Reporting practices for genomic epidemiology of tuberculosis: a systematic review of the literature using STROME-ID guidelines as a benchmark

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Summary

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Contributors
BC was responsible for screening abstracts and titles for inclusion, data extraction, statistical analysis, making the tables and figures, interpreting the data, and writing the first draft of the manuscript. MAB assisted with interpreting the data, reviewed drafts of the manuscript, and co-supervised BC. BPH and TC contributed to the protocol development and reviewed the final draft of the manuscript. TC also served as arbitrator for disagreement in study inclusion. RSL conceived and led the study, designed the protocol and ran the searches, screened abstracts and titles for inclusion, guided statistical analyses and interpretation of the data, wrote the first draft of the manuscript with BC and co-supervised BC. BC and RSL accessed and verified the data.

Declaration of interests
We declare no competing interests.

Data sharing
The data supporting the findings of this study are available within the appendices.

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**Background**—Pathogen genomics have become increasingly important in infectious disease epidemiology and public health. The Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases (STROME-ID) guidelines were developed to outline a minimum set of criteria that should be reported in genomic epidemiology studies to facilitate assessment of study quality. We evaluate such reporting practices, using tuberculosis as an example.

**Methods**—For this systematic review, we initially searched MEDLINE, Embase Classic, and Embase on May 3, 2017, using the search terms “tuberculosis” and “genom* sequencing”. We updated this initial search on April 23, 2019, and also included a search of bioRxiv at this time. We included studies in English, French, or Spanish that recruited patients with microbiologically confirmed tuberculosis and used whole genome sequencing for typing of strains. Non-human studies, conference abstracts, and literature reviews were excluded. For each included study, the number and proportion of fulfilled STROME-ID criteria were recorded by two reviewers. A comparison of the mean proportion of fulfilled STROME-ID criteria before and after publication of the STROME-ID guidelines (in 2014) was done using a two-tailed t test. Quasi-Poisson regression and tobit regression were used to examine associations between study characteristics and the number and proportion of fulfilled STROME-ID criteria. This study was registered with PROSPERO, CRD42017064395.

**Findings**—976 titles and abstracts were identified by our primary search, with an additional 16 studies identified in bioRxiv. 114 full texts (published between 2009 and 2019) were eligible for inclusion. The mean proportion of STROME-ID criteria fulfilled was 50% (SD 12; range 16–75). The proportion of criteria fulfilled was similar before and after STROME-ID publication (51% [SD 11] vs 46% [14], p=0.26). The number of criteria reported (among those applicable to all studies) was not associated with impact factor, h-index, country of affiliation of senior author, or sample size of isolates. Similarly, the proportion of criteria fulfilled was not associated with these characteristics, with the exception of a sample size of isolates of 277 or more (the highest quartile). In terms of reproducibility, 100 (88%) studies reported which bioinformatic tools were used, but only 33 (33%) reported corresponding version numbers. Sequencing data were available for 86 (75%) studies.

**Interpretation**—The reporting of STROME-ID criteria in genomic epidemiology studies of tuberculosis between 2009 and 2019 was low, with implications for assessment of study quality. The considerable proportion of studies without bioinformatics version numbers or sequencing data available highlights a key concern for reproducibility.

**Introduction**

Whole genome sequencing (WGS) has been increasingly used in genomic epidemiology studies. Its superior resolution compared with classical genotyping methods (eg, restriction fragment length polymorphism or mycobacterial interspersed repetitive unit-variable number tandem repeats for tuberculosis) provides the opportunity to gain new insights into transmission and evolution of drug resistance, and to potentially inform public health interventions. However, the ability of WGS to serve these purposes depends on the quality of the studies that use this technology. Currently, the heterogeneity of WGS bioinformatic pipelines poses challenges to the standardised reporting and interpretation of results across genomic epidemiology studies. Standardised reporting of data and software
would further facilitate comparison of WGS-based findings, and enable researchers to assess the validity of published data.⁷

In 2007, guidelines called Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) were published. These consisted of 22 criteria⁸ outlining study details that should be reported to help readers better assess quality and validity of results. In 2014, the Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases (STROME-ID) guidelines were released.⁹ These extended the original 22 STROBE criteria with 20 additional criteria for reporting of genomic epidemiology studies (appendix 1 pp 14–15). In this Article, unless otherwise stated, we define STROME-ID as the combined set of STROBE and STROME-ID criteria.

The impact of the STROBE guidelines on reporting quality has been inconsistent.¹⁰–¹³ However, higher reporting quality (ie, a larger number of criteria in the guidelines being reported) has previously been associated with greater sample size¹⁴,¹⁵ and, to a lesser degree, with journal impact factor.¹³ To our knowledge, no previous studies have investigated factors associated with reporting quality using STROME-ID for pathogen genomic epidemiology. We systematically reviewed genomic epidemiology studies, using tuberculosis as an example, to determine the extent to which STROME-ID criteria have been reported, and whether specific study or journal characteristics were associated with reporting practices.

**Methods**

**Search strategy and selection criteria**

This systematic review was done according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.¹⁶ We initially searched MEDLINE, Embase Classic, and Embase on May 3, 2017, using the terms “tuberculosis” and “genom* sequencing”. We updated this search on April 23, 2019, and included a search of bioRxiv. No restrictions were placed on start date or geographic location. References of included articles were also searched manually. A detailed search strategy is described in appendix 1 (p 3).

