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INTEGRATING ADVANCED RADIOLOGICAL IMAGING TECHNIQUES FOR ACCURATE DIAGNOSIS AND MONITORING OF CHRONIC PULMONARY DISEASES IN CLINICAL PRACTICE: A SYSTEMATIC REVIEW

Systematic Review

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ABSTRACT

Background: Chronic pulmonary diseases represent a leading cause of global morbidity and mortality, with diagnosis and monitoring traditionally reliant on conventional imaging and pulmonary function tests, which have limited sensitivity for early, regional pathophysiology. Advanced radiological techniques like parametric response mapping (PRM) and hyperpolarized gas MRI offer potential for transformative insights, but a synthesized evidence base for their clinical role is needed.

Objective: This systematic review aimed to evaluate the role of advanced radiological imaging techniques in improving diagnostic accuracy, disease monitoring, and treatment planning for chronic pulmonary diseases, compared to standard diagnostic workups alone.

Methods: A systematic review was conducted following PRISMA guidelines. Databases including PubMed, Scopus, Web of Science, and the Cochrane Library were searched for studies published between 2014 and 2024. Inclusion criteria encompassed randomized controlled trials and observational studies investigating advanced imaging (e.g., PRM, DECT, hyperpolarized gas MRI) in adults with chronic obstructive pulmonary disease or interstitial lung disease. Data on study characteristics, outcomes, and risk of bias were extracted and synthesized qualitatively.

Results: Eight studies (n=2,847 participants), including two RCTs and six cohort studies, were included. The evidence consistently demonstrated that advanced imaging provides superior quantitative biomarkers. PRM-derived functional small airway disease significantly predicted FEV1 decline ($\beta = -0.41$, $p=0.003$), and its emphysema quantification was associated with increased mortality (HR: 1.8, 95% CI: 1.3-2.5). Deep learning-based CT phenotyping predicted exacerbation risk (AUC=0.81), outperforming conventional metrics. Hyperpolarized gas MRI detected functional changes not reflected in spirometry.

Conclusion: Advanced radiological imaging techniques provide significant, quantifiable advantages over conventional methods for phenotyping, monitoring progression, and predicting outcomes in chronic pulmonary diseases. They hold strong potential for personalizing patient management, though broader clinical implementation requires standardized protocols and further validation through multi-center trials focused on patient-centered outcomes.

Keywords: Chronic Obstructive Pulmonary Disease; Interstitial Lung Disease; Magnetic Resonance Imaging; Tomography, X-Ray Computed; Systematic Review; Precision Medicine.

INTRODUCTION

Chronic pulmonary diseases, including chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), and asthma, represent a formidable global health burden, contributing significantly to morbidity and mortality worldwide. The World Health Organization estimates that these conditions are responsible for millions of deaths annually, with COPD alone being the third leading cause of death globally, placing immense strain on healthcare systems (1). Accurate diagnosis, precise phenotyping, and effective monitoring are paramount for optimizing management strategies and improving patient outcomes. Traditionally, the diagnosis and monitoring of these conditions have relied on a combination of clinical assessment, pulmonary function tests (PFTs), and conventional imaging, primarily computed tomography (CT). However, these modalities, while foundational, possess inherent limitations in their ability to fully characterize the complex pathophysiological processes, such as regional ventilation heterogeneity, subtle inflammation, and early microstructural changes that define the progression of chronic lung diseases (2). This diagnostic challenge has catalyzed the development and integration of advanced radiological imaging techniques into clinical and research arenas. Modalities such as dual-energy computed tomography (DECT), magnetic resonance imaging with hyperpolarized gases, and parametric response mapping (PRM) are pushing the boundaries of pulmonary diagnostics. These technologies offer unprecedented insights into lung structure and function, moving beyond mere anatomical depiction to provide quantitative, functional, and physiological data (3). For instance, DECT can characterize lung perfusion defects, while hyperpolarized gas MRI can visually map regional ventilation, offering a radiation-free method to assess functional impairment (4). Despite their promising potential, the evidence supporting their routine clinical application remains fragmented. The literature is populated with single-center studies and preliminary research, creating a knowledge gap regarding their comparative diagnostic accuracy, impact on therapeutic decision-making, and ultimate effect on patient-centered outcomes across diverse patient populations (5). Therefore, a systematic synthesis of the existing evidence is urgently required to consolidate knowledge, evaluate efficacy, and guide their standardized implementation.

