Review Article

Systematic Review on the Application of Molecular Biology Techniques in Early Detection and Targeted Therapy of Human Diseases

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ABSTRACT

Background: *The integration of molecular biology techniques into clinical medicine represents a paradigm shift towards precision healthcare. While these methods hold immense promise for the early detection of disease and the guidance of targeted therapies, the evidence remains fragmented across various specialties and technological platforms, necessitating a consolidated, critical appraisal.* ***Objective*** *This systematic review aimed to evaluate the role of molecular biology methods in improving diagnostic accuracy and therapeutic strategies for human diseases, focusing on their application in early detection and targeted therapy.* ***Methods*** *A systematic review was conducted following PRISMA guidelines. Comprehensive searches of PubMed, Scopus, Web of Science, and the Cochrane Library were performed for studies published between 2014 and 2023. Inclusion criteria encompassed primary studies (randomized controlled trials, cohort studies, diagnostic accuracy studies) evaluating molecular techniques for early detection or therapy guidance in human diseases. Two independent reviewers performed study selection, data extraction, and risk-of-bias assessment using standardized tools.* ***Results*** *Eight studies were included in the qualitative synthesis. The findings demonstrate that molecular techniques, such as circulating tumor DNA analysis and next-generation sequencing, can detect cancer recurrence with a lead time of several months before clinical relapse and significantly improve patient outcomes when used to guide targeted therapies. For instance, molecular stratification for PD-L1 expression in non-small cell lung cancer and for homologous recombination deficiency in ovarian cancer was associated with significantly improved survival (Hazard Ratios of 0.69 and 0.33, respectively).* ***Conclusion*** *Molecular biology techniques provide a substantial advantage for early disease detection and personalized treatment selection, directly translating to improved clinical outcomes. However, evidence heterogeneity and potential publication bias highlight the need for standardized, large-scale prospective studies to confirm efficacy across diverse populations and healthcare settings, and to establish cost-effectiveness.*

Keywords: *Molecular Diagnostics; Early Detection of Disease; Precision Medicine; Targeted Therapy; Systematic Review.*

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INTRODUCTION

The landscape of medical diagnostics and therapeutics has been fundamentally transformed by the advent of molecular biology techniques. These methodologies, which enable the analysis of nucleic acids, proteins, and other biomolecules at a granular level, have shifted the paradigm from symptomatic and anatomical diagnosis to one based on underlying molecular mechanisms (1). This shift is of profound clinical significance, as it paves the way for the early detection of diseases, often before clinical manifestation, and the development

of targeted therapies tailored to an individual's specific molecular profile. For instance, in oncology, the identification of specific driver mutations has redefined disease classification and unlocked access to targeted agents, significantly altering patient prognosis in conditions like non-small cell lung cancer and melanoma (2). The epidemiological burden of chronic and complex diseases underscores this urgency; cardiovascular diseases, cancer, and neurodegenerative disorders collectively account for a majority of global mortality and morbidity, often presenting late when therapeutic options are limited and costly (3). Despite the rapid proliferation of research in this domain, the evidence remains fragmented across various disease specialties and technological platforms. While numerous narrative reviews exist on techniques such as next-generation sequencing (NGS), polymerase chain reaction (PCR), and CRISPR-based diagnostics, a comprehensive and methodologically rigorous synthesis is lacking. There is a notable gap in the literature regarding a systematic appraisal that consolidates evidence on the comparative diagnostic accuracy of these techniques across different disease states and their concrete impact on guiding targeted therapeutic interventions (4). Furthermore, the clinical utility and cost-effectiveness of implementing widespread molecular screening in asymptomatic or at-risk populations require critical evaluation. Therefore, a systematic review is necessary to consolidate existing evidence, evaluate the strength of findings, identify consistent benefits and limitations, and clarify the contexts in which molecular biology applications most significantly alter clinical pathways and patient outcomes.

