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Does sinus surgery reduce the development of asthma and bronchiectasis in patients with CRS?

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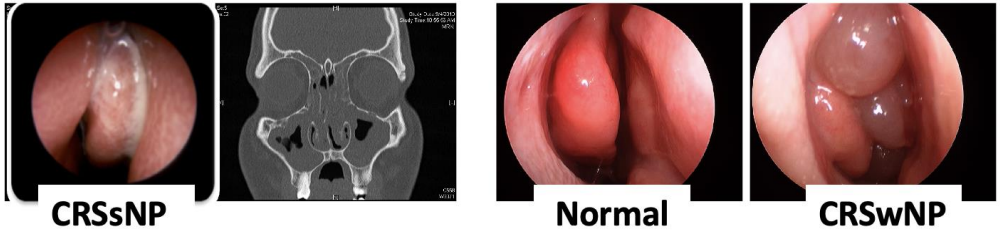
Disclosures

- I have no relevant disclosures to report

Chronic Rhinosinusitis (CRS)



- Chronic inflammation of the nasal mucosa and paranasal sinuses
- 5-12% of the general population in North America and Europe
  - CRS without nasal polyposis (CRSsNP) - 75-80%
  - CRS with nasal polyposis (CRSwNP) - ~20% of cases
  - Allergic fungal rhinosinusitis (AFRS) - <5%

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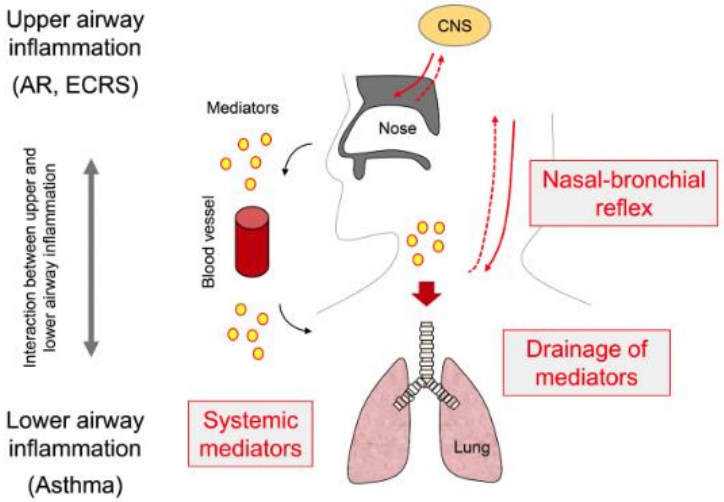
Schleimer et al. Annu Rev Pathol. 2017 January 24; 12:331–357
DeConde et al. Am J Rhinol Allergy 2016;30(2):134-9

Unified Airway Hypothesis



- Diseases of the upper and lower airway are both manifestations of a single inflammatory process within the respiratory tract

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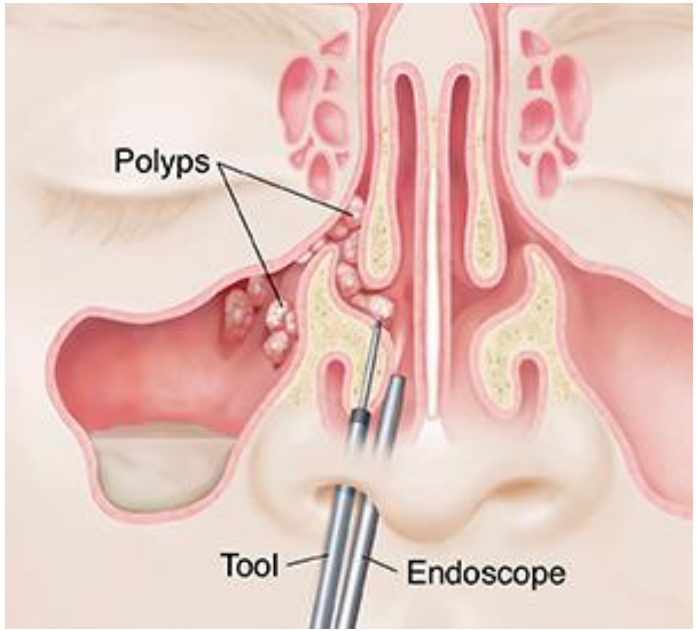
Rimmer et al. Med J Aust 2006;185(10):565-571
Kanda et al Med.Sci. 2019;7(2):27

Does Sinus Surgery Affect the Development of Lower Airway Inflammation?



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Background

- The anatomic and pathophysiological link between the nose and lung supports the rationale that CRS may lead to lower airway injury (unified airway hypothesis)
- Previous cross-sectional studies have identified that CRS and bronchiectasis commonly co-exist
- Existing evidence suggests a decrease in antibiotic prescriptions post sinus surgery in patients with CRS
- In CRS patients with known NCFB, ESS improves QoL (SNOT-22)
- In CRSwNP patient with known asthma, ESS also improves QoL (SNOT-22), along with asthma severity

Somani et al. Int Forum Allergy Rhinol 2019 Dec;9(12):1424-1429
Peters et al. J Allergy Clin Immunol Pract. 2021 Aug;9(8):3188-3195
Schlosser et al. Allergy. 2017 Mar;72(3):483-491.

Background (cont'd)

- In CRS patients without asthma, ESS performed earlier in the disease continuum appears to decrease the risk of developing asthma
- Early surgical intervention after diagnosis of CRS, with or without asthma or polyps, is associated with lower health care utilization
  - Limitations of these studies include the method used to ID patients with asthma (only looking at diagnosis without other metrics) and use of claims database coding without in depth chart review

ESS may be disease modulating by mitigating the risk of developing lower airway inflammatory disease (i.e. asthma and bronchiectasis)

Vashishta et al. Int Forum Allergy Rhinol. 2013 Oct;3(10):788-94.
Benninger et al. Otolaryngol Head Neck Surg. 2015 Mar;152(3):546-52.

