

The Incremental Yield of CMA Over Karyotype in Fetal Growth Restriction - A Systematic Review and Meta-Analysis

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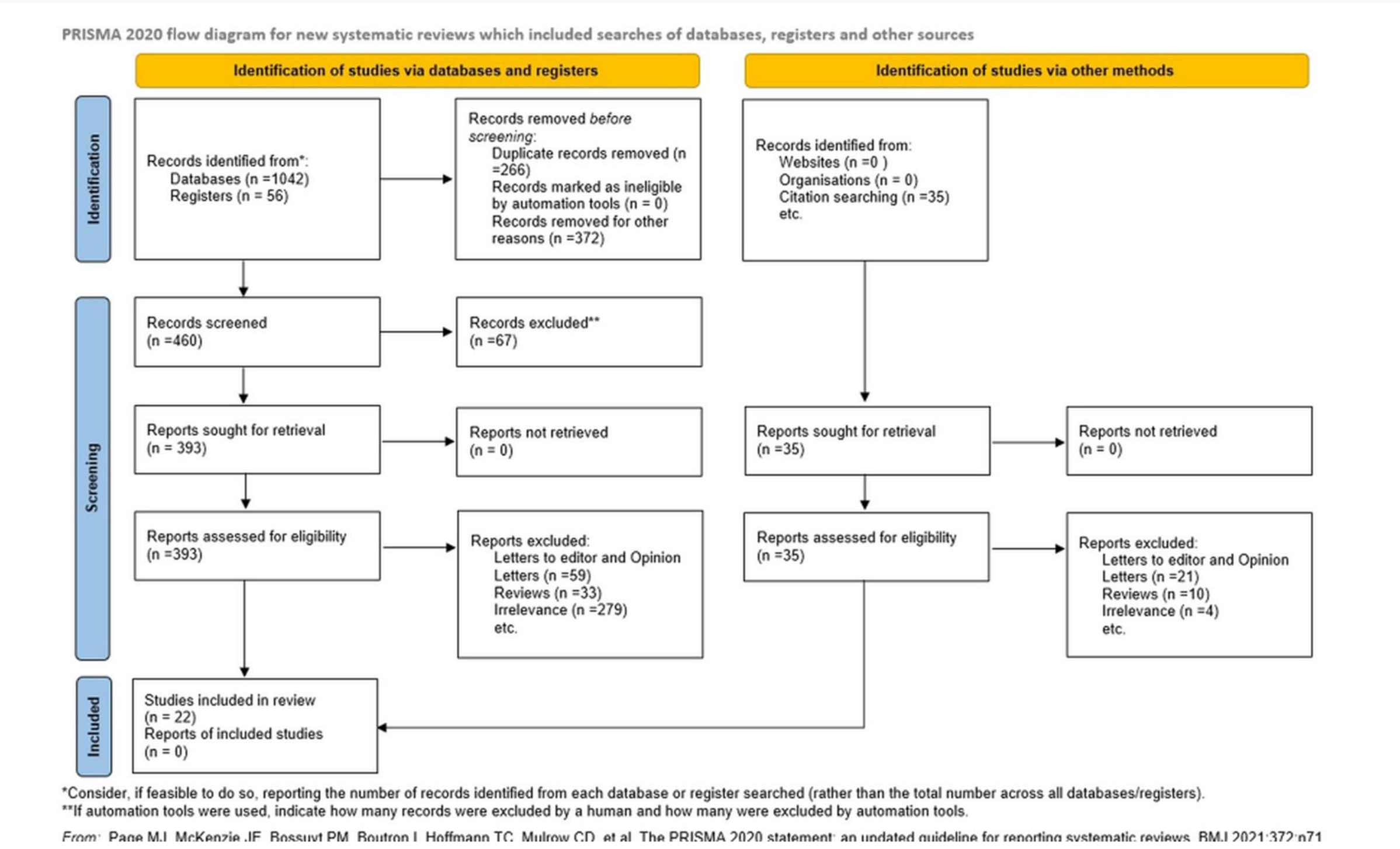


Key message
Incremental yield is phenotype-dependent: CMA adds diagnostic value after normal karyotype, especially when FGR is malformed.

STUDY FRAME

22 studies 2,275 fetuses

Meta-analysis of CMA after normal conventional cytogenetic testing in fetal growth restriction.



PRISMA flow: 1,133 records identified; 22 peer-reviewed studies included.

