SUPPLEMENTARY MATERIALS

Biological markers of antibiotic-refractory Lyme arthritis in human: A systematic review.

Supplementary Table 1: PRISMA Checklist for: Biological markers of antibiotic-refractory Lyme arthritis in human: A systematic review [10].

Supplementary Table 2: PICOST Table for: Biological markers of antibiotic-refractory Lyme arthritis in human: A systematic review

Supplementary Table 3: Variables and data collected for: Biological markers of antibiotic-refractory Lyme arthritis in human: A systematic review

Supplementary Table 1: PRISMA Checklist for: Biological markers of antibiotic-refractory Lyme arthritis in human: A systematic review [10].

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Systematic review
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.	All included in the abstract of the article. Some details in the results section.
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.	The protocol has not been registered
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.	5, supplementary table
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.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5-6, supplementary table
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).	Figure 1
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.	6
Data items	11	List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made.	Supplementary table
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 data synthesis.	Not applicable
Summary measures	13	State the principal summary measures (e.g. risk ratio, difference in means).	6
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.	Not applicable
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).	Not applicable
Additional analyses	16	Describe methods of additional analyses (e.g. sensitivity or subgroup analysis, meta-regression), if done, indicating which were pre-specified	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assess for eligibility, and included in the review, with reasons for exclusion at each stage, ideally with a flow diagram.	Fig1
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.	Table 1, pages 7-10
Risk of bias	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Not applicable
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 forest plot.	Not applicable

Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not applicable
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15)	Not applicable
Additional analysis	23	Give results of additional analyses, if done (e.g. sensitivity or subgroup analyses, meta-regression [see item 16]).	Not applicable
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).	11-14
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).	13-14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14
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.	See funding statement

Supplementary Table 2: PICOST Table for: Biological markers of antibiotic-refractory Lyme arthritis in human: A systematic review

Component	Criteria
Population	Adult or child populations (any, no restrictions)
Exposure	Lyme Arthritis
Comparator	Usual care, no intervention, any other intervention.
Outcomes	– Association with antibiotic refractory Lyme arthritis (A-RLA) – Prediction of A-RLA at the time of diagnosis
Study Design	– Observational – Interventions (randomized or non-randomized) – Exclusion: case-reports and reviews will be excluded
Time Period	1982 - onwards

Supplementary Table 3: Variables and data collected for: Biological markers of antibiotic-refractory Lyme arthritis in human: A systematic review

Variable name	Description	Entries
Study descriptors		
Manuscript Number	Number from Endnote Library	
Author	Last name of First Author	
Publication Year	Year of Publication of Manuscript	
Journal Name	Full Journal Name	
Title	Full Title of Manuscript	
Study characteristics		
Study Design	Study Design	Cohort, case-Cohort, case-control
Outcome of interest	Primary Outcome in the study	Diagnosis, prognosis, response to treatment
Sample Size (cases)	Number of cases included	
Sample Size (controls)	Number of controls included (if needed)	
Case ascertainment	Method of case ascertainment	
Country	Country where cases collected	
Sex	Sex of participants	Both, males, females
% Males	In studies of males and females % of population that is male	
Age (number)	Reported summary statistics for age	
Age (unit)	Summary provided	Mean, median
Age (interval)	CI, range or IQR if provided	
Additional Details	Additional details relevant to the population	
Biological samples collected for analyses (type)	describe type of biological samples collected	Whole blood, serum, plasma, buffy coat, synovial fluid, tissue
Biological samples collected for analyses (volume)	Include volume where collected (number)	
Biological samples collected for analyses (unit)	Include unit where collected (number)	
Immune biomarkers		
Biomarker class	Class of immune biomarkers included	
Specific biomarkers	Specific names of biomarker	
Method of measurement	Method use for measurement	
Additional details (assay)	Additional information pertaining to biomarkers included	
Effect estimate (type)	Type of effect measure for biomarkers	
Effect estimate (number)	Effect estimate provided	
Effect estimate (comparison/unit)	Unit of difference related to effect estimate	
Measure of uncertainty (type)	Type of measure of uncertainty included	
Measure of uncertainty (number)	Number for measure of uncertainty	
Additional details	Additional details related to effect estimate or measure of uncertainty	
Genomic biomarker		
Biomarker class	Class of genomic biomarkers	Leukocytes, cytokines, antigen expression, acute phase proteins
Specific biomarkers	Specific names of biomarker	
Method of measurement	Method use for measurement	Flow cytometry, ELISA
Additional details (assay)	Additional information pertaining to biomarkers included	
Effect estimate (type)	Type of effect measure for biomarkers	OR, RR, prevalence, mean difference
Effect estimate (number)	Effect estimate provided	
Effect estimate (comparison/unit)	Unit of difference related to effect estimate	
Measure of uncertainty (type)	Type of measure of uncertainty included	95% CI, SD, SE, SEM
Measure of uncertainty (number)	Number for measure of uncertainty	
Additional details	Additional details related to effect estimate or measure of uncertainty	