

Prevalence and Clinical Implications of Chronic Rhinosinusitis in People with Bronchiectasis: A Systematic Review



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What is already known about this topic? Chronic rhinosinusitis (CRS) has been reported in bronchiectasis, but its prevalence and clinical implications are unclear.

What does this article add to our knowledge? This review found that 62% of adults with bronchiectasis have CRS and it is linked to poorer quality of life and greater disease severity.

How does this study impact current management guidelines? These findings highlight the importance of considering clinical screening for CRS in patients with bronchiectasis and identifying optimal management.

BACKGROUND: Chronic rhinosinusitis (CRS) is an extrapulmonary manifestation in some individuals with bronchiectasis, but the prevalence of CRS in this population and its clinical impact has not been systematically reviewed.

OBJECTIVE: To systematically review the prevalence of CRS in bronchiectasis and identify its clinical implications.

METHODS: Four databases were searched from inception to August 2018 for studies reporting the prevalence and/or clinical impact of CRS in individuals with bronchiectasis. Clinical outcomes included health-related quality of life (HRQOL), severity of bronchiectasis, lung function, clinical and psychological symptoms, exacerbation frequency, and health care utilization. Two independent reviewers rated the quality of evidence using the risk of bias for prevalence trials tool.

RESULTS: Of 80 studies identified, 8 studies with 797 participants (all adults) were included. Mean FEV₁ % predicted was 77.7%. Overall, 5 studies were classed as low risk of bias and 3 were of moderate risk of bias. The pooled prevalence of clinical

and/or radiological CRS was 62% (95% CI, 50%-74%). CRS was associated with a greater degree of bronchiectasis severity, poorer HRQOL, reduction in smell detection, elevated levels of inflammatory markers, and reduced time to first exacerbation.

However, the association with airflow obstruction was inconsistent and there was no impact on anxiety or depression.

CONCLUSIONS: CRS is present in 62% of adults with bronchiectasis. Its presence is associated with poorer HRQOL, greater degree of disease severity, and more extensive radiological bronchiectasis. © 2019 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2019;7:2004-12)

Key words: Bronchiectasis; Chronic rhinosinusitis; Health-related quality of life; Disease severity; Clinical effects

INTRODUCTION

Bronchiectasis is characterized by irreversible dilation of the bronchi and bronchioles, and is associated with a cycle of recurrent acute exacerbations and airway inflammation. Lower airway symptoms of chronic cough and purulent sputum production due to impaired mucociliary clearance are common and are linked to poorer lung function and impaired health-related quality of life (HRQOL).¹ Chronic rhinosinusitis (CRS) affecting the upper airways in bronchiectasis has also been reported.²⁻⁴ Typical clinical symptoms of CRS include nasal obstruction or blockage, nasal discharge secondary to impaired sinonasal clearance and secretion retention, lost sense of smell, and facial pain or pressure, with persistent symptoms for greater than 3 months.⁵ Nasal polyposis and chronic inflammatory disease of the nose and sinus mucosa may also be present in those with CRS and increase the risk of recurrent infection.³ There is a wide range (45%-84%) in the reported prevalence of CRS in those with idiopathic or postinfective bronchiectasis.^{6,7}

With the upper respiratory tract (comprising of the nose and paranasal sinuses) and the lower respiratory tract sharing the same mucosal lining, recognized in the “single airway”

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Abbreviations used

COPD- chronic obstructive pulmonary disease

CRS- chronic rhinosinusitis

EPOS- European Position Paper on Rhinosinusitis and Nasal Polyps

HRQOL- health-related quality of life

concept,³⁻⁵ it is clear that CRS may impact disease severity and symptoms of the lower respiratory tract. However, the clinical implications of CRS including psychological symptoms, exercise tolerance, HRQOL, fatigue, and cough-related quality of life and other markers of bronchiectasis disease severity are less clear. Treatment options beyond pharmacology and surgery for CRS in chronic respiratory conditions currently include nasal saline irrigations, mucolytics, and ultrasound.⁸⁻¹¹ Although the optimal choice for the treatment of these approaches has not been established, it is important to identify the clinical implications, because this may inform the choice of patient-centered outcomes for future clinical treatment trials for patients with CRS and bronchiectasis.

The primary aim of this review was to identify the prevalence of CRS in individuals diagnosed with bronchiectasis. The secondary aim was to identify the clinical implications of CRS in bronchiectasis. This review has been registered with PROSPERO (no. CRD42017075548).

METHODS

This review is reported according to Preferred Reporting Items for Systematic Reviews and Meta-analysis.¹²

Search strategy

A systematic literature search was undertaken by 1 author of 4 databases from inception to August 2018 (Figure 1). The strategy for MEDLINE is outlined in Appendix E1 in this article's Online Repository at www.jaci-inpractice.org and was adapted for other databases (Excerpta Medica Database, Cumulative Index to Nursing and Allied Health Literature, and PubMed). Reference lists of retrieved articles were inspected to identify additional articles and authors contacted when necessary.

