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Atypical bacterial pathogens underlying sexually transmitted infections: A systematic scoping review

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Emerging STI

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Protocol status: Working
This is a protocol for a systematic review (scoping review). If there is any deviation from the protocol in conducting the review, ammendments will be attached in the final report of the review.

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Keywords: sexually transmitted disease, sexually transmitted infection, urethritis, cervicitis, pelvic inflammatory disease, emerging, emergence, pathogen, bacteria, systematic scoping review this systematic review, transmitted infection, systematic scoping review, atypical bacterial pathogen, sti, systematic review, scoping review

Abstract

This systematic review aims to assess and summarise current knowledge on atypical bacterial sexually transmitted infections (STI). We will explore and describe the evidence available in the literature, identify the types of studies conducted, and analyse existing knowledge gaps. Given the breadth of the research question and the exploratory nature of the topic, a scoping review is the most appropriate approach.

Attachments

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Research proposal_Sy...

80KB

Guidelines

Design and methods used for this systematic review comply with the updated guideline of JBI scoping review and will be reported in line with the PRISMA-Scr. Eligibility criteria were informed in accordance with the PRISMA and PRISMA-Scr guideline.

Eligibility criteria

1 Patient (P): Adult male and female patients suspected of urethral discharge or urethritis and cervicitis with negative STI test, respectively.
Etiology (E): Atypical bacterial pathogens (all bacterial species **except** *N. gonorrhoeae, C. trachomatis, M. genitalium, U. urealyticum, T. vaginalis, U. parvum, M. hominis*)
Outcome (O): urethral discharge or urethritis or cervicitis with negative STI test.

Information sources

2 The search will employ a variety of electronic databases, using predefined keywords (see Search strategy) from inception to 28 February 2026. There will be no language or geographical restrictions. Articles written in other languages in English will be translated with the help of Generative Artificial Intelligence (AI) in accordance with the University of Oxford's Policy for Using Generative AI in Research.

3 List of databases for literature search:
- MEDLINE and EMBASE via Ovid
- Web of Science (Core collection, Preprint citation index, and Conference proceeding citation index)
- Scopus
- Google scholar

4 To complement the literature search and increase its sensitivity, a collateral search through NCBI BioSample database will be conducted to identify rare bacterial species isolated from human infection case from urethra (in male) or cervix (in female) reported on this database. All bacterial species identified through this means will be included as additional keywords for literature search.

Search strategy

5 The search strategy will include disease outcome terms and aetiology-related terms (broad and specific). Disease outcome terms are "sexually transmitted disease", "sexually transmitted infection", "urethritis", "cervicitis, and "pelvic inflammatory disease". Broad aetiology-related terms are "emerging" OR "emergence" and "pathogen" OR "bacteria". Specific aetiology terms are specific bacterial species identified during complementary search through the NCBI BioSample database (see Data management and Selection process). An example is provided in Table 1.

6 Table 1. Example of the search strategy implemented for MEDLINE and EMBASE search via
Ovid: advanced search on 3rd December 2025.

No	Keywords	Result
1	sexually transmitted.mp.	137,867
2	disease.mp.	17,703,205
3	infection.mp.	4,892,727
4	pathogen.mp.	601,355
5	1 and 2	88,049
6	1 and 3	75,036
7	1 and 4	3,656
8	5 or 6 or 7	110,440
9	urethritis.mp.	16,097
10	cervicitis.mp.	9,922
11	pelvic inflammatory disease.mp.	21,249
12	emerging.mp.	931,026
13	emergence.mp.	383,793
14	12 or 13	1,285,409
15	bacteri*.mp.	3,981,666
16	8 or 9 or 10 or 11	146,026
17	14 and 15 and 16	1,088
18	8 and 14	2,984

Data management

7 Studies found through the literature search process will be recorded in EndNote, a software for managing bibliographies.

Software

EndNote NAME

The resulting EndNote library will be converted to an XML format and uploaded to Covidence systematic review software for deduplication and selection.

Software	
Covidence	NAME
https://www.covidence.org/	SOURCE LINK

NCBI BioSample search results will be extracted in tabular format and stored and processed as Microsoft Excel document.

Selection process

8 Eligibility criteria will be defined on Covidence for each PEO component. Two reviewers (MK
and AU) will conduct independent screening from title and abstract concurrently. Any disagreement will be settled by OH as the third reviewer. Inclusion of studies will be defined after reviewing the full-text and at this stage, discrepancies will be resolved by discussion amongst all reviewers (MK, AU, and OH).

Data items

9 A customised Covidence spreadsheet will be developed, followed by pilot testing of three randomly chosen studies passing the eligibility check. Two reviewers (MK and AU) will extract the data in this pilot scheme and improve the spreadsheet if necessary. The data items to be extracted are:

- first and last author, type of article (original research or review article),
- study design,
- method(s) to isolate and identify bacterial species,
- limitations,
- funding,
- conflict of interest,
- geographical location (country),
- patients population (male or female and number of subjects),
- sex of patients (male or female),
- presence of STI symptoms,
- specimen type and source (urethra, cervix, vagina, or fallopian tube),
- bacterial species identified, and
- number of cases for each infecting bacterial species.

If one study covers both male and female populations, data items will be collected twice, with the results within one sex group separated to the other. We will not critically appraise each study, as this is a scoping review.

Data synthesis and presentation

10 Extracted data collected in Covidence will be converted in tabular format and explored and evaluated in Microsoft Excel and Jupyter Notebook. Graphical charts will be generated with Python on Jupyter Notebook. Meta-analysis will not be performed. Codes used for data analyses and visualisation will be deposited on a GitHub repository.

Glossary

11 Bacterial infection: in the context of clinical diagnostics, this is defined as presence of a potentially
pathogenic bacterium in (a) body part(s) where it's not usually present (i.e. sterile location).[28] It can be symptomatic or asymptomatic.

Colonisation: presence of bacteria in any body part without clinical features of infection.[29]

Differentiating asymptomatic infection and colonisation: while both involve bacterial presence and growth without clinical signs/symptoms, at a cellular level, infection is set when the multiplying bacteria breach the epithelial barrier.[28] Clinically, it is not usually possible to differentiate them based on this feature; therefore other measures have been proposed. First, the bacterium in colonised individuals (also known as "carrier") present in a longer duration while in asymptomatic cases, the individuals progress through "recovery" in the same duration as symptomatic ones.[30] Secondly, the bacterial species and demographic characteristics of the affected individuals can provide "clues" to differentiate the two groups. Examples are given on Table 2.

12 Table 2. Examples of how clinical and epidemiological context helps differentiate asymptomatic infection versus colonisation.

Bacterial species	Context	Asymptomatic infection vs colonisation	Reasons
Staphylococcus epidermidis	Isolated from skin in healthy individuals in community	Colonisation	*S. epidermidis* is a part of normal skin microbiota in healthy individuals. *S. epidermidis* can be considered pathogenic, for example, in normally sterile body sites in individuals with compromised immunity or infections associated with indwelling medical device.[31]
Neisseria gonorrhoeae	Isolated from cervix of asymptomatic female patients	Asymptomatic infection	*N. gonorrhoeae* is an obligate human pathogen, and when it is present, it will invade the epithelial cells in the reproductive tract even without causing symptoms. Presence of the bacterium, even asymptomatic, is associated with ascending infection and long-term complications.[32]
Haemophilus influenzae	Isolated from upper respiratory tract of healthy children	Colonisation	*H. influenzae* is accidental human pathogenic and children are common carriers for *H. influenzae.* Typically, during the duration of colonisation, that lasts 1-5 months, there are changes in predominant strains.[33]

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