# Adverse pregnancy and perinatal outcomes associated with *Mycoplasma genitalium:* systematic review and meta-analysis

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**Text S1: Search strategy** 

1. Terms for population	"pregnancy" or "prenatal" or "antenatal"
2. Terms for exposure	"Mycoplasma genitalium"
3. Terms for outcomes	"birth outcome" or "adverse birth outcome" or "adverse pregnancy
	outcome" or "perinatal morbidity" or "perinatal mortality" or
	"perinatal outcome" or "premature birth" or "premature delivery" or
	"very preterm birth" or "preterm birth" or "preterm delivery" or
	"premature labour" or "preterm labour" or "premature labor" or
	"preterm labor" or "premature rupture of membranes" or "preterm
	rupture of membranes" or "preterm premature rupture of membranes"
	or "low birth weight" or "intrauterine growth retardation" or
	"intrauterine growth restriction" or "small for gestational age" or
	"gestational age" or "stillbirth" or "perinatal mortality" or "perinatal
	morbidity" or "perinatal death" or "neonatal mortality" or "neonatal
	morbidity" or "neonatal death" or "fetal death" or "miscarriage" or
	"spontaneous abortion" or "chorioamnionitis"

#### Text S2: Exclusion criteria at first stage

If the title mentions one of the following without reference to pregnancy, sexually transmitted infections or *M. genitalium* the article was excluded in the first stage of the screening process:

- Sexual assault
- Algorithm
- Infertility
- Contraception/ Family planning
- Ectopic/tubal pregnancy
- UTI in women
- Gonococcal arthritis
- Gynecology/gynaecology
- Induced abortion

- Syphilis (only)
- Trachomatis (only)
- Chlamydia (only)
- Treatment guidelines/ treatment schedules
- Anti-retroviral therapy
- Tetanus
- Sexual health
- Child sex abuse
- Polio

If the article was found to be a case report, review article or letter, the article was excluded at any stage of the review process.

Table S1: Preferred reporting items for systematic reviews and meta-analysis (PRISMA 2020 item checklist)

Section/topic	#	Checklist item	Section and paragraph
Title	1	Identify the report as a systematic review.	Title
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract includes as many items as allowed in word count
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction, para 3
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods, Eligibility criteria; Text S2
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods, Information sources
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Text S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods, Study selection; Text S2
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods, Study selection and data extraction
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods, Study selection and data extraction; Protocol, Codebook S2
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Protocol, Codebook S1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods, Risk of bias in individual studies
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Methods, Data synthesis and analysis

Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Methods, Data synthesis and analysis
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Methods, Data synthesis and analysis
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Methods, Data synthesis and analysis
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Methods, Data synthesis and analysis
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Risk of bias across studies and certainty of the body of evidence
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Risk of bias across studies and certainty of the body of evidence
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Risk of bias across studies and certainty of the body of evidence
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Risk of bias across studies and certainty of the body of evidence
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Results ,para 1-2, p. 6, Figure S1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Not done
Study characteristics	17	Cite each included study and present its characteristics.	Results, Table 1; Table S2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Tables S10 and S11
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Results, Table 2; Figure 1; Figure 2; Figure S2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results, named paragraph for each outcome

		Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Results, Table 2; Figure 1; Figure 2; Figure S2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Results, Risk of bias
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not done
Certainty of evidence	22		Results, Certainty of evidence; Table S12
Discussion	23a		Discussion, Comparison with other studies and interpretation
	23b	Discuss any limitations of the evidence included in the review.	Discussion, Comparison with other studies and interpretation
	23c	Discuss any limitations of the review processes used.	Discussion, Strengths and weaknesses
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion, Implications for practice and research
Registration and protocol		Provide registration information for the review, including register name and registration number, or state that the review was not registered.	After Abstract
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Methods, para 1
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	After main text
Competing interests	26	Declare any competing interests of review authors.	After main text
Availability of data, code and other materials		Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Online supplemental material