The titles and abstracts of studies were initially screened by BC and RSL to determine whether they met inclusion criteria, which was followed by full-text review. Discrepancies were resolved by discussion and third-party arbitration (TC). Eligible studies included patients with microbiologically confirmed tuberculosis and used WGS for typing of strains. Studies must have been published in English, French, or Spanish. As suggested by Field and colleagues,⁹ we considered studies to be genomic epidemiology reports if they investigated the distribution or transmission dynamics of tuberculosis across time, in a particular population, or in a geographical location in order to inform outbreaks, evaluate infection control practices, or perform surveillance. Studies were also included if they examined risk factors for transmission or if they distinguished between recurrent cases of tuberculosis as relapse or reinfection. If studies described the evolution of tuberculosis, drug resistance, or both, or if they identified and classified new tuberculosis strains or lineages, they were
included. Finally, studies were included if they investigated the association between strain types or mutations and clinical outcomes (eg, death, treatment failure, or relapse).

We excluded non-human studies, studies that were exclusively experimental (eg, in-vitro or in-vivo animal studies), or those that were purely diagnostic. Conference abstracts, editorials, and literature reviews were also excluded. A full list of exclusion criteria is provided in appendix 1 (p 3).

Data analysis
Each STROME-ID variable was assessed and scored as complete or incomplete. Some variables, evaluated by BC with consideration of the study design, were scored as not applicable. The number and proportion of fulfilled STROME-ID criteria were tabulated for each article, with the denominator for the proportions excluding criteria that were not applicable (eg, specific to a different study design). In addition, we analysed whether certain study or journal characteristics were associated with the number and proportion of fulfilled STROME-ID criteria, which were specified a priori. These were the journal impact factor, sample size of isolates, the geographic region of the senior author’s primary affiliation, and the h-index of the senior author (appendix 1 pp 3–4).

To assess differences in reporting after the publication of STROME-ID guidelines, the mean proportions of fulfilled criteria were compared before and after the publication date (April 1, 2014). A 6-month lag period was included to account for articles that were already in press when STROME-ID was published. Sensitivity analyses were also done using a 12-month lag period, and excluding articles published within 6 months and 12 months after STROME-ID publication. Differences in mean proportions of criteria were compared before and after publication using a two-tailed t test. The least and most reported STROME-ID criteria were also qualitatively assessed to explore differences between periods, excluding criteria that were not applicable for more than 20% of articles (appendix 1 pp 6–7). Finally, to evaluate potential differences in reporting according to study theme, we did a post-hoc analysis of the proportion of fulfilled STROME-ID criteria for the most common themes identified.

To examine the association between study and journal characteristics and reporting, two approaches were used. First, we used quasi-Poisson regression (to account for under-dispersion) with the number of criteria fulfilled as the dependent variable. This analysis was restricted to criteria that were applicable across all studies. Second, we used tobit regression (censored between 0 and 1) to assess the association with the proportion of criteria that were completed, including all studies in the analysis. Impact factor was used as a categorical variable (0 to <5, 5 to <10, 10 to <20, ≥20), with categories chosen based on our experience with the metric and previous studies that examined associations with impact factor. The sample size of isolates was categorised into quartiles due to low counts across a wide range of data (appendix 1 p 9). h-index was analysed as a linear variable.

Variables that had a p value of less than 0.20 in univariate analyses were included in the final model for each analysis. Pseudo-$R^2$, the Akaike information criterion, and log-likelihood were calculated to assist with model selection and to evaluate fit. All analyses were done using R (version 1.1.456).
Finally, because STROME-ID aims to support transparent reporting practices, which is important for reproducibility, we investigated whether authors reported the bioinformatics tools used, along with corresponding version numbers for software, and whether studies had uploaded their genomic data to an open-access sequence archive.

This study was registered with PROSPERO, CRD42017064395.

Role of the funding source
The funder of this study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results
Our initial search identified 976 studies, of which 274 were duplicates and were excluded. After the addition of 16 studies identified in bioRxiv, 718 titles and abstracts were screened. Of these, 138 full-text articles were screened, and 114 full texts were eligible for inclusion (figure 1). 97 of 114 studies were published after STROME-ID guidelines. No studies were excluded due to language of publication. A summary of key characteristics of included studies is shown in table 1 (further detail in appendix 2). Studies were classified into four themes based on their overall aims (these themes were not mutually exclusive): transmission (n=82), evolution (n=36), strain identification (n=11), and clinical outcomes (n=2; appendix 1 p 5). The number of patients was missing for 21 (18%) articles. Impact factor was also not available for one article published during the first year of the journal (2013) and from 15 articles published in 2019 (13%).

Overall, we found that the proportion of applicable STROME-ID criteria fulfilled among the included studies ranged from 16% to 75% (mean 50% [SD 12]). There was no significant difference between the average proportion of fulfilled criteria in studies from before and after guideline publication (table 2). Both before and after guideline publication, STROME-ID 4.1 (definitions for molecular terminology; 0% before, 11% after) and STROME-ID 8.1 (methods used to detect multiple-strain infections; 6% before, 7% after) were among the least reported criteria. Across both time periods, both STROBE-3 (study objectives and hypotheses; before 94%, after 97%) and STROME-ID 3.1 (epidemiological objectives of using molecular typing; before 100%, after 95%) were among the top reported criteria. The same 15 criteria were not applicable in at least 20% of papers both before and after STROME-ID publication (appendix 1 pp 6–7); of these, 12 (80%) were from the original STROBE guidelines, and pertained to specific epidemiological study designs or statistical analyses that are less likely to be used in genomic epidemiology studies.

The average proportions of studies that fulfilled each individual STROME-ID criterion are shown in figure 2. Before STROME-ID publication (figure 2A), six STROME-ID criteria were not fulfilled by any of the included studies, whereas after publication (with a 6-month lag period; figure 2B), a single criterion, STROBE-16(a), was not completed. Similar results were found in sensitivity analyses using a 12-month lag period or excluding articles published during the 6 or 12 months after guideline publication (appendix 1 pp 10–13).
To evaluate potential differences in reporting according to study theme, we reviewed the proportion of fulfilled STROME-ID criteria among the two most common themes: transmission and evolution. Examining potential differences in reporting for transmission-only \((n=67)\) and evolution-only \((n=21)\) studies (ie, excluding 13 manuscripts which were classified under both of these themes), proportions of criteria reported were similar before and after publication within both themes (appendix 1 pp 17–18). The average proportions of criteria reported overall were low for both themes (51% [SD 13] for transmission-only studies, 44% [12] for evolution-only studies).