Inclusion criteria

Titles and abstracts of all retrieved citations were independently screened by the 2 authors, on the basis of inclusion criteria (Table I). Studies were included if they reported the prevalence of CRS and/or reported the clinical implications of CRS. Prospective or retrospective observational studies, randomized controlled trials, or cohort, case-control, or cross-sectional studies were included, whereas case series, single case studies, and studies written in languages other than English were excluded. This was followed by a full-text review for inclusion eligibility, with any disagreement resolved by discussion. Figure 1 illustrates this process.

Data Extraction and quality assessment

Data extraction was completed independently by 2 authors, using a standardized template. Extraction included participant details, CRS prevalence, criteria for diagnosing CRS, and clinical parameters including high-resolution computed tomography scoring, spirometry, measures of HRQOL, symptoms, exercise capacity, and function. With the greater distinction between CRS with or without

nasal polyps,⁵ data specific to the presence or absence of nasal polyps for prevalence and clinical implications were also extracted. Quality assessment was conducted independently by the 2 authors using the Risk of Bias Tool, modified by Hoy et al.¹³ The tool comprises 10 sections, evaluating method rigor and bias of prevalence studies. Items are individually scored using dichotomous (yes or no) responses, correlating to a low or high risk of bias, respectively. Any disagreement between the reviewers was resolved by consensus. The summary score was determined on the basis of a numerical quality score out of 10, obtained by totaling the 10 dichotomous responses in the quality tool, with a response of low scored as 0 and a response of high scored as 1. The summary numerical score was correlated to an overall risk of bias: 0/10 to 3/10 scored as low, 4/10 to 6/10 scored as moderate, and 7/10 to 10/10 scored as high. This numerical categorization was defined by the 2 reviewers, because no previously published categorization system was identified.

Analysis

Analysis of prevalence was based on the diagnostic criteria for CRS applied in individual studies. The pooled prevalence of CRS was analyzed using MetaXL 1.3 (EpiGear International Pty Ltd, Brisbane, Australia), a tool for meta-analysis in Microsoft Excel (Microsoft Corporation, Redmond, Wash). The data were first transformed using the variance stabilizing double arcsine transformation.¹⁴ The quality effects model was then applied to determine the prevalence rate and 95% CI. This model was selected over the fixed or random effects models to explicitly address heterogeneity in pooled proportions caused by differences in study quality and distribution,^{15,16} allowing greater weighting to high-quality studies. MetaXL ensures that the pooled proportions add up to 1. Heterogeneity assumption was assessed by the Q-test and the I² test. Clinical implications of CRS were reported narratively.

RESULTS

A total of 137 articles were identified. After removing 57 duplicates, 80 were reviewed for title and abstract, and 18 full-text articles were reviewed, with 8 meeting the inclusion criteria (Figure 1).

Quality assessment

For the 8 included studies, the overall rating of quality ranged from a low to moderate risk of bias (Table II). Common methodological flaws included sampling biases, with sample frames either not specified or sourced from one clinic population, and sample selection randomization not specified. Low areas of bias were the use of method of data collection, definition of CRS applied, consistency in the mode of data collection, and definition of prevalence period.

Study characteristics

Study characteristics are outlined in Table III. Four studies were conducted in Spain,¹⁷⁻²⁰ 3 in China,²¹⁻²³ and 1 in Australia.² A total of 797 participants were included. All participants had spirometry performed, with FEV₁ ranging from 57.0% to 83.0% predicted. Two studies included a comparison group of healthy controls.^{17,20} One study examined a group of participants with a diagnosis of bronchiectasis and chronic obstructive pulmonary disease (COPD).²³ Underlying causes of bronchiectasis included idiopathic disease,^{2,18,20} post-infective,^{2,18,20} immunodeficiency,² Kartagener syndrome,² Young syndrome,² Allergic bronchopulmonary aspergillosis,²

