Endbericht:
„Systematische Auswertung des aktuellen Forschungsstands zum Kaiserschnitt“
Los 4: Schwangere mit Zustand nach Sectio

IFOM - Institut für Forschung in der Operativen Medizin (Universität Witten / Herdecke)

Barbara Prediger, Tim Mathes, Monika Becker, Stephanie Polus, Pauline Klaßen, Dawid Pieper

Datum: 25.11.16

Kontakt:
Dr. Dawid Pieper
IFOM - Institut für Forschung in der Operativen Medizin
Kommissarischer Leiter: Univ.-Prof. Dr. Rolf Lefering
Lehrstuhl für Chirurgische Forschung
Fakultät für Gesundheit, Department für Humanmedizin
Universität Witten/Herdecke
Ostmerheimer Str. 200, Haus 38
51109 Köln

Tel.: 0221 98957-40
Fax: 0221 98957-30

Inhalt

Abbildungsverzeichnis

Tabellenverzeichnis

Abkürzungsverzeichnis

AWMF	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften
AUC	Area under the curve
ÄZQ	Ärztliches Zentrum für Qualität in der Medizin
CDSR	Cochrane Database of Systematic Reviews
CS	Cesarean Section
DARE	Database of Abstracts of Reviews of Effects
DRKS	Deutsches Register Klinischer Studien
GIN	Guideline International Network
GRADE	Grades of Recommendation, Assessment, Development, and Evaluation
HTA	Health Technology Database
KI	Konfidenzintervall
MD	Mittelwertdifferenz
MRT	Magnet Resonanz Tomographie
NGC	National Guideline Clearinghouse
NICE	National Institute for Health and Care Excellence
NICU	Neonatal Intensive Care Unit
PICOS	Patienten, Interventionen, Kontrollen, Endpunkte, Studientypen
QUADAS 2	Quality assessment of diagnostic accuracy studies 2
QUIPS	Quality in Prognosis Studies
RCOG	Royal College of Obstetricians and Gynecologists
RCT	Randomized Controlled Trial
RR	Relatives Risiko
SoF	Summary of Findings
WHO	World Health Organization

1. Fragestellung

Für Los 4: Schwangere mit Zustand nach Sectio wurden folgende Fragestellungen definiert:

Frage 1: Wie genau lassen sich Plazentationsstörungen mit Sonografie und MRT diagnostizieren?

Frage 2: Hat die präpartale Prognose einer Plazentationsstörung bei Schwangeren mit Zustand nach Sectio / Uterusoperation einen positiven Einfluss auf die mütterliche Gesundheit?

2. Methoden

2.1. Review-Protokoll

Für die Erstellung dieses Systematic Reviews wurde vorab ein Protokoll für jede der beiden Fragestellungen erstellt, das die methodische Vorgehensweise darlegt und mit den Kriterien der PRISMA Gruppe übereinstimmt.[1] Das Protokoll wurde nach Fertigstellung der Koordinierungsstelle „Kaiserschnittforschung“ (ansässig Universitätsklinikum Frankfurt, Prof. Louwen) zur Kommentierung freigegeben.

2.2. Einschlusskriterien

- **Frage 1**

Folgende Einschlusskriterien für Patienten, Indextest, Referenztest, Endpunkt und Studientyp wurden formuliert:

Population:

Mindestens 80 % der eingeschlossen Patientinnen mussten Schwangere mit Zustand nach Kaiserschnitt (bei vorheriger Schwangerschaft/en) oder vorangegangener anderer Uterusoperation sein. Dies war unabhängig davon, wie viele Kaiserschnitte oder Operationen vorangegangen waren. Außerdem bezog sich die Frage nur auf Populationen aus Staaten gemäß Weltgesundheitsorganisation (WHO) Stratum-A. Dies sind Staaten mit sehr niedriger Kindersterblichkeit und Gesamtsterblichkeit, vorwiegend Staaten in Westeuropa, Nordamerika und Westpazifik.[2]

Index Test:

Zur Diagnose von Plazentationsstörungen (Plazenta Accreta, Plazenta Increta, Plazenta Percreta) wurden Sonographie und Magnet Resonanz Therapie (MRT) untersucht.

Referenztest:

Nach Entbindung, Schwangerschaftsabbruch oder Fehlgeburt wurde eine klinische und/oder histopathologische Untersuchung durchgeführt.

Outcomes:

Wie gut ist die Vorhersagekraft des Index Test:

Primäres Outcome:

Diagnostische Gütemaße (Sensitivität, Spezitifität, negativ prädiktiver Wert, positive prädiktiver Wert) oder Vierfeldertafel, anhand der diese diagnostischen Gütemaße berechnet werden können.

Studientyp:

Es wurden Kohortenstudien und Fall-Kontrollstudien eingeschlossen bei denen der Referenztest bei Geburt erfolgte

- **Frage 2**

Folgende Einschlusskriterien für Patienten, Intervention, Kontrollgruppe, Endpunkt und Studientyp (PICOS-Schema) wurden formuliert:

Population:

Mindestens 80 % der eingeschlossen Patientinnen mussten Schwangere mit Zustand nach Kaiserschnitt (bei vorheriger Schwangerschaft/en) oder vorangegangener anderer Uterusoperation sein. Dies war unabhängig davon, wie viele Kaiserschnitte oder Operationen vorangegangen waren. Außerdem bezog sich die Frage nur auf Populationen aus Staaten gemäß Weltgesundheitsorganisation (WHO) Stratum-A. Dies sind Staaten mit sehr niedriger Kindersterblichkeit und Gesamtsterblichkeit, vorwiegend Staaten in Westeuropa, Nordamerika und Westpazifik.[2]

Intervention/frühe Diagnose:

Darüber hinaus wurden interventionelle Studien zur Sonographie, MRT und klinische Symptomatik zur frühzeitigen Diagnose von Plazentationsstörungen (Plazenta Accreta, Plazenta Increata, Plazenta Percreta) eingeschlossen. Es wurde sowohl jegliche einzelne diagnostische Maßnahme als auch jegliche Diagnosekette, (Hintereinanderschaltung mehrere diagnostischer oder differentialdiagnostischer Maßnahmen) die eine der genannten diagnostischen Maßnahmen umfasst, betrachtet (z.B. klinische Symptomatik und anschließende Sonographie). Auch Studien, die ein systematisches Screening untersuchen (z.B. mit Sonographie), wurden eingeschlossen.

Es wurde Studien eingeschlossen, die den Einfluss einer frühen (prenatal) Diagnose (prognostischer Faktor) untersuchen. Hierbei war es nicht notwendig, dass die diagnostischen Maßnahmen die zu eine frühen Diagnose geführt haben standardisiert waren oder genau spezifiziert wurden.

Kontrolle/späte Diagnose:

Keine frühe Diagnosestellung (Diagnose bei Geburt).

Für interventionelle Studien wurde als Kontrollgruppe keine diagnostische Maßnahme/n bzw. Screening oder eine andere der oben genannten diagnostischen Maßnahmen definiert.

Outcomes:

Hatte die Intervention einen Einfluss auf:

Primäre Outcomes:

- Müttersterblichkeit

Sekundäre Outcomes:

- Hysterektomien
- Blutverlust, Bedarf an Bluttransfusion
- Chirurgische Eingriffe
- Chirurgische Komplikationen
- Andere schwerwiegende Komplikationen (z.B. Infektionen)
- Dauer des Krankenhausaufenthalts/Intensivstationaufenthalts
- Kaiserschnitte
- Frühgeburten (Gestationsalter)
- Gesundheit des Kindes (z.B. APGAR score, Intensivverlegung)

Studientyp:

Im Review sollten randomisierte-kontrollierte Studien (RCT), quasi randomisierte-kontrollierte Studien und Kohortenstudien untersucht werden. RCTs sollen Bias durch zufällige und damit gleichmäßige Verteilung von Risiken verringern. Bei Quasi-RCT verfehlt die Art der Randomisierung das Prinzip der Randomisierung, z.B. eine Randomisierung nach dem Tag der Aufnahme im Krankenhaus entspricht nicht dem Zufallsprinzip.[3, 4] Kohortenstudien sind Beobachtungsstudien, die eine Kohorte mit der Intervention mit einer Kontrollgruppe vergleichen, jedoch teilen sich die Personen den Gruppen de facto selbst zu.[5]

Die Einschlusskriterien für die Fragestellungen sind in Tabelle 1 und 2 zusammengefasst.

Tabelle 1: Einschlusskriterien Frage 1

	Population	Indextest	Referenztest	Outcome	Studientyp
Diagnostische Güte von bildgebenden Verfahren für Plazentationsstörungen	Schwangere mit vorangegangenem Kaiserschnitt oder anderer Uterusoperation (mind. 80% der Studienpopulation)	Sonographie, MRT	Histopathologie, klinische Untersuchung	*Primäres Outcome:* Diagnostische Gütemaße (Sensitivität, Spezifität, negativ prädiktiver Wert, positive prädiktiver Wert)	• Kohortenstudien • Fall-Kontroll-Studien

MRT: Magnet Resonanz Tomographie; RCT: randomized controlled trial

Tabelle 2: Einschlusskriterien Frage 2

	Population	Intervention	Kontrolle	Outcome	Studientyp
Patientenrelevante Endpunkte nach frühzeitiger Diagnose (prenatal) von Plazentationsstörung	Schwangere mit vorangegangenem Kaiserschnitt oder anderer Uterusoperation (mind. 80% der Studienpopulation)	Frühe Diagnose (prenatal) Sonographie, MRT, klinische Symptomatik	Späte Diagnose (bei Geburt) Keine diagnostische Maßnahme	*Primäres Outcome:* • Müttersterblichkeit Sekundäre Outcomes: • Hysterektomien • Blutverlust, Bedarf an Bluttransfusion • Chirurgische Eingriffe • Chirurgische Komplikationen • Andere schwerwiegende Komplikationen (z.B. Infektionen) • Dauer des Krankenhausaufenthalts/ Intensivstation • Frühgeburten (Gestationsalter) • Gesundheit des Kindes (z.B. APGAR score, Intensivverlegung)	• RCT • Quasi-RCT • Kohortenstudien

MRT: Magnet Resonanz Tomographie; RCT: randomized controlled trial

2.3. Datenquellen und Suchstrategie

Es wurde im Juni 2016 eine systematische Recherche in MEDLINE (via Pubmed), EMBASE (via Embase), CENTRAL (via Cochrane Library), CINAHL (via Ebsco) und Psycinfo (via Ebsco) durchgeführt. Zur Identifikation von systematischen Reviews wurden über den Zugang der Cochrane Library die Datenbanken Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE) und die Health Technology Database (HTA) recherchiert.

Es wurde für beide Fragestellungen eine gemeinsame Suchstrategie entwickelt. Die Suchstrategien wurden zunächst für eine Datenbank entwickelt und dann an jeweils andere Datenbanken und Suchoberflächen angepasst. Eine andere Person überprüfte mit Hilfe der PRESS Checkliste zur Überprüfung von elektronischen Suchstrategien die so entwickelte Recherche und passte sie gegebenenfalls an.[6] Tabelle 2 enthält die Suchstrategien bezüglich der Primärstudien. Tabelle 3 zeigt die Suchstrategie für CDSR, DARE, HTA und CENTRAL.

Zur Identifikation von Leitlinien wurden die Datenbanken der Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften AWMF, Ärztliches Zentrum für Qualität in der Medizin (ÄZQ), Guideline International Network (GIN), National Guideline Clearinghouse (NGC) sowie die Homepages der folgenden Fachgesellschaften recherchiert:

- Schweizerische Gesellschaft für Gynäkologie und Geburtshilfe
- Society of Obstetricians and Gynaecologists of Canada
- The Royal College of Obstetricians and Gynaecologists
- Österreichischen Gesellschaft für Gynäkologie und Geburtshilfe

Zur Identifikation weiterer relevanter Literatur wurden die Referenzen der systematischen Reviews, Leitlinien zu verwandten Fragestellungen und der eingeschlossenen Studien geprüft.

Zusätzlich wurden auch die Studienregister ClinicalTrials (www.clinicaltrials.gov), Deutsches Register Klinischer Studien (DRKS) (www.drks.de) sowie EU Clinical Trials Register (https://www.clinicaltrialsregister.eu/) recherchiert. Tabelle 4 enthält die Suchstrategie der Studienregister.

Die Recherchen erfolgten ohne zeitliche und sprachliche Einschränkung. Lediglich die Leitlinienrecherche war auf Veröffentlichungen ab Juni 2011 beschränkt.

Tabelle 3: Recherchestrategien Primärstudien

Datenbank (Recherchedatum)	**Suchstrategie**
MEDLINE (01.06.2016)	((placenta diseases[majr] OR Placenta Accreta[mesh] OR Placenta Previa[mesh]OR Placenta Accreta[tiab] OR Placenta Previa[tiab] OR Placenta Previa[tiab] OR placenta increta[tiab] OR placental attachment[tiab] OR placental invasion[tiab]) AND (Prenatal Diagnosis[mesh] early diagnosis[mesh] OR delayed diagnosis[mesh] OR Diagnostic Techniques, Obstetrical and Gynecological[Majr] OR Placental Function Tests[mesh] OR Magnetic Resonance Imaging[mesh] OR ((prenatal[tiab] OR antenatal [tiab] OR pregnancy[tiab]) AND (diagnosis[tiab] OR diagnostic[tiab])) OR Magnetic Resonance Imaging[tiab] OR mri[tiab] OR nmr [tiab] OR Proton Spin Tomography[tiab] OR Magnetization Transfer Contrast Imaging[tiab] OR Zeugmatography[tiab] OR screening[tiab] OR Ultrasonography, Prenatal[mesh] OR Ultrasonography[tiab] OR Echography[tiab] OR Ultrasonic[tiab] OR Ultrasound[tiab] OR sonographic[tiab] OR sonography[tiab] OR Echotomography[tiab]) NOT (animals [MeSH Terms] NOT humans [MeSH Terms])
EMBASE (01.06.2016)	('placenta disorder'/de OR 'placenta accreta'/exp OR 'placenta previa'/exp OR 'placenta accreta':ab,ti OR 'placenta previa':ab,ti OR 'placenta praevia':ab,ti OR 'placenta increta':ab,ti OR 'placental attachment':ab,ti OR 'placental invasion':ab,ti) AND ('prenatal diagnosis'/exp AND ('early diagnosis'/de) OR 'delayed diagnosis'/de OR 'gynecological examination'/de OR 'nuclear magnetic resonance imaging'/de OR (prenatal:ab,ti OR antenatal:ab,ti OR pregnancy:ab,ti AND (diagnosis:ab,ti OR diagnostic:ab,ti)) OR 'magnetic resonance imaging':ab,ti OR mri:ab,ti OR nmr:ab,ti OR 'proton spin tomography':ab,ti OR 'magnetization transfer contrast imaging':ab,ti OR zeugmatography:ab,ti OR screening:ab,ti OR 'echography'/de OR echography:ab,ti OR ultrasonography:ab,ti OR ultrasonic:ab,ti OR ultrasound:ab,ti OR sonographic:ab,ti OR sonography:ab,ti OR echotomography:ab,ti) AND ([article]/lim OR [article in press]/lim OR [review]/lim) AND humans/de AND [embase]/lim
CINAHL (01.06.2016)	S1 ((MH "Placenta Accreta") OR (MH "Placenta Praevia") OR (MH "Placenta Diseases")) OR TI (Placenta Accreta OR Placenta Previa OR Placenta Previa OR placenta increta OR placental attachment OR placental accretion) OR AB (Placenta Accreta

	OR Placenta Previa OR Placenta Previa OR placenta increta OR placental attachment OR placental invasion) S2 ((MH "Prenatal Diagnosis+") OR (MH "Early Diagnosis") OR (MM "Diagnosis, Delayed") OR (MH "Magnetic Resonance Imaging+") OR (MH "Ultrasonography, Prenatal+") OR TI (((prenatal OR antenatal OR pregnancy) AND (diagnosis OR diagnostic)) OR Magnetic Resonance Imaging OR mri OR nmr OR Proton Spin Tomography OR Magnetization Transfer Contrast Imaging OR Zeugmatography OR screening OR Echography OR Ultrasonic OR Ultrasound OR sonographic OR sonography OR Echotomography)) OR AB (((prenatal OR antenatal OR pregnancy) AND (diagnosis OR diagnostic)) OR Magnetic Resonance Imaging OR mri OR nmr OR Proton Spin Tomography OR Magnetization Transfer Contrast Imaging OR Zeugmatography OR screening OR Echography OR Ultrasonic OR Ultrasound OR sonographic OR sonography OR Echotomography)) S1 AND S2
PsycInfo (01.06.2016)	(TI Placenta Accreta OR Placenta Previa OR Placenta Previa OR placenta increta OR placental attachment OR placental accretion) OR (AB Placenta Accreta OR Placenta Previa OR Placenta Previa OR placenta increta OR placental attachment OR placental invation)
CENTRAL (01.06.2016)	Siehe Recherchestrategien Systematic Reviews CDSR

Tabelle 4: Recherchestrategien Systematic Reviews

Datenbank (Recherchedatum)	**Suchstrategie**
Frage 1	
CDSR, DARE, HTA, CENTRAL (01.06.2016)	ID Search #1 MeSH descriptor: [Placenta Diseases] explode all trees #2 MeSH descriptor: [Placenta Accreta] explode all trees #3 MeSH descriptor: [Placenta Previa] explode all trees #4 (Placenta Accreta or Placenta Previa or Placenta Previa or placenta increta or placental attachment or placental invasion):ti,ab,kw (Word variations have been searched) #5 MeSH descriptor: [Prenatal Diagnosis] explode all trees #6 MeSH descriptor: [Early Diagnosis] explode all trees #7 MeSH descriptor: [Delayed Diagnosis] explode all trees #8 MeSH descriptor: [Diagnostic Techniques, Obstetrical and Gynecological] explode all trees #9 MeSH descriptor: [Placental Function Tests] explode all trees #10 MeSH descriptor: [Magnetic Resonance Imaging] explode all trees #11 MeSH descriptor: [Ultrasonography, Prenatal] explode all trees #12 (((prenatal or antenatal or pregnancy) and (diagnosis or diagnostic)) or Magnetic Resonance Imaging or MRI or NMR or Proton Spin Tomography or Magnetization Transfer Contrast Imaging or Zeugmatography or screening or Ultrasonography or Echography or Ultrasonic or Ultrasound or sonographic or sonography or Echotomography):ti,ab,kw (Word variations have been searched) #13 (#1 or #2 or #3 or #4) and (#5 or #6 or #7 or #8 or #9 or #10 or #11 or #12)

Tabelle 5: Recherchestrategien Studienregister

Thema (Recherchedatum)	Suchstrategie
ClinicalTrials (12.09.2016)	Placenta AND (Diagnosis OR Prognosis)
EU Clinical Trials (13.09.2016)	Placenta AND (Diagnosis OR Prognosis)
DRKS (13.09.2016)	Plazenta

2.4. Studienselektion

Die identifizierten Treffer wurden in ein Literaturverwaltungsprogramm (EndNote) überführt und elektronisch auf Duplikate überprüft. Die in den Datenbanken und über die Handrecherche identifizierte Literatur wurde von zwei Gutachtern unabhängig selektiert. Zunächst wurden die Abstracts sämtlicher in den Datenbanken erzielten Treffer auf Erfüllung der a-priori definierten Einschlusskriterien hin geprüft und anschließend, bei potentieller Relevanz, die Volltexte geprüft. Unstimmigkeiten wurden bis zum Konsens diskutiert.

2.5. Datenextraktion

Die gesamte Datenextraktion wurde von einem Gutachter vorgenommen und zur Verifizierung von einem zweiten Gutachter kontrolliert. Jegliche Differenz wurde bis zum Konsens diskutiert. Die nachfolgenden Daten wurden extrahiert:

- Studientyp
- Setting (Ort, Krankenhaus etc.)
- Rekrutierungszeitraum
- Teilnehmer (Ausschlusskriterien, Anzahl randomisiert/analysiert/Drop-out, Charakteristika)
- Intervention/Exposition/Indextest
- Kontrolle/Referenztest
- Zielgröße
- Hauptergebnis

Für die Ermittlung der Sensitivität, Spezifität, positiver/negativer prognostischer Faktor wurden die Richtig-Positiven, Falsch-Positiven, Richtig-Negativen und Falsch-Negativen Befunde extrahiert. Die Konfidenzintervalle für Sensitivität und Spezifität wurden berechnet.

Für kontinuierliche Variablen wurde der Mittelwert bzw. die Mittelwertdifferenz mit Konfidenzintervallen angegeben. Für dichotome Variablen wurden nach Möglichkeit die relativen Effektmaße (Odds Ratio, Relatives Risiko, Hazard Ratio) mit Konfidenzintervallen angegeben. Der statistische Vertrauensbereich bzw. die statistische Signifikanz wurde mit Konfidenzintervallen bzw. mit p-Werten angegeben. Die relativen Effektmaße wurden vereinheitlicht, sodass die Kontrollgruppe immer die Referenzkategorie darstellt (Nenner des Bruchs). D.h. relative Effektmaße >1 für negative Endpunkte (z.B. Einweisung auf NICU) bedeuten, dass die Interventionsgruppe unterlegen ist (höhere Zahl der Einweisungen in der Interventionsgruppe). Umgekehrt gilt der Zusammenhang für Effektmaße <1. Die Ergebnisse wurden zu diesem Zweck ggf. umgepolt. Die Darstellung erfolgt soweit nicht anders angegeben, entsprechend der Intention-to-Treat Population.

Um eine Meta-Analyse durchzuführen wurden die absoluten Werte der einzelnen Studien angegeben und gepoolt. Um Daten aller Studien für die Meta-Analyse zu erhalten, wurden die Autoren der Studien, die nur adjustierte Werte publizierten, nach rohen (nicht adjustierten) Werten kontaktiert.

2.6. Risk of bias assessment

Alle als relevant identifizierten Studien wurden hinsichtlich ihres Verzerrungspotentials bewertet. Die Bewertung wurde jeweils durch zwei Gutachter unabhängig voneinander durchgeführt. Unstimmigkeiten wurden ausdiskutiert.

Die Bewertung der Studien zur diagnostischen Güte (Frage 1) wurden mit dem „quality assessment of diagnostic accuracy studies 2“ (QUADAS 2) Tool durchgeführt, siehe Appendix A. Hiermit werden Aspekte untersucht, die Hinweise auf das mögliche Vorliegen von Verzerrungen geben können. Für folgende Kategorien wurde das Risk of Bias bewertet: Patient Selection, Index Test, Reference Standard, Flow and Timing. Jede Frage wurde mit „hohes Risiko für Verzerrung“, „niedriges Risiko für Verzerrung“, oder „unklares Risiko für Verzerrung“ bewertet.[7] Zusätzlich soll mit QUADAS 2 auch die Übertragbarkeit der Ergebnisse bewertet werden („Applicability Concerns“). Diese Bewertung wurde im Rahmen dieses Berichtes jedoch noch nicht durchgeführt, da noch kein konkreter Kontext (z.B. niedergelassene Gynäkologen) festgelegt wurde.

