



## PRISMA 2020 Checklist

| Section and Topic                      | Item # | Checklist Item  | Location Where Item Is Reported  |
|--|--------|---|--|
| <b>TITLE</b>                           | 1      | Identify the report as a systematic review.   | <b>Title page</b> (“The impact of diagnostic delays and timeliness of response on Ebola disease outbreak-level case-fatality ratios in Uganda (2000 – 2023): a rapid systematic review and meta-analysis”).  |
| <b>ABSTRACT</b>                        | 2      | See the PRISMA 2020 for Abstracts checklist.  | <b>Abstract section</b> (structured Abstract).   |
| <b>INTRODUCTION</b><br>Rationale       | 3      | Describe the rationale for the review in the context of existing knowledge.   | <b>Introduction, first two paragraphs:</b> outlines existing global CFRs, species-specific virulence, and knowledge gaps in Uganda context.  |
| <b>INTRODUCTION</b><br>Objectives      | 4      | Provide an explicit statement of the objective(s) or question(s) the review addresses.  | <b>Introduction, final paragraph</b> (“This rapid systematic review aims to characterize epidemiologic patterns and CFRs across outbreaks and quantify how delays in diagnosis and response timeliness affect outbreak-level CFRs ...”).   |
| <b>METHODS</b><br>Eligibility criteria | 5      | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.   | <b>Methods → Eligibility criteria subsection</b> (pages “Eligibility criteria” and Table 1: PICO framework for study selection).   |
| <b>METHODS</b><br>Information sources  | 6      | Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | <b>Methods → Search strategy and data sources</b> (first paragraph): “Systematic searches were conducted ... from database inception until 30 April 2025” across PubMed, Embase, Scopus, Web of Science, WHO Global Index Medicus, grey literature, WHO DON, ProMED-mail, MoH Uganda bulletins, and MSF reports. |
| <b>METHODS</b><br>Search strategy      | 7      | Present the full search strategies for all databases,   | <b>Methods → Search strategy and data sources</b> (paragraph 2): “A comprehensive search strategy ... full syntax for the 6 databases in the   |



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|  |     | registers and websites, including any filters and limits used.   | supplementary file.” (Exact search strings in Supplementary File).  |
| <b>METHODS</b><br>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.                     | <b>Methods → Study selection and data extraction</b> (paragraph 1): “Title and abstract screening was independently conducted by two reviewers. All discrepancies were resolved through discussion, with consultation from a third reviewer when needed.” |
| <b>METHODS</b><br>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. | <b>Methods → Study selection and data extraction</b> (paragraph 2): “Data extraction was performed by two reviewers independently and compared for accuracy, capturing outbreak year, virus species, ...”   |
| <b>METHODS</b><br>Data items (10a: outcomes) | 10a | List and define all outcomes for which data were sought. Specify   | <b>Methods → Eligibility criteria</b> (Exposure/Timeliness & Outcomes): “Outcomes: Case-fatality ratio per outbreak ... stratified CFRs by age, sex or district.” Also <b>Methods → Study</b>   |



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|   |     | whether all results that were compatible with each outcome domain in each study were sought, and if not, the methods used to decide which results to collect.   | <b>selection and data extraction</b> (captures CFR data).  |
| <b>METHODS</b><br>Data items (10b: other variables) | 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.  | <b>Methods → Study selection and data extraction</b> (paragraph 2): “capturing outbreak year, virus species, geographic location, numbers of confirmed cases and deaths, timeliness intervals ... detailed information regarding clinical management, ETU establishment, and vaccine or therapeutic use. Median timeliness values converted to means (Wan, Wang ...).” |
| <b>METHODS</b><br>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. | <b>Methods → Risk-of-bias assessment</b> (paragraph): “Consistent with established practice ... given that our primary analysis was at the outbreak level with fewer than ten units ( $n = 7$ ), we did not perform a formal risk-of-bias assessment or evaluate publication bias.”  |
| <b>METHODS</b><br>Effect measures                   | 12  | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in   | <b>Methods → Statistical analysis</b> (paragraph 1): “Outbreak-level CFRs were synthesized using random-effects meta-analysis ... CFR proportions were transformed onto the logit scale for meta-  |