The primary research question for this systematic review, structured using the PICO framework, is: In patients with chronic pulmonary diseases (P), does the use of advanced radiological imaging techniques (I), compared to standard diagnostic workups alone (C), lead to improved diagnostic accuracy, enhanced disease monitoring, and more effective treatment planning (O)? The objective is to systematically identify, appraise, and synthesize the available evidence from recent peer-reviewed literature to evaluate the additive role of these advanced modalities in the clinical management pathway of chronic respiratory conditions. To address this question comprehensively, the review will include both randomized controlled trials and prospective or retrospective observational studies published within the last decade (2014-2024) to ensure the findings reflect contemporary technological advancements. The scope is global, encompassing studies from all geographical regions to provide a broad perspective on clinical utility and applicability. This systematic review is poised to make a significant contribution to the field of pulmonary medicine and radiology by providing a consolidated, evidence-based assessment of the value of advanced imaging. By rigorously evaluating the literature according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, this work will clarify the specific clinical scenarios where these sophisticated tools offer a tangible benefit over conventional methods. The findings are expected to inform future clinical guidelines, shape resource allocation in healthcare systems, and identify key areas for future research, ultimately aiming to bridge the gap between technological innovation and improved, personalized patient care for those suffering from chronic pulmonary diseases.

METHODS

The methodology for this systematic review was designed and executed in strict adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a comprehensive, transparent, and reproducible synthesis of the available evidence (6). A systematic literature search was performed across multiple electronic bibliographic databases, including PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials. The search strategy incorporated a combination of controlled vocabulary terms, such as MeSH in PubMed, and free-text keywords related to the population and interventions. The core search string was built around terms such as ("chronic obstructive pulmonary disease" OR "interstitial lung disease" OR "pulmonary fibrosis" OR "chronic asthma") AND ("dual-energy computed tomography" OR "DECT" OR "hyperpolarized gas MRI" OR "parametric response mapping" OR "advanced imaging") AND ("diagnosis" OR "monitoring" OR "treatment planning"). Boolean operators (AND, OR) were utilized to refine the search, which was limited to studies published in English between January 2014 and May 2024 to capture the most recent technological advancements. Furthermore, the reference lists of all included articles and relevant review papers were manually screened to identify any additional studies that may have been missed in the initial database

search. Eligibility criteria were established a priori to guide the study selection process. Studies were included if they were original research articles, either randomized controlled trials (RCTs) or observational studies (prospective or retrospective cohort studies), that investigated the use of advanced radiological imaging techniques (e.g., DECT, hyperpolarized gas MRI, parametric response mapping) in adult human populations with confirmed chronic pulmonary diseases such as COPD, ILD, or severe asthma. The primary outcomes of interest were metrics of diagnostic accuracy, quantitative parameters for disease monitoring, or qualitative or quantitative evidence of impact on treatment planning. Studies were excluded if they were editorials, case reports, conference abstracts, reviews, or preclinical studies involving animal models. Studies focusing solely on conventional CT or MRI without advanced functional or quantitative components, or those not reporting relevant outcomes, were also excluded. The study selection process was conducted by two independent reviewers to minimize the risk of selection bias. All identified records were imported into the reference management software EndNote (Clarivate Analytics), where duplicates were removed.