Hinsichtlich der Bewertung des Verzerrungspotentials der Studien zu Frage 2 wurde eine Abweichung vom Protokoll vorgenommen. Dieses sah vor RCTs mit dem Cochrane Risk of Bias Tool und Kohortenstudien mit der Newcastle-Ottawa Scale zu bewerten. Da es sich bei den Studien jedoch um Prognosestudien handelte versprach das „Quality in Prognosis Studies“ (QUIPS) Instrument eine bessere Anwendbarkeit, siehe Appendix B. Die Items Study Participation, Study Attrition, Prognostic Factor Measurement, Outcome Measurement, Study Confounding und Statistical Analysis and Reporting wurden bewertet. Jedes Item wurde mit „hohem Risiko für Verzerrung“, „niedrigem Risiko für Verzerrung“, „moderatem Risiko für Verzerrung“ bewertet.[8]

2.7. Datensynthese

Um eine qualitativ hochwertige Evidenzgrundlage zu bilden, wäre es wünschenswert den direkten Einfluss auf patientenrelevante Endpunkte durch einen diagnostischen Test und die diagnostische Güte in einer Studie zu bestimmen, im besten Fall in einer RCT. In der Praxis mangelt es aber an diesem Studiendesign und somit wird in dieser Arbeit der Ansatz der „Linked Evidence“ angewendet. Dieser soll in einem Schritt Studien zur diagnostische Güte von Tests auswerten und in einem weiteren Schritt Interventionsstudien auswerten, in denen der klinische Nutzen dieser Tests untersucht wird.[9]

Für das Management der Ergebnisse wurde der von der Cochrane Collaboration zur Verfügung gestellte Review Manager 5.3 verwendet. Die Software GRADEPro wurde verwendet, um die Summary of Findings (SoF) Tables zu erstellen, die sich aus GRADE heraus ergeben. Für Frage 2 wurden auch die Meta-Analysen mit der Software Review Manager 5.3 berechnet. Berechnungen des relativen Risikos (RR) erfolgten mit einem Random Effects Model unter Verwendung der inversen Varianzen Methode. Die inversen Varianzen wurden unter Verwendung einer Mantel-Haenszel Meta-Analyse geschätzt. Der RR wurde immer mit dazugehörigen 95% Konfidenzintervall (KI) berechnet. Für die Meta-Analyse kontinuierlicher Werte wurden die Mittelwertdifferenzen (MD) und zugehöriger 95%-KIs mittels inverser Varianzen Random-Effects-Meta-Analyse ermittelt. Forest- und Funnel Plots wurden mithilfe von Review Manager 5.3 erstellt. Wenn möglich wurden die Ergebnisse aus mehreren Studien gepoolt. Wenn es nur eine einzige Studie gab, wurde für diese auch das RR bzw. MD mit zugehörigem KI berechnet.

Für Frage 1 sollten Meta-Analysen (hierarchisches Model für Summary-Receiver Operating Characteristics) mit SAS 9.4. durchgeführt werden.

Der „Body of Evidence“ wurde mit "Grades of Recommendation, Assessment, Development, and Evaluation" (GRADE) bewertet. Im Rahmen der Leitlinienerstellung eignet sich GRADE besonders gut, da es basierend auf den GRADE Ergebnissen entsprechende Handlungsempfehlungen auf Basis der vorhandenen Evidenzlage aussprechen kann. Zur Bewertung werden zum einen der Studientyp und zum anderen Einschränkungen der Ergebnisse herangezogen. Dabei werten die Risk of Bias Bewertung, Inkonsistenzen und Ungenauigkeit der Ergebnisse, Indirekte Vergleiche und Publikationsbias die Ergebnisse um ein bis zwei Stufen ab. Allerdings können große Effekte, Dosis-Wirkungs-Beziehung und wenn Effekte durch andere Störvariablen und Bias beeinflusst werden könnten, die Ergebnisse um ein bis zwei Stufen aufwerten.[4]

3. Ergebnisse der Literaturrecherche

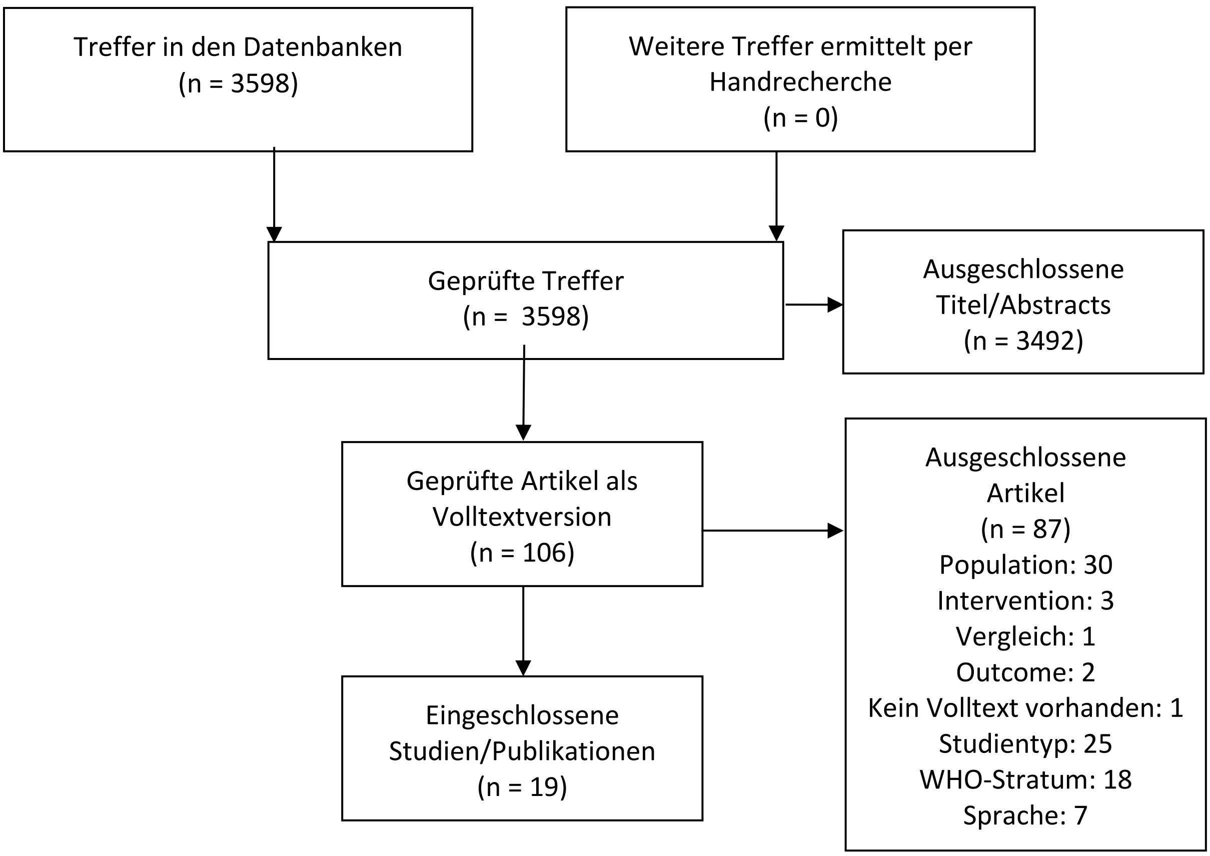
Im Rahmen der systematischen Recherche nach Primärstudien wurden in den Datenbanken Medline, EMBASE, CENTRAL, CINAHL und Psycinfo 3585 Treffer identifiziert, von denen 106 potentiell relevant erschienen und im Volltext überprüft wurden. Die Überprüfung der Volltexte resultierte in 19 Publikationen, die die Einschlusskriterien erfüllten und eingeschlossen wurden. Davon wurden 13 Publikationen Frage 1 zugeordnet und sechs Frage 2.

Im Rahmen der systematischen Recherche nach systematischen Übersichtsarbeiten konnten in den Datenbanken CDSR, DARE und HTA 13 Treffer identifiziert werden. Die Sichtung der Abstracts ergab, dass keiner die Einschlusskriterien erfüllte.

Im Weiteren wurde ein Referenzcheck durchgeführt. Dieser erbrachte keine weiteren Treffer.

Der Verlauf der Studienauswahl ist in Abbildung 1 dargestellt. Die Listen der ausgeschlossenen Volltexte sind in Appendix G aufgeführt. Die Studien, die aufgrund des Kriteriums Sprache ausgeschieden waren, waren auf Chinesisch erschienen.

Abbildung 1: Flow-chart



Bei zwei Publikationen von Bowman et al. Handelte es sich um eine Studie.[10, 11] Drei Publikationen von Rac et al. befassten sich ebenfalls mit dem gleichen Datensatz.[12-14]

Die Recherche in Studienregistern ergab zwei Treffer relevanter unveröffentlichter Studien. Die eine Studie befand sich jedoch noch in der Patientenrekrutierung (FRATTELLI) die zweite in der Auswertung (University Hospital, TOURS), siehe Appendix F.

Die Leitlinienrecherche vom 17.05.2016 ergab drei Leitlinien, die des National Institute for Health and Care Excellence (NICE) „Cesarean section" und zwei des Royal College of Obstetricians and Gynecologists (RCOG), „Birth after previous cesarean birth" und „Placenta Praevia, Placenta Praevia Accreta and Vasa Praevia: Diagnosis and Management" die eine Empfehlung zu der Fragestellung abgeben.[15-17] In Tabelle 5 sind die Leitlinien mit den dazugehörigen Empfehlungen zusammengefasst. Beide Institutionen empfehlen eine Abklärung eines Ultraschallbefundes mit MRT.

Tabelle 6: Internationale Leitlinien mit Empfehlungen

Leitlinie	Empfehlung
NICE 2011 „Cesarean section"	**Morbidly adherent placenta** If low-lying placenta is confirmed at 32–34 weeks in women who have had a previous CS, offer colour-flow Doppler ultrasound as the first diagnostic test for morbidly adherent placenta.
	If a colour-flow Doppler ultrasound scan result suggests morbidly adherent placenta: • discuss with the woman the improved accuracy of magnetic resonance imaging (MRI) in addition to ultrasound to help diagnose morbidly adherent placenta and clarify the degree of invasion • explain what to expect during an MRI procedure • inform the woman that current experience suggests that MRI is safe, but that there is a lack of evidence about any long-term risks to the baby • offer MRI if acceptable to the woman.
RCOG 2015 „Birth after previous cesarean birth"	Early recognition of placenta praevia, adopting a multidisciplinary approach and informed consent are important considerations in the management of women with placenta praevia and previous cesarean delivery.
RCOG 2011 „Placenta Praevia, Placenta Praevia Accreta and Vasa Praevia: Diagnosis and Management"	Women with a previous cesarean section require a higher index of suspicion as there are two problems to exclude: placenta praevia and placenta accreta. If the placenta lies anteriorly and reaches the cervical os at 20 weeks, a follow-up scan can help identify if it is implanted into the cesarean section scar. Women who have had a previous cesarean section who also have either placenta praevia or an anterior placenta underlying the old cesarean section scar at 32 weeks of gestation are at increased risk of placenta accreta and should be managed as if they have placenta accreta, with appropriate preparations for surgery made. Antenatal sonographic imaging can be complemented by magnetic resonance imaging in equivocal cases to distinguish those women at special risk of placenta accreta.

CS= Cesarean Section; MRI = Magnetic Resonance Imaging; NICE = National Institute for Health and Care Excellence; RCOG = Royal College of Obstetricians and Gynecologists

Die den Empfehlungen zugrundeliegende Evidenz wurde bereits in der Literaturrecherche in den Datenbanken identifiziert oder erfüllte nicht die Einschlusskriterien.

4. Studienergebnisse

4.1. Frage 1

Im folgenden Abschnitt folgt eine kurze Darstellung der wichtigsten Ergebnisse. Ergänzt werden die Ergebnisse durch detaillierte Tabellen, die aus Review Manager 5.3 exportiert wurden, siehe Appendix D.

Es wurden 10 Studien für die Beantwortung von Frage 1 (diagnostische Güte) in diesen Review eingeschlossen und ausgewertet. Dabei handelt es sich bei allen Studien um veröffentlichtes Material. In Tabelle 7 sind die allgemeinen Charakteristika der Studien dargestellt. Sechs Studien fanden in den USA statt. Fünf Studien kamen aus Europa und eine aus Neuseeland. Im Mittel dauerten die Studien sechseinhalb Jahre. Warshak et al. untersuchten in ihrer Studie sowohl die diagnostische Güte von Ultraschall, als auch die diagnostische Güte von MRT bei Patienten die ein unklares Ergebnis der Ultraschalluntersuchung hatten. [18] Um diese beiden unterschiedlichen Fragestellungen zu berücksichtigen wurden zwei Extraktionen durchgeführt.

4.1.1. Risk of Bias Bewertung mit QUADAS 2

Abbildung 2: Risk of Bias Assessment Frage 1

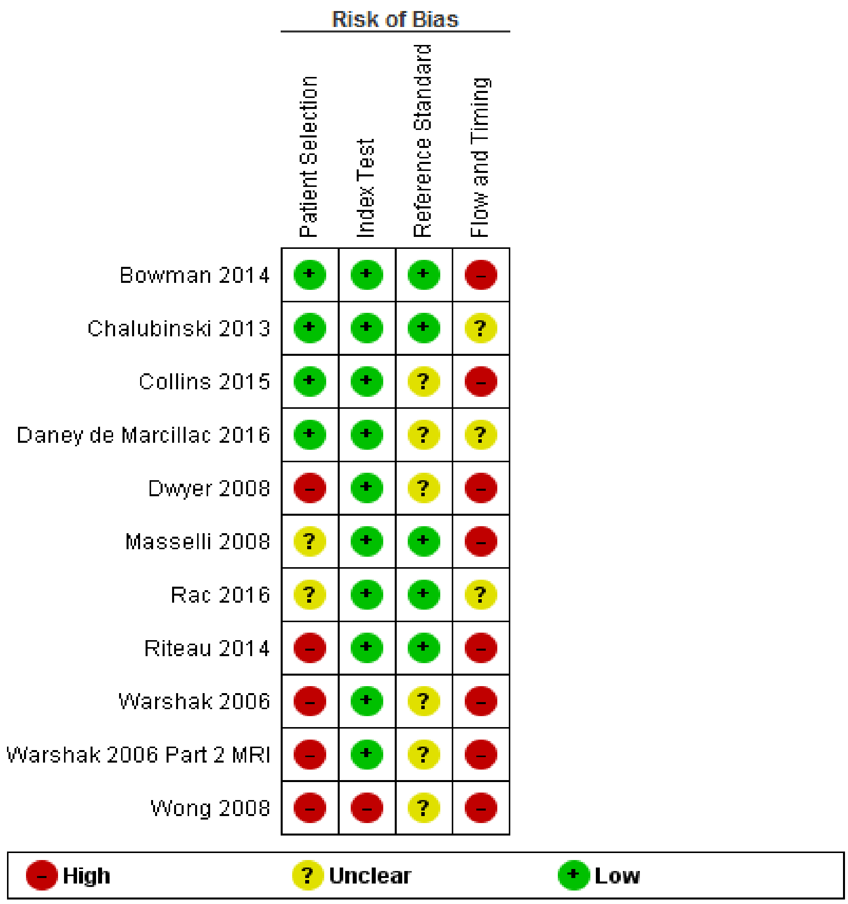


Tabelle 7: Studiencharakteristika Frage 1

Studie	Studientyp	Setting	Rekrutierungs zeitraum	Patienten-zahl	Index Test	Referenz Standard
Bowman et al. 2014	Fall-Kontroll Design	USA, Universitätsklinik	2000-2012	55	Ultraschall	Klinisch und Histopathologisch
Chalubinski et al. 2013	Kohorten-Design	Österreich, Universitätsklinik	2001-2011	232	Ultraschall	Klinisch und Histopathologisch
Collins et al. 2015	Kohorten-Design	Großbritannien/USA, NR	2012-2014	89	Ultraschall	Klinisch und Histopathologisch
Daney de Marcillac et al. 2016	Kohorten-Design	Frankreich, Level 3 Maternity-Unit	2010-2014	22	Ultraschall und MRT	Klinisch und Histopathologisch
Dwyer et al. 2008	Kohorten-Design	USA, Universitätsklinik	2001-2006	32	Ultraschall und MRT	Klinisch und Histopathologisch
Masselli et al. 2008	Kohorten-Design	Italien, NR	2006-2007	50	Ultraschall und MRT	Klinisch und Histopathologisch
Rac et al. 2016	Kohorten-Design	USA, Universitätsklinik	1997-2011	39	Ultraschall	Histopathologisch
Riteau et al. 2014	Kohorten-Design	Frankreich, Universitätsklinik	2001-2012	42	Ultraschall und MRT	Klinisch und Histopathologisch
Warshak et al. 2006	Kohorten-Design	USA, Universitätsklinik	2000-2005	453	Ultraschall	Klinisch und Histopathologisch
Warshak et al.	Kohorten-	USA, Universitätsklinik	2000-2005	40	MRT als Add-on zu unklarem	Klinisch und

2006 Part 2 MRT	Design				Ultraschall	Histopathologisch
Wong et al. 2008	Kohorten-Design	Neuseeland, NR	2004-2006	66	Ultraschall	Klinisch und Histopathologisch

MRT = Magnet Resonanz Tomographie; NR = Not Reported

4.1.2. Diagnostische Maßnahmen

Nachdem die Volltexte gesichtet waren und der Einschluss festgelegt war, wurden die Studien entsprechend der diagnostischen Maßnahme aufgeteilt (siehe Tabelle 8). Die erste Analyse bezieht sich auf Bowman et al., die in ihrer Studie einzelne Ultraschalluntersuchungen (2 pro Patientin) unabhängig voneinander durch sechs verschiedene Bewerter beurteilen ließen.[10] Die zweite Analyse untersucht die diagnostische Güte einer Ultraschalluntersuchung.[12, 18-25] Die dritte Analyse untersucht die diagnostische Güte von MRT,[21-24] während die vierte MRT als Add-on Test nach einem unklaren Ultraschallbefund untersucht.[18]

Tabelle 8: Diagnostische Maßnahmen

Nr.	Index Test	Studienanzahl
1	Einzelne Ultraschalluntersuchungen, unabhängig bewertet	1
2	Ultraschall	9
3	MRT	4
4	MRT als add-on Test nach unklarem Ultraschall	1

4.1.3. Patienten

Der Umfang der eingeschlossenen Patienten variierte und beträgt im Median 50 (Spannweite: 22 - 453, siehe Tabelle 7). Fünf Studien hatten als Einschlusskriterium eine Plazenta Previa oder „Tiefliegende Plazenta“ Diagnose.[12, 18, 20, 22, 24] Das mittlere Alter der darin eingeschlossenen Patientinnen lag in einer Spannweite von 29 bis 34 Jahren. Die meisten Frauen hatten bereits ein bis zwei Kaiserschnittgeburten und zwei bis drei Schwangerschaften erlebt. Rac et al. schlossen fast nur hispanische Patientinnen ein (100% bzw. 88% ohne Plazenta Accreta), alle anderen untersuchten hauptsächlich Patientinnen kaukasischer Herkunft. Dwyer et al. untersuchten Patientinnen aus drei verschiedenen Universitätskliniken.[21] Zwei Kliniken, Stanford und Mount Sinai, schlossen eine Risikogruppe ein, die aufgrund ihrer klinischen Vorgeschichte oder verdächtigen Ultraschallbildern den Verdacht auf eine Plazenta accreta hatten, in der dritten Klinik, Universität Washington, wurden nur Patientinnen mit sonographischem Befund zum MRT überwiesen.[21]. Somit unterschieden sich die Voraussetzungen der Patientinnen bei der MRT Untersuchung.

4.1.4. Index Test

Alle Publikationen untersuchten diagnostische Güte von Ultraschall. Vier Studien führten zusätzlich ein MRT durch und eine machte ein MRT als add-on bei unklarem Ultraschall (siehe oben). Bis auf Collins et al., Rac et al. und Wong et al. führten alle Gray Scale/2D Ultraschall und Color Doppler Ultraschall durch. Collins et al. führten nur Color Doppler Ultraschall durch, Wong et al. führten Color Doppler nur bei verdächtigen Fällen durch und Rac et al. führten keine Color Doppler Untersuchung durch.[12, 20, 25]

Bis auf Masselli et al. und Riteau et al. gaben alle Kriterien zur Diagnose, sowohl mit Ultraschall als auch MRT, einer Plazentationsstörung an, z.B. Auswölbung der Gebärmutter (siehe Tabelle 9) an. Bowman et al. ließen die Ergebnisse von sechs Gutachtern bewerten.[10] Daney de Marcillac et al., Dwyer et al., Masselli et al., Riteau et al. und Wong et al., ließen die Bewertung durch zwei Gutachter durchführen.[21-25] Collins et al., Rac et al. und Warshak et al. gaben hingegen nur eine Person an.[12, 18, 20] Darüber hinaus berichteten Bowman et al., Collins et al., Masselli et al., Rac et al. und Riteau et al., dass die Gutachter verblindet waren bzw. die Bilder deidentifiziert.[10, 12, 20, 22, 23]

4.1.5. Referenz Test

In allen Studien wurde als Referenztest eine histopathologische Untersuchung nach der Entbindung durchgeführt. Außer bei Rac et al. galten auch klinische Faktoren (z.B. komplette Ablösung der Plazenta nach Entbindung) als Referenztest.[12] Nur Chalubinski et al. beschrieben, dass die Gutachter der Histopathologie oder klinischen Symptomatik bezüglich der bildgebenden Diagnose verblindet waren.[19]

4.1.6. Outcomes

Die identifizierten Studien waren klinisch sehr heterogen (z.B. Durchführung Diagnostik, unterschiedliche Risikogruppen) und um Misinterpretationen zu vermeiden wurde auf die Durchführung einer Meta-Analyse verzichtet.[26]

Tabelle 9: Diagnostische Maßnahme 1 Einzelne Ultraschalluntersuchungen, unabhängig bewertet

Studie	RP	FP	FN	RN	Sensitivität 95% KI	Spezifizität 95% KI
Bowman 2014	371	81	220	533	0.63 [0.59, 0.67]	0.87 [0.84, 0.89]

FN = Falsch negativ; FP = Falsch positiv; KI = Konfidenzinterval; RN = Richtig negativ; RP = Richtig positiv

In Diagnostische Maßnahme 1 zeigte sich eine Sensitivität von 0.63 (95% KI 0.59-0.67) und eine Spezifität von 0.87 (95% KI 0.84-0.89) bei der unabhängigen Betrachtung von zwei Ultraschalluntersuchungen pro Patientin. [10]

Tabelle 10: Diagnostische Maßnahme 2 Ultraschall

Studie	RP	FP	FN	RN	Sensitivität 95% KI	Spezifizität 95% KI
Chalubinski 2013	32	8	3	189	0.91 [0.77, 0.98]	0.96 [0.92, 0.98]
Collins 2015	42	3	0	47	1.00 [0.92, 1.00]	0.94 [0.83, 0.99]
Daney de Marcillac 2016	12	3	1	6	0.92 [0.64, 1.00]	0.67 [0.30, 0.93]

Dwyer 2008	14	5	1	12	0.93 [0.68, 1.00]	0.71 [0.44, 0.90]
Masselli 2008	11	0	1	38	0.92 [0.62, 1.00]	1.00 [0.91, 1.00]
Rac 2016*	11	8	3	17	0.79 [0.49, 0.95]	0.68 [0.46, 0.85]
Riteau 2014	26	10	0	6	1.00 [0.87, 1.00]	0.38 [0.15, 0.65]
Warshak 2006	30	16	9	398	0.77 [0.61, 0.89]	0.96 [0.94, 0.98]
Wong 2008	Composite Score** ≥40				AUC 95% KI: 0.94 (0.91-1.06)	

AUC = Area under the curve; FN = Falsch negativ; FP = Falsch positiv; KI = Konfidenzinterval; RN = Richtig negativ; RP = Richtig positiv

* Gemessen bei myometrialer Dicke von 6mm

** “The composite score consists of the product of the likelihood ratios of the following selected criteria: obliteration of retroplacental space, placental lacuna, disruption of the placental–uterine wall interface, increased subplacental vascularity”[25]

In Diagnostische Maßnahme 2 lagen die Werte für Sensitivität zwischen 0.77 (95% KI 0.61-0.89), Warshak et al., und 1.0 (95% KI 0.92-1.0, Collins et al., bzw. 95% KI 0.87-1.0, Riteau et al.).[18, 20, 23] Vier weitere Studien erreichten jedoch auch Sensitivitätswerte über 0.9 und nur Rac et al. Erreichten auch nur 0.79 (95% KI 0.49-0.95).[12] Für die Spezifität lagen die Werte zwischen 0.38 (95% KI 0.15-0.65) bei Riteau et al. Und 1.0 (95% KI 0.91-1.0) bei Masselli et al.. Die weiteren Studien brachten Ergebnisse zwischen 0.68 und 0.96. Wong et al. Berichteten nur die area under the curve (AUC) mit 0.94 (95% KI 0.91-1.06). Es fällt jedoch auf, dass das Konfidenzintervall hier fehlerhaft berichtet wurde, es kann keinen Wert über 1.0 annehmen.[25]

Tabelle 11: Diagnostische Maßnahme 3: MRT

Studie	RP	FP	FN	RN	Sensitivität 95% KI	Spezifizität 95% KI
Daney de Marcillac 2016	11	2	2	7	0.85 [0.55, 0.98]	0.78 [0.40, 0.97]
Dwyer 2008	12	6	3	11	0.80 [0.52, 0.96]	0.65 [0.38, 0.86]
Masselli 2008	12	0	0	38	1.00 [0.74, 1.00]	1.00 [0.91, 1.00]
Riteau 2014	20	8	6	8	0.77 [0.56, 0.91]	0.50 [0.25, 0.75]

FN = Falsch negativ; FP = Falsch positiv; KI = Konfidenzinterval; RN = Richtig negativ; RP = Richtig positiv

Diagnostische Maßnahme 3 untersuchte MRT als Diagnoseverfahren. Auch hier zeigte sich eine Streuung der Sensitivität von 0.77 (95% KI 0.56-0.91) bei Riteau et al. zu 1.0 (95% KI 0.74-1.0) bei Masselli et al.[22, 23] Die Spezifität ist noch weiter gestreut mit 0.5 (95% KI 0.25-0.75) bei Riteau et al., 0.65 (95% KI 0.38-0.86) bei Dwyer et al., 0.78 (95% KI 0.4-0.97) bei Daney de Marcillac et al. und 1.0 (95% KI 0.91-1.0) bei Masselli et al. [21-24]

Tabelle 12: Diagnostische Maßnahme 4: MRT als add-on Test nach unklarem Ultraschall

Studie	RP	FP	FN	RN	Sensitivität 95% KI	Spezifizität 95% KI
Warshak 2006	23	0	3	14	0.88 [0.70, 0.98]	1.00 [0.77, 1.00]

FN = Falsch negativ; FP = Falsch positiv; KI = Konfidenzinterval; RN = Richtig negativ; RP = Richtig positiv

In Diagnostische Maßnahme 4 wird MRT als add-on zur Abklärung einer unklaren Ultraschalldiagnose eingesetzt und Warshak et al. erreichen eine Sensitivität von 0.88 (95% KI 0.7-0.98) und eine Spezifität von 1.0 (95% KI 0.77-1.0).[18]

4.1.7. Datensynthese der Ergebnisse

Die Datensynthese wurde mithilfe von GRADE durchgeführt. Jede Diagnostische Maßnahme erhielt eine eigene GRADE Summary of Findings Table, siehe Abbildungen 3-6. Die Qualitätsbewertung reichte von „very low“ bis „low“. Abstufungen in der Qualität lagen hauptsächlich daran, dass für einzelne Studien (Diagnostische Maßnahme 1 und 4) die Kriterien „Inconstency“ und „Indirectness“ nicht bewertet werden konnten, diese aber in allen anderen als „serious risk“ eingestuft wurden. Weiterhin erhielten alle Studien ein „serious risk“ in der Kategorie „Risk of Bias“ und „Imprecision“. Mögliches Confounding, das in der Studienauswertung nicht berücksichtigt wurde, konnte das Vertrauen in die meisten Ergebnisse verbessern. Allerdings führen die Einstufungen der anderen Kriterien zu so einer schlechten Bewertung, dass die Aufwertung keine Auswirkung mehr auf die Gesamtbewertung hat.