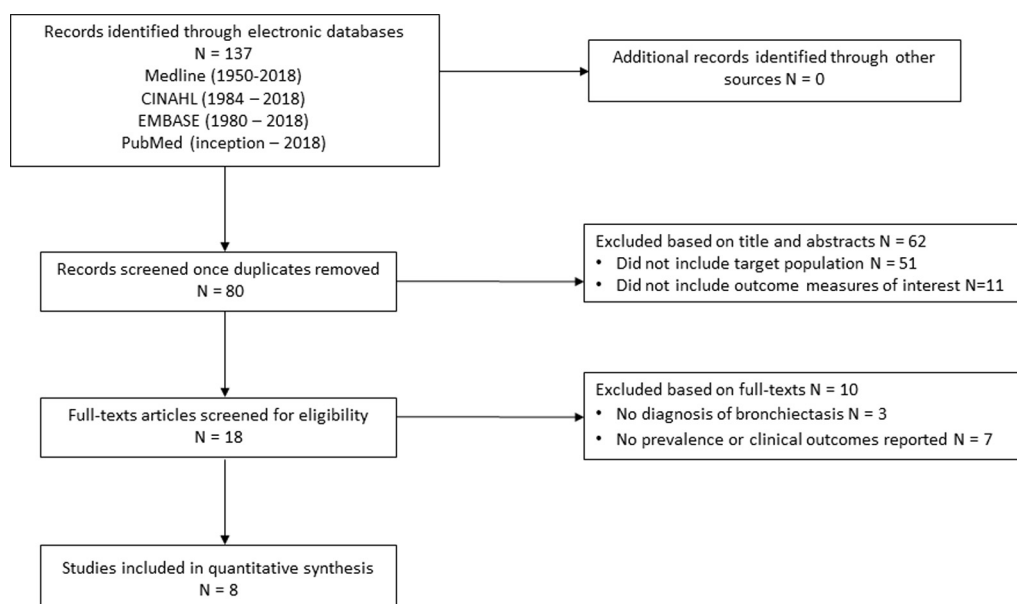


FIGURE 1. Study flow from identification to inclusion of final studies. *CINAHL*, Cumulative Index to Nursing and Allied Health Literature; *EMBASE*, Excerpta Medica Database.

TABLE I. Inclusion criteria

Criterion	Specifics
Population	Individuals diagnosed with bronchiectasis (either HRCT or physician confirmed), from any source except for cystic fibrosis
Study design	Cohort, case-control, cross-sectional, observational, randomized controlled trial study designs
Prevalence of CRS	Presence of CRS according to either symptoms, HRCT-confirmed or reports from other valid measurements (EPOS, RASP score, Lung-MacKay score for rhinosinusitis, nasal polyps). Prevalence may be reported at point prevalence or according to clinical review in the past week(s), month(s), year(s)
Outcomes	Prevalence of CRS. Data related to the severity of CRS symptoms will be reported. Clinical symptoms of CRS will be collated according to both valid and nonvalidated questionnaires/symptom review
	The association with other clinical outcomes, including HRQOL, bronchiectasis severity (BSI or HRCT scores, lung function), exercise capacity, other symptoms, cough-related QOL, comorbidities, pain, activities of daily living, and health care utilization will be included
	Studies may be included if they report prevalence or clinical implications or both

BSI, Bronchiectasis severity index; *HRCT*, high-resolution computed tomography; *HRQOL*, health-related quality of life; *QOL*, quality of life; *RASP*, grading system for nasal polyps.

rheumatoid arthritis,^{2,18} or inflammatory bowel disease¹⁸ or was not stated.^{19,21-23} Of the included studies, 3 stated that participants were in a clinically stable state.^{17,19,21} The remaining studies did not specify this detail.

The diagnosis of CRS varied significantly between studies (Table IV). Six studies made diagnosis on the basis of European Position Paper on Rhinosinusitis and Nasal polyps (EPOS) criteria,⁵ which includes both upper respiratory tract symptoms and either endoscopic signs of nasal polyps, and/or mucopurulent discharge, and/or edema/mucosal obstruction, and/or paranasal sinus computed tomography changes.^{17-21,23} Two studies predominantly diagnosed on the basis of upper respiratory symptoms alone, with variation in methods: according to the RASP classification system; the presence of chronic upper respiratory tract symptoms for more than a year; or 2 or more upper respiratory tract symptoms, including symptoms of either nasal obstruction or purulent discharge.^{2,22}

Prevalence

Prevalence was reported in 8 studies (Table IV).^{2,17-23} Overall, the pooled prevalence was 62% (95% CI, 50%-74%) (Figure 2). The heterogeneity of I^2 of 93% and Q -test = 99.9 suggest strong variability between studies. Subgroup analysis of those studies using symptoms only had a pooled prevalence of 64% (95% CI, 53%-75%); those studies using EPOS criteria had a pooled prevalence of 65% (95% CI, 44%-84%), and those with nasal polyps had a pooled prevalence of 29% (95% CI, 23%-35%).

Clinical implications

Clinical associations of CRS on subjects with bronchiectasis were reported in 6 studies, as outlined in Table IV.^{17-21,23} All 6 studies reported a range of detrimental clinical impacts on participants with CRS compared with participants without CRS. The impact on spirometry appears to be variable; 1 study reported a lower FEV₁ in those with CRS compared with those

TABLE II. Quality assessment of included studies

Authors, year	Risk of bias for individual items on methodological quality										Summary
	1	2	3	4	5	6	7	8	9	10	
Guilemany et al, ¹⁷ 2006	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
King et al, ² 2006	High	High	High	Low	Low	High	High	Low	Low	Low	Moderate
Guilemany et al, ¹⁸ 2009	High	High	Low	Low	Low	Low	Low	Low	Low	Low	Low
Guilemany et al, ¹⁹ 2009	High	High	High	High	Low	Low	Low	Low	Low	Low	Moderate
Guilemany et al, ²⁰ 2011	High	High	High	High	Low	Low	Low	Low	Low	Low	Moderate
Guan et al, ²¹ 2015	High	High	Low	Low	Low	Low	Low	Low	Low	Low	Low
Wang and Yang, ²² 2016	High	High	High	Low	Low	Low	Low	Low	Low	Low	Low
Yang et al, ²³ 2017	High	High	Low	Low	Low	Low	Low	Low	Low	Low	Low