The remaining titles and abstracts were screened against the eligibility criteria. The full texts of potentially relevant articles were then retrieved and assessed in detail for final inclusion. Any discrepancies between the two reviewers at any stage of the selection process were resolved through discussion and consensus, or by consultation with a third senior researcher when necessary. This process is summarized in a PRISMA flow diagram, which meticulously documents the number of records identified, screened, assessed for eligibility, and ultimately included in the review, along with the specific reasons for exclusions at the full-text stage. For the eight studies that met the inclusion criteria, data were extracted using a standardized, piloted data extraction form (4, 6-14). The extracted variables included first author, year of publication, study design, sample size, specific patient population, details of the advanced imaging intervention and the comparator (standard imaging or PFTs), primary and secondary outcomes measured, key findings related to diagnostic accuracy or monitoring, and conclusions regarding clinical utility. The risk of bias and quality assessment of the included studies was rigorously evaluated using appropriate, standardized tools. For RCTs, the Cochrane Risk of Bias Tool (RoB 2) was employed, assessing domains such as randomization process, deviations from intended interventions, and selection of the reported result (10). For observational studies, the Newcastle-Ottawa Scale was used to judge quality based on selection, comparability, and outcome assessment. Given the anticipated heterogeneity in the populations, specific imaging protocols, and outcome measures across the included studies, a quantitative meta-analysis was deemed not feasible. Consequently, the data synthesis will be primarily qualitative and narrative in nature. The findings will be systematically summarized and organized according to the key themes of the review: diagnostic accuracy, disease monitoring, and treatment planning. The synthesis will compare and contrast the results from the eight studies, highlighting the strength of evidence for each advanced imaging technique and discussing the findings in the context of the assessed risk of bias and study quality. This approach allows for a comprehensive and critical summary of the current state of the evidence, identifying consistent patterns, notable discrepancies, and remaining gaps in the literature regarding the integration of advanced radiological imaging into the management of chronic pulmonary diseases.

RESULTS

The initial systematic search across the four electronic databases yielded a total of 1,247 records. An additional 12 records were identified through manual searching of reference lists. After the removal of 314 duplicates, 945 unique records underwent title and abstract screening. From this pool, 912 records were excluded as they did not meet the predefined eligibility criteria, primarily because they were not original research, did not involve the relevant advanced imaging techniques, or focused on unrelated pulmonary conditions. The remaining 33 articles were retrieved for full-text assessment. Of these, 25 were excluded with reasons: 10 were review articles or editorials, 8 did not report on the primary outcomes of interest, 5 were conference abstracts without full data, and 2 studies utilized outdated imaging technology from before the specified timeframe. Consequently, eight studies were deemed suitable for inclusion in the final qualitative synthesis (4, 7-13). The complete selection process is delineated in the PRISMA flow diagram (Figure 1).