Abbildung 3: GRADE Bewertung Diagnostische Maßnahme 1 Einzelne Ultraschalluntersuchungen, unabhängig bewertet

Should ultrasound be used to diagnose placenta accreta in pregnant women with prior cesarean section?

Setting: Various ultrasound studies for a patient are independently diagnosed by six observers

Single study sensitivity: 0.63 (95% CI: 0.59 to 0.67) | **Single study specificity**: 0.87 (95% CI: 0.84 to 0.89)

Test result	Effect per 1.000 patients tested			Number of participants (studies)	Quality of the Evidence (GRADE)	Comments
	Prevalence 0.09% As seen by Fitzpatrick et al.	Prevalence 3% Seen in Silver et al. (1 CS)	Prevalence 40% Seen in Silver et al. (>3 CS)			
True positives (patients with placenta accreta)	1 (1 to 1)	19 (18 to 20)	252 (236 to 268)	591 (1)	⊕⊕◯◯ LOW [a,b]	
False negatives (patients incorrectly classified as not having placenta accreta)	0 (0 to 0)	11 (10 to 12)	148 (132 to 164)			
True negatives (patients without placenta accreta)	869 (839 to 889)	844 (815 to 863)	522 (504 to 534)	614 (1)	⊕⊕◯◯ LOW [a,b]	
False positives (patients incorrectly classified as having placenta accreta)	130 (110 to 160)	126 (107 to 155)	78 (66 to 96)			

CI: Confidence interval; CS: Cesarian

a. According to QUADAS2 ; b. No explanation was provided

Abbildung 4: GRADE Bewertung diagnostische Maßnahme 2 Ultraschall

Should ultrasound be used to diagnose placenta accreta, increata or percreta in pregnant women with prior cesarean section?

Setting: Any kind of ultrasound investigation

Range of sensitivities: 0.74 to 1.00 | **Range of specificities**: 0.38 to 1.00

Test result	Effect per 1.000 patients tested			Number of participants (studies)	Quality of the Evidence (GRADE)	Comments
	Prevalence 8.61%	Prevalence 61.9%	Prevalence 0.09%			
True positives (patients with placenta accreta, increata or percreta)	64 to 86	458 to 619	1 to 1	200 (8)	⊕◯◯◯ VERY LOW [a,b,c,d]	
False negatives (patients incorrectly classified as not having placenta accreta, increata or percreta)	0 to 22	0 to 161	0 to 0			
True negatives (patients without placenta accreta, increata or percreta)	347 to 914	145 to 381	380 to 999	762 (8)	⊕◯◯◯ VERY LOW [a,b,c,d]	
False positives (patients incorrectly classified as having placenta accreta, increata or percreta)	0 to 567	0 to 236	0 to 619			

a. According to QUADAS2 ; b. High heterogeneity; c. Ultrasound diagnosis/assessment might be different; d. Sensitivity and specificity and their CI differ widely

Abbildung 5: GRADE Bewertung Diagnostische Maßnahme 3 MRT

Should MRI be used to diagnose placenta accreta, increata or percreta in pregnant women with prior cesarean section?

Setting: Any kind of MRI

Range of sensitivities: 0.67 to 1.00 | **Range of specificities**: 0.78 to 1.00

Test result	Effect per 1.000 patients tested			**Number of participants (studies)**	**Quality of the Evidence (GRADE)**	**Comments**
	Prevalence 24%	Prevalence 61.9%	Prevalence 0.09%			
True positives (patients with placenta accreta, increata or percreta)	161 to 240	415 to 619	1 to 1	68 (4)	⨁◯◯◯ VERY LOW [a,b,c,d]	
False negatives (patients incorrectly classified as not having placenta accreta, increata or percreta)	0 to 79	0 to 204	0 to 0			
True negatives (patients without placenta accreta, increata or percreta)	593 to 760	297 to 381	779 to 999	78 (4)	⨁◯◯◯ VERY LOW [a,b,c,e]	
False positives (patients incorrectly classified as having placenta accreta, increata or percreta)	0 to 167	0 to 84	0 to 220			

MRI: magnetic resonance imaging

a. According to QUADAS2; b. High heterogeneity; c. MRI diagnosis/assessment might be different; d. No explanation was provided; e. Specificity and their CI differ widely

Abbildung 6: GRADE Bewertung Diagnostische Maßnahme 4 MRT als add-on Test nach unklarem Ultraschall

Should MRI as an add-on test be used to diagnose placenta in pregnant women with prior cesarean section?

Setting: MRI due to suspicous or inconclusive findings on previous ultrasound examination

Single study sensitivity: 0.88 (95% CI: 0.70 to 0.98) | **Single study specificity**: 1.00 (95% CI: 0.77 to 1.00)

Test result	Effect per 1.000 patients tested		Number of participants (studies)	Quality of the Evidence (GRADE)	Comments
	Prevalence 65%	Prevalence 0.09%			
True positives (patients with placenta)	572 (455 to 637)	1 (1 to 1)	26 (1)	⨁◯◯◯ VERY LOW [a,b]	
False negatives (patients incorrectly classified as not having placenta)	78 (13 to 195)	0 (0 to 0)			
True negatives (patients without placenta)	350 (269 to 350)	999 (769 to 999)	14 (1)	⨁◯◯◯ VERY LOW [a,b]	
False positives (patients incorrectly classified as having placenta)	0 (0 to 81)	0 (0 to 230)			

CI: Confidence interval; **MRI:** magnetic resonance imaging

a. According to QUADAS2; b. Wide CIs

4.2. Frage 2

Im folgenden Abschnitt folgt eine kurze Darstellung der wichtigsten Ergebnisse. Ergänzt werden die Ergebnisse durch detaillierte Tabellen, die aus Review Manager 5.3 exportiert wurden, siehe Appendix D.

Für die Beantwortung von Frage 2 (Effekte auf patientenrelevante Endpunkte durch frühzeitige Prognose) wurden sechs Studien identifiziert.[27-32] Es handelt sich bei allen Studien um veröffentlichtes Material. Im Mittel dauerten die Studien etwa zehn Jahre an (siehe Tabelle 14).

Tabelle 13: Studiencharakteristika Frage 2

Studie	Studientyp	Setting	Rekrutierungs-zeitraum	Patienten-zahl
Chantraine et al. 2013	Kohortenstudie	NR, Multizentrisch	1998-2011	66
Clouqueur et al. 2008	Kohortenstudie	Frankreich, High-Level Maternity Unit	1996-2006	21
Hall et al. 2014	Kohortenstudie	NR, Praxen	2005-2012	35
Sofiah et al. 2009	Kohortenstudie	Australien, Krankenhaus	1993-2005	40
Tikkanen et al. 2011	Kohortenstudie	Finnland, Universitätsklinik	1998-2010	44
Wong et al. 2008	Kohortenstudie	Neuseeland, Krankenhaus	2000-2006	16

4.2.1. Risk of Bias Bewertung mit QUIPS

Tabelle 14: Risk of Bias Assessment Frage 2

Studie	Study Participation	Study attrition	Prognostic factor measurement	Outcomes	Outcome measurement	Study Confounders	Statistical analysis and Reporting
Chantraine et al. 2013	+	O	-	Maternal mortality, hysterectomy, infections, uterine artery embolization, fetal mortality (intra-abdominal bleeding), gestational age at delivery	+	-	-
				Transfusions	O		
Clouqueur et al. 2008	O	O	-	Maternal mortality, hysterectomy Neonatal mortality	+	-	-
				Transfusions, estimated blood loss	O		
Hall et al. 2014	+	O	-	Maternal length of stay, ICU admission, ICU length of stay, operative injury Neonatal 5-minute Apgar scores <7 NICU admission, NICU length of stay,	+	-	-
				Transfusions, estimated blood loss	O		
Sofiah et al. 2009	O	O	-	Estimated blood loss	O	-	-
				Cesarean Section	-		
				Gestational age at delivery	+		
Tikkanen et al. 2011	+	O	-	Hysterectomy, estimated blood loss, operative complications (urinary tract injury, bleeding, hematoma, infection) length of stay, gestational age at delivery	+	-	-
				Transfusions	O		
				Cesarean Section	-		

Wong et al. 2008	**+**	**O**	**-**	hysterectomy, ICU admission, Length of stay, gestational age at delivery	**+**	**-**	**-**
				Infections, estimated blood loss	**O**		

ICU = Intensive care unit; NICU = Neonatal intensive care unit

+ low risk of bias

- high risk of bias

O moderate risk of bias

4.2.2. Patienten

In den sechs Studien wurden im Median 37 Patientinnen eingeschlossen (Spannweite: 16-66 siehe Tabelle14). Chantraine et al. schlossen Patientinnen mit „einfacher Plazenta accreta“ aus und nur Plazenta increata und percreta ein.[27] Die meisten Frauen waren etwa 33 Jahre alt (Spannweite 29-35) und hatten bereits zwei bis drei Kinder entbunden. Hall et al. berichtet, dass 89% der Frauen in der Studie kaukasischer Herkunft waren.[29]

4.2.3. Intervention

Die genannten Studien untersuchten die prenatale Diagnose von Plazentationsstörungen mittels Ultraschall. Sofiah et al. führten in 77.5% ihrer Patienten eine Ultraschalluntersuchung durch, andere prenatal diagnostizierte Fälle gehen auf „suspicions“ zurück, was nicht näher definiert ist.[30] Drei Studien zogen zusätzlich MRT in Betracht, dabei nutzten Tikkanen et al. das MRT als add-on zur Bestätigung einer Ultraschalldiagnose, bei Cloqueur et al. und Wong et al. ist nicht klar, bei welcher Patientengruppe MRT zusätzlich oder alternativ eingesetzt wurde.[28, 31, 32] Bei Chantraine et al. wurde eine Ultraschall in 42.5% der Fälle als Routine Untersuchung durchgeführt, in den anderen Fällen liegt ein Verdacht auf Placenta Accreta bereits vor (z.B. Blutungen).[27] In den anderen Veröffentlichungen wird die Bergündung für eine Ultraschalluntersuchung nicht näher erläutert.

4.2.4. Kontrolle

Die Kontrolle war intrapartale Diagnose von Placenta Accreta, Increta oder Percreta. Sowohl werden hier Fälle, die keine vorherige Diagnosemaßnahme erhalten haben, als auch Fälle, die in der prenatalen Ultraschalluntersuchung nicht identifiziert wurden, eingeschlossen.[29-31]

4.2.5. Outcome

In Abbildung 7-22 sind alle Outcomes in Forest Plots abgebildet.

Maternal

Mortalität

Das primäre Outcome maternale Mortalität wurde in zwei Studien erhoben (Chantraine et al. Und Clouqueur et al.). Im Untersuchungszeitraum trat in keiner der beiden Studien ein Todesfall auf.[27, 28]

Hysterektomie

Vier Studien zeigten, dass das Risiko einer Hysterektomie bei prenataler Diagnose signifikant niedriger ist (RR = 0.69, 95%KI (0.56-0.85)).[27, 28, 31, 32]

Kaiserschnitt

Es zeigte sich in den fünf Studien, die die Kaiserschnittanzahl angaben, dass die prenatal diagnostizierten Fälle zu fast 100% einen Kaiserschnitt bekamen.[27-31] Dies ist jedoch nicht signifikant (RR = 1.39 95% KI 0.99-1.96).

Blutungen die Transfusionen bedürfen

Chantraine et al., Clouqueur et al. und Hall et al., erhoben wie viele Patientinnen einer Bluttransfusion bedurften.[27-29] Das relative Risiko liegt bei 0.82 (95% KI 0.58-1.16).

Blutungen, geschätzt in Liter

Der geschätzte Blutverlust in Litern scheint etwas niedriger in der Interventionsgruppe zu sein, dies ist jedoch nicht signifikant MD = -1.08 95% KI -2.34-0.17).[28-32]

Einweisung auf die Intensivstation und Intensivstation Verweildauer

Die Anzahl der Einweisungen auf die Intensivstation ist in der Kontrollgruppe erhöht RR = 0.49 (95% KI 0.17-1.39).[27, 29, 32] Hall et al. gab zu dem die Verweildauer auf der Intensivstation an MD = -1.30 (95% KI -3.61- 1.01).[29]

Stationäre Verweildauer

Die allgemeine Verweildauer wurde bei Hall et al., Tikkanen et al. und Wong et al. berichtet, es konnte aber kein signifikanter Unterschied zwischen den Gruppen festgestellt werden (MD = 0.28 95% KI -0.91-1.47).[29, 31, 32]

Postnatale Infektionen

Chantraine et al. und Tikkanen et al. zeigen eine leicht erhöhte Anzahl an Infektionen in der Interventionsgruppe.[27, 31] Wong et al. berichten das Gegenteil.[32] Die Meta-Analyse zeigt ein RR von 1.31 (95% KI 0.39-4.41).

Uterus-Embolisation

Chantraine et al. und Tikkanen et al. zeigen eine nicht signifikante, leicht erhöhte Anzahl an Uterus Embolisationen in der Interventionsgruppe (Meta-Analyse: RR = 2.45 95% KI 0.48-12.63).[27, 31]

Operative Komplikationen

Die Anzahl der operativen Komplikationen ist bei Hall et al. und Tikkanen et al. signifikant höher in der Interventionsgruppe (Meta-Analyse: RR = 2.23 95% KI 1.02-4.89).[29, 31]

Neonatal

Gestationsalter

Es konnte kein signifikanter Unterschied zwischen den beiden Gruppen bezüglich des Gestationsalters festgestellt werden. Insgesamt zeigte sich aber in beiden Gruppen, dass der Mittelwert des Gestationsalter immer im Bereich der Frühgeburtlichkeit lag (<37

Schwangerschaftswoche) Die Meta-Analyse ergab ein MD von -0.10 95% KI -1.86-1.66.[27, 29-32]

Mortalität

Bei Chantraine et al. trat ein Todesfall in der Kontrollgruppe in der 25. Schwangerschaftswoche auf (RR = 0.22 95% KI 0.01, 5.19).[27]

Apgar score <7

Hall et al. erhoben den fünf-Minuten Apgar Score, konnten aber keine eindeutige Richtung des Effektes zeigen (RR = 0.48 95% KI 0.05-4.82).[29]

Einweisung NICU

Clouqueur et al. und Hall et al. zeigen ein RR von 1.74 (95% KI 0.58-5.20), Anzahl an Einweisungen in die NICU für die Interventionsgruppe.[28, 29]

Verweildauer NICU

Hall et al. misst in der Kontrollgruppe eine etwas längere, nicht signifikante Verweildauer auf der NICU (RR = -3.30 95% KI-10.02-3.42).[29]

4.2.6. Datensynthese der Ergbebnisse

Die Datensynthese wurde mithilfe von GRADE durchgeführt, siehe Abbildung 23. Die Qualitätsbewertung reichte von „very low“ bis „high“. Laut Iorio et al. sollen Prognosestudien, die einem Beobachtungsdesign entsprechen, anders als Interventionsstudien mit höchster Qualität eingestuft werden. Dementsprechend wurden alle Outcomes durch das Studiendesign erstmal mit „high“ bewertet und dann abgewertet.[33] Fast alle Outcomes wurden aufgrund ihrer Heterogenität in den Kategorien „Inconsistency“ und „Imprecision“ mindestens um einen Schritt abgewertet.. Weiterhin erhielten alle Studien ein „serious risk“ in der Kategorie „Risk of Bias“. Mögliches Confounding, das in der Studienauswertung nicht berücksichtigt wurde, konnte das Vertrauen in die meisten Ergebnisse verbessern.

Abbildung 7: Forest plot Maternal mortality

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chantraine 2013	0	40	0	26		Not estimable
Clouqueur 2008	0	6	0	15		Not estimable
Total (95% CI)		**46**		**41**		**Not estimable**
Total events	0		0			

Heterogeneity: Not applicable
Test for overall effect: Not applicable

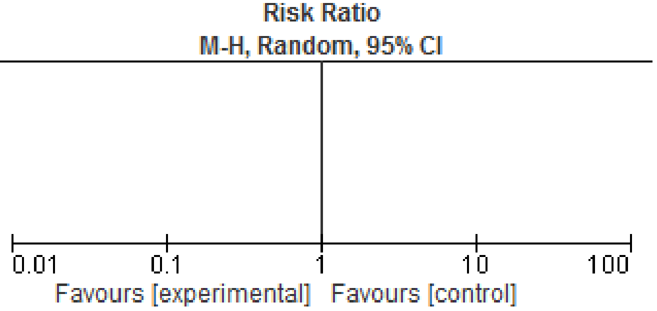


Abbildung 8: Forest plot Cesarean section

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chantraine 2013	40	40	9	26	15.8%	2.81 [1.68, 4.69]
Clouqueur 2008	6	6	12	15	19.9%	1.19 [0.85, 1.65]
Hall 2014	19	19	11	17	19.4%	1.53 [1.07, 2.18]
Sofiah 2009	26	27	12	13	23.0%	1.04 [0.88, 1.24]
Tikkanen 2011	23	24	16	20	21.9%	1.20 [0.95, 1.51]
Total (95% CI)		**116**		**91**	**100.0%**	**1.39 [0.99, 1.96]**
Total events	114		60			

Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 28.33$, df = 4 ($P < 0.0001$); $I^2 = 86\%$
Test for overall effect: Z = 1.87 (P = 0.06)

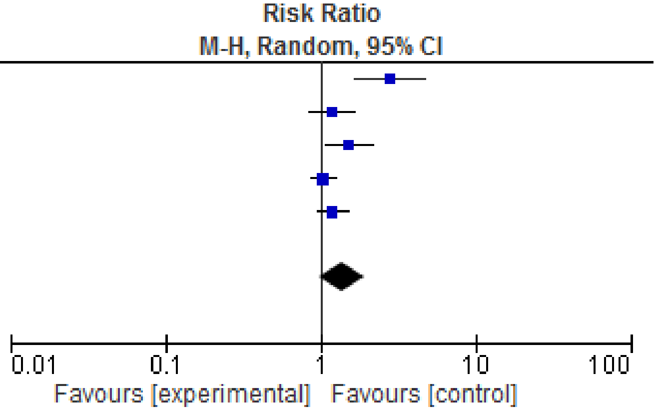


Abbildung 9: Forest Plot Maternal hysterectomy

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chantraine 2013	13	26	25	26	23.9%	0.52 [0.35, 0.77]
Clouqueur 2008	4	6	15	15	12.8%	0.66 [0.38, 1.16]
Tikkanen 2011	18	24	19	20	46.9%	0.79 [0.61, 1.02]
Wong 2008	5	7	9	9	16.4%	0.72 [0.44, 1.18]
Total (95% CI)		**63**		**70**	**100.0%**	**0.69 [0.56, 0.85]**
Total events	40		68			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 3.58$, df = 3 (P = 0.31); $I^2 = 16\%$
Test for overall effect: Z = 3.48 (P = 0.0005)

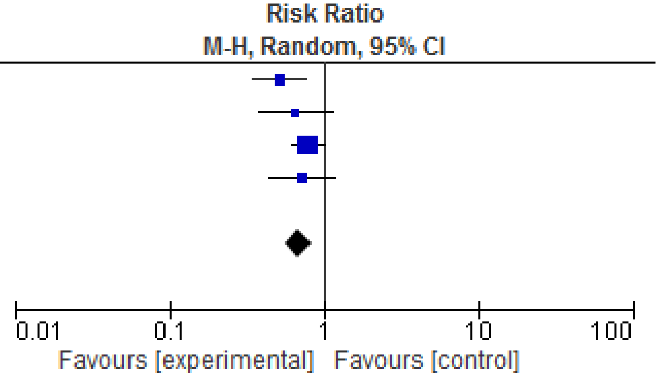


Abbildung 10: Forest plot Maternal bleeding needing transfusion

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chantraine 2013	20	40	15	26	60.6%	0.87 [0.55, 1.36]
Clouqueur 2008	3	6	14	15	18.8%	0.54 [0.24, 1.21]
Hall 2014	8	19	7	17	20.6%	1.02 [0.47, 2.22]
Total (95% CI)		**65**		**58**	**100.0%**	**0.82 [0.58, 1.16]**
Total events	31		36			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.43$, df = 2 (P = 0.49); $I^2 = 0\%$
Test for overall effect: Z = 1.11 (P = 0.27)

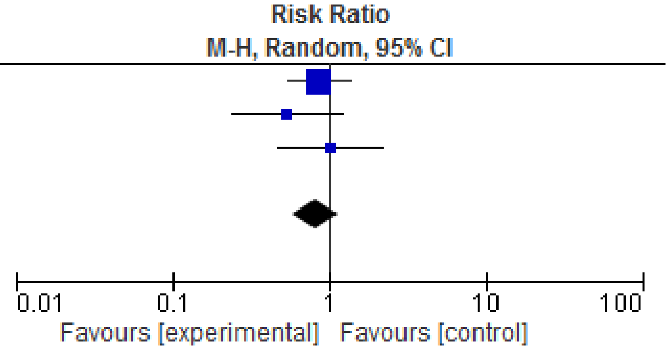


Abbildung 11: Forest plot Maternal estimated blood loss, liter

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Clouqueur 2008	2.9	2.6	6	3.6	1.9	15	16.1%	-0.70 [-2.99, 1.59]
Hall 2014	2.989	1.801	19	2.929	2.192	17	25.2%	0.06 [-1.26, 1.38]
Sofiah 2009	4.648	3.164	27	4.279	3.829	13	15.3%	0.37 [-2.03, 2.77]
Tikkanen 2011	6.025	3.827	24	8.775	3.881	20	16.1%	-2.75 [-5.04, -0.46]
Wong 2008	1.4	1	7	3.6	1.3	9	27.3%	-2.20 [-3.33, -1.07]
Total (95% CI)			**83**			**74**	**100.0%**	**-1.08 [-2.34, 0.17]**

