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Review

MicroRNAs and Long Non-Coding RNAs in Chronic Rhinosinusitis with Nasal Polyps: A Systematic Review

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Abstract

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a chronic inflammatory disorder characterized by heterogeneous molecular mechanisms and frequent disease recurrence. Advances in transcriptomics have highlighted the potential involvement of microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) in its pathogenesis. This systematic review evaluated the expression patterns, biological functions, and potential clinical implications of miRNAs and lncRNAs in CRSwNP. PubMed and Scopus were systematically searched, and 52 studies met the eligibility criteria: 41 investigated miRNAs exclusively, seven investigated lncRNAs exclusively, and four examined both RNA classes. More than 400 miRNA species and 500 lncRNAs were reported across the included studies, of which 128 miRNAs and 33 lncRNAs were examined in detail. Among the highlighted miRNAs, only 23 were investigated in more than one study, indicating limited independent replication. The identified non-coding RNAs were associated with inflammatory signaling, epithelial–mesenchymal transition, apoptosis, and tissue remodeling. Although several molecules showed potential as biomarkers or therapeutic targets, methodological heterogeneity and limited validation restrict their current clinical applicability. Further standardized, multicenter studies are needed to establish their diagnostic, prognostic, and therapeutic utility.

Keywords: miRNA; lncRNA; CRSwNP; nasal polyps

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1. Introduction

Chronic rhinosinusitis is an inflammatory condition of the nasal cavity and paranasal sinuses, characterized by persistent inflammation of the sinonasal mucosa. It is one of the most common conditions encountered in otorhinolaryngology and is classically divided into two separate phenotypes: chronic rhinosinusitis with nasal polyps (CRSwNP) and without nasal polyps (CRSsNP).

CRSwNP is defined by the presence of nasal polyps, which are bilateral benign masses that typically arise from the ethmoidal mucosa and extend through the middle meatus inside the nasal cavity. They cause varying degrees of nasal obstruction, facial pressure, hyposmia or anosmia, and rhinorrhea [1]. CRSwNP may occur as an isolated condition, or alongside comorbidities such as asthma, atopic dermatitis, or hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs). The coexistence of nasal polyposis, asthma, and NSAID

hypersensitivity is commonly known as Widal syndrome (or aspirin-exacerbated respiratory disease, AERD).

Although the exact etiology remains incompletely understood, impaired mucociliary clearance, epithelial barrier dysfunction, microbial dysbiosis, and type 2 inflammation are considered major contributors to disease development. CRSwNP may also be associated with elevated eosinophil levels in tissue and blood. Diagnosis is primarily based on clinical findings, including the presence of bilateral nasal polyps, supported by imaging to assess sinus involvement and, when indicated, histopathological examination for differential diagnosis [1].

Conservative treatment includes topical or systemic corticosteroids and saline nasal irrigation, while severe or refractory cases may require endoscopic sinus surgery [1–3]. Biologic therapies, including mepolizumab (anti-IL-5), omalizumab (anti-IgE), and dupilumab (anti-IL-4Rα), have further expanded the therapeutic options for patients with severe CRSwNP [3].

Several potential biomarkers have been proposed for CRSwNP, including blood eosinophil count, total IgE, eotaxin, and periostin. However, none has yet entered routine clinical practice [4]. Recent studies have investigated associations between non-coding RNAs, including miRNAs and lncRNAs, and the risk of disease recurrence or response to treatment.

This systematic review aims to synthesize the available evidence regarding miRNAs and lncRNAs in CRSwNP, with particular emphasis on their expression patterns, underlying biological mechanisms, and potential utility as biomarkers of disease severity, treatment response, and recurrence.

Although previous reviews have examined epigenetic mechanisms in chronic rhinosinusitis and the role of microRNAs in CRSwNP, an updated and focused synthesis of the evidence on non-coding RNA dysregulation, encompassing both microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), in CRSwNP is lacking. In particular, the existing literature has not comprehensively addressed the consistency of reported miRNA and lncRNA alterations across independent studies and their potential implications for CRSwNP pathogenesis, diagnosis, prognosis, and therapeutic development.

2. Materials and Methods

A literature search was conducted in the PubMed and Scopus databases using the search terms described below. These databases were selected because of their extensive coverage of the biomedical literature, particularly in otolaryngology and molecular biology and were considered appropriate for identifying studies directly addressing this topic. The structure of this paper was designed according to the PRISMA 2020 guidelines [5]. For the PubMed database, for miRNA studies, the following search terms were used: “miRNA nasal polyp”, “microRNA nasal polyp” and “miR nasal polyp”, yielding 86, 75, and 53 records respectively, until 22 October 2026. The search using the term “miRNA” retrieved all studies identified by the other two search strategies (“microRNA nasal polyp” and “miR nasal polyp”). Therefore, this search was selected as the primary source for study screening and selection. For consistency, we used the same “miRNA” and “nasal polyp” keyword combination for the Scopus database, obtaining 28 papers. Eligible studies investigated patients diagnosed with CRSwNP, analyzed non-coding RNAs obtained from blood or nasal polyp tissue using appropriate control specimens, and were published in English. From this review, we excluded all the other review papers on this topic, the studies that focused on obtaining the non-coding RNA from nasal fluid lavage, the papers written in foreign languages, and papers focused on other pathologies. Moreover, 1 article was retracted; therefore, it was not included in this review.

For lncRNA the following search terms were used for the PubMed database: "lncRNA nasal polyp" and "long non-coding RNA nasal polyp" yielding 17 and 14 studies, respectively, as of 22 October 2026. The search term "lncRNA nasal polyp" was retained for study selection because it encompassed the records identified by the alternative query. Furthermore, for consistency, the "lncRNA" and "nasal polyp" combination was preserved for the Scopus search, yielding 8 articles. Inclusion and exclusion criteria applied were the same as for miRNA studies.

The complete search strategies used in PubMed and Scopus, including the exact search terms, search dates, and number of records retrieved, are presented in Supplementary Table S1.

The main author coordinated the study-selection process, while the co-authors independently reviewed the eligible records. The main author performed the initial data extraction, while the extracted information and quality assessments were subsequently checked by the co-authors against the original publications to verify their accuracy and consistency. The inclusion or exclusion of each article was performed by the reading of the full text, applying the inclusion and exclusion criteria mentioned above. The main author collected all the data from the included articles, which consisted in the direction of non-coding RNA expression changes between the case and control groups.

Given the substantial heterogeneity among the included studies in terms of patient populations, biological specimens, RNA detection platforms, normalization procedures, and reported quantitative outcomes, a meta-analysis was not considered appropriate. Because quantitative results were not reported in a uniform manner across studies, fold changes and statistical estimates were not directly compared or pooled. Therefore, a structured qualitative synthesis was performed, focusing on the direction and consistency of miRNA and lncRNA expression changes across studies.

miRNA nomenclature was evaluated against miRBase, while human gene and lncRNA symbols were checked against HGNC recommendations [6,7]. To preserve consistency with the original publications and avoid introducing unsupported changes in RNA identity, historical nomenclature and study-specific transcript identifiers were retained as originally reported.