Research Question

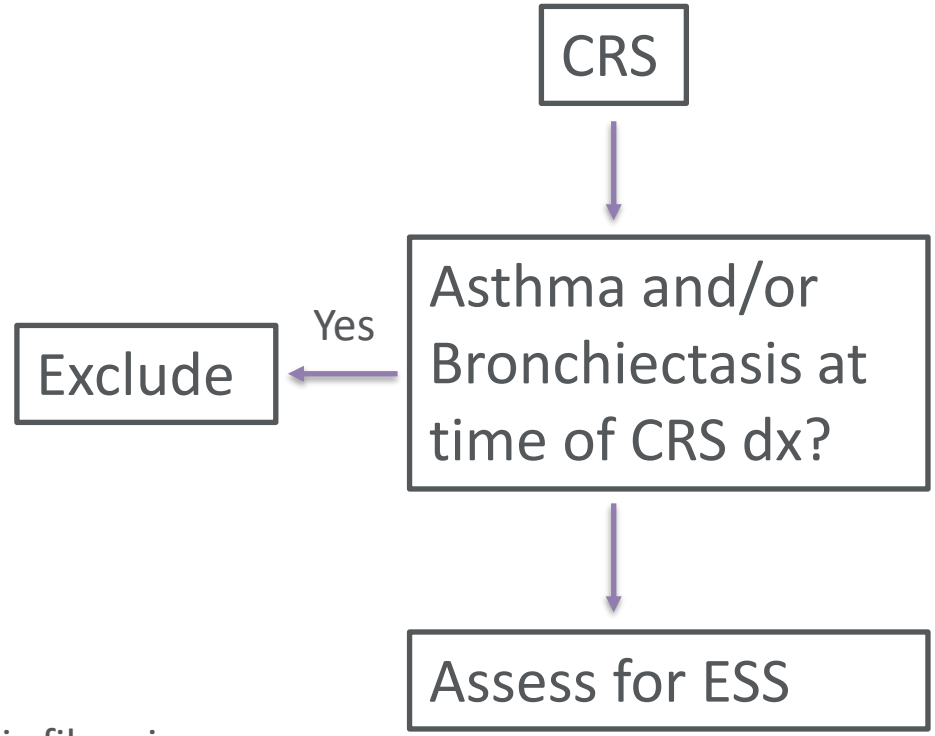
- Does sinus surgery reduce the development of asthma and bronchiectasis in patients with CRS?

Methods

- **Study design:** retrospective cohort study
- **Data source:** Northwestern's Enterprise Data Warehouse (EDW)
- **Population:** adult (≥18 yo) patients at Northwestern Medicine
  - Exclusion criteria: Diagnosis of COPD, asthma and/or bronchiectasis at time of CRS diagnosis, or prior chest CT scan
- **Exposure:** ESS in patients with CRS (without bronchiectasis or asthma) – ESS performed prior to Dec 2018
- **Control:** No ESS in patients with CRS w/o asthma/NCFB at diagnosis
- **Outcome:** New bronchiectasis on CT chest (and other new CT chest findings), New Asthma Diagnosis (ICD, lung function/FEV1, inhaler Rx)

Study Design

- CRS (Jan 2006-Dec 2013)
  - ICD code x2
  - positive sinus CT + ICD code 1mo to 3y after CT
- Asthma
  - ICD code x1
- Bronchiectasis
  - ICD code x1; Exclude dx of cystic fibrosis or primary ciliary dyskinesia at any time



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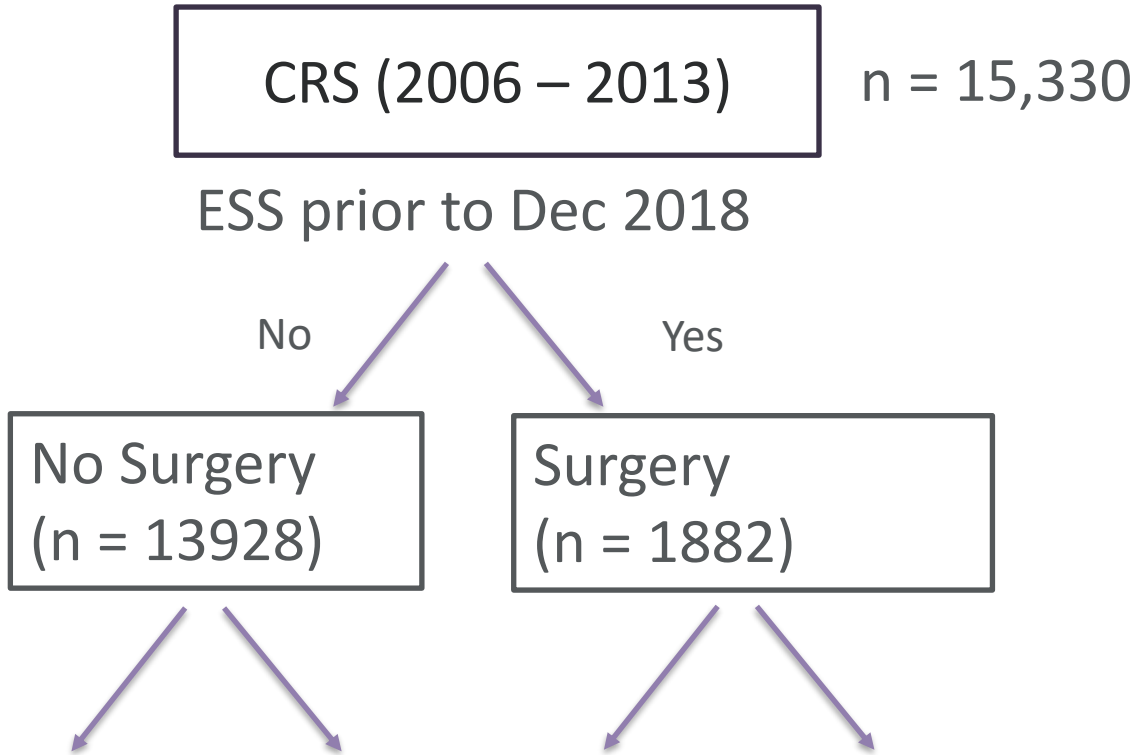
Northwestern Enterprise Data Warehouse