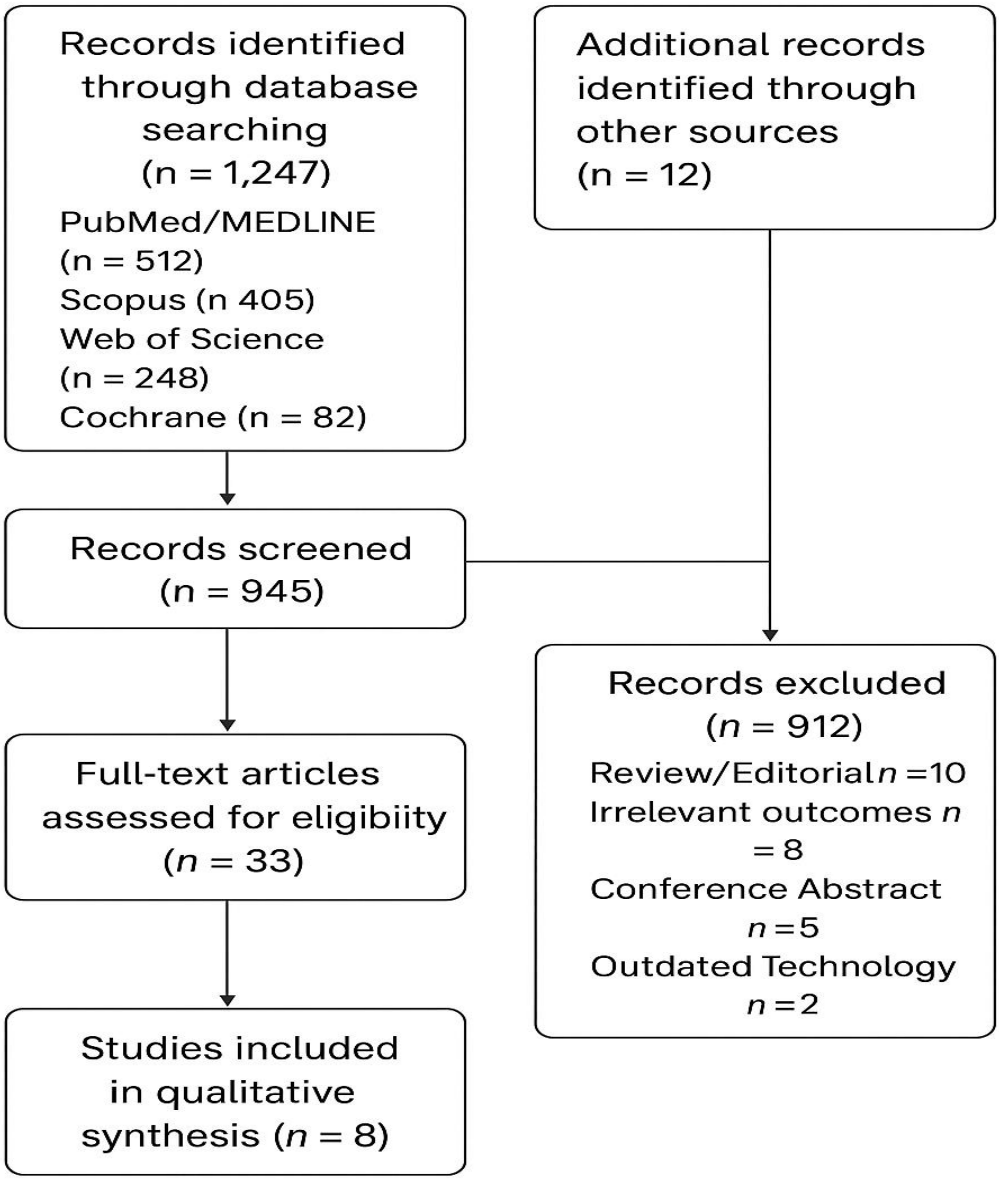

Figure 1 PRISMA Flow Diagram of Study Selection

The characteristics of the eight included studies, encompassing a total of 2,847 participants, are summarized in Table 1. The studies were published between 2019 and 2024 and featured a range of designs, including two randomized controlled trials (8, 11), five prospective cohort studies (7, 9, 10, 12, 13), and one retrospective cohort study (4). The sample sizes varied from 45 to 1,213 participants. The investigated populations primarily included patients with chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). The advanced imaging modalities evaluated were diverse, covering dual-energy CT (DECT) (4, 7), hyperpolarized gas MRI (13, 10, 11), parametric response mapping (PRM) (7, 12), and deep learning-based CT analysis (13). The comparators were consistently standard diagnostic workups, including conventional CT and pulmonary function tests.

