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Exploring the diagnostic synergy of isothermal amplifications integrated CRISPR technology for Tuberculosis: A systematic review

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Running Title: Isothermal amplification integrated CRISPR based Tuberculosis diagnosis

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Abstract

To address the problems linked with *Mycobacterium tuberculosis* (MTB) detection, we need an accurate, sensitive, and faster detection method for efficient epidemiological management for tuberculosis (TB) diagnosis. Nucleic acid-based diagnosis of TB is more sensitive and specific but majorly requires trained workers and costly infrastructure. Isothermal amplification methods due to their negligible infrastructure requirements have paved way for the efficient and rapid diagnosis of TB, however, they sometimes suffer with drawbacks like false positive results, challenges in primer designing. With progress in clustered regularly interspaced short palindromic repeats-CRISPR associated protein (CRISPR-Cas) integrated nucleic acid detection methods the above limitations are being overcome for pathogen detection. The combination of CRISPR with any suitable isothermal technologies like recombinase polymerase amplification (RPA) or loop-mediated isothermal amplification (LAMP), offers several advantages due to the higher sensitivity, specificity, versatility and reproducibility as a point of care. Thus, in this systematic review, we aimed to provide a comprehensive overview of the various isothermal amplification methods coupled CRISPR-based TB diagnostic studies that are reported in the literature. About 12 articles were included in this review using predefined selection criteria. Data were extracted for detailed review from PubMed, Google Scholar and Science Direct and the diagnostic efficiency was evaluated. The data uncovered that most of the studies were conducted in China with *IS6110* and *IS6108* as the major target genes utilised. The most used detection methods were based on fluorescence and lateral flow. Analytical sensitivity, defined by the limit of detection, ranged between 10 and 20 copies/µL. Diagnostic sensitivity and specificity were consistently high, ranging from 95 to 100 %. Diagnostic sensitivity and specificity were consistently high, ranging from 95 to 100 %. Taken together, the synergy between Isothermal amplification methods and

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CRISPR-Cas technique could be a potential alternative to qPCR, GeneXpert, and conventional acid-fast staining, particularly in low-resource regions for easy and rapid TB diagnosis.

Key words: Tuberculosis; *Mycobacterium tuberculosis*; isothermal amplification; LAMP; RPA; RAA; RCA; CRISPR-Cas

Introduction

Tuberculosis (TB), caused by the pathogen *Mycobacterium tuberculosis* (MTB), persists as a major global health threat and ranks among the foremost infectious diseases responsible for high morbidity and mortality worldwide. According to the World Health Organization (WHO), TB continues to be a major global health challenge, with an estimated 10 million people falling ill with TB in 2024 and 1.5 million deaths (WHO, 2024). TB primarily affects the lungs but can also impact other organs, leading to extrapulmonary TB. Despite significant advances in medicine, TB still presents a serious public health challenge, especially in resource-limited settings where timely and accurate diagnosis remains a critical barrier to effective treatment (Yayan et al., 2024).

Isothermal amplification techniques, including Loop-mediated Isothermal Amplification (LAMP), Recombinase Polymerase Amplification (RPA), Rolling Circle Amplification (RCA), and Recombinase-Aided Amplification (RAA), offer significant advantages over traditional PCR methods. These methods amplify DNA/RNA at a constant temperature, eliminating the need for a

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thermal cycler, which makes them more accessible and portable for use in low-resource settings (Notomi et al., 2000; Srivastava et al., 2015; Wong et al, 2018). LAMP has been widely used for the detection of various pathogens, including MTB, due to its simplicity, high sensitivity, and specificity (Bumbrah et al., 2023, Kaushik et al 2025). RPA and RAA also offer similar advantages, including rapid amplification times and the ability to operate at ambient temperatures, which enhances their suitability for field diagnostics (Liu et al., 2017, Lobato et al 2017, Li X et al 2023)

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated systems, CRISPR-Cas, have revolutionized genetic research, but their application in diagnostics has gained significant attention recently. CRISPR-Cas systems have been adapted for use in molecular diagnostics, particularly for pathogen detection, due to their high specificity, sensitivity, and ability to detect minute quantities of nucleic acid (Huang et al 2022, Koonin et al, 2017). CRISPR-based diagnostics, such as SHERLOCK and DETECTR, offer the potential for rapid, portable, and cost-effective testing for infectious diseases, including TB (Mustafa et al 2021, Yang et al 2023, Ghouneimy et al 2022, Myhrvold et al., 2018; Gootenberg et al., 2018). The integration of CRISPR-Cas systems with various isothermal amplification techniques, such as LAMP, RPA, RCA, and RAA, holds promise for creating highly sensitive and specific diagnostic platforms that

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can be used in resource-limited settings for the early detection of TB (Yigci et al 2023, Mao et al 2023, Ding et al., 2020; Li et al., 2021).

Literature survey and inclusion of studies

A systematic literature survey was carried out to identify and select relevant studies focusing on the application of isothermal amplification techniques in MTB diagnostics. The search was conducted across three scientific databases: PubMed, Google Scholar, and ScienceDirect. The time frame for the search spanned from the year 2020 to 2025. The primary keywords used during the database queries were "*Mycobacterium tuberculosis*", "Isothermal amplification techniques," “CRISPR”, LAMP, RPA, RAA and RCA. In PubMed, a total of 107 articles were retrieved, with publication dates ranging from 2003 to 2025. When the keyword "CRISPR" was included in the search within PubMed, only 3 articles were found, all of which were published between 2020 and 2025. On Google Scholar, the same keyword filters yielded 4,170 results. All eligible studies were included regardless of access status. Further narrowing the search with the term "CRISPR" brought the number down to 509. Science Direct returned 98 relevant results under the initial search conditions. Combining the results from all three databases, a total of 610 articles were identified for initial consideration. Given the recent emergence and integration of these isothermal amplification techniques into MTB diagnostics, the literature search was limited to studies published between January 2020 and March 2025. The screening process began with the exclusion

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of 64 articles that were written in languages other than English, leaving 546 English-language articles. From this pool, 207 articles were excluded due to duplication or because they focused on organisms other than MTB. This step reduced the number of eligible articles to 339. Further evaluation led to the removal of 210 articles because they did not include both isothermal amplification techniques and CRISPR-based diagnostic applications. The inclusion of CRISPR as one of the diagnostic components was a mandatory criterion for all selected studies. This refinement resulted in 129 articles that specifically addressed MTB diagnostics using isothermal amplification technologies. A closer inspection of these 129 studies resulted in the exclusion of 84 articles due to their irrelevance in content. The remaining 65 articles were then examined for methodological consistency and relevance. These articles included studies on isothermal amplification methods such as Loop-Mediated Isothermal Amplification (LAMP), Recombinase Polymerase Amplification (RPA), Rolling Circle Amplification (RCA), and Recombinase-Aided Amplification (RAA). Out of these, 53 articles were excluded, which were categorized as review papers, editorials, book chapters, commentaries, or conference abstracts, as they did not constitute original research. Ultimately, 12 articles fulfilled all the inclusion criteria and were finally considered (Figure 1) and their study characteristics are listed in Table 1 and discussed in subsequent sections.

