ‘lami’:ti,ab,kw OR ‘transitional countr*’:ti,ab,kw OR ‘transitional nation’:ti,ab,kw OR ‘transitional nations’:ti,ab,kw OR ‘transitional econom*’:ti,ab,kw OR ‘transition countr*’:ti,ab,kw OR ‘transition nation*’:ti,ab,kw OR ‘transition econom*’:ti,ab,kw OR low ‘resource setting*’:ti,ab,kw OR ‘lower resource setting*’:ti,ab,kw OR ‘middle resource setting*’:ti,ab,kw OR ‘Third World*’:ti,ab,kw OR ‘south east asia*’:ti,ab,kw OR ‘middle east*’:ti,ab,kw OR ‘Afghan*’:ti,ab,kw OR ‘Angola*’:ti,ab,kw OR ‘Angolese*’:ti,ab,kw OR ‘Angolian*’:ti,ab,kw OR ‘Armenia*’:ti,ab,kw OR ‘Bangladesh*’:ti,ab,kw OR ‘Benin*’:ti,ab,kw OR ‘Bhutan*’:ti,ab,kw OR ‘Birma*’:ti,ab,kw OR ‘Burma*’:ti,ab,kw OR ‘Birmese*’:ti,ab,kw OR ‘Burmese*’:ti,ab,kw OR ‘Boliv*’:ti,ab,kw OR ‘Botswan*’:ti,ab,kw OR ‘burkina Faso*’:ti,ab,kw OR ‘Burundi*’:ti,ab,kw OR ‘Cabo Verde*’:ti,ab,kw OR ‘Cambod*’:ti,ab,kw OR ‘Cameroon*’:ti,ab,kw OR ‘Cape Verd*’:ti,ab,kw OR ‘Central Africa*’:ti,ab,kw OR ‘Chad’:ti,ab,kw OR ‘Comoro*’:ti,ab,kw OR ‘Congo*’:ti,ab,kw OR ‘Cote d/Ivoire*’:ti,ab,kw OR ‘Djibouti*’:ti,ab,kw OR ‘East Africa*’:ti,ab,kw OR ‘Eastern Africa*’:ti,ab,kw OR ‘Egypt*’:ti,ab,kw OR ‘El Salvador*’:ti,ab,kw OR ‘Equatorial Guinea*’:ti,ab,kw OR ‘Eritre*’:ti,ab,kw OR ‘Ethiopia*’:ti,ab,kw OR ‘Gabon*’:ti,ab,kw OR ‘Gambia*’:ti,ab,kw OR ‘Gaza*’:ti,ab,kw OR ‘Georgia Republic’/exp OR

1
 2
 3 'Ghan*':ti,ab,kw OR 'Guatemal*':ti,ab,kw OR 'Guinea':ti,ab,kw OR 'Haiti*':ti,ab,kw OR
 4 'Hondur*':ti,ab,kw OR 'India*':ti,ab,kw OR 'Indones*':ti,ab,kw OR 'Ivory Coast*':ti,ab,kw OR
 5 'Kenya*':ti,ab,kw OR 'Kiribati*':ti,ab,kw OR 'Kosovo*':ti,ab,kw OR 'Kyrgyz*':ti,ab,kw OR 'Lao
 6 PDR*':ti,ab,kw OR 'Laos*':ti,ab,kw OR 'Lesotho*':ti,ab,kw OR 'Liberia*':ti,ab,kw OR
 7 'Madagascar*':ti,ab,kw OR 'Malaw*':ti,ab,kw OR 'Mali':ti,ab,kw OR 'Mauritan*':ti,ab,kw OR
 8 'Mauriti*':ti,ab,kw OR 'Micronesi*':ti,ab,kw OR 'Mocambiqu*':ti,ab,kw OR 'Moldov*':ti,ab,kw
 9 OR 'Mongolia*':ti,ab,kw OR 'Morocc*':ti,ab,kw OR 'Mozambiqu*':ti,ab,kw OR
 10 'Myanmar*':ti,ab,kw OR 'Namibia*':ti,ab,kw OR 'Nepal*':ti,ab,kw OR 'Nicaragua*':ti,ab,kw OR
 11 'Niger*':ti,ab,kw OR 'North Korea*':ti,ab,kw OR 'Northern Korea*':ti,ab,kw OR 'Democratic
 12 People/s Republic of Korea':ti,ab,kw OR 'Pakistan*':ti,ab,kw OR 'Papua New Guinea*':ti,ab,kw
 13 OR 'Philippine*':ti,ab,kw OR 'Principe':ti,ab,kw OR 'Rhodesia*':ti,ab,kw OR 'Rwanda*':ti,ab,kw
 14 OR 'Samoa*':ti,ab,kw OR 'Sao Tome*':ti,ab,kw OR 'Senegal*':ti,ab,kw OR 'Sierra
 15 Leone*':ti,ab,kw OR 'Solomon Islands*':ti,ab,kw OR 'Somalia*':ti,ab,kw OR 'South
 16 Africa*':ti,ab,kw OR 'South Sudan*':ti,ab,kw OR 'Southern Africa*':ti,ab,kw OR 'Sri
 17 Lanka*':ti,ab,kw OR 'Sub Saharan Africa*':ti,ab,kw OR 'Subsaharan Africa*':ti,ab,kw OR
 18 'Sudan*':ti,ab,kw OR 'Swaziland*':ti,ab,kw OR 'Syria*':ti,ab,kw OR 'Tajikist*':ti,ab,kw OR
 19 'Tanzan*':ti,ab,kw OR 'Timor*':ti,ab,kw OR 'Togo*':ti,ab,kw OR 'Tonga*':ti,ab,kw OR
 20 'Tunis*':ti,ab,kw OR 'Ugand*':ti,ab,kw OR 'Ukrain*':ti,ab,kw OR 'Uzbekistan*':ti,ab,kw OR
 21 'Vanuatu*':ti,ab,kw OR 'Vietnam*':ti,ab,kw OR 'West Africa*':ti,ab,kw OR 'West Bank*':ti,ab,kw
 22 OR 'Western Africa*':ti,ab,kw OR 'Yemen*':ti,ab,kw OR 'Zaire*':ti,ab,kw OR 'Zambia*':ti,ab,kw
 23 OR 'Zimbabw*':ti,ab,kw)

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28 AND

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31 ('Umbilical Arter*/exp OR 'Uterine Artery'/exp OR 'Middle Cerebral Artery'/exp OR 'Ductus
 32 Venosus'/exp OR 'Umbilical Vein*/exp OR 'Inferior Cava Vein'/exp OR 'Umbilical
 33 Arter*':ti,ab,kw OR 'Uterine Arter*':ti,ab,kw OR 'Middle Cerebral Arter*':ti,ab,kw OR 'Patent
 34 Ductus Venosus':ti,ab,kw OR 'Umbilical Vein*':ti,ab,kw OR 'Inferior Vena Cava':ti,ab,kw OR
 35 'Cerebroplacental Ratio':ti,ab,kw OR 'CPR':ti,ab,kw OR 'Fetal Descending Aorta':ti,ab,kw OR
 36 'FDA':ti,ab,kw OR 'Doppler Ultrasonography'/exp OR 'Doppler Ultrasound*':ti,ab,kw OR
 37 'Doppler Ultrasonography':ti,ab,kw OR 'Uterine Artery Doppler':ti,ab,kw)

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39
40 AND

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42 ('Stillbirth':ti,ab,kw OR 'Perinatal Death':ti,ab,kw OR 'Cesarean Section*':ti,ab,kw OR 'Caesarean
 43 Section*':ti,ab,kw OR 'Acidosis':ti,ab,kw OR 'Premature Birth':ti,ab,kw OR 'Neonatal Intensive
 44 Care':ti,ab,kw OR 'Fetal Growth Retard*':ti,ab,kw OR 'Newborn Respiratory Distress
 45 Syndrome*':ti,ab,kw OR 'Gestational Age':ti,ab,kw OR 'Birth Weight':ti,ab,kw OR 'Asphyxia
 46 Neonatorum':ti,ab,kw OR 'Apgar Score*':ti,ab,kw OR 'Length of Stay':ti,ab,kw OR 'Stillbirth'/exp
 47 OR 'Perinatal Death'/exp OR 'Perinatal Mortality'/exp OR 'Cesarean Section'/exp OR
 48 'Acidosis'/exp OR 'Prematurity'/exp OR 'Newborn Intensive Care'/exp OR 'Intrauterine Growth
 49 Retardation'/exp OR 'Neonatal Respiratory Distress Syndrome'/exp OR 'Gestational Age'/exp OR
 50 'Birth Weight'/exp OR 'Newborn Hypoxia'/exp OR 'Apgar Score'/exp OR 'Length of Stay'/exp OR
 51 'Pregnancy':ti,ab,kw OR 'Pregnancies':ti,ab,kw OR 'Gestation':ti,ab,kw OR 'Pregnant':ti,ab,kw OR
 52 'Pregnancy'/exp)

PUBMED (MEDLINE)

("Developing Countries"[Mesh] OR developing countr*[tiab] OR developing nation*[tiab] OR developing population*[tiab] OR developing econom*[tiab] OR undeveloped countr*[tiab] OR undeveloped nation*[tiab] OR "undeveloped economy"[tiab] OR "undeveloped economies"[tiab] OR least developed countr*[tiab] OR least developed nation*[tiab] OR "least developed economy"[tiab] OR "least developed economies"[tiab] OR less-developed countr*[tiab] OR less-developed nation*[tiab] OR "less-developed population"[tiab] OR "less-developed populations"[tiab] OR less-developed econom*[tiab] OR lesser developed countr*[tiab] OR lesser developed nation*[tiab] OR "lesser developed population"[tiab] OR "lesser developed populations"[tiab] OR "lesser developed economy"[tiab] OR "lesser developed economies"[tiab] OR under-developed countr*[tiab] OR under-developed nation*[tiab] OR underdeveloped countr*[tiab] OR underdeveloped nation*[tiab] OR underdeveloped population*[tiab] OR underdeveloped econom*[tiab] OR low income countr*[tiab] OR middle income countr*[tiab] OR low income nation*[tiab] OR middle income nation*[tiab] OR low income population*[tiab] OR middle income population*[tiab] OR low income econom*[tiab] OR middle income econom*[tiab] OR lower income countr*[tiab] OR lower income nation*[tiab] OR lower income population*[tiab] OR "lower income economy"[tiab] OR "lower income economies"[tiab] OR resource limited[tiab] OR low resource countr*[tiab] OR lower resource countr*[tiab] OR low resource nation*[tiab] OR low resource population*[tiab] OR "low resource economy"[tiab] OR "low resource economies"[tiab] OR underserved countr*[tiab] OR underserved nation*[tiab] OR underserved population*[tiab] OR "underserved economy"[tiab] OR "underserved economies"[tiab] OR "under-served country"[tiab] OR "under-served countries"[tiab] OR "under-served nation"[tiab] OR "under-served nations"[tiab] OR "under-served population"[tiab] OR "under-served populations"[tiab] OR "underserved economy"[tiab] OR "underserved economies"[tiab] OR derived countr*[tiab] OR "deprived nation"[tiab] OR "deprived nations"[tiab] OR derived population*[tiab] OR "deprived economy"[tiab] OR "deprived economies"[tiab] OR poor countr*[tiab] OR poor nation*[tiab] OR poor population*[tiab] OR poor econom*[tiab] OR poorer countr*[tiab] OR poorer nation*[tiab] OR poorer population*[tiab] OR poorer econom*[tiab] OR lmic[tiab] OR lmic[tiab] OR lami[tiab] OR transitional countr*[tiab] OR "transitional nation"[tiab] OR "transitional nations"[tiab] OR transitional econom*[tiab] OR transition countr*[tiab] OR transition nation*[tiab] OR transition econom*[tiab] OR low resource setting*[tiab] OR lower resource setting*[tiab] OR middle resource setting*[tiab] OR Third World*[tiab] OR south east asia*[tw] OR middle east*[tw] OR Afghan*[tw] OR Angola*[tw] OR Angolese*[tw] OR Angolian*[tw] OR Armenia*[tw] OR Bangladesh*[tw] OR Benin*[tw] OR Bhutan*[tw] OR Birma*[tw] OR Burma*[tw] OR Birmese*[tw] OR Burmese*[tw] OR Boliv*[tw] OR Botswan*[tw] OR burkina Faso*[tw] OR Burundi*[tw] OR Cabo Verde*[tw] OR Cambod*[tw] OR Cameroon*[tw] OR Cape Verd*[tw] OR Central Africa*[tw] OR Chad[tw] OR Comoro*[tw] OR Congo*[tw] OR Cote d'Ivoire*[tw] OR Djibouti*[tw] OR East Africa*[tw] OR Eastern Africa*[tw] OR Egypt*[tw] OR El Salvador*[tw] OR Equatorial Guinea*[tw] OR Eritre*[tw] OR Ethiopia*[tw] OR Gabon*[tw] OR Gambia*[tw] OR Gaza*[tw] OR "Georgia Republic"[Mesh] OR Ghan*[tw] OR Guatemal*[tw] OR Guinea[tw] OR Haiti*[tw] OR Hondur*[tw] OR India*[tw] OR Indones*[tw] OR Ivory Coast*[tw] OR Kenya*[tw] OR Kiribati*[tw] OR Kosovo*[tw] OR Kyrgyz*[tw] OR Lao PDR*[tw] OR Laos*[tw] OR Lesotho*[tw] OR Liberia*[tw] OR Madagascar*[tw] OR Malaw*[tw] OR Mali[tw] OR Mauritan*[tw] OR Mauriti*[tw] OR Micronesi*[tw] OR Mocambiqu*[tw] OR Moldov*[tw] OR Mongolia*[tw] OR Morocc*[tw] OR Mozambiqu*[tw] OR Myanmar*[tw] OR Namibia*[tw] OR Nepal*[tw] OR Nicaragua*[tw] OR Niger*[tw] OR North Korea*[tw] OR Northern Korea*[tw] OR "Democratic People s Republic of Korea"[tiab] OR "Democratic People's Republic of Korea"[Mesh] OR Pakistan*[tw] OR Papua New Guinea*[tw] OR Philippine*[tw] OR Principe[tw] OR Rhodesia*[tw] OR Rwanda*[tw] OR Samoa*[tw] OR Sao Tome*[tw] OR Senegal*[tw] OR Sierra Leone*[tw] OR Solomon Islands*[tw]

OR Somalia*[tw] OR South Africa*[tw] OR South Sudan*[tw] OR Southern Africa*[tw] OR Sri Lanka*[tw] OR Sub Saharan Africa*[tw] OR Subsaharan Africa*[tw] OR Sudan*[tw] OR Swaziland*[tw] OR Syria*[tw] OR Tajikist*[tw] OR Tanzan*[tw] OR Timor*[tw] OR Togo*[tw] OR Tonga*[tw] OR Tunis*[tw] OR Ugand*[tw] OR Ukrain*[tw] OR Uzbekistan*[tw] OR Vanuatu*[tw] OR Vietnam*[tw] OR West Africa*[tw] OR West Bank*[tw] OR Western Africa*[tw] OR Yemen*[tw] OR Zaire*[tw] OR Zambia*[tw] OR Zimbabw*[tw])

AND

("Umbilical Arteries"[Mesh] OR "Uterine Artery"[Mesh] OR "Middle Cerebral Artery"[Mesh] OR "Ductus Venosus" [Supplementary Concept] OR "Umbilical Veins"[Mesh] OR "Vena Cava, Inferior"[Mesh] OR Umbilical Arter*[tiab] OR Uterine Arter*[tiab] OR Middle Cerebral Arter*[tiab] OR Patent Ductus Venosus[tiab] OR Umbilical Vein*[tiab] OR Inferior Vena Cava[tiab] OR Cerebroplacental Ratio[tiab] OR CPR[tiab] OR Fetal Descending Aorta[tiab] OR FDA[tiab] OR "Ultrasonography, Doppler"[Mesh] OR Doppler Ultrasound*[Title/Abstract] OR Doppler Ultrasonography[Title/Abstract] OR Uterine Artery Doppler[Title/Abstract])

AND

("Stillbirth"[tiab] OR "Perinatal Death"[tiab] OR "Caesarean Section*"[tiab] OR "Caesarean Section*"[tiab] OR Acidosis[tiab] OR Premature Birth[tiab] OR Neonatal Intensive Care"[tiab] OR Fetal Growth Retard*[tiab] OR Newborn Respiratory Distress Syndrome*[tiab] OR Gestational Age[tiab] OR Birth Weight[tiab] OR Asphyxia Neonatorum[tiab] OR Apgar Score*[tiab] OR Length of Stay"[tiab] OR "Stillbirth"[Mesh] OR "Perinatal Death"[Mesh] OR "Caesarean Section"[Mesh] OR "Acidosis"[Mesh] OR "Premature Birth"[Mesh] OR "Intensive Care, Neonatal"[Mesh] OR "Fetal Growth Retardation"[Mesh] OR "Respiratory Distress Syndrome, Newborn"[Mesh] OR "Gestational Age"[Mesh] OR "Birth Weight"[Mesh] OR "Asphyxia Neonatorum"[Mesh] OR "Apgar Score"[Mesh] OR "Length of Stay"[Mesh] OR Pregnancy[Title/Abstract] OR Pregnancies[Title/Abstract] OR Gestation[Title/Abstract] OR Pregnant[Title/Abstract] OR "Pregnancy"[Mesh])

COCHRANE

‘developing countr*’ OR ‘developing nation*’ OR ‘developing population*’ OR ‘developing econom*’ OR ‘undeveloped countr*’ OR ‘undeveloped nation*’ OR ‘undeveloped economy’ OR ‘undeveloped economies’ OR ‘least developed countr*’ OR ‘least developed nation*’ OR ‘least developed economy’ OR ‘least developed economies’ OR ‘less-developed countr*’ OR ‘less-developed nation*’ OR ‘less-developed population’ OR ‘less-developed populations’ OR ‘less-developed econom*’ OR ‘lesser developed countr*’ OR ‘lesser developed nation*’ OR ‘lesser developed population’ OR ‘lesser developed populations’ OR ‘lesser developed economy’ OR ‘lesser developed economies’ OR ‘under-developed countr*’ OR ‘under-developed nation*’ OR ‘underdeveloped countr*’ OR ‘underdeveloped nation*’ OR ‘underdeveloped population*’ OR ‘underdeveloped econom*’ OR ‘low income countr*’ OR ‘middle income countr*’ OR ‘low income nation*’ OR ‘middle income nation*’ OR ‘low income population*’ OR ‘middle income population*’ OR ‘low income econom*’ OR ‘middle income econom*’ OR ‘lower income countr*’ OR ‘lower income nation*’ OR ‘lower income population*’ OR ‘lower income economy’ OR ‘lower income economies’ OR ‘resource limited’ OR ‘low resource countr*’ OR ‘lower resource countr*’ OR ‘low resource nation*’ OR ‘low resource population*’ OR ‘low resource economy’ OR ‘low resource economies’ OR ‘underserved countr*’ OR ‘underserved nation*’ OR ‘underserved

population* OR 'underserved economy' OR 'underserved economies' OR 'under-served country'
 OR 'under-served countries' OR 'under-served nation' OR 'under-served nations' OR 'under-served
 population' OR 'under-served populations' OR 'underserved economy' OR 'underserved
 economies' OR 'derived countr*' OR 'deprived nation' OR 'deprived nations' OR 'derived
 population*' OR 'deprived economy' OR 'deprived economies' OR 'poor countr*' OR 'poor
 nation*' OR 'poor population*' OR 'poor econom*' OR 'poorer countr*' OR 'poorer nation*' OR
 'poorer population*' OR 'poorer econom*' OR 'Imic' OR 'Imics' OR 'lami' OR 'transitional
 countr*' OR 'transitional nation' OR 'transitional nations' OR 'transitional econom*' OR 'transition
 countr*' OR 'transition nation*' OR 'transition econom*' OR low 'resource setting*' OR 'lower
 resource setting*' OR 'middle resource setting*' OR 'Third World*' OR 'south east asia*' OR
 'middle east*' OR 'Afghan*' OR 'Angola*' OR 'Angolese*' OR 'Angolian*' OR 'Armenia*' OR
 'Bangladesh*' OR 'Benin*' OR 'Bhutan*' OR 'Birma*' OR 'Burma*' OR 'Birmese*' OR
 'Burmese*' OR 'Boliv*' OR 'Botswan*' OR 'burkina Faso*' OR 'Burundi*' OR 'Cabo Verde*' OR
 'Cambod*' OR 'Cameroon*' OR 'Cape Verd*' OR 'Central Africa*' OR 'Chad' OR 'Comoro*' OR
 'Congo*' OR 'Cote d'Ivoire*' OR 'Djibouti*' OR 'East Africa*' OR 'Eastern Africa*' OR
 'Egypt*' OR 'El Salvador*' OR 'Equatorial Guinea*' OR 'Eritre*' OR 'Ethiopia*' OR 'Gabon*' OR
 'Gambia*' OR 'Gaza*' OR 'Georgia Republic' OR 'Ghan*' OR 'Guatemala*' OR 'Guinea' OR
 'Haiti*' OR 'Hondur*' OR 'India*' OR 'Indones*' OR 'Ivory Coast*' OR 'Kenya*' OR 'Kiribati*' OR
 'Kosovo*' OR 'Kyrgyz*' OR 'Lao PDR*' OR 'Laos*' OR 'Lesotho*' OR 'Liberia*' OR
 'Madagascar*' OR 'Malaw*' OR 'Mali' OR 'Mauritan*' OR 'Mauriti*' OR 'Micronesi*' OR
 'Mocambiqu*' OR 'Moldov*' OR 'Mongolia*' OR 'Morocc*' OR 'Mozambiqu*' OR 'Myanmar*' OR
 'Namibia*' OR 'Nepal*' OR 'Nicaragua*' OR 'Niger*' OR 'North Korea*' OR 'Northern
 Korea*' OR 'Democratic People's Republic of Korea' OR 'Pakistan*' OR 'Papua New Guinea*' OR
 'Philippine*' OR 'Principe' OR 'Rhodesia*' OR 'Rwanda*' OR 'Samoa*' OR 'Sao Tome*' OR
 'Senegal*' OR 'Sierra Leone*' OR 'Solomon Islands*' OR 'Somalia*' OR 'South Africa*' OR
 'South Sudan*' OR 'Southern Africa*' OR 'Sri Lanka*' OR 'Sub Saharan Africa*' OR 'Subsaharan
 Africa*' OR 'Sudan*' OR 'Swaziland*' OR 'Syria*' OR 'Tajikist*' OR 'Tanzan*' OR 'Timor*' OR
 'Togo*' OR 'Tonga*' OR 'Tunis*' OR 'Ugand*' OR 'Ukrain*' OR 'Uzbekistan*' OR
 'Vanuatu*' OR 'Vietnam*' OR 'West Africa*' OR 'West Bank*' OR 'Western Africa*' OR
 'Yemen*' OR 'Zaire*' OR 'Zambia*' OR 'Zimbabw*'

