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Sex differences in asthma and COPD hospital admission, readmission and mortality

Hannah Whittaker , ¹ Alexander Adamson , ¹ Philip Stone, ¹ Precious Olubori, ² James Calvert, ^{3,4} James Dodd , ^{5,6} Ian Sinha, ^{4,7} Katherine Hickman, ⁸ Sally Singh, ⁹ Jennifer K Quint ¹⁰

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For numbered affiliations see end of article.

Correspondence to

BMJ Group

Dr Hannah Whittaker; h.whittaker@imperial.ac.uk

ABSTRACT

Background Asthma and chronic obstructive pulmonary disease (COPD) outcomes vary by sex. We investigated whether males and females with asthma or COPD are managed differently in-hospital when admitted for an exacerbation.

Methods Data from the National Asthma and COPD Audit Programme were used to determine three cohorts of people hospitalised for an exacerbation: (1) adults with asthma, (2) children and young people (CYP) with asthma, and (3) adults with COPD. Outcomes included the following in-hospital interventional measures: spirometry recording, respiratory specialist review, respiratory medication administration and discharge bundle recording. Linked hospital data were used to determine 30-day and 90-day readmissions and Office for National Statistics data for 90day mortality. Random effects logistic regression was used to investigate the association between sex and in-hospital outcomes, readmission and mortality.

Results 16 370 adults with asthma, 7156 CYP with asthma and 28354 adults with COPD were included. Female adults with asthma had higher odds of being seen by a respiratory specialist (OR 0.1.13, 1.02-1.26) and higher odds of readmission within 30 and 90 days (OR 1.22, 1.10-1.37, OR 1.34, 1.23-1.46) compared with males. Female adults with COPD had higher odds of being seen by a respiratory specialist, (OR 1.10,1.02-1.19), being administered non-invasive ventilation (OR 1.18, 1.09-1.29), and receiving a discharge bundle (OR 1.07, 1.00-1.14), and lower odds of readmission within 90 days (OR 0.95, 0.90-1.01), or mortality within 90 days (OR 0.88, 0.81-0.96). Lastly, female CYP had higher odds of steroids administered within 1 hour (OR 1.13, 1.00-1.28) and higher 30-day and 90-day readmission compared with males (OR 1.21, 1.00-1.44 and 1.17, 1.03-1.34). **Interpretation** Sex differences in in-hospital care exist in adults COPD, which may impact readmissions and mortality; however, little to no sex differences in in-hospital care were seen in people with asthma yet females were more likely to be readmitted to hospital.

INTRODUCTION

Chronic respiratory diseases are among the top causes of early death in the UK and worldwide, particularly asthma and chronic obstructive pulmonary disease (COPD). In

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Exacerbations and hospitalisations are known to differ by sex in people with asthma or chronic obstructive pulmonary disease (COPD).

WHAT THIS STUDY ADDS

⇒ In-hospital care differed by males and females with COPD: however, no difference was seen for adults and children with asthma vet females were more likely to be readmitted to hospital following their original admission.

HOW THIS STUDY MIGHT AFFECT RESEARCH. PRACTICE OR POLICY

⇒ This study demonstrates how factors other than in-hospital care should be considered in terms of hospitalisations in people with asthma in order to reduce the higher burden of hospitalisation in females.

England in 2023, the prevalence of asthma in adults and children was 6.5% and the prevalence of COPD was 1.9%.²³ Chronic respiratory diseases have historically been classed as male-dominated; however, we now know that differences in incidence, mortality and exacerbations differ by sex. 4-9

Incidence of asthma across the life course differs by sex with more females likely to develop asthma in adulthood compared with males and more males in childhood compared with females.⁵ Previous studies have also found that asthma hospitalisations are more common in adult females than males.¹⁰ In 2021, the UK National Asthma and COPD Audit Programme (NACAP) reported that 71.8% of hospital admissions for asthma were in females; whereas, the children and young people (CYP) with asthma audit reported that 60.1% of asthma hospital admissions were in males. 11 12 In addition, data from the Office for National Statistics indicate that more females died of asthma compared with males consistently between 2001 and 2019.¹³ Sex





differences in COPD have also been reported. Females with COPD are more likely to be younger, experience a greater number of exacerbations, but have better lung function, have fewer pack-years smoking and survive longer compared with males. Understanding why these differences exist by sex is vital to reducing the gap in health inequalities between males and females.