Loop-Mediated Isothermal Amplification (LAMP)

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Loop-mediated isothermal amplification (LAMP) is a nucleic acid amplification method that operates at a constant temperature, typically between 60-65°C, and is facilitated by the use of a set of four to six primers that target different regions of the DNA. This technique allows for the amplification of DNA in a rapid, simple, and cost-effective manner without the need for sophisticated thermal cyclers (Notomi et al., 2000). LAMP has shown considerable promise in the detection of MTB due to its sensitivity and specificity. Studies have demonstrated that LAMP can detect low concentrations of MTB DNA in sputum samples, even in the presence of other respiratory pathogens (Parida et al., 2008). Recent advancements in CRISPR-based detection have overcome these issues by enhancing the specificity of LAMP, ensuring a more accurate and rapid diagnostic approach (Sam et al 2021, Wang et al 2021, Kaushik et al.,2025)

Recombinase Polymerase Amplification (RPA)

Recombinase polymerase amplification (RPA) is another isothermal amplification technique that is faster than traditional PCR, as it operates at a constant temperature of 37-42°C. RPA employs recombinase enzymes to facilitate strand displacement and polymerase for amplification, making it an efficient method for DNA detection (Lobato et al 2017). Notable success has been achieved in RPA base MTB detection and due to the rapid amplification duration, results are often achieved within 20 minutes making it more advantages in terms of the minimal infrastructure requirements and operational simplicity (Li et al., 2015). The combination of RPA with CRISPR technology

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further enhances the specificity and sensitivity of the assay, making it ideal for field-based diagnostics (Xu et al 2020, Jia et al 2023). CRISPR's high specificity ensures that the amplified product is accurately detected, even at low concentrations of MTB DNA, providing a highly sensitive tool for TB detection (Liu et al., 2021, Xiao et al 2023, Thakku et al 2023).

Rolling Circle Amplification (RCA)

Rolling circle amplification (RCA) is an isothermal amplification technique that uses a single-stranded DNA or RNA template to generate long, concatemeric DNA products. From less number of samples, RCA has ability to produce large quantities of DNA making it an attractive method in diagnostics (Sun et al., 2024). RCA has been utilized to detect MTB with high efficiency, in clinical samples (Huang et al., 2017). When integrated with CRISPR technology, RCA can be used to enhance detection sensitivity further. CRISPR-Cas systems, such as Cas12 and Cas13, can be utilized for the specific detection of amplified products, enabling real-time monitoring of the DNA amplification process and reducing false positives (Gootenberg et al., 2018, Sun et al 2024). This combination offers a promising tool for the rapid and accurate detection of TB in resource-limited settings.

Recombinase-Aided Amplification (RAA)

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Recombinase-aided amplification (RAA) is another isothermal amplification method similar to RPA, but it uses recombinase enzymes to bind to single-stranded DNA, forming a heteroduplex with a primer, which allows for amplification at a constant temperature (Liu et al., 2017). RAA has been shown to provide fast, accurate, and sensitive results for MTB detection, often in less than 30 minutes. The major advantage of RAA over traditional PCR is its ability to perform amplification at lower temperatures, making it more suitable for point-of-care diagnostics in low-resource settings. Coupling RAA with CRISPR systems can significantly enhance TB diagnostics by improving both sensitivity and specificity with high precision, ensuring accurate TB detection even in samples with low DNA concentrations (Li et al 2024; Myhrvold et al., 2018).

There are few key differences (Table 2) between LAMP, RPA/RAA, RCA and RCA in terms of primer design, amplification efficiency, specificity, cost and field suitability. LAMP, requires 4–6 primers targeting 6–8 regions, offers high specificity and inhibitor resistance, but primer design is complex and the method is sensitive to temperature fluctuations—false positives due to primer-dimers are well-documented. RPA/RAA, using only two primers and operating at 37–42 °C, delivers rapid results (≤20 min), tolerates more temperature variation, and is easier to design; however, it relies on proprietary enzymes that increase cost and may cause non-specific amplification without probe integration synapse. RCA uses simple padlock probes and single primers, but its reaction is slower (~1 h) and requires circular template preparation; it lends itself

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to multiplexing via concatemer production PMC offers a concise visual overview of these comparisons.

Mechanism of CRISPR-Cas in Diagnostics

CRISPR-based diagnostics show great sensitivity, specificity, speed, and cost-effectiveness. This makes them ideal for point-of-care testing, especially in resource-limited settings. The CRISPR-Cas system, originally discovered as a bacterial immune mechanism, has been adapted for use in molecular diagnostics due to its high specificity and sensitivity. The CRISPR-Cas system functions by utilizing a guide RNA (gRNA) to direct the Cas protein (typically Cas9, Cas12, or Cas13) to a specific DNA or RNA target. Upon recognition of the target sequence, Cas proteins induce a detectable change, such as DNA cleavage in the case of Cas12 or in case of Cas13 ssRNA is cleaved, making it an ideal tool for diagnostic purposes (Thabet et al 2017, Wang et al 2021, Kaushik et al 2025). For example, the CRISPR-Cas12 and Cas13 systems are often coupled with isothermal amplification techniques to increase the sensitivity of pathogen detection (Thakku et al 2023). The key advantage of using CRISPR in diagnostics is its ability to recognize specific sequences with high accuracy, even in the presence of closely related sequences, which makes it far more specific than traditional PCR-based methods (Gootenberg et al., 2018; Kaushik et al, 2025; Bhatt et al, 2022 Diagnosing MTB begins with isolating the nucleic acid in the patient sample. The extracted nucleic acid is processed and amplified using isothermal techniques like

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recombinase polymerase amplification (RPA) or loop-mediated isothermal amplification (LAMP). These methods are preferred because they need less equipment than traditional PCR. Using RPA or LAMP speeds up the diagnostic process, allowing quick and sensitive detection of MTB. This makes the CRISPR-Cas system a promising diagnostic tool for facilities with limited infrastructure (Table 2).

