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INPLASY

# Prenatal MRI biomarkers for predicting postnatal neurodevelopmental outcomes in fetal brain abnormalities: a protocol for a systematic review and meta-analysis

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**ADMINISTRATIVE INFORMATION**

**Support -** This review has not received any specific funding.

**Review Stage at time of this submission -** Preliminary searches.

**Conflicts of interest -** None declared.

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**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 April 2026 and was last updated on 30 April 2026.

## INTRODUCTION

**Review question / Objective** This systematic review and meta-analysis aims to evaluate whether prenatal magnetic resonance imaging biomarkers are associated with postnatal neurodevelopmental outcomes in fetuses with brain abnormalities.

The review question is: In fetuses with suspected or confirmed brain abnormalities who undergo prenatal MRI, which MRI findings or MRI-derived biomarkers are associated with adverse postnatal neurodevelopmental outcomes?

The population will include fetuses undergoing prenatal brain MRI for suspected or confirmed brain abnormalities. The exposure/index factors will include qualitative MRI findings, MRI-detected additional abnormalities, isolated versus non-isolated abnormalities, severity grading, and quantitative MRI-derived markers. Comparators may include fetuses without the biomarker of interest, different severity categories, isolated versus non-isolated abnormalities, or ultrasound findings when available. The primary outcome will be adverse postnatal neurodevelopmental outcome, including developmental delay, cognitive impairment, motor impairment, language delay, epilepsy, cerebral palsy, abnormal standardized developmental assessment scores, or clinically significant neurological abnormalities.

**Rationale** Fetal brain MRI is increasingly used after prenatal ultrasound to characterize suspected fetal brain abnormalities and to support prenatal counseling. Although MRI can improve anatomical assessment and reveal additional abnormalities not detected by ultrasound, its value for predicting postnatal neurodevelopmental outcomes remains uncertain.

For families and clinicians, the most important question is often not only whether a fetal brain abnormality is present, but whether the abnormality is likely to result in adverse neurodevelopment after birth. Existing studies have reported associations between specific

prenatal MRI findings and later outcomes, including ventriculomegaly, corpus callosum abnormalities, posterior fossa abnormalities, cortical developmental malformations, cerebellar abnormalities, and non-isolated brain abnormalities. However, the evidence is heterogeneous because of differences in MRI timing, abnormality classification, follow-up duration, neurodevelopmental assessment tools, and outcome definitions.

A systematic review and meta-analysis is therefore needed to synthesize the available evidence, identify prenatal MRI biomarkers associated with adverse postnatal neurodevelopmental outcomes, and evaluate their potential role in prenatal counseling, postnatal risk stratification, and early intervention planning.

**Condition being studied** Fetal brain abnormalities assessed by prenatal magnetic resonance imaging. These abnormalities include, but are not limited to, ventriculomegaly, corpus callosum abnormalities, posterior fossa abnormalities, cerebellar abnormalities, cortical developmental malformations, midline brain abnormalities, and fetal brain parenchymal abnormalities. These conditions are clinically important because they may be associated with variable postnatal neurodevelopmental outcomes, ranging from normal development to cognitive impairment, motor delay, language delay, epilepsy, cerebral palsy, or other neurological abnormalities. Prenatal MRI is increasingly used to refine the anatomical diagnosis after ultrasound and may provide prognostic information for prenatal counseling and postnatal follow-up planning.

## METHODS

**Search strategy** We will search MEDLINE/PubMed, Embase, Web of Science, Scopus, Cochrane Library, and ClinicalTrials.gov from database inception to the final search date. Reference lists of included studies and relevant reviews will also be screened manually. No language restriction will be applied during the database search.

The preliminary PubMed search strategy will be:

((fetal[Title/Abstract] OR foetal[Title/Abstract] OR prenatal[Title/Abstract] OR antenatal[Title/Abstract] OR "in utero"[Title/Abstract])
AND
("magnetic resonance imaging"[Title/Abstract] OR MRI[Title/Abstract] OR "MR imaging"[Title/Abstract])
AND
(brain[Title/Abstract] OR cerebral[Title/Abstract] OR ventriculomegaly[Title/Abstract] OR "corpus callosum"[Title/Abstract] OR "posterior fossa"[Title/Abstract] OR cerebellum[Title/Abstract] OR cortical[Title/Abstract] OR sulcation[Title/Abstract] OR "brain abnormality"[Title/Abstract])
AND
(neurodevelopment*[Title/Abstract] OR developmental[Title/Abstract] OR postnatal[Title/Abstract] OR cognitive[Title/Abstract] OR motor[Title/Abstract] OR language[Title/Abstract] OR epilepsy[Title/Abstract] OR "cerebral palsy"[Title/Abstract] OR outcome*[Title/Abstract]))

The search strategy will be adapted for each database using appropriate controlled vocabulary and syntax.