AND

'Umbilical Arter*' OR 'Uterine Artery' OR 'Middle Cerebral Artery' OR 'Ductus Venosus' OR
 'Umbilical Vein*' OR 'Inferior Cava Vein' OR 'Uterine Arter*' OR 'Middle Cerebral Arter*' OR
 'Patent Ductus Venosus' OR 'Inferior Vena Cava' OR 'Cerebroplacental Ratio' OR 'CPR' OR
 'Fetal Descending Aorta' OR 'FDA' OR 'Doppler Ultrasonography' OR 'Doppler Ultrasound*' OR
 'Doppler Ultrasonography' OR 'Uterine Artery Doppler'

AND

'Stillbirth' OR 'Perinatal Death' OR 'Caesarean Section*' OR 'Caesarean Section*' OR 'Acidosis'
 OR 'Premature Birth' OR 'Neonatal Intensive Care' OR 'Fetal Growth Retard*' OR 'Newborn
 Respiratory Distress Syndrome*' OR 'Gestational Age' OR 'Birth Weight' OR 'Asphyxia
 Neonatorum' OR 'Apgar Score*' OR 'Perinatal Mortality' OR 'Caesarean Section' OR 'Prematurity'
 OR 'Newborn Intensive Care' OR 'Intrauterine Growth Retardation' OR 'Neonatal Respiratory
 Distress Syndrome' OR 'Gestational Age' OR 'Birth Weight' OR 'Newborn Hypoxia' OR 'Length
 of Stay' OR 'Pregnancy' OR 'Pregnancies' OR 'Gestation' OR 'Pregnant'

SCOPUS

TITLE-ABS-KEY("developing countr*" OR "developing nation*" OR "developing population*" OR "developing econom*" OR "undeveloped countr*" OR "undeveloped nation*" OR "undeveloped economy" OR "undeveloped economies" OR "least developed countr*" OR "least developed nation*" OR "least developed economy" OR "least developed economies" OR "less-developed countr*" OR "less-developed nation*" OR "less-developed population" OR "less-developed populations" OR "less-developed econom*" OR "lesser developed countr*" OR "lesser developed nation*" OR "lesser developed population" OR "lesser developed populations" OR "lesser developed economy" OR "lesser developed economies" OR "under-developed countr*" OR "under-developed nation*" OR "underdeveloped countr*" OR "underdeveloped nation*" OR "underdeveloped population*" OR "underdeveloped econom*" OR "low income countr*" OR "middle income countr*" OR "low income nation*" OR "middle income nation*" OR "low income population*" OR "middle income population*" OR "low income econom*" OR "middle income econom*" OR "lower income countr*" OR "lower income nation*" OR "lower income population*" OR "lower income economy" OR "lower income economies" OR "resource limited" OR "low resource countr*" OR "lower resource countr*" OR "low resource nation*" OR "low resource population*" OR "low resource economy" OR "low resource economies" OR "underserved countr*" OR "underserved nation*" OR "underserved population*" OR "underserved economy" OR "underserved economies" OR "under-served country" OR "under-served countries" OR "under-served nation" OR "under-served nations" OR "under-served population" OR "under-served populations" OR "underserved economy" OR "underserved economies" OR "derived countr*" OR "deprived nation" OR "deprived nations" OR "derived population*" OR "deprived economy" OR "deprived economies" OR "poor countr*" OR "poor nation*" OR "poor population*" OR "poor econom*" OR "poorer countr*" OR "poorer nation*" OR "poorer population*" OR "poorer econom*" OR "lmic" OR "lmics" OR "lami" OR "transitional countr*" OR "transitional nation" OR "transitional nations" OR "transitional econom*" OR "transition countr*" OR "transition nation*" OR "transition econom*" OR low "resource setting*" OR "lower resource setting*" OR "middle resource setting*" OR "Third World*" OR "south east asia*" OR "middle east*" OR "Afghan*" OR "Angola*" OR "Angolese*" OR "Angolian*" OR "Armenia*" OR "Bangladesh*" OR "Benin*" OR "Bhutan*" OR "Birma*" OR "Burma*" OR "Birmese*" OR "Burmese*" OR "Boliv*" OR "Botswan*" OR "burkina Faso*" OR "Burundi*" OR "Cabo Verde*" OR "Cambod*" OR "Cameroon*" OR "Cape Verd*" OR "Central Africa*" OR "Chad" OR "Comoro*" OR "Congo*" OR "Cote d'Ivoire*" OR "Djibouti*" OR "East Africa*" OR "Eastern Africa*" OR "Egypt*" OR "El Salvador*" OR "Equatorial Guinea*" OR "Eritre*" OR "Ethiopia*" OR "Gabon*" OR "Gambia*" OR "Gaza*" OR "Georgia Republic" OR "Ghan*" OR "Guatemal*" OR "Guinea" OR "Haiti*" OR "Hondur*" OR "India*" OR "Indones*" OR "Ivory Coast*" OR "Kenya*" OR "Kiribati*" OR "Kosovo*" OR "Kyrgyz*" OR "Lao PDR*" OR "Laos*" OR "Lesotho*" OR "Liberia*" OR "Madagascar*" OR "Malaw*" OR "Mali" OR "Mauritan*" OR "Mauriti*" OR "Micronesi*" OR "Mocambiqu*" OR "Moldov*" OR "Mongolia*" OR "Morocc*" OR "Mozambiqu*" OR "Myanmar*" OR "Namibia*" OR "Nepal*" OR "Nicaragua*" OR "Niger*" OR "North Korea*" OR "Northern Korea*" OR "Democratic People/s Republic of Korea" OR "Pakistan*" OR "Papua New Guinea*" OR "Philippine*" OR "Principe" OR "Rhodesia*" OR "Rwanda*" OR "Samoa*" OR "Sao Tome*" OR "Senegal*" OR "Sierra Leone*" OR "Solomon Islands*" OR "Somalia*" OR "South Africa*" OR "South Sudan*" OR "Southern Africa*" OR "Sri Lanka*" OR "Sub Saharan Africa*" OR "Subsaharan Africa*" OR "Sudan*" OR "Swaziland*" OR "Syria*" OR "Tajikist*" OR "Tanzan*" OR "Timor*" OR "Togo*" OR "Tonga*" OR "Tunis*" OR "Ugand*" OR "Ukrain*" OR "Uzbekistan*" OR "Vanuatu*" OR "Vietnam*" OR "West Africa*" OR "West Bank*" OR "Western Africa*" OR "Yemen*" OR "Zaire*" OR "Zambia*" OR "Zimbabw*")

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7 TITLE-ABS-KEY("Stillbirth" OR "Perinatal Death" OR "Caesarean Section*" OR "Caesarean
8 Section*" OR "Acidosis" OR "Premature Birth" OR "Neonatal Intensive Care" OR "Fetal Growth
9 Retard*" OR "Newborn Respiratory Distress Syndrome*" OR "Gestational Age" OR "Birth
10 Weight" OR "Asphyxia Neonatorum" OR "Apgar Score*" OR "Length of Stay" OR "Stillbirth" OR
11 "Perinatal Death" OR "Caesarean Section" OR "Acidosis" OR "Premature Birth" OR "Intensive Care,
12 Neonatal" OR "Fetal Growth Retardation" OR "Respiratory Distress Syndrome, Newborn" OR
13 "Gestational Age" OR "Birth Weight" OR "Asphyxia Neonatorum" OR "Apgar Score" OR "Length
14 of Stay" OR "Pregnancy" OR "Pregnancies" OR "Gestation" OR "Pregnant" OR "Pregnancy")
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17 AND
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19 TITLE-ABS-KEY("Umbilical Arteries" OR "Uterine Artery" OR "Middle Cerebral Artery" OR
20 "Ductus Venosus" OR "Umbilical Veins" OR "Vena Cava, Inferior" OR "Umbilical Arter*" OR
21 "Uterine Arter*" OR "Middle Cerebral Arter*" OR "Patent Ductus Venosus" OR "Umbilical Vein*"
22 OR "Inferior Vena Cava" OR "Cerebroplacental Ratio" OR "CPR" OR "Fetal Descending Aorta"
23 OR "FDA" OR "Ultrasonography, Doppler" OR "Doppler Ultrasound*" OR "Doppler
24 Ultrasonography" OR "Uterine Artery Doppler")
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Appendix S2. List of full-text articles excluded with reasons

a) Country income level: 3 studies

1. El Shourbagy, S., Elsakhawy, M. (2012). Prediction of fetal anemia by middle cerebral artery Doppler. *Middle East Fertility Society Journal*, 17(4), 275-282.
2. Haley, J., Tuffnell, D. J., Johnson, N. (1997). Randomized controlled trial of cardiotocography versus umbilical artery Doppler in the management of small for gestational age fetuses. *British Journal of Obstetrics and Gynaecology*, 104(4), 431-435).
3. Morales-Rosello, J., Dias, T., Khalil, A., Fornes-Ferrer, V., Ciammella, R., Gimenez-Roca, L., Perales-Marin, A., Thilaganathan, B. (2018). Birth-weight differences at term are explained by placental dysfunction and not by maternal ethnicity. *Ultrasound Obstet Gynecol*, 52(4), 488-493.

b) Design and quality: 9 studies

1. Abidoye, I. A., Ayoola, O. O., Idowu, B., Aderibigbe, A. S., Loto, O. M. (2017). Uterine artery Doppler velocimetry in hypertensive disorder of pregnancy in Nigeria. *J Ultrason*, 17(71) 253-258.
2. Agarwal, R., Tiwari, A., Wadhwa, N., Radhakrishnan, G., Bhatt, S., Batra, P. (2017). Abnormal umbilical artery Doppler velocimetry and placental histopathological correlation in fetal growth restriction. *South African Journal of Obstetrics and Gynaecology*, 23(1), 12-16.
3. Ali, A., Ara, I., Sultana, R., Akram, F., Zaib, M. J. (2014). Comparison of perinatal outcome of growth restricted fetuses with normal and abnormal umbilical artery Doppler waveforms. *Journal of Ayub Medical College, Abbottabad: JAMC*, 26(3), 344-348.
4. Kumar, S., Datta, S., Mittal, S., Roy, K. K. (2002). Doppler flow studies in middle cerebral and umbilical arteries in growth retarded and normal pregnancies. *JK Science*, 4(0), 185-189
5. Mufenda, J., Gebhardt, S., van Rooyen, R., Theron, G. (2015). Introducing a Mobile-Connected Umbilical Doppler Device (UmbiFlow) into a Primary Care Maternity Setting: Does This Reduce Unnecessary Referrals to Specialised Care? Results of a Pilot Study in Kraaifontein, South Africa. *PLoS One*, 10(11) e0142743.
6. Nguku, S. W., Wanyoike-Gichuhi, J., Aywak, A. A. (2006). Biophysical profile scores and resistance indices of the umbilical artery as seen in patients with pregnancy induced hypertension. *East African Medical Journal*, 83(3), 96-101
7. Nkosi, S., Makin, J., Hlongwane, T. M. A. G., & Pattinson, R. C. (2019). Screening and managing a low-risk pregnant population using continuous-wave Doppler ultrasound in a low-income population: A cohort analytical study. *SAMJ: South African Medical Journal*, 109(5), 347-352.
8. Siddiqui, T. S., Asim, A., Ali, S., Tariq, A. (2014). Comparison of perinatal outcome in growth restricted fetuses retaining normal umbilical artery Doppler flow to those with diminished end-diastolic flow. *Journal of Ayub Medical College, Abbottabad: JAMC*, 26(2), 221-224.
9. Kachewar, S. G., Gandage, S. G., Pawar, H. J. (2012). An Indian study of novel non-invasive method of screening for foetal anaemia. *Journal of Clinical and Diagnostic Research*, 6(4), 688-691.

c) Outcomes: 11 studies

1. Adekanmi, A. J., Roberts, A., Akinmoladun, J. A., & Adeyinka, A. O. (2019). Uterine and umbilical artery doppler in women with pre-eclampsia and their pregnancy outcomes. *Nigerian Postgraduate Medical Journal*, 26(2), 106.
2. El Behery, M. M., Siam, S., Seksaka, M. A., Mansou, S. M. (2013). Uterine artery Doppler and urinary hyperglycosylated HCG as predictors of threatened abortion outcome. *Middle East Fertility Society Journal*, 19(1), 42-46.
3. El-Mashad, A. I., Mohamed, M. A., Elahadi Farag, M. A., Ahmad, M. K., Ismail, Y. (2011). Role of uterine artery Doppler velocimetry indices and plasma adrenomedullin level in women with unexplained recurrent pregnancy loss. *Journal of Obstetrics and Gynaecology Research*, 37(1), 51-57.
4. Geerts, L., Van der Merwe, E., Theron, A., Rademan, K. (2016). Placental insufficiency among high-risk pregnancies with a normal umbilical artery resistance index after 32 weeks. *Int J Gynaecol Obstet*, 135(1), 38-42.
5. Kumar, B. S., Sarmila, K., Prasad, K. S. (2012). Prediction of preeclampsia by midtrimester uterine artery doppler velocimetry in high-risk and low-risk women. *Journal of Obstetrics and Gynecology of India*, 62(3), 297-300.
6. Maged. A. M., Elnassery, N., Fouad, M., Abdelhafiz, A., Al Mostafa, W. (2015). Third-trimester uterine artery Doppler measurement and maternal postpartum outcome among patients with severe pre-eclampsia. *International Journal of Gynecology and Obstetrics*, 131(1), 49-53.
7. Prajapati, S. R., Maitra, N. (2013). Prediction of pre-eclampsia by a combination of history, uterine artery doppler, and mean arterial pressure (A Prospective Study of 200 Cases). *Journal of Obstetrics and Gynecology of India*, 63(1), 32-36.
8. Sebastian, A., Raj, T. S., Yenuberi, H., Job, V., Varuhghese, S., & Regi, A. (2019). Angiogenic factors and uterine artery Doppler in predicting preeclampsia and associated adverse outcomes in a tertiary hospital in south India. *Pregnancy hypertension*, 16, 26.
9. Shehata, N. A. A., Ali, H. A. A., Hassan, A., Katta, M. A., Ali, A. S. F. (2018). Doppler and biochemical assessment for the prediction of early pregnancy outcome in patients experiencing threatened spontaneous abortion. *Int J Gynaecol Obstet*, 143(2), 150-155.
10. Yusuf, M., Galadanci, H., Ismail, A., Aliyu, L. D., Danbatta, A. H. (2017). Uterine artery doppler velocimetry for the prediction of preeclampsia among high-risk pregnancies in low-resource setting: Our experience at aminu Kano teaching hospital, Kano, Nigeria. *Donald School Journal of Ultrasound in Obstetrics and Gynecology*, 11(3), 197-202
11. Puri, M. S., Deshpande, H., Kohli, S., Sharma, K., Singhanian, S. (2013). A study of uterine artery colour doppler at 20-24 weeks gestation as a predictor of pregnancy induced hypertension and intra uterine growth restriction from industrial town in Western India. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 4(1), 698-705.

Appendix S3. Pregnancy risk profiles in the selected studies

First Author	Risk Profile	Risk profile details in article
Abdallah et al., 2019	Low risk	Primigravida ≥ 37 weeks admitted in labor to the delivery unit. Women with BMI >30 kg/m ² , multiple pregnancy, fetal malpresentation, fetal demise, chorioamnionitis, meconium-stained liquor, associated medical disorder (hypertension, diabetes, autoimmune disease, etc), perinatal complication (e.g. placental abruption), fetal malformation or abnormal fetal growth were excluded from the study.
Agbaje et al., 2018	High-risk	Sickle cell anemia.
Alanwar et al., 2018	High-risk	Pregnancies complicated with severe pre-eclampsia.
Allam et al., 2013	High-risk	Suspected IUGR, oligohydramnios, preeclampsia, or placental vascular dysfunction documented by abnormal umbilical artery pulsatility index by local reference ranges.
Anshul et al., 2010	High-risk	SGA fetuses, some mothers had hypertensive disorder, anemia, and obstetric history
Bano et al., 2010	High risk	Clinical suspicion of IUGR
Dhand et al., 2011	High risk	SGA fetuses
Dorman et al., 2002	High-risk	Maternal falciparum malaria infection.
Ebrashy et al., 2005	High-risk	Pre-eclampsia women
Geerts et al., 2007	High-risk	Women with severe pre-eclampsia
Khanduri et al., 2013	High-risk	Clinical suspicion of IUGR
Kumari et al., 2019	High risk	Rhesus isoimmunized complicated pregnancies
Lakhkar et al., 2006	High risk	Preeclampsia and growth-restricted fetuses
Lakshmi et al., 2013	High-risk	IUGR, pregnancy induced hypertension, h/o previous intrauterine death
Malik et al., 2013	High-risk	IUGR; hypertensive disorder; pre-eclampsia
Masihi et al. 2019	Low risk	Women that had uncomplicated pregnancies
Mullick et al., 1993	Low and high-risk	Women attending routine antenatal (any risk profile).
Nagar et al., 2015	High risk	History of preeclampsia or eclampsia in previous pregnancy pre-existing medical disorders like: Diabetes, Renal disease, Epilepsy, Autoimmune disease, Thrombophilia, and Hypertension, History of IUGR or still birth, history of abruptio placentae, preeclampsia or pregnancy-induced hypertension current, Nulliparity, Extremes of age (<20 years and >35 years).
Najam et al., 2016	Low and high-risk	Pregnancies undergoing routine antenatal (any risk profile).
Nouh et al., 2011	High-risk	Primigravida with ovulatory polycystic ovary syndrome (PCOS)

Pares et al., 2008	High-risk	Fetuses at risk for anemia because of maternal alloimmunization to red-cell antigens
Pattinson et al., 1991	High risk	SGA, preeclampsia and pregnancy wastage
Pattinson et al., 1993	Low and high-risk	Pregnancies undergoing routine antenatal (any risk profile).
Phupong et al., 2003	Low-risk	Healthy pregnant women
Rani et al., 2016	Low and high-risk	Women attending routine antenatal (any risk profile).
Rocca et al., 1995	High risk	Pre-eclampsia women
Verma et al., 2016	Low-risk	Women with uncomplicated pregnancies
Waa et al., 2010	Low and high-risk	Women undergoing routine antenatal (any risk profile).
Yelikar et al., 2013	High-risk	Preeclampsia and growth-restricted fetuses
Zarean et al., 2018	Low-risk	Women that had uncomplicated pregnancies

^aFGR: fetal growth restriction; LBW: low birth weight; NICU: neonatal intensive care unit. High risk: pregnancies with any underlying condition that threatens the health or life of the mother or her foetus.

