Adverse pregnancy and neonatal outcomes associated with *Neisseria gonorrhoeae:* systematic review and meta-analysis

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Vallely LM, *et al. Sex Transm Infect* 2021; 97:104–111. doi: 10.1136/sextrans-2020-054653

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Figure S1: Flow chart of identified and included studies

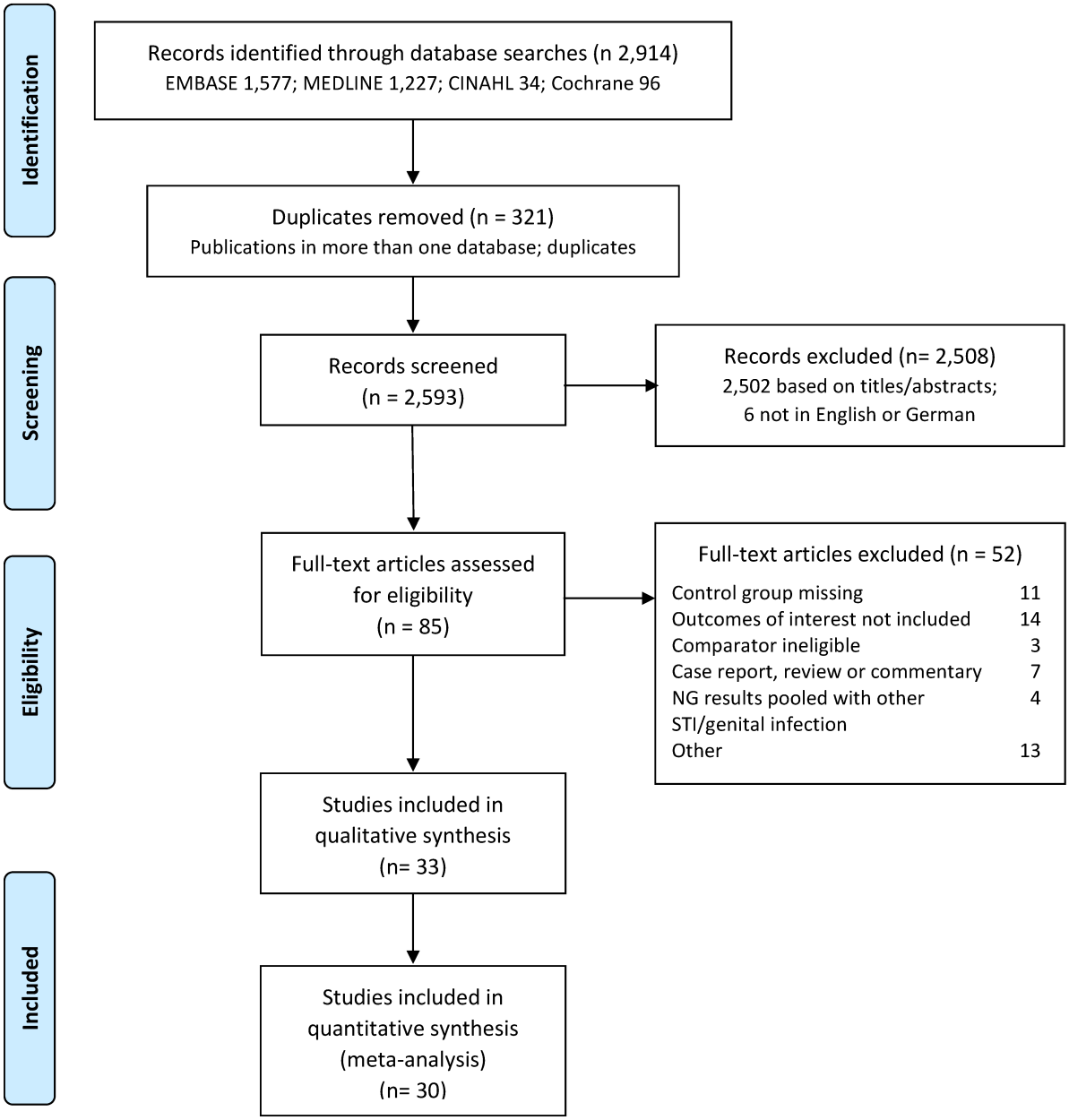

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Figure S2: Funnel plot for studies reporting on the outcome preterm birth

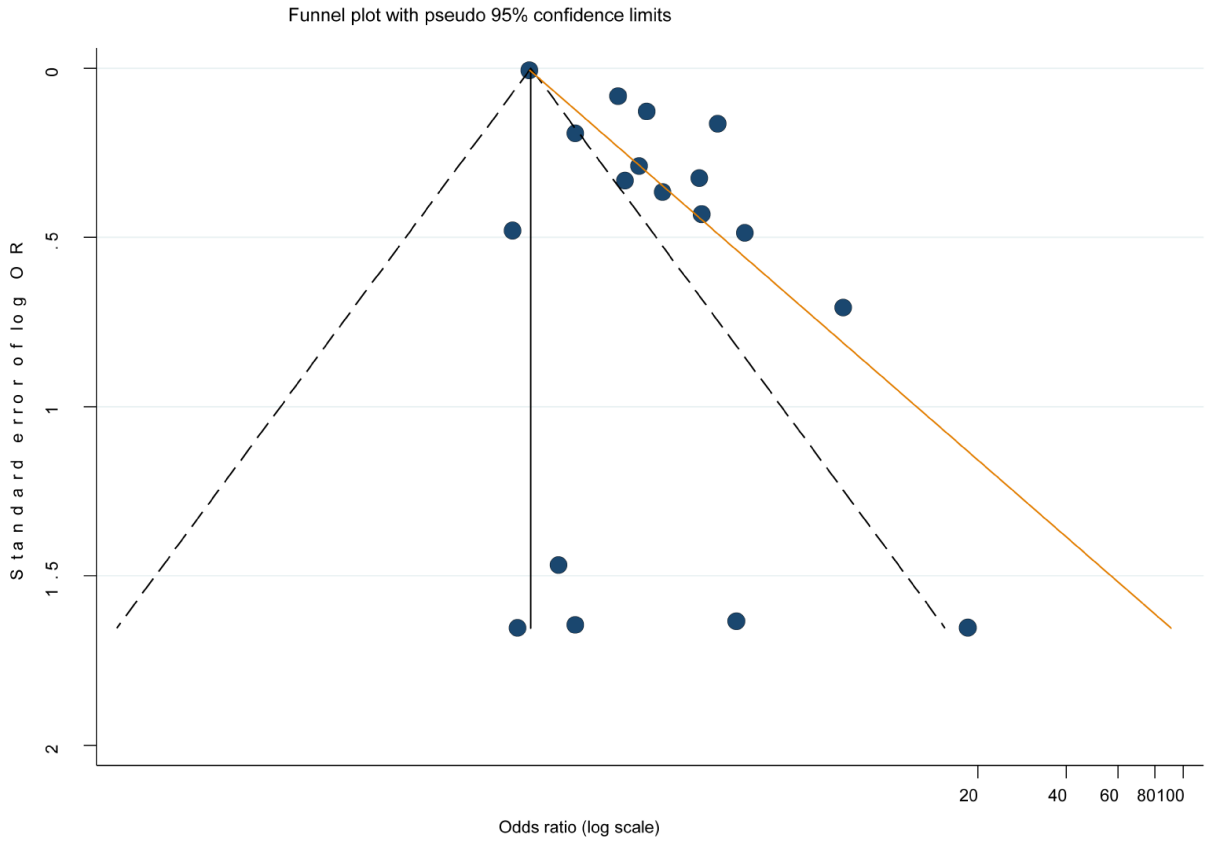

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Figure S3: Unadjusted effect sizes for association between *Neisseria gonorrhoeae* during pregnancy and preterm birth by country income group (random effects model)

