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Cervical mucus removal prior to embryo transfer in women undergoing IVF/ICSI: a systematic review and meta-analysis of randomised controlled trials

Craciunas L, Tsampras N, Fitzgerald C

Department of Reproductive Medicine, St. Mary's Hospital, Manchester, M13 0JH, UK





Introduction

- Most of the IVF/ICSI cycles reach the stage of ET
 - Small proportion of transferred embryos implant
 - ET: critical and delicate step in ART
 - Interventions:
 - pre-ET (dummy ET, endometrial preparation)
 - during ET (USS, manipulation, catheter, site)
 - post-ET (fibrin sealant, bed rest)
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Cervical mucus

- Suggested to interfere with adequate ET
 - Blocks the passage of embryos
 - Drags the embryos back from the releasing site
 - Contaminates the intra-uterine environment
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Objective

To appraise critically the published RCTs reporting on the outcome of cervical mucus removal prior to ET in women undergoing IVF/ICSI.





Methods: Literature search

- Standard medical databases up to October 2013
(Medline, EMBASE, Science Citation Index Expanded, Cochrane Central Register of Controlled Trials)
 - Medical subject headings (MeSH):
 - embryo transfer, cervical mucus, pregnancy rate, in vitro fertilization, intracytoplasmic sperm injection
 - Free terms:
 - cervical discharge, aspiration, removal, irrigation, outcome
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Methods: Selection / Endpoints

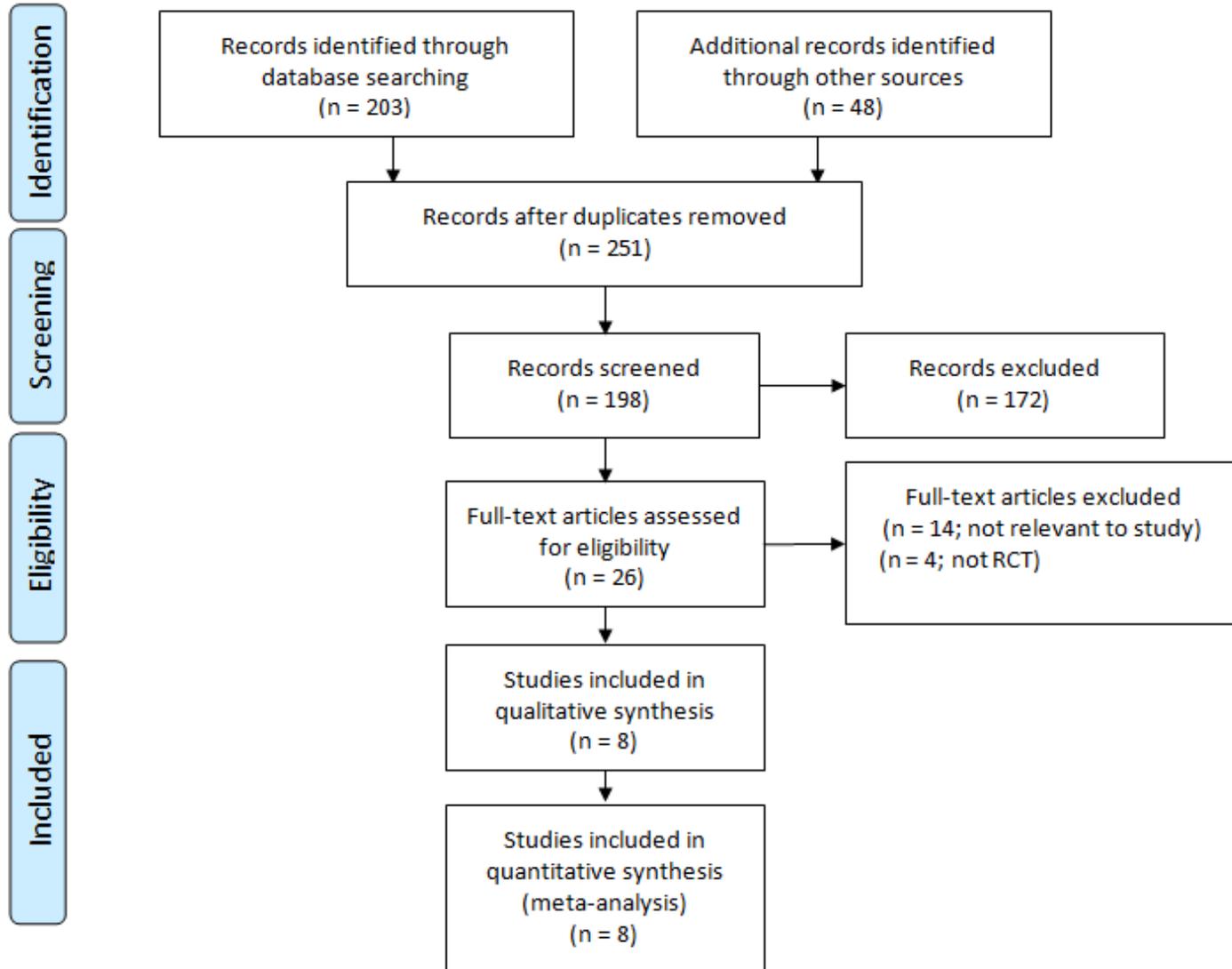
- RCTs evaluating cervical mucus removal prior to ET
 - No filters: language, country of origin, blinding, sample size
 - Primary endpoints: clinical pregnancy, implantation, live birth
 - Secondary endpoints: retained embryos, difficult ET, catheter bacterial contamination
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Methods: Statistics