Any risk profile: unselected pregnancies (pregnancies undergoing routine antenatal). Low risk: Uncomplicated pregnancies or healthy pregnant women

Appendix S4. Risk of bias assessment results of the 30 studies included in the analysis**First Author:** Abdallah et al., 2018**ID:** 68614233

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e., individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate				x	
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Agbaje et al., 2018

ID: 6377433

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?		x			
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Alanwar et al., 2018

ID: 6377464

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

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First Author: Allam et al., 2013

ID: 6377480

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]		x			
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Anshul et al., 2010

ID: 6377837

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate				x	
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	High risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).		x			
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?					x
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	High risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting			x		
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	High risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= High risk of bias						

First Author: Bano et al., 2010

ID: 74903018

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]		x			
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]			x		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	High risk of bias				
Study confounding	Do the authors address potential confounders?			x		
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	High risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= high risk of bias						

First Author: Dhand et al., 2011

ID: 6379383

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate				x	
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).		x			
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori		x			
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	High risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	High risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting			x		
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	High risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= High risk of bias						

First Author: Dorman et al., 2002

ID: 6377862

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data	x				
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Ebrashy et al., 2005

ID: 6377887

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Geerts et al., 2007

ID: 6378017

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).		x			
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Khanduri et al., 2013

ID: 6378321

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?		x			
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Kumari et al., 2019

ID: 68614385

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]		x			
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate				x	
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Lakhkar et al., 2006

ID: 74903014

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]		x			
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Lakshmi et al., 2013

ID: 6378401

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data			x		
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Malik et al., 2013

ID: 6378519

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics			x		
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	High risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).			x		
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori				x	
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	High risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= High risk of bias						

First Author: Masihi et al., 2019

ID: 68614415

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate			x		
	Participants lost to follow-up are adequately described for key characteristics			x		
	Statement as to the possible effect on the results from missing data			x		
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Mullick et al., 1993

ID: 6378675

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori		x			
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Nagar et al., 2015

ID: 6378692

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Najam et al., 2016

ID: 6378705

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]			x		
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]			x		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	High risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate		x			
	Participants lost to follow-up are adequately described for key characteristics		x			
	Statement as to the possible effect on the results from missing data			x		
	Loss to follow-up is not associated with key characteristics	High risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	High risk of bias				
Study confounding	Do the authors address potential confounders?				x	
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	High risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting			x		
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	High risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= High risk of bias						

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First Author: Nouh et al., 2011

ID: 6378752

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Pares et al., 2008

ID: 6378809

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Pattinson et al., 1991

ID: 74903015

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Pattinson et al., 1993

ID: 6378815

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Phupong et al., 2003

ID: 6378830

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Rani et al., 2016

ID: 74903020

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori		x			
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

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First Author: Rocca et al., 1995

ID: 74903016

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Verma et al., 2016

ID: 6379243

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

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First Author: Waa et al., 2010

ID: 6379255

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data	x				
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Yelikar et al., 2013

ID: 6379339

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate		x			
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Zarean et al., 2018

ID: 6379369

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

Table S1. Statistical measures of prognostic performance of Doppler ultrasound reported in the selected studies

Prognostic determinant	Outcome	Studies	Sn	Sp	PPV	NPV	AUROC	Diagnostic accuracy	OR [95% CI]	RR [95% CI]	Correlation	Normal Doppler n (%)	Abnormal Doppler n (%)	
UA flow impedance	FGR	Agbaje et al., 2018	67.00	53.00			0.63							
		Mullick et al., 1993	85.00	89.00	88.50									
		Najam et al., 2016	48.15	80.67	53.06	77.40								
		Rocca et al., 1995	92.30	91.90	77.40	97.60		92.0						
		Khanduri et al., 2013	73.80	75.90	87.70	55.40		75.00						
		Bano et al., 2010	46.70	93.30	87.50	63.60		70.00						
		Nagar et al., 2015	42.86	94.62	37.50	95.65								
	NICU Admission	Anshul et al., 2010											13 (24.07)	36 (78.2)
		Najam et al., 2016	50.00	80.30	48.90	80.95								
	Fetal Distress	Anshul et al., 2010											18 (33)	35 (76)
		Rocca et al., 1995											2 (2.5)	12 (39)
		Najam et al., 2016	66.67	78.04	74.89	89.72								
		Yelikar et al., 2013	42.10	65.90	12.10	91.10								
	Stillbirth	Anshul et al., 2010											0 (0)	4 (9.5)
		Najam et al., 2016											0 (0)	5 (8.2)
	Perinatal death	Rocca et al., 1995											0 (0)	2 (6.5)
		Anshul et al., 2010											0 (0)	9 (60)
	LBW	Anshul et al., 2010											15 (27.0)	35 (77.8)
	Apgar Score	Rocca et al., 1995	80.00	82.40	41.00	96.00		83.00						
		Anshul et al., 2010											2 (3.7)	14 (82.35)
		Najam et al., 2016											3 (60.0)	6 (85.71)
		Agbaje et al., 2018										0.378		
	Fetal Anemia	Kumari et al., 2019										0.21		
	HIE	Najam et al., 2016											1 (1.29)	8 (16.31)
	MAS	Najam et al., 2016											1 (1.29)	16 (32.65)
	CAPO	Bano et al., 2010	79.20	92.40	79.20	92.20		88.90						
		Lakhkar et al 2006	50.00	59.00	66.60	41.90								

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1		Rani et al., 2016	17.80	95.80	80.70	50.50	0.57						
2		Geerts et al., 2007	75.00			95.00			0.6 (0.1, 4.1)				
3		Malik et al., 2013	64.40	80.00	96.60	20.00							
4		Pattinson et al., 1993	12.50	91.80	22.70	84.50							
5		Ebrashy et al., 2005	53.30	36.40	81.10	30.80							
6		Waa et al., 2010	8.00	100.00	0.00	26.00							
7													
8													
9	UA AREDF	Perinatal death	Lakshmi et al., 2013						9.8 (2.1, 46.4)				
10			Najam et al., 2016								2 (2.59)	4 (33.33)	
11		RDS	Lakshmi et al., 2013						2.4 (1.1, 5.0)				
12		CAPO	Pattinson et al., 1991	75.00	90.00	69.00							
13			Lakshmi et al., 2013						8.4 (2.3, 30.5)				
14													
15													
16	MCA flow impedance	FGR	Najam et al., 2016	59.25	88.89	72.72	81.35						
17			Bano et al., 2010	8.90	100.0	100.0	52.30		54.40				
18			Khanduri et al., 2013	26.20	92.60	89.20	35.00		46.10				
19		Fetal Anemia	Pares et al., 2008	100.00	65.00	90.90	100.0		92.20				
20			Kumari et al., 2019	68.00	57.00	83.00	33.00	0.70			-0.43		
21		NICU Admission	Najam et al., 2016	64.58	88.69	70.45	85.71						
22		Neonatal Acidosis	Allam et al., 2013	87.50	64.00	74.00	82.00	0.82					
23		Fetal Distress	Najam et al., 2016	72.73	78.05	54.55	91.53						
24		Stillbirth	Najam et al., 2016									0 (0)	2 (4.5)
25		Apgar Score	Najam et al., 2016									1 (1.29)	17 (38.6)
26		HIE	Najam et al., 2016									1 (1.29)	10 (22.72)
27		MAS	Najam et al., 2016									1 (1.29)	20 (45.5)
28		CAPO	Bano et al., 2010	16.70	100.0	100.0	76.70		77.80				
29	Lakhkar et al 2006		41.60	90.90	88.20	48.70							
30	Rani et al., 2016		18.60	90.30	68.70	49.40	0.58						
31	Dhand et al., 2011		71.00	92.00	94.00	65.00							
32	Malik et al., 2013		7.70	90.00	87.50	9.80							
33	Ebrashy et al., 2005		41.00	63.60	80.00	23.30							
34	Waa et al., 2010		23.0	68.00	76.00	33.00							

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		Verma et al., 2016	48.20	95.40	84.40	78.20						
		Nouh et al., 2011	84.60	96.30	91.70	92.90						
		Malik et al., 2013	37.70	70.00	91.80	11.00						
		Zarean et al., 2018	37.50	73.30	48.40	63.70	0.55					
	FDA flow impedance	Fetal anemia	Pares et al., 2008	95.70	100.0	100.0	86.90		96.70			
		Kumari et al., 2019	87.00	57.00			0.80			-0.54		
		CAPO	Lakhkar et al 2006	44.40	59.00	64.00	56.50					
	FDA & MCA	Fetal anemia	Pares et al., 2008	98.40	100.0	100.0	91.70		98.60			
		Kumari et al., 2019	86.00	67.00	86.00	67.00						
	DV flow impedance	Neonatal Acidosis	Allam et al., 2013	100.0	57.00	72.0	100.0	0.88	80.00			
		CAPO	Geerts et al., 2007		92.0	33.0				0.3 (0.03, 4.6)		

^aUA: umbilical artery; MCA: middle cerebral artery; CPR: cerebroplacental ratio; UtA: uterine artery; FDA: fetal descending aorta; DV: ductus venosus; RI: resistive index; PI: pulsatility index; S/D ratio: systolic diastolic ratio; PSV: peak systolic velocity; MV: mean velocity; AREDF: absent and/or reversed end diastolic flow; FGR: fetal growth restriction; LBW: low birth weight; HIE: hypoxic ischemic encephalopathy; MAS: meconium aspiration syndrome; RDS: respiratory distress syndrome; NICU: neonatal intensive care unit; CAPO: composite adverse perinatal outcomes; Sn: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value; OR: odds ratio; RR: relative risk; and n (%): frequency (percentage).

Table S2. Definitions of adverse perinatal outcomes reported in the selected studies

First Author	Outcomes	Definition (detailed description in the article)
Abdallah et al., 2019	LBW	Not defined
	NICU admission	Not defined
	Stillbirth	Not defined
	Perinatal mortality	Not defined
	Low APGAR score (1min & 5min)	Not defined
Agbaje et al., 2018	FGR	Abnormal birth weight: defined as estimated foetal weight below the 10th percentile for gestational age and abdominal circumference below the 10th percentile for gestational age.
	Low APGAR score at 5 minutes	APGAR score less than 6
Alanwar et al., 2018	Acidosis	Neonatal acidemia of pH < 7.2
	NICU admission	New-born was admitted to the neo- natal intensive care unit
	Low APGAR score at 5 minutes	APGAR score < 7 at 5 min
Allam et al., 2013	Neonatal acidosis	Cord blood pH <7.25
Anshul et al., 2010	Stillbirth	Not defined
	Neonatal death	Not defined
	NICU admission	Admission required
	Foetal distress	Delivered by emergency caesarean section for suspected foetal distress
	LBW	Not defined
	Low APGAR score at birth.	APGAR score <7 at birth
Bano et al., 2010	Perinatal death	Not defined
	Foetal distress	Caesarean section for foetal distress (FD not defined)
	NICU admission	Not defined
	Low APGAR score at 5min	APGAR score <7 at 5 min
	FGR	Birth weight less than 10 th percentile for gestational age

	Composite adverse perinatal outcome	Not defined
Dhand et al., 2011	Composite adverse perinatal outcome	Abnormal foetal outcome (details not provided)
Dorman et al., 2002	Perinatal death	Not defined
	Preterm delivery	Delivery < 37 weeks
	LBW	Birth weight <2.5kg
Ebrashy et al., 2005	Acidosis	Neonatal acidaemia of pH<7.2 were present
	Composite adverse neonatal outcome	Neonatal morbidity (neonatal academia pH<7.2, 5-minute APGAR score <6, and/or admission to NICU)
Geerts et al., 2007	Composite adverse perinatal outcome	Poor outcome (perinatal demise or clinical/ultrasound signs of neurological compromise in the infant at the time of discharge from the tertiary institution)
Khanduri et al., 2013	FGR	Ponderal index was calculated as birth weight (in gm) per length (in cm ³). Ponderal index of <10 indicates growth restriction.
Kumari et al., 2019	Foetal anaemia	Haematocrit of the umbilical cord blood was used as the reference test to diagnose foetal anaemia (defined as haemoglobin <0.65 times the median for gestational age).
Lakhkar et al., 2006	Composite adverse perinatal outcome	Adverse perinatal outcome (Major and Minor). Major adverse outcomes were perinatal deaths including intrauterine and early neonatal deaths. Major complications like hypoxic ischemic encephalopathy, intraventricular haemorrhage, periventricular leukomalacia, pulmonary haemorrhage and necrotizing enterocolitis. Minor outcomes include-caesarean delivery for foetal distress, APGAR score below 7 at 5 minutes, admission to NICU (neonatal intensive care unit) for treatment.
Lakshmi et al., 2013	Neonatal death	Not defined
	Respiratory distress syndrome	Not defined
	Composite adverse perinatal outcome	Composite outcome of death or major neuro-morbidity at 12-18 months of corrected age, defined as presence of cerebral palsy or visual or hearing impairment.
Malik et al., 2013	Composite adverse perinatal outcome	Abnormal foetal outcome (IUGR, IUFD and perinatal mortality)
Masihi et al.2019	Intrapartum foetal distress	Emergency caesarean section for foetal distress
Mullick et al., 1993	FGR	Not defined
Nagar et al., 2015	FGR	Not defined
Najam et al., 2016	FGR	Not defined

	NICU admission	Not defined
	Foetal distress	Not defined
	Stillbirth	Not defined
	Neonatal death	Not defined
	Low APGAR score	Not defined
	Hypoxic ischemic encephalopathy	Not defined
	Meconium aspiration syndrome	Not defined.
Nouh et al., 2011	Composite adverse perinatal outcome	The presence of one or more of the following; miscarriage, gestational DM, PIH, PE, antepartum haemorrhage, intrauterine growth retardation, instrumental, caesarean delivery and preterm labour.
Pares et al., 2008	Foetal anaemia	Anaemia was considered moderate to severe when foetal haemoglobin concentrations were $< \text{or} = 0.64$ multiples of the median for gestational age.
Pattinson et al., 1991	Composite adverse perinatal outcome	Poor foetal outcome (details not provided).
Pattinson et al., 1993	Composite adverse perinatal outcome	Complications of pregnancy, namely intra-uterine growth retardation and proteinuric hypertension.
Phupong et al., 2003	FGR	Birth weight less than 10 percentile for gestational age.
Rani et al., 2016	Composite adverse perinatal outcome	Adverse perinatal outcome was defined as any of these: small for gestational age, still birth, APGAR score < 5 at 5 minutes, need of bag and mask ventilation for > 10 minutes or hypoxic ischemic encephalopathy, admission to neonatal intensive care unit (NICU) and caesarean section due to non-reassuring foetal heart rate.
Rocca et al., 1995	IUGR	Not defined.
	Low APGAR score 5mins	APGAR score < 7 at 5 minutes.
	Perinatal death	Not defined.
	Foetal distress	Emergency operative delivery for foetal distress.
Verma et al., 2016	FGR	Not defined.
	LBW	Birth weight < 2500 gm.
	Preterm delivery	Spontaneous delivery < 37 weeks.

	Composite adverse perinatal outcome	At least one adverse outcome (preeclampsia, FGR, low birth weight, spontaneous preterm delivery, oligohydramnios, foetal loss).
Waa et al., 2010	Composite adverse perinatal outcome	Poor outcome was defined by foetal mortality or appearance, pulse rate, grimace, activity, respiration (APGAR) score less than eight at five minutes or weight less than 10 th percentile for gestation 20 or head circumference and length below 10 th percentile for gestation.
Yelikar et al., 2013	Intrapartum foetal distress	Delivered by emergency caesarean section for suspected foetal distress.
Zarean et al., 2018	Composite adverse perinatal outcome	Adverse perinatal outcome, including preterm labour, intrauterine foetal death, PE, low 5-min APGAR score (<7), low umbilical arterial cord blood pH, admitted to Intensive Care Unit in the first 3 days of birth, low birth weight, infant with low weight, death of new-born, caesarean section for respiratory distress, and meconial amniotic fluid.

^aFGR: fetal growth restriction; FGR: intrauterine growth restriction; LBW: low birth weight; NICU: neonatal intensive care unit.

Reporting checklist for systematic review and meta-analysis.

Based on the PRISMA guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the PRISMA reporting guidelines, and cite them as:

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	Reporting Item	Page Number
Title		
	#1 Identify the report as a systematic review, meta-analysis, or both.	1
Abstract		
Structured summary	#2 Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	2
Introduction		
Rationale	#3 Describe the rationale for the review in the context of what is already known.	3
Objectives	#4 Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design	2

(PICOS).

Methods

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3	Methods		
4			
5	Protocol and	#5	Indicate if a review protocol exists, if and where it can be accessed (e.g.,
6	registration		Web address) and, if available, provide registration information including
7			the registration number.
8			
9			
10	Eligibility criteria	#6	Specify study characteristics (e.g., PICOS, length of follow-up) and report
11			characteristics (e.g., years considered, language, publication status) used
12			as criteria for eligibility, giving rational
13			
14			
15	Information	#7	Describe all information sources in the search (e.g., databases with dates
16	sources		of coverage, contact with study authors to identify additional studies) and
17			date last searched.
18			
19			
20	Search	#8	Present full electronic search strategy for at least one database, including
21			any limits used, such that it could be repeated.
22			
23			
24	Study selection	#9	State the process for selecting studies (i.e., for screening, for determining
25			eligibility, for inclusion in the systematic review, and, if applicable, for
26			inclusion in the meta-analysis).
27			
28			
29	Data collection	#10	Describe the method of data extraction from reports (e.g., piloted forms,
30	process		independently by two reviewers) and any processes for obtaining and
31			confirming data from investigators.
32			
33			
34	Data items	#11	List and define all variables for which data were sought (e.g., PICOS,
35			funding sources), and any assumptions and simplifications made.
36			
37			
38	Risk of bias in	#12	Describe methods used for assessing risk of bias in individual studies
39	individual studies		(including specification of whether this was done at the study or outcome
40			level, or both), and how this information is to be used in any data
41			synthesis.
42			
43			
44			
45	Summary	#13	State the principal summary measures (e.g., risk ratio, difference in
46	measures		means).
47			
48			
49	Planned methods	#14	Describe the methods of handling data and combining results of studies, if
50	of analysis		done, including measures of consistency (e.g., I ²) for each meta-analysis.
51			
52			
53	Risk of bias	#15	Specify any assessment of risk of bias that may affect the cumulative
54	across studies		evidence (e.g., publication bias, selective reporting within studies).
55			
56			
57	Additional	#16	Describe methods of additional analyses (e.g., sensitivity or subgroup
58			na
59			

analyses analyses, meta-regression), if done, indicating which were pre-specified.

Results

Study selection	#17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram .	6
Study characteristics	#18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citation.	6
Risk of bias within studies	#19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	5
Results of individual studies	#20	For all outcomes considered (benefits and harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	6-8
Synthesis of results	#21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency.	6-8
Risk of bias across studies	#22	Present results of any assessment of risk of bias across studies (see Item 15).	6
Additional analysis	#23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	na
Discussion			
Summary of Evidence	#24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers	8
Limitations	#25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	8
Conclusions	#26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
Funding			
Funding	#27	Describe sources of funding or other support (e.g., supply of data) for the systematic review; role of funders for the systematic review.	11

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2 This checklist was completed on 02. February 2021 using <https://www.goodreports.org/>, a tool made by the
3 [EQUATOR Network](#) in collaboration with [Penelope.ai](#)
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For peer review only

BMJ Open

Prognostic accuracy of antenatal Doppler ultrasound for adverse perinatal outcomes in low- and middle-income countries: a systematic review

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Keywords:	Ultrasound < RADIOLOGY & IMAGING, Prenatal diagnosis < OBSTETRICS, Ultrasonography < OBSTETRICS, Fetal medicine < OBSTETRICS

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5 1 **Prognostic accuracy of antenatal Doppler ultrasound for adverse perinatal outcomes in**
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7 2 **low- and middle-income countries: a systematic review**
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12 4 Sam Ali^{1,2*}, Simelina Heuving¹, Michael G. Kawooya², Josaphat Byamugisha³,
13
14 5 Diederick E. Grobbee¹, Aris T. Papageorgiou⁴, Kerstin Klipstein-Grobusch^{1,5}, Marcus
15
16
17 6 J. Rijken^{1,6}
18
19
20 7

21
22 8 ¹Julius Global Health, Julius Center for Health Sciences and Primary Care, University
23
24 9 Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.