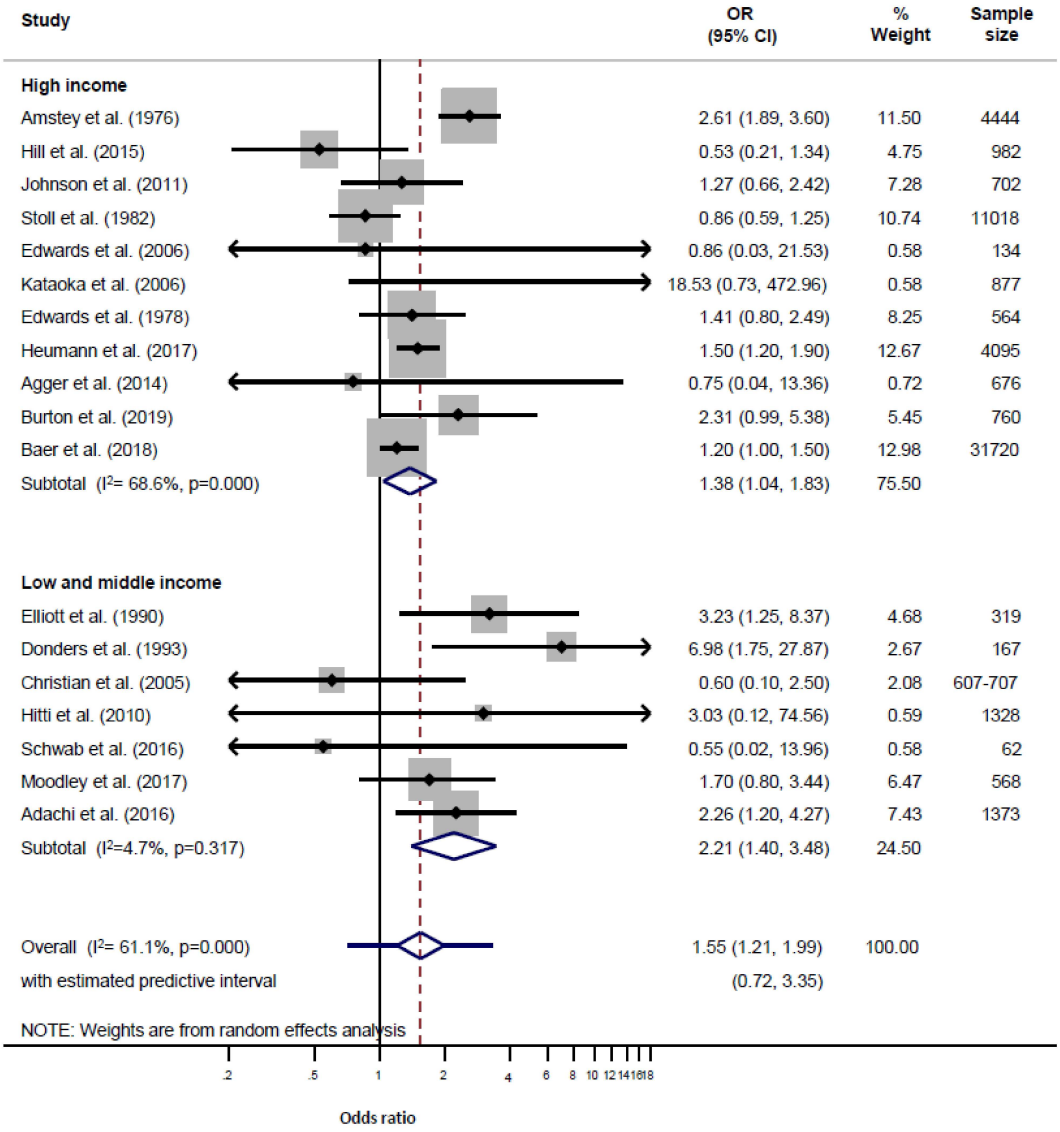

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Figure S4: Adjusted effect sizes for association between *Neisseria gonorrhoeae* during pregnancy and preterm birth by country income group (random effects model)

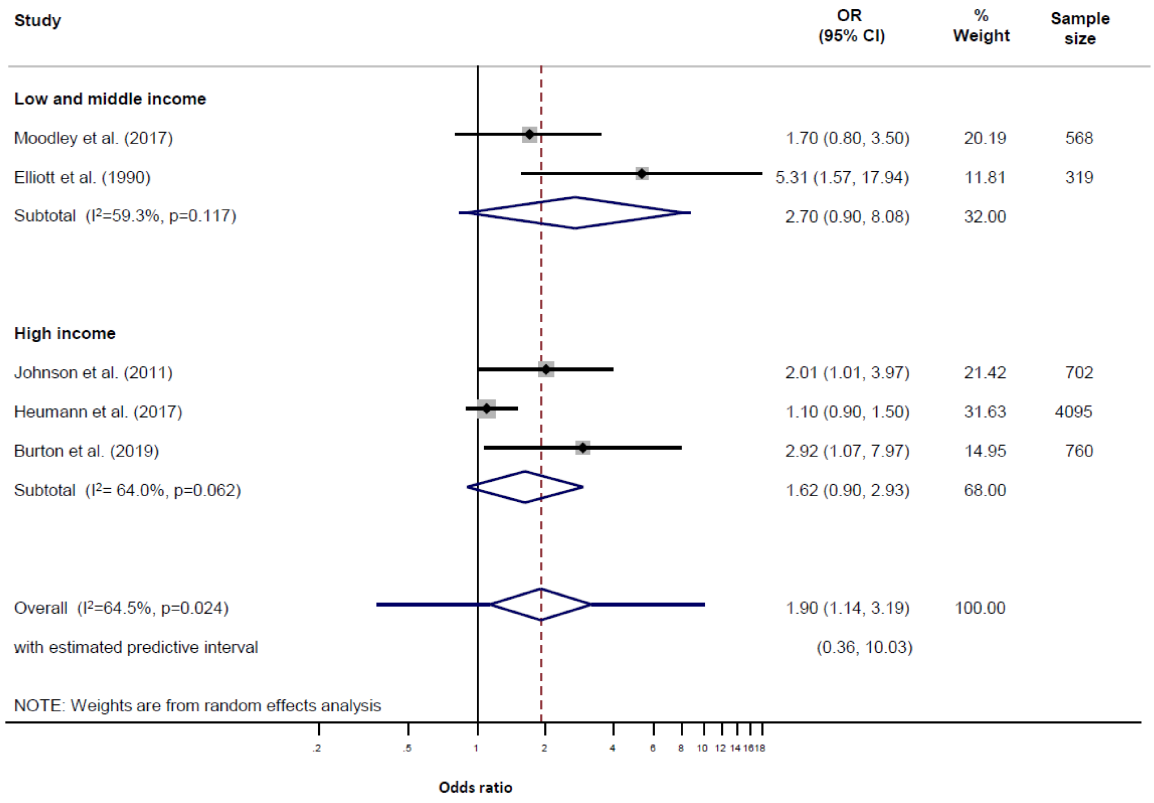

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Figure S5: Unadjusted effect sizes for association between *Neisseria gonorrhoeae* during pregnancy and spontaneous abortion (random effects model)

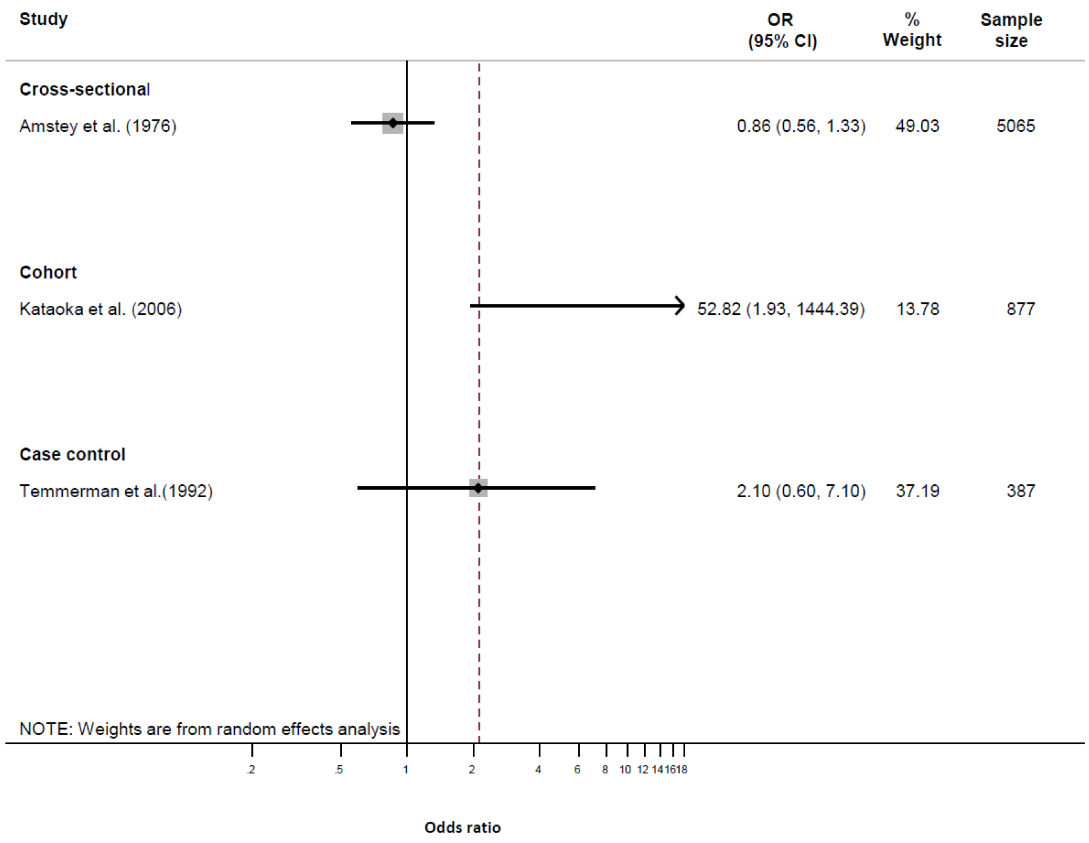

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Figure S6: Unadjusted effect sizes for association between *Neisseria gonorrhoeae* during pregnancy and premature rupture of membranes (random effects model)