We next considered whether reporting quality was associated with specific journal and author characteristics. Because we did not detect a difference between the reporting quality before and after STROME-ID publication, we included all papers published over the entire study period for this analysis. The distribution of impact factors from all studies is shown in appendix 1 (p 8). For articles published in 2019, an evaluation of impact factors between 2013 and 2018 showed little variation across these years (appendix 1 p 16); therefore, the 2018 values were used. One paper in 2013 did not have an impact factor and was excluded from the analysis. Moreover, due to low individual country counts, we analysed author affiliation by continent. There was only one study in South America, which was subsequently combined with North America to form the category Americas (appendix 1 p 19).

Univariate and multivariate analyses for quasi-Poisson regression and tobit regression models are presented in table 3 and appendix 1 (p 20), respectively. h-index did not meet the criteria for inclusion in the full multivariate model for either quasi-Poisson or tobit regression models. There was no association between sample size of isolates, impact factor, or geographic region of the senior author, and the number of STROME-ID criteria fulfilled. Similar results were found in the multivariate tobit regression analysis, although a sample size of isolates of 277 or more was significantly associated with the proportion of criteria fulfilled \((p=0.0070)\). 12 studies had more than one senior author; sensitivity analyses excluding these manuscripts yielded similar results (appendix 1 pp 21–22).

In terms of reporting of the bioinformatics tool used and the availability of genomic data, 100 (88%) articles reported the names of bioinformatic tools; however, only 33 (33%) of these provided version numbers for all of the tools (appendix 2). 86 (75%) papers reported accession numbers for their raw genomic data (appendix 1 p 23).

Given that genomic epidemiology studies aim to inform public health, we investigated whether any articles reported clinical or public health actions as a result of their findings. Possibly due to the retrospective nature of most of these studies, only three (3%) of included studies reported such changes; specifically, WGS results helped identify linked cases, guide tailored drug treatment based on drug-resistance analysis, and informed epidemiological investigations.\(^{32,50,123}\) Of note, one additional study reported their WGS findings to national tuberculosis surveillance programmes, but subsequent public health intervention was not possible because of the region’s political instability.\(^{131}\)

\(^{32}\)
Discussion

STROME-ID was developed by an interdisciplinary team with expertise in infection control and infectious diseases, to facilitate the reporting of a minimal set of study variables that were considered critical for assessment of bias and study quality. Herein, we have used STROME-ID as the framework to evaluate the reporting and transparency of genomic epidemiology studies of tuberculosis and have explored the association between specific journal or study characteristics and reporting practices.

Publication of guidelines has previously been shown to improve reporting practices. Although we hypothesised that there would be differences in variables reported following the publication of STROME-ID guidelines, we found no evidence of this in the current study. On average, only around half of STROME-ID criteria were completed both before and after their publication, a finding similar to that from other systematic reviews that evaluated reporting quality after publication of STROBE. The proportions of criteria completed in these reviews ranged from 51.4% to 76.5%. Although the proportions of criteria completed before and after STROME-ID publication were similar, we note that fewer criteria were never completed in the post-publication period. However, this difference could simply be due to temporal changes, such as an increased demand for reproducibility, and could be unrelated to STROME-ID.

There could be several reasons for the observed low reporting of STROME-ID criteria. Given that only one included article specifically cited the guidelines, lack of awareness could be an issue. Previous studies have also shown that formal journal endorsement of STROBE reporting guidelines improves reporting adherence, but to our knowledge, no publishers require authors to follow and report adherence to STROME-ID guidelines. Other practical limitations, such as article word count and absence of online supplements, could have also influenced reporting practices. Journal support of STROME-ID is probably needed to improve reporting transparency. We also did not find any articles that completed all STROME-ID criteria, which could suggest that some of the criteria in the guidelines are too vague or difficult to complete in practice.

In terms of which criteria were less likely to be reported, we found STROME-ID criteria that concerned key definitions, methods, and potential limitations to be more poorly reported. Although it might seem trivial that the least completed STROME-ID criteria related to the defining of molecular terminology, we would argue that standardisation of basic microbiological terminology is essential to allow for clear comparisons between studies and correct interpretation of results for public health. Despite this, even in the same academic field, terms such as strain, isolate, and clone are sometimes used differently by researchers. In addition, we note that STROME-ID 8.1 (methods for detecting multi-strain infections) was also reported poorly across the entire study period. Although this criterion was investigated by some of the included papers, methods for discriminating within-host diversity using WGS data are an area of active research, which could explain why these were less frequently discussed.
Journal impact factor has often been used as an indicator of quality,\textsuperscript{138} by funding organisations,\textsuperscript{139,140} and even for academic promotion.\textsuperscript{140} However, our analyses suggest that reporting quality is not associated with impact factor, adjusting for sample size of isolates and geographic region of the senior author. Similarly, we found no association between h-index and reporting quality. These findings highlight the limitations of such indicators as correlates of the quality of scientific publications, supporting previous studies.\textsuperscript{139,141,142} Moreover, sample size of isolates was not found to be associated with the number of criteria completed; studies with 153–276 isolates completed a similar number of mean criteria as those with 277 or more. Although a sample size of 277 or more was associated with a higher proportion of criteria being reported, this was equivalent to less than a 10\% increase compared with the reference group of less than 30 samples, and only a 2\% difference from a sample size of 153–276 isolates, the adjacent category. Therefore, although this result is statistically significant, we suspect that it is not an epidemiologically meaningful difference.