As an isothermal technology, LAMP works at a constant temperature, which simplifies the amplification step. In contrast, PCR needs complex equipment, such as a thermal cycler. LAMP's rapid and efficient nature enables amplification in just 30 to 60 minutes. Its integration with Cas12b, a thermostable CRISPR-associated nuclease, boosts the system’s effectiveness by allowing for one-pot detection. This method streamlines workflows, shortens diagnostic time, reduces dependence on complicated equipment, and lowers the risk of cross-contamination. Upon target recognition (cis-cleavage), Cas12 (DNA target) and Cas13 (RNA target) undergo conformational changes that induce robust trans-cleavage, enabling non-specific cutting of nearby single-stranded nucleic acid reporters (e.g., ssDNA for Cas12, ssRNA for Cas13). This collateral activity provides signal amplification, wherein one target molecule can activate multiple reporter-cleavage cycles, increasing assay sensitivity. Detection outputs include: Fluorophore-quencher reporters, yielding fluorescence upon reporter cleavage and lateral flow strips, where labelled reporters produce visual bands as shown by systematic diagram

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in (Fig 2). Moreover, CRISPR-based assays can be performed rapidly and without sophisticated equipment, making them well-suited for point-of-care diagnostics (Myhrvold et al., 2018).

Another CRISPR-based diagnostic method for TB detection is DETECTR, which utilizes Cas12 for DNA detection (Jia et al 2023). DETECTR detects MTB DNA in a two-step manner, where firstly, isothermal methods like LAMP amplify the DNA/RNA, and then CRISPR-Cas12-based detection precisely identifies (Gan et al, 2024). This combination not only enhances sensitivity but also ensures faster results compared to traditional methods such as culture and PCR. The CRISPR-Cas12 system's ability to generate a signal in the presence of amplified DNA further enhances the speed and accessibility of diagnostic testing, which is crucial in the timely management of TB cases (Thakku et al., 2023).

The sensitivity of CRISPR-based assays is also noteworthy. Because the Cas proteins can be programmed to target highly specific sequences, the system can detect even small quantities of genetic material, often down to a single copy of the target sequence (Kaushik et al 2025). This level of sensitivity is particularly beneficial when dealing with pathogens that are present in low concentrations in clinical samples, such as MTB. Additionally, CRISPR-based diagnostics can be adapted for the detection of multiple pathogens in a single assay, offering a multiplexing capability that further enhances diagnostic accuracy and utility.

Characteristics of the included studies

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The figure 3 depicted by Sankey diagram shows the number of studies from different countries that focus on using any isothermal amplification techniques combined with CRISPR to detect MTB. Out of the 12 studies included, China leads by a wide margin with 9 studies. India, the USA and Thailand each contributed one study. The figure highlights China's strong advocacy for the usage of isothermal amplification linked CRISPR diagnosis for TB. Figure 4 depicted as the bar chart shows different types of samples used in the 12 studies included in our study on CRISPR-based diagnostics for MTB. Sputum was the most used specimen, appearing in 11 of the studies. Bronchoalveolar lavage fluid (BALF) came next, used in 4 studies. Other types of specimens viz. serum, urine, tissue, blood, hythorax, and pus were each used individually in just 1 study. While sputum remains the preferred choice for MTB detection, this figure also reflects a small but notable interest in exploring other sample types. Figure 5 depicted by bar chart illustrates the distribution of target genes used across all the studies in our analysis. Each bar represents the number of articles that utilized a specific gene as their molecular target for detection or analysis. Among all, *IS6110* was the most frequently used target gene, appearing in 8 studies, highlighting its popularity and potential reliability in diagnostic assays. *IS1081* emerged as the second most frequently targeted gene, reported in 6 studies. The use of *rpoB* and *rpsl* was relatively limited, featuring in only 2 and 1 articles, respectively. This figure emphasizes the variability in gene targets chosen by different researchers and underscores *IS6110* prominence in the current body of literature. Figure 6 depicted as two pie charts shows the distribution of different detection methods (left) and reference

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standard methods (right) reported in 12 studies that focused on CRISPR-based diagnostics for MTB. We separated them to make it easier to compare how often each method was used. For detection, gel electrophoresis and fluorescence-based assays were the most common, each used in 28% of the studies (7 out of 12). RT-PCR came next at 24% (6 studies), followed by lateral flow methods at 16% (4 studies). A colorimetric method was used in just one study, making up 4%. On the reference side, GeneXpert and AFB culture was the most frequently used comparator, appearing in 33 % of the included studies respectively. While the ZN-Staining and Sanger sequencing method covering 14% and 10% of the studies, other methods like Bactec960 and qPCR made up the remaining references accounting for **5%** of the total studies.. By showing these two charts side-by-side, the figure gives a clear picture of the methods being used to detect MTB and how their performance was validated. Figure 7 depicted by bar graph shows the utilization of various isothermal techniques alongside CRISPR in studies focused on MTB diagnostics. The combination of RPA and CRISPR is featured in six studies, while LAMP and CRISPR appear in three studies. RAA and CRISPR are used in two studies, and RCA with CRISPR is used in one study. This figure highlights the growing trend of combining CRISPR with isothermal methods for rapid and sensitive MTB detection. The analytical sensitivity (limit of detection) of the assays ranged from approximately 10–20 copies/µL. Their diagnostic sensitivity and specificity—when compared against reference standards—were typically between 95–100%%. Only one study showed a specificity of 95%. Most of the studies used the DNA isolation method for the detection

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of the MTB pathogen, but one study innovatively used RNA as a template for the detection of MTB. Also, the researcher uses different types of samples such as sputum, urine, serum, BALF, tissue, pus, blood, hythorax, etc.

Recent advances showcase a range of CRISPR-based tests for the quick, sensitive, and specific detection of M. tuberculosis. For example, WATSON uses genome-wide tiled amplification along with Cas13 detection to identify fragmented cfDNA in patient plasma, providing better sensitivity than single-locus tests and working well with lateral flow formats. On the amplification-free side, a Cas12a-GFET platform combines CRISPR detection with graphene field-effect transistors to directly measure serum DNA without pre-amplification. This setup achieves a detection limit of about 2.4×10^{-18} M and delivers results in under 5 minutes.