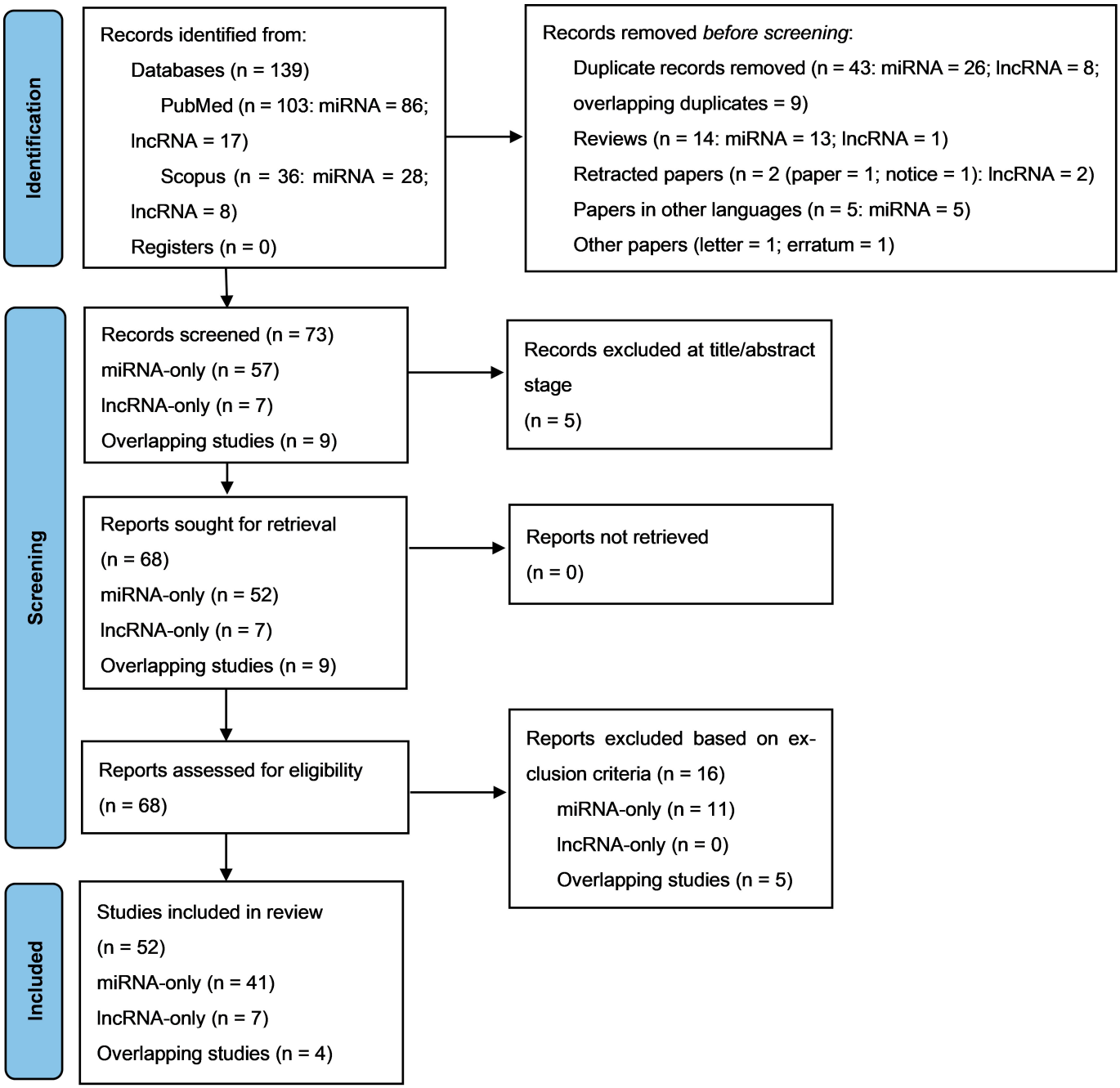
The methodological quality and risk of bias of the included studies were assessed using the Newcastle–Ottawa Scale (NOS) [8], with the results summarized in Table A1. For the interpretation of NOS scores, studies receiving 7–9 stars were classified as having a low risk of bias, those receiving 4–6 stars as moderate risk, and those receiving 0–3 stars as high risk. These thresholds were applied consistently across all included studies.

The manuscript was initially developed as a narrative review. Later, the manuscript was restructured as a systematic review. The PubMed search was first updated to include publications up to 22 October 2026. Subsequently, the systematic-review protocol was registered in PROSPERO on 26 October 2026 (CRD420261550980). The eligibility criteria and primary outcomes were defined before registration and remained unchanged thereafter. Following registration, the inclusion and exclusion criteria were reapplied to the PubMed records, and the literature search was expanded to Scopus using the same publication cutoff date. The combined records were then reassessed according to the predefined eligibility criteria, followed by the methodological quality assessment and structured qualitative synthesis.

3. Results

A total of 139 records were identified for the review from the selected databases. Following the identification, screening, and eligibility assessment processes, 52 studies met the inclusion criteria and were included in the systematic review (Scheme 1). The articles excluded following full-text assessment, together with their corresponding reasons for

exclusion, are detailed in Supplementary Table S2. Of the 52 included studies, 41 investigated miRNAs exclusively, seven investigated lncRNAs exclusively, and four investigated both RNA classes (Figure 1).



Scheme 1. Identification of studies via databases and registers.

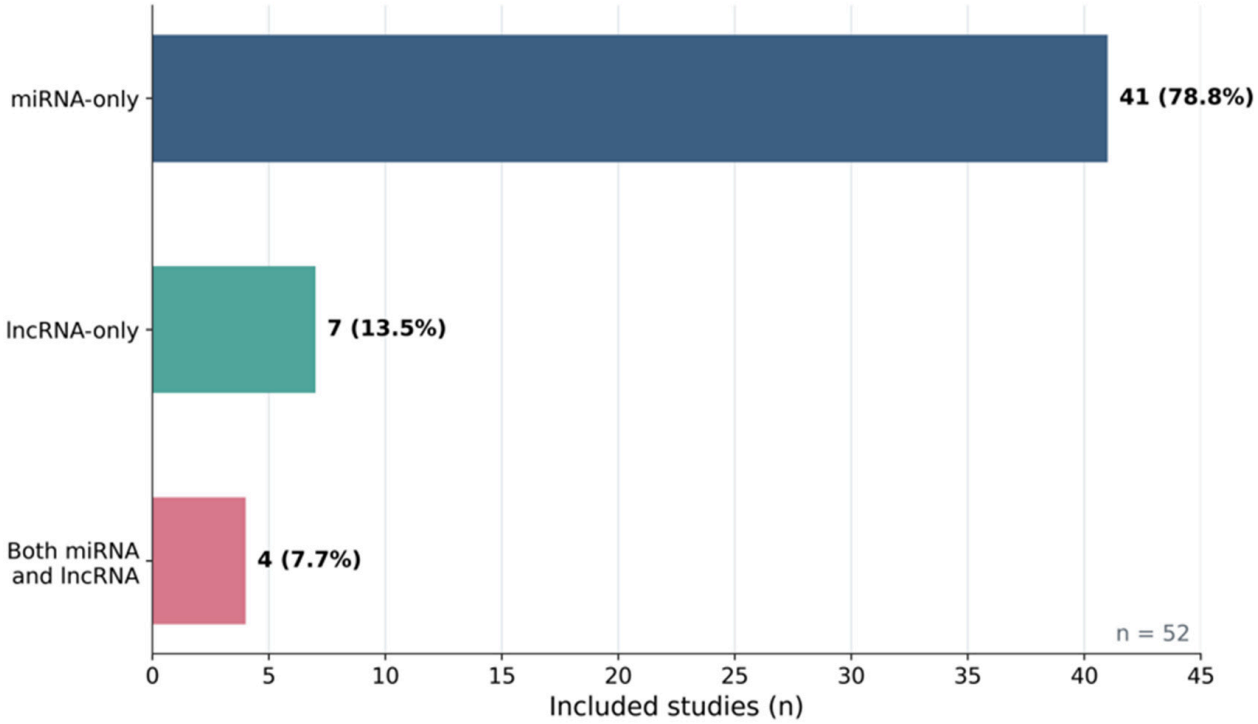


Figure 1. Distribution of included studies according to the non-coding RNA class investigated. Of the 52 studies included in this systematic review of chronic rhinosinusitis with nasal polyps (CRSwNP), 41 (78.8%) investigated microRNAs (miRNAs) exclusively, 7 (13.5%) investigated long non-coding RNAs (lncRNAs) exclusively, and 4 (7.7%) investigated both RNA classes. Each study was assigned to one mutually exclusive category to avoid double counting.

Across the included miRNA studies, more than 400 miRNA species were identified, of which 128 were examined in detail. Several miRNAs, including miR-145-5p, miR-125a, and miR-125b, were investigated in multiple studies.

Of the 128 highlighted miRNAs, 23 (17.97%) were investigated in more than one study, whereas 105 (82.03%) were reported in a single study (Figure 2). This limited overlap between investigations, together with the variability in expression direction observed for some miRNAs, highlights the need for further independent validation. The identified miRNAs and their reported expression patterns are presented in Table A2.

To further assess the reproducibility of the reported findings, a structured comparison of the 23 miRNAs investigated in more than one study was performed (Table 1). Among these, 18 showed concordant expression patterns, four were partially concordant, and one exhibited discordant results across studies. Notably, miR-145-5p consistently showed decreased expression, whereas miR-203a-3p exhibited conflicting expression patterns. These findings highlight both the potential reproducibility of certain miRNA alterations and the considerable variability across investigations. Differences in biological specimens, control groups, analytical platforms, and inflammatory endotypes may contribute to the observed heterogeneity and should be considered when interpreting these results. Additional study-level information, including sample sizes, biological specimen types, and RNA detection platforms, is provided in Supplementary Table S3, allowing methodological differences to be considered when interpreting the expression patterns summarized in Table 1.

