Supplementary Online Content


eMethods. Literature Search Strategies for Primary Literature
eTable 1. Inclusion and Exclusion Criteria
eTable 2. Quality Assessment Criteria

This supplementary material has been provided by the authors to give readers additional information about their work.
Screening
Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:

1     Syphilis/
2     Syphilis, Congenital/
3     syphilis.ti,ab.
4     treponema pallidum.ti,ab.
5     or/1-4
6     Mass screening/
7     screen$.ti,ab.
8     6 or 7
9     5 and 8
10    Syphilis Serodiagnosis/
11    ((nontreponemal or treponemal) adj (test$ or immunoassay$)).ti,ab.
12    venereal disease research laboratory.ti,ab.
13    VDRL.ti,ab.
14    Rapid plasma reagin.ti,ab.
15    Fluorescent treponemal antibody absorbed.ti,ab.
16    Treponema pallidum particle agglutination.ti,ab.
17    or/10-16
18    9 or 17
19    Pregnancy/
20    Pregnancy Trimester, First/
21    Pregnancy Trimester, Second/
22    Pregnancy Trimester, Third/
23    Pregnant women/
24    Prenatal Care/
25    Prenatal Diagnosis/
26    Pregnancy Outcome/
27    Pregnancy Complications, Infectious/
28    Infectious Disease Transmission, Vertical/
29    (pregnan$ or prenatal or pre natal or perinatal or peri natal or antenatal or ante natal or antepartum or ante partum).ti,ab.
Syphilis/
Syphilis, Congenital/
syphilis.ti,ab.
treponema pallidum.ti,ab.
or/1-4
exp Anti-Bacterial Agents/
(antibiotic$ or Penicillin or Benzylpenicillin or Amoxicillin or Ampicillin or Carbenicillin or Sulbenicillin).ti,ab.
6 or 7
Pregnancy/
Pregnancy Trimester, First/
Pregnancy Trimester, Second/
Pregnancy Trimester, Third/
Pregnant women/
Prenatal Care/
Pregnancy Outcome/
(pregnan$ or prenatal or pre natal or perinatal or peri natal or antenatal or ante natal or antepartum or ante partum).ti,ab.
Infant/
Infant, newborn/
Fetus/
(fetal or foetal or fetus$ or foetus$ or neonat$ or infant$ or newborn$).ti,ab.
exp Pregnancy Complications/
Infectious Disease Transmission, Vertical/
((vertical or maternal or mother or fetomaternal) adj3 transmission).ti,ab.
Congenital Abnormalities/
Abnormalities, Drug-Induced/
fetal mortality/
infant mortality/
perinatal mortality/
maternal mortality/
or/9-29
5 and 8 and 30
limit 31 to (english language and yr="2008 -Current")
remove duplicates from 32

Pubmed, publisher-supplied [search run on 6.2.2017]
Search
Query
#6 Search #5 AND ("2008/01/01"[Date - Publication] : "3000"[Date - Publication]) AND English[Language]
#5 Search #4 AND publisher[sb]
#4 Search #1 AND (#2 OR #3)
#3 Search (vertical[tiab] OR maternal[tiab] OR mother[tiab] OR fetomaternal[tiab]) AND transmission[tiab]
#1 Search syphilis[tiab] OR “treponema pallidum”[tiab]

