Improving Induction Outcomes: Progesterone Receptor Antagonists Reduce Cesarean Birth Risk

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INTRODUCTION

Induction of labor (IOL) is one of the most common interventions in obstetrics, with 1:3 pregnancies undergoing IOL, yet a failure to achieve active labor in the setting of IOL remains a major driver of cesarean birth. Compared to cesarean birth, vaginal birth is less costly, shortens recovery, lowers risks of complications, and reduces risks to future pregnancies. Despite the widespread use of prostaglandins and mechanical methods for IOL, outcomes remain inconsistent and resource-intensive.

Mifepristone, a *non-specific* progesterone receptor antagonist (PA), offers a mechanistically distinct approach by reducing the cellular influence of progesterone, as the dominant hormone suppressing uterine contractility and cervical ripening throughout pregnancy. Yet, it has predominantly been used only in the setting of intrauterine fetal demise or for therapeutic abortion. This meta-analysis examines whether mifepristone can shift the trajectory of labor toward safer, more efficient vaginal birth.

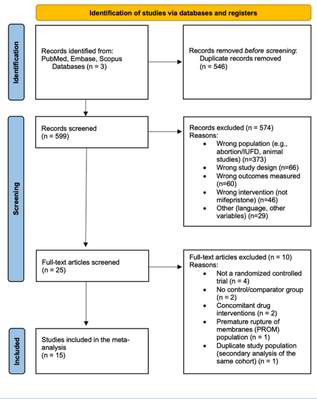
OBJECTIVE

To summarize and evaluate the extant literature reporting the effect of mifepristone on cesarean deliveries in term pregnancies undergoing IOL.

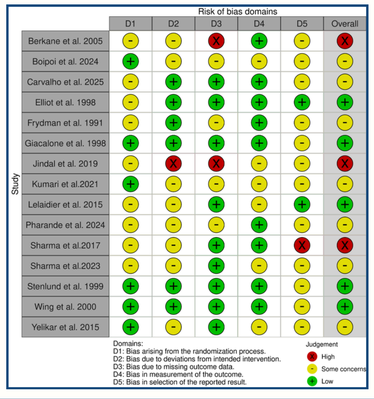
METHODOLOGY

Design: Systematic review + meta-analysis of randomized trials
Population: Term (≥37 weeks), singleton pregnancies
Intervention: Mifepristone (50-600 mg)
Control Condition: Placebo, prostaglandins, mechanical methods
Outcomes: *Primary*: Cesarean Birth. *Secondary*: Time to labor onset, time to birth, Bishop score, neonatal intensive care unit (NICU) admission, postpartum hemorrhage
Analysis: Risk of Bias Assessment (Cochrane ROB tool) and Random-effects model, heterogeneity via I^2

PRISMA FLOW DIAGRAM FOR STUDY INCLUSION



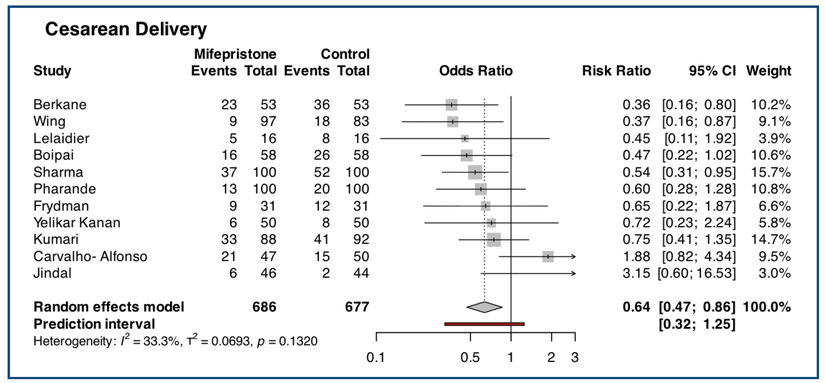
RISK OF BIAS ASSESSMENT OF INCLUDED RCTS USING THE COCHRANE ROB 2 TOOL.