25
26
27 10 ²Ernest Cook Ultrasound Research and Education Institute (ECUREI), Mengo Hospital,
28
29 11 Kampala, Uganda.

30
31
32 12 ³Department of Obstetrics and Gynecology, Makerere University College of Health
33
34 13 Sciences, Kampala, Uganda.

35
36
37 14 ⁴Nuffield Department of Women's and Reproductive Health, John Radcliffe Hospital,
38
39 15 University of Oxford, Oxford, United Kingdom.

40
41
42 16 ⁵Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health
43
44 17 Sciences, University of the Witwatersrand, Johannesburg, South Africa.

45
46
47 18 ⁶Department of Obstetrics and Gynecology, University Medical Center Utrecht, Utrecht
48
49 19 University, Utrecht, Netherlands.

50
51
52 20
53
54
55 21 **Corresponding author:**

56
57 22 Sam Ali
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60

1
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3
4
5 23 Department of research, Ernest Cook Ultrasound Research and Education Institute
6
7 24 (ECUREI), Mengo Hospital. Sir Albert Cook Road. P.O. Box 7161, Kampala, Uganda.
8
9
10 25 **Email:** S.Ali-2@umcutrecht.nl or alisambecker@gmail.com
11
12 26
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15 27 **Word count:** 2834
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20 29 **ABSTRACT**
21
22 30 **Objectives** This systematic review examined available literature on the prognostic
23
24 31 accuracy of Doppler ultrasound for adverse perinatal outcomes in LMIC.
25
26
27 32 **Design** We searched PubMed, Embase, Cochrane Library and Scopus from inception to
28
29 33 April 2020.
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31
32 34 **Setting** Observational or interventional studies from low- and middle-income countries
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34
35 35 **Participants** Singleton pregnancies of any risk profile.
36
37 36 **Interventions** Umbilical artery (UA), middle cerebral artery (MCA), cerebroplacental
38
39 37 ratio (CPR), uterine artery (UtA), fetal descending aorta (FDA), ductus venosus,
40
41 42 umbilical vein, and inferior vena cava.
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44 43
45 39 **Primary and secondary outcome measures.** Perinatal death, stillbirth, neonatal death,
46
47 40 expedited delivery for fetal distress, meconium-stained amniotic fluid, low birth weight,
48
49 41 fetal growth restriction (FGR), admission to neonatal intensive care unit, neonatal
50
51 42 acidosis, Apgar scores, preterm birth, fetal anemia, respiratory distress syndrome, length
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53 43 of hospital stay, birth asphyxia and composite adverse perinatal outcomes.
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5 44 **Results** We identified 2825 records, and 30 (including 4977 women) from Africa
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7 45 (40.0%, n= 12), Asia (56.7%, n= 17) and South America (3.3%, n= 01) were included.
8

9
10 46 Many individual studies reported associations and promising predictive values of UA
11
12 47 Doppler for various adverse perinatal outcomes mostly in high-risk pregnancies, and
13
14 48 moderate to high predictive values of MCA, CPR and UtA Dopplers for composite
15
16 49 adverse perinatal outcomes. A few studies suggested that the MCA and FDA may be
17
18 50 potent predictors of fetal anemia. No randomized clinical trial was found. Most studies
19
20 51 were of sub-optimal quality, poorly powered and characterized by wide variations in
21
22 52 outcome classifications, the timing for the Doppler tests and study populations.
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27 53 **Conclusion** Local evidence to guide how antenatal Doppler ultrasound should be used
28
29 54 in LMIC is lacking. Well-designed studies, preferably randomized clinical trials, are
30
31 55 required. Standardization of practice and classification of perinatal outcomes across
32
33 56 countries, following the international standards, is imperative.
34
35

36
37 57 **Keywords** Pregnancy, ultrasound, prenatal diagnosis, prenatal care, developing
38
39 58 countries, and systematic review.
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43 60 **Strengths and limitations of this study**

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45
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47 61 • This systematic review used the most optimal database combinations and
48
49 62 snowballing technique with no time restrictions to identify the records.
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52 63 • We comprehensively examined available literature on the prognostic accuracy of
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54 64 Doppler ultrasound for adverse pregnancy outcomes in low and middle-income
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56 65 countries.
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5 66 • Although only English language articles were included, it is unlikely that high
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7 67 impact papers were not identified.
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10 68 • Pooling and interpreting the data for wider clinical application was not possible
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12 69 due to the large heterogeneity across studies.
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71 INTRODUCTION

72 Stillbirths remain a major global challenge,¹ with nearly three million cases reported
73 annually.² The vast majority of the cases (98%) are contributed by low- and middle-
74 income countries (LMIC).³ These deaths have profound effects on the families and
75 communities involved, and strategies for reduction are of high societal importance. The
76 risk of adverse perinatal outcomes is higher in compromised fetuses than in normally
77 growing babies, and could be distinguishable using antenatal Doppler ultrasound.^{4,5}
78 Prenatal diagnosis of fetuses at risk provides a window for close monitoring and/or
79 expedited delivery of well-developed babies with the prospect of improving survival
80 and long-term wellbeing.⁴

81 The predictive performance of Doppler ultrasound for adverse perinatal
82 outcomes has been demonstrated in primary studies, systematic reviews and meta-
83 analysis from high-income countries (HIC), guiding the development of HIC practice
84 guidelines.⁶ The use of HIC guidelines for clinical guidance in LMIC without local
85 validation may be inappropriate given the differences in the prevalence of adverse
86 pregnancy outcomes in the two settings. For instance, the stillbirth rates per 1000 total
87 births (95% confidence interval) is 3.4 (3.4-3.5) in HIC, 25.5 (22.5-29.1) in Southern

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4 88 Asia and 28.7 (25.1-34.2) in sub-Saharan Africa.² Since the prevalence and severity of a
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7 89 disease influences the diagnostic or prognostic test performance, context-specific
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10 90 guidance is necessary.⁷ However, there are still knowledge gaps about the predictive
11
12 91 ability of antenatal Doppler for adverse pregnancy outcomes in LMIC.

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15 92 This systematic review examined existing literature on the prognostic accuracy
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17 93 of Doppler ultrasound for adverse perinatal outcomes in LMIC. The implications for
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20 94 clinical utility of the available local evidence to guide practice in LMIC are highlighted.

21 22 95 **MATERIAL AND METHODS**

23 24 25 96 **Protocol and registration**

26
27 97 This systematic review protocol was registered in the PROSPERO database:
28
29
30 98 CRD42019128546, and reported following the Preferred Reporting Items for a
31
32 99 Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The
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34
35 100 PRISMA-DTA Statement.⁸

36 37 101 **Eligibility criteria**

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39
40 102 We included observational (cohort or case-control) studies and randomized clinical
41
42 103 trials (RCTs) from LMIC (as per the World Bank country classifications in the year
43
44
45 104 2020) reporting the prognostic value of Doppler ultrasound for adverse perinatal
46
47 105 outcomes in singleton pregnancies of any risk profile. Doppler measurements of interest
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49
50 106 included umbilical artery (UA), middle cerebral artery (MCA), cerebroplacental ratio
51
52 107 (CPR), uterine artery (UtA), fetal descending aorta (FDA), ductus venosus (DV),
53
54
55 108 umbilical vein (UV) and inferior vena cava (IVC). Adverse perinatal outcomes (as
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57 109 defined in the included studies) were perinatal death, stillbirth, neonatal death,
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5 110 expedited delivery for fetal distress, meconium stained amniotic fluid, low birth weight,
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7 111 fetal growth restriction (FGR), admission to neonatal intensive care unit (NICU),
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10 112 neonatal acidosis, Apgar scores, preterm birth, fetal anemia, respiratory distress
11
12 113 syndrome (RDS), length of hospital stay, birth asphyxia, and composite adverse
13
14 114 perinatal outcomes (CAPO). Conference proceedings/posters that did not appear as full-
15
16 115 text papers, case reports and review articles without original data were excluded.

116 **Information sources and search**

117 We conducted a comprehensive literature search in PubMed (Medline), Embase,
118 Cochrane Library and Scopus for articles published from inception to April 07, 2020.
119 The search strategies (online supplementary appendix S1) were developed with the
120 support of a librarian at University Medical Center Utrecht. When applicable, pre-
121 defined search (Title/Abstract) and MeSH/Emtree terms were used. No limits were
122 applied to the searches.

123 **Study selection**

124 The records retrieved from the databases were exported to Endnote to eliminate
125 duplicates and then transferred to Rayyan for review and selection. Two reviewers (SA
126 and SH) independently assessed all studies for inclusion based on title and abstract.
127 Studies reporting any Doppler parameter and adverse pregnancy outcome of interest in
128 the title or abstract were further retrieved in full text and assessed by the same two
129 reviewers against full eligibility criteria. Disagreements were resolved by discussion or,
130 if required, we consulted the third review author (MJR).

131 **Data extraction**

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5 132 Using a pre-piloted data extraction sheet, two reviewers (SA and SH) independently
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7 133 extracted data on authors, study title, year of publication, aims of the study, study
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10 134 period, the number of women recruited, gestational age at Doppler ultrasound exam,
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12 135 method of pregnancy dating, pregnancy risk profile, blood vessels studied, pregnancy
13
14 136 outcomes (as defined in the primary study), and key results. If any relevant information
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16
17 137 was missing, the corresponding authors were contacted once by e-mail.

18 19 20 138 **Risk of bias assessment**

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22 139 Two raters (SA and SH) independently evaluated the risk of bias for each study using
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24 140 the quality in prognostic studies (QUIPS) tool.⁹ The risk of bias domains included study
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27 141 population, attrition, prognostic factor measurement, outcome measurement,
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30 142 confounding and statistical analysis. All the domains were separately judged by two
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32 143 raters as having a low, moderate or high risk of bias. Any disagreement during this
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35 144 process was resolved by contacting the third rater (MJR).

36 37 145 **Prognostic test accuracy measures**

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40 146 Doppler test prognostic performance measures, as reported in the selected studies, are
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42 147 presented in table S1. These included diagnostic test accuracy measures such as
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45 148 sensitivity, specificity, positive predictive values (PPV) and negative predictive values
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47
48 149 (NPV); measures of association; proportions; and correlations.

49 50 150 **Data synthesis and analysis**

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52 151 The results were narratively summarized. The large heterogeneity in the study
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55 152 populations, timing for Doppler tests, outcome definitions and prognostic performance
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5 153 measures in the included studies did not allow for a meta-analysis. If a study reported
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7 154 multiple Doppler indices, the most commonly used (pulsatility index) was selected.
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10 155 **Patient and public involvement**

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12 156 No patient was involved. The public was also not involved in the design, conduct and
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14 157 dissemination of this research.
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19 159 **RESULTS**

20 160 **Study selection**

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25 161 The 2825 records we identified through electronic searches were reduced to 2210 after
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27 162 the removal of duplicates, and 2162 were further excluded based on title and abstract
28
29
30 163 screening, retaining 48 records. After full-text assessment for eligibility, 23 studies were
31
32 164 excluded with reasons, and 25 remained (online supplementary appendix S2). Five
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35 165 additional records were identified through snowballing (Figure 1). Thirty studies,
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37 166 involving a total count of 4977 women and a median (interquartile range) sample size of
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40 167 100 (30 to 181) were included in the analysis (table 1).
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42 168 **Study characteristics**

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45 169 The selected studies were from Africa (40.0%, n = 12), Asia 17 (56.7%, n = 17) and
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47 170 South America (3.3%, n = 01). Twenty studies (67%) recruited high-risk pregnancies,
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50 171 six (16.7%) both high and low-risk populations, while five (16.7%) studied the low-risk
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52 172 group (online supplementary appendix S3). Thirteen (43.3%) studies did not specify a
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55 173 method of pregnancy dating, 13 (43.3%) assessed gestational age using last menstrual
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57 174 period (LMP) combined with ultrasound, three (10.0%) used ultrasound alone, and one
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5 175 (3.3%) study used LMP. No RCTs was identified, and no study provided data on the
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7 176 UV and IVC Dopplers (table 1). The reasons for undertaking the Doppler research
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9 177 varied by individual studies and included the prediction of the risk of FGR, fetal
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12 178 anemia, neonatal acidosis, among others (online supplementary appendix S3).

14 179 **Methodological quality of included studies**

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17 180 The results of the QUIPS assessment are provided in Figure 2 and online supplementary
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19 181 appendix S4. Overall, the risk of bias was low in 15 (50%), moderate in 10 (33.3%),
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21 182 and high in five (16.7%) studies. In the study population domain, the risk of bias was
22
23 183 low in 73.3%, moderate in 23.3%, and high in 3.3% of the studies. Selective reporting
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25 184 remarkably resulted in a moderate to high risk of bias for analysis and reporting in 20
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27 185 (66.7%) studies. We found a moderate to high risk of bias for outcome measurement in
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29 186 17 (56.7%) studies, mostly due to inconsistencies in outcome classifications (online
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31 187 supplementary table S2).

32 188 **Prognostic accuracy of antenatal Doppler ultrasound for adverse perinatal outcomes**

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35 189 Twenty studies evaluated the umbilical artery,¹⁰⁻²⁹ and seven reported its
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37 190 predictive values for FGR. The positive predictive values for FGR reported in the
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39 191 individual studies were between 77.40 and 88.5,^{11,16,21,24} while the area under the
40
41 192 receiver operating characteristic (AU ROC) curve was 0.63,¹⁷ mostly in high-risk
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43 193 pregnancies. The NPV ranged from 55.4 - 95.65.^{11,16,21,24} FGR was defined as birth
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45 194 weight or abdominal circumference below the 10th percentile in two studies,^{11,17}
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47 195 ponderal index less than 10 in one study,²¹ and was not defined in the remaining
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49 196 studies.^{16,24,26} Increased flow impedance in the UA had positive predictive values for
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5 197 composite adverse outcomes between 66.60 and 96.6 in high-risk pregnancies.^{11,13,19,23}
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7 198 All studies provided individual components of the CAPO except only one.¹¹ Absent or
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9 199 reversed end-diastolic flow (AREDF) in the UA was associated with poor pregnancy
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11 200 outcomes (perinatal death, odds ratio (OR) 9.8, 95% confidence interval (CI) 2.1 to
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13 201 46.4; CAPO: OR 2.4, 95% CI 1.1 to 5.0; and RDS: OR 8.4, 95% CI 2.3 to 30.5).^{14,22,26}
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17 202 The MCA was reported in 12 studies.^{11,12,13,15,19,21,23,26,28,30,31,32} The positive
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19 203 predictive values for fetal anemia in Rhesus (Rh) isoimmunized pregnancies requiring
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21 204 transfusion were between 83.0 - 90.9 and the AU ROC curve was 0.7.^{12,32} Fetal anemia
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23 205 was consistently defined as hemoglobin (Hb) \leq 0.64 g/dl in the two studies, though
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25 206 they recruited low numbers of women.^{12,32} MCA Doppler had a sensitivity of 87.5%,
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27 207 PPV of 74.0% and AU ROC curve of 0.82 for neonatal acidosis.³⁰ The positive
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29 208 predictive values for CAPO ranged from 80.0-100% in high-risk pregnancies,^{11,13,19,23,31}
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31 209 but two studies did not provide details of the individual components of the CAPO.^{11,31}
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37 210 Nine studies reported the prognostic value of CPR.^{11,13,15,19,20,23,26,33,34} CPR
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39 211 showed promising predictive value for adverse perinatal outcomes in unselected
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41 212 pregnancies in the third trimester. One study reported sensitivity 85.10, specificity
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43 213 89.72, PPV 80.70 and NPV 92.30 for FGR.²⁶ Two studies found sensitivity between
44
45 214 80.90 and 90.91%, and specificity between 50.0 and 78.04% for emergency caesarean
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47 215 section for fetal distress though the tests had poor positive predictive values.^{26,34}
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49 216 Abnormal CPR had positive predictive values for CAPO between 81.80 and 100% in
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51 217 high-risk pregnancies.^{11,13,15,23}
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5 218 Eight studies reported the prognostic value of UtA Doppler,^{14,23,25,35-39} and two
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7 219 showed positive predictive values of over 91.8% for CAPO in high-risk
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10 220 pregnancies.^{23,36} The remaining studies had poor predictive values for adverse perinatal
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12 221 outcomes.

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15 222 Three studies evaluated the prognostic accuracy of FDA Doppler.^{12,13,32} The
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17 223 FDA sensitivity for fetal anemia in Rh isoimmunized pregnancies ranged from 87.0% to
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19 224 95.7% when used in isolation.^{12,32} The sensitivity varied between 86.0% and 98.4% and
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21 225 positive predictive values ranged from 86.0- 100% when combined with the MCA.^{12,32}
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25 226 The DV was sampled in two studies undertaken in high-risk pregnancies.^{20,30}
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27 227 Abnormal DV had a sensitivity of 100, PPV of 72.0 and AU ROC curve of 0.88 for the
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29 228 prediction of neonatal acidosis, though this study included only 30 women between 36-
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31 229 41 weeks of gestation.³⁰ The second study found a borderline significance and positive
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33 230 predictive value of 92.0% for the prediction of composite adverse perinatal outcomes at
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35 231 24-34 weeks of gestation.²⁰
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40 232 **DISCUSSION**

41 233 **Summary of findings**

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45 234 Many individual studies showed that abnormal UA Doppler was associated with poor
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47 235 perinatal outcomes, mostly in high-risk pregnancies, and that abnormal UA, MCA, CPR
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49 236 and UtA Dopplers had moderate to high predictive values for composite adverse
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51 237 perinatal outcomes. A few studies suggested that abnormal MCA Doppler had high
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53 238 individual predictive value for fetal anemia, but performed better when combined with
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55 239 the FDA. However, the majority of the available evidence was of sub-optimal quality,
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5 240 based on a few poorly powered studies and had no RCTs. Further, wide variations in the
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7 241 populations studied, definitions of adverse perinatal outcomes and prognostic accuracy
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9 242 measures across studies was present. Thus, pooling and interpreting the evidence for
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12 243 wider clinical application was not possible.

14 244 **Implications for practice**

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17 245 Evidence from HIC suggests that adding Doppler studies into clinical diagnostic
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19 246 or prognostic rules improves pregnancy risk assessment,⁶ and are increasingly becoming
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21 247 integrated into their pregnancy management guidelines.^{4,6} The use of guidance based
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23 248 entirely on HIC data in daily practice in LMIC could be inappropriate considering the
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25 249 differences in the adverse pregnancy outcome rates in the two settings. The stillbirth
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27 250 rates in LMIC is approximately 10 times that of HIC,² a large variation likely to
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29 251 influence the predictive performance of diagnostic or prognostic tests.⁷ Thus, a proper
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31 252 understanding of existing literature from LMIC is important. This paper reports the
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33 253 findings of a systematic review of primary evidence on the prognostic value of antenatal
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35 254 Doppler ultrasound for adverse perinatal outcomes in LMIC.

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37 255 Abnormal blood flow patterns in the UA had moderate to high predictive values
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39 256 for FGR and was associated with poor outcomes in high-risk pregnancies. Similarly, a
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41 257 recent Cochrane review of RCTs from HIC suggests that using UA Doppler in high-risk
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43 258 pregnancies could reduce perinatal deaths by 30% (risk ratio 0.71, 95% CI 0.52 to 0.98),
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45 259 and lead to fewer obstetric interventions.⁴⁰ Despite some similarities with our findings,
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47 260 the definitions of adverse outcomes, including FGR were inconsistent (or not even
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49 261 defined in many studies included in this review) with recommended international
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standards,^{4,41} and with no clear distinction between early and late FGR. Scanty data from this review indicate that abnormal CPR, UA, MCA and UtA Doppler could be predictive of CAPO. However, in a previous systematic review from HIC, CPR had low predictive accuracy (pooled sensitivity: 57%, specificity: 77%, and summary positive likelihood ratio (LR): 2.5, and negative LR: 0.60) for CAPO in pregnancies with suspected FGR antenatally.⁴² In another review, CPR was significantly better than UA and MCA Doppler in predicting CAPO ($P < 0.001$) and emergency delivery for fetal distress in singleton pregnancies of all risk profiles,⁴³ but the primary studies reviewed had numerous methodological limitations.⁴³ Further, first-trimester UtA Doppler had very low sensitivity 25.8% (95% CI 15.5 to 39.7) for CAPO in a systematic review of 18 studies (involving 55974 women).⁴⁴ More data from HIC indicate that MCA-PSV reliably predicts fetal anemia in un-transfused fetuses.⁴⁵ The area under the hierarchical summary ROC curve for moderate-severe anemia in untransfused fetuses was 87%, pooled sensitivity 86% (95% CI 75 to 93%) and specificity 71% (95% CI 49 to 87%).⁴⁵ Similarly, in our study, MCA alone or when combined with FDA had high predictive values for fetal anemia in Rh isoimmunized pregnancies, but this was based on only three studies. Overall, this review found that high-quality studies on the predictive accuracy of Doppler ultrasound for adverse perinatal outcomes in LMIC were scarce. The large heterogeneity across studies precluded a meta-analysis and between-study comparisons.