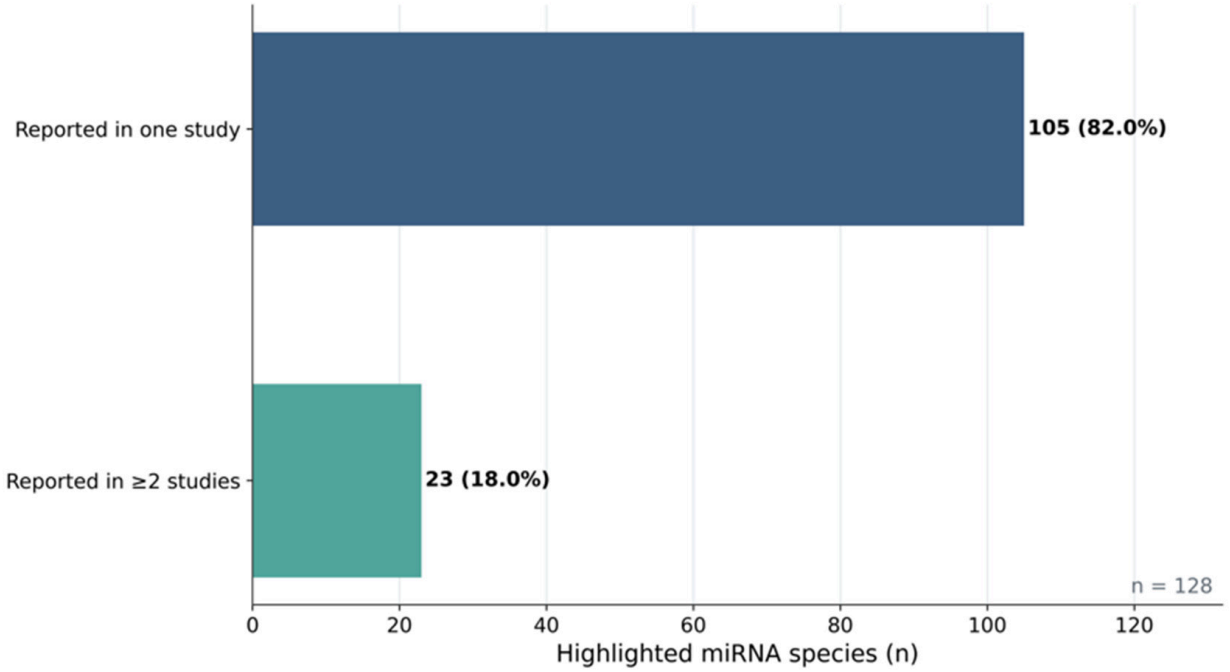


Figure 2. Frequency of investigation of individual miRNA species across the included studies. Among the 128 distinct high-lighted miRNA species, 105 (82.03%) were reported in a single study, whereas 23 (17.97%) were reported in two or more studies. Repeated investigation indicates that the same miRNA species was examined in multiple studies, but does not by itself imply agreement in expression direction.

Table 1. Direction and consistency of expression changes among recurrently investigated miRNAs in CRSwNP.

miRNA	Studies (n)	References	Expression Direction	Consistency	Risk-of-Bias Context
miR-203a-3p	2	[9,10]	Increased (1); decreased (1)	Discordant	No high-risk study identified
miR-143-3p	3	[11–13]	Decreased in all studies	Concordant	Includes high-risk study [12]
miR-145-5p	7	[9,14–19]	Decreased in all studies	Concordant	No high-risk study identified
miR-214-5p	2	[14,16]	Decreased in all studies	Concordant	No high-risk study identified
miR-27b-3p	2	[14,17]	Decreased in all studies	Concordant	No high-risk study identified
miR-23b-3p	2	[14,16]	Decreased in all studies	Concordant	No high-risk study identified
miR-138-5p	2	[14,16]	Decreased in all studies	Concordant	No high-risk study identified
miR-187-3p	2	[14,16]	Decreased in all studies	Concordant	No high-risk study identified
miR-23a-5p	2	[14,20]	Decreased in all studies	Concordant	No high-risk study identified
miR-132-3p	3	[14,16,17]	Decreased in all studies	Concordant	No high-risk study identified
miR-375	2	[14,20]	Decreased in all studies	Concordant	No high-risk study identified
miR-125a-5p	3	[14,16,17]	Decreased (2); no difference (1)	Partially concordant	No high-risk study identified
miR-125b	4	[10,21–23]	Increased in all studies	Concordant	No high-risk study identified
miR-125b-5p	2	[24,25]	Increased in all studies	Concordant	No high-risk study identified
miR-21	2	[26,27]	Increased in all studies	Concordant	No high-risk study identified
miR-155	2	[22,28]	Increased in all studies	Concordant	No high-risk study identified
miR-155-5p	2	[29,30]	Increased in all studies	Concordant	No high-risk study identified

Table 1. *Cont.*

miRNA	Studies (n)	References	Expression Direction	Consistency	Risk-of-Bias Context
miR-223-5p	2	[11,31]	Increased in all studies	Concordant	No high-risk study identified
miR-449a	2	[31,32]	Increased in all studies	Concordant	No high-risk study identified
miR-221-3p	2	[32,33]	Increased in all studies	Concordant	No high-risk study identified
miR-18a	2	[34,35]	Increased (1); no difference (1)	Partially concordant	No high-risk study identified
miR-377-5p	2	[20,36]	Decreased (1); no difference (1)	Partially concordant	No high-risk study identified
miR-92a	2	[22,35]	Decreased (1); no difference (1)	Partially concordant	No high-risk study identified

46 miRNAs (35.94%) were increased in CRSwNP patients in comparison to the control groups, 7 miRNAs (5.47%) presented no differences between the studied groups, 5 miRNAs (3.91%) had different values across multiple studies, while the rest of 70 (54.69%) were decreased in the case groups (Figure 3).

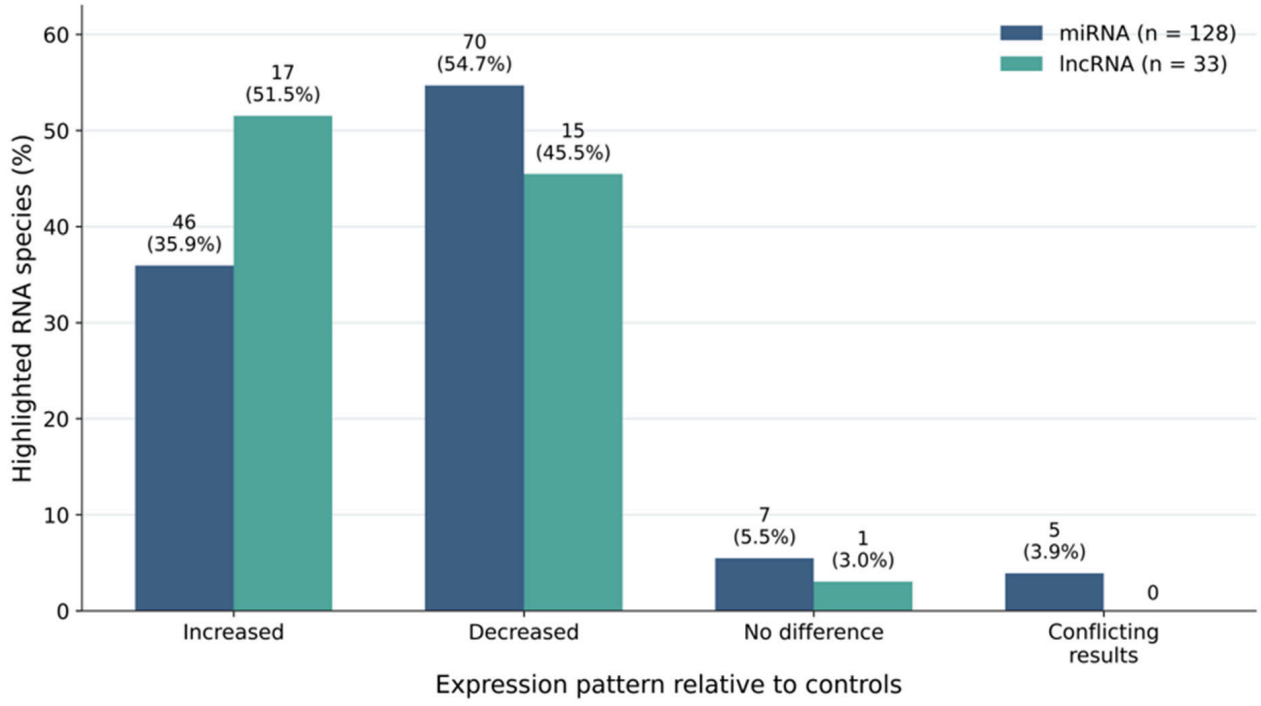


Figure 3. Differential expression patterns of highlighted miRNAs and lncRNAs in chronic rhinosinusitis with nasal polyps (CRSwNP) relative to control groups. Among the 128 highlighted miRNA species, 46 (35.94%) showed increased expression, 70 (54.69%) showed decreased expression, 7 (5.47%) showed no significant difference, and 5 (3.91%) exhibited conflicting results across studies. Among the 33 highlighted lncRNAs, 17 (51.52%) showed increased expression, 15 (45.45%) showed decreased expression, and 1 (3.03%) showed no significant difference. No conflicting expression patterns were reported among the highlighted lncRNAs. Bars represent percentages, and labels indicate absolute counts and percentages.