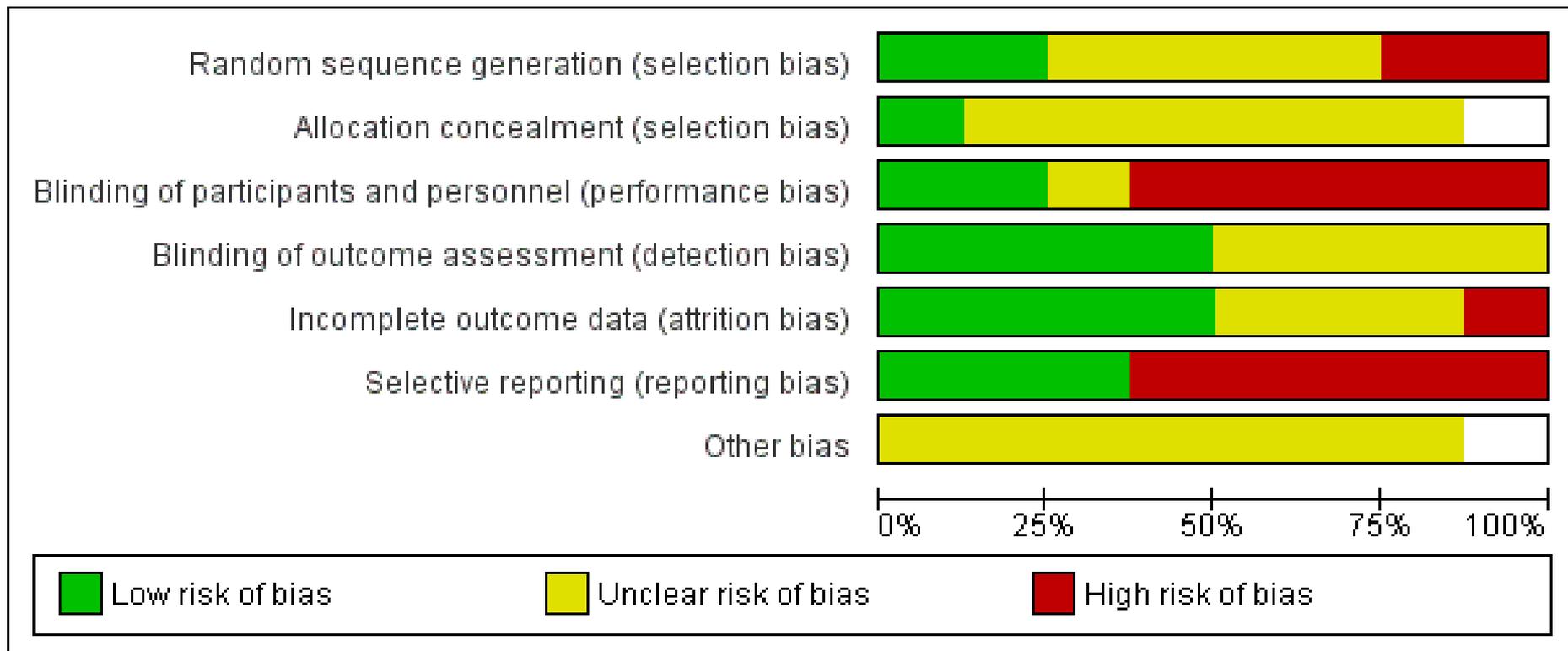
- RevMan 5.2.7 (Cochrane Collaboration)
 - RR with a 95% CI
 - Heterogeneity: measured using the χ^2 , quantified using I^2
 - Risk of bias: guideline of the Cochrane Collaboration
 - Results displayed as forest plots
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Results: PRISMA flow chart