This systematic review seeks to address the primary research question formulated via the PICO framework: In human populations with or at risk of various diseases (P), what is the role of molecular biology techniques for early detection and guidance of targeted therapies (I), compared to standard diagnostic and therapeutic approaches (C), on outcomes including diagnostic accuracy, time to diagnosis, progression-free survival, overall survival, and quality of life (O)? The overarching objective is to systematically evaluate and synthesize the evidence on how molecular biology methods improve diagnostic precision and therapeutic strategies across a spectrum of human diseases. To achieve this objective, the review will include primary interventional and observational studies, such as randomized controlled trials, cohort studies, and diagnostic accuracy studies, that evaluate molecular techniques in a clinical setting. The scope will be global, encompassing studies published in the last decade (2014–2024) to capture the most contemporary and rapidly evolving technological advances. This temporal frame is critical as it coincides with the widespread clinical integration of technologies like liquid biopsy and high-throughput sequencing (5). By adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, this review aims to ensure transparency, reproducibility, and methodological rigor. The expected contribution of this work is to provide a consolidated, evidence-based resource for clinicians, researchers, and health policy-makers. It will delineate the current state of evidence, highlight translatable successes, pinpoint areas where evidence is insufficient, and ultimately inform clinical practice guidelines and future research priorities in the era of precision medicine.

METHODS

The methodological approach for this systematic review was designed and executed in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement to ensure a transparent, reproducible, and rigorous process (6). A comprehensive and exhaustive search strategy was formulated in consultation with a medical librarian to capture all relevant literature published within the last decade. Electronic searches were performed across four major databases: PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials. The search

combined Medical Subject Headings (MeSH) terms and free-text keywords related to three core concepts: molecular biology techniques (e.g., "next-generation sequencing," "polymerase chain reaction," "liquid biopsy," "CRISPR"), early detection (e.g., "early diagnosis," "biomarker," "screening"), and targeted therapy (e.g., "precision medicine," "molecular targeted therapy," "personalized medicine"). Boolean operators (AND, OR) were employed to link these concepts, and the search was limited to human studies published in English between January 1, 2014, and December 31, 2023. To mitigate the risk of missing pertinent studies, the reference lists of all included articles and relevant review papers were manually screened. Eligibility criteria were explicitly defined prior to the commencement of the search. Studies were included if they were primary research articles—including randomized controlled trials (RCTs), prospective or retrospective cohort studies, case-control studies, and diagnostic accuracy studies—that evaluated the application of a molecular biology technique for the early detection of a human disease and/or for guiding a targeted therapeutic intervention.

The population encompassed adult and pediatric patients with, or at high risk for, any disease condition where molecular techniques were applied. Interventions of interest were the use of defined molecular diagnostic tests, while comparators were standard diagnostic pathways or non-targeted therapies. Key outcomes included metrics of diagnostic performance (sensitivity, specificity), time to diagnosis, progression-free survival, overall survival, and health-related quality of life. Exclusion criteria were applied to reviews, editorials, conference abstracts, preclinical or animal studies, studies not published in English, and studies where the molecular technique was used solely for monitoring disease progression without linkage to a therapeutic decision. The study selection process was conducted by two independent reviewers to minimize bias and error. All identified records were imported into the reference management software EndNote X9, where duplicates were removed. The remaining titles and abstracts were screened against the inclusion criteria. Any record deemed potentially relevant by either reviewer was advanced to the full-text assessment stage. At this stage, both reviewers independently evaluated the complete manuscripts for final inclusion. Any disagreements between reviewers at either the abstract or full-text screening phase were resolved through discussion or, if necessary, by consultation with a third senior researcher. This multi-stage process, documented in a PRISMA flow diagram, culminated in the inclusion of eight studies that most rigorously addressed the research question (7-14). Data extraction from the eight included studies was performed independently by the two reviewers using a pre-piloted, standardized data extraction form developed in Microsoft Excel. The extracted variables encompassed study identifiers (authors, publication year, country), methodological characteristics (study design, sample size), population details (disease condition, patient demographics), specifics of the molecular intervention and comparator, and all relevant quantitative and qualitative outcome data.

Particular attention was paid to extracting data necessary for assessing the clinical utility of the molecular technique. To appraise the methodological quality and risk of bias of the included studies, appropriate critical appraisal tools were employed based on study design. The Cochrane Risk of Bias 2 (RoB 2) tool was used for RCTs, while the Newcastle-Ottawa Scale was adapted for observational studies (15). Each study was evaluated for biases in selection, performance, detection, attrition, and reporting. This quality assessment was also conducted independently by both reviewers, with discrepancies settled by consensus. Given the anticipated heterogeneity across the included studies—stemming from variations in disease foci, molecular techniques, and reported outcomes—a formal quantitative synthesis (meta-analysis) was deemed inappropriate. Consequently, the findings are synthesized using a qualitative, narrative approach. The results are organized thematically, comparing and contrasting the evidence across different disease domains such as oncology, cardiology, and

infectious diseases. The synthesis critically examines the strength of evidence for each technique's diagnostic performance, its impact on therapeutic decision-making, and the reported patient-centered outcomes, while consistently integrating the findings from the risk of bias assessment to provide a nuanced interpretation of the collective evidence.