Across the included lncRNA studies, more than 500 differentially expressed lncRNAs were identified, although only 33 were highlighted and discussed in detail. XLOC_010280 was the only highlighted lncRNA replicated across multiple studies. The subtypes are presented in Table A3.

One lncRNA (3.03%) had similar values between the groups, while the increased group was represented by 17 different subtypes (51.52%) and the decreased group was represented by 15 different subtypes (45.45%) (Figure 3).

4. Discussion

The findings of this systematic review highlight the involvement of miRNAs and lncRNAs in multiple biological processes associated with CRSwNP. The following sections discuss the reported expression patterns, their consistency across studies, the potential underlying molecular mechanisms, and their clinical implications, while considering the limitations of the available evidence.

4.1. miRNA

The miR-145 family was among the most frequently investigated, with one study examining miR-145-3p [11], and seven studies investigating miR-145-5p [9,14–19]. Both strands showed decreased expression in CRSwNP compared with the respective control groups.

The miR-125 family was also frequently investigated. Four studies examined miR-125a and its variants: three investigated miR-125a-5p [14,16,17], with two reporting decreased expression and one reporting no difference between groups, while one study investigated miR-125a-3p [11] and reported increased expression. Seven studies examined miR-125b and its variants [10,20–25], including two investigating miR-125b-5p [24,25], and one investigating miR-125b-2-3p [20]. Increased expression was reported in all studies except the latter, which observed decreased expression [20].

Morawska-Kochman M et al. [9] suggested that the unchanged expression of miR-146a-5p between groups may reflect a compensatory response aimed at limiting inflammation. They also associated decreased miR-17-5p and miR-145-5p expression, together with increased miR-203a-3p expression, with enhanced apoptosis in CRSwNP. Gata A et al. [10] reported decreased expression of miR-203a-3p, which was observed especially in patients with environmental allergies, accompanied by increased levels of miR-125b. The decreased levels of miR-145-5p were also observed by Zhang M et al. [14], who described the link between increased TGF-β1 which promoted the epithelial–mesenchymal transition and the decreased miR. Li X et al. [27] revealed the same pathway in the polyp development, but through increased levels of miR-21. Its variant, miR-21-5p was observed by Luan G et al. [37] to target glucagon-like peptide-1 receptor/IL-33 pathway, aggravating the type 2 inflammation.

miR-21 has been implicated in inflammatory processes relevant to CRSwNP. Liu R et al. [26] suggested that miR-21 may modulate inflammatory responses in CRSwNP through mechanisms involving IL-10.

The increased levels of miR-125b were also observed and described in studies performed by Song L et al. [21] (activating the Wnt/β-catenin signaling pathway through increased Sp1 which worked as an upstream regulator promoting the transcription of the miR in nasal polyps), Xia G et al. [22], Zhang XH et al. [23] (enhancing type I IFN expression in eosinophilic CRSwNP by suppression of 4E-BP1) and Li K et al. [24] (presenting the increased expression of IFN-β targeting 4E-BP1), the latter also obtaining 357 de-creased miRNA species. A downregulated miR-125b-2-3p, among other 18 decreased miRNA and 5 upregulated miRNAs were studied by Xuan L et al. [20] concluding the mucin type O-glycan pathway in upregulated variants and TGF-β1 in the downregulated group. Although the study was performed on children, the paper of Yu H et al. [38] demonstrates the role of miR-663 in the regulation and expression of TGF-β1 gene, and thus its role in the development and onset of nasal polyps.

Sun Q et al. [39] postulated in their study the decreased levels of miR-1260b and miR-6507-5p and classified them as key regulators in competitive endogenous RNA networks in the development of CRSwNP.

A study performed by Li H et al. [15] revealed decreased levels of miR-145-5p and miR-582-5p in nasal polyps, with no differences between groups regarding miR-450-5p.

Qing X et al. [40] evaluated the implications of miR-142-3p in the development of CRSwNP. Increased levels of miR-142-3p were observed through lipopolysaccharide-TNF-α pathway, with increased TNF-α levels detected in the human nasal epithelial cells in the case group, compared to the control group.

Chen JC et al. [16] identified a potential regulatory axis in CRSwNP through MIAT/miR-125a-IRF4 axis, constructing a potential lnc-RNA-miRNA-mRNA network for an in depth understanding of the pathogenesis.

Yu J et al. [17] offered strong evidence of the implication of miR-145-5p in the development and occurrence of CRSwNP, after discovering and evaluating 192 significant downregulated and no upregulated miRNAs in the case group.

Increased miRNA values were observed by Jiang W et al. [41] who studied the epithelial-to-mesenchymal transition (EMT) and polyp formation due to increased levels of miR-182, Yang N et al. [29] who concluded the prevention of EMT by targeting miR-155-5p, and Zhang W et al. [42] who pointed out the role of miR-22-3p in the regulation of vascular permeability by targeting the vascular-endothelial-cadherin. The EMT can also be prevented by targeting miR-30a-5p, as its downregulated levels are associated with increased EMT, as observed in a study published by Zhang T et al. [43]. Wang X et al. [44] observed increased values of miR-375-3p and its EMT-inducing effects in Eos-CRSwNP.

A downregulated miR-4492 level was observed and analyzed, together with increased IL-10 values by Li L et al. [45] acting through Jak/STAT signaling pathway. Increased expression of STAT1 and miR-18a promoted EMT through STAT1/miR-18a-PTEN axis, as observed by Jian B et al. [34]. Du J et al. [28] described the higher relapse risk of Eos CRSwNP caused by upregulated NF-kB/miR-155 via COX2 induction.

Silveira MLC et al. [32] reported increased expression of six miRNAs implicated in cell cycle regulation, apoptosis and inflammation, with emphasis on miR-205-5p being increased in patients with higher T2 inflammation through increased levels of IL-5. Bu X et al. [31] discovered multiple miRNA-mRNA regulatory networks, highlighting the roles of miR-154, miR-221, miR-223 in the development of Eos CRSwNP and miR-449 in non-Eos variant. Hartung F et al. [11] observed downregulated miR-143-3p and miR-145-3p and 6 upregulated miRNAs (miR-125a-3p, miR-1246, miR-182-5p, miR-223-5p, miR-9-5p and let-7f) with emphasis on the implication of let-7 family in the aberrant response of macrophages described in NSAID-exacerbated respiratory disease. The association between downregulated miR-143-3p and severe CRSwNP was also observed and published by Tubita V et al. [12] and Tang P et al. [13]. Furthermore, the role of let-7 family through let-7a-5p was described by Zhang J et al. [46] through Ras-MAPK pathway.

Callejas-Díaz B et al. [47] concluded the malfunction of cilia and ciliogenesis caused by altered expression of miR-34 and miR-449 families. A distinct miR-200 family variant (miR-200a-3p) was downregulated in a study performed by Wu Y et al. [48], concluding its role in the development of EMT.

Another pathway described in the literature in the inflammatory response of CRSwNP was through aryl hydrocarbon receptor (AHR) which was negatively correlated with the decreased levels of miR-124 in the work of Liu CC et al. [49]. Wang Z et al. [50] studied the overexpression of miR-214 in both CRSwNP and CRSsNP patients and its regulatory role in lipopolysaccharide-mediated inflammation.

Shuman Li et al. [51] concluded the implication of miR-199-3p modulation of EMT through miR-199-3p/PAK4 axis. He S et al. [52] described the exosomal miRNA profile of patients with CRSwNP, expanding the knowledge and understanding of the regulatory mechanisms in pathogenesis, describing 93 increased and 66 decreased subtypes.

In their work, Wang G et al. [36] expanded the list of potential biomarkers to be used in the diagnosis and the treatment of CRSwNP, by observing the values and implication of several miRNAs. With emphasis on miR-141-3p and miR-3679-5p, between different 3 sets of case–control groups, they described their potential as novel biomarkers and therapeutic targets.

The paper of Tepebaşi MY et al. [30] offered insight into the potential role of miR-155-5p as a therapeutic target and its role in the PIK3K/AKT/HIF-1 pathway.

Another pathway of miR-145-5p was described by Wang L et al. [18], mentioning the regulation of inflammatory response by targeting CD40.

Luo XQ et al. [35] concluded in their research the potential involvement of miR-19a in the suppression of IL-10 and its potential as a target for novel therapeutic agents. Liu Zhuohui et al. [53] acknowledged the role of miR-29b-3p/MMP-9 signaling pathway as a potential target for future therapeutic investigation.