Heterogeneity: Tau² = 1.16; Chi² = 10.11, df = 4 (P = 0.04); I² = 60%
Test for overall effect: Z = 1.70 (P = 0.09)

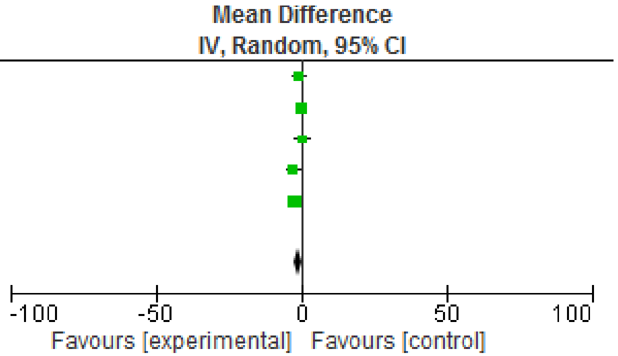


Abbildung 12: Forest plot Maternal admission to the ICU

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chantraine 2013	0	40	1	26	10.9%	0.22 [0.01, 5.19]
Hall 2014	3	19	6	17	72.9%	0.45 [0.13, 1.52]
Wong 2008	1	7	1	9	16.2%	1.29 [0.10, 17.14]
Total (95% CI)		**66**		**52**	**100.0%**	**0.49 [0.17, 1.39]**
Total events	4		8			

Heterogeneity: Tau² = 0.00; Chi² = 0.80, df = 2 (P = 0.67); I² = 0%
Test for overall effect: Z = 1.33 (P = 0.18)

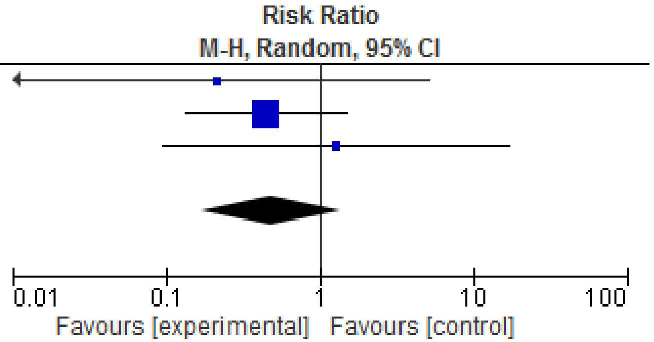


Abbildung 13: Forest plot Maternal ICU length of stay, days

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Hall 2014	0.3	0.8	19	1.6	4.8	17	100.0%	-1.30 [-3.61, 1.01]
Total (95% CI)			**19**			**17**	**100.0%**	**-1.30 [-3.61, 1.01]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)

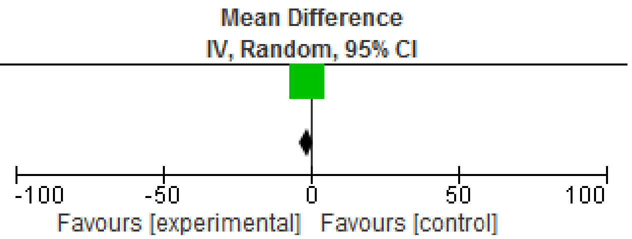


Abbildung 14: Forest plot Maternal length of stay, days

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Hall 2014	5.5	2.3	19	6.4	10.7	17	5.3%	-0.90 [-6.09, 4.29]
Tikkanen 2011	6.5	2.2	24	6.1	2	20	91.9%	0.40 [-0.84, 1.64]
Wong 2008	8.6	4.9	7	9.9	9.3	9	2.8%	-1.30 [-8.38, 5.78]
Total (95% CI)			**50**			**46**	**100.0%**	**0.28 [-0.91, 1.47]**

Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 2 (P = 0.81); I² = 0%
Test for overall effect: Z = 0.47 (P = 0.64)

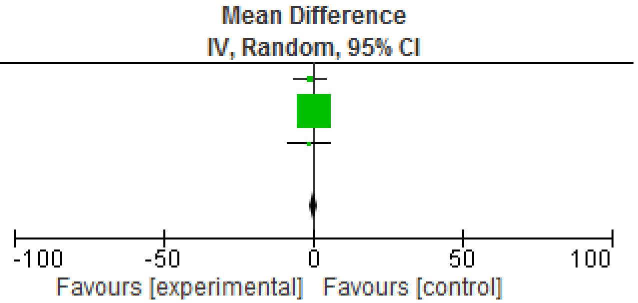


Abbildung 15: Forest Plot Maternal postnatal infections

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chantraine 2013	8	40	3	26	58.0%	1.73 [0.51, 5.94]
Tikkanen 2011	3	24	1	20	25.5%	2.50 [0.28, 22.20]
Wong 2008	0	7	3	9	16.5%	0.18 [0.01, 2.98]
Total (95% CI)		**71**		**55**	**100.0%**	**1.31 [0.39, 4.41]**
Total events	11		7			

Heterogeneity: Tau² = 0.27; Chi² = 2.52, df = 2 (P = 0.28); I² = 21%
Test for overall effect: Z = 0.43 (P = 0.67)

Risk Ratio
M-H, Random, 95% CI

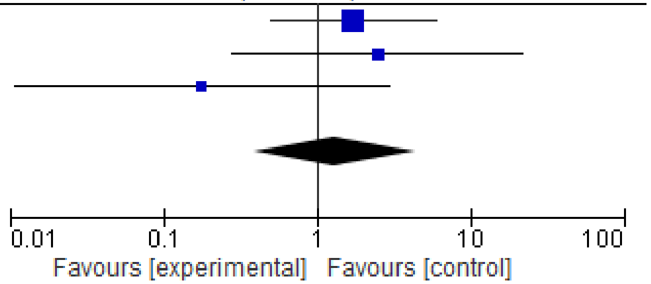


Abbildung 16: Forest plot Maternal uterine artery embolization

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chantraine 2013	7	40	3	26	73.4%	1.52 [0.43, 5.34]
Tikkanen 2011	5	24	0	20	26.6%	9.24 [0.54, 157.57]
Total (95% CI)		**64**		**46**	**100.0%**	**2.45 [0.48, 12.63]**
Total events	12		3			

Heterogeneity: Tau² = 0.54; Chi² = 1.43, df = 1 (P = 0.23); I² = 30%
Test for overall effect: Z = 1.07 (P = 0.28)

Risk Ratio
M-H, Random, 95% CI

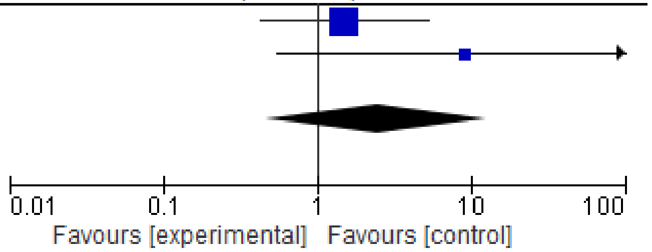


Abbildung 17: Forest plot Maternal operative complications

	Experimental		Control			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Chantraine 2013	3	40	4	26		Not estimable
Hall 2014	3	19	1	17	13.2%	2.68 [0.31, 23.43]
Tikkanen 2011	13	24	5	20	86.8%	2.17 [0.93, 5.04]
Total (95% CI)		**43**		**37**	**100.0%**	**2.23 [1.02, 4.89]**
Total events	16		6			

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%
Test for overall effect: Z = 2.00 (P = 0.05)

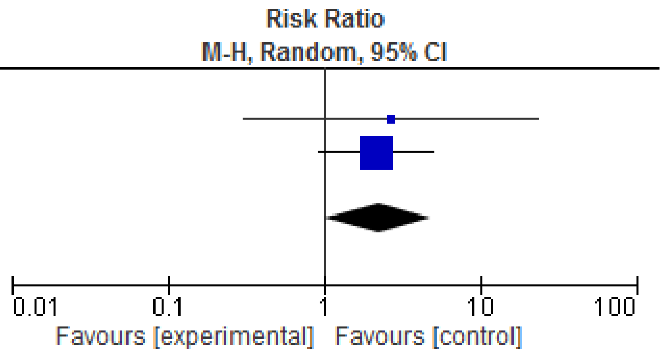


Abbildung 18: Forest plot Gestational age at birth, weeks

	Experimental			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Chantraine 2013	32.25	4.4	40	34.25	3.8	26	28.3%	-2.00 [-4.00, -0.00]
Hall 2014	36.4	1.4	20	35.5	4.8	19	25.9%	0.90 [-1.34, 3.14]
Sofiah 2009	34.3	4.3	27	33.6	10.8	13	7.0%	0.70 [-5.39, 6.79]
Tikkanen 2011	35.1	2.7	24	36	3.7	20	28.9%	-0.90 [-2.85, 1.05]
Wong 2008	35.9	2.1	7	31.4	7.2	9	9.9%	4.50 [-0.45, 9.45]
Total (95% CI)			**118**			**87**	**100.0%**	**-0.10 [-1.86, 1.66]**

Heterogeneity: Tau² = 1.81; Chi² = 7.88, df = 4 (P = 0.10); I² = 49%
Test for overall effect: Z = 0.11 (P = 0.91)

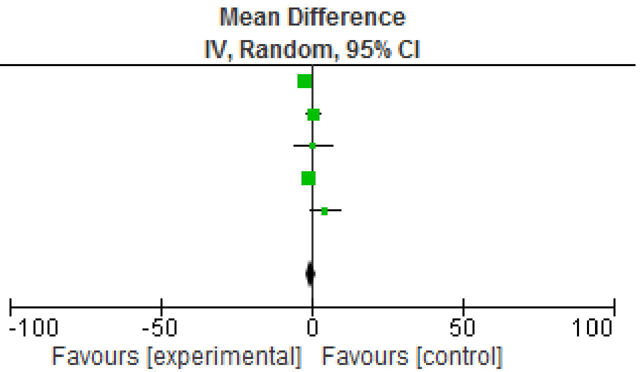


Abbildung 19: Forest plot Fetal death

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chantraine 2013	0	40	1	26	100.0%	0.22 [0.01, 5.19]
Total (95% CI)		**40**		**26**	**100.0%**	**0.22 [0.01, 5.19]**
Total events	0		1			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (P = 0.35)						

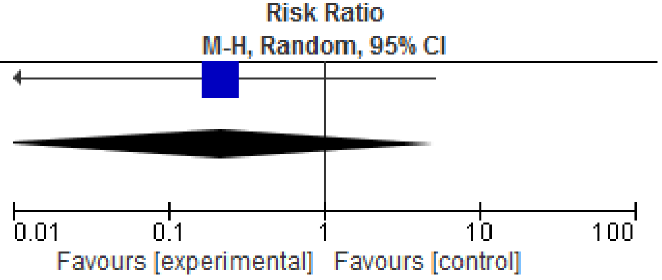


Abbildung 20: Forest plot Neonatal Apgar Score <7

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Hall 2014	1	20	2	19	100.0%	0.47 [0.05, 4.82]
Total (95% CI)		**20**		**19**	**100.0%**	**0.48 [0.05, 4.82]**
Total events	1		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.63 (P = 0.53)						

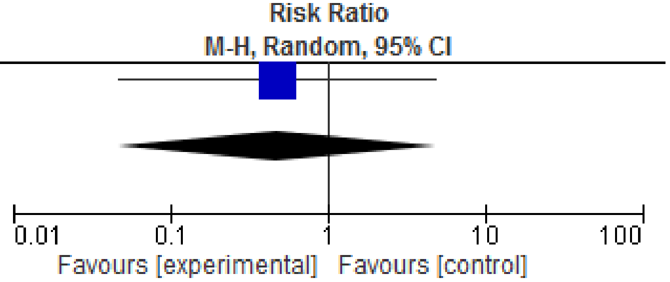


Abbildung 21: Forest plot Neonatal NICU admission

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Clouqueur 2008	6	7	4	15	45.3%	3.21 [1.32, 7.84]
Hall 2014	11	20	10	19	54.7%	1.04 [0.58, 1.87]
Total (95% CI)		**27**		**34**	**100.0%**	**1.74 [0.58, 5.20]**
Total events	17		14			

Heterogeneity: $Tau^2 = 0.48$; $Chi^2 = 4.27$, df = 1 (P = 0.04); $I^2 = 77\%$
Test for overall effect: Z = 0.99 (P = 0.32)

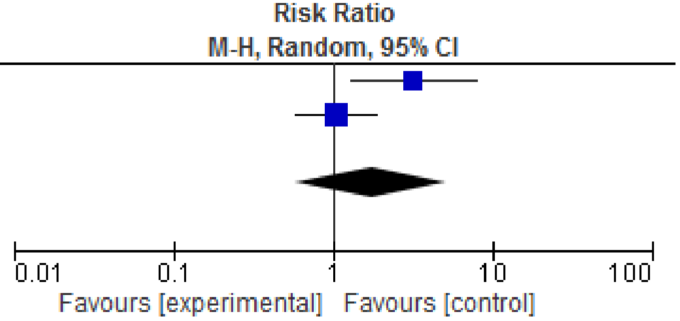


Abbildung 22: Forest plot Neonatal length of stay, days

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Hall 2014	11.5	6.8	20	14.8	13.4	19	100.0%	-3.30 [-10.02, 3.42]
Total (95% CI)			**20**			**19**	**100.0%**	**-3.30 [-10.02, 3.42]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)

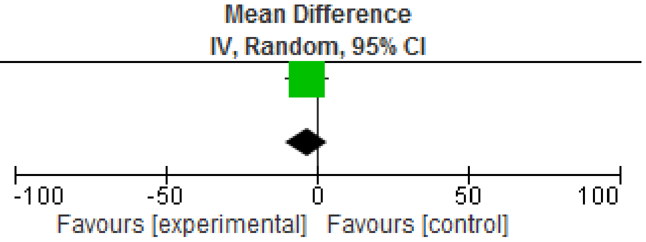


Abbildung 23: GRADE Evidence Profile

Summary of findings:

Prenatal diagnosis compared to intrapartal diagnosis in pregnant women with prior cesarean section or uterus surgery

Patient or population: pregnangt women with prior cesarean section or uterus surgery

Setting:

Intervention: Prenatal diagnosis

Comparison: intrapartal diagnosis

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with intrapartal diagnosis	Risk with Prenatal diagnosis				
Maternal mortality	not pooled	not pooled	not pooled	87 (2 cohort studies)	⊕◯◯◯ VERY LOW [a]	No Events occured
Cesarean Section	659 per 1.000	**916 per 1.000** (653 to 1.000)	**RR 1.39** (0.99 to 1.96)	207 (5 cohort studies)	⊕◯◯◯ VERY LOW [b,c,d,e,f]	
Maternal hysterectomy	971 per 1.000	**670 per 1.000** (544 to 826)	**RR 0.69** (0.56 to 0.85)	133 (4 cohort studies)	⊕⊕⊕◯ MODERATE [a,b]	
Maternal bleeding needing transfusion	621 per 1.000	**509 per 1.000** (360 to 720)	**RR 0.82** (0.58 to 1.16)	123 (3 cohort studies)	⊕⊕⊕◯ MODERATE [b,g]	
Maternal estimated blood loss, liter	The mean maternal estimated blood loss, liter was **0**	The mean maternal estimated blood loss, liter in the intervention group was 1,08 lower (2,34 lower to 0,17 higher)	-	157 (5 cohort studies)	⊕⊕◯◯ LOW [a,b,c,h]	

Summary of findings:

Prenatal diagnosis compared to intrapartal diagnosis in pregnant women with prior cesarean section or uterus surgery

Patient or population: pregnangt women with prior cesarean section or uterus surgery

Setting:

Intervention: Prenatal diagnosis

Comparison: intrapartal diagnosis

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with intrapartal diagnosis	**Risk with Prenatal diagnosis**				
Maternal admission to the ICU	154 per 1.000	**75 per 1.000** (26 to 214)	**RR 0.49** (0.17 to 1.39)	118 (3 cohort studies)	⨁⨁⨁⨁ HIGH [b,f]	
Maternal ICU length of stay, days	The mean maternal ICU length of stay, days was **0**	The mean maternal ICU length of stay, days in the intervention group was 1,3 lower (3,61 lower to 1,01 higher)	-	36 (1 cohort study)	⨁⨁◯◯ LOW [a,b]	
Maternal length of stay, days	The mean maternal length of stay, days was **0**	The mean maternal length of stay, days in the intervention group was 0,28 higher (0,91 lower to 1,47 higher)	-	96 (3 cohort studys)	⨁⨁⨁◯ MODERATE [b,f]	
Maternal postnatal infections	127 per 1.000	**167 per 1.000** (50 to 561)	**RR 1.31** (0.39 to 4.41)	126 (3 cohort studies)	⨁◯◯◯ VERY LOW [a,b,f,i]	
Maternal uterine artery embolization	65 per 1.000	**160 per 1.000** (31 to 824)	**RR 2.45** (0.48 to 12.63)	110 (2 cohort studies)	⨁⨁◯◯ LOW [a,b,f]	

Summary of findings:

Prenatal diagnosis compared to intrapartal diagnosis in pregnant women with prior cesarean section or uterus surgery

Patient or population: pregnangt women with prior cesarean section or uterus surgery

Setting:

Intervention: Prenatal diagnosis

Comparison: intrapartal diagnosis

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with intrapartal diagnosis	**Risk with Prenatal diagnosis**				
Maternal operative complications	162 per 1.000	**362 per 1.000** (165 to 793)	**RR 2.23** (1.02 to 4.89)	80 (2 cohort studies)	⊕⊕⊕◯ MODERATE [a,b,j]	
Gestational age at birth, weeks	The mean gestational age at birth, weeks was **0**	The mean gestational age at birth, weeks in the intervention group was 0,1 lower (1,86 lower to 1,66 higher)	-	205 (5 cohort studies)	⊕⊕◯◯ LOW [b,c,f]	
Fetal death	38 per 1.000	**8 per 1.000** (0 to 200)	**RR 0.22** (0.01 to 5.19)	66 (1 cohort study)	⊕⊕◯◯ LOW [b,f]	
Neonatal Apgar score <7	105 per 1.000	**51 per 1.000** (5 to 507)	**RR 0.48** (0.05 to 4.82)	39 (1 cohort study)	⊕◯◯◯ VERY LOW [b,f]	
Neonatal NICU admission	412 per 1.000	**716 per 1.000** (239 to 1.000)	**RR 1.74** (0.58 to 5.20)	61 (2 cohort studies)	⊕◯◯◯ VERY LOW [b,c,d,f]	

Summary of findings:

Prenatal diagnosis compared to intrapartal diagnosis in pregnant women with prior cesarean section or uterus surgery

Patient or population: pregnangt women with prior cesarean section or uterus surgery

Setting:

Intervention: Prenatal diagnosis

Comparison: intrapartal diagnosis

Outcomes	**Anticipated absolute effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with intrapartal diagnosis	**Risk with Prenatal diagnosis**				
Neonatal NICU length of stay, days	The mean neonatal NICU length of stay, days was **0**	The mean neonatal NICU length of stay, days in the intervention group was 3,3 lower (10,02 lower to 3,42 higher)	-	39 (1 cohort study)	⊕⊕◯◯ LOW [b,f]	

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio; **RR:** Risk ratio; **MD:** Mean difference; **ICU:** Intensive care unit; **NICU:** Neonatal intensive care unit

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. No explanation was provided; b. According to QUIPS; c. High heterogeneity; d. Non overlapping CI; e. Diagnostic test/assessment may not be comparable; f. Wide CI include potential benefits and harms; g. Blood products may be provided with the diagnosis; h. Estimate of blood loss may differ; i. Infections not specified; j. Operative injuries not specified

5. Diskussion

Frage 1

Zur Beantwortung der Frage 1 „Wie genau lassen sich Plazentationsstörungen mit Sonografie und MRT diagnostizieren?“ konnten 10 Studien identifiziert werden. Dabei untersuchte eine Studie, ob verschiedene Bewerter bei einzelnen Ultraschalluntersuchungen (2 pro Patientin) zu dem gleichen Ergebnis kommen (Placenta accreta ja/nein).[10] Neun Studien prüften die diagnostische Güte von Ultraschalluntersuchungen zur Identifikation von Plazentationsstörungen.[12, 18-25] Davon untersuchten vier zusätzlich die diagnostische Güte von einer MRT Untersuchung zur Identifikation von Plazentationsstörungen (Patienten identisch mit denen die auch Ultraschalluntersuchung erhielten).[21-24] Eine andere prüfte die Genauigkeit von MRT zur Diagnose von Plazentationsstörungen als add-on Test bei unklarem Ultraschallbefund.[18] Wie in den Ergebnissen bereits berichtet, zeigte sich, dass die Studien, die Ultraschall als Diagnoseverfahren untersuchten, vor allem in Hinblick auf die Spezifität, aber auch in Hinblick auf Sensitivität zu sehr unterschiedlichen Ergebnissen kommen. Bowman et al. zeigten, dass die Diagnose von einer Placenta accreta auf zwei unterschiedlichen Ultraschallbildern/-untersuchungen häufig nicht übereinstimmt.[10] Dies deutet darauf hin, dass die tatsächliche diagnostische Güte von Ultraschall unklar ist und möglicherweise nur in bestimmten Populationen, oder Settings zu einer hohen Aussagekraft führen kann. Ein besonderes Augenmerk liegt dabei auf Hochrisikopopulationen. Je mehr Kaiserschnitte eine Frau bereits hatte, desto höher ist die Wahrscheinlichkeit, dass sie eine Plazentationsstörung bei vorliegender Plazenta Previa entwickelt.[34] Die drei Studien, die besonders gute Werte in der Prüfung zur diagnostischen Güte erreichen, sind Collins et al., Masselli et al. und Riteau et al..[20, 22, 23] Collins et al., erreichen sowohl eine hohe Sensitivität als auch Spezifität in einer eher großen Patientengruppe (n=89). Sie haben keine eindeutigen Kriterien definiert, sondern messen einen bestimmten Bereich („The largest area of confluent three-dimensional power Doppler signal“[20]) in der 4D Darstellung. Weiterhin werden die Bilder von nur einem Betrachter bewertet. Dafür wurden nur Patientinnen mit diagnostizierter Plazenta Previa eingeschlossen, was auf eine Verzerrung deuten kann, dadurch dass die Patientinnen bereits als Risikogruppe identifiziert wurden.[20] Bei Masselli et al., die auch eine hohe Sensitivität und Spezifität erreichen, werde hingegen nur 50 Patientinnen untersucht. Auch diese hatten alle bereits eine Plazenta Previa Diagnose. Es wurden keine Diagnosekriterien berichtet, dafür wurde aber die Bewertung von zwei Personen durchgeführt.[22] Riteau et al. erreichen bei einer Sensitivität von 100% eine Spezifität von nur 38% (95% KI 0.15-0.65). Es wurden allerdings auch nur 42 Patientinnen eingeschlossen und keine Diagnosekriterien berichtet. Die Bewertung wurde von zwei Personen mit mindestens fünf Jahren Erfahrung in der Diagnose von Plazentationsstörungen durchgeführt.[23] Es konnte sich kein eindeutiges Kriterium zeigen, für das Ultraschall zur Diagnose von Plazentationsstörungen eine hohe diagnostische Güte hat. Die beiden größten Studien, Chalubinski et al. mit 232 Patientinnen und Warshak et al. mit 453 Patientinnen erreichten beide spezifische Ergebnisse (96%), allerdings war auch der Anteil der Patientinnen, die tatsächlich eine Plazentationsstörung hatten, wesentlich geringer (ca. 10%).[18, 19] In den anderen Studien war der Anteil der Patientinnen mit Plazentatationsstörungen deutlich höher (bis 60%), was darauf zurückzuführen ist, dass vielmals Patientinnen mit Verdacht auf Plazentationsstörungen in die jeweiligen Kliniken überwiesen wurden. Dies könnte möglicherweise bedeuten, dass die Patienten bereits eine Ultraschalluntersuchung hatten und dadurch wäre wiederum der Vergleich dieser

Patientengruppe mit der ohne Verdacht auf Plazentationsstörungen nicht vergleichbar. Außerdem ist damit eine Übertragung auf die Allgemeinbevölkerung eingeschränkt. Laut einer Studie von Fitzpatrick et al. liegt die Prävalenz bei nur 0.09% bei Patientinnen mit mindestens einem vorangegangenem Kaiserschnitt.[35]

Im Gegensatz zu den Ultraschallbewertungen, schließen die Studien, die MRT untersuchen, alle weniger als 50 Patientinnen ein. Die Werte streuen bei MRT Untersuchungen aufgrund der geringen Patientenzahl noch mehr und es lässt sich keine Erkenntnis über die Güte von MRT Untersuchungen ableiten. Masselli et al. fallen jedoch auch bei der MRT Untersuchung durch eine hohe diagnostische Güte auf. In der Publikation zeigt sich dennoch kein Kriterium wie, Patientencharakteristika, Diagnosekriterien o.ä., das die hohe diagnostische Güte beeinflusst haben könnte.[22] Weiterhin ist sowohl für Ultraschall als auch MRT zu beachten, dass es neben unterschiedlichen Diagnosekriterien, Bewertern und Patientengruppen immer auch um unterschiedliche Geräte und deren Einstellungen geht. Dies ist vor allem ein wichtiger Hinweis, wenn es zur Übertragbarkeit der Studienergebnisse auf eine Zielgruppe geht. So sind die Ausstattung und das Personal, das mit diesem umgeht, anders einzuschätzen als in einem Krankenhaus der Regelversorgung mit geburtshilflicher Station. Falls eine Übertragung auf niedergelassene Ärzte erreicht werden soll, birgt dies wieder Abweichungen, hier auch vor allem bei der Patientenpopulation.