In addition to STROME-ID criteria, we also investigated whether bioinformatics tools (at a minimum) were well documented in tuberculosis genomic epidemiology papers, because reproducibility is a critical concern in genomic studies.\textsuperscript{143,144} Although we found that articles frequently reported the name of the tool, the corresponding version number of the software was reported much less frequently, consistent with a recent analysis of RNA-seq methodology.\textsuperscript{145} The inclusion of version numbers is essential to evaluate bias, reproduce workflows, and compare results across studies, which, as proposed by Simoneau and colleagues,\textsuperscript{145} suggests the need for standardised reporting of these methodological details. Even more surprisingly, we found that nearly a quarter of studies did not provide a Sequence Read Archive or Genbank accession number for their sequencing data, with no improvement across the study period. This is problematic because it not only prevents researchers from reproducing analyses and verifying results,\textsuperscript{146} but in the context of infectious diseases, it can hinder public health investigations that rely on global strain depositions for genomic context or for evaluation of cross-jurisdictional transmission. We therefore suggest that data deposition should be a requirement for publication, rather than just a social norm in genomic epidemiology. However, such a change will be unlikely without collaboration (and enforcement) by funders, publishers, or both.\textsuperscript{143}

Overall, this study has several strengths. First, it represents a comprehensive review of reporting practices in tuberculosis genomic epidemiology studies, starting with the first publication in tuberculosis genomic epidemiology in 2009,\textsuperscript{147} and including a search of unpublished literature. Using STROME-ID guidelines, we have identified key gaps in current reporting practices that could affect interpretation of results, adding to previous work that highlighted the implications of differences in analytic pipelines.\textsuperscript{4} To our knowledge, this is the first study to examine the application of STROME-ID guidelines (to tuberculosis or any other pathogen) and will serve as a template for other such investigations that employ similar genomic methods. In terms of analysis, we used a rigorous analytical approach and did numerous sensitivity analyses to assess the robustness of our results, lending further support to our inferences. Finally, in addition to STROME-ID criteria, we also examined variables related to reproducibility, highlighting that even in a field that has arguably
embraced open science, a large proportion of studies continue to not share their underlying genomic data.

The study has also several limitations. First, we note that, given that the STROME-ID guidelines were only published in 2014, there may have not been enough time for widespread uptake of these reporting guidelines at the time this study was done. However, because we did not observe increased reporting practices even in 2019, 5 years after publication, we consider this to be unlikely. This view is supported by other studies suggesting low adherence to STROBE guidelines after their publication.\textsuperscript{12,13,148} Furthermore, because of the small number of studies in each time period, we were not able to do an analysis controlling for secular trends (eg, an interrupted time-series). However, because we did not see evidence of any such trends on visual assessment by year, this is unlikely to affect our comparison of reporting before and after guideline publication. In our regression analyses, we specifically accounted for the time-varying nature of impact factor by using the impact factor from the study’s year of publication. We also note that, as bioinformatics pipelines are not yet standardised,\textsuperscript{4} our review of the reporting of bioinformatics tools was qualitative and did not require adherence to a specific pipeline or set of steps. Had we required a minimum set of tools or analytic steps be reported, we expect the reproducibility would have been assessed as being even lower. Finally, we did not separate STROME-ID criteria that required multiple pieces of information (eg, STROBE-19, which required reporting of both limitations and direction of bias); thus, if the entire criterion was not met, it was assigned as incomplete. Similarly, for bioinformatics version numbers, we considered reporting to be complete only if steps were reported with versions for all included tools; there could be differences in the reporting of version numbers across different steps in the analysis.

In this comprehensive review, we systematically examined reporting quality using STROME-ID guidelines as a benchmark. We have shown that, in general, only around 50% of STROME-ID criteria were met, potentially hindering assessment of study quality. Although good reporting practices themselves do not guarantee a study is of high quality, transparency of design, methods, and results are critical for such an assessment. The scope of the current study is limited to tuberculosis, but we expect that many of these reporting and transparency issues also apply to genomic epidemiology studies of other pathogens as well. The reasons underlying the low level of reporting are unclear, although similar reporting practices have been found with other guidelines for other types of studies.\textsuperscript{149,150} Possible reasons include adherence to strict word limits, low author awareness or understanding of guidelines, and, possibly, resistance to change. Alternatively, these guidelines may be too difficult to implement in practice. Further study is warranted to investigate these hypotheses.

Finally, in addition to STROME-ID, we also identified key reproducibility issues in many studies, pertaining to methods of analysis and data sharing. To improve data sharing, we suggest that data deposition should be a requirement for publication of genomic epidemiology studies. This stance will require active support from journals, with real consequences for failing to meet this obligation.\textsuperscript{145}
Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Research in context**

**Evidence before this study**

Pathogen genomics are playing an increasingly important role in infectious disease epidemiology and public health. However, the ability of genome sequencing to inform interventions depends on the quality of the studies that use this technology. In 2014, guidelines called the Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases (STROME-ID) were published by a team of experts in the field, to provide authors with a minimum set of criteria for reporting and to help readers assess the validity of study methodology and results. To date, however, overall reporting practices of genomic epidemiology studies have not been evaluated with STROME-ID. Evidence of the impact of reporting guidelines on reporting practices in other fields is mixed.

**Added value of this study**

In this study, we evaluated reporting practices of genomic epidemiology studies of tuberculosis using the STROME-ID guidelines as our benchmark. Overall, we found that reporting quality was low; the mean proportion of STROME-ID criteria fulfilled was only 50% (SD 12). There was no significant difference in reporting before versus after STROME-ID publication, nor did reporting appear to be associated with impact factor, h-index, geographical region of the senior author, or with the number of isolates included in the study. We also examined several important considerations for reproducibility of these studies. We found that, although 88% of studies reported which bioinformatic tools were used, only a third reported corresponding version numbers, and less than 80% of studies had made pathogen sequencing data available.