Management of males and females admitted to hospital with acute respiratory exacerbations has not been explored. Investigating whether chronic respiratory disease management differs by sex is important to better understand where future interventions can be applied to reduce sex disparities in chronic respiratory disease outcomes. We aimed to investigate whether in-hospital management of adults with asthma, children and young people with asthma, and adults with COPD differed by sex. Second, we investigated whether readmission and mortality varied by sex in these asthma and COPD populations.

METHODS

Data source and study population

NACAP contains pseudonymised data collected from hospitals across England and Wales for individuals admitted to hospital with a primary diagnosis of an asthma or COPD exacerbation. We used data from the NACAP adult asthma database, the NACAP CYP asthma database and the NACAP COPD database. The adult asthma database included information on individuals aged 18 years or older admitted to hospital for an asthma exacerbation and discharged between 1 April 2019 and 30 March 2020. The CYP asthma database included information on individuals aged less than 18 years admitted to hospital for an asthma exacerbation and discharged between 1 June 2019 and 31 January 2020. The COPD adult database included information on individuals aged 18 years or older admitted to hospital for a COPD exacerbation and discharged between 1 October 2019 and 29 February 2020. Data were recorded for admissions lasting at least 4hours. Datasets were linked to additional hospital data from the Hospital Episode Statistics (HES) for England and the Patient Episode Database for Wales (PEDW) and mortality data from the Office for National Statistics (ONS) to determine 30-day and 90-day readmission and 90-day mortality. Data were linked by patient's unique NHS number, admission date and discharge date. The Healthcare Quality Improvement Partnership (HQIP) commissioned the NACAP, and funding was primarily provided by NHS England and the Welsh government. Using the NACAP adult asthma data, the CYP asthma data and the COPD data, three cohorts were created, and data were analysed separately.

Exposure and outcomes

The exposure of interest was sex. Sex was recorded as male or female. People with missing sex were excluded from this study.

Outcomes in all cohorts were in-hospital processes of care. In the adult asthma cohort, these included a record of (1) peak expiratory flow (PEF) on admission, (2) PEF recorded within 1 hour of admission, (3) a respiratory specialist review on admission, (4) a respiratory specialist review within 24 hours of admission, (5) beta-2-agonist administered on admission, (6) beta-2-agonist administered within 1 hour of admission, (7) steroid administered on admission, (8) steroid administered within 1 hour of admission and (9) discharge bundle received.

In the CYP asthma cohort, outcomes included a record of (1) PEF on admission, (2) a respiratory specialist review on admission, (3) beta-2-agonist administered, (4) beta-2-agonist administered within 1 hour of admission, (5) steroid administered, (6) steroid administered within 1 hour of admission and (7) discharge bundle received.

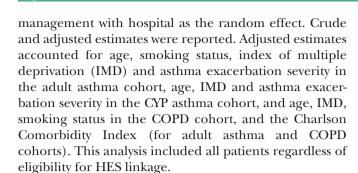
In the COPD cohort, in-hospital outcomes included a record of (1) a respiratory specialist review on admission, (2) a respiratory specialist review within 24 hours of admission, (3) non-invasive ventilation (NIV) treatment, (4) NIV treatment within 2 hours of admission and (5) discharge bundle received. For each cohort, all outcome variables were binary and coded as having a record of the specific outcome or not having a record of the outcome. Missing data were reported where necessary.

In addition, further outcomes included 30-day and 90-day readmission and 90-day mortality from patients' initial hospital admission were determined through HES and ONS records, respectively. Cause-specific 90-day readmission was determined through ICD-10 codes for respiratory and cardiovascular-related causes in the first position (see additional methodology in the supplementary material for specific ICD-10 codes). The top 5 most common causes of 90-day readmission were also described.