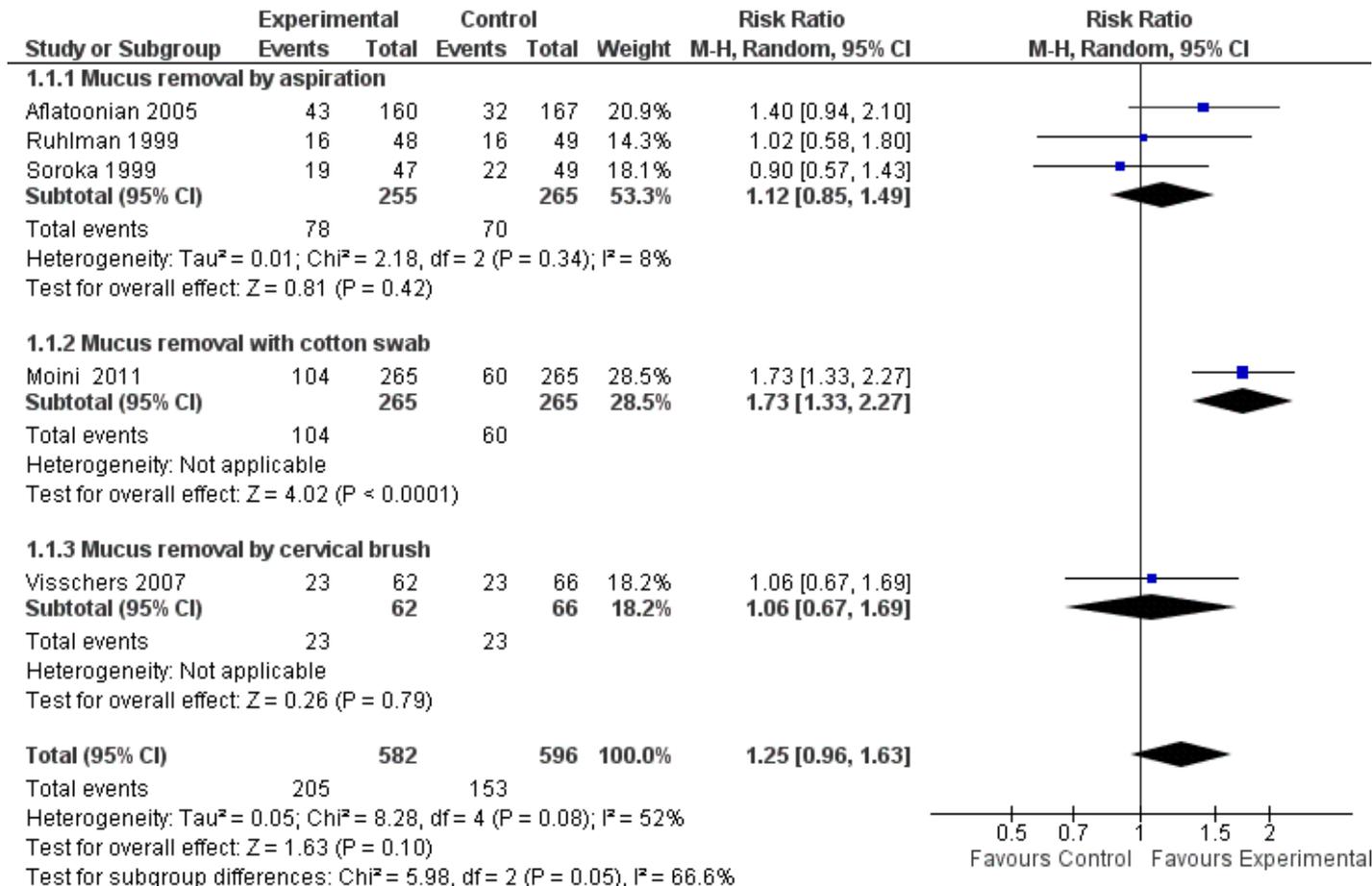
Results: Methodological quality

- Moderate to poor: inadequate concealment technique, blinding and possible reporting bias in abstracts.