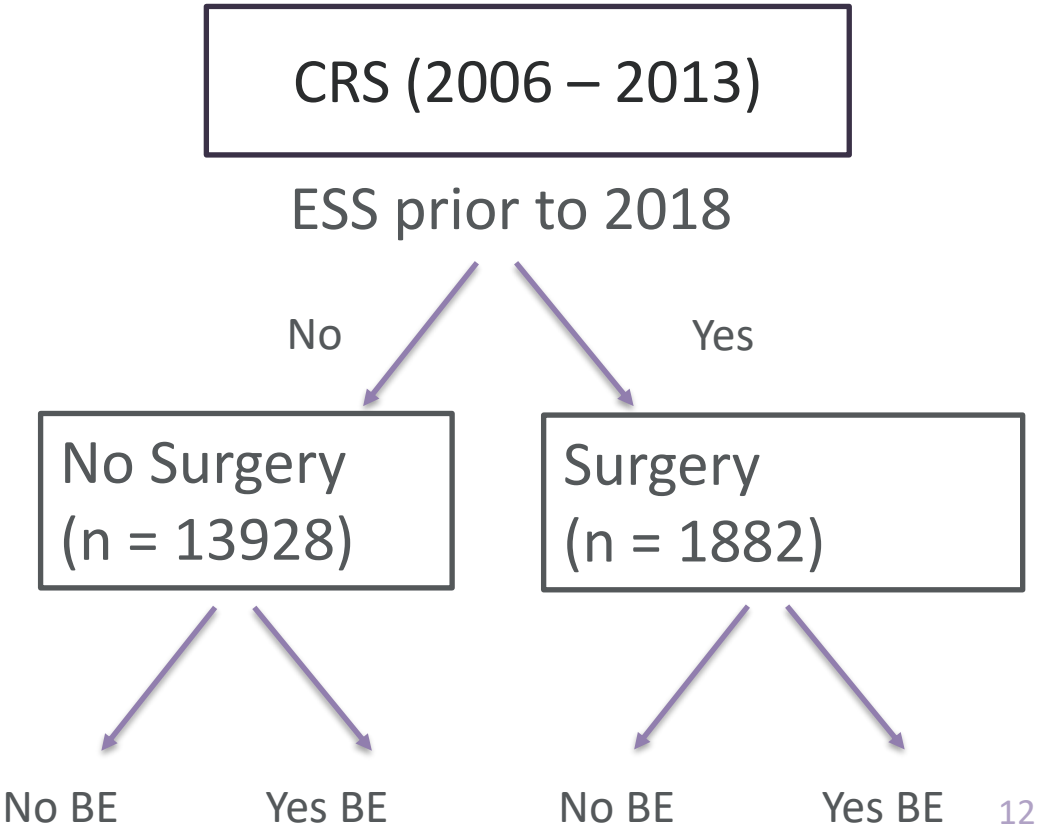
- For Patients who undergo ESS
  - Exclude if they have diagnosis of Asthma or Bronchiectasis prior to ESS date

Asthma development: ICD code x2, or ICD code x1 and Rx for Inhaler



Northwestern Enterprise Data Warehouse

- Bronchiectasis
  - Surgery group: Chest CT at least 6 months after surgery
  - Non surgery group: Chest CT 6 months after CRS Dx



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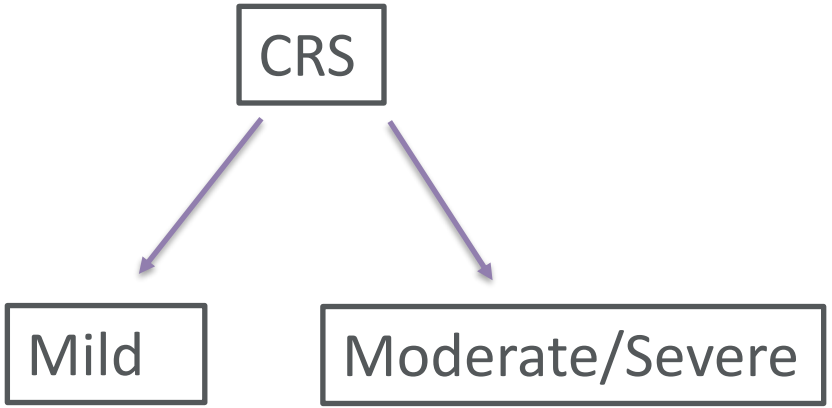
CRS Severity

- Patients with more severe CRS may be more likely to undergo ESS
- Must therefore control for severity of disease (based on CT Scan Radiologist Reading or Lund Mackay Scoring - radiographic scoring):



Lund–Mackey system.

Sinus	Right sinus	Left sinus
Frontal	0–2	0–2
Anterior ethmoids	0–2	0–2
Posterior ethmoids	0–2	0–2
Maxillary	0–2	0–2
Sphenoid	0–2	0–2
Ostiomeatal complex	0 or 2	0 or 2

For the sinuses: 0 = no inflammation; 1 = partial inflammation; 2 = 100% inflammation.
For the ostiomeatal complex: 0 = not occluded; 2 = occluded.
Maximum total score: 24.

CRSwNP vs CRSsNP

CRS

CRSwNP
(n = 1439)

CRSsNP
(n = 13891)

Potential Modifiers

- Allergies
- AERD
- GERD
- BMI
- Age
- Gender
- Race
- Immunodeficiency

- Autoimmune disease
- ABPA
- Smoking history

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Demographics & Clinical Characteristics

	No ESS n = 13453	ESS n = 1877
Mean Age (SD)	43.5 (13.7)	42.0 (13.4)
Female (%)	8484 (63.1%)	844 (45.0%)
Race/Ethnicity (%)		
White	10278 (76.4%)	1383 (73.7%)
Black	807 (6.0%)	106 (5.6%)
Hispanic	692 (5.1%)	99 (5.3%)
Other/unknown	1676 (12.5%)	289 (15.4%)
BMI (SD)	27.6 (6.0)	26.9 (5.4)
Smoking Status (%)		
Current	971 (7.2%)	98 (5.2%)
Former	1822 (13.5%)	200 (10.7%)
Never	6881 (51.2%)	753 (40.1%)
Unknown	3779 (28.1%)	826 (44.0%)

Table 1. Clinical characteristics of patients included in the study.