1: Was the study's target population a close representation of the national population in relation to relevant variables? 2: Was the sampling frame a true or close representation of the target population? 3: Was some form of random selection used to select the sample, or, was a census undertaken? 4: Was the likelihood of nonresponse bias minimal? 5: Were data collected directly from the subjects? 6: Was an acceptable case definition used in the study? 7: Was the study instrument that measured the parameter of interest shown to have reliability and validity? 8: Was the same mode of data collection used for all subjects? 9: Was the length of the shortest prevalence period for the parameter of interest appropriate? 10: Were the numerator(s) and denominator(s) for the parameter of interest appropriate? Summary: Overall risk of study bias.

TABLE III. Characteristics of included studies

Authors, year	Study design	No. of participants	Age (y), mean $\pm$ SD	Sex (% female)	FEV ₁ % predicted, mean $\pm$ SD	Clinical outcomes
Guilemany et al, ¹⁷ 2006	Cohort	60	52 $\pm$ 16	65	81.0 $\pm$ 3.4	SF-36
King et al, ² 2006	Cross-sectional	103	56 $\pm$ 14	63	76.0 $\pm$ 26.0	NR
Guilemany et al, ¹⁸ 2009	Cohort	88	55 $\pm$ 2	69	83.0 $\pm$ 3.0	CRP, lung function (spirometry), bronchiectasis severity (HRCT scoring, 0-3; 0, no involvement; 1, single segment; 2, more than 1 segment; 3, gross cystic bronchiectasis of entire lobe)
Guilemany et al, ¹⁹ 2009	Cohort	80	57 $\pm$ 2	71	80.8 $\pm$ 2.8	Bronchiectasis severity (HRCT scoring, 0-3; 0, no involvement; 1, single segment; 2, more than 1 segment; 3, gross cystic bronchiectasis of entire lobe), SNOT-20, SF-36, SGRQ
Guilemany et al, ²⁰ 2011	Cohort	91	54 $\pm$ 3	68	82.5 $\pm$ 3	BAST-24 Olfactometry (smell characteristics of detection, identification, and forced choice)
Guan et al, ²¹ 2015	Cohort	148	CRS group: 44 $\pm$ 15 No CRS group: 45 $\pm$ 13	63	CRS group: 68.2 $\pm$ 24.8 No CRS group: 74.8 $\pm$ 21.2	No exacerbations, lung function (spirometry), health care utilization, HRCT scores, HADS, PA colonization, BSI
Wang and Yang, ²² 2016	Cohort	161	Total: NR Rhinosinusitis group: 55 $\pm$ 9	50	73.0 (NR)	NR
Yang et al, ²³ 2017	Cohort	66*	71 $\pm$ 11*	16*	57.0 $\pm$ 18.1*	Smith score for extent of bronchiectasis, Bhalla scoring for severity of bronchiectasis, inflammatory markers

BAST-24, Barcelona Smell Test-24; BSI, bronchiectasis severity index; CRP, C-reactive protein; HADS, hospital anxiety and depression scale; HRCT, high-resolution computed tomography; NR, not reported; PA, *Pseudomonas aeruginosa*; SF-36, short form-36 health survey; SGRQ, St George's Respiratory questionnaire; SNOT-20, Sinonasal Outcome Test-20.

*Values are for total group (mixed COPD/bronchiectasis diagnosis).

without CRS,¹⁹ whereas 2 studies found no difference.^{18,21} A single study reported higher C-reactive protein levels in those with CRS.¹⁸ Elevated levels of inflammatory markers were also reported in those with bronchiectasis, COPD, and CRS.²³ Three

studies reported a higher bronchiectasis severity score based on high-resolution computed tomography scoring in those with CRS.^{18,19,23} The presence or absence of nasal polyps in those with CRS did not influence lung function or measures of disease