**Participant or population** The population will include fetuses who underwent prenatal brain MRI because of suspected or confirmed fetal brain abnormalities and who had postnatal neurodevelopmental, neurological, clinical, or imaging follow-up. Eligible fetal brain abnormalities may include ventriculomegaly, corpus callosum abnormalities, posterior fossa abnormalities, cerebellar abnormalities, cortical developmental malformations, midline brain abnormalities, and brain parenchymal abnormalities. Studies including singleton or multiple pregnancies will be eligible if data for fetuses with prenatal MRI and postnatal outcome assessment can be extracted. Studies limited to postnatal MRI without prenatal MRI data will be excluded.

**Intervention** No therapeutic intervention will be evaluated in this review. The index factors of interest are prenatal MRI biomarkers and MRI findings used for prognostic assessment. These may include qualitative MRI findings, MRI-detected additional abnormalities, isolated versus non-isolated fetal brain abnormalities, severity grading of abnormalities, and quantitative MRI-derived markers such as ventricular size, brain volume, cerebellar measurements, corpus callosum measurements, cortical development, sulcation markers, diffusion-related metrics, or other MRI biomarkers reported by the included studies.

**Comparator** Comparators may include fetuses without the MRI biomarker of interest, fetuses with normal or less severe MRI findings, isolated versus non-isolated fetal brain abnormalities, different severity categories of the same abnormality, or ultrasound findings when available. For studies without an explicit comparator group, prognostic associations between prenatal MRI findings and

postnatal outcomes will be extracted and synthesized when possible.

**Study designs to be included** Prospective and retrospective cohort studies, case-control studies, and observational studies reporting prenatal MRI findings and postnatal neurodevelopmental, neurological, clinical, or imaging outcomes will be included. Prediction model and prognostic factor studies will also be eligible if relevant data can be extracted.

**Eligibility criteria** Studies will be eligible if they meet the following criteria:
1. include fetuses who underwent prenatal brain MRI for suspected or confirmed fetal brain abnormalities;
2. report at least one prenatal MRI finding, MRI-derived measurement, or MRI biomarker;
3. provide postnatal neurodevelopmental, neurological, clinical, or imaging follow-up; and
4. report sufficient data to extract or calculate outcome frequencies, effect estimates, diagnostic/prognostic accuracy measures, or associations between MRI findings and postnatal outcomes.

Eligible fetal brain abnormalities may include ventriculomegaly, corpus callosum abnormalities, posterior fossa abnormalities, cerebellar abnormalities, cortical developmental malformations, midline brain abnormalities, and fetal brain parenchymal abnormalities.

Exclusion criteria will include case reports, narrative reviews, editorials, commentaries, conference abstracts without full data, animal studies, phantom studies, purely technical MRI studies without postnatal outcome data, studies limited to postnatal MRI without prenatal MRI findings, and studies reporting only pregnancy termination, stillbirth, or perinatal mortality without neurodevelopmental or neurological outcome assessment.

**Information sources** The following electronic databases will be searched from inception to the final search date: MEDLINE/PubMed, Embase, Web of Science, Scopus, Cochrane Library, and ClinicalTrials.gov. Reference lists of included studies and relevant reviews will also be manually screened to identify additional eligible studies. Grey literature and trial or study registries will be considered when relevant. If important data are missing or unclear, study authors may be contacted for additional information. No language restriction will be applied during the database search, and non-English studies will be translated when feasible.

**Main outcome(s)** The primary outcome will be adverse postnatal neurodevelopmental outcome after prenatal MRI assessment of fetal brain abnormalities. Adverse neurodevelopmental outcome will include developmental delay, cognitive impairment, motor impairment, language delay, epilepsy, cerebral palsy, abnormal standardized developmental assessment scores, or clinically significant neurological abnormalities during postnatal follow-up. When available, outcomes assessed at 12 months or later will be prioritized. Effect measures may include odds ratios, risk ratios, hazard ratios, proportions, sensitivity, specificity, or other reported measures of association between prenatal MRI biomarkers and postnatal outcomes.