Die Studien wurden mit dem QUADAS 2 Tool für Diagnosestudien bewertet. Chalubinski et al. und Bowman et al. wurden am besten bewertet, hier gab es nur Zweifel am Kriterium „Flow and Timing“. Dies wurde allerdings bei allen Studien als negativ oder unklar bewertet, was zu einem Teil an der Bewertung des Zeitraums zwischen diagnostischem Test und Referenztest (Klinik/Histopathologie bei Geburt) lag. Hierbei handelt es sich auch um das größte Verzerrungspotential der Studien, da keine Studie direkt nach dem Indextest einen Referenztest einsetzt, was im vorliegenden Studienaufbau auch nicht möglich ist, da der Referenztest erst bei Geburt erfolgen kann. Es handelt sich also bei genauerer Betrachtung eher um Prognosestudien, da die Vorhersage des Ereignisses erst bei dessen Eintreten bestätigt wird. In der Literatur werden diese Studien allerdings alle als Diagnosestudien bezeichnet. Die Einschätzung mit GRADE zeigte ein niedriges bis sehr niedriges Vertrauen in die Studienergebnisse.

Frage 2

Zur Beantwortung von Frage 2: „Hat die präpartale Prognose einer Plazentationsstörung bei Schwangeren mit Zustand nach Sectio / Uterusoperation einen positiven Einfluss auf die mütterliche Gesundheit?“ wurden sechs Studien identifiziert. Es konnten keine Bewertung des Nutzen durch prenatale Diagnose hinsichtlich Mortalität (primäres Outcome) vorgenommen werden, da im Studienzeitraum kein Ereignis auftrat. In der Gruppe prenatale Diagnose gab es signifikant weniger Hysterektomien bei der Geburt (RR = 0.69 95% KI 0.56-0.85)) aber signifikant mehr operative Komplikationen (RR = 2.23 95% KI 1.02-4.89). Alle anderen Endpunkte zeigten keine signifikanten Unterschiede in den Gruppen und einige Studien zeigten positive Effekte während andere negative zeigten, so dass noch nicht einmal eine Effektrichtung bestimmt werden konnte. Der Endpunkt Kaiserschnitt zeigte zwar eine (nicht signifikant) höhere Rate in der Interventionsgruppe, aber dieser Endpunkt ist so wie einige andere auch eine Managemententscheidung. Hall et al. berichten, dass alle positiv diagnostizierten einen elektiven Kaiserschnitt zwischen der 35. und 37. Schwangerschaftswoche erhalten.[29] Es ist nicht möglich den Unterschied zwischen den Kaiserschnitten, die als Managemententscheidung durchgeführt worden von denen zu unterscheiden, die aufgrund klinischer Ursachen erfolgten. Dennoch scheinen mehr Kaiserschnitte bei Patientinnen mit Plazentationsstörungen mit weniger Hysterektomien einherzugehen. Ein weiterer Punkt, dem eine Managemententscheidung vorausgeht, ist die Anzahl der Bluttransfusionen und der geschätzte Blutverlust. Auch hier berichten Hall et al. dass vier Packungen Erythrozyten Konzentrat und ein „Cell Saver“ bei positiver Diagnose im OP-Saal vorliegen. Auch wurde die Blutbank über den geplanten Eingriff informiert.[29] Somit zeigten die drei Studien, die den Gebrauch von Blutprodukten erfassten, eine leicht höhere Tendenz in der Gruppe der prenatal diagnostizierten.[27-29]

Insgesamt schlossen die Studien alle eine kleine Zahl an Patientinnen ein, was daran liegt, dass es sich um eine seltene Erkrankung handelt.[35] Das Verzerrungspotential wurde mit dem QUIPS Tool für Prognosestudien bewertet. Die Studien zeigten alle ein mehr oder weniger hohes Risiko für Verzerrungen. Die Kategorien „Prognostic Factor Measurement“, „Study Confounding“ und „Statistical Analysis and Reporting“ wurden für alle Studien mit einem hohen Risiko bewertet. Bei „Outcome Measurement“ wurden die Endpunkte der Studien einzeln bewertet, z.B. nicht weiter spezifizierte Infektionen haben ein höheres Verzerrungspotential als Hysterektomien. Die Beurteilung mit GRADE zeigte in den meisten Outcomes eine niedrige oder sehr niedrige Einschätzung über das Vertrauen in die Ergebnisse. Ein Outcome erreichte eine Bewertung mit „high“ und vier Outcomes „moderate“, darunter Hysterektomien, das auch das einzige war, das signifikant niedrigere Fallzahlen in der Interventionsgruppe erreichte.

Die Übertragbarkeit der Ergebnisse ist eingeschränkt, da es sich bei den Studien um ausländische Publikationen handelt und es möglicherweise landesspezifische Managementstrategien gibt. Hinzu kommen die Ausstattung und das medizinische Personal, dass die Diagnose vornimmt, das sich national auf Klinikebene unterscheidet. Weiterhin sind die Studien sehr heterogen hinsichtlich der Einschlusskriterien. So berichtet Hall et al. dass die Patientinnen in der Kontrollgruppe zum Großteil eine Ultraschalluntersuchung erhielten, diese aber Falsch-negativ war (14 von 17 Fällen).[29] Chantraine et al. berichten nur, dass die Kontrollgruppe keine Diagnose erhielt.[27] Genauso wurden auch Teilnehmer in der Interventionsgruppe unterschiedlich eingeschlossen. Chantraine et al. schlossen 57.5% mit einem Verdacht auf Plazenta accreta in die Diagnosegruppe ein.[27]

Eine Aussage über sowohl die diagnostische Güte von Ultraschall und MRT und deren patientenrelevanten Nutzen ist abschließend nicht möglich. Der Forschungsstand zum Thema Diagnose von Plazentationsstörungen nach vorangegangenem Kaiserschnitt ist ungenügend. Es wurden zwar einige Studien identifiziert, jedoch schlossen diese wenige Patientinnen ein und das Verzerrungspotential war hoch. Eine Tendenz, dass Ultraschall eine hohe Sensitivität erreichen kann und die diagnostische Güte von MRT insgesamt eher schwach ist, lässt sich ableiten. Bezüglich des patientenrelevanten Nutzen scheint eine frühe Diagnose zu einer geringeren Anzahl von Hysterektomien zurückzuführen sein, was durch eine höhere Kaiserschnittrate (als Managemententscheidung) begründbar sein mag. Allerdings führen die hohe Anzahl an Falsch-positiven in einer Population mit geringem Risiko, welches der Allgemeinbevölkerung betrifft, die getestet werden soll, zu möglicherweise negativen Auswirkung, z.B. eine erhöhte Kaiserschnittrate. Für eine Beantwortung der Frage, ob prenatale Diagnose durch Ultraschall oder MRT eine Auswirkung auf die mütterliche Gesundheit hat, wurde in dieser Arbeit das Konzept „linked evidence“ angewendet. Wünschenswert sind qualitativ hochwertige Studien, die beide Schritte kombinieren, sowohl diagnostische Güte bewerten als auch Effekte der Diagnose (z.B. randomisierte Screeningstudien).

6. Appendix

Appendix A: QUADAS 2 Tool

DOMAIN	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING
Description	Describe methods of patient selection Describe included patients (previous testing, presentation, intended use of index test and setting)	Describe the index test and how it was conducted and interpreted	Describe the reference standard and how it was conducted and interpreted	Describe any patients who did not receive the index tests or reference standard or who were excluded from the 2 x 2 table (refer to flow diagram) Describe the interval and any interventions between index tests and the reference standard
Signaling questions (yes, no, or unclear)	Was a consecutive or random sample of patients enrolled? Was a case-control design avoided? Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standards? If a threshold was used, was it prespecified?	Is the reference standard likely to correctly classify the target condition? Were the reference standard results interpreted without knowledge of the results of the index tests?	Was there an appropriate interval between index tests and reference standard? Did all patients receive a reference standard? Did all patients receive the same reference standard? Were all patients included in the analysis?
Risk of bias (high, low, or unclear)	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct, or its interpretation have introduced bias?	Could the patient flow have introduced bias?
Concerns about applicability (high, low, or unclear)	Are there concerns that the included patients do not match the review question?	Are there concerns that the index test, its conduct, or its interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	

Whiting, P. F., et al. (2011). "Quadas-2: A revised tool for the quality assessment of diagnostic accuracy studies." Annals of Internal Medicine 155(8): 529-536.

Appendix B: QUIPS Tool

Domains	Prompting items for Consideration	Ratings
Study Participation	a. Adequate participation in the study by eligible persons b. Description of the source population or population of interest c. Description of the baseline study sample d. Adequate description of the sampling frame and recruitment e. Adequate description of the period and place of recruitment f. Adequate description of inclusion and exclusion criteria	**High bias**: The relationship between the PF and outcome is very likely to be different for participants and eligible nonparticipants **Moderate bias**: The relationship between the PF and outcome may be different for participants and eligible nonparticipants **Low bias**: The relationship between the PF and outcome is unlikely to be different for participants and eligible nonparticipants
Study Attrition	a. Adequate response rate for study participants b. Description of attempts to collect information on participants who dropped out c. Reasons for loss to follow-up are provided d. Adequate description of participants lost to follow-up e. There are no important differences between participants who completed the study and those who did not	**High bias**: The relationship between the PF and outcome is very likely to be different for completing and non-completing participants **Moderate bias**: The relationship between the PF and outcome may be different for completing and non-completing participants **Low bias**: The relationship between the PF and outcome is unlikely to be different for completing and non-completing participants
Prognostic Factor Measurement	a. A clear definition or description of the PF is provided b. Method of PF measurement is adequately valid and reliable c. Continuous variables are reported or appropriate cut points are used d. The method and setting of measurement of PF is the same for all study participants e. Adequate proportion of the study sample has complete data for the PF f. Appropriate methods of imputation are used for missing PF data	**High bias**: The measurement of the PF is very likely to be different for different levels of the outcome of interest **Moderate bias**: The measurement of the PF may be different for different levels of the outcome of interest **Low bias**: The measurement of the PF is unlikely to be different for different levels of the outcome of interest
Outcome Measurement	a. A clear definition of the outcome is provided b. Method of outcome measurement used is adequately valid and reliable	**High bias**: The measurement of the outcome is very likely to be different related to the baseline level of

	c. The method and setting of outcome measurement is the same for all study participants	the PF **Moderate bias**: The measurement of the outcome may be different related to the baseline level of the PF **Low bias**: The measurement of the outcome is unlikely to be different related to the baseline level of the PF
Study Confounding	a. All important confounders are measured b. Clear definitions of the important confounders measured are provided c. Measurement of all important confounders is adequately valid and reliable d. The method and setting of confounding measurement are the same for all study participants e. Appropriate methods are used if imputation is used for missing confounder data f. Important potential confounders are accounted for in the study design g. Important potential confounders are accounted for in the analysis	**High bias:** The observed effect of the PF on the outcome is very likely to be distorted by another factor related to PF and outcome **Moderate bias:** The observed effect of the PF on outcome may be distorted by another factor related to PF and outcome **Low bias:** The observed effect of the PF on outcome is unlikely to be distorted by another factor related to PF and outcome
Statistical Analysis and Reporting	a. Sufficient presentation of data to assess the adequacy of the analytic strategy b. Strategy for model building is appropriate and is based on a conceptual framework or model c. The selected statistical model is adequate for the design of the study d. There is no selective reporting of results	**High bias**: The reported results are very likely to be spurious or biased related to analysis or reporting **Moderate bias**: The reported results may be spurious or biased related to analysis or reporting **Low bias**: The reported results are unlikely to be spurious or biased related to analysis or reporting

Hayden, J. A., et al. (2013). "Assessing bias in studies of prognostic factors." Ann Intern Med **158**(4): 280-286.

Appendix C: GRADE, Assessing the quality of a body of evidence

Levels of quality of a body of evidence in the GRADE approach	
Underlying methodology	**Quality rating**
Randomized trials; or double-upgraded observational studies.	High
Downgraded randomized trials; or upgraded observational studies.	Moderate
Double-downgraded randomized trials; or observational studies.	Low
Triple-downgraded randomized trials; or downgraded observational studies; or case series/case reports.	Very low
Factors that may decrease the quality level of a body of evidence	
1. Limitations in the design and implementation of available studies suggesting high likelihood of bias. 2. Indirectness of evidence (indirect population, intervention, control, outcomes). 3. Unexplained heterogeneity or inconsistency of results (including problems with subgroup analyses). 4. Imprecision of results (wide confidence intervals). 5. High probability of publication bias.	
Factors that may increase the quality level of a body of evidence	
1. Large magnitude of effect. 2. All plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect. 3. Dose-response gradient.	

Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P and Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. In: S HJG, editor. Cochrane Handbook for Systematic Reviews of Interventions Version 510 (updated March 2011). www.cochrane-handbook.org.: The Cochrane Collaboration; 2011.

Appendix D: Studiencharakteristika der eingeschlossenen Studien

Frage 1

Bowman 2014	
Patient Sampling	Case-control design, patients with documentation of diagnosis of placenta accreta were matched to patients with placenta previa but no accreta. Recruitment period: 2000 - 2012
Patient characteristics and setting	**Sample size (analysed):** 55 **Inclusion criteria:** Women with either placenta previa or placenta accrete **Patient characteristics accreta/previa without accreta:** Age (mean; SD): 32.4; 5.2 / 31.3; 6.9 BMI (mean; SD): 29.0; 9.4 / 31.9; 6.9 Gravidity (median, range): 5 (2-18) / 4 (1-14) Parity (median, range): 3 (1-7) / 2 (0-10) ***Cesarean delivery (%)*** 0: 1.8 / 28.6 1: 30.9 / 44.6 2: 29.1 / 16.1 3+: 38.2 / 10.7 Gestational age at study, wk (median, interquartile range): 29.2 (25.1 -32.4) / 29.3 (23.9-33.6) Delivery gestational age, wk (mean; SD): 33.8; 3.0 / 34.9; 4.0 **Setting:** University clinic, USA
Index tests	**Device:** Ultrasound/Color Doppler **Procedure:** 229 Ultrasound studies (images) were reviewed (116 from the 55 cases, 113 from 56 controls). Senesitivity and specificity were calculated for studies. Investigator scored presence of placenta accreta as "yes", "no" or "unable to determine". Confidence for each imaging study was scored from 0 (none) to 10 (certain) and image quality was scored from 1 (very poor) to 10 (best). **Criteria:** Findings associated with diagnosis: number of lacunae, loss of retroplacental clear space, loss of visualization of the myometrium and bladder wall irregularity. If colour Doppler was used, investigators further identified the presence or absence of the following: subplacental vascularity,vessels bridging from the placenta to the uterine margin, gaps in myometrial blood flow, vessels crossing interface disruption sites, or turbulent lacunae. **Rater:** three obstetric radiologists and three maternal-fetal medicinephysicians with at least eight years of experience. Raters were blinded to clinical history
Target condition and reference standard(s)	clinical, documentation of abnormal adherence of the placenta or evidence of gross placental invasion at the time of surgery, or histopathologic, documentation of placental invasion into the myometrium

Flow and timing	See above (gestational age at study and gestational age at delivery). About four-five weeks. Index test at a gestational age of greater than or equal to 16 weeks. Diagnosis at delivery. Clinical or histopathologic diagnosis of placenta accreta. Patients were included if they had ultrasound images of the placenta available

SD: standard deviation; wk: week;

Chalubinski 2013	
Patient Sampling	Cohort-design. 232 consecutive patients who were included in this screening program. Recruitment period: 01.2001 - 01.2011.
Patient characteristics and setting	**Sample size (analysed):** 232 **Inclusion criteria:** patients with one of these risk factors: - placenta previa - history of more than one uterine surgery (CS, dilatation and curettage, myomectomy) - history of manual placenta separation during a previous delivery, according to the guidelines for peripartum hemorrhage of the German society of Gynecology and Obstetrics **Patient characteristics:** Age (years, median; range): 33; 21-49 age > 35 (%): 38.8 Multiparity (%): 11.2 History of manual placenta separation (%): 6 One or more previous CS (%): 36.2 One or more previous dilatation and curettage procedures (%): 27.6 One or more myomectomy procedures (%): 4.3 IVF treatment (%): 8.6 Cesarean delivery (%): 78.1 **Setting:** Department of Fetomaternal Medicine of the Medical University of Vienna, Austria
Index tests	**Device:** commercially available real-time equipment, with standard 3.75-MHz linear or sector transducers transabdominally and 7.5- MHz sector transducers transvaginally. Two-dimensional gray-scale, color and power Doppler ultrasound imaging. **Procedure:** ultrasound focusing on the placenta and the retroplacental myometrial zone. Transvaginal examinations were performed with a partially filled bladder to optimize evaluation of the uterine and bladder serosa. The whole placenta was scanned in a systematic manner using both gray-scale ultrasound and color-flow mapping. Performed by one highly experienced operator **Criteria:** Normal placentation was assumed when the placental–uterine wall interface was intact in all places during the dynamic sonographic examination.

	Degree of placental invasion: (i) placenta accreta: placental 'cones' disrupted the decidual zone with mildly increased vascularization around these cones; (ii) placenta increta: placental invasion into the myometrium was sonographically suspected as a result of the presence of irregular and diffuse demarcation of the placental–uterine wall interface and thinning of the myometrium that was overlying the placental–myometrial tissue. Placenta increta was also characterized by increased vascularization and irregularly shaped intraplacental vascular lacunae, resembling the characteristic 'moth damage' appearance; (iii) placenta percreta: complete absence of the myometrium, with the placenta extending to the serosa, or beyond, including vascular breakthrough.Placenta percreta was also characterized by massive subplacental hypervascularization, with vessels extending irregularly into the placental–myometrial tissue and with numerous large intraplacental lacunae. Patients with placental invasion underwent regular follow-up examinations every 2 weeks (when placenta increta or percreta were suspected) to 4 weeks (when placenta accreta was suspected) until delivery.
Target condition and reference standard(s)	Sonographic findings were compared with the clinical outcome during and after delivery and the histomorphological examination of the placenta, performed by pathologists experienced in obstetric histopathology, who were blinded to the sonographic findings. **Crtiteria:** abnormally retained placenta was defined as a placenta that did not separate promptly and thus remained attached to the uterine wall after delivery of the fetus, but was not associated with any histopathological signs of placental invasion (i.e. placenta accreta, increta or percreta; see below). This was thought to be mostly caused by reduced uterine contractility. Patients for whom normal placentation or placenta accreta had been suspected during antepartum ultrasound examinations underwent a vaginal delivery when CS was not indicated for other reasons. The obstetric team waited for spontaneous placental separation and the placenta was examined for completeness afterwards. Placenta accreta was then defined by failed attempts to remove the placenta during the third stage of labor or during CS. At histological examination of the specimen (either the curettement or the removed uterus, if any), placenta accreta was characterized by placental villi that were partially incorporated into the decidua basalis. All women with a suspected placenta increta or percreta underwent planned CS at a gestational age of 34–36 completed weeks. When gross placental invasion (fusion of the placenta and myometrial tissue) was evident at surgery, no attempt to remove the placenta manually was made and a hysterectomy

	was performed. At histological examination of the removed uterus, placenta increta was defined by a partially missing decidua basalis and united trophoblastic cell structures in the myometrium and placenta percreta was diagnosed when placental villi reached, or extended beyond, the serosa.
Flow and timing	One woman with placental invasion only into the uterine cervix was observed and excluded from the present analysis because the cervix differs anatomically from other parts of the uterus in that the cervix consists of primarily collagenous tissue and only 10% muscle. In order to assess any progression of the condition, patients with placental invasion underwent regularfollow-up examinations every 2 weeks (when placenta increta or percreta were suspected) to 4 weeks (when placenta accreta was suspected) until delivery. Data for the final ultrasound examination before delivery were included in the present analysis. The maximum interval between the final ultrasound examination and delivery was 2 weeks.