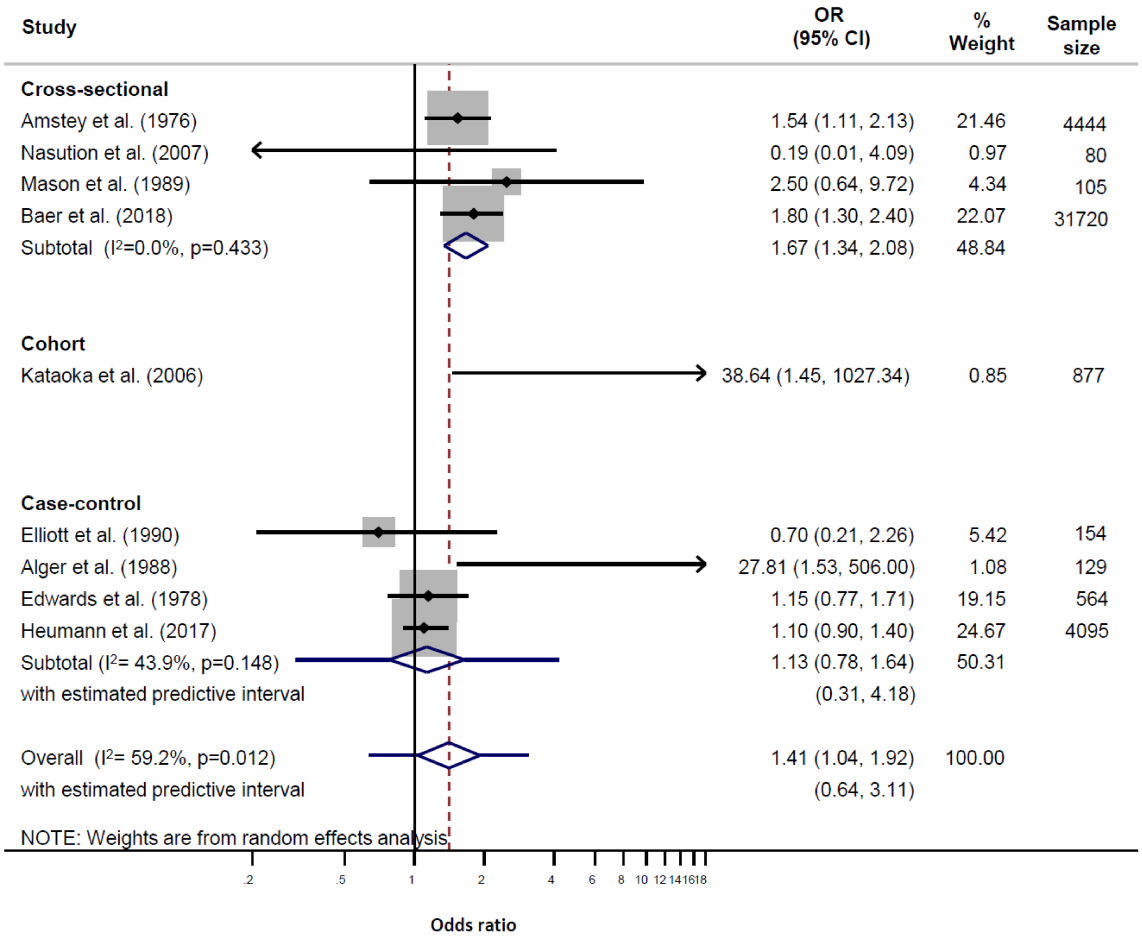

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Figure S7: Unadjusted effect sizes for association between *Neisseria gonorrhoeae* during pregnancy and perinatal mortality (random effects model)

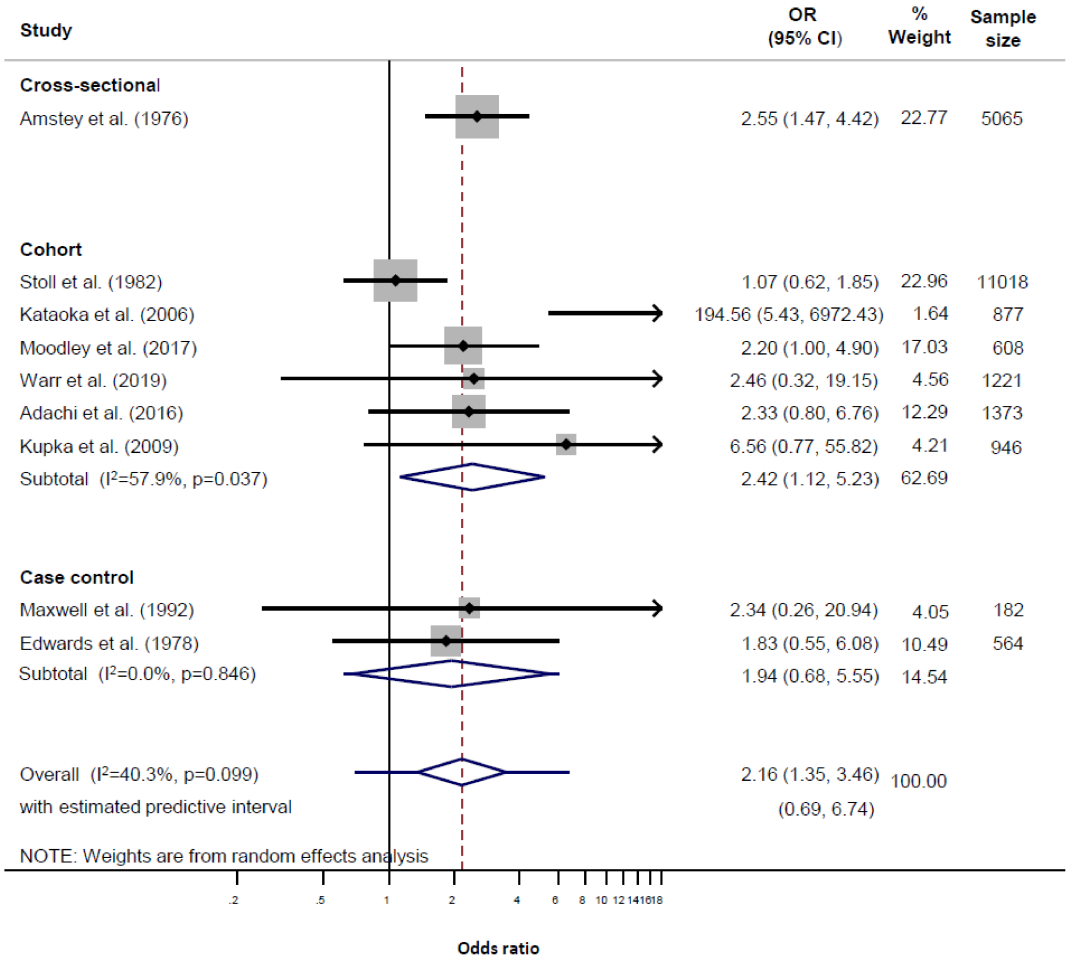

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Figure S8: Unadjusted effect sizes for association between *Neisseria gonorrhoeae* during pregnancy and low birth weight (random effects model)