Methods that involve amplification, like MTB-MCDA-CRISPR, use isothermal multiple cross displacement amplification (MCDA) before Cas12a detection. This approach reaches 40 fg sensitivity in less than an hour and performs similarly to Xpert assays. Another isothermal method combines ERA (exonuclease-based amplification) with Cas12a, completing tests in about 40 minutes and offering nearly perfect predictive values, making it suitable for lateral flow readings. A simple Cas12a assay targeting IS6110 can be done in under 15 minutes, detecting roughly 3 CFU/mL while clearly distinguishing it from other bacteria. An in situ Cas12a-based assay applied to macrophages and BALF samples achieved 94% sensitivity, compared to 67–78% for culture or Xpert, and 100% specificity. While most reviewed assays report excellent sensitivity (95–100%) and low limits of detection (10–20 copies/μL), our analysis highlights several significant

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limitations rooted in study design and implementation. First, in the half of the studies employed case-control designs using convenience samples, potentially introducing spectrum bias—leading to inflated accuracy compared to performance in real-world, heterogeneous populations. Second, there was considerable heterogeneity in reference standards, with some studies using GeneXpert, others relying on culture or qPCR for confirmation. This raises concerns about verification bias and limits the validity of cross-study comparisons. Third, inconsistent fluorescence or signal thresholds across studies may explain variability in reported specificity (85–100%), emphasizing the need for standardized cut-offs. Fourth, only one study explicitly addressed negative or discordant results, suggesting the presence of publication bias, where studies reporting less favorable outcomes may remain unpublished.

Lastly, a multiplexed RCA-Cas12a system that targets the rpoB gene improves point-of-care detection for resistance and strain typing, though complete performance data were not provided. Overall, these platforms highlight important trends: genome-wide tiling, electrical sensing without amplification, fast isothermal amplification, and direct application on clinical samples. They deliver sub-femtomolar sensitivity, high specificity, and turnaround times of under an hour, showing strong promise for near-patient TB diagnostics.

Limitations and future directions

Despite the numerous advantages, there are several challenges associated with the integration of CRISPR and isothermal amplification techniques. One of the primary concerns is the sensitivity and detection limits of these integrated systems. While CRISPR enhances the specificity of

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isothermal amplification, detecting very low concentrations of DNA can still be challenging. In some cases, false negatives may occur if the amplification process is not efficient enough to generate a detectable signal (Myhrvold et al., 2018). To mitigate this, optimizing the amplification conditions and improving CRISPR systems for better sensitivity is crucial (Liu et al., 2021). Another significant challenge is the potential for false positives or negatives. False positives could arise due to non-specific amplification or contamination, while false negatives could occur if the CRISPR system does not efficiently detect low amounts of the target DNA. These issues can be overcome by carefully designing CRISPR guide RNAs to ensure high specificity, implementing stringent quality control measures, and using internal controls to confirm the validity of the results (Gootenberg et al., 2018; Li et al., 2015, Kaushik et al 2025, Bhatt et al 2022). Scalability and implementation in resource-limited settings are also critical challenges. While CRISPR-integrated isothermal amplification assays are cost-effective and portable, scaling them up for widespread use in low-resource settings requires significant investment in infrastructure, training, and supply chains. Moreover, ensuring the availability of reagents and consumables, such as CRISPR enzymes and primers, could pose challenges in remote regions (Ding et al., 2020). Addressing these issues will require collaboration between researchers, healthcare providers, and policymakers to ensure that these technologies are accessible and sustainable. Finally, regulatory and ethical considerations must be considered when developing CRISPR-based diagnostic tools. The use of gene-editing technologies in diagnostics raises concerns about potential misuse, data

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privacy, and regulatory approval processes. It is essential to establish clear regulatory frameworks to ensure that CRISPR-based diagnostics are safe, reliable, and compliant with ethical standards. Additionally, public acceptance and understanding of CRISPR technology will be vital for its successful integration into clinical practice. To address these limitations, future research should: (a) prioritize prospective, field-based studies in mixed patient cohorts to reduce spectrum bias; (b) adopt uniform reference standards or parallel validation methods to minimize verification bias; (c) establish harmonized detection threshold guidelines, ideally validated across multiple platforms; and (d) pre-register protocols and commit to publishing both positive and negative results to mitigate publication bias.. Such targeted strategies will strengthen the scientific rigor, reproducibility, and real-world applicability of isothermal amplification–CRISPR diagnostics for MTB.

Conclusion

The integration of isothermal amplification technologies, such as LAMP, RPA, RCA, and RAA, with CRISPR-Cas systems has the potential to revolutionize TB diagnostics. These integrated systems combine the strengths of both amplification techniques and CRISPR, resulting in highly sensitive, specific, and rapid diagnostic platforms. Isothermal amplification methods allow for efficient DNA amplification without the need for complex thermal cycling, making them ideal for field-based applications. When paired with CRISPR's ability to specifically target and cleave DNA

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or RNA, these systems can detect MTB with unprecedented accuracy, even in samples containing low amounts of DNA. This integration enhances the speed and cost-effectiveness of TB diagnosis, making it more accessible in resource-limited settings.

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Figure Legends

Figure 1: PRISMA flowchart depicts search of the literature and screening strategy for the study.

Figure 2 : Schematic diagram showing isothermal amplification and CRISPR-Cas 12 and 13mediated detector assay.

Figure 3 : Country-wise distribution of included studies (n=12) reported in the present investigation.

Figure 4: Distribution of types of specimens for detection of MTB in the included studies (n=12).

Figure 5: Distribution of target genes reported in the included studies (n=12).

Figure 6: Distribution of type of detection (left) and reference (right) methods for MTB in the included studies (n=12).

Figure 7: Distribution of Isothermal Techniques combined with CRISPR in MTB diagnostics across selected studies (n=12).

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Data availability statement

Since it is review therefore the data that support the findings of this study are publicly available.