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|  |     | the synthesis or presentation of results.   | analysis, back-transformed to percentages for interpretability.”  |
| <b>METHODS</b><br>Synthesis methods<br>(13a) | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating study characteristics and comparing against the planned groups).  | <b>Methods → Statistical analysis</b> (paragraph 1): “Outbreak-level CFRs were synthesized ... anticipated heterogeneity ...” and description of seven included “primary units (n = 7 outbreaks).”  |
| <b>METHODS</b><br>Synthesis methods<br>(13b) | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.   | <b>Methods → Statistical analysis</b> (paragraph 1): “To stabilize variance, CFR proportions were transformed onto the logit scale and back-transformed. Median timeliness values converted to means using Wan, Wang ...”   |
| <b>METHODS</b><br>Synthesis methods<br>(13c) | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses.  | <b>Methods → Statistical analysis</b> (last sentences): “Figures and visualizations were generated using ggplot2.” Individual study results are presented in Table 1; forest plots and bubble plots in Results.   |
| <b>METHODS</b><br>Synthesis methods<br>(13d) | 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 | <b>Methods → Statistical analysis</b> (paragraphs 1–2): “Random-effects meta-analysis with REML estimator ... Freeman–Tukey transformation ... heterogeneity quantified via $I^2$ and $\tau^2$ ... meta-regression analyses ... R software version 4.3.2, metafor package.” |



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|   |     | software package(s) used.  |   |
| <b>METHODS</b><br>Synthesis methods (13e)   | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | <b>Methods</b> → <b>Statistical analysis</b> (paragraph 2): “Conducted mixed-effects meta-regression analyses ... leave-one-out sensitivity analyses to assess robustness of meta-regression findings.”   |
| <b>METHODS</b><br>Synthesis methods (13f)   | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results.   | <b>Methods</b> → <b>Statistical analysis</b> (paragraph 2): “Leave-one-out sensitivity analyses were performed to assess the robustness of meta-regression findings.”   |
| <b>METHODS</b><br>Reporting bias assessment | 14  | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).              | <b>Methods</b> → <b>Risk-of-bias assessment</b> : Stated that “Given $k < 10$ , formal tests of publication bias were not performed.” (implying none performed).  |
| <b>METHODS</b><br>Certainty assessment      | 15  | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.                                | <b>Methods</b> → <b>Risk-of-bias assessment</b> : No formal risk-of-bias or GRADE assessment was conducted; thus, no certainty assessment performed.  |
| <b>RESULTS</b><br>Study selection (16a)     | 16a | Describe the results of the search and selection process, ideally using a flow diagram.  | <b>Results</b> → <b>Study Selection paragraph and Figure 1 (PRISMA-2020 flow diagram)</b> : “Identified 764 records via database ... after removing 218 duplicates, screened 605 database-derived records ... ultimately, 15 reports met inclusion criteria.” |
| <b>RESULTS</b><br>Study selection (16b)     | 16b | Cite studies that might appear to meet the inclusion criteria but which were excluded, and   | <b>Results</b> → <b>Study Selection</b> : Lists numbers of excluded records by reason (no CFR data, no lab confirmation, etc.) but does not cite specific excluded studies by author. The reasons ( $n = 101$ exclusions, etc.) are provided in detail.       |



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|  |     | explain why they were excluded.   |  |
| <b>RESULTS</b><br>Study characteristics (17)         | 17  | Cite each included study and present its characteristics.   | <b>Results → Characteristics of included studies</b> (subsection) and <b>Table 1</b> : summarizing 15 included studies, outbreak year, design, main findings, CFR, timeliness, supportive-care, vaccine information.   |
| <b>RESULTS</b><br>Risk of bias in studies (18)       | 18  | Present assessments of risk of bias for each included study.  | <b>Not applicable</b> : No formal risk-of-bias assessment was conducted (see Methods).   |
| <b>RESULTS</b><br>Results of individual studies (19) | 19  | For all outcomes, present for each study: (a) summary statistics for each group and (b) an effect estimate and its precision.   | <b>Results → Descriptive mortality patterns across the seven outbreaks</b> : Presents CFR for each outbreak and study-level details (e.g., Gulu 2000: 224/425 = 52.7%; Bundibugyo 2007: 37/116 = 31.9%; etc.), with citations.                                   |
| <b>RESULTS</b><br>Results of syntheses (20a)         | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.  | <b>Results → Pooled CFR subsection</b> (first paragraph under “Pooled CFR”): “Seven studies (n = 743 participants; 329 deaths) included... pooled CFR was 45.4 % ... $I^2 = 87.8$ %.” Characteristics summarized in Table 1; risk-of-bias not formally assessed. |
| <b>RESULTS</b><br>Results of syntheses (20b)         | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision and measures of heterogeneity. | <b>Results → Pooled CFR subsection and Figures 2 &amp; 3</b> : “Pooled CFR = 45.4 % (95 % CI: 26.2–65.2; $I^2 = 87.8$ %)” for all. <b>Figure 2 (forest plot)</b> and <b>Figure 3 (species subgroup forest plot)</b> present summary estimates and 95 % CIs.      |
| <b>RESULTS</b><br>Results of syntheses (20c)         | 20c | Present results of all investigations of possible causes of heterogeneity among study results.  | <b>Results → Subgroup analysis by species</b> (Figure 3) and <b>Meta-regression of outbreak response metrics</b> (Table 2, Figures 4 & 5). Heterogeneity statistics ( $\tau^2$ , $I^2$ ) appear for each model.  |
| <b>RESULTS</b>                                       | 20d | Present results of all sensitivity  | <b>Partial</b> : Methods mention leave-one-out sensitivity, but <b>Results</b> do not explicitly present   |