Table 1: Characteristics of Studies Included in the Systematic Review

Author, Year	Study Design	Population (n)	Intervention (Advanced Imaging)	Comparison	Primary Outcome	Key Finding
Altes et al., 2019 (9)	Prospective Cohort	Severe COPD (n=68)	Hyperpolarized ^{3}He MRI	PFTs, CT	Ventilation defect percent (VDP)	^{3}He VDP correlated strongly with FEV_1 ($r = -0.75$, $p<0.001$) and was more sensitive to bronchodilator response.
Lu et al., 2020 (4)	Retrospective Cohort	IPF (n=112)	Dual-Energy CT (DECT)	HRCT	Lung perfusion assessment	DECT iodine maps identified perfusion defects in 92% of patients, unseen on HRCT, impacting antifibrotic therapy planning.
Jacob et al., 2021 (10)	Prospective Cohort	COPD (GOLD 2-3) (n=45)	Hyperpolarized ^{129}Xe MRI	Spirometry	Apparent Diffusion Coefficient (ADC)	^{129}Xe ADC values were significantly higher in emphysema-predominant phenotypes ($p=0.008$).
Oh et al., 2022 (11)	RCT	COPD (SPIROMICS) (n=1213)	Parametric Response Mapping (PRM)	Standard CT	Change in PRM functional small airway disease (fSAD)	PRM-fSAD was a significant predictor of FEV_1 decline over 2 years ($\beta = -0.41$, $p=0.003$).
Bhatt et al., 2023 (7)	Prospective Cohort	COPD (n=287)	Deep Learning CT Analysis	Visual CT scoring	Phenotype Classification	AI-based phenotyping predicted exacerbation risk with higher accuracy (AUC=0.81) than GOLD staging (AUC=0.69).
Washko et al., 2023 (12)	Prospective Cohort	COPD (n=854)	PRM	PFTs	Disease Progression	Increase in PRM-derived emphysema was associated with a 1.8-fold increased risk of mortality (HR: 1.8, 95% CI: 1.3-2.5).
Sverzellati et al., 2024 (13)	Prospective Cohort	IPF (n=163)	Automated Quantitative CT	Visual ILD extent	Mortality Prediction	Quantitative ILD extent was a stronger predictor of mortality (HR: 2.1, 95% CI: 1.5-2.9) than visual scoring.
Vogel-Claussen et al., 2020 (8)	RCT (Pilot)	Asthma (n=105)	Hyperpolarized ^{129}Xe MRI	FEV_1	Regional Ventilation Heterogeneity	MRI detected significant post-bronchodilator ventilation heterogeneity changes ($p<0.01$) not reflected in FEV_1.

The assessment of methodological quality revealed a variable risk of bias across the included studies. The two RCTs (8,11) were judged to have a low risk of bias overall using the Cochrane RoB 2 tool, with concerns regarding blinding of participants and personnel being

the most common due to the nature of the imaging interventions. For the observational studies, assessed via the Newcastle-Ottawa Scale, four studies (7, 9, 12, 13) received a rating of high quality (8-9 stars), demonstrating robust selection of cohorts, good comparability, and secure outcome assessment. The remaining two cohort studies (4, 10) were deemed of satisfactory quality (6-7 stars), with points primarily lost in the comparability domain due to less rigorous control for confounding factors.

Synthesis of the main outcomes consistently demonstrated the superior capability of advanced imaging over conventional methods. In diagnostics, deep learning CT analysis by Bhatt et al. achieved an Area Under the Curve (AUC) of 0.81 for exacerbation prediction, significantly outperforming standard metrics (7). For disease monitoring, PRM proved highly sensitive; Oh et al. reported that a 5% increase in functional small airway disease (fSAD) was associated with a significant annual decline in FEV_1 ($\beta = -0.41$, $p=0.003$) (11). Similarly, Washko et al. found that quantitative progression of emphysema on PRM carried a hazard ratio of 1.8 (95% CI: 1.3-2.5) for all-cause mortality (12). In the context of treatment planning, DECT altered clinical management in 31% of IPF patients by revealing significant perfusion defects not apparent on standard CT (4). Furthermore, hyperpolarized gas MRI provided unique functional insights in asthma, with Vogel-Claussen et al. showing significant changes in regional ventilation heterogeneity post-bronchodilator ($p<0.01$) that were not captured by spirometric FEV_1 measurements (8), suggesting a potential role in guiding biologic therapy.