Statistical analysis

Baseline characteristics were described for each of the three cohorts. Baseline characteristics included age at admission, smoking status (never smoker, ex-smoker, current smoker and current vaper for adult asthma and COPD cohorts based on status on admission), index of multiple deprivation in 2019 (quintile 1 was the most deprived and quintile 5 was the least deprived), PEF per cent predicted (for the adult asthma cohort), asthma exacerbation severity (moderate or severe for asthma cohorts; see additional methodology in the supplementary material for exacerbation severity definitions), oxygen saturation (for asthma cohorts), FEV1% predicted prior to admission (for COPD cohort), the Charlson Comorbidity Index (for adult asthma and COPD cohort) and length of stay in hospital. Continuous variables were reported as medians and IQRs and categorical variables were reported as numbers and proportions. Missing data were reported where necessary.

Random effects logistic regression was used to investigate the association between sex and in-hospital



Random effects logistic regression was also used to compare 30 and 90-day hospital readmission and 90-day mortality (all-cause and cause-specific) between males and females with hospital as the random effect. This analysis included only those patients who were eligible for HES linkage. Adjusted estimates accounted for age, smoking status (for adult cohorts only), IMD, length of stay in hospital, asthma exacerbation severity on initial admission (for the asthma cohorts) and the Charlson Comorbidity Index (for adult cohorts only). In the CYP population, 90-day mortality was not investigated due to small mortality numbers.

Patient and public involvement

Patients and the public were not involved in the design of this study.

RESULTS

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A total of 16370 adults with asthma were included, of whom 11546 (70.5%) were female, 7156 children and young people with asthma were included, of whom 2755 (38.5%) were female, and 28354 adults with COPD were

included, of whom 15565 (54.9%) were female (figure 1). In addition, 14973 (91.5%) adults with asthma, 6617 (92.5%) CYP with asthma and all 28354 (100%) adults with COPD were eligible for HES linkage (figure 1).

In-hospital management of adults with asthma

Females admitted to hospital for asthma were more likely to be never smokers compared with males (46.4% vs 37.9%, respectively) and had higher PEF per cent predicted compared with males (median 60% vs 55%, respectively) but were similar to males in terms of age, IMD, median oxygen saturation, Charlson Comorbidity Index, and asthma exacerbation severity on admission, and length of stay in hospital (online supplemental table S1). Females had a higher odds of being seen by a respiratory specialist compared with males (OR 1.13, 1.02-1.26, p=0.021) but similar odds of having PEF recorded, having a record of beta-2-agonist administered during admission and within 1 hour of admission, having a record of steroids administered during admission and within 1 hour of admission, and receiving the discharge bundle compared with males, figure 2 and online supplemental table S2.

In-hospital management of children and young people with asthma

Females under the age of 18 who were admitted to hospital with asthma were slightly older (median age 6 vs 7, respectively) and were more likely to have severe asthma exacerbation on admission (67.2% vs 62.4%, respectively) compared with males under 18 years old (online supplemental table S3). CYP with asthma were similar in terms of IMD, oxygen saturation and median length

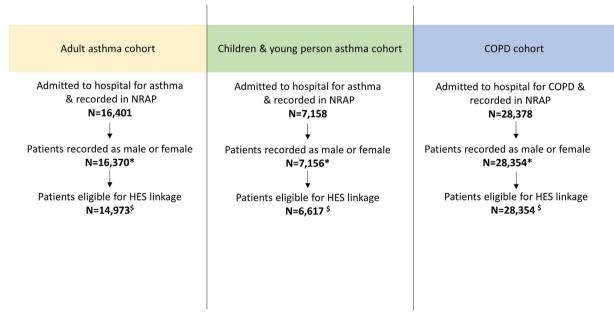


Figure 1 Patients included in the adult asthma cohort, children and young persons cohort, and COPD cohort. Legend: NACAP (National Respiratory Audit Programme), COPD (chronic obstructive pulmonary disease). *Patients included in the analysis investigating the association between sex and in-hospital outcomes. \$Patients included in the analysis investigating the association between sex and 30-day and 90-day readmission and mortality.

