Effects of tobacco smoking on recurrent hospitalisation with pneumonia: a population-based cohort study

Vadsala Baskaran 1,2,3, Wei Shen Lim2, Tricia M McKeever1,3

ABSTRACT
The incidence of and risk factors for recurrent hospitalisation for pneumonia were investigated using data from Hospital Episode Statistics, linked to a UK primary care database. Within 90 days and 1 year of follow-up, 1733 (3.1%) and 5064 (9.0%), developed recurrent pneumonia respectively. Smoking status at the time of hospitalisation with index pneumonia was associated with the risk of readmission with recurrent pneumonia within a year of discharge: current versus never smokers: adjusted subhazard ratio (sHR) 1.42, 95% CI 1.32 to 1.53, p<0.001, and ex smokers versus never smokers: adjusted sHR 1.24, 95% CI 1.15 to 1.34, p<0.001. Other independent risk factors associated with recurrent pneumonia were age, gender, deprivation and underlying comorbidities.

INTRODUCTION
Preventing hospitalisation for pneumonia, especially during winter, is one of the priorities for respiratory disease in the NHS Long Term Plan and for the British Thoracic Society. However, there are few studies related to recurrent hospitalisation for pneumonia and specifically no studies from the UK. Studies from the past two decades suggest recurrent hospitalisation for pneumonia occurs in 9%–17.6% of adults during a follow-up of 1–3 years following index admission with pneumonia. 1–3 Non-modifiable factors associated with increased risk of recurrent pneumonia included increasing age, impaired functional status, comorbidities and medications. 4 Although there is a well-described dose-dependent association of tobacco smoking with the development of pneumonia, the evidence in recurrent pneumonia is mixed. 5–8

The aims of this study were to determine the incidence of recurrent hospitalisation with pneumonia in England and the association of tobacco smoking, a potentially modifiable risk factor.

METHODS
Hospitalisation data from Hospital Episode Statistics (HES, England), linked to the Clinical Practice Research Datalink (CPRD) and death registration data from the Office for National Statistics, were used for this study.

Adults aged ≥18 years with the first episode of hospitalisation for pneumonia (index date) recorded in HES between 1 July 2002 and 30 June 2017 were included. The Public Health England ‘epidemiological year’ definition of July–June was used as the unit of time to avoid the winter peak of pneumonia traversing two calendar years. Pneumonia was defined based on J12–J18 International Classification of Diseases, 10th Revision (ICD-10), codes recorded as the primary code for the first episode of hospitalisation. Recurrent pneumonia was defined as at least one episode of hospitalisation for pneumonia more than 30 days after index pneumonia. Patients were excluded if they had less than a year of time registered to the practice before admission, hospital-acquired pneumonia (admission for at least a day in the 10 days preceding the index admission) or readmission within 30 days of discharge. Patients were followed up from day 1 after the date of hospital discharge to either the date of admission for recurrent pneumonia, end of data collection (30 June 2017), date of transfer out of practice, date of last data collection for the practice or date of death, whichever came first.

Read code lists for smoking status were developed using validated read codes from previous research. The most recent documented smoking status (current smoker, ex-smoker and never smokers) in CPRD before the index admission was used; ‘never smokers’ with previous smoking history were recorded as ‘ex-smoker’.

Descriptive statistics for the patient population were calculated. ‘Time to first recurrence’ was measured from day 1 after discharge from the hospital to admission with recurrent pneumonia. The proportion of patients who developed recurrent pneumonia during a 5-year follow-up period was determined. Incidence rates (per 100 person-years) for recurrent pneumonia at different time intervals were determined (90 days, 1 year and 5 years). Directed acyclic graph (DAG) was used to identify the minimum set of confounders to close the backdoor paths, which included age, gender, deprivation, alcohol consumption and comorbidities (online supplemental file 1). Multiple imputation using chained equations was performed with 10 imputed datasets for smoking status (2.7% missing data) and alcohol consumption (15.0% missing data) (online supplemental file 2). Competing-risks regression (CRR) analyses were conducted to determine the effect of tobacco smoking on hospitalisation for recurrent pneumonia with death as a competing event. Statistical analyses were performed using StataMP V15.
RESULTS
The study cohort comprised 56,396 patients (figure 1). The median age of the study cohort was 75 years (IQR 61–84 years) and 49.7% were male.