Fig. 1

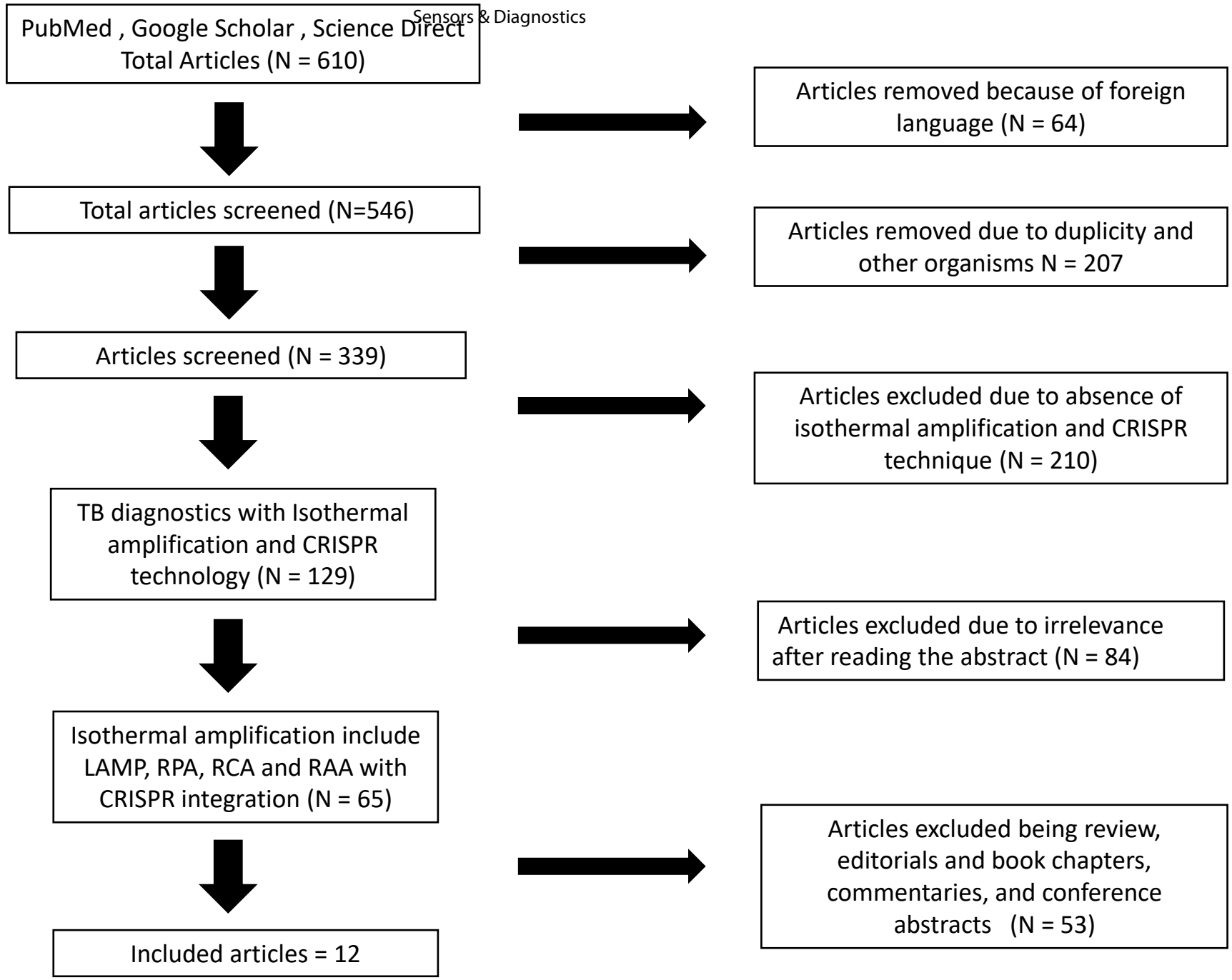


Fig. 2