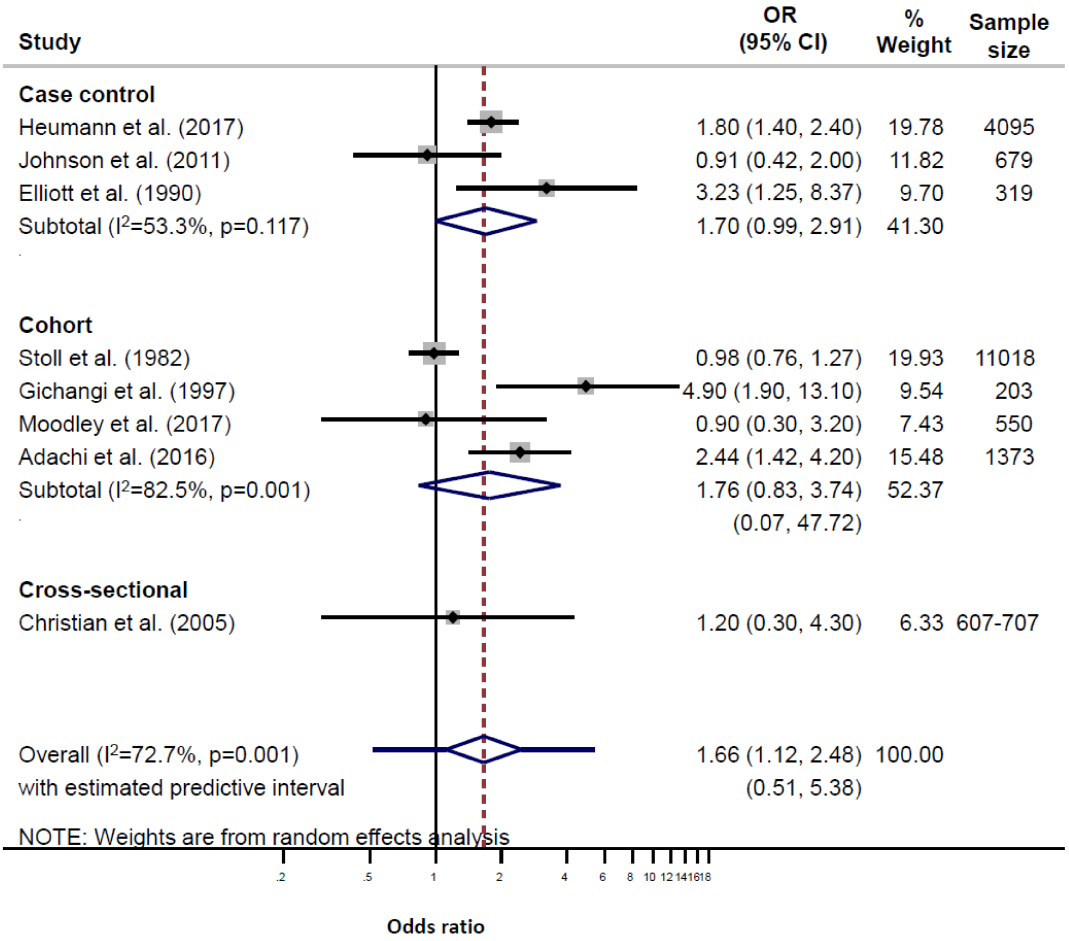

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Figure S9: Adjusted effect sizes for association between *Neisseria gonorrhoeae* during pregnancy and low birth weight (random effects model)

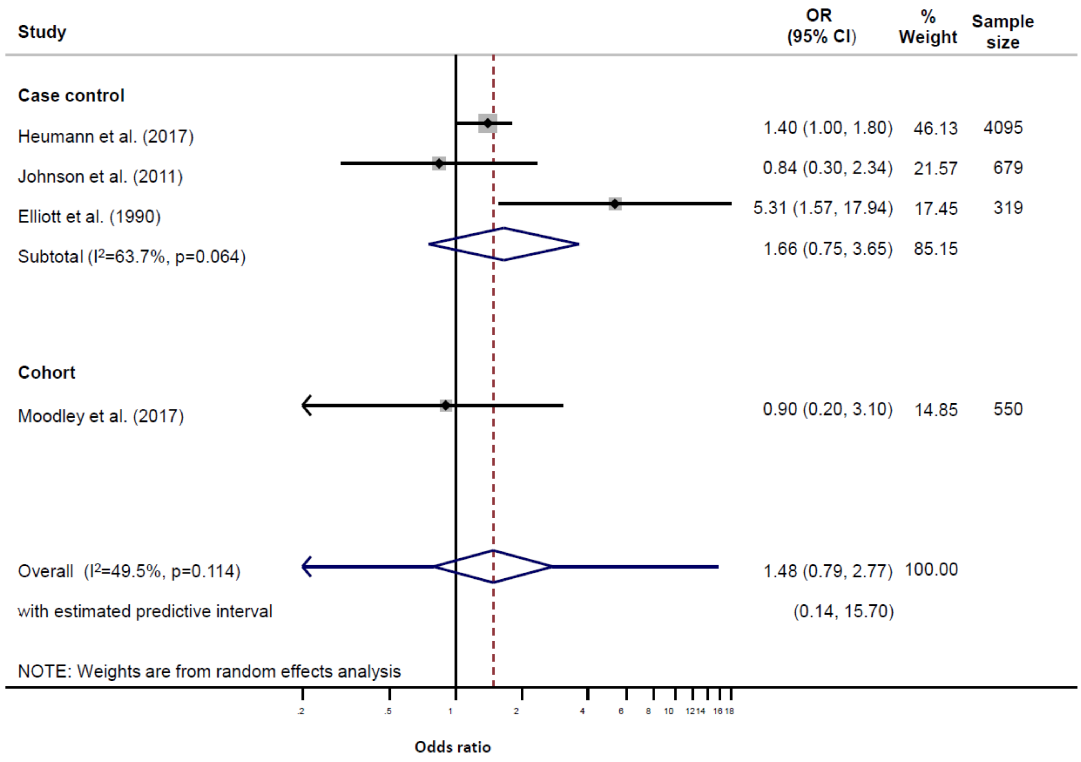

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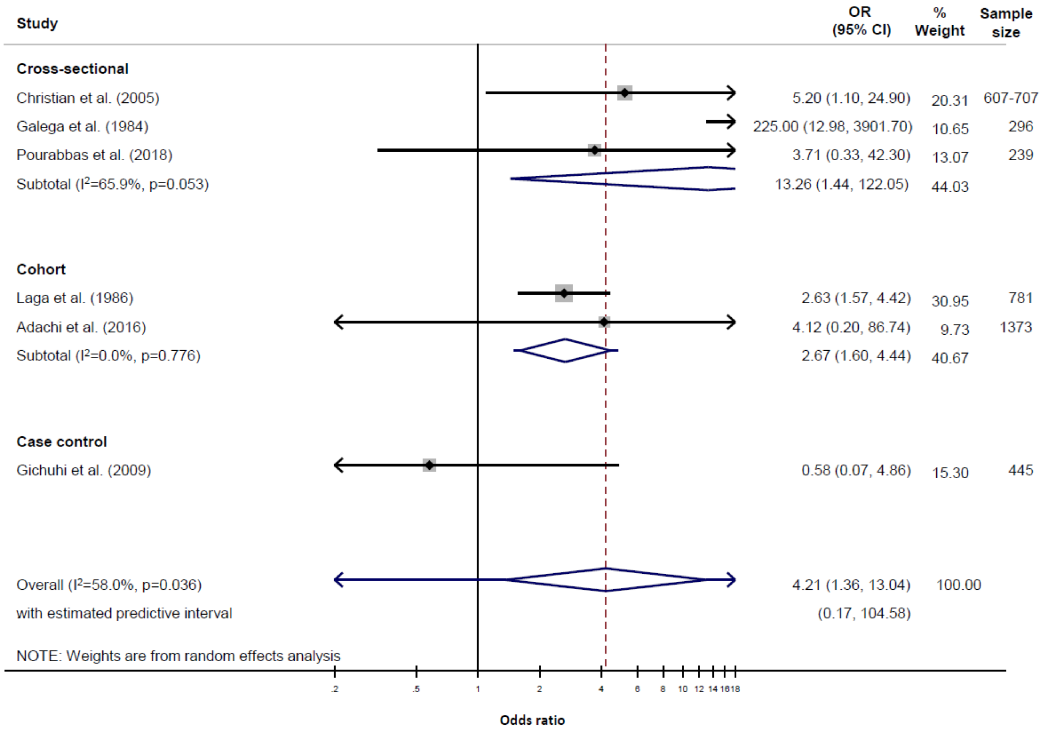
Figure S10: Unadjusted effect sizes for association between *Neisseria gonorrhoeae* during pregnancy and ophthalmia neonatorum (random effects model)



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Text File S1: Search strategy

1. Terms for population	"pregnancy" or "prenatal" or "antenatal"
2. Terms for exposure	"*Neisseria gonorrhoeae"* or "gonorrhoeae" or "gonorrhoea"
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 death" or "neonatal mortality" or "neonatal morbidity" or "neonatal death" or "fetal death" or "miscarriage" or "spontaneous abortion" or "ophthalmia neonatorum" or "chorioamnionitis"
4. Search = #1 + # 2 + # 3	

Free text terms in the search strategy will use truncated and wildcard forms e.g. pregn, gono**

The "explode" function was applied to each MeSH heading.