In their paper, Shi M et al. [19] described the role of miR-145-5p through circRNA_0021727-miR-145-5p-ADAM12 pathway in eosinophilic CRSwNP.

The role of miR-221-3p as an inhibitor for mast cells-dependent type 2-inflammation was verified and explained by Liu R et al. [33]. Moreover, the regulation of dendritic cells in different types of CRS through distinctive patterns of miRNA gene expression was published by Ma ZX et al. [25].

4.2. lncRNA

Among the 11 included studies investigating lncRNAs, XLOC_010280 was the only highlighted lncRNA examined in two independent investigations.

Liu Z et al. [54] investigated the involvement of upregulated LINC01094 in the EMT process in the nasal mucosa and pyroptosis through HMGB1 pathway. Li H et al. [15] evaluated hundreds of non-coding RNAs, including 230 differentially expressed lncRNAs, involved in multiple biological pathways, focused also on inflammation and immunity. Similarly, Li K et al. [24], also studied hundreds of competing endogenous RNA in the pathophysiology of eosinophilic CRSwNP.

Liu M et al. [55] described the role of lncRNA XLOC_010280 in the regulation of CCL18 and inflammation and the role of RP11 798M19.6 in regulating GALNT7 and cell proliferation. Chen JC et al. [16] analyzed the role of MIAT in the development of CRSwNP through MIAT/miR-125a/IRF4 axis.

Wang M et al. [56] observed the upregulation of LINC01146 and its role in T cell receptor signaling pathway, cell differentiation of Th1 and Th2, cytotoxicity mediated by natural killer cells and phagocytosis. Wang W et al. [57] studied the eosinophilic inflammation in their study, concluding the role of lncRNA XLOC_010280 in regulating CCL18.

Another study published by Ma Y et al. [58] described the decreased levels of NRON (although much lower in the CRSsNP) compared to the control group and the influence of IL-17A and dexamethasone over its levels.

Zhou X et al. [59] reported that MALAT1 and XIST, lncRNA previously described to be related to the occurrence in cancer, are also significantly downregulated in CRSwNP group, compared to healthy patients' group, and thus implies a possible common path-way in CRSwNP and cancer development.

The role of NEAT1 in EMT through miR-199-3p/PAK4 axis, as well as its role as a potential biomarker and therapeutic target was described by Li Shuman et al. [51], while Li

Shenting et al. [60] presented PVT1 as a possible new therapeutic target and its purpose in epithelial barrier function impairment.

4.3. Signaling Pathways and Underlying Mechanisms

The findings of this review provide further evidence that non-coding RNAs, particularly miRNAs, are involved in several of the biological processes underlying chronic rhinosinusitis with nasal polyps (CRSwNP). Rather than being associated with a single inflammatory pathway, the identified miRNAs were implicated in inflammation, epithelial–mesenchymal transition (EMT), apoptosis, tissue remodeling, vascular permeability, ciliogenesis and type-2 eosinophilic inflammation [9–12,14–17,20–24,26–29,31,32,34,37–45,47–50]. This broad involvement is consistent with the current understanding of CRSwNP as a heterogeneous inflammatory disease in which multiple molecular pathways interact to determine disease phenotype and severity. The increasing recognition of distinct CRSwNP endotypes has emphasized the need to identify molecular mechanisms and biomarkers that can better characterize individual patients beyond the conventional presence or absence of nasal polyps.

Among the miRNAs identified in this review, miR-145-5p represents one of the most consistently investigated candidates. Its decreased expression was reported in several studies and was associated with mechanisms relevant to epithelial integrity, apoptosis and EMT [9,14–19]. The relationship between reduced miR-145-5p expression and increased TGF-β1 activity is particularly relevant, as TGF-β signaling is an important mediator of epithelial remodeling and fibrosis. Therefore, reduced miR-145-5p may contribute to the persistence of pathological epithelial remodeling and polyp formation. The repeated identification of miR-145-5p across independent studies strengthens its potential biological relevance. Nevertheless, the available evidence remains insufficient to establish whether its decreased expression is a primary driver of disease or a consequence of the inflammatory microenvironment.

The miR-125 family, particularly miR-125b, represents another important group. In contrast to miR-145-5p, miR-125b was predominantly reported as upregulated. Several studies linked its expression to Wnt/β-catenin signaling, Sp1 regulation, type I interferon responses and 4E-BP1. These findings suggest that miR-125b may participate in the interaction between epithelial abnormalities and inflammatory signaling. However, the observation of decreased miR-125b-2-3p in another study highlights the importance of distinguishing individual strands and variants rather than treating a miRNA family as a single biological entity. This strand-specific behavior may partly explain apparently contradictory results across studies [10,20–24].

Other recurrent findings further support the involvement of non-coding RNAs in the regulation of the inflammatory and remodeling environment. Increased miR-21 and miR-21-5p were associated with inflammatory signaling and EMT, including the GLP-1R/IL-33 pathway and IL-10-related mechanisms [26,37]. Similarly, miR-155, miR-182 and miR-375-3p were associated with EMT and tissue remodeling [28,41,44], while miR-22-3p was implicated in vascular permeability through regulation of vascular endothelial cadherin [42]. The involvement of these molecules suggests that miRNAs may act at the interface between persistent inflammation, epithelial dysfunction and structural remodeling rather than representing isolated markers of inflammation.

The findings concerning type 2 inflammation are particularly relevant to contemporary models of CRSwNP. Increased miR-205-5p was associated with higher T2 inflammation and increased IL-5 [32], while miR-125b was linked to eosinophilic inflammatory mechanisms in several studies [10,20–24]. These observations suggest that specific miRNA profiles may reflect or potentially regulate the intensity of type 2 inflammatory responses. This is clinically relevant because T2 inflammation is an important determinant of disease severity

and treatment selection in CRSwNP, particularly in the era of biologic therapies. However, current evidence indicates that biomarkers are generally more useful for identifying inflammatory endotypes than for reliably selecting one specific biologic over another [61].

The involvement of miRNAs in ciliogenesis and epithelial homeostasis provides another important dimension to their biological significance. Altered expression of the miR-34 and miR-449 families was associated with impaired ciliary function and ciliogenesis [31,32,47]. Because effective mucociliary clearance is essential for sinonasal homeostasis, dysregulation of these pathways could contribute to persistence of inflammation by impairing the ability of the sinonasal epithelium to remove mucus, pathogens and environmental stimuli. Similarly, the reported involvement of miR-124, miR-200 family members and other miRNAs in epithelial and inflammatory signaling suggests that non-coding RNAs may participate in maintaining the abnormal epithelial state characteristic of chronic disease [48,49].

Although several miRNAs demonstrated recurrent associations, the overall evidence was characterized by considerable heterogeneity. The most notable examples were miR-145-5p and miR-125b, for which multiple independent studies reported alterations in expression and proposed biologically plausible mechanisms. These recurrent findings provide stronger evidence than observations reported by individual studies alone.

However, consistency was considerably weaker for many other miRNAs. miR-125a-5p showed different results between studies, miR-203a-3p was reported as both increased and decreased between studies, and miR-450-5p did not consistently demonstrate a significant difference between CRSwNP and control groups. Such discrepancies indicate that differential expression alone may not be sufficient to establish a miRNA as a disease-specific marker.

Several factors may contribute to these inconsistencies. CRSwNP encompasses multiple inflammatory endotypes, including type 1, type 2 and type 3 patterns, and molecular profiles may differ according to eosinophilic status, allergy, disease severity, recurrence and comorbidities. Differences in tissue source, control tissue, sample size, analytical platform, normalization strategy and miRNA strand identification may further contribute to variation. The current evidence should be interpreted as demonstrating biological plausibility and repeated associations rather than definitive causal relationships.

The methodological quality of the included studies also influenced the interpretation of the findings. According to the Newcastle–Ottawa Scale assessment (Table A1), 37 studies (71.15%) were classified as having a low risk of bias, 12 (23.08%) as moderate risk, and three (5.77%) as high risk [12,50,53]. Findings supported primarily by studies at high risk of bias were interpreted with greater caution, particularly when independent validation was lacking. In contrast, the consistently decreased expression of miR-145-5p across seven studies not classified as high risk of bias [9,14–19] provides comparatively stronger evidence of a reproducible association with CRSwNP, as none of the seven contributing studies fell into this category. However, the influence of excluding high-risk studies on the broader findings was not systematically reassessed. Nevertheless, differences in study populations, sample sources, and analytical methods limit the strength of the conclusions, and even consistent findings cannot establish causality or clinical biomarker validity.