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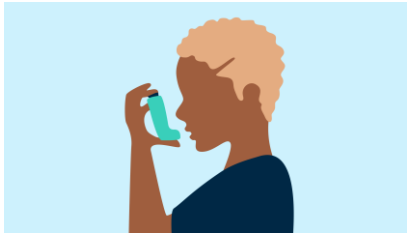
Asthma



ESS vs no ESS	Unadjusted OR [95% CI]	Adjusted OR [95% CI]
CRS w/ Asthma	0.81 [0.70-0.95]	0.85 [0.73-0.99]

Table 2. Multivariable logistic regression analysis for asthma development in CRS patients without controlling for confounders and after controlling for age, gender, race/ethnicity, chronic rhinitis and smoking status.

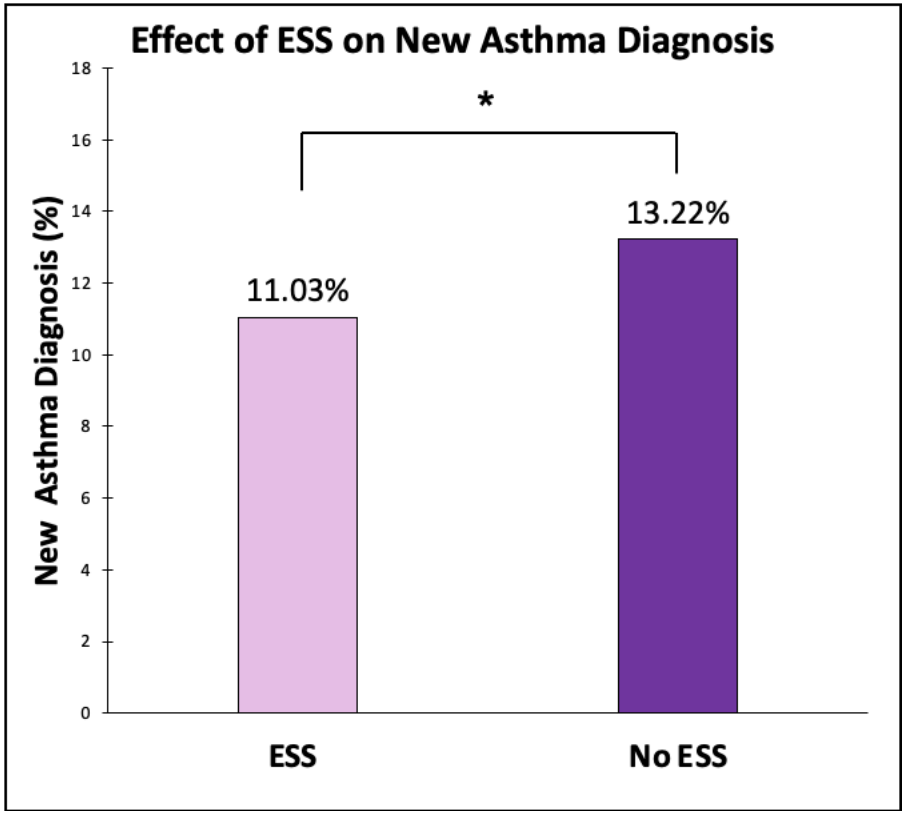


Figure 1. New asthma diagnosis in CRS patients in the sinus surgery (ESS) vs no ESS groups. (* P < 0.05)

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CRSwNP: Asthma Development

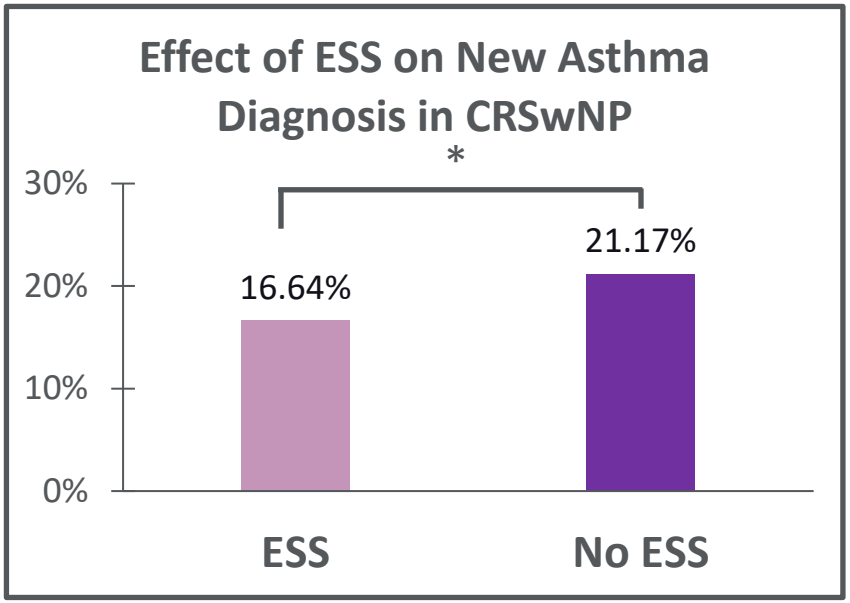

Figure 2. New asthma diagnosis in CRSwNP patients in the sinus surgery (ESS) vs no ESS groups. (* P=0.03)

ESS vs no ESS	Unadjusted OR [95% CI]	Adjusted OR [95% CI]
CRSwNP w/ Asthma	**0.74 [0.57-0.97]**	**0.79 [0.60-1.04]**

Table 3. Multivariable logistic regression analysis for asthma development in CRSwNP patients without controlling for confounders and after controlling for age, gender, race/ethnicity, chronic rhinitis and smoking status.