KEY FINDINGS

36% Reduction in Cesarean Birth

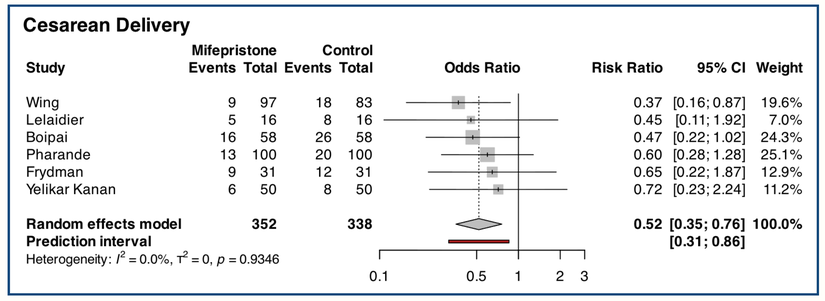
RR 0.64 (95% CI 0.47–0.86)



48% Reduction In High-Quality Trials

Limited to low risk of bias trials and placebo controlled conditions.

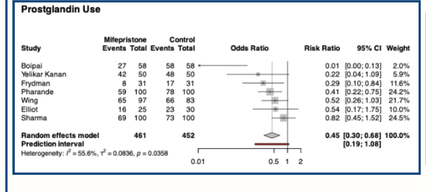
RR 0.52 (95% CI 0.35–0.76) (I^2 = 0%)



Women were nearly 50% less likely to require cesarean birth in high-quality trials.

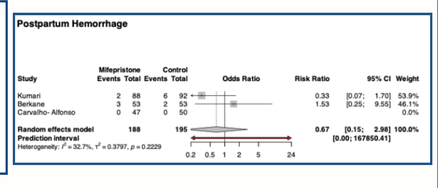
55% Reduction in Prostaglandin Use

RR 0.45 (95% CI 0.30–0.68)



No Significant Difference in Postpartum Hemorrhage

RR 0.67 (95% CI 0.15–2.98)



ANALYSIS

Mifepristone **targets the mechanisms that maintain pregnancy at term** and results in a clinically meaningful effect on IOL by addressing one of its most critical limitations: **An unprepared cervix.**

The primary analysis demonstrated a significant reduction in odds for cesarean birth with mifepristone (RR 0.64, 95% CI 0.47–0.86), with low–moderate heterogeneity (I^2 = 33%) compared to control group outcomes. Sensitivity analysis excluding high-risk-of-bias studies strengthened the effect (RR 0.52, 95% CI 0.35–0.76) and eliminated heterogeneity (I^2 = 0%), confirming a robust and consistent treatment effect across higher-quality trials.

Across randomized trials, the consistent reduction in cesarean birth, coupled with improvements in cervical ripening and time from intervention to birth, supports a model in which mifepristone enables a more **physiological progression into labor by antagonizing the mechanisms that prevent uterine contraction and cervical remodeling**. This upstream effect distinguishes it from conventional IOL strategies that aim to directly stimulate cervical softening (PGE) or uterine contractions (PGE/OXT).

LIMITATIONS/ FUTURE STUDY



We identified several important limitations in the current evidence base for the use of mifepristone for the induction of labor.

1. Moderate heterogeneity in induction protocols and comparator groups.
2. Limited power for safety outcomes (e.g., PPH) due to low event rates.
3. Variable outcome definitions across studies.
4. Small sample sizes contribute to imprecision and wide confidence intervals

Future studies should include standardized, adequately powered randomized trials with optimization of dosing and timing strategies, stratification by key clinical subgroups, and evaluation of safety outcomes and real-world implementation.

CONCLUSION

Mifepristone for cervical ripening and IOL is associated with a significant reduction in cesarean birth. This effect is strengthened and becomes highly consistent when analyses are restricted to studies at low risk of bias, supporting the robustness and internal validity of the findings. These results suggest that mifepristone is an effective and reliable intervention for improving labor outcomes in term pregnancies. Given the consistency across high-quality trials and the absence of heterogeneity in sensitivity analyses, the incorporation of mifepristone into clinical IOL protocols may reduce cesarean rates and associated maternal morbidity.

Rather than intensifying contractions in an unprepared cervix, mifepristone improves labor outcomes by blocking the inhibition of labor onset.

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