282 **Implications for research**

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5 283 Future studies need to specify the methods and timing for pregnancy dating.
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7 284 Accurate dating is crucial for timing the Doppler tests and interventions to expedite
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10 285 delivery in compromised fetuses. The interpretation and comparison of Doppler studies
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12 286 could be improved by using standard outcome definitions and completeness in
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15 287 reporting.⁴⁶ Most primary studies in this review studied the predictive ability of a single
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17 288 variable (Doppler test) for the outcome(s) of interest, without considering existing
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19 289 characteristics of clinical importance to estimate pregnancy risk. The predictive
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22 290 accuracies of new determinants need to be assessed individually and by multivariable
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25 291 analysis to facilitate the clinical applicability of the findings. The clinical applicability
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27 292 of Doppler ultrasound also depends on the clinical judgement of the Doppler
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30 293 measurements and the feasibilities of local healthcare systems to interpret and respond
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32 294 to the results of the Doppler scan. Along the same line, our recently concluded
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35 295 prospective cohort study in a rural sub-Saharan African setting will soon highlight the
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37 296 prognostic value of Doppler ultrasound in the late third trimester and the feasibilities of
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40 297 integrating such advanced technologies into routine antenatal care in LMIC.

41 42 298 **Strengths and limitations**

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45 299 A strength of this systematic review is that it was conducted according to a registered
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47 300 protocol, using the most optimal database combinations and snowballing with no time
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50 301 restrictions. However, it is possible that some studies performed in low-resource
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52 302 settings, may not have been indexed in the searched databases. Although we only
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55 303 included English language articles, it is unlikely that high impact papers were not
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57 304 identified. Further, this review primarily aimed to thoroughly examine the current
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5 305 evidence on the predictive value of Doppler ultrasound for adverse perinatal outcomes
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7 306 in LMIC using a meta-analysis. However, due to the inherent limitations in the included
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10 307 studies such as large heterogeneity in the study populations, inconsistencies in the
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12 308 definition of pregnancy outcomes, differences in the gestational age at the Doppler
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15 309 study and prognostic accuracy measures reported, we were only able to present our
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17 310 findings narratively. A future updated systematic review and meta-analysis of high-
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20 311 quality evidence is recommended.

21 22 312 **CONCLUSION**

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25 313 This review demonstrated that a scientific basis to provide evidence for how antenatal
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27 314 Doppler should be used in LMIC is lacking. Well-designed studies, preferably
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30 315 randomized clinical trials, testing application models of antenatal Doppler while
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32 316 respecting the local conditions are needed. Moreover, local practice and classification of
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35 317 perinatal outcomes need to be standardized, utilizing approaches consistent with
36
37 318 international consensus.

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49
50 323 language review.

51 52 324 **Author contributions**

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4 325 SA, SH, KKG, and MJR drafted the protocol and conducted the review. MGK, JB,
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7 326 DEG, and ATP critically reviewed the work for important intellectual content. All the
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10 327 authors approved the final manuscript.

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19
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21 332 **Competing interests**

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23
24 333 None

25 334 **Data sharing statement**

26
27 335 No additional data are available.

28 336 **Ethics statements**

29 337 **Patient consent for publication**

30 338 Not required.

31 339 **Ethics approval**

32 340 Given this is a systematic review, ethics approval is not required.

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17 490 outcome sets in women’s and newborn health: a systematic review. *BJOG An Int*
18 491 *J Obstet Gynaecol.* 2017 Sep 1;124(10):1481–9.
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30 496 **LEGENDS**

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33 497 **Online supplementary data legends**

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35 498 **Appendix S1.** Search strings for the databases used to retrieve articles.

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37 499 **Appendix S2.** List of full-text articles excluded with reasons.

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39 500 **Appendix S3.** The aims of the selected studies and risk profiles of the women recruited

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41 501 **Appendix S4.** Risk of bias assessment results of the 30 studies included in the analysis.

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43 502 **Table S1.** Statistical measures of prognostic performance of Doppler ultrasound

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45 503 reported in the selected studies.

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47 504 **Table S2.** Definitions of adverse perinatal outcomes reported in the selected studies

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51 506 **Figures legends**

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53 507 **Figure 1.** PRIMA flow diagram
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5 508 **Figure 2.** Risk of bias assessment results of the 30 included studies

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10 510 **Figure 2 key**

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12 511  Low-risk of bias

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17 513  Moderate-risk of bias

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22 515  High-risk of bias

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27 517 **Table legends**

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30 518 **Table 1** Summary of studies included in the systematic review of current evidence on
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32 519 the prognostic value of Doppler ultrasound for predicting adverse pregnancy outcomes
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35 520 in LMIC.

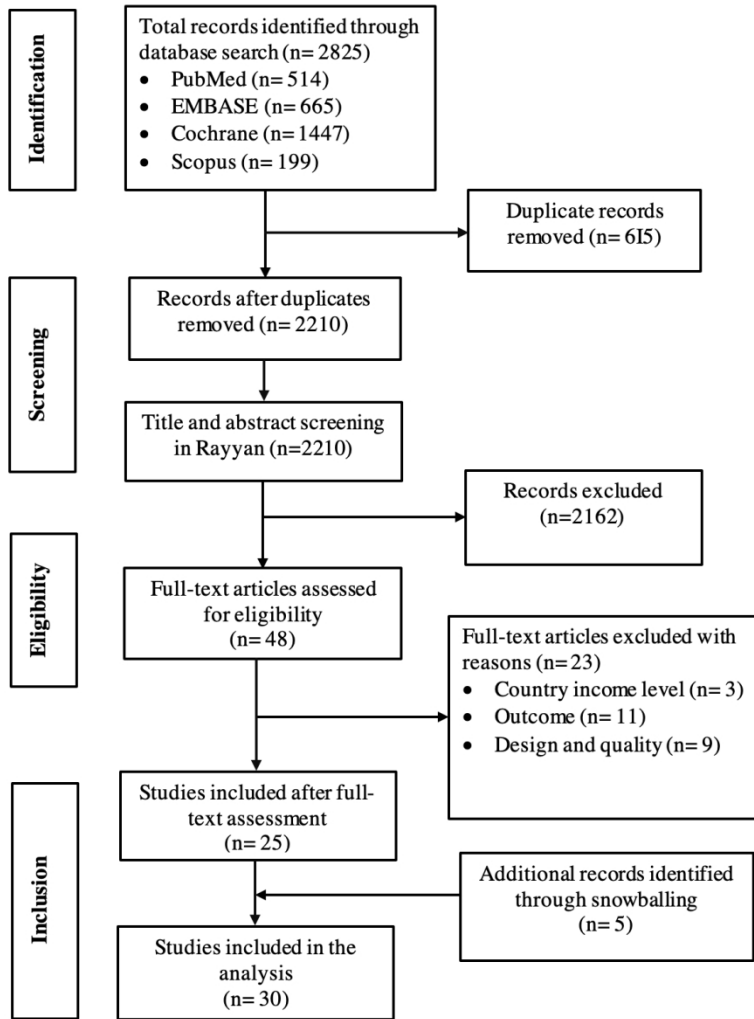
Table 1

Author, Year	Country	Study Period	Women	Weeks	Study Design	Vessels	Abnormal Doppler Thresholds
Abdallah, 2019. ¹⁰	Egypt	2015-2017	92	≥ 37	Cohort	UA	UA (RI, PI and S/D ratio) > 95 th centile
Agbaje, 2018. ¹⁷	Nigeria	2014-2015	120	26	Cohort	UA	S/D ratio > 95 th percentile, RI > 95 th percentile, and AREDF.
Alanwar, 2018. ³³	Egypt	2017	100	30 - 40	Cohort	CPR	CPR PI < 1 or CPR PI < 5 th percentile.
Allam, 2013. ³⁰	Egypt	2007- 2010	30	36 - 41	Cohort	MCA, DV	MCA S/D ratio <4.37, DV RI > 0.29, or Decrease in a-, v- and d- waves, or reversed flow in both a- and v-waves.
Anshul, 2010. ¹⁸	India	2005-2007	100	≥ 28	Cohort	UA	S/D ratio ≥ 3 or AREDF.
Bano, 2010. ¹¹	India	Not stated	90	30 - 41	Cohort	UA, MCA, CPR	MCA < 2SD; UA > 2SD or CPR PI < 1.08
Dhand, 2011. ³¹	India	2005- 2006	121	28 - 41	Cohort	MCA	Not specified
Dorman, 2002. ³⁵	Kenya	1996- 1997	854	24 - 31	Cohort	UtA	Early diastolic notch or mean/ipsilateral UtA RI ≥ 0.58
Ebrashy, 2005. ¹⁹	Egypt	2002- 2003	80	≥ 28	Case-control	UA, MCA, CPR	UA RI > 0.72, MCA RI < 0.69, CPR RI < 1.0
Geerts, 2007. ²⁰	South Africa	Not stated	113	24 - 34	Cohort	UA, CPR, DV	UA PI >95 th centile; UA/MCA >1; DV PI > 95 th centile.
Khanduri, 2013. ²¹	India	2009- 2011	60	23 - 37	Cohort	UA, MCA	UA PI > 1.42 or UA RI > 0.72, MCA PI < 1.1, MCA RI < 0.59

Kumari, 2019. ¹²	India	2015-2016	30		Cohort	UA, MCA, FDA	MCA PSV > 1.50 MoM, FDA PSV delta > 70. Not specified for UA
Lakhkar, 2006. ¹³	India	2001-2002	58	> 30	Cohort	UA, MCA, CPR, FDA	S/D ratio, RI or PI of UA > 2SD; MCA < 5 th centile; FDA > 2SD; CPR PI or S/D ratio < 1.0
Lakshmi, 2013. ²²	India	2007- 2008	238	< 35	Cohort	UA	Absent and/or reversed end-diastolic flow (AREDF)
Malik, 2013. ²³	India	2010- 2011	100	31 - 41	Cohort	UA, MCA, CPR, UtA	Not specified
Masihi, 2019. ³⁴	Iran	2016- 2017	181	38 - 40	Cohort	CPR	CPR PI <1.94
Mullick, 1993. ²⁴	India	Not stated	73	22 - 26, 30 - 32, > 37	Cohort	UA	S/D ratio >= 4 (26 weeks), 3.5 (30-32 weeks) and 3 (37-40 weeks)
Nagar, 2015. ²⁵	India	2009 - 2011	500	26 - 30	Cohort	UA, UtA	UA (S/D ratio or RI) > 95 th centile or AREDF. UtA S/D ratio > 95 th centile
Najam, 2016. ²⁶	India	Not stated	150	28 - 40	Cohort	UA, MCA, CPR	UA S/D ratio > 2SD, or AREDF, MCA SD ratio < 5 th percentile, MCA/UA SD ratio of < 1.0
Nouh, 2011. ³⁶	Egypt	2009-2011	80	8 - 12, 26	Case-control	UtA	UtA PI > 95 th percentile, and/or Unilateral or bilateral notch
Pares, 2008. ³²	Brasil	1997- 2005	46	20 - 34	Cohort	MCA, FDA	FDA-MV >= 2SD MCA-PSV >= 1.5 MoM

Pattinson, 1991. ¹⁴	South Africa	1987-1989	53	16 - 28	Cohort	UA, UtA	UA RI > 95 th centile UtA RI > 0.58
Pattinson, 1993. ²⁷	South Africa	1990	496	16 - 24	Cohort	UA	UA RI > 95 th centile
Phupong, 2003. ³⁷	Thailand	2000- 2001	322	22 - 28	Cohort	UtA	Unilateral or bilateral early diastolic notch
Rani, 2016. ¹⁵	India	2012-2014	223	30 - 36	Cohort	UA, MCA, CPR	UA PI > 1.03, UA RI > 0.695; MCA PI < 1.2 MCA RI < 0.75; CPR PI < 1.08 or CPR RI < 1.05.
Rocca, 1995. ¹⁶	Egypt	Not stated	113	>= 28	Cohort	UA	UA S/D ratio >= 3
Verma, 2016. ³⁸	India	Not stated	165	22 - 24	Cohort	UtA	Bilateral diastolic notches or mean UtA PI > 1.15 (UtA PI > 95 th centile).
Waa, 2010. ²⁸	Kenya	2007	100	>= 28	Cohort	MCA, UA	MCA RI < 0.71, and UA > 0.71.
Yelikar, 2013. ²⁹	India	Not stated	189	> 32	Cohort	UA	UA S/D ratio > 90 th centile or AREDF
Zarean, 2018. ³⁹	Iran	2015- 2016	100	30 - 34	Cohort	UtA	UtA PI > 95 th centile

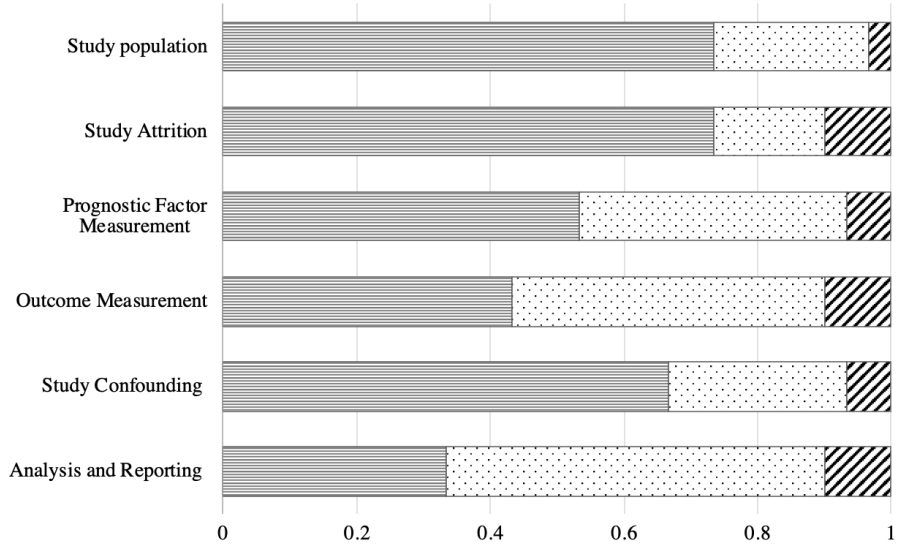
^aLMP: last menstrual period; UA: umbilical artery; MCA: middle cerebral artery; CPR: cerebroplacental ratio; UtA: uterine artery; FDA: fetal descending aorta; DV: ductus venosus; RI: resistive index; PI: pulsatility index; S/D ratio: systolic diastolic ratio; PSV: peak systolic velocity; MV: mean velocity; AREDF: absent and/or reversed end diastolic flow.



PRISMA flow diagram

273x283mm (144 x 144 DPI)

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Risk of bias assessment results of the 30 included studies

482x350mm (72 x 72 DPI)

Appendix S1. Search strings for the databases used to retrieve articles

EMBASE

(‘developing countr*’:ti,ab,kw OR ‘developing nation*’:ti,ab,kw OR ‘developing population*’:ti,ab,kw OR ‘developing econom*’:ti,ab,kw OR ‘undeveloped countr*’:ti,ab,kw OR ‘undeveloped nation*’:ti,ab,kw OR ‘undeveloped economy’:ti,ab,kw OR ‘undeveloped economies’:ti,ab,kw OR ‘least developed countr*’:ti,ab,kw OR ‘least developed nation*’:ti,ab,kw OR ‘least developed economy’:ti,ab,kw OR ‘least developed economies’:ti,ab,kw OR ‘less-developed countr*’:ti,ab,kw OR ‘less-developed nation*’:ti,ab,kw OR ‘less-developed population’:ti,ab,kw OR ‘less-developed populations’:ti,ab,kw OR ‘less-developed econom*’:ti,ab,kw OR ‘lesser developed countr*’:ti,ab,kw OR ‘lesser developed nation*’:ti,ab,kw OR ‘lesser developed population’:ti,ab,kw OR ‘lesser developed populations’:ti,ab,kw OR ‘lesser developed economy’:ti,ab,kw OR ‘lesser developed economies’:ti,ab,kw OR ‘under-developed countr*’:ti,ab,kw OR ‘under-developed nation*’:ti,ab,kw OR ‘underdeveloped countr*’:ti,ab,kw OR ‘underdeveloped nation*’:ti,ab,kw OR ‘underdeveloped population*’:ti,ab,kw OR ‘underdeveloped econom*’:ti,ab,kw OR ‘low income countr*’:ti,ab,kw OR ‘middle income countr*’:ti,ab,kw OR ‘low income nation*’:ti,ab,kw OR ‘middle income nation*’:ti,ab,kw OR ‘low income population*’:ti,ab,kw OR ‘middle income population*’:ti,ab,kw OR ‘low income econom*’:ti,ab,kw OR ‘middle income econom*’:ti,ab,kw OR ‘lower income countr*’:ti,ab,kw OR ‘lower income nation*’:ti,ab,kw OR ‘lower income population*’:ti,ab,kw OR ‘lower income economy’:ti,ab,kw OR ‘lower income economies’:ti,ab,kw OR ‘resource limited’:ti,ab,kw OR ‘low resource countr*’:ti,ab,kw OR ‘lower resource countr*’:ti,ab,kw OR ‘low resource nation*’:ti,ab,kw OR ‘low resource population*’:ti,ab,kw OR ‘low resource economy’:ti,ab,kw OR ‘low resource economies’:ti,ab,kw OR ‘underserved countr*’:ti,ab,kw OR ‘underserved nation*’:ti,ab,kw OR ‘underserved population*’:ti,ab,kw OR ‘underserved economy’:ti,ab,kw OR ‘underserved economies’:ti,ab,kw OR ‘under-served country’:ti,ab,kw OR ‘under-served countries’:ti,ab,kw OR ‘under-served nation’:ti,ab,kw OR ‘under-served nations’:ti,ab,kw OR ‘under-served population’:ti,ab,kw OR ‘under-served populations’:ti,ab,kw OR ‘underserved economy’:ti,ab,kw OR ‘underserved economies’:ti,ab,kw OR ‘derived countr*’:ti,ab,kw OR ‘deprived nation’:ti,ab,kw OR ‘deprived nations’:ti,ab,kw OR ‘derived population*’:ti,ab,kw OR ‘deprived economy’:ti,ab,kw OR ‘deprived economies’:ti,ab,kw OR ‘poor countr*’:ti,ab,kw OR ‘poor nation*’:ti,ab,kw OR ‘poor population*’:ti,ab,kw OR ‘poor econom*’:ti,ab,kw OR ‘poorer countr*’:ti,ab,kw OR ‘poorer nation*’:ti,ab,kw OR ‘poorer population*’:ti,ab,kw OR ‘poorer econom*’:ti,ab,kw OR ‘Imic’:ti,ab,kw OR ‘Imics’:ti,ab,kw OR ‘lami’:ti,ab,kw OR ‘transitional countr*’:ti,ab,kw OR ‘transitional nation’:ti,ab,kw OR ‘transitional nations’:ti,ab,kw OR ‘transitional econom*’:ti,ab,kw OR ‘transition countr*’:ti,ab,kw OR ‘transition nation*’:ti,ab,kw OR ‘transition econom*’:ti,ab,kw OR low ‘resource setting*’:ti,ab,kw OR ‘lower resource setting*’:ti,ab,kw OR ‘middle resource setting*’:ti,ab,kw OR ‘Third World*’:ti,ab,kw OR ‘south east asia*’:ti,ab,kw OR ‘middle east*’:ti,ab,kw OR ‘Afghan*’:ti,ab,kw OR ‘Angola*’:ti,ab,kw OR ‘Angolese*’:ti,ab,kw OR ‘Angolian*’:ti,ab,kw OR ‘Armenia*’:ti,ab,kw OR ‘Bangladesh*’:ti,ab,kw OR ‘Benin*’:ti,ab,kw OR ‘Bhutan*’:ti,ab,kw OR ‘Birma*’:ti,ab,kw OR ‘Burma*’:ti,ab,kw OR ‘Birmese*’:ti,ab,kw OR ‘Burmese*’:ti,ab,kw OR ‘Boliv*’:ti,ab,kw OR ‘Botswan*’:ti,ab,kw OR ‘burkina Faso*’:ti,ab,kw OR ‘Burundi*’:ti,ab,kw OR ‘Cabo Verde*’:ti,ab,kw OR ‘Cambod*’:ti,ab,kw OR ‘Cameroon*’:ti,ab,kw OR ‘Cape Verd*’:ti,ab,kw OR ‘Central Africa*’:ti,ab,kw OR ‘Chad’:ti,ab,kw OR ‘Comoro*’:ti,ab,kw OR ‘Congo*’:ti,ab,kw OR ‘Cote d/Ivoire*’:ti,ab,kw OR ‘Djibouti*’:ti,ab,kw OR ‘East Africa*’:ti,ab,kw OR ‘Eastern Africa*’:ti,ab,kw OR ‘Egypt*’:ti,ab,kw OR ‘El Salvador*’:ti,ab,kw OR ‘Equatorial Guinea*’:ti,ab,kw OR ‘Eritre*’:ti,ab,kw OR ‘Ethiopia*’:ti,ab,kw OR ‘Gabon*’:ti,ab,kw OR ‘Gambia*’:ti,ab,kw OR ‘Gaza*’:ti,ab,kw OR ‘Georgia Republic’/exp OR