CS: cesarean section; IVF: in vitro fertilization; MHz: Megahertz

Collins 2015	
Patient Sampling	Cohort design, Patients were referred from two referal centers. Recruitment period: 04.2012 - 03.2014
Patient characteristics and setting	**Sample size (analysed):** 89 **Inclusion criteria:** Women diagnosis of a placenta previa and a history of previous uterine surgery or ultrasound findings suggestive of abnormally invasive placenta on routine ultrasound scan **Exclusion criteria:** Multiple gestation, age younger than 16 years (United Kingdom) or younger than 18 years (United Staates) and inability to provide informed concsent **Patient characteristics Abnormally Invasive Placenta/Not Abnormally Invasive Placenta:** BMI (mean; SD): 26.1; 5.3 (17.9-43.4) / 26.7; 95.4 (18.1 - 43.0) Hysterectomy performed (%): 86 / 6 Admission to ICU (%): 7 / 0 *Parity (%)* 0: 5 / 11 1: 36 / 47 2: 24 / 26 3 or greater: 36 / 17 *Gestational age (week, median; range)* At delivery: 34 3/7 (21 5/7-26 4/7) / 37 1/7 (28 2/7-42) At ultrasound scan: 32 4/7 (15 2/7-39 2/7) / 32 1/7 (17 1/7-33 6/7) *Ethnicity (%)* White (non-Hispanic): 53 / 50 Hispanic: 26 / 19

	Black: 9 / 9 Asian 9 / 7 Other (including mixed race): 2/15 *Prior Cesarean delivery (%)* 0: 5 / 21 1: 50 / 47 2: 21 / 19 3+: 24 / 13 *Placenta previa (%)* Major placenta previa (placenta over os): 76 / 36 Marginal placenta previa (2 cm or less from os): 17 /15 Cesarean delivery scar and major placenta previa: 71 / 23 *Previous uterine surgery (%)* Evacuation of retained products of conception: 31 / 19 Myomectomy: 5 / 6 Transcervical resection of fibroids: 2 / 2 Endometrial ablation: 2 / 0 Assisted reproductive technology (%): 7 / 2 **Setting:** NR, UK and USA
Index tests	**Device:** RAB4-8-D 3D/4D curved array abdominal transducer (4-8,5 MHz) on a Volusion E8. static, transabdominal three-dimensional power Doppler ultrasound. **Procedure:** Patients underwent diagnostic imaging according to the local unit protocol. In addition, static, transabdominal three-dimensional power Doppler ultrasound scan were examined offline by a blinded observer. The ultrasound volumes of the placental bed were obtained according to a predefined protocol with the participant in a semirecumbentposition and a full bladder **Criteria:** The largest area of confluent three-dimensional power Doppler signal (Area of Confluence "Acon") at the uteroplacental interface was measured and compared. **Rater:** All the static volumes were opened in 4D View and examined by one operator. images were coded (deidentified) and the analysis was conducted blinded to pregnancy outcome.
Target condition and reference standard(s)	The presence and severity of abnormally invasive placentation were assessed at delivery according to their clinical grading system by an attending obstetrician who had seen more than 10 cases of abnormally invasive placenta and from histopathology results in which histerectomy was performed. All histopathology was undertaken by senior pathologists in each unit who have special expertise in placentology. **Clinical Grading System:** 1 At cesarean or vaginal delivery: complete placental separation at third stage; not abnormally invasive placenta 2 At cesarean delivery or laparotomy: no placental tissue seen invaded through the serosal surface of the uterus; only partial separation with synthetic oxytocin and gentle controlled cord traction, manual removal of placenta required for

	remaining tissue AND parts of placenta thought to be abnormally adherent by a senior, experienced clinician At vaginal delivery; manual removal of placenta required AND parts of placenta thought to be abnormally adherent by a senior, experienced clinician 3 At cesarean delivery or laparotomy: no placental tissue seen invaded through the serosal surface of the uterus; no signs of any separation with synthetic oxytocin and gentle controlled cord traction, manual removal of placenta required AND the whole placental bed thought to be abnormally adherent by a senior, experienced clinician At vaginal delivery: manual removal of placenta required AND the whole placental bed thought to be abnormally adherent by a senior, experienced clinician 4 At cesarean delivery or laparotomy: placental tissue seen to have invaded through the serosal surface of the uterus but NOT passing into any surrounding structures (including the posterior wall of the urinary bladder); a clear surgical plane can be identified between the bladder and uterus to allow nontraumatic reflection of the urinary bladder at hysterectomy 5 At cesarean delivery or laparotomy: placental tissue seen to have invaded through the serosal surface of the uterus AND invaded into the urinary bladder ONLY (consequently, a clear surgical plane cannot be identified between the bladder and uterus to allow nontraumatic reflection of the urinary bladder at hysterectomy) 6 At cesarean delivery or laparotomy: placental tissue seen to have invaded through the serosal surface of the uterus AND invaded into the pelvic side wall or any organ other than the urinary bladder, with or without invasion into the urinary bladder
Flow and timing	Two were lost to follow-up, one was excluded for an incomplete scan of the uteroplacental interface, and one was excluded because the woman was unable to fill her bladder sufficiently to adequately visualize the uterovesical interface. Women in the abnormal invasive placenta group had two weeks in median between ultrasound and delivery (with histopathology), women in the not abnormal invasive placenta group had five weeks in median between ultrasound and delivery (with histopathology). median gestation for all included scans was 32 weeks. There was no difference in the gestational age at ultrasonography for the women diagnosed with abnormally invasive placenta (median 32 1/7 weeks of gestation, range 17 1/7–33 6/7 weeks of gestation) and those without abnormally invasive placenta (32 4/7 weeks of gestation, range 15 2/7 - 39 2/7 weeks of gestation)

ICU: intensive care unit; NR: not reported; SD: standard deviation;

Daney de Marcillac 2016	
Patient Sampling	Cohort-design, potential cases of placenta accreta (patients with an anterior placenta praevia with history of scarred uterus). Recruitment period: 01.2010 - 12.2014
Patient characteristics and setting	**Inclusion criteria:** Women with either placenta previa or placenta accreta **Patient characteristics Cases placenta accreta/Controls placenta non-accreta:** Age (mean; SD): 34.3; 2 / 29; 3.8 Gravidity (mean; SD): 3.92; 1.0 / 2.31; 1.43 Parity (mean; SD): 2.31; 1.4 / 1.6; 1.5 Number of previous Cesarean delivery (mean, SD): 2.15; 1.4 / 2.2; 1.8 Scarred uterus (%): 100 / 100 Previous Currettage (%): 8 / 22 Low-lying placenta (%): 100 / 67 Normal placenta (%): 0 / 33.3 **Setting:** Level 3 Maternity Unit, Strasbourg, France
Index tests	The patients that were suspected to have a placenta accreta through ultrasound were assessed by 2 experienced sonographers using 2D and color doppler ultrasound with a Voluson E8 General Electrics ultrasound system. Systematically, when they found signs towards risk of having a placenta acreta but even when no signs pointed towards a placenta accreta diagnosis, an MRI was used as a second step. They used Ultrafast spin echo sequences T2 HASTE, short T1 inversion recovery STIR which allowed to limit signal from fats, 3D TSE and TFI turbo spin echo. Interpretation was done with one single radiologic experiment. **Criteria:** Ultrasound - various hypoechogenic placental lacunae - Anormal placental vascularization - loss of the retroplacental hypoechoic clear zone - bladder wall irregularity MRI: - myometrial interface/placental lobe with bulging in myometrium (loss of its piriform) - intraplacental bands on T2-weighted images - intraplacental vascularization - heterogenous placenta - bulging of the placenta into the inner orifice - bladder wall irregularity
Target condition and reference standard(s)	The diagnosis of placenta accreta were confirmed through histology of a piece taken from hysterectomy in case of hemostatic hysterectomy or clinically in case of succesful conservative treatment
Flow and timing	NR Index test were performed once they were referred to the maternity center with suspicion of placental disorder. Diagnosis

	at delivery. Clinical or histopathologic diagnosis of placenta accreta. All patients were included except one person which was lost to follow-up due to missing data on birth and final indec test results.

HASTE: Half Fourier Acquisition Single Shot Turbo Spin Echo; MRI: magnetic resonance imaging; NR: not reported; SD: standard deviation; STIR: Short tau inversion recovery; TSE: Turbo-Spin-Echo

Dwyer 2008	
Patient Sampling	Cohort design design. Retrospective searches using databases and codes from the International Classification of Diseases, Ninth Revision, for placenta previa, placenta accreta, cesarean delivery with placental abnormalities, and cesarean hysterectomy were performed at each institution.Identified patients who underwent both prenatal transabdominal sonography and MRI to evaluate for suspected diagnosis of placenta accreta. Recruitment period: 2001 – 2006.
Patient characteristics and setting	**Sample size:** 32 **Inclusion criteria:** Women who were clinically at high risk for placenta accreta because of suspicious sonographic (2 centres); patients with sonographic findings suspicious for placenta accreta (1 centre) Placenta previa (%): 66 Prior uterine surgery (%): 81 Placenta previa and prior uterine surgery (%): 47 Diagnosis of placenta accreta clinically at delivery, by pathologic examination, or both (n): 15 *Placenta location (%):* Anterior: 44 Posterior: 38 Lateral: 3 Central: 41 *Correct / incorrect / inconclusive sonographic and MRI findings for diagnosing Placenta Accreta (%):* Sonography: 69 / 16 /16 MRI: 59 / 16 / 25 **Setting:** Stanford University, University of Washington and Sinai medical centers, USA
Index tests	**Device and procedure:** At Stanford University, examinations were performed on Acuson Sequoia ultrasound systems. The entire placental volume was imaged in the transverse and longitudinal planes with a 4- or 6-MHz curved array transducer. At Mount Sinai, examinations were performed on a Voluson 730 Expert system using a 5-MHz transducer or ATL HDI 3500 system using a 4-MHz transducer. At the University of Washington, examinations were performed with an iU22 system using a C5–2 MHz curved array transducer. Magnetic Resonance Imaging Without Gadolinium—At Stanford

	University and the University of Washington, MRI was performed on a 1.5-T whole-body MRI scanner. The maternal pelvis was imaged in the axial, coronal, and sagittal planes with an 8-channel phased array cardiac coil. After a 3-plane localizing scan, T1-weighted fast gradient echo sequences were acquired in the sagittal, coronal, and axial planes through the maternal abdomen with repetition/echo times of 165/2.5 milliseconds, a flip angle of 90°, a 384 × 192 data matrix, and a slice thickness of 5 mm. The field of view was usually 38 cm but was occasionally increased to optimize for the uterine size. T2-weighted single-shot fast spin echo sequences were acquired in the axial, sagittal, and coronal planes with repetition/echo times of 6000/160 milliseconds, a 288 × 224 data matrix, a slice thickness of 5 mm, and a typical field of view 38 cm. Intravenous gadolinium was not used in any of the MRI studies. At Mount Sinai, MRI was performed on a 1.5-T whole-body MRI scanner. Details were identical to those described above, except that a 6-channel body matrix coil was used. T2-weighted sequences used a 256 × 218 data matrix and a slice thickness of 6mm. T1-weighted sequences were acquired at the attending physician's discretion. Sonography with gray scale and color Doppler imaging was performed by registered sonographers and by a perinatologist or radiologist. **Criteria:** Doppler findings that were considered suggestive of placenta accreta included loss of the retroplacental hypoechoic clear zone, loss of the bladder wall-uterine interface, presence of placental lacunae (vascular spaces), and presence of hypervascularity of the interface between the uterine serosa and the bladder wall on color Doppler imaging. MRI findings considered suggestive of placenta accreta included ocal thinning or absence of the myometrium at the site of placental implantation, a nodularinterface between the placenta and the uterus, a mass effect of the placenta on the uterus causing an outer bulge, heterogeneous signal intensity within the placenta, dark intraplacental bands on T2-weighted images, and loss of the tissue plane between the placenta and bladder wall. For both sonography and MRI, if the report concluded low or no probability of placenta accreta, the findings were considered negative. A second analysis designating studies as correct, incorrect, or inconclusive was done. Examples of studies designated inconclusive included the following: (1) a study in which a single nonspecific feature of placenta accreta was seen on imaging, but the overall study was thought to have low probability; and (2) a study that was limited by poor quality. **Rater:** Sonograms and MRIs were read by an attending perinatologist or radiologist (all fellowship trained) at the original institution. Reports were retrospectively reviewed by the senior

	authors, with more than 5 years of experience, at the coordinating center.
Target condition and reference standard(s)	Maternal delivery records and delivery databases were reviewed for delivery outcomes. Placenta accreta was defined by clinical criteria at the time of delivery and by pathologic diagnosis. If pathologic findings were not available, then placenta accreta was defined by clinical criteria alone, including an adherent placenta and maternal hemorrhage.
Flow and timing	Pathologic findings were not available for patient 2 because hysterectomy was not performed. For patients 6 and 12, pathologic findings were not available in the database. For patient 15, the pathologic findings were inconclusive because the uterine specimen was fragmented.

MHz: Megaherz; MRI: Magnetic resonance imaging

Masselli 2008	
Patient Sampling	Cohort-design. Patients with diagnosis of placenta previa and at least one previous cesarean section were referred to the clinic for detailed color Doppler and MRI.Fifty women for whom complete information was available regarding clinical and pathological diagnosis were included in this study. Recruitment period: 03.2006 - 06.2007
Patient characteristics and setting	**Sample size:** 50 **Inclusion criteria:** Women in the third trimester of pregnancy with a diagnosis of placenta previa and at least one previous CS **Patient characteristics:** Age (years, mean; range): 31; 22-38 Clinical and pathological confirmation of PAD (n): 12 Gestational Age at diagnosis (weeks, mean; range): 30; 20-37 *Clinical findings and pathology reports (n):* Placenta accreta: 7 Placenta increta: 2 Placenta percreta: 3 Total hysterectomy (n): 7 **Setting:** NR, Italy
Index tests	**Device:** Gray-scale B-mode sonography was used to screen the placental tissue in a systematic fashion and in addition superimposed color Doppler flow. Magnetic resonance scans were performed on a Siemens Magnetom Avanto 1.5-T scanner equipped with high-performance gradients and phase array coils **Procedure:** In the absence of normal subplacental venous complex or in the presence of placental sonolucent lakes and/or irregularities of the bladder uterine serosa assessment of the placenta was completed using superimposed color Doppler flow. Doppler power settings were at the level approved for fetal use. Patients were supine, with their feet entering the magnet bore first to minimize feelings of claustrophobia. All US Doppler and

	MR exams were obtained with a partially full bladder. Following a localizer scan, sagittal, axial and coronal half-Fourier acquisition with single-shot turbo spin echo (HASTE) (min/90.0 repetition time, ms/echo time, ms), (256×224 matrix, 4-mm thickness with no gap, echo train length of 94, receiver bandwidth of 62.50 kHz) were acquired during breath-hold. Next, sagittal, coronal and axial true fast-imaging with steady-state precession (True FISP) (3.5/1.8 repetition time, ms/echo time, ms), 256×224 matrix, one signal acquired, 5-mm thickness with no gap, 50 flip angle, receiver bandwidth of 125 kHz were acquired. Finally, a sagittal T1 three-dimensional (3D) volume interpolated breath-hold examination (VIBE) (4.2/2/15 repetition time, ms/echo time, ms/inversion time, ms), 256×224 matrix, one signal acquired, 2.5-mm thickness with no intersection gap, 12 flip angle, receiver bandwidth of 62.50 kHz was acquired. Breath-holding by the mother was utilized to minimize respiratory motion artifact. **Criteria:** The levels of placental invasion determined by US Doppler and MRI were labelled: 0, for absence of invasion; A, for accreta; I for, increta; P, for percreta. According to the previous topographic characterization of Palacios et al., sagittal images obtained through MRI allow the division of anterior placenta invasion into two sectors, delimited by a plane perpendicular to the center of the so-called upper bladder axis. The uterine sectors bordering the upper and lower posterior bladder wall were called S1 and S2, respectively . For the case of different grades of placenta penetration and combined S1 and S2 invasions, the score was assigned according to the highest percentage of invasion. After this first analysis, a second interpretation was performed by the same two reviewers, who reached a consensus in evaluating both the degree of invasion and the topographic evaluation of invasion. **Rater:** Two reviewers, blinded to results of US and pathologic examinations
Target condition and reference standard(s)	The final degree of placental penetration and its specific topography were compared in the operating room according to clinical and anatomical criteria. Placenta was considered accreta if firmly attached to the endometrium and showing a non-self-controlled bleeding when detached, increta when requiring surgical curettage to remove invasive tissue deeply implanted in the myometrium and percreta when extending through the myometrium into the neighbouring organs. A true negative was defined as an uncomplicated placental removal without excessive bleeding after cesarean delivery. All true positive diagnoses, as well as false-positive and negative diagnoses, were confirmed by pathologic examination (hysterectomy, curettings, or fragments of myometrium adherent to the placenta). The diagnosis of placenta accreta required that the anchoring villi directly abut the

	myometrium: invasive trophoblastic cells were evidenced with the Giemsa staining.
Flow and timing	Fifty women for whom complete information was available (from 56 who were referred) regarding clinical and pathological diagnosis were included in this study. The mean gestational age at diagnosis with MRI/US was 30 weeks, with a range of 20–37 weeks

CS: cesarean section; HASTE: Half Fourier Acquisition Single Shot Turbo Spin Echo; kHz: kilohertz MRI: magnetic resonance imaging; ms: millisecond; NR: not reported; PAD: placental adhesive disorder US: ultrasound VIBE: Volume Interpolated Breathhold Examination

Rac 2016	
Patient Sampling	Cohort design. retrospective review of the obstetric ultrasound database for patients with a history of prior cesarean delivery who had placenta previa or low-lying placenta diagnosed on third-trimester sonography. Recruitment period: 09.1997 - 10.2011.
Patient characteristics and setting	**Sample size:** 39 (analysed) **Inclusion criteria:** Women with a phistory of prior cesarean delivery who had placenta previa or low-lying placenta diagnosed on third-trimester. From this group, only those women with a first-trimester sonographic examination during the same pregnancy and who delivered at our institution were included in the study. **Characteristics of Patients With Invasion / Without Invasion at Delivery** Age (years, mean; SD): 31.4; 5.6 / 30.9;4.8 *Race (%)* Black: 0 / 8 White 0 / 4 Hispanic: 100 / 88 Other: 0 / 0 Gravidity (mean; SD): 4.3;1.6 / 3.8;1.4 Parity (mean; SD): 2.7; 1.1 / 2.2; 1.3 *Cesareans* (mean; SD): 2.36; 0.74 / 1.32; 0.48 1 (%): 7 / 68 2 (%): 57 / 32 3 or more (%): 36 / 0 Prior dilation and curettage (%): 14 / 20 Gestational age at 1st-trimester sonography, (weeks, mean; SD): 8.3; 2. 2 / 9.8; 2.7 Transvaginal sonography (%): 79 / 40 *Indication for 1st-trimester sonography (%):* Bleeding: 64 / 44 Pain: 7 / 16 Gestational age assessment: 21 / 28 Other: 7 / 12 Gestational age at 3rd-trimester sonography (week, mean;SD): 35.5;2. / 36.7;2.3

	Delivery Outcomes Gestational age at delivery (week, mean; SD): 35.5;2.3 / 36.7;2.3 *Indication for delivery (%):* Scheduled delivery: 50 / 44 Labor: 29 / 24 Bleeding: 21 / 36 Other: 7 / 12 Estimated blood loss (ml, first quartile, third quartile): 2750 (2000, 4625) / 1500 (1000, 2000) Anterior placentation (%): 52 / 93 *Degree of Invasion (%):* Accreta: 86 / 0 Increta: 7 / 0 Percreta: 7 / 0 **Setting:** University of Texas Southwestern Medical Center, USA
Index tests	As routine first-trimester imaging was not standardly performed at our institution during the study period, all sonographic examinations were performed for clinical indications. **Criteria:** Sonographic parameters assessed included distance from the inferior border of the gestational sac to the external cervical os, location of the decidua basalis, presence of anechoic areas, uterine-bladder interface irregularity, and smallest myometrial thickness (<9mm), defined as the smallest distance from the anterior trophoblastic border of the gestational sac to the uterine serosa. Color Doppler parameters were not assessed because color Doppler sonography was not a standard part of first-trimester imaging during the study period. **Rater:** Images were obtained by certified registered diagnostic medical sonographers, and digitally stored first-trimester transvaginal images were reviewed by a single investigator, who was blinded to both pregnancy outcomes and sonographic reports. If transvaginal imaging was not performed, transabdominal images were reviewed.
Target condition and reference standard(s)	Placental invasion was established if placenta accreta, increta, or percreta was diagnosed after a standardized histologic examination of the cesarean or hysterectomy specimen by our pathology department.
Flow and timing	See above (gestational age at first trimester sonography and gestational age at delivery), gestational age at first-trimester screening (invasion/no invasion, week, mean;SD) 8.3; 2. 2 / 9.8; 2.7

SD: standard deviation

Riteau 2014	
Patient Sampling	Cohort-design, medical records of all patients referred for suspected placenta accreta to two university hospitals. Women who had been investigated by both ultrasound and prenatal MRI. Recruitment period: 01.2001 - 05.2012
Patient characteristics and setting	**Sample size:** 42 **Patient characteristics** Age (in years, mean; SD): 34;4.7 Gravidity (mean; SD): 4.2; 2.3 Parity (mean; SD): 2.1;1.5 Previous cesarean delivery (%): 88 Gestational age at the time of diagnosis by ultrasonography (in weeks, mean): 28.7 Gestational age at the time of MRI (in weeks, mean): 30.8 *Placental insertion (%)* Previa: 76,2 Low-lying: 11,9 Non-low-lying: 11.9 *Final diagnosis (%)* Placenta accreta / increta: 38 Placenta Percreta: 24 Non-adherent placenta: 38 *Surgical management at delivery* Vaginal: 2 cesarean delivery: 40 **Setting:** Two university hospitals, France
Index tests	**Device:** IU 22 system and the GE Voluson 730 or E8 with 4–9 MHz or 5–9 MHz transabdominal transducers, and 3–9 MHz and 4–8 MHz endovaginal transducers. MRI was performed with a 1.5 Tesla scanner . **Procedure:** Ultrasound and MRI were performed by obstetricians or radiologists experienced in abnormal adherent placenta. The MRI protocols were similar in both hospitals and included T1-weighted sequences in the sagittal and axial planes, single-shot fast spin-echo T2-weighted MR sequences (HASTE, single shot TSE) and true fast imaging with steady-state precession (TrueFISP, FIESTA) in the axial, sagittal and coronal planes. 7 MRI scans were done after intravenous injection of gadolinium, 6 were MR diffusion-weighted imaging. No fetal sedation was used. **Rater:** Ultrasound images and MRI were blindly reassessed by 2 raters with more than 5 years of experience in the evaluation of placentation disorders. They were blinded to the patient's diagnosis and were asked to score features previously described in the literature as useful for predicting placental invasion.
Target condition and reference standard(s)	Placenta accreta was defined by clinical criteria at the time of delivery and by pathologic findings. The placenta was considered normal if it was easily removed during cesarean delivery without any bleeding complications. Ideally, the standard of reference for

	the diagnosis of abnormal adherent placenta is confirmation of the final histology after hysterectomy has been performed. If pathologic examination was not available, the diagnosis was based on clinical information provided at the time of delivery and surgery. The placenta was considered as accreta when the delivery was impossible and as percreta when it was evident that the placenta had reached the uterine serosa or the adjacent organs.
Flow and timing	Pathologic examination was not performed in 10 cases because of conservative treatment and in 5 cases because delivery was complete and no postpartum haemorrhage occurred (the five placentas were considered normal).Average gestational age at the time of diagnosis by ultrasonography (in weeks) 28. 7. Average gestational age at the time of MRI (in weeks) 30.8

HASTE: Half Fourier Acquisition Single Shot Turbo Spin Echo; MHz: Megaherz; MRI: magnetic resonance imaging; SD: standard deviation; TSE: Turbo-spin-echo

Warshak 2006	
Patient Sampling	Cohort-design, pregnant women from the obstetric and radiologic databases. Recruitment period: 01.2000 - 06.2005
Patient characteristics and setting	**Sample size:** 453 (analysed) **Inclusion criteria:** Patients with a diagnosis of placenta previa, low-lying placenta with a previous cesarean delivery, or myomectomy and those referred for pelvic MRI because of suspicious or inconclusive findings for placenta accreta on previous ultrasound examination. **Exclusion criteria:** incomplete information regarding clinical (gestational age at the time of diagnosis, previous uterine surgery, parity, clinical findings at the time of surgery, and pathologic diagnosis)and pathologic diagnosis **Patient characteristics** Gestational age at diagnosis (weeks, mean; range): 25; 11-37 **Clinical characteristics of women with false positives on ultrasonography** Age (y) / Gravidity / Parity / Prior CD / Ultrasound findings / MRI findings / GA at delivery (wk) / Delivery findings / operative EBL (mL) / pathology findings 1. 29 / 3 / 2 / 1 / Previa with heterogeneity / negative / 38 / uncomplicated CD / 900 / mature placenta 2. 31 / 3 / 1 / 0 / Previa with hypoechoic areas / negative / 37 / uncomplicated CD / 800 / matureplacenta 3. 41 / 3 / 2 / 2 / Previa suspicious for PA / negative / 36 / classic CD / 1200 / Negative for placenta accreta 4. 23 / 5 / 2 / 2 / Anterior placenta with multiple lakes / negative / 39 / classic CD / 1800 / mature placenta 5. 39 / 3 / 2 / 0 / Heterogenous anterior placenta / negative / 38 /

	SVD / 350 / mature placenta 6. 34 / 5 / 2 / 2 / Previa, irregular placenta, no well-defined border / negative / 32 / uncomplicated CD / 1000 / immature placenta 7. 33 / 6 / 5 / 2 / Heterogenous previa with multiple lakes / negative / 39 / uncomplicated CD / 1000 / mature placenta 8. 31 / 8 / 7 / 2 / Previa suspicious for accreta / negative / 39 / uncomplicated / 800 / mature placenta 9. 24 / 3 / 2 / 2 / Marginal previa, PA cannot be excluded / negative / 21 / Dilation and evacuation for multiple anomalies / 400 / immature placenta 10. 30 / 6 / 3 / 2 / Anterior placenta, suspicious for PA / Negative / 39 / SVD, Postpartum hemorrhage / 1200 / mature placenta 11. 31 / 1 / 0 / 0 / Posterior placenta with lakes / Negative / 39 / SVD / 400 / mature placenta 12. 29 / 4 / 1 / 1 / Posterior placenta with hypoechoic area / Negative / 40 / SVD / 350 / mature placenta 13. 38 / 5 / 2 / 2 / Previa suspicious for PA / negative / 39 / Uncomplicated CD / 1000 / mature placenta 14. 27 / 1 / 0 / 0 / Fundal placenta with increased vascularity, PA cannot be excluded / Negative / 40 / SVD / 500 / Mature placenta 15. 37 / 1 / 0 / 0 / Previa with increased vascularity / No MRI / 39 / Uncomplicated CD / 900 / No evidence of PA 16. 26 / 4 / 3 / 2 / Anterior with possible PA / No MRI / 39 / Uncomplicated CD / 900 / Mature placenta **Clinical characteristics of women with false negatives on ultrasonography** Age (y) / Gravidity / Parity / Prior CD / Ultrasound findings / MRI findings / GA at delivery (wk) / Delivery findings / operative EBL (mL) / pathology findings 17. 43 / 3 / 0 / 0 / Marginal previa / None / 40 / CD to hysterectomy / 3100 / PA 18. 38 / 2 / 0 / 0 / Complete previa / None / 37 / CD, placenta notably adherent to the uterus / 2000 / PA 19. 41 / 3 / 1 / 1 / Anterior placenta / None / 39 / Elective repeat CD / 1000 / PA 20. 32 / 4 / 2 / 2 / Complete previa / None / 28 / CD to hysterectomy / 2500 / Focal PA in lower uterine segment 21. 29 / 6 / 2 / 0 / Fundal placenta / None / 40 / SVD with densely adherent placenta, D&C / 1500 / PA with pale villous tissue associated with myometrium 22. 28 / 1 / 0 / 0 / Low-lying placenta / None / 40 / Uncomplicated CD / 1000 / Small focus of PA 23. 34 / 2 / 1 / 1 / Posterior placenta / None / 36 / CD to hysterectomy / 1500 / PA 24. 36 / 5 / 4 / 4 / Previa / None / 35 / Planned cesarean hysterectomy / 750 / PA 25. 36 / 1 / 0 / Myomectomy / Posterior placenta / Negative / 36 / Cesarean hysterectomy / 2500 / PA