TABLE IV. Prevalence and outcomes of included studies

Authors, year	Prevalence of CRS (% total participants)	Diagnostic process for CRS	Clinical impact of CRS in bronchiectasis (mean $\pm$ SD unless otherwise stated)
Guilemany et al, ¹⁷ 2006	25 of 60 (42)	Presence of upper airway symptoms diagnosed on the basis of nasal obstruction, loss of smell, rhinorrhea (anterior and posterior), facial pain, itching, and sneezing, scored using RASP criteria. Consistent with EPOS criteria. Presence of nasal polyps (size scored for each nasal cavity on Lildholdt's classification).	Participants with bronchiectasis and CRS had lower quality-of-life scores in all domains of the SF-36 compared with the general Spanish population, including the PCS (46.5 [26.7] vs 82.7 [23.3]) and the MCS (39.7 [27.3] vs 84.5 [19.3]) (all $P < .05$). No differences were noted between those with NP and those without NPs.
King et al, ² 2006	73 of 103 (71)	Chronic upper respiratory tract symptoms present for more than a year. History of ENT surgery for recurrent rhinosinusitis. Radiological abnormalities of upper airways (mucosal thickening to severe pansinusitis).	NR
Guilemany et al, ¹⁸ 2009	68 of 88 (77)	EPOS criteria: Nasal symptom score, nasal endoscopy, and/or sinonasal CT scan, scored using the Lund-Mackay score system, nasal function, and nasal NO. Nasal congestion/obstruction/blockage, reduced/loss in smell, anterior rhinorrhea, postnasal drip, facial pain/pressure, itching, and sneezing, scored using RASP criteria. Presence of nasal polyps (size scored for each nasal cavity on Lildholdt's classification).	CRP levels were higher in participants with CRS compared with participants without CRS (1.3 [0.2] mg/dL vs 0.6 [0.2] mg/dL; $P < .05$), but there was no difference in FEV ₁ . There were no differences between those with or without NPs. A higher bronchiectasis severity score (according to HRCT) was evident in those with CRS compared with those without CRS (7.2 [0.5] vs 3.7 [0.7]; $P < .001$). There were no differences between those with or without NPs.
Guilemany et al, ¹⁹ 2009	60 of 80 (75)	EPOS criteria: Nasal symptom score, nasal endoscopy, and/or sinonasal CT scan, scored using the Lund-Mackay score system. Nasal congestions/obstruction/blockage, reduced/loss in smell, anterior rhinorrhea, postnasal drip, facial pain/pressure, itching, and sneezing scored using RASP criteria. Presence of nasal polyps (size scored for each nasal cavity on Lildholdt's classification).	FEV ₁ was lower in participants with CRS compared with participants without CRS (75.8% [3%] vs 90% [4%]; $P < .05$). Bronchiectasis severity scores (according to HRCT) were higher in those with CRS compared with those without CRS (6.2 [0.5] vs 4.2 [0.7]; $P < .001$). There was no difference between those with or without NPs. SNOT-20 total score was higher in participants with CRS compared with participants without CRS (2.1 [0.1] vs 0.4 [0.06]; $P < .001$). SGRQ total score was higher in participants with CRS compared with participants without CRS (43.7 [2.2] vs 24.7 [2.5]; $P < .001$), with higher scores in symptoms, activities, and impact (all $P < .001$). There was no difference between those with or without NPs. SGRQ total score and SF-36 PCS and MCS scores correlated with SNOT-20 total score. Total nasal symptom score correlated with SGRQ total score ($r = 0.67$; $P < .01$) and SF-36 PCS and MCS score ($r = -0.72$; $P < .01$ and $r = -0.48$; $P < .01$). SF-36 PCS and MCS scores were lower in participants with CRS compared with participants without CRS (64 [3.4] vs 76.2 [3.3]; $P < .05$ and 65.5 [4.7] vs 78.3 [5.3]; $P < .05$). There was no difference between those with or without NPs.
Guilemany et al, ²⁰ 2011	73 of 91 (80)	EPOS criteria: Nasal symptom score, nasal endoscopy, and sinonasal CT scan, scored using the Lund-Mackay score system Nasal congestion/obstruction/blockage, reduced/loss in smell, anterior rhinorrhea, postnasal	Participants with CRS had worse scores in smell detection compared with those without CRS. There was no difference in smell identification or forced choice between participants with or without CRS. Those with CRS and NP had

(continued)

TABLE IV. (Continued)

Authors, year	Prevalence of CRS (% total participants)	Diagnostic process for CRS	Clinical impact of CRS in bronchiectasis (mean $\pm$ SD unless otherwise stated)
		drip, facial pain/pressure, itching, and sneezing scored on Likert classification. Presence of nasal polyps (size scored for each nasal cavity on Lildholdt's classification).	poorer smell detection ($P < .05$) and worse scores in first choice ($P < .05$) compared with those with CRS without NPs, but there was no difference in smell identification between groups.
Guan et al, ²¹ 2015	47 of 148 (32)	EPOS criteria: Two or more symptoms of nasal and paranasal sinuses inflammation, for at least 12 wk, nasal blockage/obstruction/congestion or discharge, plus facial pain/pressure or reduced/loss in smell, and/or CT changes (mucosal changes of ostiomeatal complex and/or sinuses).	Participants with CRS had a shorter time to first exacerbation within a 1-y follow-up period compared with participants without CRS ($P = .02$). There was no difference in BSI or FEV ₁ , proportion of participants colonized with <i>Pseudomonas aeruginosa</i> , or chest HRCT scores in those with CRS compared with participants without CRS. Participants with CRS had a lower proportion of cystic bronchiectasis (42.6% vs 61.4%; $P = .03$). There was no difference in the frequency of use of oral antibiotics or health care utilization in those with CRS compared with those without CRS. There was no difference in the proportion of participants with anxiety or depression between those with CRS vs those without CRS.
Wang and Yang, ²² 2016	161 of 273 (59)	Two or more symptoms including nasal obstruction, viscous or purulent nasal discharge, headaches, hyposmia, or anosmia. Symptoms must include 1 of nasal obstruction and viscous or purulent discharge. Nasal endoscope and Sinus CT.	NR
Yang et al, ²³ 2017	38 of 66 (58)	EPOS criteria: nasal obstruction/blockage, nasal or postnasal discharge/purulence, headache, facial pain/pressure/fullness, hyposmia/anosmia. At least 2 major symptoms, for at least 12 consecutive wks.	Higher bronchiectasis severity score (according to Bhalla scoring) in those with CRS (median, 3.0 [IQR, 2-5] vs 2 [2-3]; $P = .034$). No different in Smith score ($P = .179$). Higher level of eosinophils ($P = .036$), IL-6 ($P = .037$), IL-8 ($P = .027$), and MMP-9 ($P = .025$) in those with bronchiectasis and CRS compared with those without CRS.