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CRSsNP: Asthma Development

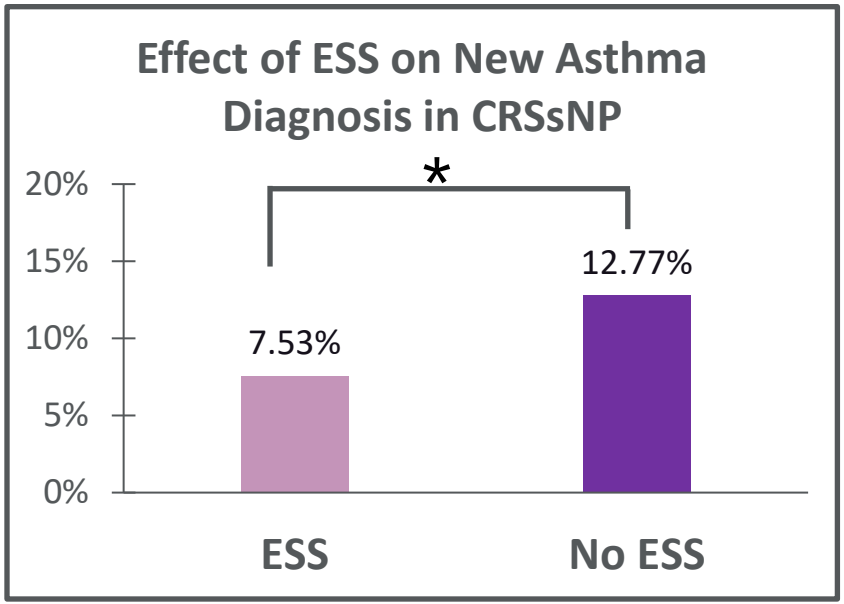

Figure 3. New asthma diagnosis in CRSsNP patients in the sinus surgery (ESS) vs no ESS groups. (* P< 0.0001)

ESS vs no ESS	Unadjusted OR [95% CI]	Adjusted OR [95% CI]
CRSsNP w/ Asthma	**0.56 [0.44-0.70]**	**0.57 [0.45-0.71]**

Table 4. Multivariable logistic regression analysis for asthma development in CRSsNP patients without controlling for confounders and after controlling for age, gender, race/ethnicity, chronic rhinitis and smoking status.

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Bronchiectasis

ESS vs no ESS	Unadjusted OR [95% CI]	Adjusted OR [95% CI]
CRS w/ BE	0.98 [0.70-1.37]	1.22 [0.84-1.77]

Table 5. Multivariable logistic regression analysis for bronchiectasis development in CRS patients without controlling for confounders and after controlling for age, gender, race/ethnicity, BMI, smoking status, and comorbidities.

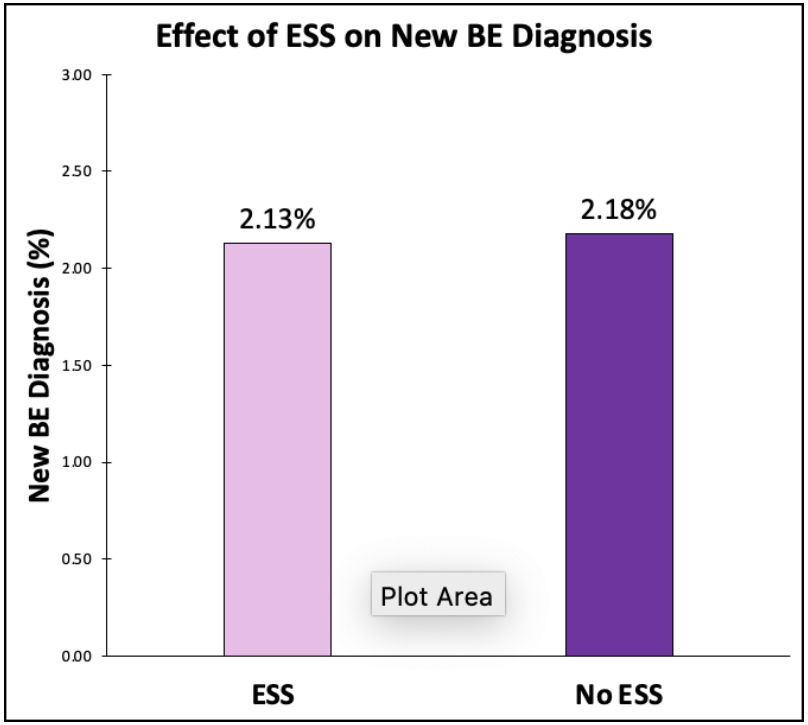

Figure 4. New bronchiectasis (BE) diagnosis in CRS patients in the sinus surgery (ESS) vs no ESS groups. (P=1.0)

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CRSwNP: BE Development

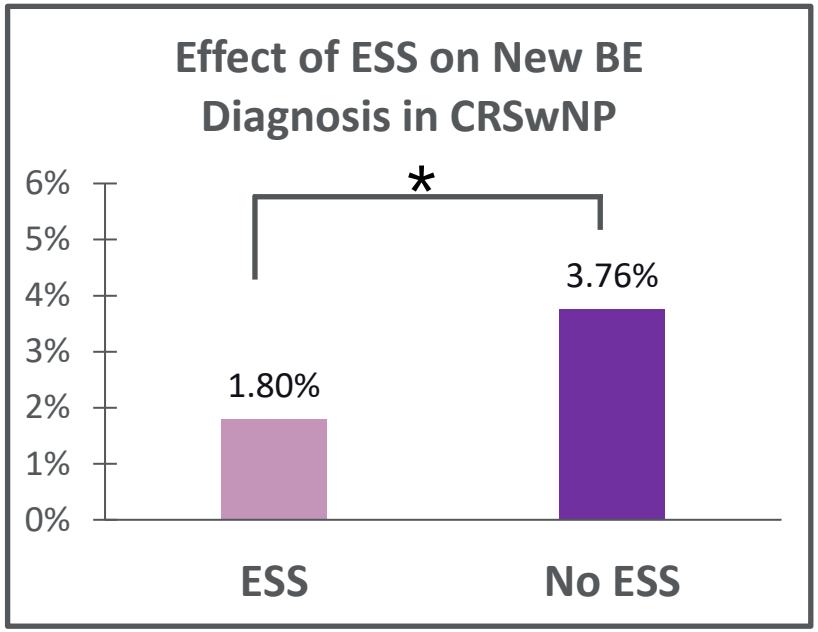

Figure 5. New bronchiectasis (BE) diagnosis in CRSwNP patients in the sinus surgery (ESS) vs no ESS groups. (P=0.02)

ESS vs no ESS	Unadjusted OR [95% CI]	Adjusted OR [95% CI]
CRSwNP w/ BE	**0.47 [0.24-0.92]**	**0.57 [0.26-1.21]**

Table 6. Multivariable logistic regression analysis for bronchiectasis development in CRSwNP patients without controlling for confounders and after controlling for age, gender, race/ethnicity, BMI, smoking status, and comorbidities.