DISCUSSION

This systematic review synthesized evidence from eight recent studies to evaluate the role of advanced radiological imaging in the management of chronic pulmonary diseases. The findings consistently demonstrate that modalities such as parametric response mapping, hyperpolarized gas MRI, dual-energy CT, and deep learning-enhanced CT analysis provide significant added value over conventional diagnostic workups. The evidence indicates that these techniques offer superior sensitivity in detecting early pathophysiological changes, enable precise phenotyping of heterogeneous diseases like COPD and IPF, and provide robust quantitative biomarkers for monitoring disease progression and predicting clinically relevant outcomes such as exacerbation risk and mortality (7, 11, 12, 13). The overall strength of this evidence is bolstered by the inclusion of several large, prospective cohort studies and RCTs, which collectively point towards a paradigm shift from purely anatomical to functional and quantitative lung imaging. When contextualized within the broader scientific landscape, these findings both confirm and extend the conclusions of earlier, more focused investigations. A previous review by Vogel-Claussen et al. had highlighted the potential of novel MRI and CT biomarkers, and the current synthesis provides substantial new data from subsequent years that validates this potential in larger, multi-center cohorts (8). For instance, the results from the SPIROMICS and COPDGene studies, included in this review, provide a level of evidence previously unavailable, firmly establishing the prognostic value of PRM-derived metrics (11, 12). Similarly, while the concept of quantitative CT analysis in IPF has been explored before, the study by Sverzellati et al. (13) directly demonstrates its superiority over visual scoring for mortality prediction, a finding that resolves prior ambiguity in the literature. The review also identifies a growing consensus on the ability of hyperpolarized gas MRI to uncover functional deficits that remain occult to spirometry, a consistency that strengthens the argument for its use in specific clinical scenarios, particularly severe asthma and complex COPD (9, 8). A principal strength of this review lies in its rigorous methodological adherence to PRISMA guidelines, which minimizes selection bias and enhances the reproducibility of its conclusions (6). The comprehensive search strategy across multiple databases, coupled with a dual-reviewer selection and data extraction process, ensures that the findings are based on a thorough and critical appraisal of the current evidence base.

Furthermore, the application of standardized risk-of-bias tools provides a transparent assessment of the included studies' quality, allowing for a nuanced interpretation of the results. The focus on the most recent five-year literature ensures that the review captures the rapid technological advancements in this field, making its conclusions highly relevant for contemporary clinical and research practice. Notwithstanding these strengths, several limitations warrant consideration. The heterogeneity in the specific imaging protocols, outcome measures, and patient populations across the included studies precluded a quantitative meta-analysis, limiting the synthesis to a qualitative summary. While the included studies were generally of high quality, the inherent challenges in blinding personnel to advanced imaging interventions introduce a potential for performance bias in some of the RCTs. Furthermore, the focus on peer-reviewed, English-language publications may have omitted relevant data presented in other formats or languages, potentially introducing publication bias. The generalizability of findings for some modalities, particularly hyperpolarized gas MRI, may be constrained by its limited availability outside major academic centers, reflecting a disparity between research utility and widespread clinical implementation. The implications of these findings are substantial for both clinical practice and future research. For clinicians, this review provides a compelling evidence base supporting the integration of advanced imaging into the diagnostic and monitoring algorithms for complex chronic pulmonary diseases. The ability to precisely phenotype COPD patients using PRM or deep learning can

guide more personalized treatment plans, including targeted lung volume reduction or selection of specific biologic therapies (7, 11). In IPF, DECT and quantitative CT can offer critical prognostic information that informs the timing of interventions and discussions with patients (4, 13). For the research community, this review underscores the need for larger, multi-center randomized trials designed with patient-centered outcomes as primary endpoints to definitively establish the impact of these technologies on long-term morbidity and quality of life. Future studies should also aim to standardize imaging protocols and analytical pipelines to facilitate cross-study comparisons and accelerate the translation of these powerful tools from research laboratories into routine clinical practice.

CONCLUSION

In conclusion, this systematic review consolidates robust evidence that advanced radiological imaging techniques, including parametric response mapping, hyperpolarized gas MRI, and dual-energy CT, significantly enhance the diagnostic precision, phenotyping, and monitoring of chronic pulmonary diseases beyond the capabilities of conventional imaging and pulmonary function tests. The clinical significance of these findings is profound, as they provide a pathway towards more personalized medicine by enabling clinicians to identify specific disease phenotypes, predict individual patient trajectories for outcomes like exacerbations and mortality, and make more informed decisions regarding treatment planning. While the collective evidence from recent high-quality studies is compelling and underscores the transformative potential of these technologies, their current application remains largely confined to research-oriented centers, highlighting a critical need for future efforts focused on standardizing protocols, demonstrating cost-effectiveness, and validating their impact on patient-centered outcomes in diverse, real-world clinical settings to fully realize their integration into routine care.

AUTHOR CONTRIBUTIONS

Author	Contribution
Fatima Mahboob	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Mohammad Bilal Ayad	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Rabia Khattak*	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Muhammad Affan Nadeem	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammed Zakria	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Faiza Shabir Abro	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Aqsa Iqbal	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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