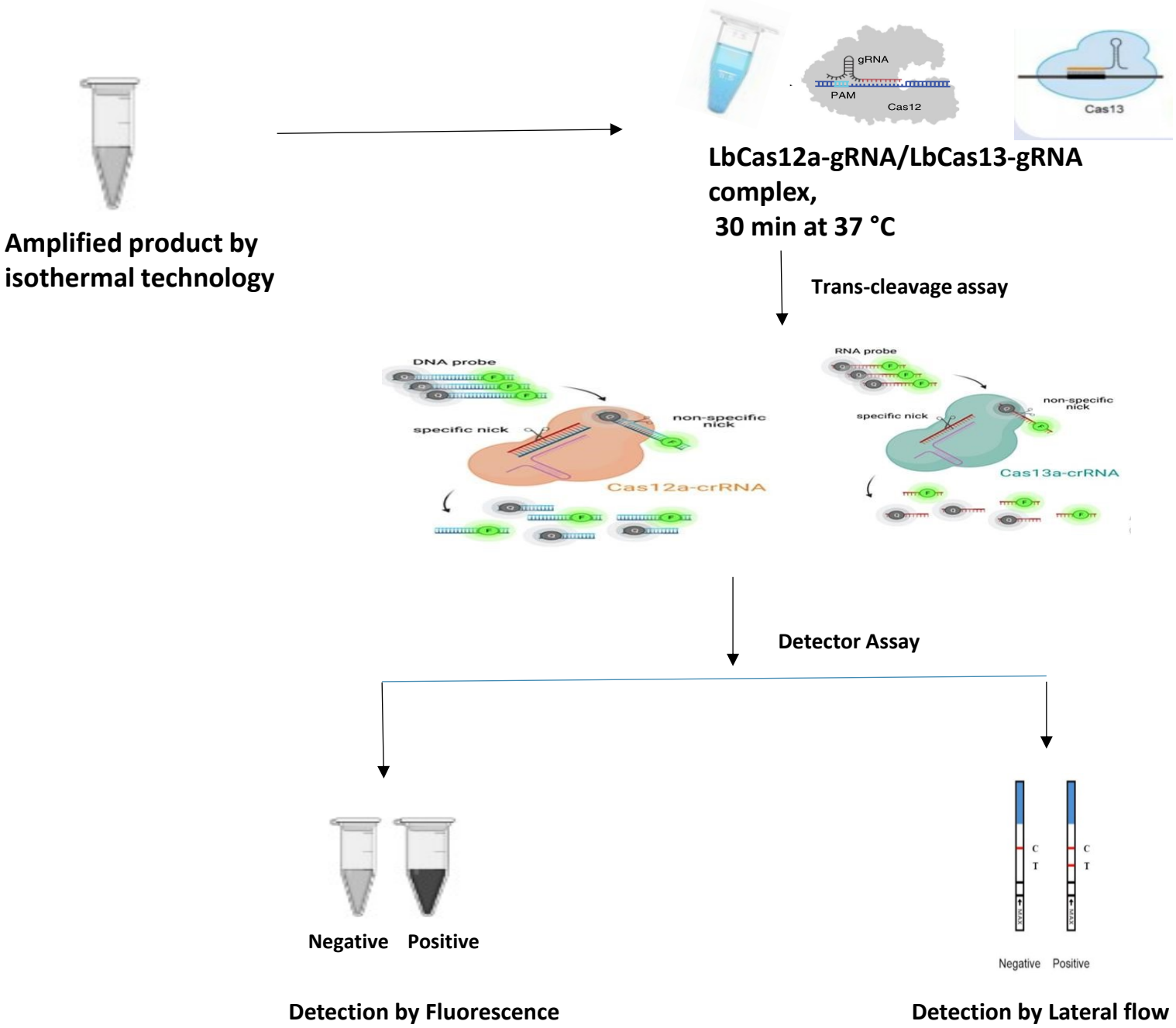
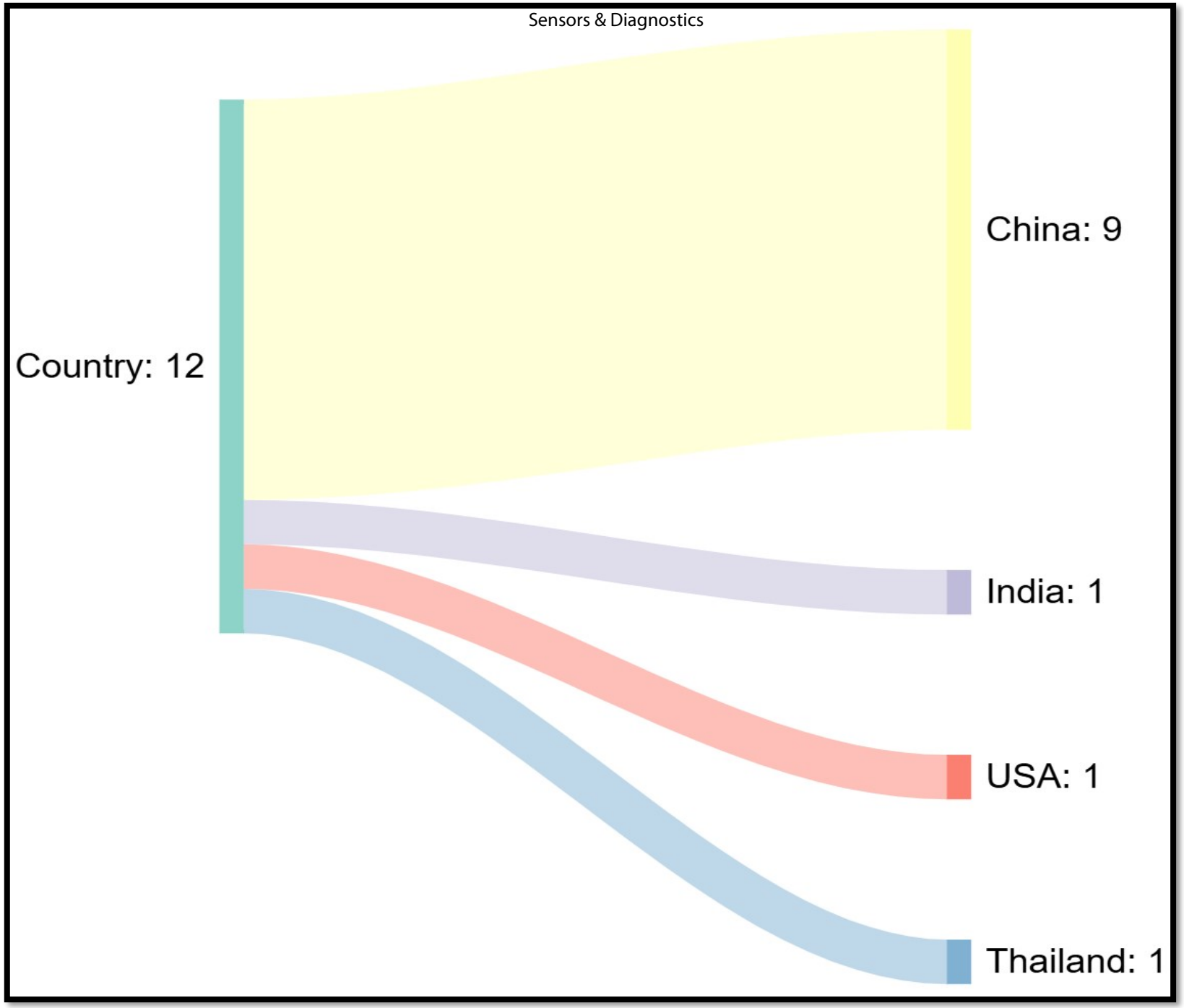