Taken together, the findings suggest that miRNAs may function as molecular regulators connecting several major components of CRSwNP pathogenesis. Dysregulated miRNAs may consequently reinforce the inflammatory environment and contribute to the persistence and recurrence of nasal polyps.

The identified pathways also illustrate the considerable interconnection between inflammatory and structural mechanisms. For example, TGF-β-related signaling, EMT, apoptosis and type 2 inflammation should not necessarily be regarded as independent processes. Instead, they may form interconnected regulatory networks in which changes in one pathway influence several downstream biological processes. The identification of miRNA–mRNA

and lncRNA–miRNA–mRNA regulatory axes therefore provides a more comprehensive perspective than examination of individual cytokines or proteins alone.

Regarding the lncRNA findings, although the evidence base was considerably smaller, molecules such as LINC01094, XLOC_010280, MIAT, LINC01146, NRON, MALAT1 and XIST were implicated in inflammation, EMT, pyroptosis, immune-cell signaling and cell proliferation [16,54,56–59]. The MIAT/miR-125a/IRF4 axis [16] is especially relevant because it illustrates how different classes of non-coding RNA can interact within a regulatory network. Rather than acting independently, lncRNAs may function as upstream regulators or competing endogenous RNAs that modify miRNA availability and consequently alter downstream gene expression. However, the limited independent replication of individual lncRNAs across the included studies substantially reduces confidence in the generalizability of these findings. The current lncRNA evidence should therefore be regarded primarily as hypothesis-generating.

An important distinction should be made between correlative and mechanistic evidence regarding the involvement of non-coding RNAs in CRSwNP. Although numerous studies have reported differential miRNA and lncRNA expression between patients with CRSwNP and control groups, these observations primarily establish associations and do not necessarily demonstrate a causal role in disease pathogenesis. Stronger mechanistic evidence is provided by studies incorporating functional experiments, such as RNA overexpression or inhibition, target-gene validation, and assessment of downstream signaling pathways. Nevertheless, findings obtained from in vitro experimental models may not fully reflect the complexity of the inflammatory microenvironment in human nasal polyps. Therefore, the proposed involvement of individual non-coding RNAs in inflammation, epithelial–mesenchymal transition, apoptosis, and tissue remodeling should be interpreted according to the strength of the underlying experimental evidence, with causal conclusions requiring further validation.

The mechanistic findings also raise the possibility that non-coding RNAs could represent therapeutic targets. Restoration of downregulated miRNAs or inhibition of pathogenic upregulated miRNAs could theoretically modify several disease pathways simultaneously. For example, restoring miR-145-5p could potentially influence TGF-β-associated EMT and inflammatory remodeling, whereas modulation of miR-21, miR-125b or miR-155 could alter inflammatory signaling.

The potential clinical utility of non-coding RNAs should also be considered in the context of currently available biologic therapies for CRSwNP, including dupilumab, omalizumab, and mepolizumab, which target key components of type 2 inflammatory signaling. Although several miRNAs identified in this review, particularly miR-125b, miR-145-5p, and miR-205-5p, have been associated with inflammatory pathways relevant to CRSwNP, their ability to predict treatment response or guide the selection of specific biologic agents has not been established. Current biomarker-based approaches primarily support the identification of inflammatory endotypes rather than reliable discrimination between responses to individual biologic therapies [62,63].

However, because individual miRNAs can regulate numerous target genes, manipulation of their expression could produce unintended effects in multiple biological pathways. An important future direction would therefore be to determine whether miRNA modulation can complement, rather than replace, existing targeted therapies. Thus, miRNA signatures could potentially be investigated as biomarkers of treatment response or resistance, rather than considered therapeutic targets themselves.

Future prospective studies should investigate whether circulating or tissue-derived non-coding RNA signatures correlate with clinical outcomes, including changes in nasal polyp burden, symptom severity, olfactory function, and disease recurrence following biologic

treatment. Until such associations are independently validated, miRNAs and lncRNAs should be regarded as promising investigational biomarkers rather than established tools for personalized therapeutic decision-making.

Several important knowledge gaps remain. The relatively limited replication of individual miRNA findings and the limited independent replication of lncRNA findings indicate a need for larger, independent validation cohorts. Future studies should use standardized protocols for tissue collection, RNA extraction, normalization and reporting of miRNA strands. There is a need for more longitudinal studies. Most available evidence describes miRNA expression at a single point in time. Serial sampling before and after corticosteroids, surgery or biologic therapy could determine whether specific miRNAs are associated with disease activity, treatment response or recurrence.

Moreover, future research should evaluate multimarker signatures rather than individual molecules. Given the biological heterogeneity of CRSwNP and the current limitations of single biomarkers, combinations of non-coding RNAs with established inflammatory markers, clinical characteristics and endoscopic or radiological parameters may ultimately provide greater diagnostic and prognostic value.

Overall, this review synthesizes the available evidence on non-coding RNA dysregulation in CRSwNP and identifies potential directions for future research, particularly the development of therapies targeting these molecules and their associated regulatory pathways.

4.4. Limitations and Disclosure

Although this systematic review provides a comprehensive overview of the current evidence regarding microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) in chronic rhinosinusitis with nasal polyps (CRSwNP), several limitations should be acknowledged.

First, the literature search was restricted to two biomedical databases, PubMed and Scopus, and included only articles published in English. Consequently, potentially relevant studies indexed exclusively in other databases or published in other languages may have been overlooked. Moreover, the exclusion of studies relying exclusively on nasal fluid or lavage specimens may have omitted potentially relevant evidence regarding non-invasive biomarkers for CRSwNP. Furthermore, this review focused specifically on miRNAs and lncRNAs, excluding other classes of non-coding RNAs, such as circular RNAs (circRNAs), as well as studies investigating biological specimens outside the predefined eligibility criteria. These restrictions may limit the comprehensiveness and generalizability of the findings. An additional methodological limitation concerns the timing of PROSPERO registration. Although the eligibility criteria and primary outcomes remained unchanged following registration, the original narrative review and updated PubMed search preceded protocol registration. Therefore, the review did not fully meet the principles of prospective registration, and the possibility of bias arising from methodological decisions made before registration cannot be entirely excluded. Although the extracted data and methodological quality assessments were subsequently verified by the co-authors, independent duplicate data extraction was not performed. This may have introduced some risk of extraction errors or subjective interpretation, despite the additional verification process.

Second, considerable methodological and biological heterogeneity was observed across the included studies. Differences in patient characteristics, inflammatory endotypes, disease severity, associated comorbidities, biological sample sources, control-group selection, RNA extraction methods, and analytical techniques may have influenced the reported expression profiles. Variations in normalization strategies and miRNA strand identification may further contribute to discrepancies between studies, limiting direct comparisons and the possibility of a meaningful quantitative synthesis.

Third, many of the investigated non-coding RNA species were reported in individual studies, with limited independent validation. Among the 128 miRNAs highlighted in this review, only 23 were investigated in more than one study, while only one of the 33 highlighted lncRNAs was independently replicated across two different investigations. Furthermore, conflicting expression patterns were reported for certain miRNAs. These findings highlight the preliminary nature of much of the available evidence and emphasize the need for larger, multicenter studies using standardized methodologies.

Additionally, most included studies relied on relatively small patient cohorts and cross-sectional comparisons, which limit the ability to establish causal relationships between altered non-coding RNA expression and CRSwNP pathogenesis. Although several studies proposed regulatory mechanisms involving inflammation, epithelial–mesenchymal transition, apoptosis, and tissue remodelling, the clinical significance of these findings remains incompletely established. In particular, the diagnostic, prognostic, and therapeutic utility of the identified molecules requires further validation in independent cohorts and prospective longitudinal studies.

Finally, the heterogeneity of the investigated RNA species, biological specimens, analytical approaches, and reported outcomes limited the feasibility of performing a meta-analysis. Therefore, the findings were synthesized narratively, and the conclusions should be interpreted in the context of the methodological limitations and variable quality of the available evidence.

Although findings from studies classified as having a high risk of bias were interpreted with greater caution, a formal sensitivity analysis excluding these studies was not performed. Consequently, their potential influence on the overall conclusions could not be quantitatively assessed.