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 6 PDR*':ti,ab,kw OR 'Laos*':ti,ab,kw OR 'Lesotho*':ti,ab,kw OR 'Liberia*':ti,ab,kw OR
 7 'Madagascar*':ti,ab,kw OR 'Malaw*':ti,ab,kw OR 'Mali*':ti,ab,kw OR 'Mauritan*':ti,ab,kw OR
 8 'Mauriti*':ti,ab,kw OR 'Micronesi*':ti,ab,kw OR 'Mocambiqu*':ti,ab,kw OR 'Moldov*':ti,ab,kw
 9 OR 'Mongolia*':ti,ab,kw OR 'Morocc*':ti,ab,kw OR 'Mozambiqu*':ti,ab,kw OR
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 17 Lanka*':ti,ab,kw OR 'Sub Saharan Africa*':ti,ab,kw OR 'Subsaharan Africa*':ti,ab,kw OR
 18 'Sudan*':ti,ab,kw OR 'Swaziland*':ti,ab,kw OR 'Syria*':ti,ab,kw OR 'Tajikist*':ti,ab,kw OR
 19 'Tanzan*':ti,ab,kw OR 'Timor*':ti,ab,kw OR 'Togo*':ti,ab,kw OR 'Tonga*':ti,ab,kw OR
 20 'Tunis*':ti,ab,kw OR 'Ugand*':ti,ab,kw OR 'Ukrain*':ti,ab,kw OR 'Uzbekistan*':ti,ab,kw OR
 21 'Vanuatu*':ti,ab,kw OR 'Vietnam*':ti,ab,kw OR 'West Africa*':ti,ab,kw OR 'West Bank*':ti,ab,kw
 22 OR 'Western Africa*':ti,ab,kw OR 'Yemen*':ti,ab,kw OR 'Zaire*':ti,ab,kw OR 'Zambia*':ti,ab,kw
 23 OR 'Zimbabw*':ti,ab,kw)

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31 ('Umbilical Arter*/exp OR 'Uterine Artery'/exp OR 'Middle Cerebral Artery'/exp OR 'Ductus
 32 Venosus'/exp OR 'Umbilical Vein*/exp OR 'Inferior Cava Vein'/exp OR 'Umbilical
 33 Arter*':ti,ab,kw OR 'Uterine Arter*':ti,ab,kw OR 'Middle Cerebral Arter*':ti,ab,kw OR 'Patent
 34 Ductus Venosus':ti,ab,kw OR 'Umbilical Vein*':ti,ab,kw OR 'Inferior Vena Cava':ti,ab,kw OR
 35 'Cerebroplacental Ratio':ti,ab,kw OR 'CPR':ti,ab,kw OR 'Fetal Descending Aorta':ti,ab,kw OR
 36 'FDA':ti,ab,kw OR 'Doppler Ultrasonography'/exp OR 'Doppler Ultrasound*':ti,ab,kw OR
 37 'Doppler Ultrasonography':ti,ab,kw OR 'Uterine Artery Doppler':ti,ab,kw)

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42 ('Stillbirth':ti,ab,kw OR 'Perinatal Death':ti,ab,kw OR 'Cesarean Section*':ti,ab,kw OR 'Caesarean
 43 Section*':ti,ab,kw OR 'Acidosis':ti,ab,kw OR 'Premature Birth':ti,ab,kw OR 'Neonatal Intensive
 44 Care':ti,ab,kw OR 'Fetal Growth Retard*':ti,ab,kw OR 'Newborn Respiratory Distress
 45 Syndrome*':ti,ab,kw OR 'Gestational Age':ti,ab,kw OR 'Birth Weight':ti,ab,kw OR 'Asphyxia
 46 Neonatorum':ti,ab,kw OR 'Apgar Score*':ti,ab,kw OR 'Length of Stay':ti,ab,kw OR 'Stillbirth'/exp
 47 OR 'Perinatal Death'/exp OR 'Perinatal Mortality'/exp OR 'Cesarean Section'/exp OR
 48 'Acidosis'/exp OR 'Prematurity'/exp OR 'Newborn Intensive Care'/exp OR 'Intrauterine Growth
 49 Retardation'/exp OR 'Neonatal Respiratory Distress Syndrome'/exp OR 'Gestational Age'/exp OR
 50 'Birth Weight'/exp OR 'Newborn Hypoxia'/exp OR 'Apgar Score'/exp OR 'Length of Stay'/exp OR
 51 'Pregnancy':ti,ab,kw OR 'Pregnancies':ti,ab,kw OR 'Gestation':ti,ab,kw OR 'Pregnant':ti,ab,kw OR
 52 'Pregnancy'/exp)

PUBMED (MEDLINE)

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OR Somalia*[tw] OR South Africa*[tw] OR South Sudan*[tw] OR Southern Africa*[tw] OR Sri Lanka*[tw] OR Sub Saharan Africa*[tw] OR Subsaharan Africa*[tw] OR Sudan*[tw] OR Swaziland*[tw] OR Syria*[tw] OR Tajikist*[tw] OR Tanzan*[tw] OR Timor*[tw] OR Togo*[tw] OR Tonga*[tw] OR Tunis*[tw] OR Ugand*[tw] OR Ukrain*[tw] OR Uzbekistan*[tw] OR Vanuatu*[tw] OR Vietnam*[tw] OR West Africa*[tw] OR West Bank*[tw] OR Western Africa*[tw] OR Yemen*[tw] OR Zaire*[tw] OR Zambia*[tw] OR Zimbabw*[tw])

AND

("Umbilical Arteries"[Mesh] OR "Uterine Artery"[Mesh] OR "Middle Cerebral Artery"[Mesh] OR "Ductus Venosus" [Supplementary Concept] OR "Umbilical Veins"[Mesh] OR "Vena Cava, Inferior"[Mesh] OR Umbilical Arter*[tiab] OR Uterine Arter*[tiab] OR Middle Cerebral Arter*[tiab] OR Patent Ductus Venosus[tiab] OR Umbilical Vein*[tiab] OR Inferior Vena Cava[tiab] OR Cerebroplacental Ratio[tiab] OR CPR[tiab] OR Fetal Descending Aorta[tiab] OR FDA[tiab] OR "Ultrasonography, Doppler"[Mesh] OR Doppler Ultrasound*[Title/Abstract] OR Doppler Ultrasonography[Title/Abstract] OR Uterine Artery Doppler[Title/Abstract])

AND

("Stillbirth"[tiab] OR "Perinatal Death"[tiab] OR "Caesarean Section*"[tiab] OR "Caesarean Section*"[tiab] OR Acidosis[tiab] OR Premature Birth[tiab] OR Neonatal Intensive Care"[tiab] OR Fetal Growth Retard*[tiab] OR Newborn Respiratory Distress Syndrome*[tiab] OR Gestational Age[tiab] OR Birth Weight[tiab] OR Asphyxia Neonatorum[tiab] OR Apgar Score*[tiab] OR Length of Stay"[tiab] OR "Stillbirth"[Mesh] OR "Perinatal Death"[Mesh] OR "Caesarean Section"[Mesh] OR "Acidosis"[Mesh] OR "Premature Birth"[Mesh] OR "Intensive Care, Neonatal"[Mesh] OR "Fetal Growth Retardation"[Mesh] OR "Respiratory Distress Syndrome, Newborn"[Mesh] OR "Gestational Age"[Mesh] OR "Birth Weight"[Mesh] OR "Asphyxia Neonatorum"[Mesh] OR "Apgar Score"[Mesh] OR "Length of Stay"[Mesh] OR Pregnancy[Title/Abstract] OR Pregnancies[Title/Abstract] OR Gestation[Title/Abstract] OR Pregnant[Title/Abstract] OR "Pregnancy"[Mesh])

COCHRANE

‘developing countr*’ OR ‘developing nation*’ OR ‘developing population*’ OR ‘developing econom*’ OR ‘undeveloped countr*’ OR ‘undeveloped nation*’ OR ‘undeveloped economy’ OR ‘undeveloped economies’ OR ‘least developed countr*’ OR ‘least developed nation*’ OR ‘least developed economy’ OR ‘least developed economies’ OR ‘less-developed countr*’ OR ‘less-developed nation*’ OR ‘less-developed population’ OR ‘less-developed populations’ OR ‘less-developed econom*’ OR ‘lesser developed countr*’ OR ‘lesser developed nation*’ OR ‘lesser developed population’ OR ‘lesser developed populations’ OR ‘lesser developed economy’ OR ‘lesser developed economies’ OR ‘under-developed countr*’ OR ‘under-developed nation*’ OR ‘underdeveloped countr*’ OR ‘underdeveloped nation*’ OR ‘underdeveloped population*’ OR ‘underdeveloped econom*’ OR ‘low income countr*’ OR ‘middle income countr*’ OR ‘low income nation*’ OR ‘middle income nation*’ OR ‘low income population*’ OR ‘middle income population*’ OR ‘low income econom*’ OR ‘middle income econom*’ OR ‘lower income countr*’ OR ‘lower income nation*’ OR ‘lower income population*’ OR ‘lower income economy’ OR ‘lower income economies’ OR ‘resource limited’ OR ‘low resource countr*’ OR ‘lower resource countr*’ OR ‘low resource nation*’ OR ‘low resource population*’ OR ‘low resource economy’ OR ‘low resource economies’ OR ‘underserved countr*’ OR ‘underserved nation*’ OR ‘underserved

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 OR 'Congo*' OR 'Cote d'Ivoire*' OR 'Djibouti*' OR 'East Africa*' OR 'Eastern Africa*' OR
 'Egypt*' OR 'El Salvador*' OR 'Equatorial Guinea*' OR 'Eritre*' OR 'Ethiopia*' OR 'Gabon*'
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 'Haiti*' OR 'Hondur*' OR 'India*' OR 'Indones*' OR 'Ivory Coast*' OR 'Kenya*' OR 'Kiribati*'
 OR 'Kosovo*' OR 'Kyrgyz*' OR 'Lao PDR*' OR 'Laos*' OR 'Lesotho*' OR 'Liberia*' OR
 'Madagascar*' OR 'Malaw*' OR 'Mali' OR 'Mauritan*' OR 'Mauriti*' OR 'Micronesi*' OR
 'Mocambiqu*' OR 'Moldov*' OR 'Mongolia*' OR 'Morocc*' OR 'Mozambiqu*' OR 'Myanmar*'
 OR 'Namibia*' OR 'Nepal*' OR 'Nicaragua*' OR 'Niger*' OR 'North Korea*' OR 'Northern
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 OR 'Philippine*' OR 'Principe' OR 'Rhodesia*' OR 'Rwanda*' OR 'Samoa*' OR 'Sao Tome*'
 OR 'Senegal*' OR 'Sierra Leone*' OR 'Solomon Islands*' OR 'Somalia*' OR 'South Africa*' OR
 'South Sudan*' OR 'Southern Africa*' OR 'Sri Lanka*' OR 'Sub Saharan Africa*' OR 'Subsaharan
 Africa*' OR 'Sudan*' OR 'Swaziland*' OR 'Syria*' OR 'Tajikist*' OR 'Tanzan*' OR 'Timor*'
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 'Vanuatu*' OR 'Vietnam*' OR 'West Africa*' OR 'West Bank*' OR 'Western Africa*' OR
 'Yemen*' OR 'Zaire*' OR 'Zambia*' OR 'Zimbabw*'

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'Umbilical Arter*' OR 'Uterine Artery' OR 'Middle Cerebral Artery' OR 'Ductus Venosus' OR
 'Umbilical Vein*' OR 'Inferior Cava Vein' OR 'Uterine Arter*' OR 'Middle Cerebral Arter*' OR
 'Patent Ductus Venosus' OR 'Inferior Vena Cava' OR 'Cerebroplacental Ratio' OR 'CPR' OR
 'Fetal Descending Aorta' OR 'FDA' OR 'Doppler Ultrasonography' OR 'Doppler Ultrasound*'
 OR 'Doppler Ultrasonography' OR 'Uterine Artery Doppler'

AND

'Stillbirth' OR 'Perinatal Death' OR 'Caesarean Section*' OR 'Caesarean Section*' OR 'Acidosis'
 OR 'Premature Birth' OR 'Neonatal Intensive Care' OR 'Fetal Growth Retard*' OR 'Newborn
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 OR 'Newborn Intensive Care' OR 'Intrauterine Growth Retardation' OR 'Neonatal Respiratory
 Distress Syndrome' OR 'Gestational Age' OR 'Birth Weight' OR 'Newborn Hypoxia' OR 'Length
 of Stay' OR 'Pregnancy' OR 'Pregnancies' OR 'Gestation' OR 'Pregnant'

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TITLE-ABS-KEY("developing countr*" OR "developing nation*" OR "developing population*" OR "developing econom*" OR "undeveloped countr*" OR "undeveloped nation*" OR "undeveloped economy" OR "undeveloped economies" OR "least developed countr*" OR "least developed nation*" OR "least developed economy" OR "least developed economies" OR "less-developed countr*" OR "less-developed nation*" OR "less-developed population" OR "less-developed populations" OR "less-developed econom*" OR "lesser developed countr*" OR "lesser developed nation*" OR "lesser developed population" OR "lesser developed populations" OR "lesser developed economy" OR "lesser developed economies" OR "under-developed countr*" OR "under-developed nation*" OR "underdeveloped countr*" OR "underdeveloped nation*" OR "underdeveloped population*" OR "underdeveloped econom*" OR "low income countr*" OR "middle income countr*" OR "low income nation*" OR "middle income nation*" OR "low income population*" OR "middle income population*" OR "low income econom*" OR "middle income econom*" OR "lower income countr*" OR "lower income nation*" OR "lower income population*" OR "lower income economy" OR "lower income economies" OR "resource limited" OR "low resource countr*" OR "lower resource countr*" OR "low resource nation*" OR "low resource population*" OR "low resource economy" OR "low resource economies" OR "underserved countr*" OR "underserved nation*" OR "underserved population*" OR "underserved economy" OR "underserved economies" OR "under-served country" OR "under-served countries" OR "under-served nation" OR "under-served nations" OR "under-served population" OR "under-served populations" OR "underserved economy" OR "underserved economies" OR "derived countr*" OR "deprived nation" OR "deprived nations" OR "derived population*" OR "deprived economy" OR "deprived economies" OR "poor countr*" OR "poor nation*" OR "poor population*" OR "poor econom*" OR "poorer countr*" OR "poorer nation*" OR "poorer population*" OR "poorer econom*" OR "lmic" OR "lmics" OR "lami" OR "transitional countr*" OR "transitional nation" OR "transitional nations" OR "transitional econom*" OR "transition countr*" OR "transition nation*" OR "transition econom*" OR low "resource setting*" OR "lower resource setting*" OR "middle resource setting*" OR "Third World*" OR "south east asia*" OR "middle east*" OR "Afghan*" OR "Angola*" OR "Angolese*" OR "Angolian*" OR "Armenia*" OR "Bangladesh*" OR "Benin*" OR "Bhutan*" OR "Birma*" OR "Burma*" OR "Birmese*" OR "Burmese*" OR "Boliv*" OR "Botswan*" OR "burkina Faso*" OR "Burundi*" OR "Cabo Verde*" OR "Cambod*" OR "Cameroon*" OR "Cape Verd*" OR "Central Africa*" OR "Chad" OR "Comoro*" OR "Congo*" OR "Cote d'Ivoire*" OR "Djibouti*" OR "East Africa*" OR "Eastern Africa*" OR "Egypt*" OR "El Salvador*" OR "Equatorial Guinea*" OR "Eritre*" OR "Ethiopia*" OR "Gabon*" OR "Gambia*" OR "Gaza*" OR "Georgia Republic" OR "Ghan*" OR "Guatemal*" OR "Guinea" OR "Haiti*" OR "Hondur*" OR "India*" OR "Indones*" OR "Ivory Coast*" OR "Kenya*" OR "Kiribati*" OR "Kosovo*" OR "Kyrgyz*" OR "Lao PDR*" OR "Laos*" OR "Lesotho*" OR "Liberia*" OR "Madagascar*" OR "Malaw*" OR "Mali" OR "Mauritan*" OR "Mauriti*" OR "Micronesi*" OR "Mocambiqu*" OR "Moldov*" OR "Mongolia*" OR "Morocc*" OR "Mozambiqu*" OR "Myanmar*" OR "Namibia*" OR "Nepal*" OR "Nicaragua*" OR "Niger*" OR "North Korea*" OR "Northern Korea*" OR "Democratic People/s Republic of Korea" OR "Pakistan*" OR "Papua New Guinea*" OR "Philippine*" OR "Principe" OR "Rhodesia*" OR "Rwanda*" OR "Samoa*" OR "Sao Tome*" OR "Senegal*" OR "Sierra Leone*" OR "Solomon Islands*" OR "Somalia*" OR "South Africa*" OR "South Sudan*" OR "Southern Africa*" OR "Sri Lanka*" OR "Sub Saharan Africa*" OR "Subsaharan Africa*" OR "Sudan*" OR "Swaziland*" OR "Syria*" OR "Tajikist*" OR "Tanzan*" OR "Timor*" OR "Togo*" OR "Tonga*" OR "Tunis*" OR "Ugand*" OR "Ukrain*" OR "Uzbekistan*" OR "Vanuatu*" OR "Vietnam*" OR "West Africa*" OR "West Bank*" OR "Western Africa*" OR "Yemen*" OR "Zaire*" OR "Zambia*" OR "Zimbabw*")

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7 TITLE-ABS-KEY("Stillbirth" OR "Perinatal Death" OR "Caesarean Section*" OR "Caesarean
8 Section*" OR "Acidosis" OR "Premature Birth" OR "Neonatal Intensive Care" OR "Fetal Growth
9 Retard*" OR "Newborn Respiratory Distress Syndrome*" OR "Gestational Age" OR "Birth
10 Weight" OR "Asphyxia Neonatorum" OR "Apgar Score*" OR "Length of Stay" OR "Stillbirth" OR
11 "Perinatal Death" OR "Caesarean Section" OR "Acidosis" OR "Premature Birth" OR "Intensive Care,
12 Neonatal" OR "Fetal Growth Retardation" OR "Respiratory Distress Syndrome, Newborn" OR
13 "Gestational Age" OR "Birth Weight" OR "Asphyxia Neonatorum" OR "Apgar Score" OR "Length
14 of Stay" OR "Pregnancy" OR "Pregnancies" OR "Gestation" OR "Pregnant" OR "Pregnancy")
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17 AND
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20 TITLE-ABS-KEY("Umbilical Arteries" OR "Uterine Artery" OR "Middle Cerebral Artery" OR
21 "Ductus Venosus" OR "Umbilical Veins" OR "Vena Cava, Inferior" OR "Umbilical Arter*" OR
22 "Uterine Arter*" OR "Middle Cerebral Arter*" OR "Patent Ductus Venosus" OR "Umbilical Vein*"
23 OR "Inferior Vena Cava" OR "Cerebroplacental Ratio" OR "CPR" OR "Fetal Descending Aorta"
24 OR "FDA" OR "Ultrasonography, Doppler" OR "Doppler Ultrasound*" OR "Doppler
25 Ultrasonography" OR "Uterine Artery Doppler")
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Appendix S2. List of full-text articles excluded with reasons

a) Country income level: 3 studies

1. El Shourbagy, S., Elsakhawy, M. (2012). Prediction of fetal anemia by middle cerebral artery Doppler. *Middle East Fertility Society Journal*, 17(4), 275-282.
2. Haley, J., Tuffnell, D. J., Johnson, N. (1997). Randomized controlled trial of cardiotocography versus umbilical artery Doppler in the management of small for gestational age fetuses. *British Journal of Obstetrics and Gynaecology*, 104(4), 431-435).
3. Morales-Rosello, J., Dias, T., Khalil, A., Fornes-Ferrer, V., Ciammella, R., Gimenez-Roca, L., Perales-Marin, A., Thilaganathan, B. (2018). Birth-weight differences at term are explained by placental dysfunction and not by maternal ethnicity. *Ultrasound Obstet Gynecol*, 52(4), 488-493.