Table S2: Descriptive characteristics of included studies

First author, publication year	Assessment of gestational age	Timing of specimen collection	Specimen type	Total number enrolled	size for	MG+	Outcome+ MG-	Outcome- MG+	Outcome- MG-	Outcom	e Outcome definition
Agger, 2014	NR	1 <sup>st</sup> or 2 <sup>nd</sup> trimester	Endocervical swab	783	676	0	54	9	613	PTB	< 37 weeks
Averbach, 2013	USS, LMP	1st or 2nd trimester	Endocervical swab	100	66	1	10	4	51	PTB	24-36 weeks
				100	81	1	10	6	64	LBW	< 2500g
				100	81	1	8	6	66	SAB	NR
Choi, 2012	NR	NR	Vaginal swab	217	191	0	100	0	91	PTB	NR
Edwards, 2006	NR	NR	Not clear	137	134	NR	NR	NR	NR	PTB	< 37 weeks
Hitti, 2010	USS, LMP, NN	<48 hours post-partum	Endocervical swab	1338	1328	29	632	12	655	PTB	20-36 weeks
Kataoka, 2006	USS, LMP	1 <sup>st</sup> trimester	Vaginal swab	1040	871	0	15	7	849	PTB	< 34 weeks <sup>1</sup>
				1040	871	0	7	7	857	PROM	NR
				1040	877	0	5	7	865	SAB	NR
				1040	872	0	1	7	864	PND	NR
Labbé, 2002	NR	<24 hours post-partum	Endocervical swab	1014	799	16	183	36	564	PTB	< 37 weeks
				1014	653	2	51	36	564	SAB	< 20 weeks
				1014	725	8	117	36	564	PND	> 20 weeks
Oakeshott, 2004	LMP	1st trimester	Urine	1216	699	0	39	3	657	PTB	< 37 weeks
				1216	894	1	91	5	797	SAB	<16 weeks
Rahimkhani, 2018	NR	1st or 2nd trimester	Urine	119	119	6	25	15	73	SAB	NR
Short, 2010	NR	NR	Urine	216	213	3	79	9	125	SAB	< 22 weeks

**Abbreviations:** LBW, low birth weight; LMP, last menstrual period; NN, neonatal; NR, not reported; PROM, premature rupture of membranes; PND perinatal death; PTB, preterm birth; SAB, spontaneous abortion; USS, ultrasound scan.

<sup>&</sup>lt;sup>1</sup> Included spontaneous abortion (n=5 at 11-15 weeks) and intrauterine death (n=1 at 24 weeks). These outcomes were extracted separately

Table S3: Income group and socio-demographic characteristics in included studies

First author, year	Country of study	World bank classification	Urban or rural location	Age in years (mean(SD)/median (IQR)/min-max)	Ethnic group/racial categories/nationality	Smokers included (%)	Multiple pregnancies
Agger, 2014	USA	High income	Mixed	NR <sup>1</sup>	Mixed	NR	Yes <sup>2</sup> (5/783)
Averbach, 2013	USA	High income	Urban	NR/25.0 (22.0-30.0)/NR	Mixed	Yes (11.6%)	No
Choi, 2012	South Korea	High income	Urban	NR	Asian	NR	NR
Edwards, 2006	USA	High income	Urban	NR	Mixed	Yes (15.67%)	No
Hitti, 2010	Peru	Non-high income	Urban	NR <sup>3</sup>	NR	Yes (6.48%)	Yes (73/1328)
Kataoka, 2006	Japan	High income	Urban	NR	Asian	NR	No
Labbé, 2002	Guinea- Bissau	Non-high income	NR	NR	Black	NR	NR
Oakeshott, 2004	United Kingdom	High income	Urban	31 (NR)/NR/16-48	Mixed	NR	NR
Rahimkhani, 2018	Iran	Non-high income	NR	29 (NR)/NR/NR	NR	NR	NR
Short, 2010	USA	High income	Urban	NR <sup>4</sup>	Mixed	Yes (34.72%)	NR

Abbreviations: IQR, interquartile range; NR, not reported; SD, standard deviation

Ages only available for subgroups
Multiple Pregnancies were excluded from the analysis
Ages only available for subgroups
Ages only available for subgroups

Table S4: Reported antibiotic treatment in included studies

First author, year	Antibiotic treatment provided	Timing of antibiotic treatment
Agger, 2014	Yes, some positive women	NR
Averbach, 2013	NR	NR
Choi, 2012	NR	NR
Edwards, 2006	NR	NR
Hitti, 2010	Yes, some positive women	NR
Kataoka, 2006	Yes, some positive women <sup>1</sup>	1st or 2nd trimester
Labbé, 2002	NR	NR
Oakeshott, 2004	NR	NR
Rahimkhani, 2018	NR	NR
Short, 2010	NR	NR