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Text File S2: Exclusion criteria at first stage

1. Any article in which the title mentions the following without reference to pregnancy, sexually transmitted infections or *N. gonorrhoeae* was excluded in the first stage of the screening process:

Title contains

- Sexual assault
- Algorithm
- Infertility
- Contraception/ Family planning
- Ectopic/tubal
- UTI in women
- Gonococcal arthritis
- Gynecology/gynaecology
- Induced abortion
- Pelvic inflammatory disease
- Syphilis (only)
- Trachomatis (only)
- Chlamydia (only)
- Treatment guidelines/ treatment schedules
- Anti-retroviral therapy
- Tetanus
- Sexual health
- Child sex abuse
- Polio

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

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Table S1: Preferred reporting items for systematic review and meta-analysis (PRISMA)

Section/topic	#	Checklist item	Page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2,3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4,5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	4
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	4
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5,6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6,7
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6,7
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	7,8
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	8
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	9,10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	9,10
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	10

Table S2: Descriptive tables: Study design, cohort studies (n=14)

First author, publication year, location of study	Assessment of Gestational age	Timing of specimen collection	Specimen type; collection method	Laboratory test	Total number enrolled	Outcomes	Definition Provided
Adachi, 2016 Brazil, South Africa, Argentina, USA	NR/unclear	Intrapartum or postpartum	Urine	NAAT	1373	PTB LBW PM ON	32-36 weeks <2500g Not defined [a]
Agger, 2014 USA	NR/unclear	1st or 2nd trimester	Endocervical swab; clinician collected	NAAT	676	PTB	<37 weeks
Charles, 1970 USA	NR/unclear	NR/unclear	Endocervical swab; clinician collected	Culture	2160	PROM ON	Not defined [a]
Donders, 1993 South Africa	NR/unclear	NR/unclear	Endocervical swab; clinician collected	Culture	167	PTB	<37 weeks
Edwards, 2006 USA	NR/unclear	NR/unclear	Endocervical swab; clinician collected	NAAT	134	PTB	<37 weeks
Gichangi, 1997 Kenya	LMP	Postpartum	Endocervical swab; clinician collected	Culture	203	LBW	<2500g
Hill, 2015 USA	NR/unclear	1st, 2nd or 3rd trimester	NR/unclear	NAAT	1120	PTB PROM	Not defined Not defined
Kataoka, 2006 Japan	US/LMP	1st trimester	Vaginal swab; clinician collected	NAAT	877	PTB SA PROM PM	<34 weeks Not defined Not defined Not defined

First author, publication year, location of study	Assessment of Gestational age	Timing of specimen collection	Specimen type; collection method	Laboratory test	Total number enrolled	Outcomes	Definition Provided
Kupka, 2009 Tanzania	LMP	1st, 2nd and 3rd trimester	Endocervical swab; vaginal swab/clinician collected	NR	1017	PM	≥28 weeks[a]
Laga, 1986 Kenya	Newborn assessment	Postpartum	Endocervical swab; clinician collected	Culture	781	ON	[b]
Moodley, 2017 South Africa	US/FH/LMP	1st, 2nd and 3rd trimester and postpartum[c]	NR/unclear	NAAT	615	PTB LBW PM	<37 weeks <2500 g ≥21 weeks
Schwab, 2015 Indonesia	LMP	2nd trimester	Vaginal swab; NR/unclear	NAAT	62	PTB	<37 weeks
Stoll, 1982 USA	NR/Unclear	1st, 2nd or 3rd trimester	Endocervical swab; clinician collected	Culture	11018	PTB LBW PM	<35 weeks ≤2500 g Not defined
Warr, 2019 Kenya	US/FH/LMP	2nd and 3rd trimester and postpartum	Vaginal swab, self-collected	NAAT	1221	PM^	≥20 weeks <28 days

Abbreviations: FH, fundal height; LMP, last menstrual period; LBW, low birth weight; NAAT, nucleic acid amplification tests; NN, neonatal; NR, not reported; ON, ophthalmia neonatorum; PROM, premature rupture of membranes; PTB, preterm birth; SA, spontaneous abortion; US, ultrasound; [a] Data for fresh stillbirths (without signs or symptoms of skin disintegration or maceration) included in meta-analysis; [b] assumes standard definition of acute, mucopurulent infection occurring in the first 4 weeks of life; [c] the trimester of swab collection is not clear from the study; postpartum swabs were taken at 14 weeks postpartum. ^ Includes infants who died between 1-27 days of age.

Table S3: Descriptive tables: Study design, case control studies (n=11)

First author, publication year, study location	Assessment of Gestational age	Timing of specimen collection	Specimen type; collection method	Laboratory test	Total number enrolled	Outcomes	Definition provided
Alger, 1988 USA	US/FH/LMP	2nd or 3rd trimester	Endocervical swab; clinician collected	Culture	136	PROM	>20 up to 37 weeks
Burton, 2019 Australia	NR/unclear	1st, 2nd & 3rd trimester and postpartum	Urine collection, vaginal swab; NR/unclear	NAAT & culture	760	PTB	<37 weeks
Choi, 2012 South Korea	NR/unclear	NR /unclear	Vaginal swab; clinician collected	NAAT	217	PTB	Not defined
Edwards, 1978 USA	NR/unclear	NR/unclear	NR/unclear; NR/unclear	Culture	564	PTB PROM PM	Not defined Not defined Not defined
Elliott, 1990 Kenya	Newborn assessment	Postpartum	Endocervical swab; clinician collected	Culture	341	PTB PROM LBW	<37 weeks RoM before onset labour ≤2500 g
Gichuhi, 2009 Kenya	NR/unclear	3rd trimester	Endocervical swab; clinician collected	NAAT	510	ON	[a]
Heumann, 2017 USA	US	NR/unclear	NR/unclear; NR/unclear	NR/unclear	4095	PTB PROM LBW	<37 weeks ≥12 hours before labour <2500 g
Hitti, 2010 Peru	US/LMP/ newborn assessment	Postpartum	Endocervical swab; clinician collected	NAAT	1328	PTB	20-36 weeks
Johnson, 2011 USA	Newborn assessment	NR/unclear	NR/unclear; clinician collected	Culture	730	PTB LBW	<37 weeks <2500 g

First author, publication year, study location	Assessment of Gestational age	Timing of specimen collection	Specimen type; collection method	Laboratory test	Total number enrolled	Outcomes	Definition provided
Maxwell, 1992 USA	US/LMP	2nd or 3rd trimester	Endocervical swab; clinician collected	Culture	182	PROM PM	PROM 26-33 weeks Not defined
Temmerman, 1992 Kenya	NR/unclear	1st, 2nd or 3rd trimester	Endocervical swab, vaginal swab; clinician collected	Culture	390	SA	<20 weeks

Abbreviations: FH, fundal height; LMP, last menstrual period LBW, Low Birth Weight; NAAT, nucleic acid amplification test; NN, neonatal; NR, not reported; ON, ophthalmia neonatorum; PROM, premature rupture of membranes; PTB, Preterm birth; SA, spontaneous abortion; US, ultrasound; [a] assumes standard definition of acute, mucopurulent infection occurring in the first 4 weeks of life.

Table S4: Descriptive tables: Study design, cross sectional studies (n=8)

First author, publication year, location of study	Assessment of Gestational age	Timing of specimen collection	Specimen type; collection method	Laboratory test	Total number enrolled	Outcomes	Definition provided
Amstey, 1976 USA	NR/unclear	1st or 3rd trimester or intrapartum	Endocervical swab; clinician collected	Culture	5065	PTB PROM SA PM	Not defined RoM before onset labour Not defined Not defined
Baer, 2019 USA	NR/unclear	2nd or 3rd trimester	NR/unclear; NR/unclear	NR/Unclear	31,720	PTB PROM	<37 weeks <37 weeks
Christian, 2005 Nepal	LMP	Postpartum	Urine; self-collected	NAAT	709	PTB LBW ON	<37 weeks <2500g [a]
Galega, 1984 Cameroon	NR/unclear	Intrapartum	Vaginal swab; NR/unclear	Culture	296	ON	[a]
Mann, 2010 USA	NR/unclear	NR/unclear	NR/unclear; NR/unclear	NR/unclear	86654	PTB	<37 weeks
Mason, 1989 Zimbabwe	NR/unclear	Intrapartum	Endocervical swab; clinician collected	Culture	214	PROM	RoM 12 hours before onset labour
Nasution, 2007 Malaysia	NR/unclear	Intrapartum and postpartum	Vaginal swab, placental swab & blood; clinician collected	NAAT and culture	180	PTB PROM	<37 weeks <37 weeks
Pourabbas, 2018 Iran	NR/unclear	3rd trimester	Endocervical swab; clinician collected	NAAT	239	ON	[a]

Abbreviations: LBW, low birth weight; NAAT, nucleic acid amplification tests; NN, neonatal; NR, not reported; ON, ophthalmia neonatorum; PM, perinatal mortality (neonatal death and/or stillbirth); PROM, premature rupture of membranes; PTB, preterm birth; RoM, rupture of membranes; SA, spontaneous abortion; [a] assumes standard definition of acute, mucopurulent infection occurring in the first 4 weeks of life.