b) Design and quality: 9 studies

1. Abidoye, I. A., Ayoola, O. O., Idowu, B., Aderibigbe, A. S., Loto, O. M. (2017). Uterine artery Doppler velocimetry in hypertensive disorder of pregnancy in Nigeria. *J Ultrason*, 17(71) 253-258.
2. Agarwal, R., Tiwari, A., Wadhwa, N., Radhakrishnan, G., Bhatt, S., Batra, P. (2017). Abnormal umbilical artery Doppler velocimetry and placental histopathological correlation in fetal growth restriction. *South African Journal of Obstetrics and Gynaecology*, 23(1), 12-16.
3. Ali, A., Ara, I., Sultana, R., Akram, F., Zaib, M. J. (2014). Comparison of perinatal outcome of growth restricted fetuses with normal and abnormal umbilical artery Doppler waveforms. *Journal of Ayub Medical College, Abbottabad: JAMC*, 26(3), 344-348.
4. Kumar, S., Datta, S., Mittal, S., Roy, K. K. (2002). Doppler flow studies in middle cerebral and umbilical arteries in growth retarded and normal pregnancies. *JK Science*, 4(0), 185-189
5. Mufenda, J., Gebhardt, S., van Rooyen, R., Theron, G. (2015). Introducing a Mobile-Connected Umbilical Doppler Device (UmbiFlow) into a Primary Care Maternity Setting: Does This Reduce Unnecessary Referrals to Specialised Care? Results of a Pilot Study in Kraaifontein, South Africa. *PLoS One*, 10(11) e0142743.
6. Nguku, S. W., Wanyoike-Gichuhi, J., Aywak, A. A. (2006). Biophysical profile scores and resistance indices of the umbilical artery as seen in patients with pregnancy induced hypertension. *East African Medical Journal*, 83(3), 96-101
7. Nkosi, S., Makin, J., Hlongwane, T. M. A. G., & Pattinson, R. C. (2019). Screening and managing a low-risk pregnant population using continuous-wave Doppler ultrasound in a low-income population: A cohort analytical study. *SAMJ: South African Medical Journal*, 109(5), 347-352.
8. Siddiqui, T. S., Asim, A., Ali, S., Tariq, A. (2014). Comparison of perinatal outcome in growth restricted fetuses retaining normal umbilical artery Doppler flow to those with diminished end-diastolic flow. *Journal of Ayub Medical College, Abbottabad: JAMC*, 26(2), 221-224.
9. Kachewar, S. G., Gandage, S. G., Pawar, H. J. (2012). An Indian study of novel non-invasive method of screening for foetal anaemia. *Journal of Clinical and Diagnostic Research*, 6(4), 688-691.

c) Outcomes: 11 studies

1. Adekanmi, A. J., Roberts, A., Akinmoladun, J. A., & Adeyinka, A. O. (2019). Uterine and umbilical artery doppler in women with pre-eclampsia and their pregnancy outcomes. *Nigerian Postgraduate Medical Journal*, 26(2), 106.
2. El Behery, M. M., Siam, S., Seksaka, M. A., Mansou, S. M. (2013). Uterine artery Doppler and urinary hyperglycosylated HCG as predictors of threatened abortion outcome. *Middle East Fertility Society Journal*, 19(1), 42-46.
3. El-Mashad, A. I., Mohamed, M. A., Elahadi Farag, M. A., Ahmad, M. K., Ismail, Y. (2011). Role of uterine artery Doppler velocimetry indices and plasma adrenomedullin level in women with unexplained recurrent pregnancy loss. *Journal of Obstetrics and Gynaecology Research*, 37(1), 51-57.
4. Geerts, L., Van der Merwe, E., Theron, A., Rademan, K. (2016). Placental insufficiency among high-risk pregnancies with a normal umbilical artery resistance index after 32 weeks. *Int J Gynaecol Obstet*, 135(1), 38-42.
5. Kumar, B. S., Sarmila, K., Prasad, K. S. (2012). Prediction of preeclampsia by midtrimester uterine artery doppler velocimetry in high-risk and low-risk women. *Journal of Obstetrics and Gynecology of India*, 62(3), 297-300.
6. Maged, A. M., Elnassery, N., Fouad, M., Abdelhafiz, A., Al Mostafa, W. (2015). Third-trimester uterine artery Doppler measurement and maternal postpartum outcome among patients with severe pre-eclampsia. *International Journal of Gynecology and Obstetrics*, 131(1), 49-53.
7. Prajapati, S. R., Maitra, N. (2013). Prediction of pre-eclampsia by a combination of history, uterine artery doppler, and mean arterial pressure (A Prospective Study of 200 Cases). *Journal of Obstetrics and Gynecology of India*, 63(1), 32-36.
8. Sebastian, A., Raj, T. S., Yenuberi, H., Job, V., Varuhghese, S., & Regi, A. (2019). Angiogenic factors and uterine artery Doppler in predicting preeclampsia and associated adverse outcomes in a tertiary hospital in south India. *Pregnancy hypertension*, 16, 26.
9. Shehata, N. A. A., Ali, H. A. A., Hassan, A., Katta, M. A., Ali, A. S. F. (2018). Doppler and biochemical assessment for the prediction of early pregnancy outcome in patients experiencing threatened spontaneous abortion. *Int J Gynaecol Obstet*, 143(2), 150-155.
10. Yusuf, M., Galadanci, H., Ismail, A., Aliyu, L. D., Danbatta, A. H. (2017). Uterine artery doppler velocimetry for the prediction of preeclampsia among high-risk pregnancies in low-resource setting: Our experience at aminu Kano teaching hospital, Kano, Nigeria. *Donald School Journal of Ultrasound in Obstetrics and Gynecology*, 11(3), 197-202
11. Puri, M. S., Deshpande, H., Kohli, S., Sharma, K., Singhania, S. (2013). A study of uterine artery colour doppler at 20-24 weeks gestation as a predictor of pregnancy induced hypertension and intra uterine growth restriction from industrial town in Western India. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 4(1), 698-705.

Appendix S3. The aims of the selected studies and risk profiles of the women recruited

First Author	Aim of study	Dating method	Risk Profile	Participant risk profile details in the article
Abdallah et al., 2019	To study the value of umbilical artery Doppler indices in predicting the risk of intrapartum and neonatal outcomes in pregnancies with and without nuchal cord.	LMP or first trimester ultrasound	Low risk	Primigravida ≥ 37 weeks admitted in labor to the delivery unit. Women with BMI >30 kg/m ² , multiple pregnancy, fetal malpresentation, fetal demise, chorioamnionitis, meconium-stained liquor, associated medical disorder (hypertension, diabetes, autoimmune disease, etc.), perinatal complication (e.g. placental abruption), fetal malformation or abnormal fetal growth were excluded from the study.
Agbaje et al., 2018	To assess umbilical artery Doppler findings in women with sickle cell anemia in the local environment at the onset of the third trimester and compare with obstetric outcomes.	LMP and/or early dating sonograms	High-risk	Sickle cell anemia.
Alanwar et al., 2018	To assess the efficacy of fetal middle cerebral artery/umbilical artery pulsatility index ratio (cerebroplacental ratio CPR) in predicting the occurrence of adverse perinatal outcomes in pregnancies complicated with severe pre-eclampsia.	Not specified	High-risk	Pregnancies complicated with severe pre-eclampsia.
Allam et al., 2013	To investigate, in high-risk pregnancies, the prediction of neonatal acidosis using DV, MCA and UA Doppler studies and subsequently to determine the best parameters and cutoff values.	Not specified	High-risk	Suspected IUGR, oligohydramnios, preeclampsia, or placental vascular dysfunction documented by abnormal umbilical artery pulsatility index by local reference ranges.
Anshul et al., 2010	To evaluate the role of umbilical artery Doppler in growth-restricted fetuses.	LMP and first trimester dating scan	High-risk	SGA fetuses, some mothers had hypertensive disorder, anemia, bad obstetric history.
Bano et al., 2010	To evaluate the usefulness of the pulsatility index (PI) of the umbilical artery (UA) and that of the middle cerebral artery (MCA), as well as the ratio of the MCA PI to the UA PI (C/U ratio), in the diagnosis of small-for-gestational-age (SGA) fetuses and the prediction of adverse perinatal outcome.	Not specified	High risk	Clinical suspicion of FGR

1 2 3 4 5	Dhand et al., 2011	To compare the role of the middle cerebral artery and umbilical artery Doppler pulsatility indices in predicting the fetal outcome in intrauterine growth restriction.	LMP and fetal biometry <22weeks	High risk	SGA fetuses
6 7 8 9 10 11	Dorman et al., 2002	To determine whether impaired uteroplacental blood flow might account for the low infant birth weight associated with maternal falciparum malaria infection.	LMP and fetal biometry	High-risk	Maternal falciparum malaria infection.
12 13 14 15 16 17 18	Ebrashy et al., 2005	To evaluate the accuracy of middle cerebral/umbilical artery resistance index (C/U RI) ratio in predicting acidemia and low Apgar score at 5 minutes after birth in the infants of women with preeclampsia.	Fetal biometry (BPD, AC and FL)	High-risk	Pre-eclampsia women
19 20 21 22 23	Geerts et al., 2007	To assess the prognostic value of ultrasound findings and fetoplacental Doppler indices in severe preterm preeclampsia in identifying fetuses at high risk of death, major morbidity or long-term compromise.	LMP and fetal biometry	High-risk	Women with severe pre-eclampsia
24 25 26 27 28	Khanduri et al., 2013	To measure the pulsatility index (PI) and resistive index (RI) of the middle cerebral artery (MCA) and umbilical artery (UA) in predicting fetal growth restriction.	LMP and first or second trimester ultrasound	High-risk	Clinical suspicion of FGR
29 30 31 32 33	Kumari et al., 2019	To assess the correlation between fetal blood vessel Doppler measurements and fetal anemia among Rhesus isoimmunized pregnancies after two intrauterine transfusions as a potential guide to therapy.	Not specified	High risk	Rhesus isoimmunized complicated pregnancies
34 35 36 37 38 39 40 41 42 43	Lakhkar et al., 2006	To determine and compare the diagnostic performance of Doppler sonography of fetal middle cerebral artery (MCA), descending abdominal aorta (DAA), umbilical artery (UA), umbilical vein (UV) and inferior vena cava (IVC) for prediction of adverse perinatal outcome in suspected intrauterine growth retardation (IUGR) and pre-eclampsia (PET).	LMP, clinical gestational age, 1 st or 2 nd trimester biometry	High risk	Preeclampsia and suspicion of growth-restricted fetuses

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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	Lakshmi et al., 2013	To determine outcomes of preterm infants with history of absent/reversed end-diastolic umbilical artery Doppler flow (AREDF) vs. infants with forward end-diastolic flow (FEDF).	LMP or first trimester ultrasound	High-risk	FGR, pregnancy induced hypertension, h/o previous intrauterine death
	Malik et al., 2013	To determine the role of ultrasonography in screening high-risk mothers for detection of IUGR, to find out the impact of fetal parameters on the extent of IUGR, correlation between the sonographic pattern of IUGR and the birth weight, and to find out the sensitivities of various fetal parameters and their evaluation against each other and against the birth weight.	LMP	High-risk	FGR; hypertensive disorder; pre-eclampsia
	Masihi et al.2019	To determine the relationship between the fetal middle cerebral artery and the umbilical artery ratio on color Doppler sonography with fetal distress at 38-40 weeks of gestation.	First trimester ultrasound	Low risk	Women that had uncomplicated pregnancies
	Mullick et al., 1993	To explore whether measurement of umbilical artery blood velocity waveform between 22 and 26 weeks might predict pregnancies destined to become complicated by pregnancy could induce hypertension (PIH) and/or fetal growth restriction (IUGR).	Not specified	Low and high-risk	Women attending routine antenatal (any risk profile).
	Nagar et al., 2015	To evaluate the predictive values of Uterine and Umbilical artery Doppler indices in high-risk pregnancies.	LMP and ultrasound before 21 weeks	High risk	History of preeclampsia or eclampsia in previous pregnancy pre-existing medical disorders like: Diabetes, Renal disease, Epilepsy, Autoimmune disease, Thrombophilia, and Hypertension, History of IUGR or still birth, history of abruptio placentae, preeclampsia or pregnancy-induced hypertension current, Nulliparity, Extremes of age (<20 years and >35 years).

Najam et al., 2016	To assess the predictive value of the cerebroplacental ratio in the detection of perinatal outcome in high-risk pregnancies in comparison to its components.	Not specified	Low and high-risk	Pregnancies undergoing routine antenatal (any risk profile).
Nouh et al., 2011	To assess the value of uterine artery Doppler screening during pregnancy in predicting adverse pregnancy outcomes in women with polycystic ovary syndrome (PCOS).	LMP and first trimester ultrasound	High-risk	Primigravida with ovulatory polycystic ovary syndrome (PCOS)
Pares et al., 2008	To evaluate the accuracy of middle cerebral artery peak systolic velocity (MCA-PSV) associated with descending thoracic aorta mean velocity (DTA-MV) in the prediction of fetal anemia.	Sonographic exam at <= 20 weeks	High-risk	Fetus at risk for anemia because of maternal alloimmunization to red-cell antigens
Pattinson et al., 1991	To investigate whether abnormalities in Doppler waveform can predict the outcome of pregnancy accurately before other clinical signs develop	LMP and biometry: 16-20 weeks	High risk	SGA, preeclampsia and pregnancy wastage
Pattinson et al., 1993	To describe the prevalence and natural history of absent end-diastolic velocities (AEDV) in the umbilical artery of the fetus between 16 and 24 weeks gestation, and to evaluate its role as a screening test for identifying high-risk pregnancies.	Not specified	Low and high-risk	Pregnancies undergoing routine antenatal (any risk profile).
Phupong et al., 2003	To assess the value of uterine artery notching as a screening test for preeclampsia and fetal growth restriction in a low-risk population of healthy pregnant women.	LMP and first trimester ultrasound	Low-risk	Healthy pregnant women
Rani et al., 2016	To assess the accuracy of the middle cerebral artery (MCA) and umbilical artery (UmA), pulsatility index (PI) and resistance index (RI) in predicting perinatal outcome in pregnancies complicated by preeclampsia with or without intrauterine growth restriction (IUGR).	Not specified	Low and high-risk	Women attending routine antenatal (any risk profile).

1 2 3 4	Rocca et al., 1995	To test the value of routine Doppler study of the umbilical artery to predict the perinatal outcome in pre-eclamptic patients.	Not specified	High risk	Pre-eclampsia women
5 6 7 8	Verma et al., 2016	To assess the predictive value of uterine artery Doppler imaging at 22-24 weeks of gestation for adverse pregnancy outcomes.	Not specified	Low-risk	Women with uncomplicated pregnancies
9 10 11 12 13	Waa et al., 2010	To assess the value of umbilical and middle cerebral artery doppler ultrasound values in predicting foetal outcome in high and low-risk pregnancies.	Not specified	Low and high-risk	Women undergoing routine antenatal (any risk profile).
14 15 16 17	Yelikar et al., 2013	To study the efficacy of fetal Doppler and Non-Stress Test (NST) in predicting fetal compromise in preeclampsia and growth-restricted fetuses.	Not specified	High-risk	Preeclampsia and growth-restricted fetuses
18 19 20 21	Zarean et al., 2018	To assess the diagnostic value of UtA-PI in the prediction of the adverse perinatal outcome at 30–34 week's gestation.	Not specified	Low-risk	Women that had uncomplicated pregnancies

^aFGR: fetal growth restriction; LBW: low birth weight; NICU: neonatal intensive care unit. High risk: pregnancies with any underlying condition that threatens the health or life of the mother or her foetus.

Any risk profile: unselected pregnancies (pregnancies undergoing routine antenatal). Low risk: Uncomplicated pregnancies or healthy pregnant women

Appendix S4. Risk of bias assessment results of the 30 studies included in the analysis**First Author:** Abdallah et al., 2018**ID:** 68614233

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e., individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate				x	
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Agbaje et al., 2018

ID: 6377433

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?		x			
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Alanwar et al., 2018

ID: 6377464

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Allam et al., 2013

ID: 6377480

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]		x			
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

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First Author: Anshul et al., 2010

ID: 6377837

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate				x	
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	High risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).		x			
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?					x
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	High risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting			x		
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	High risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= High risk of bias						

First Author: Bano et al., 2010

ID: 74903018

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]		x			
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]			x		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	High risk of bias				
Study confounding	Do the authors address potential confounders?			x		
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	High risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= high risk of bias						

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First Author: Dhand et al., 2011

ID: 6379383

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate				x	
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).		x			
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori		x			
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	High risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	High risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting			x		
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	High risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= High risk of bias						

First Author: Dorman et al., 2002

ID: 6377862

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data	x				
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Ebrashy et al., 2005

ID: 6377887

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Geerts et al., 2007

ID: 6378017

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).		x			
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Khanduri et al., 2013

ID: 6378321

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?		x			
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Kumari et al., 2019

ID: 68614385

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]		x			
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate				x	
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Lakhkar et al., 2006

ID: 74903014

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]		x			
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Lakshmi et al., 2013

ID: 6378401

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data			x		
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Malik et al., 2013

ID: 6378519

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics			x		
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	High risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).			x		
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori				x	
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	High risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= High risk of bias						

First Author: Masihi et al., 2019

ID: 68614415

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate			x		
	Participants lost to follow-up are adequately described for key characteristics			x		
	Statement as to the possible effect on the results from missing data			x		
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Mullick et al., 1993

ID: 6378675

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori		x			
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Nagar et al., 2015

ID: 6378692

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Najam et al., 2016

ID: 6378705

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]			x		
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]			x		
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	High risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate		x			
	Participants lost to follow-up are adequately described for key characteristics		x			
	Statement as to the possible effect on the results from missing data			x		
	Loss to follow-up is not associated with key characteristics	High risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors			x		
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?			x		
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	High risk of bias				
Study confounding	Do the authors address potential confounders?				x	
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	High risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting			x		
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	High risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= High risk of bias						

First Author: Nouh et al., 2011

ID: 6378752

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

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First Author: Pares et al., 2008

ID: 6378809

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Pattinson et al., 1991

ID: 74903015

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

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First Author: Pattinson et al., 1993

ID: 6378815

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Phupong et al., 2003

ID: 6378830

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?	x				
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Rani et al., 2016

ID: 74903020

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori		x			
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Rocca et al., 1995

ID: 74903016

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate					x
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Verma et al., 2016

ID: 6379243

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?	x				
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Low risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

First Author: Waa et al., 2010

ID: 6379255

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics	x				
	Statement as to the possible effect on the results from missing data	x				
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?		x			
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Moderate risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Yelikar et al., 2013

ID: 6379339

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]	x				
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Low risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate		x			
	Participants lost to follow-up are adequately described for key characteristics				x	
	Statement as to the possible effect on the results from missing data				x	
	Loss to follow-up is not associated with key characteristics	Moderate risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors		x			
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?			x		
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Moderate risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting		x			
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Moderate risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Moderate risk of bias						