Abbreviations: NR, not reported

 $<sup>^{1}</sup>$  Antibiotics were administered to women in whom *C. trachomatis* and/or *N. gonorrhoeae* was detected but not to those in whom any mycoplasma was detected in the absence of *C. trachomatis* or *N. gonorrhoeae* 

Table S5: Overview of *C. trachomatis* infections and co-infections in study populations in included studies

First author, year	All CT+1	CT+ in MG+ <sup>2</sup>	CT+ in MG- <sup>3</sup>
Agger, 2014	33/676 (4.9%)	NR	NR
Averbach, 2013	6/94 (6.4%)	1/8 (12.5%)	5/86 (5.8%)
Choi, 2012	3/126 (2.4%)	NR	NR
Edwards, 2006	10/134 (7.5%)	NR	NR
Hitti, 2010	98/1328 (7.4%)	9/41 (22.0%)	89/1287 (6.9%)
Kataoka, 2006	28/877 (3.2%)	NR	NR
Labbé, 2002	NR	NR	NR
Oakeshott, 2004	20/914 (2.2%)	0/20 (0.0%)	20/894 (2.2%)
Rahimkhani, 2018	8/119 (6.7%)	NR	NR
Short, 2010	15/216 (6.9%)	NR	NR

Abbreviations: CT, C. trachomatis; MG, M. genitalium; NR, not reported

<sup>&</sup>lt;sup>1</sup> Total number of participants tested positive for CT/total number of participants tested for this infection

<sup>&</sup>lt;sup>2</sup> Total number of participants tested positive for CT and MG/total number of participants tested positive for MG

<sup>&</sup>lt;sup>3</sup> Total number of participants tested positive for CT and negative for MG/total number of participants tested negative for MG

Table S6: Overview of N. gonorrhoeae infections and co-infections in study populations in included studies

First author, year	All NG+1	NG+ in MG+ <sup>2</sup>	NG+ in MG- <sup>3</sup>
Agger, 2014	7/676 (1.0%)	NR	NR
Averbach, 2013	1/94 (1.1%)	0/8 (0.0%)	1/86 (1.2%)
Choi, 2012	0/126 (0.0%)	NR	NR
Edwards, 2006	1/134 (0.7%)	NR	NR
Hitti, 2010	1/1328 (0.1%)	0/41 (0.0%)	1/1287 (0.1%)
Kataoka, 2006	1/877 (0.1)	NR	NR
Labbé, 2002	78/986 (7.9%)	6/63 (9.5%)	72/923 (7.8%)
Oakeshott, 2004	NR	NR	NR
Rahimkhani, 2018	NR	NR	NR
Short, 2010	NR	NR	NR

Abbreviations: NG, N. gonorrhoeae; MG, M. genitalium; NR, not reported

<sup>&</sup>lt;sup>1</sup> Total number of participants tested positive for NG/total number of participants tested for this infection

 $<sup>^2</sup>$  Total number of participants tested positive for NG and MG/total number of participants tested positive for MG

 $<sup>^3</sup>$  Total number of participants tested positive for NG and negative for MG/total number of participants tested negative for MG

Table S7: Overview of *T. pallidum* infections and co-infections in study populations in included studies

First author, year	All TP+1	TP+ in MG+ <sup>2</sup>	TP+ in MG- <sup>3</sup>
Agger, 2014	NR	NR	NR
Averbach, 2013	1/95 (1.1%)	0/8 (0.0%)	1/86 (1.2%)
Choi, 2012	0/126 (0.0%)	NR	NR
Edwards, 2006	0/134 (0.0%)	NR	NR
Hitti, 2010	NR	NR	NR
Kataoka, 2006	NR	NR	NR
Labbé, 2002	49/1014 (4.8%)	4/63 (6.3%)	45/951 (4.7%)
Oakeshott, 2004	NR	NR	NR
Rahimkhani, 2018	NR	NR	NR
Short, 2010	NR	NR	NR

Abbreviations: MG, M. genitalium; NR, not reported; TP, T. pallidum

Table S8: Overview of bacterial vaginosis and co-infections in study populations in included studies