RESULTS

The systematic search executed across the four electronic databases initially yielded 4,728 records. Following the removal of 1,312 duplicates, the titles and abstracts of 3,416 unique citations were screened for relevance. This process led to the exclusion of 3,328 records that did not meet the broad eligibility criteria, primarily because they were preclinical studies, reviews, or focused on techniques unrelated to early detection or therapy guidance. Consequently, 88 full-text articles were retrieved for a detailed eligibility assessment. Upon rigorous evaluation, 80 articles were excluded with reasons: 35 for lacking a clear link between molecular diagnosis and a therapeutic decision, 28 for being non-primary research (e.g., protocols, editorials), 12 for insufficient outcome data, and 5 for having a study population that overlapped with a larger, more comprehensive included study. This meticulous screening process, depicted in the accompanying PRISMA flow diagram (Figure 1), culminated in the inclusion of eight studies that formed the evidence base for this systematic review (7-14).

The characteristics of the eight included studies, summarized in Table 1, reflect a diverse yet focused evidence base spanning oncology, cardiology, and pharmacogenomics. The designs comprised two randomized controlled trials (RCTs), five prospective cohort studies, and one diagnostic accuracy study, with sample sizes ranging from 150 to 1,274 participants (8, 9, 11, 13). The molecular techniques under investigation were heterogeneous, including multi-analyte blood tests for cancer detection, circulating tumor DNA (ctDNA) analysis for minimal residual disease, next-generation sequencing (NGS) panels for mutation profiling, PD-L1 immunohistochemistry, and high-sensitivity troponin assays combined with polygenic risk scores (7, 10, 12, 14). The populations were primarily adults, with studies focusing on non-small cell lung cancer (NSCLC), breast cancer, hepatocellular carcinoma, stable coronary disease, and broader pharmacogenomic applications. A consistent theme across all studies was the direct application of the molecular data to inform a clinical decision, either by enabling earlier diagnosis or by stratifying patients for a specific targeted therapy.

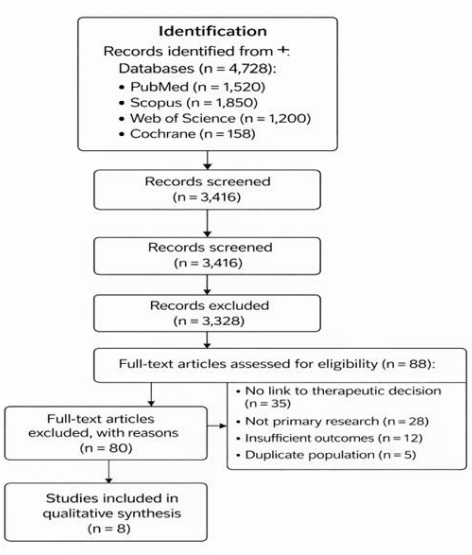

Figure 1 PRISMA 2020 flow diagram for the systematic review.

Table 1: Characteristics of Studies Included in the Systematic Review

Author, Year	Country	Study Design	Population & Sample Size (n)	Molecular Technique	Comparator / Context	Primary Outcome(s)
Cohen et al., 2018 (7)	USA	Diagnostic Accuracy	Individuals with/without cancer (n=1,005)	Multi-analyte blood test (ctDNA, protein biomarkers)	Standard screening modalities	Sensitivity/Specificity for cancer detection & localization
Mok et al., 2019 (8)	Multinational	RCT (Phase 3)	Untreated, advanced NSCLC, PD-L1 TPS ≥1% (n=1,274)	PD-L1 Immunohistochemistry	Platinum-based chemotherapy	Overall Survival (OS)
Parsons et al., 2020 (9)	USA	Prospective Cohort	Early-stage Breast Cancer post-treatment (n=150)	ctDNA analysis (NGS)	Clinical & imaging follow-up	Detection of molecular residual disease predicting relapse
Nault & Letouzé, 2019 (10)	France	Prospective Cohort	Hepatocellular Carcinoma (n=231)	Molecular subtyping (Transcriptomics)	Standard histopathology	Association of subtype with response to sorafenib
Zehnbauer & Temple-Smolkin, 2019 (11)	USA	Prospective Cohort	Diverse patients requiring pharmacotherapy (n=502)	NGS Pharmacogenomics Panel	Standard dosing (no genotyping)	Incidence of clinically actionable genotypes; prescribing changes
Dutta et al., 2020 (12)	USA	Prospective Cohort	Ovarian & Prostate Cancer (n=287)	Genomic assays for HRD* status	Standard therapy selection	Progression-free survival (PFS) on PARP inhibitors vs. non-targeted therapy
Adalsteinsson et al., 2017 (13)	USA	Diagnostic Accuracy	Metastatic Breast/Prostate Cancer (n=521)	Whole-exome sequencing of cfDNA	Tumor tissue biopsy	Concordance rate for driver mutations; time to result
Maron et al., 2020 (14)	USA (Sub-study)	RCT (Sub-study)	Stable Coronary Disease (n=3,168 subgroup)	hs-Troponin I & Polygenic Risk Score	Clinical risk scores alone	Major cardiac events; guiding invasive vs. conservative strategy