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CRSsNP: BE Development

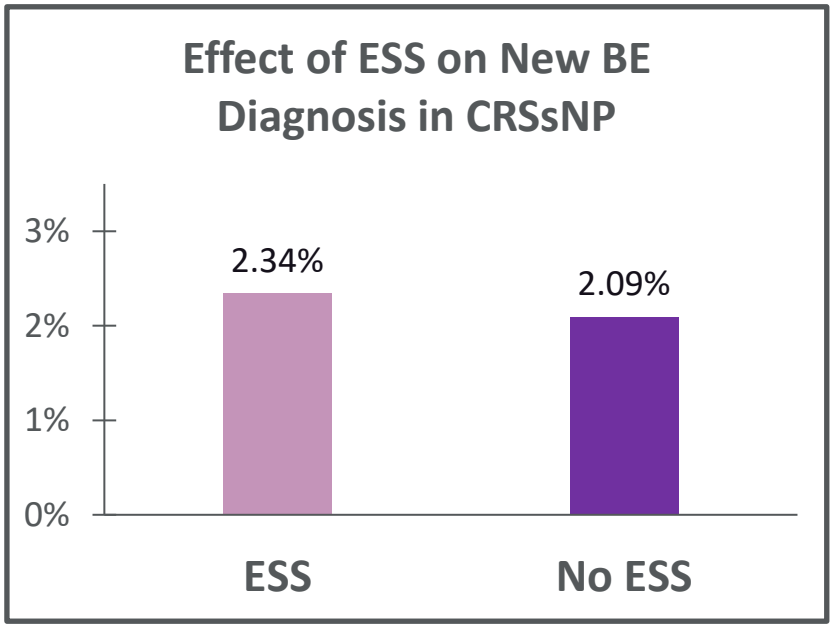

Figure 6. New bronchiectasis (BE) diagnosis in CRSsNP patients in the sinus surgery (ESS) vs no ESS groups. (P=0.58)

ESS vs no ESS	Unadjusted OR [95% CI]	Adjusted OR [95% CI]
CRSsNP w/ BE	**1.12 [0.75-1.67]**	**1.45 [0.94-2.27]**

Table 7. Multivariable logistic regression analysis for bronchiectasis development in CRSsNP patients without controlling for confounders and after controlling for age, gender, race/ethnicity, BMI, smoking status, and comorbidities.

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Time to Diagnosis?

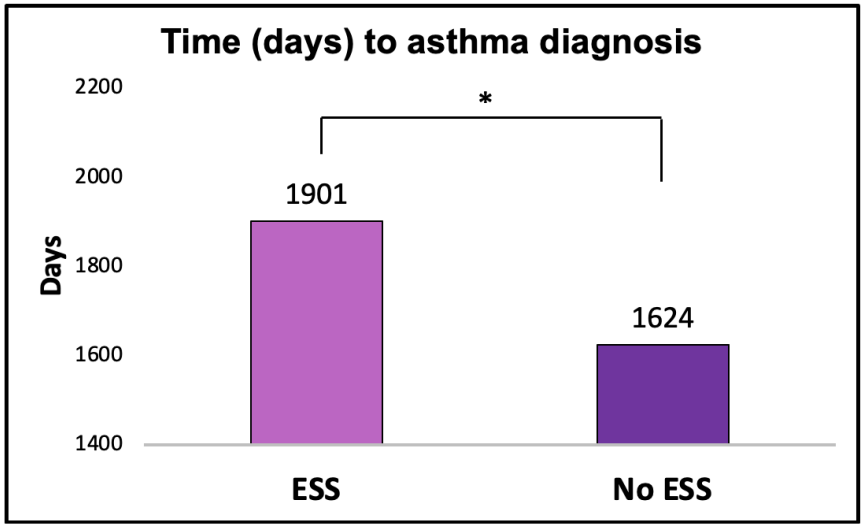

Figure 7. Average time in days to asthma diagnosis following CRS diagnosis. ($P < 0.05$)

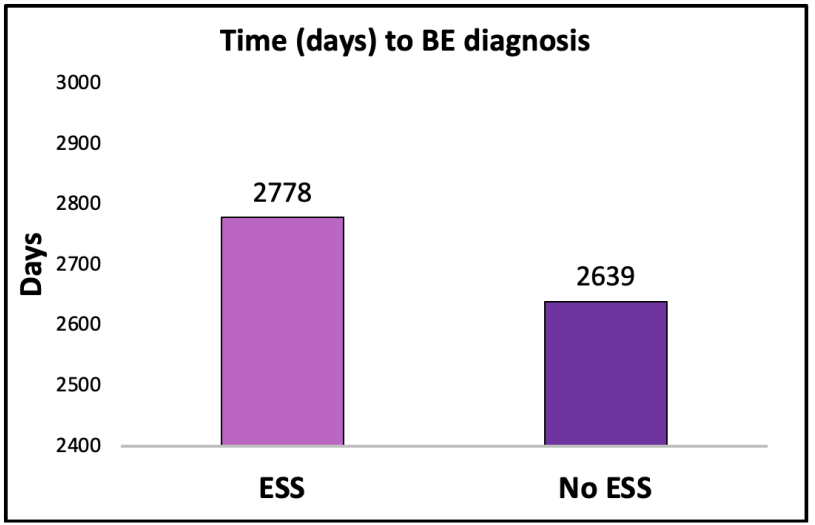

Figure 8. Average time in days to bronchiectasis diagnosis following CRS diagnosis. ($P = 0.57$)