First author, year	All BV <sup>1</sup>	BV+ in MG+ <sup>2</sup>	BV+ in MG- <sup>3</sup>
Agger, 2014	NR	NR	NR
Averbach, 2013	42/75 (56.0%)	6/8 (75%)	36/67 (53.7%)
Choi, 2012	1/126 (0.8%)	NR	NR
Edwards, 2006	18/134 (13.4%)	NR	NR
Hitti, 2010	NR	NR	NR
Kataoka, 2006	NR	NR	NR
Labbé, 2002	NR	NR	NR
Oakeshott, 2004	128/859 (14.9%)	3/128 (2.3%)	125/731 (17.1%)
Rahimkhani, 2018	NR	NR	NR
Short, 2010	NR	NR	NR

Abbreviations: BV, bacterial vaginosis; MG, M. genitalium; NR, not reported

<sup>&</sup>lt;sup>1</sup> Total number of participants tested positive for BV/total number of participants tested for this infection

<sup>&</sup>lt;sup>2</sup> Total number of participants tested positive for BV and MG/total number of participants tested positive for MG

<sup>&</sup>lt;sup>3</sup> Total number of participants tested positive for BV and negative for MG/total number of participants tested negative for MG

Table S9: Overview of overall positivity of genital infections in study populations in included studies<sup>1</sup>

First author, year	All M. hominis <sup>2</sup>	All U. urealyticum³	All <i>U. parvum</i> <sup>4</sup>	All T. vaginalis <sup>5</sup>	All herpes <sup>6</sup>	All HIV <sup>7</sup>
Agger, 2014	119/676 (17.6%)	50/676 (7.4%)	331/676 (49.0%)	NR	34/676 (5.0%)	NR
Averbach, 2013	NR	NR	NR	NR	NR	NR
Choi, 2012	16/126 (12.7%)	79/126 (62.7%)	NR	NR	NR	NR
Edwards, 2006	NR	NR	NR	10/134 (7.5%)	NR	NR
Hitti, 2010	NR	NR	NR	33/1328 (2.5%)	NR	NR
Kataoka, 2006	98/877 (11.2%)	76/877 (8.7%)	456/877 (52.0%)	NR	NR	NR
Labbé, 2002	NR	NR	NR	194/884 (22.0%)	NR	95/1011 (9.4%)
Oakeshott, 2004	NR	NR	NR	NR	NR	NR
Rahimkhani, 2018	NR	NR	NR	NR	NR	NR
Short, 2010	NR	NR	NR	NR	NR	NR

**Abbreviations:** HIV, human immunodeficiency virus; M. hominis, Mycoplasma hominis; NR, not reported; T. vaginalis, Trichomonas vaginalis; U. parvum, Ureaplasma parvum; U. urealyticum, Ureaplasma urealyticum

<sup>&</sup>lt;sup>1</sup> Prevalence of C. trachomatis, N. gonorrhoeae, T. pallidum and bacterial vaginosis is listed in table 2 to 5 in the thesis under all CT+, all NG+, all TP+ and all BV+

<sup>&</sup>lt;sup>2</sup> Total number of participants tested positive for M. hominis/total number of participants tested for this infection

<sup>&</sup>lt;sup>3</sup> Total number of participants tested positive for *U. urealyticum*/total number of participants tested for this infection

<sup>&</sup>lt;sup>4</sup> Total number of participants tested positive for *U. parvum*/total number of participants tested for this infection

<sup>&</sup>lt;sup>5</sup> Total number of participants tested positive for *T. vaginalis*/total number of participants tested for this infection

<sup>&</sup>lt;sup>6</sup> Total number of participants tested positive for herpes/total number of participants tested for this infection

<sup>&</sup>lt;sup>7</sup> Total number of participants tested positive for HIV/total number of participants tested for this infection