**Implications of all the available evidence**

Detailed reporting of study methodology is critical to properly evaluate quality and determine how (and whether) results can inform public health interventions. Similarly, open sharing of pathogen genomic data is crucial for reproducibility of results, and as a resource for the greater scientific community. Our study suggests reporting practices in genomic epidemiology studies of tuberculosis require considerable improvement to meet guidelines. We would anticipate that many of the reporting and transparency issues identified here also apply to genomic epidemiology studies of other pathogens. We suggest that active support from scientific journals might be essential in addressing these crucial issues.
Figure 1: Study selection
Full texts were excluded for the following reasons: conference abstract or case report (n=3), no epidemiological aims (n=12), drug resistance prediction (n=2), inadequate or no use of whole genome sequencing (n=6), did not meet inclusion criteria (n=2).
Figure 2: Proportion of STROME-ID criteria fulfilled before (A) and after (B) publication of the STROME-ID guidelines

For this analysis, a 6-month lag period was used; studies published within 6 months of STROME-ID publication were classified as before publication instead of after publication. Definitions of the criteria are provided in appendix 1 (pp 14–15). STROBE=Strengthening the Reporting of Observational Studies in Epidemiology. STROME-ID=Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases.
Table 1:
Summary of included studies

| Year | Study aims | Location | Sample size of isolates | Sample size of patients | Sequencing platforms |
|------|------------|----------|-------------------------|-------------------------|----------------------|
| 2018 | Elucidate transmission dynamics and describe resistance-conferring mutations | Saudi Arabia | 205 | NR | Illumina NextSeq |
| 2019 | Compare genotype techniques to determine transmission in a low-incidence country | Sweden | 100 | 52 | Illumina HiSeq |
| 2019 | Explore countrywide transmission routes, strain dynamics, and bacterial evolution | Serbia | 103 | 110 | Illumina MiSeq, HiSeq |
| 2016 | Describe XDR-TB cluster in the UK | UK | 4 | 35 | NR |
| 2018 | Determine genomic transmission links between individuals without an epidemiologic link | South Africa | 342 | 386 | Illumina MiSeq |
| 2018 | Infer whether cases represent important or local transmission | Norway | 129 | 127 | Illumina MiSeq, NextSeq |
| 2018 | Describe strains driving the epidemic and associated drug resistance mutations | Papua New Guinea (Daru Island) | 100 | NR | Illumina MiSeq |
| 2019 | Examine transmission in remote, high-incidence region | Tunisia | 46 | 46 | Illumina MinSeq |
| 2017 | Distinguish between outbreak cases of relapse from reactivation in UK | UK (England) | 17 | 25 | Illumina MiSeq |
| 2016 | Describe genomic epidemiology of subpopulations in two cities | USA | 71 | NR | Illumina HiSeq |
| 2013 | Estimate usefulness of the molecular clock to refute and affirm epidemiological links | Amsterdam, Estonia | 199 | 199 | Illumina Genome Analyzer IIx |
| 2019 | Assess association between exposure to community settings and MDR-TB infection | Peru | 59 | 59 | NR |
| 2018 | Describe WGS-based model for tuberculosis diagnosis and surveillance | Italy | 298 | 56 | Illumina MinSeq |
| 2012 | Examine microevolution of Beijing strains and spread of drug resistance | Russia | 2348 | 2348 | Illumina Genome Analyzer GAII |
| 2014 | Explore molecular mechanisms determining transmissibility and prevalence of drug-resistant strains | Russia | 1000 | 2348 | Illumina Genome Analyzer GAIL, HiSeq |
| 2016 | Compare WGS and MIRU-VNTR to resolve the transmission network within outbreak | UK (England) | 344 | 501 | Illumina HiSeq |
| 2017 | Characterise genotypic drug resistance | India | 74 | NR | Illumina MiSeq |
| 2013 | Understand emergence and acquisition of MDR-TB among treated patients with tuberculosis | Uganda | 51 | 41 | Illumina HiSeq |
| 2015 | Describe evolution of XDR-TB | African continent | 337 | 337 | Illumina HiSeq |
| Year   | Study aims                                                                 | Location                | Sample size of isolates | Sample size of patients | Sequencing platforms       |
|--------|-----------------------------------------------------------------------------|-------------------------|-------------------------|--------------------------|-----------------------------|
| 2015   | Describe population genomics in Africa and evolutionary origin of tuberculosis | Ethiopia                | 285                     | 2151                     | Illumina HiSeq              |
| 2013   | Describe evolutionary history of humans and tuberculosis                    | 46 countries            | 259                     | 259                      | Illumina, model unspecified |
| 2015   | Describe the genomic epidemiology of MDR-TB among refugees in the USA       | USA                     | 57                      | 45                       | Illumina HiSeq              |
| 2017   | Analyse transmission dynamics of patients with XDR-TB                       | African continent       | 149                     | 237                      | Illumina HiSeq              |
| 2019   | Study evolution of isolates within an MDR-TB cluster                        | Peru (Lima)             | 61                      | 60                       | Illumina HiSeq              |
| 2018   | Describe the epidemiological and genomic determinants of two outbreaks       | Canada                  | 75                      | 75                       | Illumina HiSeq              |
| 2017   | Determine timeline of drug-resistance evolution during an outbreak           | Argentina               | 252                     | NR                       | Illumina HiSeq, MiSeq       |
| 2017   | Investigate cross-border MDR-TB transmission                                 | Austria, Romania, Germany | 10                      | 13                       | Illumina MiSeq              |
| 2011   | Describe outbreak transmission with WGS and social network analysis         | Canada                  | 36                      | 41                       | Illumina Genome Analyzer II |
| 2018   | Describe the genomic epidemiology of tuberculosis in Tasmania               | Australia (Tasmania)    | 18                      | 18                       | Illumina MiSeq              |
| 2017   | Analyse the genomic content of the Rangipo strain                           | New Zealand             | 9                       | NR                       | Illumina MiSeq              |
| 2019   | Describe tracing of linked cases in an outbreak using WGS                   | France                  | 14                      | 14                       | Illumina MiSeq              |
