Exacerbations Are Associated With Lung Function Trajectory in a Broad Asthma Population in England, Scotland, and Wales 1950-2019

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Rationale

- Progressive deterioration of lung function can result in **severe asthma** and **permanent airflow obstruction.**[1]
- Severe **asthma exacerbations** may be a cause; however, previous studies are small and/or inconclusive.[2,3]

Aim Assess the association between exacerbation burden and lung function decline in a broad asthma patient population

Study Design Observational historical cohort

Data Source Optimum Patient Care Research Database UK: Quality controlled longitudinal primary care clinical data (https://opcrd.co.uk/)

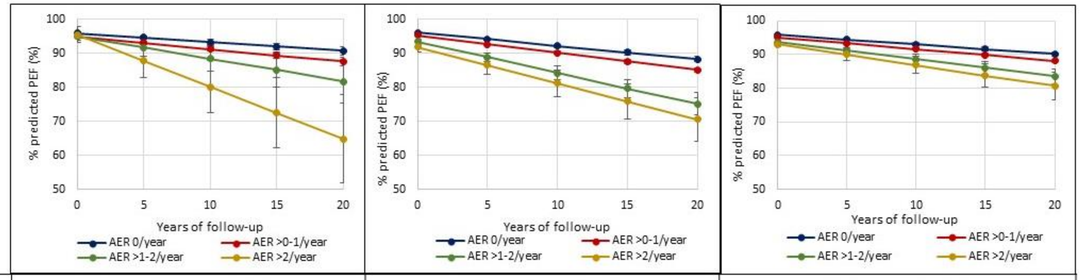
109,182 patients with asthma:

- Quality outcomes framework (QoF)-defined asthma diagnosis[4]
- 2+ asthma prescriptions during follow-up
- No COPD at baseline
- 5+ years of follow-up and 3+ peak expiratory flow (PEF) readings on or after 18th birthday
- Baseline = 1st eligible PEF reading

Outcome Slope of percent predicted PEF[5]

Repeat exacerbations are a key driver of lung function decline in asthma, which is significantly accelerated in younger patients aged under 40 years

Figure. Estimated declines in % predicted PEF (ppPEF) over 20 years according to annual exacerbation rate



AER	18 – 24 years old at baseline		25 – 39 years old at baseline		40+ years old at baseline	
	Decline in ppPEF/yr (95% CI)	Average difference in ppPEF decline/yr (95% CI)	Decline in ppPEF/yr (95% CI)	Average difference in ppPEF decline/yr (95% CI)	Decline in ppPEF/yr (95% CI)	Average difference in ppPEF decline (95% CI)
0/yr	**-0.26** (-0.31, -0.21)	**comparator**	**-0.39** (-0.43, -0.36)	**comparator**	**-0.29** (-0.32, -0.26)	**comparator**
>0-1/yr	**-0.37** (-0.41, -0.32)	**-0.11** (-0.18, -0.04) p = 0.001	**-0.51** (-0.54, -0.48)	**-0.11** (-0.16, -0.07) p <0.001	**-0.35** (-0.37, -0.32)	**-0.06** (-0.09, -0.02) p = 0.003
>1-2/yr	**-0.67** (-0.92, -0.41)	**-0.41** (-0.67, -0.14) p = 0.002	**-0.91** (-1.04, -0.78)	**-0.52** (-0.65, -0.38) p <0.001	**-0.51** (-0.6, -0.42)	**-0.22** (-0.32, -0.13) p <0.001
>2/yr	**-1.53** (-2.07, -1.0)	**-1.27** (-1.81, -0.73) p <0.001	**-1.06** (-1.31, -0.81)	**-0.67** (-0.92, -0.41) p <0.001	**-0.62** (-0.79, -0.45)	**-0.33** (-0.5, -0.16) p <0.001

Analysis ● **Mixed effects growth model** ● Assessed **interaction of AER and time** on % predicted PEF
● **Adjusted for** patient age, BMI, gender, length of follow-up, baseline lung function, and smoking status

Conclusions

- **Largest population-based assessment of asthma exacerbation burden and lung function decline.**
- **Exacerbations are associated with faster lung function decline, which is most accelerated in patients aged under 40 years and is not entirely prevented by ICS.**
- **Earlier intervention with appropriate management in younger asthma patients could be of value to prevent excessive lung function decline.**