Table S10: Risk of bias assessment, case control studies

Assessment criteria	Choi 2012	Hitti 2010	Labbé 2002	Short 2010
Appropriate and clearly focused question.	WC	WC	AA	WC
The cases and controls are taken from comparable populations.	NR	AA	AA	AA
The same exclusion criteria are used for both cases and controls.	NAD	AA	NAD	AA
What was the participation rate for each group (cases)?	NA	$98.7\%^{1}$	NA	NA
What was the participation rate for each group (controls)?	NA	$99.9\%^{2}$	NA	NA
Both groups are compared to establish their similarities or differences.	PA	WC	NAD	WC
Cases are clearly defined and differentiated from controls.	WC	WC	WC	WC
It is clearly established that controls are not cases.	WC	WC	WC	WC
Measures taken to prevent knowledge of primary exposure from influencing case ascertainment.	NA	NA	NA	NA
Exposure status is measured in a standard, valid and reliable way.	WC	WC	WC	WC
Main potential confounders are accounted for in design/analysis.	NAD	AA	NAD	WC
Confidence intervals provided?	No	Yes	Yes	Yes
Study results internally valid?	+	++	+	++
Study results externally valid?	+	+	+	-

**Abbreviations:** AA, adequately addressed; NA, not applicable; NAD, not addressed; NR, not reported; PA, poorly addressed; WC, well covered; ++, all or most of checklist criteria fulfilled; + some of checklist criteria fulfilled; - few or no checklist criteria fulfilled

<sup>&</sup>lt;sup>1</sup> Data were omitted for 5 cases with gestational age < 20 weeks or no documentation of gestational age assessment, 2 cases with higher-order multiple gestations and 2 additional subject who did not have cervical samples collected for *M. genitalium*.

<sup>&</sup>lt;sup>2</sup> Data were omitted for 1 case who did not have cervical samples collected for *M. genitalium*.

Table S11: Risk of bias assessment, cohort studies

Assessment criteria	Agger 2014	Averbach 2013	Edwards 2006	Kataoka 2006	Oakeshott 2004	Rahimkhani 2018
The method of allocation to exposure groups was unrelated to potential confounding factors.	NA	NA	NA	NA	NA	NA
Attempts made within design or analysis to balance both groups for potential confounders.	Yes	Yes	Yes	Yes	No	No
The groups were comparable at baseline, including all major confounding factors.	No	No	No	No	Unclear	Unclear
Based on above answers, was selection bias present?	High	High	High	High	Unclear	Unclear
If so, what is the likely direction of its effect?	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
The comparison groups received the same care and support apart from the exposure(s) studied.	Unclear	Yes	Unclear	Unclear	Unclear	Unclear
Participants receiving care and support were kept "blind" to intervention allocation.	NA	NA	NA	NA	NA	NA
Individuals administering care and support were kept "blind" to intervention allocation.	NA	NA	NA	NA	NA	NA
Based on above answers, was performance bias present?	Unclear	Low	Unclear	Unclear	Unclear	Unclear
If so, what is the likely direction of its effect?	Unclear	NA	Unclear	Unclear	Unclear	Unclear
All groups followed up for an equal length of time?	Yes	Yes	Yes	Yes	Yes	Yes
Number of participants who did not complete the intervention in each group?	NA	NA	NA	NA	NA	NA
The groups were comparable for intervention completion.	NA	NA	NA	NA	NA	NA

Assessment criteria	Agger 2014	Averbach 2013	Edwards 2006	Kataoka 2006	Oakeshott 2004	Rahimkhani 2018
For how many participants were no outcome data available?	107/783 (13.7%)	14/95 (14.7%)	3/137 (2.2%)	148/1040 (14.2%)	301/1216 (24.8%)	0/119 (0.0%)
Were groups comparable for outcome data? (there were no important or systematic differences between groups in terms of those who did not complete the intervention)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Based on above answers, was attrition bias present?	Unclear	Unclear	Low	Unclear	Unclear	Unclear
If so, what is the likely direction of its effect?	Unclear	Unclear	NA	Unclear	Unclear	Unclear
The study had an appropriate length of follow-up.	Yes	Yes	Yes	Yes	Yes	Yes
The study used a precise definition of outcome.	Yes	Yes	Yes	No	Yes	No
A valid, reliable method used to determine the outcome?	Unclear	Yes	Unclear	Yes	No	Unclear
Investigators were kept "blind" to participants' exposure to the intervention.	NA	NA	NA	NA	NA	NA
Investigators were kept "blind" to other important confounding factors.	NA	NA	NA	NA	NA	NA
Based on above answers, was detection bias present?	Unclear	Low	Unclear	Low	High	Unclear
If so, what is the likely direction of its effect?	Unclear	NA	Unclear	NA	Unclear	Unclear
Overall assessment of internal validity	+	+	+	+	+	-
Overall assessment of external validity	+	-	+	-	-	-

**Abbreviations:** AO, adverse outcomes; High, high risk of bias; Low, low risk of bias; NA, not applicable; NK, not known; STI, sexually transmitted infections; Unclear, unclear of risk of bias; ++, all or most of checklist criteria fulfilled; + some of checklist criteria fulfilled; - few or no checklist criteria fulfilled.