Table S5. Studies or data not included in meta-analysis

First author, publication year	Outcomes not included	Reason not included in meta-analysis	NG+/ outcome+	NG-/ outcome+	NG+/ outcome-	NG-/ outcome-
Charles, 1970	PROM	NG+/PROM-=m; NG-/PROM-=m	1	m	148	m
	ON	NG+/ON+=0; NG-/ON+=0	0	0	158	2002
Choi, 2012	PTB	NG+/PTB+=0; NG+/PTB-=0	0	100	0	117
Hill, 2015[a]	PROM	NG+/PROM+=0; NG+/PROM-=0	0	37	0	896
Mann, 2010	PTB	NG+/PTB-=m; NG-/PTB-=m	749	7182	m	m
Maxwell, 1992[b]	PROM	NG+/PROM-=m; NG-/PROM-=m	11	171	m	m
Nasution, 2007[c]	PTB	NG+/PTB+=0; NG+/PTB-=0	0	30	0	30

[a] Data for PTB included in meta-analysis; [b] data for NN death included in meta-analysis; [c] data for PROM included in meta-analysis.

Abbreviations: m, missing; ON, ophthalmia neonatorum; PROM, premature rupture of membranes; PTB, preterm birth; +, positive; -, negative

Table S6: Study setting and socio-demographics, cohort studies (n=14)

First author, year of publication	Study setting	Urban /rural location	Age in years (range/mean/ median)	Ethnicity	Smokers included/ (%)	Multiple pregnancies
Adachi, 2016	NR/ Unclear	NR/ Unclear	NR/26.9/26.0	Mixed	Yes/ 32.1%	NR/ unclear
Agger, 2014	Health Facility	Mixed	NR/NR/NR	Mixed	NR/ unclear	Yes
Charles, 1970	Health Facility	NR/ Unclear	14-39/22.3/NR	Black	NR/ unclear	NR/ unclear
Donders, 1993	Health Facility	Urban	NR/26.8/NR	Black	NR/ unclear	No
Edwards, 2006	Health Facility	Urban	NR/NR/NR	Mixed	Yes/ 15.7%	No
Gichangi, 1997	Health Facility	Urban	NR/NR/NR	Black	NR/ unclear	NR/ unclear
Hill, 2015	Health Facility	Urban	NR/NR/NR	Mixed	NR/ unclear	NR/ unclear
Kataoka, 2006	Health Facility	Urban	NR/NR/NR	Asian	NR/ unclear	No
Kupka, 2009	Health Facility	Urban	NR/24.7/NR	NR/ unclear	NR/ unclear	No
Laga, 1986	Health Facility	Urban	NR/NR/NR	NR/ unclear	NR/ unclear	Yes
Moodley, 2017	Health Facility	Mixed	NR/25.4/NR	NR/ unclear	NR/ unclear	NR/ unclear
Schwab, 2015	Health Facility	Rural	17-42/26.6/NR	NR/ unclear	NR/ unclear	NR/ unclear
Stoll, 1982	Health Facility	Urban	NR/NR/NR	NR/ unclear	NR/ unclear	NR/ unclear
Warr, 2019	Health Facility	Rural	19-27/22/NR	NR/ unclear	NR/ unclear	No

Abbreviations: NR, not reported

Table S7: Study setting and socio-demographics, case control studies (n=11)

First author, year of publication	Study setting	Urban /rural location	Age in years (range/mean/ median)	Ethnicity	Smokers included/ (%)	Multiple pregnancies
Alger, 1988	Health Facility	Urban	NR/NR/NR	Mixed	NR/ unclear	NR/ unclear
Burton, 2019	Health Facility	Urban	NR/NR/NR	Mixed	Yes/ 57.1%	No
Choi, 2012	Health Facility	Urban	NR/NR/NR	Asian	NR/ unclear	NR/ unclear
Edwards, 1978	Health Facility	NR/ Unclear	14-34/19.8/NR	Mixed	NR/ unclear	NR/ unclear
Elliott, 1990	Health Facility	Urban	NR/NR/NR	Black	NR/ unclear	No
Gichuhi, 2009	Health Facility	Urban	NR/NR/25	NR/ unclear	NR/ unclear	NR/ unclear
Heumann, 2017	NR/ unclear	NR/ Unclear	NR/NR/NR	Mixed	Yes/ 14.3%	No
Hitti, 2010	Health Facility	Urban	NR/NR/NR	NR/ unclear	Yes/ 6.5%	Yes
Johnson, 2011	Health Facility	Urban	13-24/NR/NR	Mixed	Yes/ unclear	No
Maxwell, 1992	Health Facility	Urban	NR/NR/NR	Mixed	NR/ unclear	No
Temmerman, 1992	Health Facility	Urban	NR/NR/NR	Black	NR/ unclear	NR/ unclear

Abbreviations: NR, not reported

Table S8: Study setting and socio-demographics, cross-sectional studies (n=8)

First author, year of publication	Study setting	Urban /rural location	Age in years (range/mean/ median)	Ethnicity	Smokers included/ (%)	Multiple pregnancies
Amstey, 1976	Health Facility	NR/ unclear	NR/NR/NR	NR/ unclear	NR/ unclear	NR/ unclear
Baer, 2019	NR/Unclear	NR/ unclear	NR/NR/NR	Mixed	Yes/ 9.3%	No
Christian, 2005	Community	Rural	NR/NR/NR	Asian	Yes/ unclear	NR/ unclear
Galega, 1984	Health Facility	Urban	15-39/NR/NR	Black	NR/ unclear	Yes
Mann, 2010	NR/unclear	NR/ unclear	NR/NR/NR	Mixed	Yes/ 19.9%	No
Mason, 1989	Health Facility	Urban	NR/NR/NR	Black	NR/ unclear	NR/ unclear
Nasution, 2007	Health Facility	NR/ unclear	24-38/NR/NR	Asian	NR/ unclear	NR/ unclear
Pourabbas, 2018	Health Facility	NR/ unclear	18-45/27.7/NR	NR/ unclear	NR/ unclear	NR/ unclear

Abbreviations: NR, Not reported

Table S9: Treatment provided *for Neisseria gonorrhoeae* and other STIs included in study, cohort studies (n=14)

First author, year of publication	Treatment provided for NG infection	Time provided	Other STI in study population[a]
Adachi, 2016	Unclear	NR/Unclear	CT 249/1373 (18.1%) HIV 1373/1373 (100.0%) Syphilis 129/1373 (9.4%)
Agger, 2014	Some positive women	NR/Unclear	CT 33/676 (4.9%) MG 9/676 (1.3%)
Charles, 1970	Some positive women	NR/Unclear	Syphilis 4/158 (2.5%)
Donders, 1993	Some positive women	NR/Unclear	CT 22/167 (13.2%) Syphilis 15/167(9.0%)
Edwards, 2006	Unclear	NR/Unclear	BV 18/134 (13.4%) CT 10/134 (7.5%) MG 27/134 (20.2%) Syphilis 0/134 (0.0%) TV 10/134 (7.5%)
Gichangi, 1997	Some positive women	2nd, 3rd trimester	HIV 17/209 (8.1%) Syphilis 9/207 (4.3%)
Hill, 2015	Unclear	NR/unclear	CT 160/1120 (14.2%)
Kataoka, 2006	Some positive women	1st, 2nd trimester	CT 28/877 (3.2%) MG 7/877 (0.8%)
Kupka, 2009	Unclear	NR/Unclear	HIV 1017/1017 (100%) Syphilis 155/947 (16.4%)
Laga, 1986	All positive women	Postpartum	CT 201/938 (21%)
Moodley, 2017	All positive women	Timing unclear but symptomatic women, same day; asymptomatic at next visit	CT 115/615 (18.7%) HIV 230/615 (37.4%) TV 91/615 (14.8%)
Schwab, 2015	Unclear	NR/unclear	BV 10/62 (16.1%) CT 1/62 (1.6%)
Stoll, 1982	Some positive women	NR/unclear	NR
Warr, 2019	All positive women	2nd, 3rd trimester or postpartum	BV 271/1221 (22.2%) CT 65/1221 (5.3%) HIV 0/1221 (0.0%) Syphilis 10/1221(0.8%) TV 79/1221 (6.5%)

Abbreviations: BV, bacterial vaginosis; CT, *Chlamydia trachomatis*; HIV, human immunodeficiency virus; MG, *Mycoplasma genitalium*; NG, *Neisseria gonorrhoeae*; NR, not reported; TV, *Trichomonas vaginalis*.