**Additional outcome(s)** Secondary outcomes will include disease-specific rates of adverse neurodevelopmental outcome, outcome differences between isolated and non-isolated fetal brain abnormalities, prognostic value of MRI-detected additional abnormalities, associations between abnormality severity and outcome, and postnatal imaging abnormalities related to prenatal MRI findings. Additional analyses may include outcomes according to abnormality type, such as ventriculomegaly, corpus callosum abnormalities, posterior fossa abnormalities, cerebellar abnormalities, cortical developmental malformations, midline abnormalities, or fetal brain parenchymal abnormalities.

**Data management** All records identified from electronic databases will be imported into reference management software and duplicate records will be removed. Two reviewers will independently screen titles and abstracts, assess full texts, and extract data using a standardized data extraction form. Disagreements will be resolved through discussion or consultation with a third reviewer. Extracted data will include study characteristics, population characteristics, MRI timing, fetal brain abnormality type, MRI findings or biomarkers, postnatal follow-up duration, outcome assessment tools, and effect estimates or raw data required for meta-analysis. The study selection process will be documented using a PRISMA flow diagram.

**Quality assessment / Risk of bias analysis** Two reviewers will independently assess the methodological quality and risk of bias of included studies. Prognostic factor studies will be assessed using the Quality in Prognosis Studies tool. Prediction model studies will be assessed using PROBAST when applicable. Diagnostic or prognostic accuracy studies will be assessed

using QUADAS-2 when applicable. Key domains will include participant selection, measurement of prenatal MRI biomarkers, outcome assessment, follow-up completeness, confounding, and statistical analysis. Disagreements will be resolved by consensus or by a third reviewer.

**Strategy of data synthesis** A narrative synthesis will first be conducted to summarize study characteristics, fetal brain abnormality types, MRI biomarkers, follow-up duration, and outcome definitions. If at least three studies report sufficiently comparable MRI biomarkers and outcomes, random-effects meta-analysis will be performed. Pooled odds ratios, risk ratios, hazard ratios, proportions, or diagnostic/prognostic accuracy estimates will be calculated as appropriate. Heterogeneity will be assessed using the $I^2$ statistic and $\tau^2$. Sources of heterogeneity will be explored through subgroup and sensitivity analyses. If quantitative synthesis is not appropriate because of clinical or methodological heterogeneity, results will be summarized narratively.

**Subgroup analysis** Planned subgroup analyses will include fetal brain abnormality type, isolated versus non-isolated abnormalities, severity of ventriculomegaly, corpus callosum abnormalities, posterior fossa abnormalities, cerebellar abnormalities, cortical developmental malformations, MRI gestational age, follow-up duration, standardized versus non-standardized neurodevelopmental assessment, and studies with normal versus abnormal genetic testing when available. Subgroup analyses will be performed only when sufficient data are available.

**Sensitivity analysis** Sensitivity analyses will be performed to examine the robustness of the findings. Planned sensitivity analyses include excluding studies at high risk of bias, studies with follow-up duration shorter than 12 months, studies without standardized neurodevelopmental assessment, studies with incomplete reporting of MRI findings or outcomes, and studies with very small sample sizes. Additional sensitivity analyses may be conducted according to study design, outcome definition, or availability of adjusted effect estimates.

**Language restriction** No language restriction will be applied during the database search. Non-English studies will be translated when feasible.

**Country(ies) involved** China.

**Other relevant information** This review will focus on prenatal MRI biomarkers as prognostic index factors rather than therapeutic interventions. The review will be conducted and reported in accordance with the PRISMA 2020 statement. Any protocol amendments, including changes to eligibility criteria, outcomes, or analysis methods, will be documented and reported transparently in the final manuscript.

**Keywords** fetal MRI; prenatal MRI; fetal brain abnormalities; neurodevelopmental outcome; prognostic biomarker; meta-analysis.

**Dissemination plans** The findings of this systematic review and meta-analysis will be submitted for publication in a peer-reviewed neurology, fetal medicine, or medical imaging journal. The results may also be presented at relevant academic conferences. The review aims to inform prenatal counseling, postnatal risk stratification, and future research on fetal brain MRI biomarkers.

**Contributions of each author**

Author 1 - Gan Tian - Author 1 conceived the review, developed the protocol, designed the search strategy and eligibility criteria, and will supervise study selection, data extraction, risk of bias assessment, data synthesis, and manuscript drafting.
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Author 3 - Fengying Chen - Author 3 will resolve disagreements during study selection and data extraction, advise on statistical analysis, interpret results, and critically revise the manuscript.
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