BSI, Bronchiectasis severity index; CRP, C-reactive protein; CT, computed tomography; ENT, ear, nose, and throat; HRCT, high-resolution computed tomography; IQR, interquartile range; MCS, mental component summary; MMP-9, matrix metalloproteinase 9; NP, nasal polyp; NR, not reported; PCS, physical component summary; QOL, quality of life; RASP, grading system for nasal polyps; SF-36, short form-36 health survey; SGRQ, St George Respiratory Questionnaire; SNOT-20, Sinonasal Outcome Test-20.

severity.^{18,19} A single study found that participants with CRS had a greater risk of experiencing exacerbations, despite no difference in other risk factors for exacerbations: the bronchiectasis severity index, proportion of individuals colonized with *Pseudomonas aeruginosa*, frequency of use of oral antibiotics, or health care utilization.²¹

Two studies reported on HRQOL, using both disease-specific and generic questionnaires.^{17,19} Compared with the general Spanish population, those with bronchiectasis and CRS have lower HRQOL in all domains of the short form-36 Health Survey,¹⁷ although there was no comparison in HRQOL in those with bronchiectasis in the absence of CRS. According to the St George's Respiratory questionnaire, higher total, activity, impact, and symptoms scores (indicating worse quality of life) were evident in those with CRS compared with those without CRS; similarly, lower physical component summary and mental component summary scores were evident in those with CRS.¹⁹ A higher total Sinonasal Outcome Test-20 score was evident in those with CRS.¹⁹ Poorer HRQOL according to both the St George's

Respiratory Questionnaire total score and short form-36 health survey physical component summary and mental component summary was related to greater symptoms of CRS based on the Sinonasal Outcome Test-20.¹⁹ However, these clinical effects did not appear to be influenced by the presence or absence of nasal polyps in individuals with CRS and bronchiectasis.¹⁷⁻¹⁹ The presence of nasal polyps was reported to reduce the ability to detect smells in those with CRS compared with those without CRS,^{17,18,20} although further impairment in quality of life in those with nasal polyps was not noted.¹⁷ No significant difference in anxiety and depression was found between those with CRS compared with those without CRS.²¹ No outcomes related to exercise capacity, cough-related quality of life, comorbidities, pain, or activities of daily living with respect to CRS were reported.

DISCUSSION

This systematic review shows that CRS is present in most adults with bronchiectasis (prevalence of 62%). CRS is associated

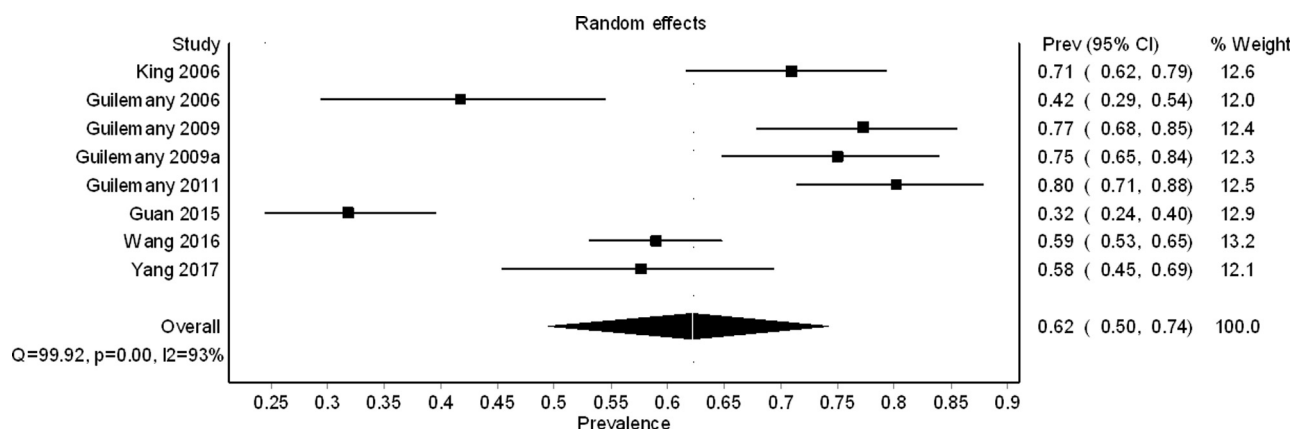


FIGURE 2. Pooled prevalence of CRS in bronchiectasis in all studies.

with an increase in bronchiectasis severity and a poorer HRQOL. Limited evidence suggests higher levels of baseline systemic inflammation and a greater risk of experiencing an acute exacerbation of bronchiectasis in individuals with CRS.