[a] Data were extracted for BV, CT, HIV, MG, Syphilis and TV only

Table S10: Treatment provided *for Neisseria gonorrhoeae* and other STIs included in study, case control studies (n=11)

First author, year of publication	Treatment provided for NG infection	Time provided	Other STI in study population[a]
Alger, 1988	All positive women	2nd , 3rd trimester	CT 36/136 (26.5%)
Burton, 2019	Some positive women	1st, 2nd, 3rd trimester and postpartum	CT 40/760 (5.3%) TV 93/760 (12.2%) Syphilis 3/760 (0.4%)
Choi, 2012[b]	Unclear	NR/Unclear	CT 3/126 (2.4%) MG 0/126 (0.0%) TV 0/126 (0.0%)
Edwards, 1978	Some positive women	1st, 2nd, 3rd trimester	NR
Elliott, 1990	Unclear	NR/Unclear	BV 46/276 (16.6%) CT 42 /284 (14.8%) HIV 9/194 (4.6%) Syphilis 13/290 (4.5%)
Gichuhi, 2009	All positive women	3rd trimester	BV 164/427 (38.4%) CT 20/472 (4.2%) HIV 510/510 (100%) Syphilis 3/173 (1.7%) TV 77/479 (16.1%)
Heumann, 2017	Unclear	NR/Unclear	CT 434/4095 (10.6%) Syphilis 12/4095 (0.3%)
Hitti, 2010	Some positive women	NR/Unclear	CT 98/1328 (7.4%) MG 41/1328 (3.1%) TV 33/1328 (2.5%)
Johnson, 2011	All positive women	NR/Unclear	BV 220/730 (30.1%) CT 101/730 (13.8%) HIV 1/730 (0.1%) Syphilis 6/730 (0.8%) TV 109/730 (14.9%)
Maxwell, 1992	All positive women	2nd, 3rd trimester	CT 0/182 (0.0%)
Temmerman, 1992	Some positive women	NR/Unclear	HIV 40/390 (10.3%) Syphilis 17/386 (4.4%)

Abbreviations: BV, bacterial vaginosis; CT, *Chlamydia trachomatis*; HIV, human immunodeficiency virus; MG, *Mycoplasma genitalium*; NG, *Neisseria gonorrhoeae*; NR, not reported; TV, *Trichomonas vaginalis*

[a] Data were extracted for BV, CT, HIV, MG, Syphilis and TV only

[b] Control group was not tested for STI and not included

Table S11: Treatment provided *for Neisseria gonorrhoeae* and other STIs included in study, cross-sectional studies (n=8)

First author, year of publication	Treatment provided for NG infection	Time provided	Other STI in study population[a]
Amstey, 1976	Some positive women	NR/Unclear	NR
Baer, 2019	Unclear	NR/Unclear	CT 13633/15860 (86.0%) Syphilis 1180/15860 (7.4%)
Christian, 2005	Some positive women	Postpartum	CT 10/1014 (1.0%)
Galega, 1984	All positive women	Postpartum	NR
Mann, 2010	Unclear	NR/Unclear	CT 650/108346 (0.6%) TV 3034/108346 (2.8%)
Mason, 1989	Unclear	NR/Unclear	CT 17/188 (9.0%) TV 39/214 (18.2%)
Nasution, 2007	Unclear	NR/Unclear	CT 13/180 (7.2%)
Pourabbas, 2018	No treatment	NA	CT 37/239 (15.5%)

Abbreviations: CT, *Chlamydia trachomatis*; HIV, human immunodeficiency virus; MG, *Mycoplasma genitalium*; NA, not applicable; NR, not reported; TV, *Trichomonas vaginalis*.

[a] Data were extracted for BV, CT, HIV, MG, Syphilis and TV only

Table S12: Risk of bias assessment, cohort studies (n=14)

	Adachi 2016	Agger 2014	Charles 1970	Donders 1993	Edwards 2006	Gichangi 1997	Hill 2015	Kataoka 2006
The method of allocation to intervention group was unrelated to potential confounding factors	NA	NA	NA	NA	NA	NA	NA	NA
Attempts made within design or analysis to balance the both groups for potential confounders.	Yes	Yes	No	Yes	Yes	Yes	No	Yes
The groups were comparable at baseline, including all major confounding factors.	No	No	Unclear	Unclear	No	Unclear	No	No
Based on above answers, was selection bias present?	High	High	Unclear	High	High	Unclear	High	High
If so, what is the likely direction of its effect?	↑ AO	Unclear	Unclear	↑ AO & STI	Unclear	Unclear	↑ AO & STI	Unclear
The comparison groups received the same care and support apart from the exposure(s) studied.	Yes	Unclear	No	No	Unclear	Yes	Unclear	Unclear
Participants receiving care and support were kept 'blind' to intervention allocation.	NA	NA	NA	NA	NA	NA	NA	NA
Individuals administering care and support were kept 'blind' to intervention allocation.	NA	NA	NA	NA	NA	NA	NA	NA
Based on above answers, was performance bias present?	Low	Unclear	High	High	Unclear	Low	Unclear	Unclear
If so, what is the likely direction of its effect?	NA	Unclear	Unclear	Unclear	Unclear	NA	Unclear	Unclear
All groups followed up for an equal length of time?	Yes	Yes	No	No	Yes	Yes	Unclear	Yes
Number of participants did not complete the intervention in each group?	NA	NA	NA	NA	NA	NA	NA	NA
The groups were comparable for intervention completion.	NA	NA	NA	NA	NA	NA	NA	NA
For how many participants were no outcome data available?	311/1684 (18.5%)	107/783 (13.7%)	0/2160 (0.0%)	75/256 (29.3%)	3/137 (2.2%)	117/320 (36.6%)	602/1722 (35.0%)	148/1040 (14.2%)
Were groups comparable for outcome data?	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

	Adachi 2016	**Agger 2014**	**Charles 1970**	**Donders 1993**	**Edwards 2006**	**Gichangi 1997**	**Hill 2015**	**Kataoka 2006**
Based on above answers, was attrition bias present?	Low	Unclear	Unclear	High	Low	High	High	Unclear
If so, what is the likely direction of its effect?	NA	Unclear	Unclear	↑ AO & STI	NA	Unclear	↑ AO & STI	Unclear
The study had an appropriate length of follow-up.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
The study used a precise definition of outcome.	Yes	Yes	No	Yes	Yes	Yes	No	No
A valid, reliable method used to determine the outcome?	Yes	Unclear	No	Unclear	Yes	Yes	Yes	Yes
Investigators were kept 'blind' to participants' exposure to the intervention.	NA	NA	NA	NA	NA	NA	NA	NA
Investigators were kept 'blind' to other important confounding factors.	NA	NA	NA	NA	NA	NA	NA	NA
Based on above answers, was detection bias present?	Low	Unclear	High	Low	Unclear	Low	Unclear	Low
If so, what is the likely direction of its effect?	NA	Unclear	↑ AO	NA	Unclear	NA	Unclear	NA
Overall assessment of internal validity	++	+	-	-	+	+	+	+
Overall assessment of external validity	++	+	-	-	+	+	++	-