Cochrane Central Register of Controlled Trials: Issue 5 of 12, May 2017

#1 syphilis:ti,ab,kw
#2 "treponema pallidum":ti,ab,kw
#3 #1 or #2
#4 (pregnan* or prenatal or pre natal or perinatal or peri natal or antenatal or ante natal or antepartum or ante partum):ti,ab,kw
#5 (fetal or foetal or fetus* or foetus* or neonat* or infant* or newborn*):ti,ab,kw
#6 ((vertical or maternal or mother or fetomaternal) near/3 transmission):ti,ab,kw
#7 #4 or #5 or #6
#8 #3 and #7 Publication Year from 2008 to 2017 in Trials
## eTable 1. Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Category</th>
<th>Include</th>
<th>Exclude</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Populations</strong></td>
<td>KQs 1, 2: Asymptomatic pregnant adolescents or adult women, at any time during pregnancy, who are not known to have syphilis infection</td>
<td>KQs 1, 2: Women who are known to have syphilis infection, have symptoms, or are not pregnant; studies in women living with HIV</td>
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<td></td>
<td>KQ 3: Studies of penicillin treatment in pregnant women with syphilis infection</td>
<td>KQ 3: Studies of penicillin treatment in nonpregnant women or men; studies of penicillin treatment for any condition other than syphilis</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>KQs 1, 2: Two-step screening for syphilis with a nontreponemal and treponemal test (traditional or reverse sequence algorithms)</td>
<td>KQs 1, 2: Screening tests not currently used in U.S. primary care settings</td>
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<tr>
<td></td>
<td>KQ 3: Treatment of syphilis with penicillin started during pregnancy</td>
<td>KQ 3: Other types of treatment of syphilis; treatment of syphilis with penicillin outside of pregnancy</td>
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<tr>
<td><strong>Comparisons</strong></td>
<td>KQ 1: No screening</td>
<td>KQ 1: Alternate screening strategy or no comparator</td>
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<td></td>
<td>KQ 2: No comparator necessary for studies on psychosocial harms; studies on screening test in accuracy must define their criteria for false-positive and false-negative results</td>
<td></td>
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<td></td>
<td>KQ 3: No comparator necessary</td>
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<tr>
<td><strong>Outcomes</strong></td>
<td>KQ 1: Vertical transmission of syphilis (incidence of congenital syphilis); prevalence of congenital syphilis after implementation of a screening program; stillbirth; maternal or infant morbidity and mortality</td>
<td>Cost-effectiveness or cost-related outcomes</td>
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<td>KQ 2: Harms of screening (e.g., false-positive and false-negative results, stigma, psychosocial harms)</td>
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<tr>
<td></td>
<td>KQ 3: Harms of treatment of syphilis with penicillin during pregnancy (e.g., allergic reaction, premature labor, Jarish-Herxheimer reaction, fetal harms, other maternal harms)</td>
<td></td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>Primary care and primary care–referable settings (e.g., obstetrics/gynecology clinics, prenatal clinics, ambulatory care, family planning clinics, correctional facilities, sexually transmitted infection clinics)</td>
<td></td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>Studies conducted in countries categorized as “high” or “very high” on the Human Development Index (as defined by the United Nations Development Programme)</td>
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<tr>
<td><strong>Study design</strong></td>
<td>KQ 1: Randomized, controlled trials; before-after and ecologic studies reporting effect of implementing a widespread screening program with historical or geographic comparator; systematic reviews and meta-analyses (of included study designs)</td>
<td>Narrative reviews, editorials, and case reports</td>
</tr>
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<td></td>
<td>KQs 2, 3: Randomized, controlled trials; cohort studies; case-control studies; diagnostic accuracy studies; large case series; systematic reviews and meta-analyses (of included study designs)</td>
<td></td>
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<tr>
<td><strong>Publication Language</strong></td>
<td>English-language only</td>
<td>Languages other than English</td>
</tr>
<tr>
<td><strong>Study quality</strong></td>
<td>Fair- or good-quality studies</td>
<td>Poor-quality studies</td>
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### eTable 2. Quality Assessment Criteria

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Criteria</th>
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<tr>
<td>Randomized and nonrandomized controlled trials, adapted from the U.S. Preventive Services Task Force methods&lt;sup&gt;1&lt;/sup&gt;</td>
<td>• Was there valid random assignment? (NA for non-randomized controlled trials)&lt;br&gt;• Was allocation concealed?&lt;br&gt;• Was eligibility criteria specified?&lt;br&gt;• Were groups similar at baseline?&lt;br&gt;• Were outcome assessors blinded?&lt;br&gt;• Were measurements equal, valid and reliable?&lt;br&gt;• Was there adequate adherence to the intervention?&lt;br&gt;• Were the statistical methods acceptable?&lt;br&gt;• Was the handling of missing data appropriate?&lt;br&gt;• Was there acceptable followup?&lt;br&gt;• Was there evidence of selective reporting of outcomes?&lt;br&gt;• Was there risk of contamination?</td>
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<td>Cohort studies, adapted from the Newcastle-Ottawa Scale&lt;sup&gt;2&lt;/sup&gt;</td>
<td>• Was the exposed cohort(s) representative of the general population?&lt;br&gt;• Was the non-exposed cohort selected from the same community as exposed cohort?&lt;br&gt;• How was “exposure” ascertained?&lt;br&gt;• Was it demonstrated that the outcome of interest was not present at the start of the study?&lt;br&gt;• Were the cohorts comparable on the basis of the design or analysis?&lt;br&gt;• Were outcome assessors blind?&lt;br&gt;• Was followup long enough for outcomes to occur?&lt;br&gt;• Was there adequate followup of cohorts?</td>
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<td>National Heart, Lung, and Blood Institute tool for before-after (pre-post) studies with no control group&lt;sup&gt;3&lt;/sup&gt;</td>
<td>• Was the study question or objective clearly stated?&lt;br&gt;• Were eligibility/selection criteria prespecified and clearly described?&lt;br&gt;• Were the participants representative of the general population?&lt;br&gt;• Were all eligible participants enrolled?&lt;br&gt;• Was the sample size sufficiently large?&lt;br&gt;• Was the test/service/intervention clearly described and delivered consistently?&lt;br&gt;• Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently?&lt;br&gt;• Were outcome assessors blind?&lt;br&gt;• Was loss to followup ≤20% and those lost to follow-up accounted for in analysis?&lt;br&gt;• Did statistical methods examine changes in outcome measures from before to after the intervention? Were p values provided?&lt;br&gt;• Were outcome measures taken multiple times before and after the intervention?&lt;br&gt;• If a group-level intervention, did statistical analysis take into account the use of individual-level data to determine group-level effects?</td>
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</tbody>
</table>