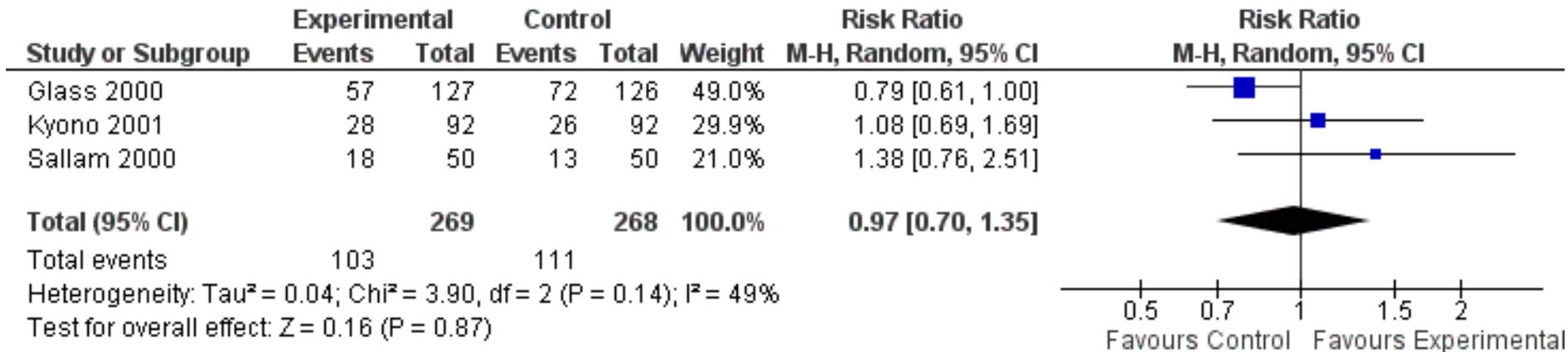
Results: Clinical pregnancy rate

- Similar results (RR, 1.25; 95% CI, 0.96 to 1.63; $z = 1.63$; $p = 0.10$) between the groups when the cervical mucus was removed.