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

Table S12: Risk of bias assessment, cohort studies (n=14), continued

	Kupka 2009	Laga 1986	Moodley 2017	Schwab 2015	Stoll 1982	Warr 2019
The method of allocation to intervention group was unrelated to potential confounding factors	NA	NA	NA	NA	NA	NA
Attempts made within design or analysis to balance the both groups for potential confounders.	Yes	No	Yes	No	No	Yes
The groups were comparable at baseline, including all major confounding factors.	Unclear	Unclear	Unclear	Unclear	Unclear	Yes
Based on above answers, was selection bias present?	Low	High	Low	High	High	Low
If so, what is the likely direction of its effect?	NA	Unclear	NA	Unclear	Unclear	NA
The comparison groups received the same care and support apart from the exposure(s) studied.	Yes	Unclear	Yes	Unclear	No	Yes
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	Unclear	Low	Unclear	High	Low
If so, what is the likely direction of its effect?	Unclear	Unclear	NA	Unclear	↑AO	NA
All groups followed up for an equal length of time?	Yes	No	Yes	No	No	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
For how many participants in were no outcome data available?	71/1017 (7.0%)	232/1013 (22.9%)	36/615 (5.9%)	97/159 (61.0%)	0/11081 (0.0%)	3/211 (0.2%)
Were groups comparable for outcome data?	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Based on above answers, was attrition bias present?	Low	High	Unclear	High	High	Low
If so, what is the likely direction of its effect?	NA	Unclear	Unclear	Unclear	Unclear	NA

	Kupka 2009	**Laga 1986**	**Moodley 2017**	**Schwab 2015**	**Stoll 1982**	**Warr 2019**
The study had an appropriate length of follow-up.	Yes	Yes	Yes	Yes	Yes	Yes
The study used a precise definition of outcome.	Yes	No	Yes	Yes	Yes	Yes
A valid, reliable method used to determine the outcome?	Yes	Yes	Yes	No	Unclear	Yes
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?	No	Unclear	Low	High	Unclear	Low
If so, what is the likely direction of its effect?	NA	Unclear	NA	Unclear	Unclear	NA
Overall assessment of internal validity	+	+	++	-	+	++
Overall assessment of external validity	+	-	+	-	-	+

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

Table S13: Risk of bias assessment, case control studies (n=11)

	Alger 1988	Burton 2019	Choi 2012	Edwards 1978	Elliot 1990	Gichuhi 2009	Heumann 2017	Hitti 2010	Johnson 2011	Maxwell 1992	Temmer-man 1992
Appropriate and clearly focused question.	WC	WC	WC	PA	AA	WC	AA	WC	AA	AA	WC
The cases and controls are taken from comparable populations.	AA	PA	NR	AA	PA	AA	PA	AA	AA	AA	PA
The same exclusion criteria are used for both cases and controls.	AA	WC	NAD	NR	WC	NR	AA	AA	PA	NR	PA
What was the participation rate for each group (cases)?	NR	NA	NR	NA	NR	NR	NA	98.7%	NA	NA	96.4%
What was the participation rate for each group (controls)?	NR	NA	NR	NA	NR	NR	NA	99.9%	NA	NA	97.0%
Both groups are compared to establish their similarities or differences.	NR	WC	PA	NR	WC	NR	NR	WC	WC	NR	NR
Cases are clearly defined and differentiated from controls.	WC	WC	WC	AA	WC	WC	WC	WC	WC	AA	WC
It is clearly established that controls are not cases.	WC	WC	WC	AA	WC	WC	WC	WC	WC	WC	WC
Measures taken to prevent knowledge of primary exposure from influencing case ascertainment.	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Exposure status is measured in a standard, valid and reliable way.	AA	PA	WC	NR	AA	WC	NR	WC	PA	AA	AA
Main potential confounders are accounted for in design/analysis	AA	AA	NAD	AA	AA	AA	AA	AA	WC	NAD	AA
Confidence intervals provided?	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes
Study results internally valid?	+	+	+	+	++	+	+	++	++	-	+
Study results externally valid?	+	-	+	+	+	+	++	+	++	-	+

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

Table S14: Risk of bias assessment, cross-sectional studies (n=8)

	Amstey 1976	Baer 2019	Christian 2005	Galega 1984	Mann 2010	Mason 1989	Nasution 2007	Pourabbas 2018
Source population, source area well described?	NR	++	+	-	+	+	-	+
Is the eligible population or area representative of the source population?	+	++	-	NR	-	+	NR	NR
Do the selected participants or areas represent the eligible population or area?	++	++	-	NR	-	+	NR	NR
Selection of exposure (and comparison) group. How was selection bias minimised?	+	++	+	+	+	NR	-	+
Was the selection of explanatory variables based on a sound theoretical basis?	NR	+	-	-	+	-	-	-
Was the contamination acceptably low?	++	++	++	++	++	++	++	++
How well were likely confounding factors identified and controlled?	-	-	-	-	+	-	-	-
Outcome measures and procedures reliable?	-	NR	+	+	NR	NR	NR	+
Were the outcome measurements complete?	++	NR	-	NR	NR	+	++	++
Were all the important outcomes assessed?	++	+	++	-	+	+	+	+
Was there a similar follow-up time in exposure and comparison groups?	++	NR	+	-	++	+	++	++
Was follow-up time meaningful?	++	++	++	+	++	++	++	++
Was the study sufficiently powered to detect an exposure effect? (if one exists)	NR	++	NR	NR	NR	NR	NR	NR
Were multiple explanatory variables considered in analyses?	-	-	-	-	+	-	-	-
Were the analytical methods appropriate?	+	+	+	+	+	+	-	+
Was the precision of association given or calculable?	++	++	+	+	+	+	+	+
Overall assessment of internal validity	-	+	-	+	+	+	-	+
Overall assessment of external validity	-	++	-	-	-	+	-	-

Abbreviations: ++, yes; +, mostly; -, no; NR, not reported; NA, not applicable; ++, all or most of checklist criteria fulfilled; + some of checklist criteria fulfilled; - few or no checklist criteria fulfilled.

Table S15: Variables adjusted for in multivariable analysis

	Elliott et al 1990	Johnson et al 2011	Moodley et al 2017	Burton et al 2018	Heumann et al 2017
Preterm birth					
Age	X	X	X		
Marital status					X
Parity			X		
History of preterm birth		X		X	
Pregnancy factors	X	X		X	
Socio-economic status			X		
HIV, CT, TV			X		
Number of antenatal visits				X	
Method of gestation assessment				X	
Smoking				X	X
Low birth weight					
Age	X	X	X		
Marital status					X
Parity			X		
History of preterm birth		X			
Pregnancy factors	X	X			
Socio-economic status			X		
HIV, CT, TV			X		
Number of antenatal visits					
Method of gestation assessment					
Smoking					X

Abbreviations: CT, *Chlamydia trachomatis*; HIV, human immunodeficiency virus; TV, *Trichomonas vaginalis*.

Table S16: Summary estimates from fixed effects analysis

Adverse outcome Study design	Number of studies	Summary estimate OR (95% CI)	I^2 (%)
Unadjusted estimates			
Preterm birth			
Case control studies	6	1.55 (1.28-1.88)	0.0
Cross-sectional studies	3	1.48 (1.25-1.76)	88.4
Cohort studies	9	1.20 (0.91-1.57)	60.1
All studies	18	1.45 (1.29-1.63)	61.1
Spontaneous abortion			
Case control studies	1	2.10 (0.60-7.10)	NA
Cross-sectional studies	1	0.86 (0.56-1.33)	NA
Cohort studies	1	52.82 (1.93-1444.39)	NA
All studies	3	1.01 (0.67-1.52)	72.8
Premature rupture of membrane			
Case control studies	4	1.11 (0.92-1.35)	43.9
Cross-sectional studies	4	1.67 (1.34-2.08)	0.0
Cohort studies	1	38.64 (1.45-127.34)	NA
All studies	9	1.33 (1.15-1.54)	59.2
Perinatal mortality			
Case control studies	2	1.94 (0.68-5.55)	0.0
Cross-sectional studies	1	2.55 (1.47-4.42)	NA
Cohort studies	6	1.67 (1.12-2.48)	57.9
All studies	9	1.93 (1.42-2.62)	40.3
Low birth weight			
Case control studies	3	1.75 (1.37-2.24)	53.3
Cross-sectional studies	1	1.20 (0.30-4.30)	NA
Cohort studies	4	1.24 (0.99-1.55)	82.5
All studies	8	1.45 (1.23-1.70)	72.7
Ophthalmia neonatorum			
Case control studies	1	0.58 (0.07-4.83)	NA
Cross-sectional studies	3	9.27 (2.81-30.54)	65.9
Cohort studies	2	2.67 (1.60-4.44)	0.0
All studies	6	2.98 (1.89-4.72)	58.0
Adjusted estimates			
Preterm birth			
Case control studies	4	1.31 (1.04,1.64)	72.3
Cohort studies	1	1.70 (0.81-3.56)	NA
All studies	5	1.34 (1.08-1.67)	64.5
Low birth weight			
Case control studies	3	1.44 (1.10-1.90)	63.7
Cohort studies	1	0.90 (0.23-3.54)	NA
All studies	4	1.42 (1.08-1.86)	49.5

Abbreviations: CI, confidence interval; NA, not applicable