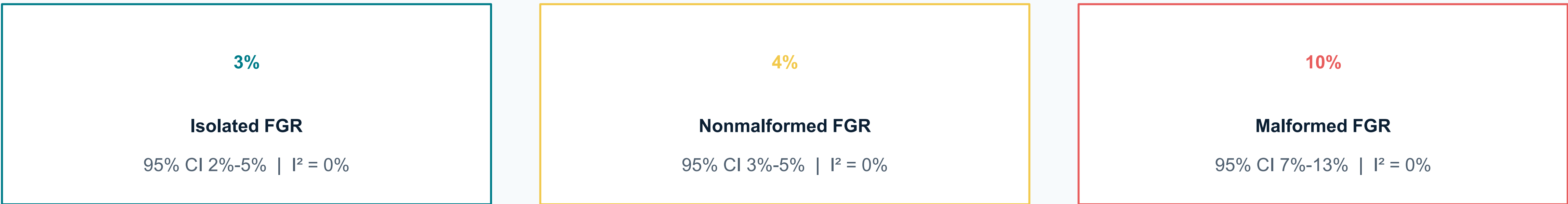
METHODS SNAPSHOT

- PRISMA/MOOSE design; PROSPERO CRD420251082633.
- Search through 31 March 2025: MEDLINE, Scopus, ClinicalTrials.gov, EMBASE, CENTRAL and Google Scholar.
- Outcome: pathogenic/likely pathogenic CNVs missed by conventional cytogenetic testing.
- Effect measure: risk difference; random-effects synthesis; VUS excluded.

FGR PHENOTYPES

- Isolated: FGR only.
- Nonmalformed: FGR + soft signs, Doppler or fluid abnormality.
- Malformed: FGR + structural anomaly.

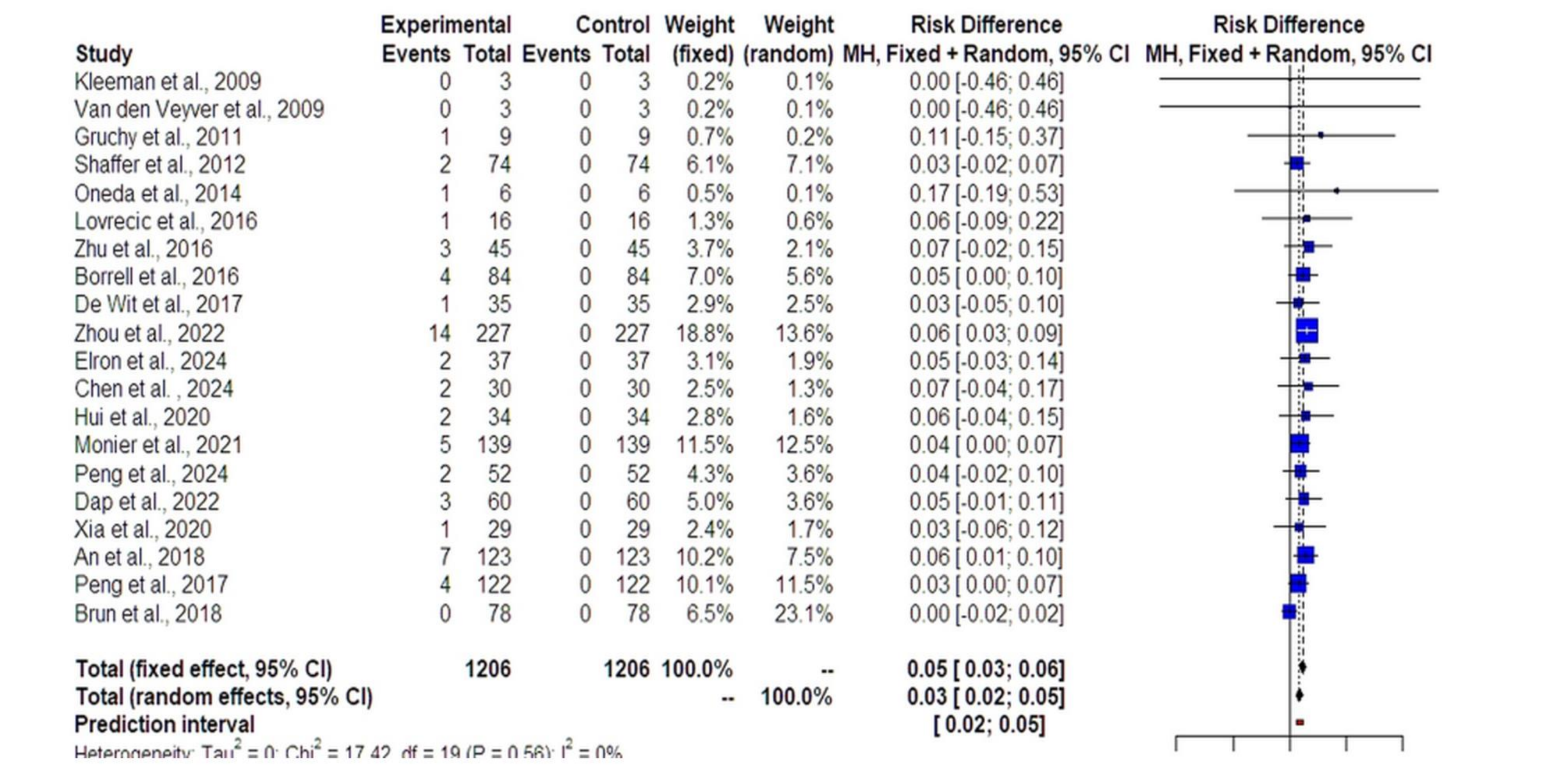
PRIMARY OUTCOME: INCREMENTAL CMA YIELD BEYOND KARYOTYPE



Observed study-level yield ranges: 0%-17% for isolated and nonmalformed FGR; 0%-21% for malformed FGR.