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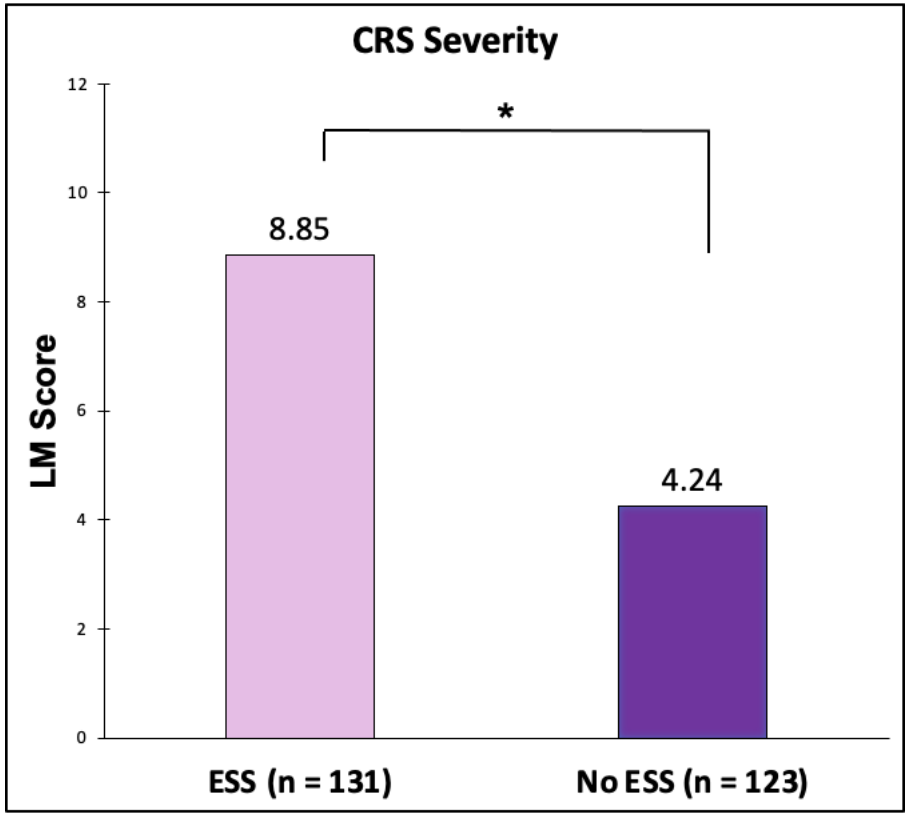
What about disease severity?

Lund-Mackay CT scan assessment
Paranasal sinuses
Maxillary (0, 1, 2)
Anterior ethmoid (0, 1, 2)
Posterior ethmoid (0, 1, 2)
Sphenoid (0, 1, 2)
Frontal (0, 1, 2)
Ostiomeatal complex (0, 2)*
Total
0 - With no abnormalities
1 - Partial opacification
2 - Total opacification

* 0: Without obstruction; 2: Obstructed.

Figure 9. Assessment of CRS disease severity by calculating Lund-Mackay (LM) scores on sinus CT scans in a random subgroup of patients from both the sinus surgery (ESS) and no ESS groups. (* $P < 0.05$)



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Freitas MR et al. 2013 Aug;79(4):480-6.

How do rates compare in those with moderate/severe sinus disease?

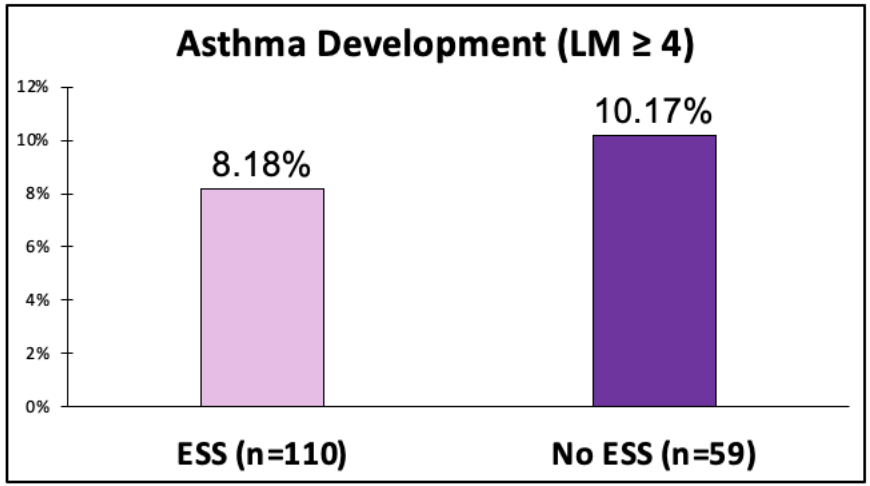

Figure 10. Rate of asthma development in patient with more severe CRS (LM ≥ 4) in the sinus surgery (ESS) vs no ESS groups. (P=0.78)

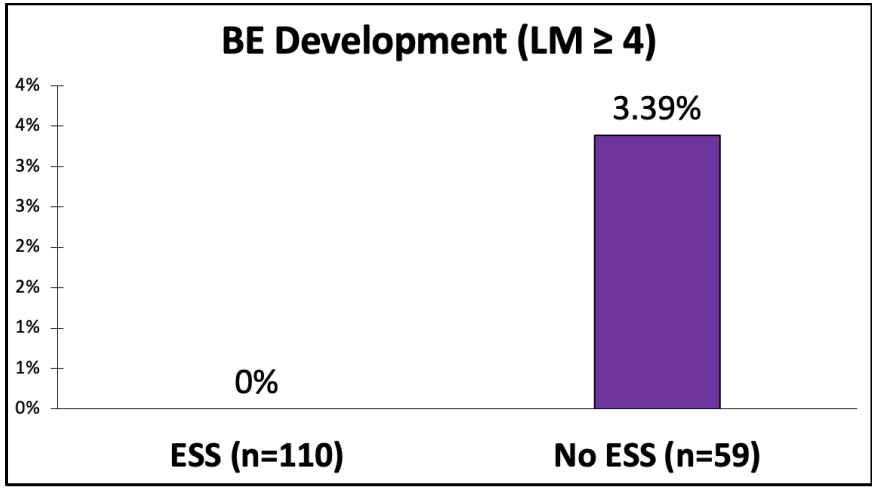

Figure 11. Rate of bronchiectasis (BE) development in patient with more severe CRS (LM ≥ 4) in the sinus surgery (ESS) vs no ESS groups. (P=0.12)

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Does the timing of ESS matter?