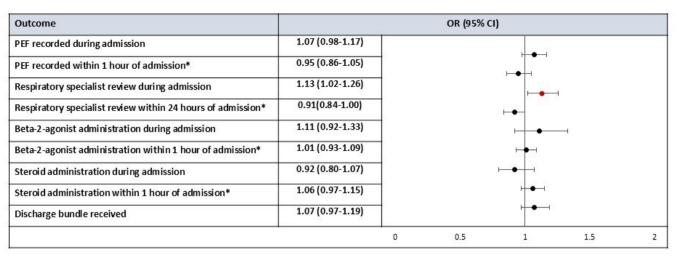


Figure 2 Adjusted ORs (95% CI) for the association between sex and in-hospital management outcomes in adults with asthma. PEF (peak expiratory flow). Estimates show ORs and 95% CIs for females compared with males. Estimates are adjusted for age, smoking status, asthma exacerbation severity, IMD and the Charlson Comorbidity Index. IMD, index of multiple deprivation.

of stay in hospital. Females had a higher odds of steroid administration within 1 hour of admission compared to males (OR 1.13, 1.00-1.28; p=0.048) but a similar odds of having PEF recorded, being seen by a respiratory specialist, having a record of beta-2-agonist administered during admission and within 1 hour of admission, having a record of steroids administered during admission, and receiving the discharge bundle compared with males (figure 3 and online supplemental table S4).

In hospital management of adults with COPD

In people with COPD, females were more likely to be current smokers compared with males (37.7% vs 33.8%, respectively) and had a lower mean FEV1% predicted compared with males (43% vs 48%, respectively), had a shorter median length of stay in hospital compared with males (3 days vs 4 days, respectively) and had fewer comorbidities (Charlson Comorbidity Index 1–2: males 67.8%, females 72.4%) but were similar to males in terms of age, IMD and FEV1/FVC ratio (online supplemental table S5). Compared with males, females with COPD had higher odds of having a respiratory specialist review during admission (OR 1.10, 1.02 to 1.19), higher odds of being administered NIV during admission (OR 1.18, 1.09-1.29) and higher odds of receiving a discharge bundle (OR 1.07, 1.00-1.14, p-value=0.038; figure 4 and online supplemental table S6).

Readmission and mortality following discharge in adults with asthma

Of the 14973 adults with asthma who were eligible for HES linkage, 2017 (13.5%) were readmitted to hospital within 30 days of their initial asthma admission; 1491 of 10 536 (14.2%) females and 526 of 4437 (11.9%) males were readmitted within 30 days. In addition, 3890 (26.0%) people were readmitted to hospital within 90 days of their initial asthma admission; 2916 (27.7%) females and 974 (22.0%) males were readmitted within

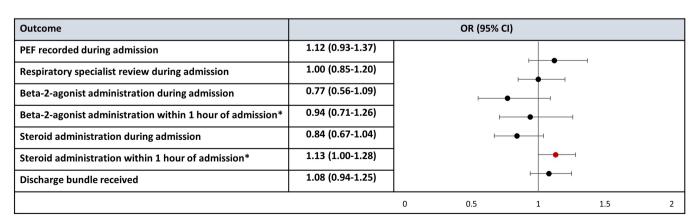


Figure 3 Adjusted ORs (95% CI) for the association between sex and in-hospital management outcomes in children and young people with asthma. PEF (peak expiratory flow). Estimates show ORs and 95% CIs for females compared with males. Estimates are adjusted for age, asthma exacerbation severity and IMD. IMD, index of multiple deprivation.

Adjusted ORs (95% CI) for the association between sex and in-hospital management outcomes in adults with COPD. FEV1 (forced expiratory flow in 1s), FVC (forced vital capacity), NIV (non-invasive ventilation). Estimates show ORs and 95% CIs for females compared with males. Estimates are adjusted for age, smoking status, IMD and the Charlson Comorbidity Index. IMD, index of multiple deprivation.