| 2015   | Assess cases attributed to transmission from close contacts                  | Malawi                  | 406                     | 1907                     | Illumina HiSeq              |
| 2015   | Conduct district-wide analysis to examine transmission over time            | Malawi                  | 1687                    | 2332                     | Illumina HiSeq              |
| 2015   | Assess effect of different factors on the rate of recurrence due to reinfection or relapse | Malawi                  | 1933                    | 903                      | Illumina HiSeq              |
| 2016   | Understand local transmission in a low-incidence setting                     | Australia               | 30                      | 1692                     | Ion Torrent                 |
| 2018   | Understand transmission dynamics of paediatric tuberculosis in a low-incidence setting | Canada                  | 49                      | 49                       | Illumina HiSeq              |
| 2018   | Describe extent of transmission based on a mass-screening exercise          | Singapore               | 10                      | 6                        | Illumina, model unspecified |
| 2018   | Describe results of an outbreak investigation                               | UK (England)            | 2                       | 2                        | Illumina HiSeq              |
| 2018   | Examine transmission dynamics                                               | Vietnam                 | 1635                    | 2091                     | Illumina HiSeq              |
| 2019   | Describe the epidemiological and drug-resistance characteristics of MDR-TB  | China                   | 357                     | 357                      | Illumina HiSeq              |
| 2009   | Investigate the causes and evolution of drug resistance                     | South Africa            | 11                      | NR                       | Illumina GAII               |
| 2010   | Understand the mechanism of drug resistance among a subgroup of the Beijing strain | South Africa            | 14                      | NR                       | Illumina, model unspecified |
| 2018   | Determine drug resistance and assess criteria against putative resistance associated with variants | South Africa            | 391                     | 401                      | Illumina MiSeq              |
| Year | Study aims                                                                 | Location        | Sample size of isolates | Sample size of patients | Sequencing platforms       |
|------|-----------------------------------------------------------------------------|-----------------|-------------------------|-------------------------|---------------------------|
| 2018 | Analyse transmission dynamics among asylum seekers and assess precision of VNTR typing versus WGS | Netherlands     | 40                       | 40                      | Illumina NextSeq          |
| 2018 | Investigate if WGS more accurately predicts epidemiological links between patients than VNTR | Netherlands     | 535                      | 527                     | Illumina HiSeq            |
| 2018 | Determine incidence of tuberculosis in close contacts and transmission       | China           | 4584                     | 1765                    | NR                        |
| 2018 | Describe the microevolution during an outbreak of drug susceptible tuberculosis | USA             | 9                        | 11                      | Illumina, model unspecified |
| 2013 | Identify genomic differences between Beijing and Manila families              | USA             | 82                       | NR                      | Illumina MiSeq            |
| 2019 | Investigate tuberculosis transmission clusters using WGS versus VNTR typing  | USA             | 16                       | 15                      | Illumina MiSeq            |
| 2018 | Characterise genomic diversity of foreign-born and Japan-born residents in Tokyo | Japan           | 259                      | 91                      | Illumina MiSeq            |
| 2015 | Determine whether recurrent cases were caused by relapse versus reinfection  | Finland         | 21                       | 21                      | Illumina MiSeq            |
| 2016 | Delinete transmission networks and investigate benefits of WGS during cluster investigation | UK (England)   | 22                       | 22                      | Illumina MiSeq, Genome Analyzer II, HiSeq |
| 2018 | Determine extent of primary acquired MDR-TB cases                           | South Africa    | 97                       | NR                      | Illumina Genome Analyzer IIX |
| 2015 | Explore epidemiological links during an outbreak                             | Canada          | 42                       | 933                     | Illumina MiSeq            |
| 2015 | Describe genomic features of an epidemiologically successful strain over time | Canada          | 163                      | NR                      | Illumina MiSeq            |
| 2015 | Characterise global diversity of 358 Beijing strains                         | China           | 908                      | NR                      | Illumina HiSeq            |
| 2015 | Compare VNTR and WGS to study the transmission in a highburden setting       | China           | 32                       | 42                      | Illumina HiSeq            |
| 2015 | Explore transmission dynamics of an outbreak in a boarding school            | China           | 33                       | 46                      | Ion Torrent               |
| 2015 | Compare WGS and classical genotyping methods to determine transmission chains | Portugal        | 83                       | 83                      | Illumina MiSeq            |
| 2019 | Identify drug-resistant mutations in an endemic region                       | Mexico          | 91                       | 91                      | Illumina NextSeq          |
| 2019 | Examine transmission dynamics and drug resistance-conferring mutations among patient with tuberculosis and HIV coinfection | Vietnam         | 200                      | 200                     | Illumina NextSeq          |
| 2018 | Determine if MDR-TB strains genotypically similar to those in Eswatini were also present in South Africa | South Africa    | 277                      | 277                     | Illumina HiSeq, MiSeq     |
| 2018 | Determine the population structure and transmission dynamics                 | Congo           | 75                       | 211                     | Illumina MiSeq            |
| 2017 | Describe prevalence of strains and evolution of drug-resistance mutations    | India           | 223                      | 196                     | Illumina HiSeq            |
| 2017 | Determine acquisition timeline of MDR drug-resistance mutations             | 48 countries    | 5310                     | NR                      | Illumina, model unspecified |