	Setting: University Center, USA
Index tests	**Device:** Grayscale and color Doppler ultrasonography. Siemens Sonoline Elegra and GE Voluson 730 with 3.5- or 5-MHz curvilinear, sector, and endovaginal transducers. **Procedure:** Pelvic ultrasonography scans were performed by registered sonographers using both grayscale and color Doppler ultrasonography, and perinatal or radiological faculty interpreted all studies. **Criteria:** The ultrasound findings considered to be consistent with placenta accreta included: 1) obliteration of the bladder wall–uterine interface with loss of the hypoechoic retroplacental myometrial zone; 2) adjacent placental sonolucent spaces; and 3) increased vascularity proximate to the bladder wall by color Doppler. An ultrasound study was considered to be positive if the final interpretation included findings suggestive of, or conclusive for, placenta accreta. All studies considered to be suggestive but not conclusive underwent MRI evaluation.
Target condition and reference standard(s)	Pathology databases were searched to verify the presence or absence of placenta accreta A clinical diagnosis of placenta accreta was made when the placenta was found to be adherent to the myometrium and difficult to remove and when hemorrhage ensued after attempts at placental delivery. All pathological specimens were reviewed by one of the authors (K.B.). The diagnosis of placenta accreta required that the anchoring villi directly abut the myometrium, without any intervening decidua basalis. The absence of decidual cells confirmed the diagnosis. The Gomori silver technique was employed to verify the nature of the basal cells by identifying decidual stromal cells possessing a distinctly silver-positive cell membrane, which is absent from the invasive extracellular trophoblastic cells. All true positive, as well as false positive and negative diagnoses were confirmed by pathologic examination (hysterectomy, curettings, or fragments of myometrium adherent to the placenta). A true negative was defined as an uncomplicated placental removal without excessive bleeding after vaginal or cesarean delivery.
Flow and timing	The mean GA at diagnosis was 25.0 weeks

CD: cesarean delivery; EBL: estimated blood loss; HASTE: Half Fourier Acquisition Single Shot Turbo Spin Echo; GA: gestational age; MRI: magnetic resonance imaging; ms: millisecond; PA: placenta accreta; VIBE: Volume Interpolated Breathhold Examination; wk: week

Warshak 2006 Part 2 MRI	
Patient Sampling	Warshak 2006, MRI as add on test, supporting the suspicion of placenta accreta. Cohort-design, pregnant women from the obstetric and radiologic databases. All ultrasound studies considered to be suggestive but not conclusive underwent MRI evaluation. Recruitment period: 01.2000 - 06.2005

Patient characteristics and setting	**Sample size:** 40 (analysed) **Inclusion criteris:** MRI because of suspicious or inconclusive findings for placenta accreta on previous ultrasound examination. Gestational age at MRI (weeks, mean; range): 28; 18-37 **Clinical Characteristics of Women With False Negative Magnetic Resonance Images** Age(y) / Gravidity / Parity / Prior CD / US Findings / MRI Findings / GA at delivery (wk) / Delivery Findings / EBL (mL) / Pathology 1. 36 / 1 / 0 / Myomectomy / Posterior placenta / Negative / 36 / Cesarean hysterectomy / 2500 / PA 2. 22 / 4 / 2 / 2 / Anterior placenta, PA strongly suspected / Negative / 34 / Planned cesarean hysterectomy / 850 / PA 3. 39 / 9 / 8 / 4 / Previa, suspect PA / Negative / 34 / Planned cesarean hysterectomy / 1700 / Small focus of PA **Setting:** University Center, USA
Index tests	**Device:** Magnetic resonance imaging scans were performed on a Siemens Magnetom Symphony 1.5 Tesla scanner equipped with high-performance gradients and phase-array coils. **Procedure:** Patients were placed on the scan table headfirst in whatever position they found most comfortable or turned toward a left lateral decubitus position. Following a localizer scan, true patient sagittal and coronal scan series were acquired using the Half-fourier Acquisition with Single shot Turbo spin Echo (HASTE) with an effective echo-time of 90 ms in continuous 8-mm thickness slices covering the entire abdomen and pelvis. Additional HASTE sequences were then acquired to cover the entire placenta in three orthogonal planes, followed by selected oblique planes that are perpendicular to the placentauterine interface that is suspected. The HASTE sequence acquires sequential single slices rather than the full volume, where each image is acquired in a subsecond to freeze fetal motion. Additionally, two T1-weighted gradient echo turbo–flash sequences were then acquired orthogonal to each other and perpendicular to the suspect placenta-uterine interface to assess the outer uterine margin and acquire T1 and T2 signal characteristics of uterine, placenta, and parametrial tissues. The HASTE and T1-weighted scans are rapid and required intermittent breathholding to minimize patient motion artifacts. If the appearance of the placenta was suspect for placenta accreta, a dynamic gadolinium-enhanced MR series was then acquired perpendicular to the plane of the placenta-uterine interface suspected of being abnormal. The dynamic series is a Volume Interpolated Breathhold Examination (VIBE) acquired in the arterial phase and then again in the venous and equilibrium phases over the identical slices. This sequence is a 3D acquisition that used interpolated echoes and rapid fat-suppression where each series is acquired during a single breath-hold. The dose of gadolinium used was up to 0.1 mM/kg.

	Criteria: appearance of the placenta on the precontrast examination 1) thickened dark nodular contour of the placenta-uterine interface with extensions of the dark bands within the placenta; 2) mass effect of the placenta on the uterus causing an outer bulge; 3) heterogeneous placental signal on the T2-weighted HASTE sequences with large placental lakes or vessels. Assessment of the integrity of cervix, myometrium, bladder, and parametrial structures was also evaluated. The gadolinium-enhanced images acquired in the arterial phase defined the location of the outer placental surface relative to the myometrium, which was enhanced on the later sequences, and were used in all cases suspected to have placenta accreta. This confirmed the presence of deep invasion. **Rater:** A radiologist with MR expertise monitored the entire study and guided the imaging work-up as is done with real-time ultrasound imaging. All studies were interpreted by the same radiologist (R.F.M.).
Target condition and reference standard(s)	Pathology databases were searched to verify the presence or absence of placenta accreta A clinical diagnosis of placenta accreta was made when the placenta was found to be adherent to the myometrium and difficult to remove and when hemorrhage ensued after attempts at placental delivery. All pathological specimens were reviewed by one of the authors (K.B.). The diagnosis of placenta accreta required that the anchoring villi directly abut the myometrium, without any intervening decidua basalis. The absence of decidual cells confirmed the diagnosis. The Gomori silver technique was employed to verify the nature of the basal cells by identifying decidual stromal cells possessing a distinctly silver-positive cell membrane, which is absent from the invasive extracellular trophoblastic cells. All true positive, as well as false positive and negative diagnoses were confirmed by pathologic examination (hysterectomy, curettings, or fragments of myometrium adherent to the placenta). A true negative was defined as an uncomplicated placental removal without excessive bleeding after vaginal or cesarean delivery.
Flow and timing	Mean GA at diagnosis was 28 weeks. Two women were included but did not tolerate the procedure and did not complete the study

CD: cesarean delivery; EBL: estimated blood loss GA: Gestational age; HASTE: Half Fourier Acquisition Single Shot Turbo Spin Echo; MRI: magnetic resonance imaging; PA: placenta accreta; US: ultrasound; VIBE: Volume Interpolated Breathhold Examination; wk: weeks; y: years;

Wong 2008	
Patient Sampling	Cohort design. Women were referred from January 2004 to December 2006The sonograms were reviewed retrospectively Recruitment period: 2004 – 2005 and prospectively in 2006
Patient characteristics and setting	**Sample size:** 66 **Inclusion criteria:** exclusion of placenta accreta because of the

	presence of risk factors including placenta previa, previous cesarean section, previous dilatation and curettage or miscarriage, previous myomectomy, previous manual removal of placenta, or previous placenta accreta **Patient characteristics accreta/non-accreta** Age (mean; SD): 33.3 ; 5.6 / 33.9; 5.7 Gravidity (mean; SD): 3.9; 1.6 / 3.3 ; 1.8 Parity (mean; SD): 2.4; 1.1 / 1.3; 1.3 Gestational age at diagnosis (week, mean; SD): 27.1; 9.6 / 32; 3.4 **Setting:** NR, New Zealand
Index tests	**Device:** 5–2-MHz curvedarray transducer and/or a 12–5-MHz linear-array transducer were used for transabdominal examination, whereas an 8–4-MHz endovaginal probe was used for transvaginal sonography. Gray-scale imaging was performed in all women. Color and/ or power Doppler sonography was used to evaluate any suspicious area as described previously. **Criteria:** the presence or absence of the following criteria on gray-scale imaging: obliteration of the retroplacental clear space (including focal obliteration); interruption of interface between the posterior bladder wall and the uterus; presence of focal exophytic mass with same echogenicity as the placenta beyond the uterine serosa; placental lacunae; smallest myometrial thickness adjacent to the placenta <1 mm; and disruption of the placental–uterine wall interface. The criteria on color or power Doppler imaging included: increased subplacental vascularity (by comparing the vascularity in the subplacental area to that in the adjacent non-subplacental area); flow in the placental lacunae; hypervascularity of the bladder–uterine serosa interface; vessels extending from the placenta to the bladder; vessels bridging the placenta and uterine margin (or serosa); and vessels crossing the sites of interface disruption. A cutoff value of the composite score was selected (cutoff value of 40) **Rater:** The sonograms were reviewed by 2 reviewers
Target condition and reference standard(s)	Hospital records were reviewed in all cases and information was collected on the delivery and postnatal course. Histological or clinical confirmation.
Flow and timing	Seventy-three women were identified with our inclusion criteria. Seven were lost to follow-up and were thus excluded from the study Gestational age at diagnosis (weeks, mean; SD) 27.1; 9.6 (accreta), 32; 3.4 (no accreta)

MHz: megahertz; NR: not reported; SD: standard deviation

Frage 2

Chantraine 2013	
Methods	**Study type:** Cohort study **Setting:** Multicenter Study (country NR) **Recruitement period:** 1998-2011
Participants	**Intervention/Control (prenatal/Intrapartum diagnosis) Characteristics:** n= 40 / 26 Age (in years, median, range): 31 (26-42) / 29 (23-35) Gravidity (median, range): 3 (2-12) / 3 (2-7) Parity (median, range): 2 (1-8) /2 (1-3) Gestational age at diagnosis (in weeks, median, range): 31 (14-37) / 36 (25-40) Gestational age at delivery (in weeks, median, range): 36 (19-38) / 36 (25-40) Previous CS (number, median, range): 32 (1-3) / 10 (1-2) Previous uterine curettages (number of dilatation and curretage, median, range): 18 (1-4) / 11 (1-3) **Exclusion criteria:** Women with simple placenta accreta (Anchoring villi are attached to the myometrium (as opposed to only the decidua); requires manual removal of curettage to fully retrieve the placenta, but placenta can be removed completely without the need for further procedures) **Drop outs:** NR
Interventions	**Prognostic factor** Prenatal diagnosis (recognized before the onset of labor or cesarean delivery, suspected cases, confirmed by ultrasound) **Reference category** diagnosis at time of delivery or CS
Outcomes	Maternal **Maternal mortality,** hysterectomy, bleeding needing transfusion, infections, uterine artery embolization, fetal mortality (intra-abdominal bleeding) Neonatal fetal death, gestational age at delivery

CS: cesarean section; NR: not reported

Clouqueur 2008	
Methods	**Study type:** Cohort study **Setting:** High-level maternity unit, France **Recruitement period:** 1996-2006
Participants	**Inclusion criteria:** Cases of placenta accreta (including accreta, increata or percreta) detected with pathologic analysis (in case of radiologic or clinic suspicion) and one case which was

	successfully treated conservatively. **Intervention/Control (prenatal diagnosis/without prenatal diagnosis)** **Characteristics:** n= 6 / 15 Age (in years, mean; SD): 33.8; 2.4 / 32.9; 5.0 Gravidity (mean; SD): 4.5; 2.9 / 4.1; 1.5 Parity (mean; SD): 2.8; 0.7 / 3.1; 1.0 Gestational age at delivery (in weeks, mean; SD): 32.2; 3.1 / 36.5; 3.7 At least one previous CS (%): 100 / 66.7 Anteroir curettage (all in %): 44 CS for delivery (%): 100 / 80 Planned CS for placenta accreta with mounted embolization probes(%): 83 / 0 **Drop outs:** NR
Interventions	**Prognostic factor** Antenatal diagnosis (suspected cases by ultrasound and partly by MRI) **Reference category** diagnosis at time of delivery or CS
Outcomes	Maternal **Mortality,** hysterectomy, estimated bleeding, needing blood transfusion

CS: cesarean section; MRI: magnetic resonance imaging; NR: not reported; SD: standard deviation

Hall 2014	
Methods	**Study type:** Cohort study **Setting:** Practices **Recruitment period:** 01.01.2005 -31.12.2012
Participants	**Inclusion criteria:** pathology-proven placentas accreta/increta/percreta from a single tertiary center **Intervention/Control (prenatal/Intrapartum diagnosis)** **Characteristics:** n= 19 / 16 Maternal Age (years, mean; SD): 32.8; 6.1 / 33.5 ; 6.3 Caucasion (%): 89.5 / 88.2 *Parity (%)* 0: 5.3 / 47.1 1: 31.6 / 11.8 >=2: 63.2 / 41.2 Singleton (%): 94.7 / 88.2 *Prior Cesarean (%)* 0: 10.5 / 76.5 1: 36.8 / 17.6

	>=2: 52.6 / 5.9 *Cesarean to conception interval (months)* <12: 47.4 / 0 12-24: 10.5 / 0 >24: 31.6 / 23.5 mean; SD: 22.8; 21.4 / 108; 7.6 Prior uterine surgery (other than CS) (%): 42.1 / 52.9 Year delivered (%) 2005-2008: 42.1 / 35.3 2009-2012: 57.9 / 64.7 Smoker (%): 15.8 / 29.4 IVF conception (%) 0 / 29.4 Placentation (%) Accreta: 47.4 / 70.6 Increta: 15.8 / 17.6 Percreta: 36.8 / 11.8 **Drop Outs:** NR
Interventions	**Prognostic test** Diagnosis prenatally (physician's interpretation in the final report regarding the presence or absence of an accreta was used to categorize the accreta as prenatally diagnosed by ultrasound or not.) Management of prenatally diagnosed accretas included cesarean delivery, typically scheduled between 35 and 37 weeks based on the patient's clinical status. Four units of packed red blood cells and a cell saver were available in the main operating room. Blood bank was aware of the scheduled surgery and prepared to activate a massive transfusion protocol **Reference category** Prenatally undiagnosed cases (14 of 17 had an ultrasound but were undetected)
Outcomes	Maternal estimated blood loss, transfusion (> 4 units red cells), length of stay, intensive care unit (ICU) admission, ICU length of stay, operative injury Neonatal ICU admission, ICU length of stay, 5-minute Apgar scores <7

CS: cesarean section; ICU: intensive care unit; IVF: in vitro fertilization; NR: not reported; SD: standard deviation

Sofiah 2009	
Methods	**Study type:** Cohort study **Setting:** Mater Mothers' Hospital Brisbane, Australia **Recruitment period:** 1993-2005
Participants	**inclusion criteria:** patients who had hysterectomy following vaginal or cesarean section deliveries

	Charasteristics of all patients with placenta accreta: n: 27/13 Age (mean): 35 Age > 35 years (%): 44.7 Age < 25 years (%): 5.3 Gravidity (mean): 9 Parity (mean): 4.5 Number of previous CS (mean): 1.6 One or more previous CS (%): 35 Number of previous curettage (mean): 1.07 one ore more previous curettages (%): 25 coexisting placenta praevia(%): 77.5 nulliparous (%): 7.5 Gestational age at delivery (weeks, mean): 35 gestation at first suspected diagnosis (weeks) (mean): 28.3 Elective CS: 16 Emergency CS: 21 **Drop Outs:** NR
Interventions	**Prognostic test** diagnosis prenatally (suspicions or ultrasonographic confirmed diagnosis) **Reference category** diagnosis at delivery (no ultrasound scan done, no antenatal suspicion not confirmed diagnosis)
Outcomes	Maternal estimated blood loss, CS Neonatal gestational age at delivery

CS: cesarean section; NR: not reported

Tikkanen 2011	
Methods	**Study type:** Cohort study **Setting:** Department of Obstetrics and Gynecology, University Central Hospital, Helsinki, Finland **Recruitment period:** 1998 - 2010
Participants	**Inclusion criteria:** women with a diagnosis of placenta accreta **Intervention / Control (antenatal diagnosis / intrapartum diagnosis)** **Characteristics** n : 24/20 *Age* (mean; SD): 34.2; 3.6 / 32.7; 5.9 >=35 (years, %): 33 / 35 *Gravidity (%)* 1: 0 / 25 >=2: 100 / 75 *Parity (%)*

	0: 0 / 45 >=1: 100 / 55 Uterine malformation (%): 13 / 5 *History of prior curettage (%)* 1: 42 / 45 >=2: 58 / 55 *History of CS (%)* 0: 13 / 55 >=1: 88 / 45 History of placenta previa (%): 8 / 0 History of manual extraction of placenta (%): 29 / 5 Other uterine surgery (%): 8 / 5 **Drop Outs:** NR
Interventions	**Prognostic test** Diagnosis prenatally with ultrasound and confirmation by MRI. For those women with antenatal diagnosis of placenta accreta, the elective cesarean section was mostly scheduled at the 35th or 36th gestational weeks. Diagnostic cystoscopy was performed if placenta percreta invading or compressing the bladder was suspected. Ureteral stents were placed in proven cases with placenta percreta invading or compressing the bladder. A multidisciplinary team, including a perinatologist, a gynecologic oncologist, an anesthesiologist, an interventional radiologist, a neonatologist and, in some cases, a urologist,was involved at delivery. Internal iliac artery catheterswere placed preoperatively and the balloons inflated after the baby was delivered by classical cesarean incision. If placental removal by gentle manipulation failed, the uterine incision was closed and cesarean hysterectomy performed. **Reference category** intrapartum diagnosed cases (not identified with ultrasound)
Outcomes	Maternal hysterectomy, CS, estimated blood loss, operative complications (urinary tract injury, bleeding, hematoma, infection) length of stay, Neonatal gestational age at delivery

CS: cesarean section; MRI: magnetic resonance imaging; NR: not reported; SD: standard deviation

Wong 2008	
Methods	**Study type:** Cohort study **Setting:** Wellington Hospital, Wellington, New Zealand **Recruitment period:** 01.01.2000-31.12.2006
Participants	**Intervention / Control (antenatal diagnosis / intrapartum diagnosis)** **Characteristics**

	n= 7/9 Age (years, mean; SD): 33.6; 3.7 / 34.7; 4.8 Gravidity (mean; SD): 3.9; 1.3 / 4.8; 1.9 Parity (mean; SD): 2.9; 1.3 / 4.8; 1.9 *No. of previous CS* 0: 1 / 3 1: 1 / 5 >1: 5 / 1 *No. of previous curretage* 0: 7 / 3 1: 0 / 2 >1: 0 / 4 No. of previous manual removal of placenta 0: 6 / 7 1: 0 / 2 >1: 1 / 0 Previous history of placenta accreta (n): 1 / 1 placenta previa in current pregnancy (n): 6 / 5 **Drop Outs:** NR
Interventions	**Prognostic test** antenatal diagnosed cases by ultrasound and/or MRI **Reference category** intrapartum diagnosed cases
Outcomes	Maternal: estimated blood loss, hysterectomy, infection, ICU admission, Length of stay, Neonatal: gestational age at delivery

CS: cesarean section; ICU: intensive care unit; MRI: magnetic resonance imaging; NR: not reported; SD: standard deviation

Appendix E: Ergebnisse Frage 2

1 Prenatal diagnosis vs. intrapartal diagnosis

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Maternal mortality	2	87	Risk Ratio (M-H, Random, 95% CI)	Not estimable
1.2 Cesarean Section	5	207	Risk Ratio (M-H, Random, 95% CI)	1.39 [0.99, 1.96]
1.3 Maternal hysterectomy	4	133	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.56, 0.85]
1.4 Maternal bleeding needing transfusion	3	123	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.58, 1.16]
1.5 Maternal estimated blood loss, liter	5	157	Mean Difference (IV, Random, 95% CI)	-1.08 [-2.34, 0.17]
1.6 Maternal admission to the ICU	3	118	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.17, 1.39]
1.7 Maternal ICU length of stay, days	1	36	Mean Difference (IV, Random, 95% CI)	-1.30 [-3.61, 1.01]
1.8 Maternal length of stay, days	3	96	Mean Difference (IV, Random, 95% CI)	0.28 [-0.91, 1.47]
1.9 Maternal postnatal infections	3	126	Risk Ratio (M-H, Random, 95% CI)	1.31 [0.39, 4.41]
1.10 Maternal uterine artery embolization	2	110	Risk Ratio (M-H, Random, 95% CI)	2.45 [0.48, 12.63]
1.11 Maternal operative complications	2	80	Risk Ratio (M-H, Random, 95% CI)	2.23 [1.02, 4.89]
1.12 Gestational age at birth, weeks	5	205	Mean Difference (IV, Random, 95% CI)	-0.10 [-1.86, 1.66]
1.13 Fetal death	1	66	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.01, 5.19]
1.14 Neonatal Apgar score <7	1	39	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.05, 4.82]

1.15 Neonatal NICU admission	2	61	Risk Ratio (M-H, Random, 95% CI)	1.74 [0.58, 5.20]
1.16 Neonatal NICU length of stay, days	1	39	Mean Difference (IV, Random, 95% CI)	-3.30 [-10.02, 3.42]

Appendix F: Liste der unveröffentlichten Studien

FRATELLI

https://clinicaltrials.gov/ct2/show/record/NCT02442518?term=placenta+AND+%28diagnosis+OR+prognosis%29&rank=1

University clinic, TOURS

https://clinicaltrials.gov/ct2/show/NCT02302573?term=placenta+AND+%28diagnosis+OR+prognosis%29&rank=8

Appendix G: Liste der ausgeschlossenen Volltexte

Primärstudien

Abbasi, S., et al., Role of clinical and ultrasound findings in the diagnosis of retained products of conception. Ultrasound Obstet Gynecol, 2008. 32(5): p. 704-7.

Abdel Moniem, A.M., et al., Accuracy of three-dimensional multislice view doppler in diagnosis of morbid adherent placenta. Journal of the Turkish German Gynecology Association, 2015. 16(3): p. 126-136.

Adeyomoye, A.A., et al., Comparison of the accuracy of trans-abdominal sonography (TAS) and transperineal sonography (TPS) in the diagnosis of Placenta Praevia. The Nigerian postgraduate medical journal, 2006. 13(1): p. 21-5.

Aitken, K., et al., MRI Significantly Improves Disease Staging to Direct Surgical Planning for Abnormal Invasive Placentation: A Single Centre Experience. J Obstet Gynaecol Can, 2016. 38(3): p. 246-251 e1.

Alamo, L., et al., Detection of suspected placental invasion by MRI: Do the results depend on observer' experience? European Journal of Radiology, 2013. 82(2): p. e51-e57.

Alchalabi, H., et al., Morbidly adherent placenta previa in current practice: Prediction and maternal morbidity in a series of 23 women who underwent hysterectomy. Journal of Maternal-Fetal and Neonatal Medicine, 2014. 27(17): p. 1734-1737.