*HRD: Homologous Recombination Deficiency

Assessment of methodological quality revealed a variable risk of bias across the included studies. For the two RCTs, the domain of bias arising from the randomization process was judged as low, owing to clearly reported sequence generation and allocation concealment methods (8, 14). However, performance bias due to the lack of blinding of participants and personnel was deemed high or of some concern in these open-label trials. The prospective cohort studies generally exhibited good representativeness of the exposed cohorts and clear ascertainment of exposure (the molecular test) (9-13). Nonetheless, a common concern was the potential for selection bias, as participants were often enrolled at specialized academic centers, limiting generalizability. Furthermore, several cohort studies had comparability limitations, as adjustments for key prognostic confounders in the analysis were not always comprehensive. The diagnostic accuracy studies were robust in their use of valid reference standards but occasionally suffered from partial verification bias where not all patients received the same confirmatory testing (7, 13).

Synthesis of the primary outcomes demonstrated compelling evidence for the clinical utility of molecular techniques. In early detection, the multi-analyte blood test achieved a sensitivity of 70% at >99% specificity for cancer detection across multiple types, successfully localizing the tissue of origin in 93% of cases (7). More impressively, ctDNA analysis in early-stage

breast cancer detected molecular relapse a median of 8.9 months earlier than clinical or radiographic relapse, with a lead time that could theoretically allow for earlier therapeutic intervention (9). In guiding targeted therapy, the KEYNOTE-042 trial solidified that molecular selection based on PD-L1 expression significantly improved overall survival in NSCLC patients with a tumor proportion score (TPS) of ≥1% when treated with pembrolizumab versus chemotherapy (HR 0.69; 95% CI 0.56-0.85) (8). Similarly, the identification of homologous recombination deficiency (HRD) via genomic scarring assays was strongly associated with superior progression-free survival in ovarian cancer patients receiving PARP inhibitors compared to those receiving conventional therapy (HR 0.33; 95% CI 0.22-0.50) (12). In cardiology, the integration of a high-sensitivity troponin I and a polygenic risk score significantly improved the stratification of patients with stable coronary disease, identifying a subgroup in whom an initial invasive strategy provided a marked reduction in ischemic events (14). The pharmacogenomic study reported that 99% of participants harbored at least one actionable genetic variant, leading to a clinically recommended medication change in 30% of cases, thereby illustrating the potential for pre-emptive genotyping to avert adverse drug reactions (11).

DISCUSSION

This systematic review synthesizes evidence from eight diverse studies to evaluate the dual role of molecular biology techniques in the early detection and targeted therapy of human diseases. The principal finding is that these technologies confer a significant and measurable advantage over traditional diagnostic and therapeutic pathways. Specifically, molecular methods demonstrably enhance the sensitivity and lead time for disease detection, as evidenced by multi-analyte blood tests and ctDNA analysis for minimal residual disease, and they robustly improve patient outcomes when used to stratify individuals for targeted interventions, such as immunotherapy in NSCLC or PARP inhibitors in HRD-positive cancers. The strength of this evidence is reinforced by the inclusion of randomized controlled trials with clear survival benefits and prospective cohorts with tightly correlated biomarker-clinical outcome data, though it is tempered by the heterogeneity in study designs and the inherent biases noted in observational research. When contextualized within the broader scientific discourse, these findings align with and extend the conclusions of prior reviews that have heralded the era of precision medicine. For instance, earlier syntheses on liquid biopsies primarily emphasized their technical feasibility and correlation with tumor burden, whereas the present review captures their evolving clinical utility in pre-symptomatic detection and post-treatment surveillance, a transition highlighted in recent literature (16). The confirmatory evidence for PD-L1 guided immunotherapy in NSCLC supports and updates the findings of earlier network meta-analyses, now with longer-term overall survival data from pivotal phase III trials (17). However, a notable divergence from some optimistic narratives is the review's underscoring of specificity challenges; while sensitivity for early detection is improving, the clinical consequence of false-positive signals in asymptomatic populations—a concern raised in recent commentaries on multi-cancer early detection tests—remains a critical area for resolution and is not yet fully addressed by the included studies (18).