First Author: Zarean et al., 2018

ID: 6379369

Potential Bias	Items to be considered for assessment of potential opportunity for bias	Yes	Partly	No	Unsure	NA*
Study population /sample selection	Inclusion and exclusion criteria are adequately described [including explicit diagnostic criteria, start/finish date of recruitment]	x				
	Baseline study sample [i.e. individuals entering the study and their key characteristics and sampling frame are adequately described]		x			
	Study sample represents population of interest on key characteristics, sufficient to limit potential bias to results	Moderate risk of bias				
Study attrition	Response rate (i.e., proportion of study sample completing the study and providing outcome data) is adequate	x				
	Participants lost to follow-up are adequately described for key characteristics					x
	Statement as to the possible effect on the results from missing data					x
	Loss to follow-up is not associated with key characteristics	Low risk of bias				
Prognostic factor measurement	Clear definition of the prognostic factors measured is provided (e.g. imaging modality method, measurement, and timing described).	x				
	Specified instrument and personnel for measurement of predictive factors	x				
	Continuous variables are reported or appropriate (i.e. not data- dependent) cut-off points are used and specified a priori	x				
	Blinding: were estimators of risk factor status and of outcomes blinded?				x	
	The prognostic factor(s) of interest is (are) adequately measured in study participants to sufficiently limit potential bias	Low risk of bias				
Outcome measurement	Is the outcome(s) clearly defined?		x			
	The outcome measure and method used are adequately valid and reliable to limit misclassification bias	Moderate risk of bias				
Study confounding	Do the authors address potential confounders?	x				
	Important potential confounders are appropriately accounted for, limiting potential bias with respect to the prognostic factor of interest.	Low risk of bias				
Analysis and reporting	There is sufficient presentation of data to assess the adequacy of the analysis strategy and there is no selective reporting	x				
	The statistical analysis is appropriate for the study design, limiting potential for the presentation of invalid results	Low risk of bias				
NA*: not applicable. Note: The above table was adapted from: Hayden et al., 2013.						
Overall opinion of study quality= Low risk of bias						

Table S1. Statistical measures of prognostic performance of Doppler ultrasound reported in the selected studies

Prognostic determinant	Outcome	Studies	Sn	Sp	PPV	NPV	AUROC	Diagnostic accuracy	OR [95% CI]	RR [95% CI]	Correlation	Normal Doppler n (%)	Abnormal Doppler n (%)	
UA flow impedance	FGR	Agbaje et al., 2018	67.00	53.00			0.63							
		Mullick et al., 1993	85.00	89.00	88.50									
		Najam et al., 2016	48.15	80.67	53.06	77.40								
		Rocca et al., 1995	92.30	91.90	77.40	97.60		92.0						
		Khanduri et al., 2013	73.80	75.90	87.70	55.40		75.00						
		Bano et al., 2010	46.70	93.30	87.50	63.60		70.00						
		Nagar et al., 2015	42.86	94.62	37.50	95.65								
	NICU Admission	Anshul et al., 2010											13 (24.07)	36 (78.2)
		Najam et al., 2016	50.00	80.30	48.90	80.95								
	Fetal Distress	Anshul et al., 2010											18 (33)	35 (76)
		Rocca et al., 1995											2 (2.5)	12 (39)
		Najam et al., 2016	66.67	78.04	74.89	89.72								
		Yelikar et al., 2013	42.10	65.90	12.10	91.10								
	Stillbirth	Anshul et al., 2010											0 (0)	4 (9.5)
		Najam et al., 2016											0 (0)	5 (8.2)
	Perinatal death	Rocca et al., 1995											0 (0)	2 (6.5)
		Anshul et al., 2010											0 (0)	9 (60)
	LBW	Anshul et al., 2010											15 (27.0)	35 (77.8)
	Apgar Score	Rocca et al., 1995	80.00	82.40	41.00	96.00		83.00						
		Anshul et al., 2010											2 (3.7)	14 (82.35)
		Najam et al., 2016											3 (60.0)	6 (85.71)
		Agbaje et al., 2018										0.378		
	Fetal Anemia	Kumari et al., 2019										0.21		
	HIE	Najam et al., 2016											1 (1.29)	8 (16.31)
	MAS	Najam et al., 2016											1 (1.29)	16 (32.65)
	CAPO	Bano et al., 2010	79.20	92.40	79.20	92.20		88.90						
		Lakhkar et al 2006	50.00	59.00	66.60	41.90								

1			Rani et al., 2016	17.80	95.80	80.70	50.50	0.57						
2			Geerts et al., 2007	75.00			95.00			0.6 (0.1, 4.1)				
3			Malik et al., 2013	64.40	80.00	96.60	20.00							
4			Pattinson et al., 1993	12.50	91.80	22.70	84.50							
5			Ebrashy et al., 2005	53.30	36.40	81.10	30.80							
6			Waa et al., 2010	8.00	100.00	0.00	26.00							
7														
8														
9	UA AREDF	Perinatal death	Lakshmi et al., 2013							9.8 (2.1, 46.4)				
10			Najam et al., 2016									2 (2.59)	4 (33.33)	
11		RDS	Lakshmi et al., 2013							2.4 (1.1, 5.0)				
12		CAPO	Pattinson et al., 1991	75.00	90.00	69.00								
13			Lakshmi et al., 2013							8.4 (2.3, 30.5)				
14														
15														
16	MCA flow impedance	FGR	Najam et al., 2016	59.25	88.89	72.72	81.35							
17			Bano et al., 2010	8.90	100.0	100.0	52.30		54.40					
18			Khanduri et al., 2013	26.20	92.60	89.20	35.00		46.10					
19		Fetal Anemia	Pares et al., 2008	100.00	65.00	90.90	100.0		92.20					
20			Kumari et al., 2019	68.00	57.00	83.00	33.00	0.70				-0.43		
21		NICU Admission	Najam et al., 2016	64.58	88.69	70.45	85.71							
22		Neonatal Acidosis	Allam et al., 2013	87.50	64.00	74.00	82.00	0.82						
23		Fetal Distress	Najam et al., 2016	72.73	78.05	54.55	91.53							
24		Stillbirth	Najam et al., 2016										0 (0)	2 (4.5)
25		Apgar Score	Najam et al., 2016										1 (1.29)	17 (38.6)
26		HIE	Najam et al., 2016										1 (1.29)	10 (22.72)
27		MAS	Najam et al., 2016										1 (1.29)	20 (45.5)
28														
29	CAPO	Bano et al., 2010	16.70	100.0	100.0	76.70			77.80					
30		Lakhkar et al 2006	41.60	90.90	88.20	48.70								
31		Rani et al., 2016	18.60	90.30	68.70	49.40	0.58							
32		Dhand et al., 2011	71.00	92.00	94.00	65.00								
33		Malik et al., 2013	7.70	90.00	87.50	9.80								
34		Ebrashy et al., 2005	41.00	63.60	80.00	23.30								
35		Waa et al., 2010	23.0	68.00	76.00	33.00								
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CPR	FGR	Najam et al., 2016	85.10	89.72	80.70	92.30								
		Bano et al., 2010						72.20						
	NICU Admission	Najam et al., 2016	75.00	82.92	63.15	89.47								
		Alanwar et al., 2018	62.50	71.42	29.40	90.90								
	Foetal Distress	Najam et al., 2016	90.91	78.04	52.63	96.97								
		Masihi et al.2019	80.95	50.00	17.50	95.20								
	Stillbirth	Najam et al., 2016										0 (0)	4 (7.14)	
	Apgar Score	Najam et al., 2016										1 (1.29)	19 (33.33)	
		Alanwar et al., 2018	50.0	88.10	44.40	90.20								
	Neonatal Acidosis	Ebrashy et al., 2005	64.10	72.70	89.30	36.40					1 (1.2, 1.7)			
		Alanwar et al., 2018	43.75	69.05	21.21	86.57								
	HIE	Najam et al., 2016										1 (1.29)	12 (21.05)	
	MAS	Najam et al., 2016	96.15			99.20						1 (1.29)	25 (43.85)	
	CAPO	Bano et al., 2010	83.30	100.0	100.00	94.30			95.60					
Lakhkar et al 2006		47.20	86.30	85.00	50.00									
Rani et al., 2016		7.60	98.00	81.80	48.30	0.60								
Malik et al., 2013		68.80	100.00	100.0	26.30									
Geerts et al., 2007				57.0				1.1 (0.1, 14.6)						
UtA flow impedance	FGR	Verma et al., 2016	45.0	84.10	28.10	91.70								
		Phupong et al., 2003	67.0	82.90	6.90	99.20					9.5 (1.7, 48.5)			
		Nagar et al., 2015	25.0	94.56	28.57	93.55								
	Perinatal Death	Dorman et al., 2002									2.5 (1.3, 4.3)			
	LBW	Verma et al., 2016	45.40	84.60	31.30	90.90								
		Dorman et al., 2002									2.5 (1.5, 4.2)			
	Preterm Birth	Verma et al., 2016	57.10	63.20	18.50	91.00								
		Dorman et al., 2002									1 (0.9, 2.4)			

1		Verma et al., 2016	48.20	95.40	84.40	78.20							
2		Nouh et al., 2011	84.60	96.30	91.70	92.90							
3		Malik et al., 2013	37.70	70.00	91.80	11.00							
4		Zarean et al., 2018	37.50	73.30	48.40	63.70	0.55						
5													
6													
7													
8	FDA flow impedance	Fetal anemia	Pares et al., 2008	95.70	100.0	100.0	86.90		96.70				
9		Kumari et al., 2019	87.00	57.00			0.80				-0.54		
10		CAPO	Lakhkar et al 2006	44.40	59.00	64.00	56.50						
11													
12													
13	FDA & MCA	Fetal anemia	Pares et al., 2008	98.40	100.0	100.0	91.70		98.60				
14		Kumari et al., 2019	86.00	67.00	86.00	67.00							
15													
16													
17	DV flow impedance	Neonatal Acidosis	Allam et al., 2013	100.0	57.00	72.0	100.0	0.88	80.00				
18		CAPO	Geerts et al., 2007		92.0	33.0				0.3 (0.03, 4.6)			
19													

^aUA: umbilical artery; MCA: middle cerebral artery; CPR: cerebroplacental ratio; UtA: uterine artery; FDA: fetal descending aorta; DV: ductus venosus; RI: resistive index; PI: pulsatility index; S/D ratio: systolic diastolic ratio; PSV: peak systolic velocity; MV: mean velocity; AREDF: absent and/or reversed end diastolic flow; FGR: fetal growth restriction; LBW: low birth weight; HIE: hypoxic ischemic encephalopathy; MAS: meconium aspiration syndrome; RDS: respiratory distress syndrome; NICU: neonatal intensive care unit; CAPO: composite adverse perinatal outcomes; Sn: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value; OR: odds ratio; RR: relative risk; and n (%): frequency (percentage).

Table S2. Definitions of adverse perinatal outcomes reported in the selected studies

First Author	Outcomes	Definition (detailed description in the article)
Abdallah et al., 2019	LBW	Not defined
	NICU admission	Not defined
	Stillbirth	Not defined
	Perinatal mortality	Not defined
	Low APGAR score (1min & 5min)	Not defined
Agbaje et al., 2018	FGR	Abnormal birth weight: defined as estimated foetal weight below the 10th percentile for gestational age and abdominal circumference below the 10th percentile for gestational age.
	Low APGAR score at 5 minutes	APGAR score less than 6
Alanwar et al., 2018	Acidosis	Neonatal acidemia of pH < 7.2
	NICU admission	New-born was admitted to the neo- natal intensive care unit
	Low APGAR score at 5 minutes	APGAR score < 7 at 5 min
Allam et al., 2013	Neonatal acidosis	Cord blood pH <7.25
Anshul et al., 2010	Stillbirth	Not defined
	Neonatal death	Not defined
	NICU admission	Admission required
	Foetal distress	Delivered by emergency caesarean section for suspected foetal distress
	LBW	Not defined
	Low APGAR score at birth.	APGAR score <7 at birth
Bano et al., 2010	Perinatal death	Not defined
	Foetal distress	Caesarean section for foetal distress (FD not defined)
	NICU admission	Not defined
	Low APGAR score at 5min	APGAR score <7 at 5 min
	FGR	Birth weight less than 10 th percentile for gestational age

	Composite adverse perinatal outcome	Not defined
Dhand et al., 2011	Composite adverse perinatal outcome	Abnormal foetal outcome (details not provided)
Dorman et al., 2002	Perinatal death	Not defined
	Preterm delivery	Delivery < 37 weeks
	LBW	Birth weight <2.5kg
Ebrashy et al., 2005	Acidosis	Neonatal acidaemia of pH<7.2 were present
	Composite adverse neonatal outcome	Neonatal morbidity (neonatal academia pH<7.2, 5-minute APGAR score <6, and/or admission to NICU)
Geerts et al., 2007	Composite adverse perinatal outcome	Poor outcome (perinatal demise or clinical/ultrasound signs of neurological compromise in the infant at the time of discharge from the tertiary institution)
Khanduri et al., 2013	FGR	Ponderal index was calculated as birth weight (in gm) per length (in cm ³). Ponderal index of <10 indicates growth restriction.
Kumari et al., 2019	Foetal anaemia	Haematocrit of the umbilical cord blood was used as the reference test to diagnose foetal anaemia (defined as haemoglobin <0.65 times the median for gestational age).
Lakhkar et al., 2006	Composite adverse perinatal outcome	Adverse perinatal outcome (Major and Minor). Major adverse outcomes were perinatal deaths including intrauterine and early neonatal deaths. Major complications like hypoxic ischemic encephalopathy, intraventricular haemorrhage, periventricular leukomalacia, pulmonary haemorrhage and necrotizing enterocolitis. Minor outcomes include-caesarean delivery for foetal distress, APGAR score below 7 at 5 minutes, admission to NICU (neonatal intensive care unit) for treatment.
Lakshmi et al., 2013	Neonatal death	Not defined
	Respiratory distress syndrome	Not defined
	Composite adverse perinatal outcome	Composite outcome of death or major neuro-morbidity at 12-18 months of corrected age, defined as presence of cerebral palsy or visual or hearing impairment.
Malik et al., 2013	Composite adverse perinatal outcome	Abnormal foetal outcome (IUGR, IUFD and perinatal mortality)
Masihi et al.2019	Intrapartum foetal distress	Emergency caesarean section for foetal distress
Mullick et al., 1993	FGR	Not defined
Nagar et al., 2015	FGR	Not defined
Najam et al., 2016	FGR	Not defined

	NICU admission	Not defined
	Foetal distress	Not defined
	Stillbirth	Not defined
	Neonatal death	Not defined
	Low APGAR score	Not defined
	Hypoxic ischemic encephalopathy	Not defined
	Meconium aspiration syndrome	Not defined.
Nouh et al., 2011	Composite adverse perinatal outcome	The presence of one or more of the following; miscarriage, gestational DM, PIH, PE, antepartum haemorrhage, intrauterine growth retardation, instrumental, caesarean delivery and preterm labour.
Pares et al., 2008	Foetal anaemia	Anaemia was considered moderate to severe when foetal haemoglobin concentrations were $< \text{or} = 0.64$ multiples of the median for gestational age.
Pattinson et al., 1991	Composite adverse perinatal outcome	Poor foetal outcome (details not provided).
Pattinson et al., 1993	Composite adverse perinatal outcome	Complications of pregnancy, namely intra-uterine growth retardation and proteinuric hypertension.
Phupong et al., 2003	FGR	Birth weight less than 10 percentile for gestational age.
Rani et al., 2016	Composite adverse perinatal outcome	Adverse perinatal outcome was defined as any of these: small for gestational age, still birth, APGAR score < 5 at 5 minutes, need of bag and mask ventilation for > 10 minutes or hypoxic ischemic encephalopathy, admission to neonatal intensive care unit (NICU) and caesarean section due to non-reassuring foetal heart rate.
Rocca et al., 1995	IUGR	Not defined.
	Low APGAR score 5mins	APGAR score < 7 at 5 minutes.
	Perinatal death	Not defined.
	Foetal distress	Emergency operative delivery for foetal distress.
Verma et al., 2016	FGR	Not defined.
	LBW	Birth weight < 2500 gm.
	Preterm delivery	Spontaneous delivery < 37 weeks.

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	Composite adverse perinatal outcome	At least one adverse outcome (preeclampsia, FGR, low birth weight, spontaneous preterm delivery, oligohydramnios, foetal loss).
Waa et al., 2010	Composite adverse perinatal outcome	Poor outcome was defined by foetal mortality or appearance, pulse rate, grimace, activity, respiration (APGAR) score less than eight at five minutes or weight less than 10 th percentile for gestation 20 or head circumference and length below 10 th percentile for gestation.
Yelikar et al., 2013	Intrapartum foetal distress	Delivered by emergency caesarean section for suspected foetal distress.
Zarean et al., 2018	Composite adverse perinatal outcome	Adverse perinatal outcome, including preterm labour, intrauterine foetal death, PE, low 5-min APGAR score (<7), low umbilical arterial cord blood pH, admitted to Intensive Care Unit in the first 3 days of birth, low birth weight, infant with low weight, death of new-born, caesarean section for respiratory distress, and meconial amniotic fluid.

^aFGR: fetal growth restriction; FGR: intrauterine growth restriction; LBW: low birth weight; NICU: neonatal intensive care unit.

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Reporting checklist for systematic review and meta-analysis.

Based on the PRISMA guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMA reporting guidelines, and cite them as:

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

	Reporting Item	Page Number
Title		
	#1 Identify the report as a systematic review, meta-analysis, or both.	1
Abstract		
Structured summary	#2 Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	2
Introduction		
Rationale	#3 Describe the rationale for the review in the context of what is already known.	3

1	Objectives	#4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
2				
3				
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6	Methods			
7				
8				
9	Protocol and registration	#5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address) and, if available, provide registration information including the registration number.	4
10				
11				
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14	Eligibility criteria	#6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rational	4
15				
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19	Information sources	#7	Describe all information sources in the search (e.g., databases with dates of coverage, contact with study authors to identify additional studies) and date last searched.	4
20				
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24	Search	#8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
25				
26				
27				
28	Study selection	#9	State the process for selecting studies (i.e., for screening, for determining eligibility, for inclusion in the systematic review, and, if applicable, for inclusion in the meta-analysis).	4-5
29				
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34	Data collection process	#10	Describe the method of data extraction from reports (e.g., piloted forms, independently by two reviewers) and any processes for obtaining and confirming data from investigators.	5
35				
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39	Data items	#11	List and define all variables for which data were sought (e.g., PICOS, funding sources), and any assumptions and simplifications made.	4
40				
41				
42				
43	Risk of bias in individual studies	#12	Describe methods used for assessing risk of bias in individual studies (including specification of whether this was done at the study or outcome level, or both), and how this information is to be used in any data synthesis.	5
44				
45				
46				
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49	Summary measures	#13	State the principal summary measures (e.g., risk ratio, difference in means).	5
50				
51				
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53	Planned methods of analysis	#14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	5
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1	Risk of bias	#15	Specify any assessment of risk of bias that may affect the cumulative	5
2	across studies		evidence (e.g., publication bias, selective reporting within studies).	
3				
4				
5	Additional	#16	Describe methods of additional analyses (e.g., sensitivity or subgroup	na
6	analyses		analyses, meta-regression), if done, indicating which were pre-	
7			specified.	
8				
9				
10	Results			
11				
12	Study selection	#17	Give numbers of studies screened, assessed for eligibility, and included	6
13			in the review, with reasons for exclusions at each stage, ideally with a	
14			flow diagram .	
15				
16				
17				
18	Study	#18	For each study, present characteristics for which data were extracted	6
19	characteristics		(e.g., study size, PICOS, follow-up period) and provide the citation.	
20				
21				
22	Risk of bias	#19	Present data on risk of bias of each study and, if available, any	5
23	within studies		outcome-level assessment (see Item 12).	
24				
25				
26	Results of	#20	For all outcomes considered (benefits and harms), present, for each	7-9
27	individual studies		study: (a) simple summary data for each intervention group and (b)	
28			effect estimates and confidence intervals, ideally with a forest plot.	
29				
30				
31	Synthesis of	#21	Present the main results of the review. If meta-analyses are done,	7-9
32	results		include for each, confidence intervals and measures of consistency.	
33				
34				
35	Risk of bias	#22	Present results of any assessment of risk of bias across studies (see Item	6
36	across studies		15).	
37				
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39	Additional	#23	Give results of additional analyses, if done (e.g., sensitivity or subgroup	na
40	analysis		analyses, meta-regression [see Item 16]).	
41				
42	Discussion			
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44	Summary of	#24	Summarize the main findings, including the strength of evidence for	8
45	Evidence		each main outcome; consider their relevance to key groups (e.g., health	
46			care providers, users, and policy makers	
47				
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50	Limitations	#25	Discuss limitations at study and outcome level (e.g., risk of bias), and at	10
51			review level (e.g., incomplete retrieval of identified research, reporting	
52			bias).	
53				
54				
55	Conclusions	#26	Provide a general interpretation of the results in the context of other	11
56			evidence, and implications for future research.	
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Funding

Funding [#27](#) Describe sources of funding or other support (e.g., supply of data) for the systematic review; role of funders for the systematic review. 11

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