Exposure

Annual exacerbation rate (AER)
- Total exacerbations/total years of follow-up

Definition of exacerbation[6]:
- Asthma related hospital visit/stay or acute prescription for 3+ days of prednisolone

Patients with higher annual exacerbation rates tended to be **sicker at baseline.**

Table. Patient demographic and clinical characteristics: Overall and by annual exacerbation rate (AER)

Characteristics	Overall 100% (109,182)	AER 0 40.4% (44,107)	AER >0-1 55.8% (60,927)	AER >1-2 3.0% (3,236)	AER 2+ 0.8% (912)
Median age at baseline (IQR)	**42** (30-55)	**39** (28-53)	**43** (32-57)	**50** (37-61)	**47** (37-60)
% Male (n)	**40.9%** (44,697)	**47.1%** (20,791)	**37.1%** (22,577)	**31.1%** (1007)	**35.3%** (322)
Median years of follow-up (IQR)	**10.4** (7.5 -14.1)	**9.3** (6.9-12.8)	**11.2** (8.1-15.1)	**10.9** (7.9-14.7)	**10.6** (7.7-14.1)
Median BMI at baseline (IQR)	**27.0** (24.0-30.9)	**26.3** (23.5-29.9)	**27.5** (24.3-31.6)	**28.1** (24.6-32.6)	**28.1** (24.4-32.9)
% Non-smoker (n)	**35.1%** (38,287)	**37.7%** (16,637)	**33.5%** (20,388)	**30.4%** (983)	**30.6%** (279)
% Ex-smoker (n)	**18.4%** (20,120)	**17.8%** (7865)	**18.8%** (11,436)	**19.7%** (637)	**20.0%** (182)
% Current smoker (n)	**15.5%** (16,873)	**14.5%** (6381)	**16.1%** (9818)	**16.2%** (524)	**16.5%** (150)
% Smoking status not recorded (n)	**31.1%** (33,902)	**30.0%** (13,224)	**31.7%** (19,285)	**33.8%** (1092)	**33.0%** (301)
Median exacerbations at baseline (IQR)	**0.2** (0.6)	**0.00** (0-0)	**0.0** (0-0)	**0.0** (0-1)	**1.0** (0-3)
Median SABA prescriptions at baseline (IQR)	**2** (1-4)	**2** (1-4)	**2** (1-5)	**3** (2-7)	**5** (2-9)
Mean ICS dosage/year categorised[a]					
lowest tercile ICS (0-147.1 mcg/day), n (%)	**37652** (34.5)	**20950** (47.5)	**16488** (27.1)	**181** (5.6)	**33** (3.6)
medium tercile ICS (147.1-463.7 mcg/day, n (%)	**37770** (34.6)	**14693** (33.3)	**22264** (36.5)	**686** (21.2)	**127** (13.9)
highest tercile (>463.7mcg), n (%)	**33760** (30.9)	**8464** (19.2)	**22175** (36.4)	**2369** (73.2)	**752** (82.5)

[a]patients were ranked by mean yearly ICS dosage in mg into 33.33% percentile groups. Bottom tercile ICS: 0-53,726.8 mg/yr; middle tercile ICS: >53,726.8 to 169,368.4 mg/yr; top tercile (>169,368.4 mg/yr)

References
1. M. R. Sears et al **2007** 'Lung function decline in asthma', *ERJ*. doi: 10.1183/09031936.00080007.
2. T. R. Bai et al **2007** 'Severe exacerbations predict excess lung function decline in asthma', *ERJ*, doi: 10.1183/09031936.00165106.
3. H. Coumou et al **2018** 'Predictors of accelerated decline in lung function in adult-onset asthma', *ERJ*, doi: 10.1183/13993003.01785-2017.
4. Quality Outcomes Framework (QOF). NHS Digital. https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/general-practice-data-hub/quality-outcomes-framework-qof
5. J. L. Hankinson et al, **1999** 'Spirometric Reference Values from a Sample of the General U.S. Population', *Am J Respir Crit Care Med*, doi: 10.1164/ajrccm.159.1.9712108.
6. C. C. Thomson et al. **2014** 'Severe Asthma', *Annals ATS*, doi: 10.1513/AnnalsATS.201405-199CME.

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