Algebally, A.M., et al., The value of ultrasound and magnetic resonance imaging in diagnostics and prediction of morbidity in cases of placenta previa with abnormal placentation. Pol J Radiol, 2014. 79: p. 409-16.

Ananth, C.V., J.C. Smulian, and A.M. Vintzileos, The effect of placenta previa on neonatal mortality: a population-based study in the United States, 1989 through 1997. American Journal of Obstetrics & Gynecology, 2003. 188(5): p. 1299-1304 6p.

Archibong, E.I. and E.S.M. Ahmed, Risk factors, maternal and neonatal outcome in major placenta previa: A prospective study. Annals of Saudi medicine, 2001. 21(3-4): p. 245-247.

Armstrong, C.A., et al., Is placenta accreta catching up with us? Australian and New Zealand Journal of Obstetrics and Gynaecology, 2004. 44(3): p. 210-213.

Bauwens, J., et al., Placenta accreta: Can prenatal diagnosis be performed? Ultrasound and MRI interests. about 27 cases. Gynecologie Obstetrique Fertilite, 2014. 42(5): p. 306-311.

Berkley, E.M. and A.Z. Abuhamad, Prenatal diagnosis of placenta accreta: is sonography all we need? J Ultrasound Med, 2013. 32(8): p. 1345-50.

Blouin, D. and C. Rioux, Routine third trimester control ultrasound examination for low-lying or marginal placentas diagnosed at mid-pregnancy: is this indicated? J Obstet Gynaecol Can, 2012. 34(5): p. 425-8.

Bowie, J.D., et al., Accuracy of placental localization by ultrasound. Radiology, 1978. 128(1): p. 177-80.

Bricker, L., J.P. Neilson, and T. Dowswell, Routine ultrasound in late pregnancy (after 24 weeks' gestation). Cochrane Database of Systematic Reviews, 2008(4).

Buetow, M.P., Sonography of placenta percreta during the first trimester. American Journal of Roentgenology, 2002. 179(2): p. 535.

Cali, G., et al., Morbidly adherent placenta: evaluation of ultrasound diagnostic criteria and differentiation of placenta accreta from percreta. Ultrasound Obstet Gynecol, 2013. 41(4): p. 406-12.

Cao, M.M., et al., MRI features of placenta accreta. Chinese Journal of Radiology (China), 2012. 46(7): p. 629-632.

Chen, C.M. and J. Zhang, Prenatal MRI diagnosis of placental invasion. Chinese Journal of Medical Imaging Technology, 2011. 27(8): p. 1655-1658.

Chen, X., et al., MRI features of placenta percreta. Chinese Journal of Radiology (China), 2015. 49(11): p. 833-837.

Chen, Y.F., et al., Exaggerated placenta site in placenta previa: An imaging differential diagnosis of placenta accreta, placental site trophoblastic tumor and molar pregnancy. Taiwanese Journal of Obstetrics and Gynecology, 2012. 51(3): p. 440-442.

Cho, H.Y., et al., Diagnosis of Placenta Accreta by Uterine Artery Doppler Velocimetry in Patients With Placenta Previa. J Ultrasound Med, 2015. 34(9): p. 1571-5.

Chou, M.M., E.S.C. Ho, and Y.H. Lee, Prenatal diagnosis of placenta previa accreta by transabdominal color Doppler ultrasound. Ultrasound in Obstetrics and Gynecology, 2000. 15(1): p. 28-35.

Chou, M.M., J.J. Tseng, and E.S. Ho, The application of three-dimensional color power Doppler ultrasound in the depiction of abnormal uteroplacental angioarchitecture in placenta previa percreta. Ultrasound Obstet Gynecol, 2002. 19(6): p. 625-7.

Chou, M.M., J.J. Tseng, and E.S. Ho, Usefulness of gray-scale ultrasound and complementary color Doppler ultrasound in the prenatal diagnosis of placenta previa accreta. Am J Obstet Gynecol, 2005. 192(4): p. 1349; author reply 1350.

Chou, M.M., et al., Sonographic appearance of tornado blood flow in placenta previa accreta/increta. Ultrasound in Obstetrics and Gynecology, 2001. 17(4): p. 362-363.

Comstock, C.H., et al., Sonographic detection of placenta accreta in the second and third trimesters of pregnancy. American Journal of Obstetrics & Gynecology, 2004. 190(4): p. 1135-1140 6p.

Desai, N., et al., Elevated first trimester PAPP-A is associated with increased risk of placenta accreta. Prenatal diagnosis, 2014. 34(2): p. 159-162.

DiGiacinto, D. and A. Hildebrand, Placenta accreta. Radiologic Technology, 2006. 78(2): p. 165-168 4p.

Dreux, S., et al., Second-trimester maternal serum markers and placenta accreta. Prenat Diagn, 2012. 32(10): p. 1010-2.

Dudenhausen, J.W., et al., Placenta pathology: Disorders of placental location, placental implantation and cord insertion. Ultraschall in der Medizin, 2008. 29(1): p. 4-23.

Elhawary, T.M., N.L. Dabees, and M.A. Youssef, Diagnostic value of ultrasonography and magnetic resonance imaging in pregnant women at risk for placenta accreta. Journal of Maternal-Fetal & Neonatal Medicine, 2013. 26(14): p. 1443-1449 7p.

Esakoff, T.F., et al., Diagnosis and morbidity of placenta accreta. Ultrasound Obstet Gynecol, 2011. 37(3): p. 324-7.

Finberg, H.J. and J.W. Williams, Placenta accreta: Prospective sonographic diagnosis in patients with placenta previa and prior cesarean section. Journal of Ultrasound in Medicine, 1992. 11(7): p. 333-343.

Giambattista, E., et al., Predicting factors for emergency peripartum hysterectomy in women with placenta previa. Arch Gynecol Obstet, 2012. 285(4): p. 901-6.

Hamisa, M., et al., Role of Doppler US and MRI in diagnosis of placenta accreta. Alexandria Journal of Medicine, 2015. 51(3): p. 225-230.

Hasegawa, J., et al., Predisposing factors for massive hemorrhage during Cesarean section in patients with placenta previa. Ultrasound in Obstetrics and Gynecology, 2009. 34(1): p. 80-84.

Heer, I.M., S. Muller-Egloff, and A. Strauss, Placenta praevia--comparison of four sonographic modalities. Ultraschall Med, 2006. 27(4): p. 355-9.

Japaraj, R.P., T.S. Mimin, and K. Mukudan, Antenatal diagnosis of placenta previa accreta in patients with previous cesarean scar. Journal of Obstetrics & Gynaecology Research, 2007. 33(4): p. 431-437 7p.

Jaraquemada, J.M.P., et al., Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of placenta accreta...Warshak CR, Eskander R, Hull AD, Scioscia AL, Mattrey RF, Benirschke K, et al. Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of placenta accreta. Obstet Gynecol 2006;108:573-81. Obstetrics & Gynecology, 2007. 109(1): p. 203-203 1p.

Jiang, K.M., et al., Prenatal MRI and pathological features of placental invasion. Chinese Journal of Medical Imaging Technology, 2013. 29(6): p. 1002-1005.

Kayem, G., C. Deneux-Tharaux, and L. Sentilhes, PACCRETA: Clinical situations at high risk of Placenta ACCRETA/Percreta: Impact of diagnostic methods and management on maternal morbidity. Acta obstetricia et gynecologica Scandinavica, 2013. 92(4): p. 476-482.

Kumar, I., et al., Invasive placental disorders: a prospective US and MRI comparative analysis. Acta Radiol, 2016.

Lam, G., J. Kuller, and M. McMahon, Use of magnetic resonance imaging and ultrasound in the antenatal diagnosis of placenta accreta. Journal of the Society for Gynecologic Investigation, 2002. 9(1): p. 37-40.

Lauria, M.R., et al., The use of second-trimester transvaginal sonography to predict placenta previa. Ultrasound Obstet Gynecol, 1996. 8(5): p. 337-40.

Lax, A., et al., The value of specific MRI features in the evaluation of suspected placental invasion. Magnetic Resonance Imaging, 2007. 25(1): p. 87-93.

Leerentveld, R.A., et al., Accuracy and safety of transvaginal sonographic placental localization. Obstet Gynecol, 1990. 76(5 Pt 1): p. 759-62.

Lerner, J.P., S. Deane, and I.E. Timor-Tritsch, Characterization of placenta accreta using transvaginal sonography and color Doppler imaging. Ultrasound Obstet Gynecol, 1995. 5(3): p. 198-201.

Levine, D., et al., Placenta accreta: Evaluation with color Doppler US, power Doppler US, and MR imaging. Radiology, 1997. 205(3): p. 773-776.

Maher, M.A., A. Abdelaziz, and M.F. Bazeed, Diagnostic accuracy of ultrasound and MRI in the prenatal diagnosis of placenta accreta. Acta obstetricia et gynecologica Scandinavica, 2013. 92(9): p. 1017-1022.

Mansour, S.M. and W.M. Elkhyat, Placenta previa - Accreta: Do we need MR imaging? Egyptian Journal of Radiology and Nuclear Medicine, 2011. 42(3-4): p. 433-442.

Martinez, M., Magnetic resonance imaging in 300 cases of placenta accreta: surgical correlation of new findings. Acta Obstet Gynecol Scand, 2006. 85(3): p. 377; author reply 378-9.

Megier, P., V. Gorin, and A. Desroches, [Ultrasonography of placenta previa at the third trimester of pregnancy: research for signs of placenta accreta/percreta and vasa previa. Prospective color and pulsed Doppler ultrasonography study of 45 cases]. J Gynecol Obstet Biol Reprod (Paris), 1999. 28(3): p. 239-44.

Moodley, J., N.F. Ngambu, and P. Corr, Imaging techniques to identify morbidly adherent placenta praevia: A prospective study. Journal of Obstetrics and Gynaecology, 2004. 24(7): p. 742-744.

Naghshineh, E., E. Khorvash, and S. Kamali, A comparison of cell-free placental messenger ribonucleic acid and color Doppler ultrasound for the prediction of placental invasion in patients with placenta accreta. Adv Biomed Res, 2015. 4: p. 31.

N'Guessan, K., et al., [Placenta praevia: maternal and featal prognosis in University Hospital of Cocody (Abidjan-Cote d'Ivoire)]. Mali Med, 2009. 24(2): p. 57-9.

Noda, Y., et al., Prenatal MR imaging diagnosis of placental invasion. Abdominal Imaging, 2015. 40(5): p. 1273-1278.

Oyelese, Y. and J.C. Smulian, Placenta previa, placenta accreta, and vasa previa. Obstetrics & Gynecology, 2006. 107(4): p. 927-941 15p.

Palacios Jaraquemada, J.M. and C. Bruno, Gadolinium-enhanced MR imaging in the differential diagnosis of placenta accreta and placenta percreta. Radiology, 2000. 216(2): p. 610-1.

Palacios Jaraquemada, J.M. and C.H. Bruno, Magnetic resonance imaging in 300 cases of placenta accreta: Surgical correlation of new findings. Acta obstetricia et gynecologica Scandinavica, 2005. 84(8): p. 716-724.

Peker, N., et al., Assessment of total placenta previa by magnetic resonance imaging and ultrasonography to detect placenta accreta and its variants. Ginekol Pol, 2013. 84(3): p. 186-92.

Philip S, L., et al., Utility of ultrasound and MRI in prenatal diagnosis of placenta accreta: A pilot study. American Journal of Roentgenology, 2011. 197(6): p. 1506-1513.

Pilloni, E., et al., Accuracy of ultrasound in antenatal diagnosis of placental attachment disorders. Ultrasound Obstet Gynecol, 2016. 47(3): p. 302-7.

Pongrojpaw, D., et al., Prenatal diagnosis of placenta accreta by colour doppler ultrasonography: 5-year review. Journal of the Medical Association of Thailand, 2014. 97((Pongrojpaw D., pongrojpaw@gmail.com; Chanthasenanont A.; Nanthakomon T.; Suwannarurk K.) Maternal Fetal Medicine Unit, Department of Obstetrics and Gynaecology, Thammasat University, Pathumthani, Thailand): p. S171-S174.

Rahim, N., T. Rehana, and A. Ara, Risk factors associated with major placenta previa. Journal of Medical Sciences (Peshawar), 2014. 22(2): p. 63-65.

Rahimi-Sharbaf, F., et al., Ultrasound detection of placenta accreta in the first trimester of pregnancy. Iranian Journal of Reproductive Medicine, 2014. 12(6): p. 421-426.

Rezk, M.A.A. and M. Shawky, Grey-scale and colour Doppler ultrasound versus magnetic resonance imaging for the prenatal diagnosis of placenta accreta. Journal of Maternal-Fetal and Neonatal Medicine, 2016. 29(2): p. 218-223.

Sanderson, D.A. and P.J.D. Milton, The effectiveness of ultrasound screening at 18-20 weeks gestational age for prediction of placenta praevia. Journal of Obstetrics and Gynaecology, 1991. 11(5): p. 320-323.

Satija, B., et al. (2015) Indian journal of radiology & imaging, 464-70 DOI: 10.4103/0971-3026.169456.

Shawky, M., E. AbouBieh, and A. Masood, Gray scale and Doppler ultrasound in placenta accreta: Optimization of ultrasound signs. Egyptian Journal of Radiology and Nuclear Medicine, 2016((Shawky M.) Department of Radiodiagnosis, Faculty of Medicine, Menoufia University, Egypt).

Shi, H., P. Pi, and Y. Ding, [Diagnosis of placenta previa accreta by two dimensional ultrasonography and color doppler in patients with cesarean section]. Zhong Nan Da Xue Xue Bao Yi Xue Ban, 2012. 37(9): p. 939-43.

Shih, J.C., et al., Role of three-dimensional power Doppler in the antenatal diagnosis of placenta accreta: Comparison with gray-scale and color Doppler techniques. Ultrasound in Obstetrics and Gynecology, 2009. 33(2): p. 193-203.

Stirnemann, J.J., et al., Screening for placenta accreta at 11-14 weeks of gestation. American Journal of Obstetrics & Gynecology, 2011. 205(6): p. 547.e1-6 1p.

Sumigama, S., et al., Placenta previa increta/percreta in Japan: a retrospective study of ultrasound findings, management and clinical course. Journal of Obstetrics & Gynaecology Research, 2007. 33(5): p. 606-611 6p.

Taipale, P., V. Hiilesmaa, and P. Ylöstalo, Transvaginal ultrasonography at 18-23 weeks in predicting placenta previa at delivery. Ultrasound in Obstetrics and Gynecology, 1998. 12(6): p. 422-425.

Taipale, P., et al., Prenatal diagnosis of placenta accreta and percreta with ultrasonography, color Doppler, and magnetic resonance imaging. Obstetrics & Gynecology, 2004. 104(3): p. 537-540 4p.

Tanaka, Y.O., et al., High temporal resolution dynamic contrast MRI in a high risk group for placenta accreta. Magnetic Resonance Imaging, 2001. 19(5): p. 635-642.

Tanimura, K., et al. (2015) Prediction of adherent placenta in pregnancy with placenta previa using ultrasonography and magnetic resonance imaging. European Journal of Obstetrics Gynecology and Reproductive Biology, 41-4 DOI: 10.1016/j.ejogrb.2015.02.017.

Ueno, Y., et al., Evaluation of interobserver variability and diagnostic performance of developed MRI-based radiological scoring system for invasive placenta previa. Journal of Magnetic Resonance Imaging, 2016((Ueno Y., yoshiu@med.kobe-u.ac.jp; Maeda T.; Tanaka U.; Kitajima K.; Suenaga Y.; Takahashi S.; Sugimura K.) Department of RadiologyKobe University Graduate School of MedicineKobe Japan).

Underhill, R.A., Diagnosis of placenta praevia by ultrasound. Midwife Health Visit, 1974. 10(11): p. 346-50.

Woodring, T.C., et al., Prediction of placenta accreta by ultrasonography and color Doppler imaging. Journal of Maternal-Fetal & Neonatal Medicine, 2011. 24(1): p. 118-121 4p.

Yang, J.I., et al., Sonographic findings of placental lacunae and the prediction of adherent placenta in women with placenta previa totalis and prior Cesarean section. Ultrasound in Obstetrics and Gynecology, 2006. 28(2): p. 178-182.

Yoon, S.Y., et al., A combined ultrasound and clinical scoring model for the prediction of peripartum complications in pregnancies complicated by placenta previa. European journal of obstetrics, gynecology, and reproductive biology, 2014. 180: p. 111-5.

Yu, M., et al., Diagnosis and treatment of placenta accreta in the second trimester of pregnancy. Acta Academiae Medicinae Sinicae, 2010. 32(5): p. 501-504.

Zelop, C.C., et al., Second trimester sonographically diagnosed placenta previa: Prediction of persistent previa at birth. International Journal of Gynecology and Obstetrics, 1994. 44(3): p. 207-210.

Zhang, L., et al., [Value of prenatal diagnosis of placenta previa with placenta increta by transabdominal color Doppler ultrasound]. Zhonghua Fu Chan Ke Za Zhi, 2006. 41(12): p. 799-802.

Zlatnik, M.G., et al., When should women with placenta previa be delivered? A decision analysis. Journal of Reproductive Medicine, 2010. 55(9-10): p. 373-381 9p.

Reviews

D'Antonio, F., et al. (2013). "Prenatal identification of invasive placentation using ultrasound: systematic review and meta-analysis." Ultrasound Obstet Gynecol **42**(5): 509-517.

D'Antonio, F., et al. (2014). "Prenatal identification of invasive placentation using magnetic resonance imaging: systematic review and meta-analysis." Ultrasound Obstet Gynecol **44**(1): 8-16.

Meng, X., et al. (2013). "Comparing the diagnostic value of ultrasound and magnetic resonance imaging for placenta accreta: A systematic review and meta-analysis." Ultrasound in Medicine and Biology **39**(11): 1958-1965.

Rahaim, N. S. A. and E. H. Whitby (2015). "The MRI features of placental adhesion disorder and their diagnostic significance: Systematic review." Clinical Radiology **70**(9): 917-925.

Referenzen

1. Moher, D., et al., *Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.* PLoS Med, 2009. **6**(7): p. e1000097.
2. WHO. *List of Member States by WHO Region and Mortality Stratum*. 2016 [cited 2016 07.06.2016]; Available from: http://www.who.int/choice/demography/mortality_strata/en/.
3. Fletcher RH, F.S., Wagner EH, Haerting J., *Klinische Epidemiologie : Grundlagen und Anwendung.* Deutschsprachige Ausg. 2. Aufl. . 2007, Hans Huber Verlag GmbH, 2007.
4. Higgins, J., Green, S (editors). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011].* The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.
5. ÄZQ. *Klinische Studie*. 2015 09.06.2016]; Available from: http://www.leitlinien.de/leitlinienmethodik/leitlinien-glossar/glossar/klinische-studie.
6. McGowan, J., et al., *PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement.* J Clin Epidemiol, 2016. **75**: p. 40-6.
7. Whiting, P.F., et al., *Quadas-2: A revised tool for the quality assessment of diagnostic accuracy studies.* Annals of Internal Medicine, 2011. **155**(8): p. 529-536.
8. Hayden, J.A., et al., *Assessing bias in studies of prognostic factors.* Ann Intern Med, 2013. **158**(4): p. 280-6.
9. Merlin, T., et al., *THE "LINKED EVIDENCE APPROACH" TO ASSESS MEDICAL TESTS: A CRITICAL ANALYSIS.* International Journal of Technology Assessment in Health Care, 2013. **29**(3): p. 343-350.
10. Bowman, Z.S., et al., *Accuracy of ultrasound for the prediction of placenta accreta.* American Journal of Obstetrics & Gynecology, 2014. **211**(2): p. 177.e1-7 1p.
11. Bowman, Z.S., et al. *Interobserver variability of sonography for prediction of placenta accreta*. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine, 2014. 2153-8 DOI: 10.7863/ultra.33.12.2153.
12. Rac, M.W., et al., *Sonographic Findings of Morbidly Adherent Placenta in the First Trimester.* J Ultrasound Med, 2016. **35**(2): p. 263-9.
13. Rac, M.W.F., et al., *Ultrasound predictors of placental invasion: the Placenta Accreta Index.* American Journal of Obstetrics & Gynecology, 2015. **212**(3): p. 343.e1-7 1p.
14. Rac, M.W.F., et al., *Placenta accreta and vaginal bleeding according to gestational age at delivery.* Obstetrics & Gynecology, 2015. **125**(4): p. 808-813 6p.
15. National Institute for Health and Care Excellence (NICE). *Caesarean section*. 2011 17.05.2016]; Available from: https://www.nice.org.uk/guidance/cg132.
16. Royal College of Obstetricians and Gynaecologists (RCOG). *Placenta Praevia, Placenta Praevia Accreta and Vasa Praevia: Diagnosis and Management*. 2011 17.05.2016].
17. Royal College of Obstetricians and Gynecologists (RCOG). *Birth after Previous Caesarean Birth*. 2015 17.05.2016]; Available from: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg45/.
18. Warshak, C.R., et al., *Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of placenta accreta.* Obstetrics & Gynecology, 2006. **108**(3 part 1): p. 573-581 9p.
19. Chalubinski, K.M., et al., *Prenatal sonography can predict degree of placental invasion.* Ultrasound Obstet Gynecol, 2013. **42**(5): p. 518-24.
20. Collins, S.L., et al., *Three-Dimensional Power Doppler Ultrasonography for Diagnosing Abnormally Invasive Placenta and Quantifying the Risk.* Obstet Gynecol, 2015. **126**(3): p. 645-53.
21. Dwyer, B.K., et al., *Prenatal diagnosis of placenta accreta: Sonography or magnetic resonance imaging?* Journal of Ultrasound in Medicine, 2008. **27**(9): p. 1275-1281.
22. Masselli, G., et al., *Magnetic resonance imaging in the evaluation of placental adhesive disorders: Correlation with color Doppler ultrasound.* European Radiology, 2008. **18**(6): p. 1292-1299.

23. Riteau, A.S., et al., *Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of placenta accreta.* PLoS ONE, 2014. **9**(4).
24. Daney De Marcillac, F., et al., *Accuracy of placenta accreta prenatal diagnosis by ultrasound and MRI in a high-risk population.* Journal de Gynecologie Obstetrique et Biologie de la Reproduction, 2016. **45**(2): p. 198-206.
25. Wong, H.S., et al., *Evaluation of sonographic diagnostic criteria for placenta accreta.* Journal of Clinical Ultrasound, 2008. **36**(9): p. 551-559.
26. Harbord, R.M., et al., *An empirical comparison of methods for meta-analysis of diagnostic accuracy showed hierarchical models are necessary.* J Clin Epidemiol, 2008. **61**(11): p. 1095-103.
27. Chantraine, F., et al., *Prenatal diagnosis of abnormally invasive placenta reduces maternal peripartum hemorrhage and morbidity.* Acta obstetricia et gynecologica Scandinavica, 2013. **92**(4): p. 439-444.
28. Clouqueur, E., et al., *Placenta accreta: Diagnosis and management in a French high-level maternity.* Journal de Gynecologie Obstetrique et Biologie de la Reproduction, 2008. **37**(5): p. 499-504.
29. Hall, T., et al., *Prenatal sonographic diagnosis of placenta accreta--impact on maternal and neonatal outcomes.* J Clin Ultrasound, 2014. **42**(8): p. 449-55.
30. Sofiah, S. and L.Y.C. Fung, *Placenta accreta: Clinical risk factors, accuracy of antenatal diagnosis and effect on pregnancy outcome.* Medical Journal of Malaysia, 2009. **64**(4): p. 298-302.
31. Tikkanen, M., et al., *Antenatal diagnosis of placenta accreta leads to reduced blood loss.* Acta obstetricia et gynecologica Scandinavica, 2011. **90**(10): p. 1140-1146.
32. Wong, H.S., et al., *The maternal outcome in placenta accreta: The significance of antenatal diagnosis and non-separation of placenta at delivery.* New Zealand Medical Journal, 2008. **121**(1277): p. 30-38.
33. Iorio, A., et al., *Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients.* Bmj, 2015. **350**: p. h870.
34. Silver, R.M., et al., *Maternal morbidity associated with multiple repeat cesarean deliveries.* Obstet Gynecol, 2006. **107**(6): p. 1226-32.
35. Fitzpatrick, K.E., et al., *Incidence and risk factors for placenta accreta/increta/percreta in the UK: a national case-control study.* PLoS One, 2012. **7**(12): p. e52893.