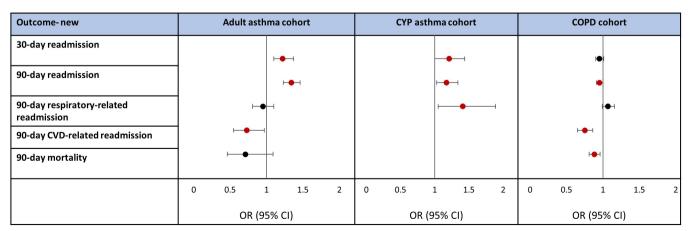
90 days (online supplemental figure S1). In females who were readmitted within 90 days, 1571 (53.9%) were readmitted for respiratory-related causes, 183 (6.3%) for cardiovascular-related causes and 1162 (39.9%) for other causes. In males, 527 (54.1%) were readmitted for respiratory-related causes, 84 (8.6%) for cardiovascularrelated causes and 363 (37.3%) for other causes. The top 5 causes of readmission within 90 days for males and females were similar and consisted of allergic asthma (ICD-10 code [45), chronic obstructive pulmonary disease (ICD-10 code J44), bronchopneumonia (ICD-10 code [18] and status asthmaticus (ICD-10 code [46). Eosinophilic asthma (ICD-10 code [82) was more commonly recorded in males; whereas, dyspnoea (ICD-10 code R06) was more common in females. In addition, 109 (0.7%) people died from any cause within 90 days of their initial admission. In females, 0.7% died within 90 days and in males, 0.8% died within 90 days.

Overall, females with asthma had higher odds of readmission within 30 and 90 days of their initial asthma admission compared with males (OR 1.22, 1.10 to 1.37 and OR 1.34, 1.23-1.46, respectively). While the odds of being readmitted for respiratory-related causes within 90 days was similar between males and females, females

had lower odds of readmission for cardiovascular-related causes (OR 0.73, 0.56-0.97) and there was no difference in 90-day mortality between males and females with asthma (figure 5 and online supplemental table S7).

Readmission following discharge in CYP with asthma

Of the 6617 CYP with asthma who were eligible for HES linkage, 631 (9.5%) were readmitted to hospital within 30 days of their initial asthma admission; 262 of 2524 (10.4%) females and 369 of 4093 (9.0%) males were readmitted within 30 days (online supplemental figure S1). In addition, 1272 (19.2%) were readmitted to hospital within 90 days of their initial asthma admission; 507 (20.1%) females and 765 (18.7%) males were readmitted within 90 days. In female children who were readmitted within 90 days, 376 (74.2%) were readmitted for respiratory-related causes and in male children, 505 (66.0%). There was no difference in the top 5 causes of readmissions between male and female children: (allergic asthma (ICD-10 code J45), status asthmaticus (ICD-10 code J46), dyspnoea (ICD-10 code R06), adenovirus infection (ICD-10 code B34) and unspecific acute lower respiratory infection (ICD-10 code [22). Overall,



Adjusted ORs (95% CI) for the association between sex and 30 and 90-day readmission and mortality. CYP (children and young people), COPD (chronic obstructive pulmonary disease), CVD (cardiovascular disease). Estimates show ORs and 95% CIs for females compared with males.

female children had a higher odds of 30 and 90 day readmission (OR 1.21, 1.00 to 1.44, p=0.039 and 1.17, I 1.03 to 1.34) compared with male children (figure 5 and online supplemental table S8).

Readmission and mortality following discharge in adults with **COPD**

Of the 28 354 COPD patients eligible for HES linkage, 6842 (24.1%) were readmitted to hospital within 30 days of their initial COPD admission; 3670 of 15 565 (23.6%) females and 3172 of 12 789 (24.8%) males were readmitted within 30 days (online supplemental figure S1). 11620 (41.0%) were readmitted within 90 days of their initial COPD admission; 6280 (40.4%) of females and 5340 (41.8%) of males were readmitted within 90 days. In females who were readmitted within 90 days, 4039 (64.3%) were readmitted for respiratory-related causes, 426 (6.8%) for cardiovascular-related causes and 1815 (28.9%) for other causes. In males, 3323 (62.2%) were readmitted for respiratory-related causes, 483 (9.0%) for cardiovascular-related causes and 1534 (28.8%) for other causes. The top 5 causes of readmission within 90 days for in males and females were similar and consisted of COPD (ICD-10 code J44), bronchopneumonia (ICD-10 code [18), acute respiratory failure (ICD-10 code [96) and heart failure (ICD-10 code I50). Sepsis due to Staphylococcus aureus (ICD-10 code A41) was more commonly recorded in males; whereas, pain in the throat and chest (ICD-10 code R07) was more common in females. In addition, 3521 (12.4%) died from any cause within 90 days of their initial admission; 1828 (11.7%) of females and 1693 (13.2%) of males. Overall, females had lower odds readmission within 90 days compared with males (OR 0.95, 0.90–1.00, p=0.047), lower odds of readmission for cardiovascular-related causes (OR 0.75, 0.65–0.86), and lower odds of death within 90 days of their initial COPD admission compared with males (OR 0.88, 0.81-0.96, respectively) (figure 5 and online supplemental table S9).