Table S12: Summary of findings table for studies examining the association between *Mycoplasma genitalium* and adverse pregnancy outcomes

Outcomes	Relative effect (95% CI)	Number of participants (studies)	Certainty of evidence (GRADE) <sup>a</sup>
Preterm birth (PTB)	OR 1.91	4573	$\oplus \oplus \bigcirc \bigcirc$
	(1.29 to 2.81)	(5 cohort, 2 case-control studies)	$Low^b$
Spontaneous abortion	OR 1.00	2837	ФФООс
(SAB)	(0.53 to 1.89)	(4 cohort, 2 case-control studies)	Low
Premature rupture of	OR 7.62	871	ФООО
membranes (PROM)	(0.40 to 145.86)	(1 cohort study)	Very low <sup>d</sup>
Low birth weight	OR 1.07	81	ФООО
(LBW)	(0.02 to 10.39)	(1 cohort study)	Very low <sup>d</sup>
Perinatal death (PND)	Not estimated <sup>e</sup>	1597	ФООО
		(1 cohort, 1 case-control study)	Very low <sup>d</sup>

CI, confidence interval; OR, odds ratio.

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

<sup>&</sup>lt;sup>a</sup> Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group grades of evidence

<sup>&</sup>lt;sup>b</sup> Only two studies control for confounding, high risk of selection bias;

<sup>&</sup>lt;sup>c</sup> Only one study controlled for confounding; high risk of selection bias;

<sup>&</sup>lt;sup>d</sup> No study controlled for confounding, imprecise estimates owing to small number of studies;

<sup>&</sup>lt;sup>e</sup> Effect estimates not combined, owing to heterogeneity.

Figure S1: Flow chart of identified and selected studies for inclusion

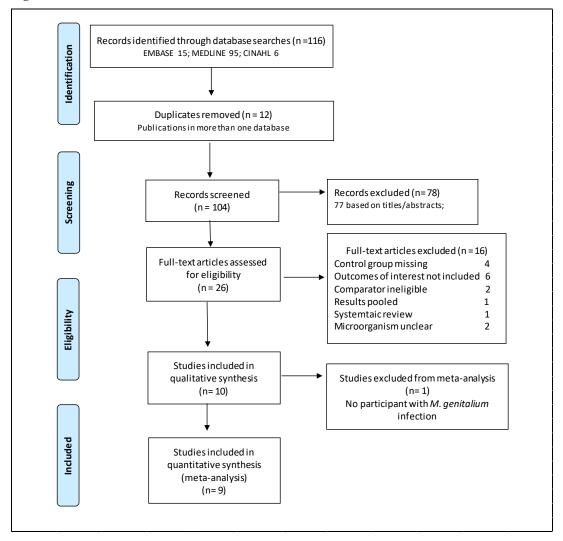
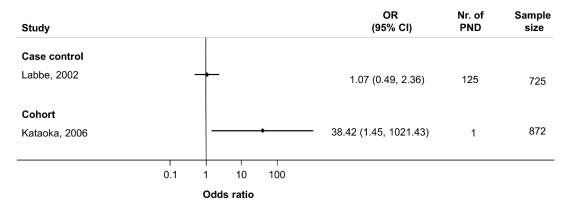


Figure S2: Forest plot of unadjusted effect sizes for association between *M. genitalium* during pregnancy and perinatal death



 $I^2 = 77\%$ 

Abbreviations: CI, confidence interval; OR, odds ratio; PND, perinatal death

Notes: For Kataoka et al., there were no *M. genitalium*-infected women who experienced perinatal death. The odds ratio is calculated by adding 0.5 to each cell in the 2x2 table. The sample size is the number of women, excluding the continuity correction.

Codebook S1, study and population characteristics, appended Codebook S2, Mycoplasma genitalium variables, appended