5. Conclusions

CRSwNP remains a clinically challenging disease characterized by persistent inflammation and a high risk of recurrence. The therapeutic armamentarium has expanded considerably during the past decade, particularly with the introduction of biologic agents. Advances in *omics* technologies have improved our understanding of the underlying pathophysiological mechanisms, while offering potential new targets for the development of future targeted therapies. In CRSwNP, miRNAs have been investigated more extensively than lncRNAs, providing a broader evidence base for their involvement in disease pathogenesis. Although several miRNAs demonstrated consistent expression patterns across independent studies, only 23 of the 128 highlighted miRNAs were investigated more than once, limiting the overall reproducibility of the findings. Among these, 18 showed concordant expression patterns, while five exhibited partially concordant or discordant results. These observations emphasize the need for larger, multicenter studies to validate the identified molecular alterations. Overall, the findings of this review support a biologically meaningful role for non-coding RNAs in CRSwNP, with miRNAs particularly implicated in the interaction between inflammation, epithelial dysfunction, EMT, apoptosis and tissue remodeling. The heterogeneous results observed for miRNAs emphasize the complexity of the disease. The lncRNA findings expand this concept by suggesting that higher-order regulatory networks involving lncRNA–miRNA–mRNA interactions may contribute to disease pathogenesis, although the current evidence is insufficient to establish individual lncRNAs as reproducible disease markers.

Thus, the principal contribution of the available evidence is not the identification of a single definitive molecular biomarker, but rather the demonstration that non-coding RNAs form part of a complex regulatory landscape underlying CRSwNP. Their future clinical value may lie in the development of multimolecular signatures capable of defining

disease endotypes, predicting severity and recurrence, monitoring treatment response and identifying new therapeutic targets.

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Abbreviations

The following abbreviations are used in this manuscript:

CRS	Chronic rhinosinusitis
CRSwNP	Chronic rhinosinusitis with nasal polyps
CRSsNP	Chronic rhinosinusitis without nasal polyps
miRNA	microRNA
lncRNA	Long non-coding RNA
EMT	Epithelial-to-mesenchymal transition

Appendix A

Table A1. Risk of bias assessment using the Newcastle–Ottawa Scale.

No.	Reference	Selection				Comparability	Exposure			Risk of Bias
		Is the Case Definition Adequate?	Representative-ness of the Cases	Selection of Controls	Definition of Controls	Comparability of Cases and Controls on the Basis of the Design or Analysis	Ascertain-ment of Exposure	Same Method of Ascertainment for Cases and Control	Non-Response Rate	
1	Hartung F 2024 [11]	*	*	*	*	*	*	*	*	Low
2	Morawska-Kochman M 2022 [9]	*	*		*	*	*	*	*	Low
3	Zhang M 2024 [14]	*	*		*	*	*	*	*	Low
4	Li H 2023 [15]	*	*	*	*	*	*	*	*	Low
5	Chen JC 2022 [16]	*	*	*	*		*	*	*	Low
6	Yu J 2021 [17]	*	*	*	*	*	*	*	*	Low
7	Song L 2022 [21]		*			*	*	*	*	Moderate
8	Gata A 2023 [10]	*	*	*	*		*	*	*	Low
9	Xia G 2015 [22]		*	*			*	*	*	Moderate
10	Zhang XH 2012 [23]	*	*	*	*		*	*	*	Low
11	Li K 2022 [24]		*			*	*	*	*	Moderate
12	Xuan L 2019 [20]	*	*	*	*		*	*	*	Low
13	Li X 2019 [27]	*	*	*	*	*	*	*	*	Low
14	Luan G 2022 [37]	*	*	*	*	*	*	*	*	Low
15	Liu R 2021 [26]	*	*	*	*		*	*	*	Low
16	Yu H 2018 [38]	*	*	*	*	*	*	*	*	Low
17	Sun Q 2022 [39]	*	*			*	*	*	*	Moderate
18	Qing X 2021 [40]			*		*	*	*	*	Moderate
19	Jiang W 2024 [41]	*	*	*	*	*	*	*	*	Low
20	Yang N 2020 [29]	*	*	*	*	*	*	*	*	Low
21	Zhang W 2020 [42]	*	*	*	*		*	*	*	Low
22	Zhang T 2021 [43]	*	*	*	*		*	*	*	Low
23	Wang X 2024 [44]	*	*	*	*		*	*	*	Low
24	Li L 2019 [45]	*	*	*	*		*	*	*	Low
25	Jian B 2022 [34]		*				*	*	*	Moderate
26	Du J 2020 [28]	*	*	*	*	*	*	*	*	Low

Table A1. *Cont.*

No.	Reference	Selection				Comparability	Exposure			Risk of Bias
		Is the Case Definition Adequate?	Representative-ness of the Cases	Selection of Controls	Definition of Controls	Comparability of Cases and Controls on the Basis of the Design or Analysis	Ascertain-ment of Exposure	Same Method of Ascertainment for Cases and Control	Non-Response Rate	
27	Silveira MLC 2021 [32]	*	*	*	*	*	*	*	*	Low
28	Bu X 2021 [31]	*	*	*	*	*	*	*	*	Low
29	Tubita V 2024 [12]						*	*	*	High
30	Callejas-Díaz B 2020 [47]	*	*	*	*	*	*	*	*	Low
31	Wu Y 2024 [48]	*	*	*	*		*	*	*	Low
32	Liu CC 2018 [49]		*	*	*	*	*	*	*	Low
33	Wang Z 2023 [50]						*	*	*	High
34	Liu Z 2024 [54]	*	*	*	*	*	*	*	*	Low
35	Liu M 2019 [55]		*			*	*	*	*	Moderate
36	Wang M 2020 [56]	*	*	*	*		*	*	*	Low
37	Wang W 2016 [57]	*	*	*	*	*	*	*	*	Low
38	Ma Y 2018 [58]	*	*	*	*		*	*	*	Low
39	Zhou X 2020 [59]	*	*	*	*	*	*	*	*	Low
40	Li Shuman 2025 [51]		*	*	*		*	*	*	Moderate
41	He S 2022 [52]	*		*	*	*	*	*	*	Low
42	Wang G 2024 [36]	*	*	*	*	*	*	*	*	Low
43	Tepebaşi MY 2026 [30]		*	*	*	*	*	*	*	Low
44	Wang L 2025 [18]		*	*	*		*	*	*	Moderate
45	Zhang J 2021 [46]		*	*		*	*	*	*	Moderate
46	Luo XQ 2017 [35]		*				*	*	*	Moderate
47	Liu Zhuohui 2021 [53]						*	*	*	High
48	Tang P 2025 [13]					*	*	*	*	Moderate
49	Li Shenting 2026 [60]	*	*	*	*		*	*	*	Low
50	Shi M 2026 [19]	*	*	*	*	*	*	*	*	Low
51	Liu R 2025 [33]	*	*	*	*		*	*	*	Low
52	Ma ZX 2015 [25]	*	*	*	*	*	*	*	*	Low

The asterisk * indicates that the study met the corresponding quality-assessment criterion according to the Newcastle–Ottawa Scale.

Table A2. miRNA subtypes. RNA identifiers are presented as reported in the original studies. Historical and study-specific nomenclature was retained to ensure consistency with the source publications and does not necessarily indicate current database validation.

miRNA	Expression Level (Case vs. Control)	Reference
miR-203a-3p	increased decreased	Morawska-Kochman M et al. [9] Gata A et al. [10]
miR-17	no difference	Luo XQ et al. [35]
miR-17-5p	decreased	Morawska-Kochman M et al. [9]
miR-142-3p	increased	Qing X et al. [40]
miR-143-3p	decreased	Hartung F et al. [11] Tubita V et al. [12] Tang P et al. [13]
miR-145-3p	decreased	Hartung F et al. [11]
miR-145-5p	decreased	Morawska-Kochman M et al. [9] Zhang M et al. [14] Li H et al. [15] Chen JC et al. [16] Yu J et al. [17] Wang L et al. [18] Shi M et al. [19]
miR-146a-5p	no difference	Morawska-Kochman M et al. [9]
miR-139-3p	decreased	Zhang M et al. [14]
miR-28-5p	decreased	Zhang M et al. [14]
miR-214	increased	Wang Z et al. [50]
miR-214-5p	decreased	Zhang M et al. [14] Chen JC et al. [16]
miR-27b-3p	decreased	Zhang M et al. [14] Yu J et al. [17]
miR-23b-3p	decreased	Zhang M et al. [14] Chen JC et al. [16]
miR-628-5p	decreased	Zhang M et al. [14]
miR-138-5p	decreased	Zhang M et al. [14] Chen JC et al. [16]
miR-187-3p	decreased	Zhang M et al. [14] Chen JC et al. [16]
miR-23a-5p	decreased	Zhang M et al. [14] Xuan L et al. [20]
miR-132-3p	decreased	Zhang M et al. [14] Chen JC et al. [16] Yu J et al. [17]
miR-99b-3p	decreased	Zhang M et al. [14]
miR-193a-5p	decreased	Zhang M et al. [14]
miR-193b-5p	decreased	Zhang M et al. [14]
miR-29c-5p	decreased	Zhang M et al. [14]
miR-30a-3p	decreased	Zhang M et al. [14]
miR-30a-5p	decreased	Zhang T et al. [43]
miR-30b-3p	decreased	Zhang M et al. [14]
miR-151b	decreased	Zhang M et al. [14]
miR-1287-5p	decreased	Zhang M et al. [14]
miR-328-3p	decreased	Zhang M et al. [14]