| Year       | Study aims                                                                 | Location                          | Sample size of isolates | Sample size of patients | Sequencing platforms          |
|------------|---------------------------------------------------------------------------|-----------------------------------|-------------------------|-------------------------|-------------------------------|
| 2017       | Use WGS data to identify within-host heterogeneity among patients in British Columbia | Canada                            | 25                      | NR                      | Illumina HiSeq               |
| 2018       | Identify transmission events associated with cases due to ON-A strain       | Canada                            | 61                      | 57                      | Illumina, model unspecified  |
| 2015       | Reconstruct evolutionary history of Beijing lineage                        | 99 countries                      | 4987                    | NR                      | Illumina MiSeq               |
| 2015       | Analyse evolutionary history of drug resistance and transmission networks of MDR-TB isolates | Uzbekistan                        | 277                     | 277                     | Illumina MiSeq, HiSeq        |
| 2018       | Examine mutation rates in Beijing strains from regions with MDR-TB        | Germany, Georgia, Uzbekistan      | NR                      | 3                       | Illumina, model unspecified  |
| 2013       | Describe molecular epidemiology of patients with tuberculosis living in localised area | Japan                             | 169                     | 169                     | Illumina MiSeq               |
| 2017       | Describe evolutionary origin of NEW-1 family in the EuroAmerican lineage  | China, Tibet, Iran, Russia, Kazakhstan | 5715                   | NR                      | Illumina MiSeq               |
| 2017       | Characterised population genetics of known drug resistance loci           | Russia, South Africa              | 1161                    | NR                      | Illumina HiSeq               |
| 2018       | Evaluate XDR-TB transmission within and between municipal districts in KwaZulu-Natal | South Africa                      | 344                     | 344                     | Illumina MiSeq               |
| 2018       | Report use of WGS to delineate an outbreak                                | Norway                            | 22                      | 24                      | Illumina MiSeq, NextSeq      |
| 2017       | Investigate suspected outbreak of eight cases                             | Haiti                             | 8                       | 8                       | Illumina HiSeq               |
| 2019       | Reconstruct lineage-specific patterns of spread in Africa and Eurasia     | 51 countries                      | 552                     | NR                      | NR                            |
| 2018       | Compare evolution of tuberculosis and influence of human migration from two lineages | Ghana                             | 214                     | NR                      | Illumina HiSeq, NextSeq      |
| 2018       | Clarify transmission pathways and explore the evolution of an outbreak     | Australia                         | 23                      | 23                      | Illumina HiSeq               |
| 2016       | Investigate transmission within an educational institution                | UK (England)                     | 5                       | 10                      | Illumina MiSeq               |
| 2019       | Evaluate genetic makeup of tuberculosis lineages circulating in the Middle East | Lebanon                           | 13                      | 13                      | Illumina MiSeq               |
| 2018       | Analyse reinfection and reactivation rates                                | Australia                         | 15                      | 18                      | Illumina NextSeq             |
| 2018       | Determine genomic diversity and microevolution of MDR-TB and XDR-TB       | Portugal                          | 56                      | NR                      | Illumina HiSeq               |
| 2014       | Examine microevolution of tuberculosis within intrapatient and interpatient scenarios | Spain                             | 36                      | NR                      | Illumina HiSeq               |
| 2014       | Investigate outbreak of MDR-TB                                            | Thailand                          | 64                      | 148                     | Illumina HiSeq               |
| 2015       | Identify outbreak-related transmission chains                              | Germany                           | 86                      | 86                      | Illumina, model unspecified  |
| 2013       | Examine acquisition and spread of MDR-TB                                  | Ireland                           | 42                      | 41                      | Illumina MiSeq               |
| 2018       | Examine association between tuberculosis genotype and susceptibility to tuberculosis meningitis | Indonesia                         | 106                     | 322                     | Illumina HiSeq               |
| Year | Study aims |
|------|------------|
| 2018 | Determine geographical origin of Beijing strain and spread across Africa |
| 2019 | Assess distribution of Beijing lineage |
| 2015 | Examine genetic variation of outbreak samples |
| 2016 | Use WGS to study epidemiology of an outbreak |
| 2010 | Understand epidemiology and genetics of MDR-TB |
| 2017 | Define recent transmission clusters and timing of transmission |
| 2018 | Describe population-level transmission of XDR-TB |
| 2017 | Describe outbreak using WGS and IGRA |
| 2018 | Assess prevalence of mixed infection and correlation with patient characteristics and outcomes |
| 2018 | Study outbreak dynamics |
| 2015 | Assess transmission among Swiss-born and foreign-born patients with tuberculosis |
| 2016 | Understand global population structure of lineage 4 and its evolution |
| 2016 | Characterise genomic diversity of outbreak clusters |
| 2017 | Explore drug resistance and transmission dynamics |
| 2019 | Estimate genetic diversity of related strains and investigate community outbreaks |
| 2013 | Explore epidemiology of transmission |
| 2014 | Describe origin of transmission cluster |
| 2018 | Understand geographic distribution of lineages 5 and 6 |
| 2016 | Determine proportion of cases attributable to relapse and reinfection |
| 2017 | Understand evolution of MDR-TB and XDR-TB |
| 2017 | Determine proportion of linked tuberculosis isolates that are closely genomically related |
| 2018 | Assess transmission of MDR-TB and identify transmission risk factors |
| 2017 | Describe transmission dynamics in an urban setting |