The studies included in this review reported a wide range of CRS prevalence. To some degree, this may have been due to differing diagnostic criteria applied for CRS. A similar pooled prevalence was reported in studies whose diagnostic criteria was predominantly based on symptoms compared with the EPOS criteria. The application of this diagnostic approach using cardinal symptoms or questionnaires has been previously associated with an inflated prevalence of CRS in other studies.^{24,25} This appears to have minimal impact in the current review and may be influenced by the additional information used to confirm the presence of CRS in individual studies.^{2,22} One study identified prevalence on the basis of retrospective reporting of symptoms alone, which increases the risk of bias associated with diagnosis.² Although a lower prevalence of CRS and nasal polyps was reported (29%), this rate is similar to a previous report of the proportion of people with CRS with nasal polyps (~25%-30%).²⁶ Nasal polyps can be clinically silent²⁷ and not all studies in the current review included investigations using anterior rhinoscopy or nasal endoscopy.²⁸ For this reason, the prevalence reported in the subgroup analysis in people with bronchiectasis and CRS should be interpreted with caution.

The difference in populations of individuals with bronchiectasis studied and the varying etiologies of the disease may also account for the variable prevalence. Cigarette smoking has been correlated with the development of CRS.²⁹ A history of smoking was documented in some studies,^{2,18,19,23} though this was not consistently linked to CRS,¹⁹ and one study was biased by a comorbid diagnosis of COPD.²³ Some causes of bronchiectasis are associated with absent or impaired ciliary motility, including Kartagener syndrome and primary ciliary dyskinesia,⁴ and may account for CRS in a small proportion of participants.² Immune deficiencies are more common in people with CRS.³⁰⁻³² A proportion of included studies identified underlying causes of bronchiectasis to be immunodeficiencies.^{2,20} Although this may account for the prevalence in these studies and is a possible cause of CRS, the inconsistent reporting of etiologies in all included studies limits the ability to determine the precise contribution of each bronchiectasis etiology to the variation in CRS prevalence. Indeed,

one study reported a similar incidence of CRS in individuals with postinfective and idiopathic bronchiectasis.¹⁹

Other demographic factors may influence the variable prevalence rates between studies. Prevalence was lower in those studies in which participants' mean age was lower; this suggests that including participants of an older age may increase the likelihood that CRS symptoms develop over time. It is unclear whether these findings vary in pediatric populations, because only adult participants were included in the selected studies. Epidemiological studies reported that women have a higher rate of CRS compared with men,^{33,34} whereas other studies have reported no difference.³⁵ Women may be more likely to report symptoms or give poor self-evaluation of health, which may bias self-reported data toward increased prevalence.³⁶ Three studies in this review reported a higher prevalence of CRS in females, all of which did not rely on symptom reporting only for diagnosis.¹⁸⁻²⁰ Although this lends support for a possible role of sex in bronchiectasis and CRS, in the absence of consistent reporting in all studies, this requires further clarification. Finally, the differing sample size between studies is also a likely factor, ranging from 60 to 161 participants.

The significance of nasal polyps was variable. Although it did not appear to have an impact on disease severity or quality of life, nasal polyps are perceived as an indicator of disease involving the upper and lower respiratory tracts.³⁷ Their presence in selected studies included in this review lends support to the concept of the united airways in bronchiectasis and the stance that treating upper airway symptoms when required may influence the overall clinical status of an individual with bronchiectasis and CRS.

The prevalence of CRS in people with bronchiectasis highlights the complex relationship between these 2 conditions. It has been hypothesized that CRS may lead to the development of bronchiectasis.³⁸ This may originate from migration of secretions from the upper airway to the lower airway, bacterial inflammation of the upper airway affecting the lower airway, or an inflammatory response originating in the upper airway and extending to the lower airway.³⁸ Bronchiectasis has been diagnosed in people with CRS.^{39,40} The precise nature of this complex relationship between the 2 conditions requires further study to ensure optimal management and prevention where possible.