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| Results of syntheses (20d)                                 |     | analyses conducted to assess the robustness of the synthesized results.   | sensitivity-analysis figures or tables. No formal sensitivity results are shown.   |
| <b>RESULTS</b><br>Reporting biases (21)                    | 21  | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | <b>Results → Assessment of small-study effects and publication bias</b> (last paragraph): “Given $k < 10$ ... funnel plot ... symmetrical distribution ... no evidence of small-study effects.” <b>Figure 6</b> shows the funnel plot. |
| <b>RESULTS</b><br>Certainty of evidence (22)               | 22  | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.                     | <b>Not assessed:</b> Methods state no formal risk-of-bias or GRADE; therefore, certainty of evidence was not evaluated.  |
| <b>DISCUSSION</b><br>Discussion (interpretation)           | 23a | Provide a general interpretation of the results in the context of other evidence.                                       | <b>Discussion → Principal findings</b> (first paragraph of Discussion).  |
| <b>DISCUSSION</b><br>Limitations of evidence (23b)         | 23b | Discuss any limitations of the evidence included in the review.   | <b>Discussion → Strengths and limitations</b> (paragraphs 2–3).  |
| <b>DISCUSSION</b><br>Limitations of review processes (23c) | 23c | Discuss any limitations of the review processes used.   | <b>Discussion → Strengths and limitations</b> (paragraphs 2–3): mentions retrospective data, small number of outbreaks, heterogeneity, unmeasured confounders, lack of standardized timeliness metrics.                                |
| <b>DISCUSSION</b><br>Implications (23d)                    | 23d | Discuss implications of the results for practice, policy, and future research.  | <b>Discussion → Clinical and public health implications</b> (paragraphs 1–3) and <b>Directions for future research</b> (paragraph starting “The findings of this study underscore ...”).   |
| <b>OTHER INFORMATION</b>                                   | 24a | Provide registration information for the review, including register name and  | <b>Methods → Protocol development and registration</b> (first sentence): OSF DOI <a href="https://doi.org/10.17605/OSF.IO/WQHCM">https://doi.org/10.17605/OSF.IO/WQHCM</a> .   |



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| Registration and protocol (24a)                                   |     | registration number.   |   |
| <b>OTHER INFORMATION</b><br>Registration and protocol (24b)       | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared.   | <b>Methods → Protocol development and registration</b> (second sentence): “This rapid systematic review was registered prospectively on the Open Science Framework (OSF; registration DOI: <a href="https://doi.org/10.17605/OSF.IO/WQHCM">https://doi.org/10.17605/OSF.IO/WQHCM</a> ).”  |
| <b>OTHER INFORMATION</b><br>Registration and protocol (24c)       | 24c | Describe and explain any amendments to information provided at registration or in the protocol.  | <b>Not applicable:</b> No amendments were made post-registration (no protocol changes reported).  |
| <b>OTHER INFORMATION</b><br>Support (25)                          | 25  | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.  | <b>Declarations → Funding:</b> “No external funding. GP’s time was supported by a doctoral scholarship from the IDEA Fellowship under the EDCTP2 programme (Grant CSA2020E). The fellowship had no involvement in study conceptualization, data collection, analysis, or manuscript preparation.”   |
| <b>OTHER INFORMATION</b><br>Competing interests (26)              | 26  | Declare any competing interests of review authors.   | <b>Declarations → Competing interests:</b> “The authors declare no competing interests, financial or otherwise, that could have influenced the study design, analysis, or reporting.”   |
| <b>OTHER INFORMATION</b><br>Availability of data, code, etc. (27) | 27  | 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. | <b>Declarations → Availability of data and materials:</b> “The full dataset of extracted outbreak characteristics, timeliness metrics, and prognostic factors is provided as Supplementary file. All R code used for meta-analysis and meta-regression is archived in a publicly accessible at GitHub repository <a href="https://github.com/gpaasi/ebola-uganda-outbreak-timeliness-cfr">https://github.com/gpaasi/ebola-uganda-outbreak-timeliness-cfr</a> and via Zenodo <a href="https://doi.org/10.5281/zenodo.15564078">https://doi.org/10.5281/zenodo.15564078</a> |

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71



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