DISCUSSION

To our knowledge, this is the first study to compare in-hospital management of people with asthma and COPD by sex in a nationally representative UK sample. We found differences by sex in presentation, in hospital management, and readmission and mortality in all three cohorts. Females with asthma had similar in-hospital management but were more likely to be readmitted; whereas, females with COPD tended to have better in-hospital management and were less likely to be readmitted.

Adult asthma

Our study found that females and males were similar in terms of in-hospital management after adjusting for asthma exacerbation severity on admission and comorbidities. Previous studies suggest that in people hospitalised

for acute asthma, males were less likely to have taken inhaled corticosteroids 4weeks prior to hospital admission compared with females indicating that females may have been better managed in primary care prior to admission.¹⁴ However, other studies show that females are more likely to be symptomatic, less likely to be on maintenance therapy but have better lung function and FeNo. 15 Our study adds to the literature and shows that while the proportion of females hospitalised with asthma remains higher than males, management once in hospital is similar between males and females.

Despite this, females were more likely to be readmitted within 30 and 90 days compared with males for causes not related to respiratory or cardiovascular disease. It is well known that females are more likely to be hospitalised than males in adulthood, notably for exacerbations; however, this was not seen in our cohort for respiratory readmissions.⁵ ¹⁶ Females had a similar likelihood of being readmitted for respiratory-related reasons and a greater proportion of females were readmitted for other causes.

CYP asthma

In-hospital markers of management were also similar between female and male children. However, females had a higher odds of 90-day readmission compared with males. This finding differs to previous studies that have shown that males under the age of 16 years old are more likely to go to A&E and females are more likely to have diagnostic tests.¹⁷ A small proportion of children and young adults were readmitted to hospital and larger studies are needed to confirm these findings. Overall, it is possible that children hospitalised for an acute asthma attack are likely to be treated the same, regardless, due to their age.

COPD

We found that females with COPD were more likely to receive NIV, more likely to be seen by a respiratory specialist on admission, and more likely to receive a discharge bundle compared with males. Females had a slightly lower FEV1% predicted compared with males and previous studies suggest that in those hospitalised due to an exacerbation, females showed signs of more severe exacerbation events with respiratory failure compared with males. 18 19 In addition, studies suggest that females are more likely to report more severe dyspnoea and cough compared with males regardless of lung function, age or smoking status.⁶ This might explain why in-hospital management differed between males and females with COPD. Despite this, analyses for the COPD cohort were not adjusted by exacerbation or disease severity on admission. While data on FEV1% predicted was available, there was a high degree of missing data which led to a limited number of patients available for complete case analysis. Therefore, results for the COPD analyses should

be interpreted with caution due to residual confounding as no marker of disease severity was accounted for.

Females were also less likely to be readmitted within 90 days for any cause but had a similar likelihood of being admitted for respiratory-related causes within 90 days and were less likely to be readmitted for cardiovascular-related causes. A previous study using the Toward a Revolution in COPD Health (TORCH) study found that females had a lower all-cause mortality rates compared with males but had similar causes of death.²⁰ A study using data from the National Health and Nutrition Examination Survey (NHANES) also found that males with COPD had a lower survival rate compared with females.²¹ While it could be possible that females were less likely to die compared with males due to better in-hospital management, there could be other reasons for this such as differences in comorbidities.²¹ In addition, it is well known that males with COPD have a higher prevalence of cardiovascular-related comorbidities and a higher risk of cardiovascular-related death compared with females. 21 22 It is possible that this association was driving the lower likelihood of all-cause mortality in females in our cohort.