| Location |
|----------|
| Africa |
| Guatemala |
| UK (England) |
| Netherlands |
| Nigeria |
| USA |
| South Africa |
| Finland |
| Malawi, Portugal |
| Switzerland |
| Switzerland |
| 100 countries |
| Canada |
| Iran |
| England |
| England |
| Germany, Switzerland, France, England, Somalia, Ethiopia, Eritrea |
| Mali |
| South Africa, Zimbabwe, Botswana, Zambia |
| Belarus |
| England |
| China |
| China |

| Sample size of isolates | Sample size of patients | Sequencing platforms |
|-------------------------|-------------------------|----------------------|
| 781                     | 781                     | Illumina HiSeq       |
| 5                       | 5                       | Illumina HiSeq, MiSeq |
| 16                      | NR                      | Illumina HiSeq       |
| 3                       | NR                      | Genome Sequencer     |
| 63                      | 5                       | Illumina MiSeq       |
| 21                      | 82                      | Illumina MiSeq       |
| 298                     | 404                     | Illumina MiSeq       |
| 12                      | 14                      | NR                   |
| 48                      | 10                      | Illumina HiSeq, MiSeq |
| 69                      | 68                      | Illumina, model unspecified |
| 90                      | 93                      | Illumina HiSeq, MiSeq, NextSeq |
| 293                     | NR                      | Illumina MiSeq, HiSeq2000/250, NextSeq |
| 233                     | NR                      | Illumina NextSeq     |
| 38                      | 892                     | Illumina NextSeq     |
| 390                     | 254                     | Illumina HiSeq       |
| 247                     | 269                     | Illumina HiSeq       |
| 58                      | 29                      | Illumina, model unspecified, Ion Torrent |
| 92                      | NR                      | Illumina, model unspecified |
| 36                      | 51                      | Illumina HiSeq       |
| 138                     | 97                      | Illumina HiSeq       |
| 1999                    | 1999                    | Illumina MiSeq       |
| 324                     | 324                     | Illumina HiSeq       |
| 218                     | NR                      | Illumina HiSeq       |
| Year | Study aims | Location | Sample size of isolates | Sample size of patients | Sequencing platforms |
|------|------------|----------|-------------------------|-------------------------|----------------------|
| 2018 | Identify genomic features of lineage 7 strains | Ethiopia | 30 | NR | Illumina MiSeq |

NR=not reported. XDR-TB=extensively drug-resistant tuberculosis. MDR-TB=multidrug-resistant tuberculosis. WGS=whole genome sequencing. MIRU-VNTR=mycobacterial interspersed repetitive unit-variable number tandem repeats. VNTR=variable number tandem repeats. IGRA=interferon γ release assay.
Table 2:
Mean proportions of STROME-ID criteria fulfilled before and after guideline publication

|                | Proportion of criteria fulfilled before STROME-ID publication (%) | Proportion of criteria fulfilled after STROME-ID publication (%) | p value |
|----------------|------------------------------------------------------------------|-----------------------------------------------------------------|---------|
| 6-month lag period * | 51% (11)                                                          | 46% (14)                                                        | 0.26    |
| 12-month lag period   | 48% (14)                                                          | 51% (11)                                                        | 0.52    |
| 6-month exclusion period † | 46% (14)                                                          | 46% (14)                                                        | 0.98    |
| 12-month exclusion period ‡ | 48% (14)                                                          | 49% (14)                                                        | 0.71    |

Data are mean (SD). STROME-ID=Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases.

* For these analyses, studies published within either 6 or 12 months of STROME-ID publication were classified as before publication instead of after publication (ie, we assumed that authors might not have seen the guidelines or had the opportunity to incorporate them within the first 6 or 12 months).

† For these analyses, papers published within 6 or 12 months of STROME-ID publication were excluded from the analysis altogether.
Table 3:
Quasi-Poisson univariate and multivariate analyses of study characteristics

| Impact factor of journal | Univariate analysis | Multivariate analysis |
|--------------------------|---------------------|-----------------------|
|                          | IRR (95% CI)        | p value               | IRR (95% CI)        | p value               |
| 0 to <5                  | 1 (ref)             | -                     | 1 (ref)             | -                     |
| 5 to <10                 | 1·10 (1·00–1·21)    | 0·062                 | 1·09 (0·98–1·22)    | 0·11                  |
| 10 to <20                | 1·20 (1·03–1·38)    | 0·020                 | 1·18 (1·00–1·39)    | 0·055                 |
| ≥20                      | 1·13 (1·00–1·28)    | 0·049                 | 1·11 (0·97–1·28)    | 0·14                  |
| h-index                  | 1·00 (1·00–1·00)    | 0·37                  | NA                  | NA                    |

| Continent of senior author | Univariate analysis | Multivariate analysis |
|----------------------------|---------------------|-----------------------|
| Americas *                 | 1 (ref)             | -                     | 1 (ref)             | -                     |
| Africa                     | 0·97 (0·79–1·18)    | 0·79                  | 0·98 (0·80–1·19)    | 0·83                  |
| Asia                       | 0·93 (0·81–1·08)    | 0·37                  | 0·96 (0·80–1·12)    | 0·62                  |
| Europe                     | 0·93 (0·84–1·02)    | 0·13                  | 0·92 (0·83–1·01)    | 0·90                  |
| Oceania                    | 0·91 (0·76–1·09)    | 0·30                  | 0·95 (0·79–1·14)    | 0·60                  |

| Sample size of isolates   | Univariate analysis | Multivariate analysis |
|----------------------------|---------------------|-----------------------|
| <30                        | 1 (ref)             | -                     | 1 (ref)             | -                     |
| 30–152                     | 1·03 (0·92–1·15)    | 0·65                  | 1·00 (0·89–1·13)    | 0·97                  |
| 153–276                    | 1·05 (0·90–1·21)    | 0·53                  | 1·01 (0·86–1·18)    | 0·95                  |
| ≥277                       | 1·11 (0·99–1·25)    | 0·088                 | 1·04 (0·91–1·19)    | 0·55                  |

IRR=incidence rate ratio. NA=not applicable.

* North America and South America were combined because only one study was from South America.