FOREST PLOT EVIDENCE

Isolated FGR



Nonmalformed FGR

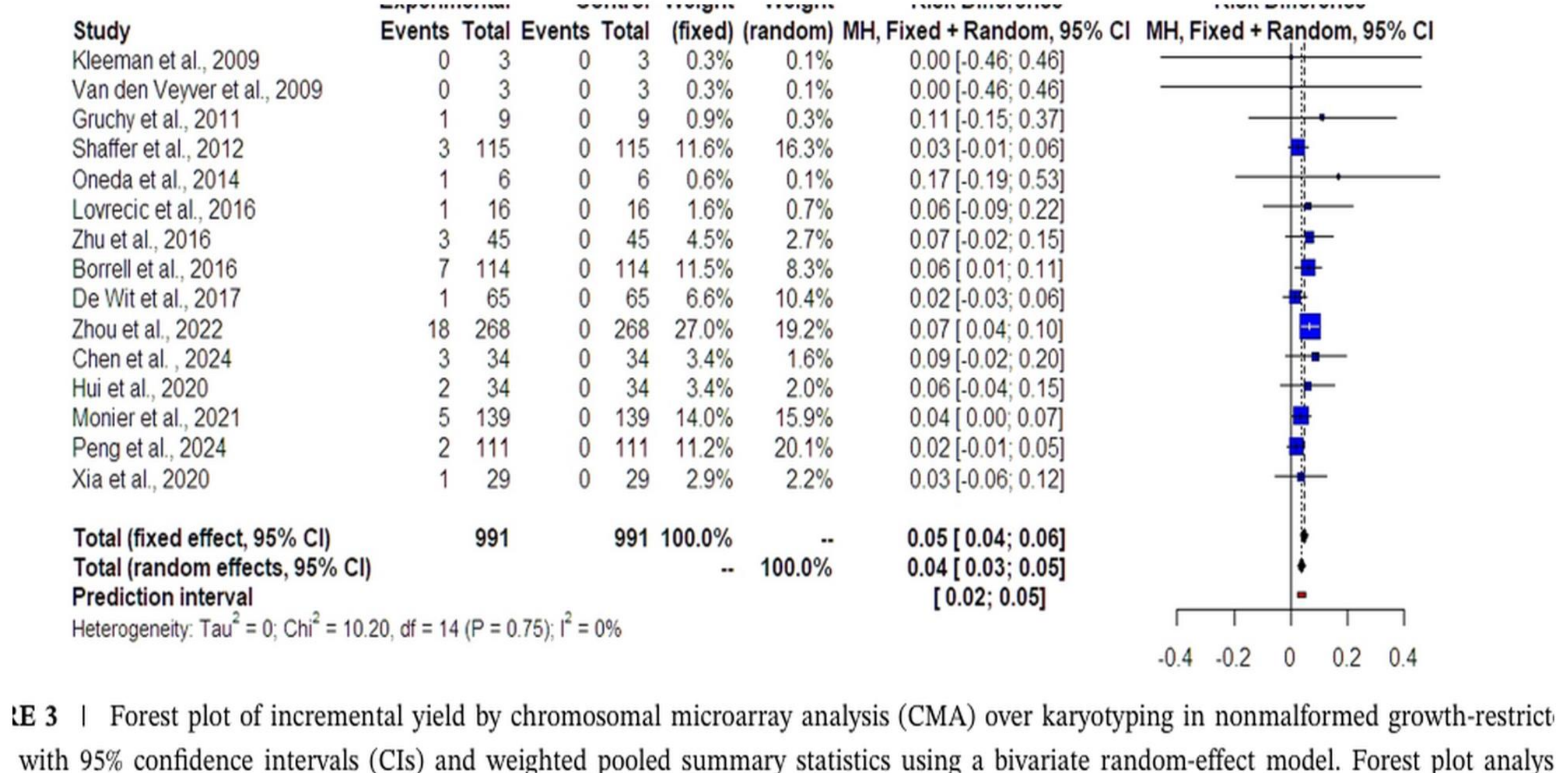
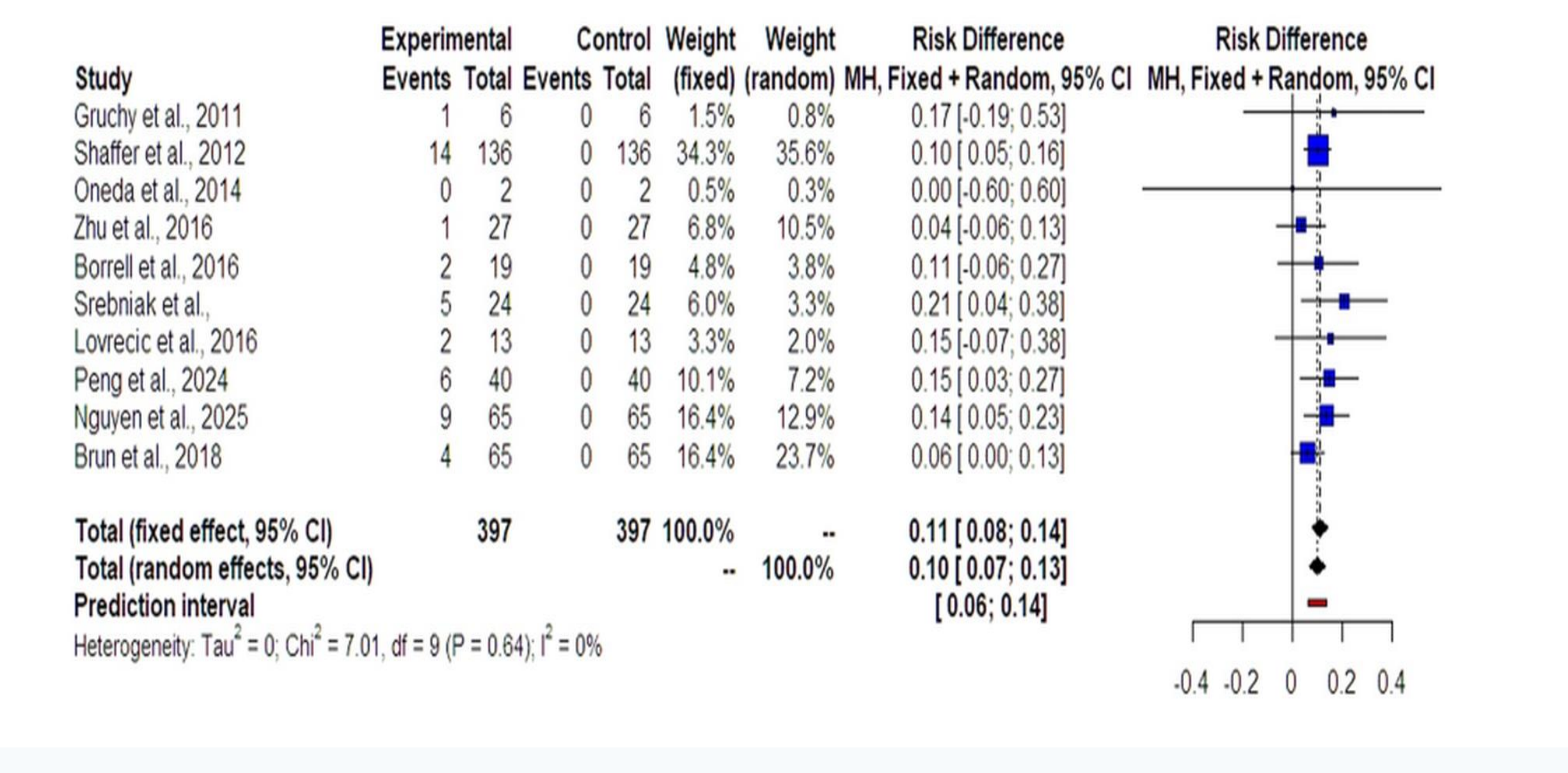


Figure 3 | Forest plot of incremental yield by chromosomal microarray analysis (CMA) over karyotyping in nonmalformed growth-restricted fetuses with 95% confidence intervals (CIs) and weighted pooled summary statistics using a bivariate random-effect model. Forest plot analysis.

Malformed FGR



CLINICAL IMPLICATIONS

Counseling should be phenotype-stratified.
A normal karyotype does not exclude clinically relevant submicroscopic imbalance. CMA should be discussed when invasive testing is clinically indicated, especially in malformed FGR.

TAKE-HOME

CMA provides an additional 3%-10% diagnostic yield beyond karyotype in FGR, with the highest yield in malformed cases.

STRENGTHS AND LIMITATIONS

- Largest updated synthesis in FGR with explicit separation of isolated, nonmalformed and malformed phenotypes.
- Limitations: heterogeneous FGR definitions, limited stratified data by gestational age/maternal age and mostly retrospective evidence.