Results: Clinical pregnancy rate

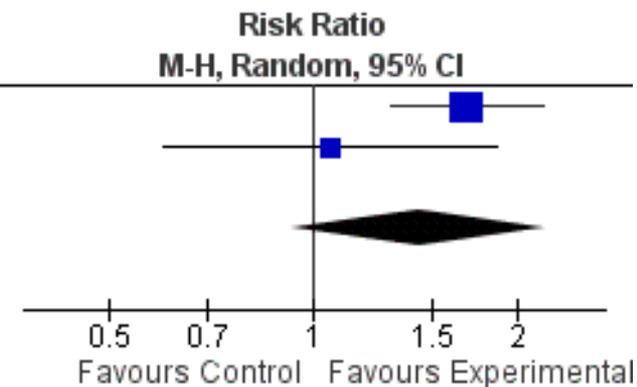
- Similar results for cervical irrigation after cervical mucus removal (RR, 0.97; 95% CI, 0.70 to 1.35; $z = 0.16$; $p = 0.87$).



Results: Implantation rate

- No difference between the groups (RR, 1.44; 95% CI, 0.93 to 2.21; $z = 1.64$; $p = 0.10$).

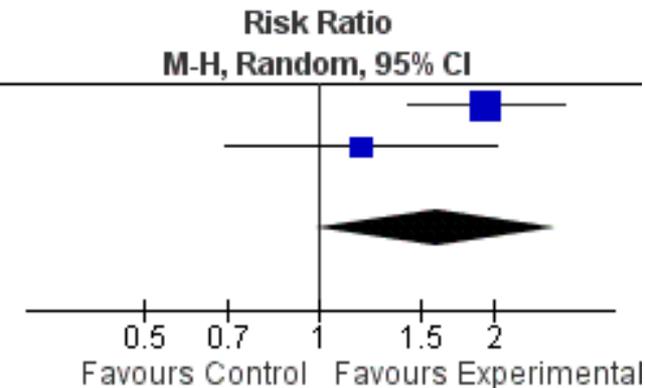
Study or Subgroup	Experimental		Control		Weight	Risk Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI
Moini 2011	135	658	78	641	65.4%	1.69 [1.30, 2.18]
Ruhlman 1999	22	168	20	162	34.6%	1.06 [0.60, 1.87]
Total (95% CI)		826		803	100.0%	1.44 [0.93, 2.21]
Total events	157		98			
Heterogeneity: $\tau^2 = 0.06$; $\chi^2 = 2.14$, $df = 1$ ($P = 0.14$); $I^2 = 53\%$						
Test for overall effect: $Z = 1.64$ ($P = 0.10$)						



Results: Live birth rate

- Similar results (RR, 1.59; 95% CI, 0.99 to 2.55; $z = 1.92$; $p = 0.05$).

Study or Subgroup	Experimental		Control		Weight	Risk Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI
Moini 2011	89	265	46	265	60.1%	1.93 [1.42, 2.64]
Visschers 2007	20	62	18	66	39.9%	1.18 [0.69, 2.02]
Total (95% CI)		327		331	100.0%	1.59 [0.99, 2.55]
Total events	109		64			
Heterogeneity: $\text{Tau}^2 = 0.07$; $\text{Chi}^2 = 2.44$, $\text{df} = 1$ ($P = 0.12$); $I^2 = 59\%$						
Test for overall effect: $Z = 1.92$ ($P = 0.05$)						





Limitations

- RCTs with fewer patients may not have been sufficient to recognise small differences in outcomes.
 - Quality of included RCTs was not good due to inadequate concealment technique, blinding and possible reporting bias.
 - Significant heterogeneity due to clinical and methodological diversity.
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Conclusion

- Very little evidence of an overall benefit of cervical mucus removal prior to embryo transfer for women undergoing IVF/ICSI.
 - Future RCTs should be powered adequately and be conducted according to the CONSORT guidelines in order to be able to identify the possible small effect of the intervention.
 - Should report both primary and secondary endpoints (difficult embryo transfer, retained embryos and catheter contamination rates) to explain the mechanism of the intervention.
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Thank you!