Time to ESS (days)	Asthma (n)	% Asthma	BE (n)	% BE
<88	107	**11.44**	14	**1.50**
89-307	48	**10.17**	11	**2.33**
>307	52	**11.06**	14	**3.19**

Table 8. Frequency of asthma and bronchiectasis development based on the timing of sinus surgery following CRS diagnosis.

Time to ESS (<88 vs >307 days)	Odds Ratio	95% CI
CRS w/ Asthma	0.99	0.70 – 1.43
CRS w/ BE	2.32	1.08 – 4.98

Table 9. Multivariable logistic regression analysis of asthma and bronchiectasis development in patients undergoing early (<88 days) versus late (>307 days) ESS following CRS diagnosis after controlling for age, gender, race, BMI and smoking status.

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Might Gender Play a Role?

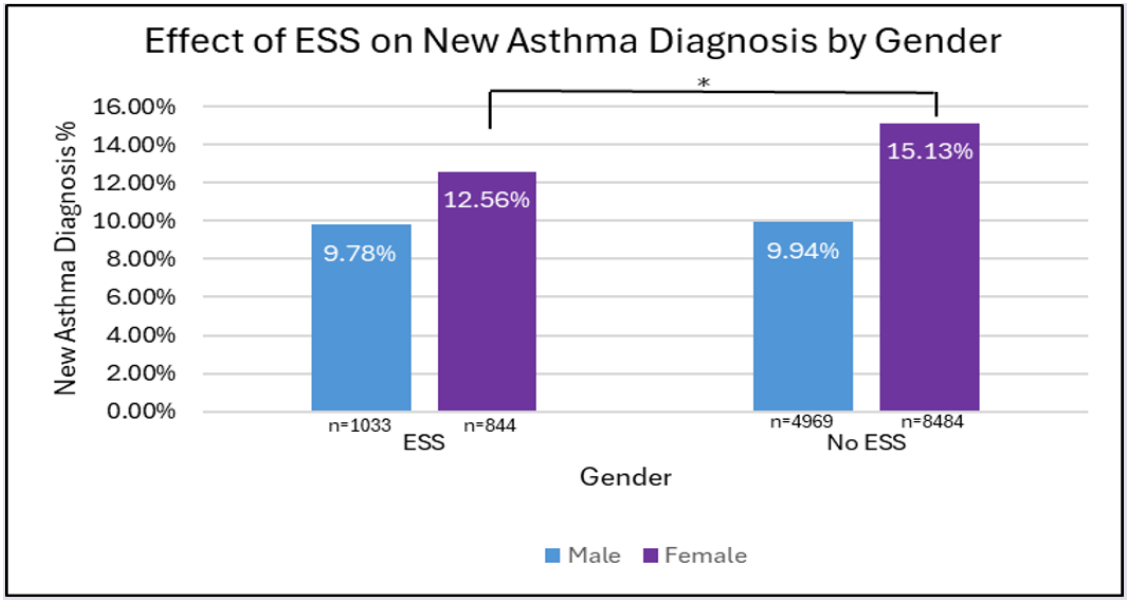

Figure 12. New Asthma Diagnosis in ESS vs no ESS groups (*p=0.045)

Table 10. Multivariable logistic regression analysis for asthma development after controlling for age, race/ethnicity, BMI, smoking status, and rhinitis

	Female ESS		Male ESS	
	Unadjusted OR [95% CI]	**Adjusted OR [95% CI]**	**Unadjusted OR [95% CI]**	**Adjusted OR [95% CI]**
New Asthma Dx	0.81 [0.65-0.99]	0.73 [0.59-0.91]	0.98 [0.78-1.23]	0.95 [0.75-1.19]

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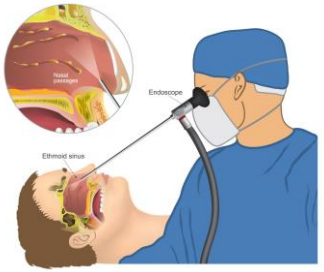
Conclusions



- Patients with CRS who undergo surgery vs medical management had a **19% lower likelihood of being diagnosed with asthma in the future**. The likelihood of a new asthma diagnosis remained significantly lower in the surgery group after controlling for confounders.
- Those with Nasal Polyps (**CRSwNP**) had a **26% lower** likely of developing asthma in the future following ESS. Those with Nasal Polyps (**CRSsNP**) had a **43% lower** likelihood of developing asthma if they underwent ESS, even after controlling for confounders.

Conclusions

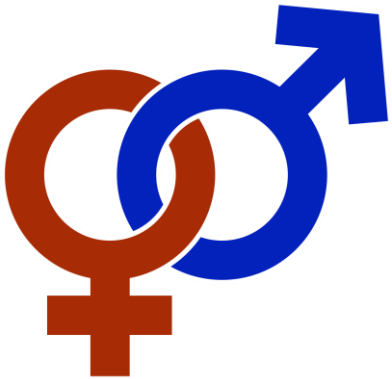
- Despite having higher sinus disease severity at baseline (based on Lund-Mackay scoring), patients undergoing ESS had a **similar risk of developing bronchiectasis** compared to the control group when controlling for confounders.
- Patient with **CRSwNP** had a **53% reduction in bronchiectasis** development when undergoing ESS compared to the control group, although this reduction was no longer significant when controlling for confounders.

Conclusions

- Patients who underwent ESS took significantly **longer to develop asthma** that those who did not undergo surgery
- Although a small group size did not allow for statistical comparison, when adjusting for more severe CRS disease (LM ≥ 4), **a smaller percentage of patients developed asthma and BE after undergoing ESS.**
- **Earlier ESS following CRS diagnosis reduces the risk of bronchiectasis development** but does not impact the risk of asthma development.

Conclusions

- ESS significantly **decreased** the risk of developing asthma in **female CRS patients**
- Despite higher CRS severity at baseline compared to the no ESS group, males undergoing ESS did not have a higher risk of developing asthma



Team Appreciation

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Questions?

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Thank You

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