Fig. 3



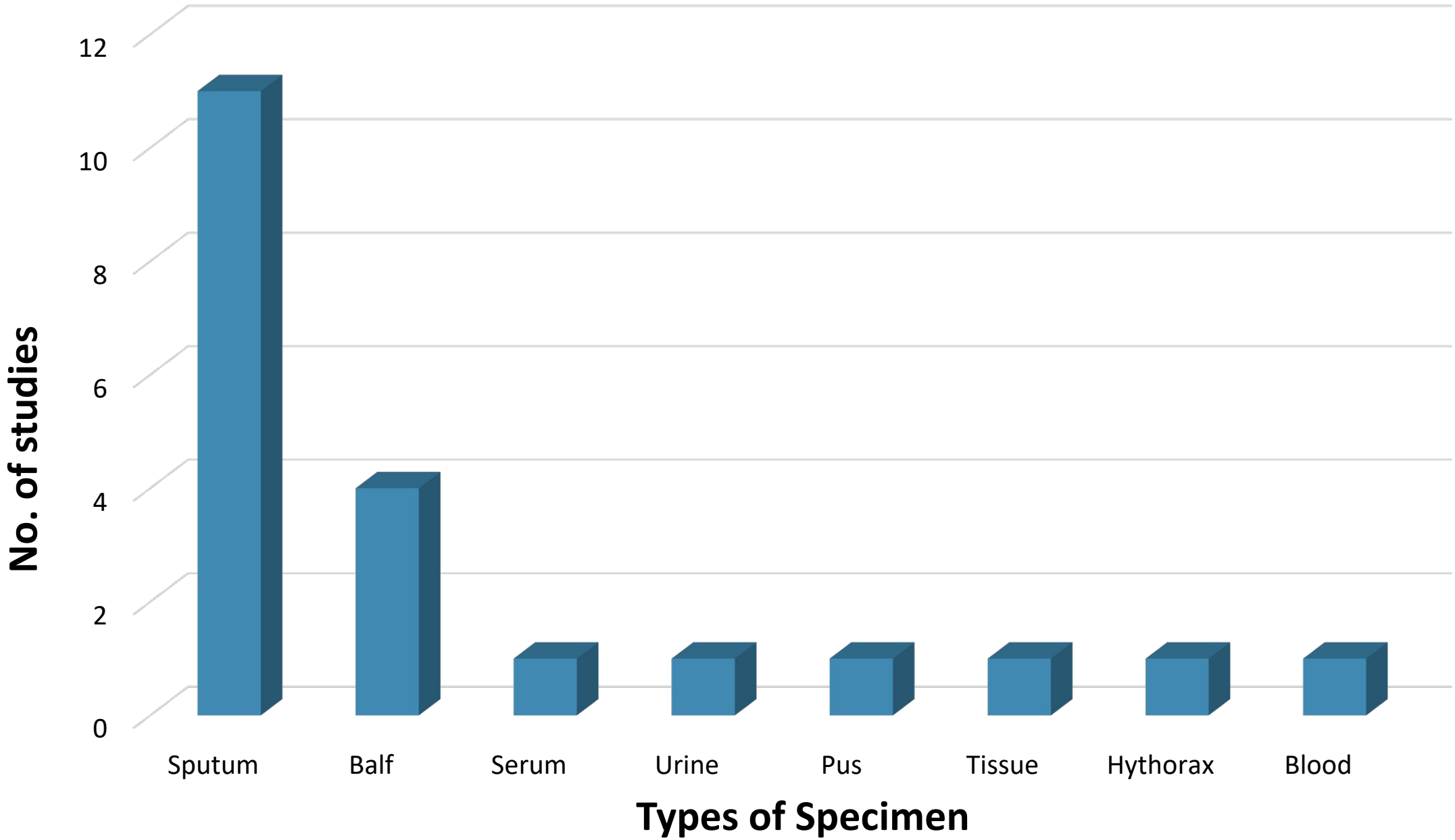


Fig. 5

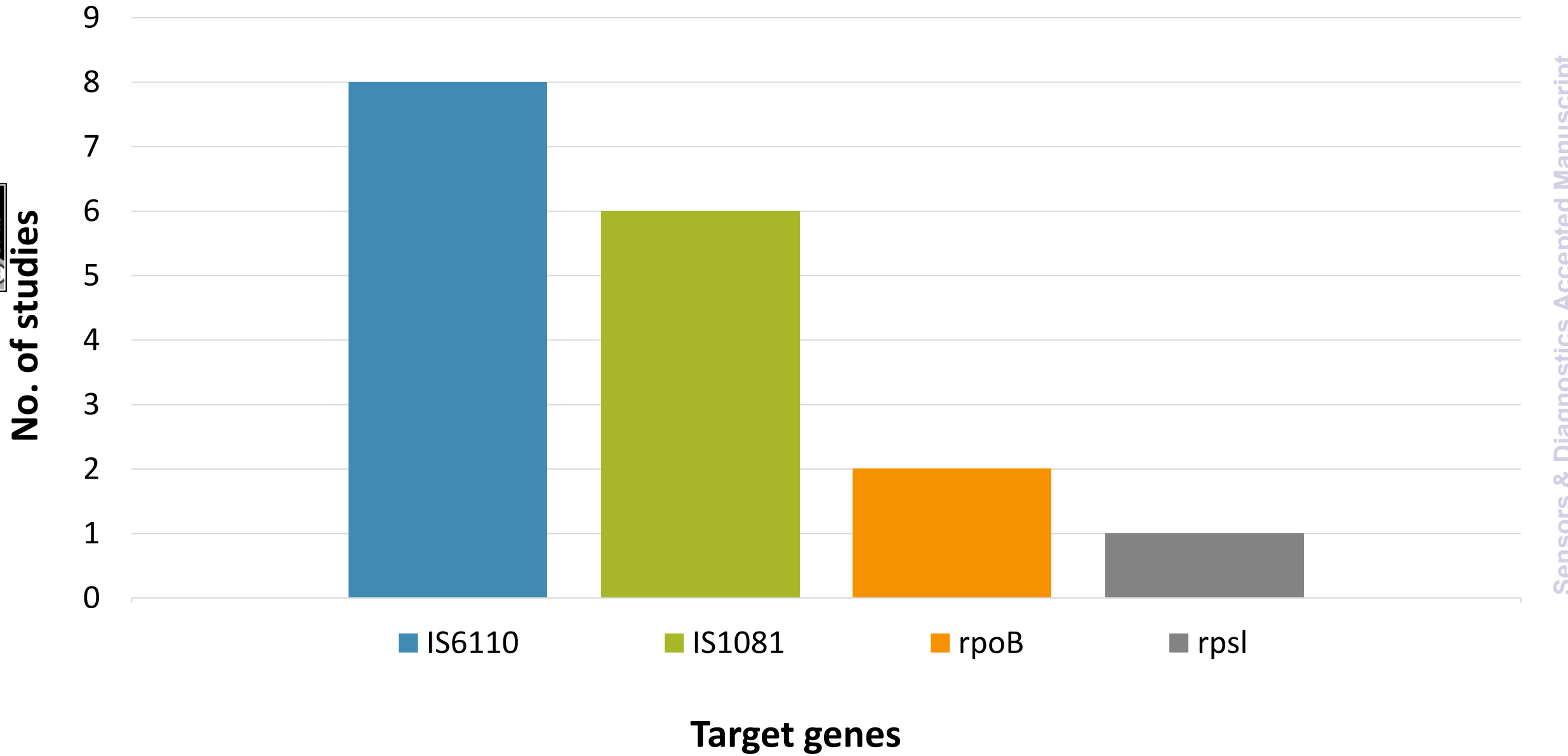


Fig. 6

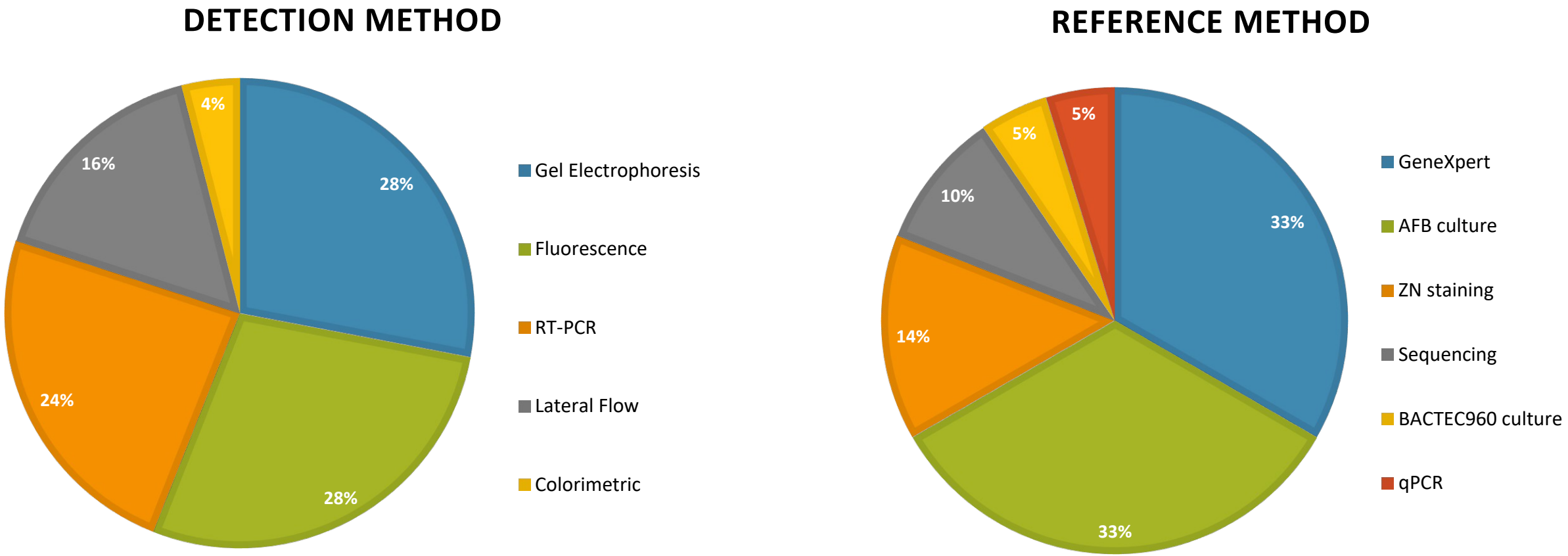


Fig. 7

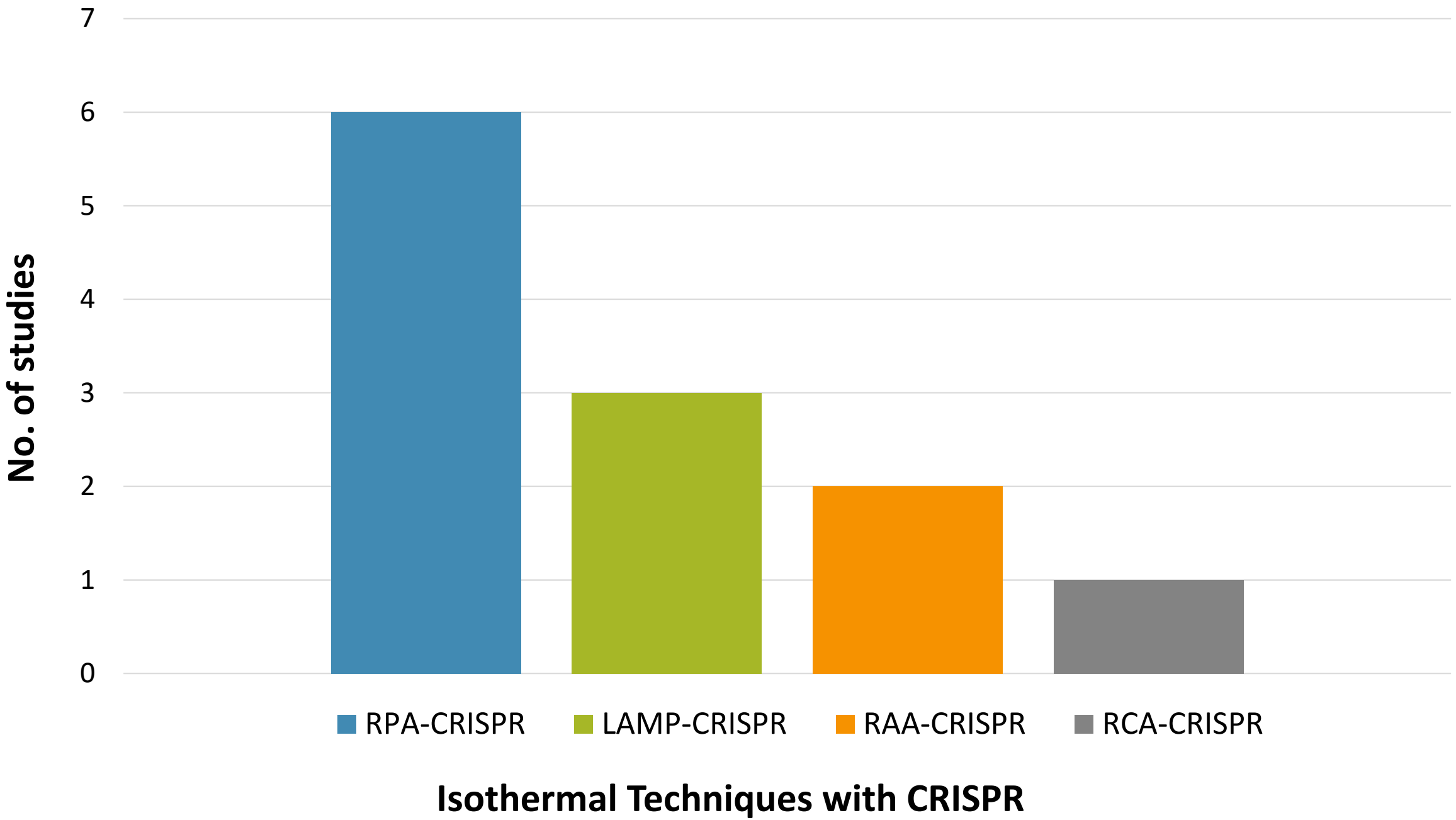


Table 1: Characteristics of the included studies (n=12).

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S.No.	Author	Country	Sample size	Type of Specimen	Targ
1	Compiro et.al., 2024	Thailand	82	Sputum	r
2	Xiao et.al., 2023	China	147	Sputum	IS IS
3	Liu et.al., 2022	China	49	Sputum	r
4	Ren et.al., 2023	China	401	Balf, Sputum, Pus	IS
5	Li et.al., 2024	China	151	Sputum	IS IS
6	Sam et. al., 2021	China	148	Balf, Sputum	IS
7	Wang et.al., 2021	China	44	Sputum	IS
8	Sun et.al., 2024	China	38	Balf, Sputum	r
9	Xu et.al., 2020	China	193	Sputum	IS IS
10	Zhang et.al., 2023	China	504	Balf, Sputum, Tissue, Hythorax	IS IS
11	Thakku et al., 2023	USA	52	Blood	IS IS
12	Kaushik et.al., 2025	India	232	Sputum, Urine, Serum	IS