The median time to recurrence was 1.3 years (IQR 0.5–2.6 years). The incidence rates (per 100 person-years) for recurrent pneumonia at 90 days, 1 year and 5 years were 13.6 (95% CI 13.0 to 14.2), 11.1 (95% CI 10.8 to 11.4) and 7.10 (95% CI 6.97 to 7.23) correspondingly. Within 90 days and 1 year of follow-up, 1733 (3.1%) and 5064 (9.0%) developed recurrent pneumonia respectively, with 1866 (36.9%) patients hospitalised for more than one recurrence during the 1-year follow-up period. The 30-day mortality for a recurrent pneumonia hospitalisation was 23.7% (n=3011). Over the period 2002–2017, the proportion of recurrent pneumonia within 1 year of index admission increased from 5.6% to 11.4% (figure 2).

Current smoking at index admission was independently associated with a 42% increased risk of recurrent pneumonia compared with having never smoked at any point in time (table 1). This risk was halved in ex-smokers. Other factors independently associated with recurrent pneumonia were age, gender, deprivation and Charlson Comorbidity Index score.

DISCUSSION
To our knowledge, this is the first UK study to investigate the incidence of and risk factors for recurrent hospitalisation for pneumonia. Current tobacco smoking status at index hospitalisation for pneumonia was independently associated with a higher risk of recurrent pneumonia.

Studies from other countries have reported a range of incidences of recurrent pneumonia over different time periods: 16.3% during a median follow-up of 475 days in Japan to 3.5% over an 11-year period in Sweden.9 Marked differences in study methodology and healthcare system are likely to account for the variation, emphasising the importance of country-specific data. Our results are similar to data from Canada and Sweden; 2% recurrent pneumonia at 30–90 days from index admission, 17.6% recurrent pneumonia during a mean follow-up of under 3 years.2,7 Of note, we observed a 23.7% 30-day mortality for recurrent pneumonia, twice as high as 30-day inpatient mortality for index pneumonia based on the BTS National Pneumonia Audit data.10 Similarly, Ishifuji et al found that patients with recurrent pneumonia were almost three times more likely to have fatal outcomes during over a year’s follow-up compared with those without (HR 2.81, p<0.001).3 Our study also revealed a significant trend of increasing proportion of recurrent pneumonia between 2002 and 2017. Conversely, the BTS National Pneumonia Audit observed a decrease in mortality from index pneumonia over a 10-year period (2009–2019).10 Whether these trends in survival are related to the trends in pneumonia recurrence requires further investigation.

Tobacco smoking is associated with an increased risk of developing community-acquired pneumonia.5 We extend this observation to an association between tobacco smoking and recurrent pneumonia. In a case–control study, El Sohl et al reported that current smokers were twice more likely to be admitted with recurrent pneumonia compared with never smokers (HR=2.04, 95% CI 1.48 to 2.82).6 Conversely, two prospective cohort studies (Canada, n=2709 and Spain, n=1556) did not find any association between smoking and recurrent pneumonia.7 8 These studies included younger patients (mean cohort ages 63 and 67 years).

A key strength of this study is the large sample size representative of the English population with a long-term follow-up. We considered all key variables in our DAG; vaccination status, dysphagia, severity of index pneumonia, cardiac complications after index pneumonia, functional status, oropharyngeal hygiene and medications were not listed in the minimal sufficient adjustment set of confounders to close the backdoor paths. A potential weakness is that we cannot exclude the possibility of information bias from miscategorisation of the study exposure, confounders and outcomes. Missing data in smoking status and alcohol consumption were handled using multiple imputation. Another limitation is that data regarding the

Figure 1 Flowchart of the study population. CPRD, Clinical Practice Research Datalink; HAP, hospital-acquired pneumonia; ICD-10, International Classification of Diseases, 10th Revision.