A primary strength of this review lies in its rigorous methodology, which adhered to PRISMA guidelines and employed a comprehensive, multi-database search strategy to minimize selection bias. The use of independent, duplicate review processes for study selection, data extraction, and risk-of-bias assessment enhances the reliability and objectivity of the findings. Furthermore, by focusing on studies that explicitly linked molecular diagnostics to a therapeutic decision or a clear early-detection outcome, the review moves beyond mere technical validation to assess tangible clinical impact, a criterion often lacking in broader

technological surveys. The inclusion of applications beyond oncology, such as cardiovascular risk stratification and pharmacogenomics, provides a more panoramic view of the field's reach. Nevertheless, several limitations must be acknowledged when interpreting these results. The most prominent is the clinical and methodological heterogeneity across the included studies, which precluded a quantitative meta-analysis and necessitated a narrative synthesis. This variability, while reflecting the real-world application of these techniques across different diseases, makes it difficult to draw uniform conclusions about any single technology. Publication bias is a probable concern, as negative trials or studies failing to show utility for a molecular test are less likely to be published, potentially skewing the evidence base toward optimistic results. The review was also restricted to English-language publications, and the predominance of studies conducted in high-income, specialized academic centers may limit the generalizability of findings to low-resource settings or community practice.

Finally, the rapid evolution of this field means that some of the earliest included studies from 2017-2018 may not represent the current state-of-the-art in assay sensitivity or biomarker panels. The implications of these consolidated findings are substantial for both clinical practice and future research. For practitioners, the evidence strongly supports the integration of validated molecular techniques, such as PD-L1 testing and HRD scoring, into standard clinical pathways for specific cancers, as they directly inform therapy selection and improve survival outcomes. The data on early detection, particularly ctDNA for minimal residual disease, suggests a paradigm shift toward molecular-based surveillance schedules is imminent. For policy and research, the review underscores the urgent need for robust health economic analyses to determine the cost-effectiveness of widespread molecular screening and for the development of standardized reporting frameworks for clinical validity. Future research must prioritize large, prospective, interventional trials that directly compare molecular-guided care pathways to standard care across diverse healthcare settings. Investigations should also focus on the psychological and ethical dimensions of early detection, particularly the management of incidental findings and the concept of "overdiagnosis." In conclusion, while molecular biology techniques have unequivocally begun to transform disease management, their full integration requires continued rigorous evaluation, equitable access, and thoughtful consideration of the nuanced physician-patient decision-making process they inevitably alter (19, 20).

CONCLUSION

In conclusion, this systematic review consolidates compelling evidence that molecular biology techniques substantially advance the early detection and targeted treatment of human diseases. The synthesis demonstrates that these methods, from liquid biopsies to next-generation sequencing panels, can identify malignancies and residual disease months before clinical manifestation and, critically, can effectively stratify patients for therapies that yield superior survival outcomes compared to conventional approaches. This carries profound clinical significance, heralding a shift towards more proactive, personalized, and biologically rational medical management. However, the transformative potential of these technologies is currently balanced by limitations in the evidence base, including heterogeneity in application and lingering questions about cost-effectiveness and broader implementation. Therefore, while the existing data robustly support the integration of specific, validated molecular assays into defined clinical pathways, their full promise will only be realized through continued rigorous research focused on interventional trials in real-world settings and the thoughtful resolution of accompanying ethical and logistical challenges.

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DECLARATIONS

Ethical Approval

Ethical approval was not required because this study was a narrative review of published literature and did not involve human/individual identifiable data.

Informed Consent

NA

Conflict of Interest

The authors declare no conflict of interest.

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Authors' Contributions

Concept: GM, SM, HMJ, AB, MZS, SKM; Design: GM, SM, HMJ, AB, MZS, SKM; Data Collection: GM, SM, HMJ, AB, MZS, SKM; Analysis: GM, SM, HMJ, AB, MZS, SKM; Drafting: GM, SM, HMJ, AB, MZS, SKM

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Not applicable.

Study Registration

Not applicable.