Table A2. *Cont.*

miRNA	Expression Level (Case vs. Control)	Reference
miR-375	decreased	Zhang M et al. [14] Xuan L et al. [20]
miR-375-3p	increased	Wang X et al. [44]
miR-124	decreased	Liu CC et al. [49]
miR-125a-5p	decreased no difference	Zhang M et al. [14] Chen JC et al. [16] Yu J et al. [17]
miR-125a-3p	increased	Hartung F et al. [11]
miR-125b	increased	Song L et al. [21] Gata A et al. [10] Xia G et al. [22] Zhang XH et al. [23]
miR-125b-5p	increased	Li K et al. [24] Ma ZX et al. [25]
miR-125b-2-3p	decreased	Xuan L et al. [20]
miR-21	increased	Liu R et al. [26] Li X et al. [27]
miR-21-5p	increased	Luan G et al. [37]
miR-1260b	decreased	Sun Q et al. [39]
miR-6507-5p	decreased	Sun Q et al. [39]
miR-450-5p	no difference	Li H et al. [15]
miR-582-5p	decreased	Li H et al. [15]
miR-181b	decreased	Xia G et al. [22]
miR-182	increased	Jiang W et al. [41]
miR-182-5p	increased	Hartung F et al. [11]
miR-154	increased	Bu X et al. [31]
miR-155	increased	Du J et al. [28] Xia G et al. [22]
miR-155-5p	increased	Yang N et al. [29] Tepebaşi MY et al. [30]
miR-22-3p	increased	Zhang W et al. [42]
miR-4492	decreased	Li L et al. [45]
miR-205-5p	increased	Silveira MLC et al. [32]
miR-221	increased	Bu X et al. [31]
miR-221-3p	increased	Silveira MLC et al. [32] Liu R et al. [33]
miR-222-3p	increased	Silveira MLC et al. [32]
miR-223-3p	increased	Bu X et al. [31]
miR-223-5p	increased	Bu X et al. [31] Hartung F et al. [11]
miR-378a-3p	increased	Silveira MLC et al. [32]
miR-449	decreased	Callejas-Díaz B et al. [47]
miR-449a	increased	Silveira MLC et al. [32] Bu X et al. [31]
miR-449b-5p	increased	Silveira MLC et al. [32]
miR-18a	increased no difference	Jian B et al. [34] Luo XQ et al. [35]

Table A2. *Cont.*

miRNA	Expression Level (Case vs. Control)	Reference
miR-210-3p	increased	Ma ZX et al. [25]
miR-210-5p	increased	Xuan L et al. [20]
miR-3178	increased	Xuan L et al. [20]
miR-585-3p	increased	Xuan L et al. [20]
miR-3146	increased	Xuan L et al. [20]
miR-320e	increased	Xuan L et al. [20]
miR-320	increased	He S et al. [52]
miR-32-3p	decreased	Xuan L et al. [20]
miR-1299	decreased	Xuan L et al. [20]
miR-3196	decreased	Xuan L et al. [20]
miR-3924	decreased	Xuan L et al. [20]
miR-548e-3p	decreased	Xuan L et al. [20]
miR-3184-5p	decreased	Xuan L et al. [20]
miR-377-5p	decreased no difference	Xuan L et al. [20] Wang G et al. [36]
miR-574-5p	decreased	Xuan L et al. [20]
miR-3149	decreased	Xuan L et al. [20]
miR-500a-5p	decreased	Xuan L et al. [20]
miR-1914-5p	decreased	Xuan L et al. [20]
miR-532-3p	decreased	Xuan L et al. [20]
miR-612	decreased	Xuan L et al. [20]
miR-1298-5p	decreased	Xuan L et al. [20]
miR-1226-3p	decreased	Xuan L et al. [20]
miR-668-3p	decreased	Xuan L et al. [20]
let-7a-5p	decreased	Zhang J et al. [46]
let-7f-5p	increased	Hartung F et al. [11]
let-7a	decreased	Zhang XH et al. [23]
miR-1246	increased	Hartung F et al. [11]
miR-9-5p	increased	Hartung F et al. [11]
miR-34	decreased	Callejas-Díaz B et al. [47]
miR-92a	decreased no difference	Xia G et al. [22] Luo XQ et al. [35]
miR-26a	decreased	Zhang XH et al. [23]
miR-26b	decreased	Xia G et al. [22]
miR-200a-3p	decreased	Wu Y et al. [48]
miR-663	increased	Yu H et al. [38]
miR-199-3p	decreased	Li Shuman et al. [51]
miR-677	increased	He S et al. [52]
miR-1037	increased	He S et al. [52]
miR-79	increased	He S et al. [52]
miR-357	increased	He S et al. [52]
miR-1058	increased	He S et al. [52]
miR-757	increased	He S et al. [52]

Table A2. *Cont.*

miRNA	Expression Level (Case vs. Control)	Reference
miR-228	increased	He S et al. [52]
miR-551	increased	He S et al. [52]
miR-839	increased	He S et al. [52]
miR-410-3p	decreased	He S et al. [52]
miR-667	decreased	He S et al. [52]
miR-594	decreased	He S et al. [52]
miR-376	decreased	He S et al. [52]
miR-9-3p	decreased	He S et al. [52]
miR-595	decreased	He S et al. [52]
miR-923	decreased	He S et al. [52]
miR-4	decreased	He S et al. [52]
miR-1022	decreased	He S et al. [52]
miR-192	decreased	He S et al. [52]
miR-141-3p	increased	Wang G et al. [36]
miR-18a-5p	decreased	Wang G et al. [36]
miR-3679-5p	decreased	Wang G et al. [36]
miR-5701	no difference	Wang G et al. [36]
miR-374a-3p	no difference	Wang G et al. [36]
miR-19a	increased	Luo XQ et al. [35]
miR-19b	no difference	Luo XQ et al. [35]
miR-20a	no difference	Luo XQ et al. [35]
miR-29b-3p	decreased	Liu Zhuohui et al. [53]
miR-708-5p	decreased	Ma ZX et al. [25]
miR-126-3p	decreased	Ma ZX et al. [25]
miR-150-5p	increased	Ma ZX et al. [25]

Table A3. lncRNA subtypes. RNA identifiers are presented as reported in the original studies. Historical and study-specific nomenclature was retained to ensure consistency with the source publications and does not necessarily indicate current database validation.

lncRNA/Transcript ID	Expression Level (Case vs. Control)	Reference
LINC01094	increased	Liu Z et al. [54]
LINC01146	increased	Wang M et al. [56]
PART1	decreased	Li H et al. [15]
PARD6G-AS1	decreased	Li H et al. [15]
MIR503HG	increased	Li H et al. [15]
MIAT	increased	Chen JC et al. [16]
NRON	decreased	Ma Y et al. [58]
MALAT1	decreased	Zhou X et al. [59]
XIST	decreased	Zhou X et al. [59]
SCAMP1	no difference	Zhou X et al. [59]
lnc-FBXO45-1/XLOC_003006	increased	Liu M et al. [55]
XLOC_016248	increased	Liu M et al. [55]

Table A3. *Cont.*

lncRNA/Transcript ID	Expression Level (Case vs. Control)	Reference
XLOC_017561	increased	Liu M et al. [55]
lnc-FOXF1-1/XLOC_011814	increased	Liu M et al. [55]
XLOC_018649	increased	Liu M et al. [55]
XLOC_015500	increased	Liu M et al. [55]
XLOC_018891	increased	Liu M et al. [55]
lnc-ZCCHC17-1/XLOC_000122	increased	Liu M et al. [55]
lnc-USP12-9/XLOC_010540	decreased	Liu M et al. [55]
lnc-SGCG-5/XLOC_010305	decreased	Liu M et al. [55]
XLOC_018529	decreased	Liu M et al. [55]
XLOC_025155	decreased	Liu M et al. [55]
lnc-FBXO5-1/XLOC_005882	decreased	Liu M et al. [55]
XLOC_018024	decreased	Liu M et al. [55]
XLOC_015712	decreased	Liu M et al. [55]
XLOC_019396	decreased	Liu M et al. [55]
XLOC_010280	increased	Wang W et al. [57] Liu M et al. [55]
lnc-RDH10-1/ENSG00000253339.1	increased	Liu M et al. [55]
LINC02432/ENSG00000248810.1	increased	Liu M et al. [55]
LINC02106/ENSG00000250360.1	decreased	Liu M et al. [55]
ENSG00000181123.4	decreased	Liu M et al. [55]
NEAT1	increased	Shuman Li et al. [51]
PVT1	increased	Shenting Li et al. [60]

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