Limitations

The main limitation of this study was the high degree of missing data, specifically for lung function tests. One reason for this could be that patients were too unwell to perform spirometry or that data were not contemporaneous. This is why spirometry was not included in adjusted models to minimise selection bias and the exclusion of more severe patients. Interestingly, our results suggest that females may receive more appropriate care when they have a more severe disease such as COPD but not when they experience asthma, regardless of the disease severity. This may highlight the additive effect of gender, specifically gender biases in the way in which individuals are managed and treated in hospital as well as differences in behaviours of patients. However, this may have been due to the lack of adjustment for disease severity in the COPD cohort (as spirometry or previous exacerbations were not adjusted for. Similarly, we do not have data recorded prior to the hospital admission and were unable to include variables such as prior exacerbations, medication use or compliance, prior hospitalisations, or disease phenotypes in our adjusted models. In addition, mortality was not investigated in the CYP cohort due to the small number of cases and risk of identification. Similarly, people recorded as transgender were excluded due to the small number of individuals and the risk of identification. Therefore, while this study investigated sex differences, results may only be applicable to cisgender individuals. Lastly, models for cause-specific readmission were unable to converge and fixed effects regression was used. However, crude estimates for fixed and random effects models were similar and we do not anticipate large differences in results between these two models.

Implications

Based on the results from this study, there is some evidence that females with COPD might have better in-hospital management and that this may reflect on lower readmissions and mortality, but analyses were not adjusted for disease severity. It is possible that females were more severe on admission and were therefore more likely to receive certain aspects of care compared with males. In people with asthma, males and females are managed similarly in hospital and yet females are more likely to be hospitalised than males. This suggests that for asthma, factors other than in-hospital management are contributing towards higher hospital admissions in females. This might include management within primary care, steroid responsiveness or hormonal differences. 10 Further work is needed to better understand this relationship with the use of additional data sources to help contextualise these findings.

CONCLUSION

We found little to no sex differences in in-hospital management of people with asthma but some differences in people with COPD whereby females were more likely to be seen by a respiratory specialist, have NIV treatment and be given a discharge bundle. However, sex differences in readmissions, and mortality in both people with asthma and COPD remain. Overall our study suggests that other factors are likely contributing towards higher hospital admissions in females with asthma and males with COPD.

Author affiliations

¹School of Public Health, Imperial College London, London, UK

²School of Medicine, Imperial College London, London, UK

³Aneurin Bevan Health Board, Newport, UK

⁴Royal College of Physicians, London, UK

⁵Academic Respiratory Unit, North Bristol NHS Trust, Westbury on Trym, UK

⁶MRC Integrative Epidemiology Unit, Bristol, UK

⁷Alder Hey Children's Hospital, Liverpool, UK

8West Yorkshire Health and Care Partnership, Wakefield, UK

⁹Cardiac/Pulmonary Rehabilitation, University Hospitals of Leicester NHS

Trust, Leicester, UK

¹⁰NHLI, Imperial College London, London, UK

Contributors HW conceptualised the project, analysed the data and wrote the draft manuscript. AA and PS cleaned the data and reviewed the manuscript. JKQ reviewed the manuscript and is the guarantor . PO, JC, JD, IS, KH and SS reviewed

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.



Patient consent for publication Consent obtained directly from patient(s).

Ethics approval The audit operates under Section 251 approval from the Confidentiality Advisory Group (CAG) of the Health Research Authority (HRA). The reference number is CAG-8-06(b)/2013. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Data may be obtained from a third party and are not publicly available. Data collected on behalf of HQIP by all NCAPOP projects are routinely reported and these reports are available in the 'Resources' section of the HQIP website (https://www.hqip.org.uk/resources/). The reported data are also placed on the data.gov.uk website. Data are also placed upon MyNHS and NHS Choices. For details of how to apply for data that is not in the public domain, please see HQIP's data access webpages (https://www.hqip.org.uk/national-programmes/accessing-ncapop-data/).

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ORCID iDs

Hannah Whittaker http://orcid.org/0000-0002-7705-0300 Alexander Adamson http://orcid.org/0000-0003-0265-5900 James Dodd http://orcid.org/0000-0003-4805-5759

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