Within the individual studies, the presence of CRS was associated with greater bronchiectasis severity, according to the

bronchiectasis severity score from high-resolution computed tomography or the bronchiectasis severity index.^{18,19,23} In contrast, the presence of CRS in bronchiectasis was not linked to the severity of airflow obstructions, with mean FEV₁ being greater than 70% in all but 1 study, which included individuals with both bronchiectasis and COPD.²³ Similarly, there were inconsistent reports on the effect of CRS on FEV₁.^{18,19} This suggests that measures that are specific to bronchiectasis and that incorporate a range of variables may be more sensitive outcomes for assessing the impact of CRS in bronchiectasis.

Greater levels of inflammatory markers and shorter time to exacerbation within a 1-year follow-up period were reported in individuals with bronchiectasis and CRS; however, there was no link to health care utilization.^{21,23} Although examined only in 1 study to date, exacerbations in bronchiectasis have a significant negative impact on morbidity and mortality⁴¹ and future examination of the relationship between CRS and exacerbations is required. The lack of influence on health care utilization is likely attributed to the limited 1-year study duration, which is insufficient to adequately capture the effect of this outcome.²¹ Further exploration of the long-term impact on health care utilization of CRS in bronchiectasis is warranted.

The presence of CRS was associated with poorer scores in all domains of the St George's Respiratory Questionnaire, as well as both the physical component summary score and the mental component summary score of the short form-36 health survey. This report of greater impairment in HRQOL in individuals with CRS and CRS symptoms highlights the clinical importance of CRS in bronchiectasis. These outcomes are comparable to the published research on the impact of CRS on individuals with cystic fibrosis.⁴² It emphasizes the significance of the united airways or the "one airway, one disease"²¹ concept in bronchiectasis and that considering the impact of upper airway symptoms in HRQOL in this population should be considered a key component within clinical practice. Interventions directed toward addressing CRS should consider the effect on HRQOL in those with bronchiectasis.

The reduction in smell detection in individuals with bronchiectasis and CRS was identified in 4 studies. Although it was not linked to a poorer quality of life,¹⁷ it may reflect the presence of severe CRS in people with bronchiectasis.²⁰ From a clinical perspective, an enquiry of an individual with bronchiectasis' sense of smell may serve as an initial guide to the potential presence of CRS.²⁰ The broader clinical implications of loss of smell on daily function in this population requires further study.

Various treatment options for CRS are available, including pharmacological, nonpharmacological, and surgical interventions; however, their impact was not evaluated in this review because of the limited evidence in this population. With the higher prevalence reported in studies in which participants' mean age was more, it suggests that symptoms of or screening for CRS ideally should be sought and managed as early as possible. Further research is necessary to establish the definitive effects and patient-centered outcomes of treatment options for CRS in this population to inform clinical practice.

This review was limited by the diverse procedures applied in the diagnosis of CRS between studies, varying from the use of EPOS criteria, to clinical symptoms alone or identification of nasal polyps. The EPOS definition of CRS is symptom based, with the presence of supporting findings, from either endoscopy or sinus computed tomography, being important to exclude

differential diagnoses and verify the clinical symptoms.⁵ However, the EPOS recognize that it is the presence of symptoms that prompts an individual to seek medical attention for their CRS, and a diagnosis based on symptoms alone remains the mainstay of diagnosis in primary care.⁵ A second limitation in this review is the heterogeneous etiologies of bronchiectasis, which is a factor likely to influence the CRS prevalence reported. The risk of bias between studies ranged from low to moderate. The criteria at highest risk of bias were the representation of each study's target population and the method of sample selection. The small study sample sizes (60-161) introduced a risk of missing clinically important effects and precluded clinical outcome comparisons within studies.

In conclusion, this review demonstrates the high prevalence of CRS in adults with bronchiectasis. Nasal polyps were prevalent in 29% of individuals with bronchiectasis and CRS. The associations between the presence of CRS with more severe bronchiectasis and poorer HRQOL highlight important clinical consequences for CRS. Further research to establish optimal patient-centered treatment options for CRS in bronchiectasis and the effect on HRQOL would be of value to clinicians.

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ONLINE REPOSITORY

Appendix E1. Search strategy for MEDLINE

- #1. MeSH Heading "Bronchiectasis" OR "bronch\$"
- #2. MeSH Heading "sinus\$" OR "sinusitis" OR "chronic sinusitis" OR "rhino\$" OR "rhinosinusitis" OR "rhinosinusus"
- #3. MeSH Heading "Symptom*" OR "breathless*" OR "dyspnea" OR "dyspnoea" OR "short\$ of breath\$" OR "quality of life" OR "QOL" OR "life quality" OR "health-related quality of life" OR "HRQOL" OR "fatigue" OR "perceive* exertion" OR "perceive* fatigue" OR "exercise" OR "exercise* capacity" OR "exercise tolerance" OR "lung function" OR "disease severity" OR "lung severity" OR "anxiety" OR "depression."
- #4. MeSH Heading "causality" OR "cohort stud\$" OR "cross-sectional stud\$" OR "epidemiolog\$" OR "epidemiologic factor\$" OR "follow-up study" OR "prevalence" OR "prevalence stud\$" OR "prospective stud\$."
- # 5. #1 AND #2 AND #3 AND #4.

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