Figure 2 Trend of recurrence of pneumonia within 31–90 days and 1 year of index pneumonia admission. Note: 1-year recurrence refers to recurrence between 31 and 365 days after discharge for index pneumonia. Patients readmitted to the hospital within 30 days of discharge were considered to be readmissions for the index episode and hence were excluded.
### Table 1  Factors independently associated with recurrent pneumonia within a year of discharge: Competing-risks regression (CRR) analysis with death as competing event

| Patients (total n) | With recurrence | Multivariate CRR |
|-------------------|-----------------|------------------|
|                   | N               | n (%)            | sHR (95% CI)     | P value |
| Number of patients| 56 396          | 5064             |                  |         |
| Smoking status    |                 |                  |                  |         |
| Never             | 18 179          | 1274 (7.0)       | 1.00             | Reference |
| Ex                | 14 512          | 1517 (10.5)      | 1.24 (1.15 to 1.34) | <0.001 |
| Current           | 23 678          | 2273 (9.6)       | 1.42 (1.32 to 1.53) | <0.001 |
| Age (years)       |                 |                  |                  |         |
| 18–49             | 8208            | 247 (3.0)        | 1.00             | Reference |
| 50–64             | 8830            | 556 (6.3)        | 1.76 (1.51 to 2.05) | <0.001 |
| 65–74             | 10 499          | 986 (9.4)        | 2.37 (2.05 to 2.75) | <0.001 |
| 75–84             | 15 317          | 1692 (11.0)      | 2.78 (2.41 to 3.22) | <0.001 |
| ≥85               | 13 542          | 1583 (11.7)      | 3.17 (2.73 to 3.67) | <0.001 |
| Gender            |                 |                  |                  |         |
| Male              | 28 002          | 2719 (9.7)       | 1.00             | Reference |
| Female            | 28 394          | 2345 (8.3)       | 0.85 (0.80 to 0.90) | <0.001 |
| Alcohol status    |                 |                  |                  |         |
| Non-drinker       | 14 780          | 1451 (9.8)       | 1.00             | Reference |
| Former drinker    | 3319            | 381 (11.5)       | 1.08 (0.96 to 1.22) | 0.176 |
| Occasional drinker| 9047            | 854 (9.4)        | 0.95 (0.87 to 1.04) | 0.237 |
| Moderate drinker  | 21 468          | 1772 (8.3)       | 0.88 (0.82 to 0.95) | 0.001 |
| Heavy drinker     | 7782            | 606 (7.8)        | 0.90 (0.81 to 1.01) | 0.063 |
| IMD (patient- level) |               |                  |                  |         |
| 1 (least deprived)| 10 596          | 875 (8.3)        | 1.00             | Reference |
| 2                 | 11 407          | 1023 (9.0)       | 1.06 (0.97 to 1.16) | 0.195 |
| 3                 | 11 909          | 1068 (9.0)       | 1.06 (0.97 to 1.16) | 0.228 |
| 4                 | 11 263          | 977 (8.7)        | 1.02 (0.93 to 1.12) | 0.689 |
| 5 (most deprived) | 11 171          | 1117 (10.0)      | 1.21 (1.10 to 1.32) | <0.001 |
| Unknown           | 50              | 4 (8.0)          | 1.14 (0.45 to 2.89) | 0.776 |
| Charlson Index    |                 |                  |                  |         |
| 0                 | 13 636          | 608 (4.5)        | 1.00             | Reference |
| 1                 | 12 290          | 955 (7.8)        | 1.43 (1.29 to 1.59) | <0.001 |
| 2                 | 9912            | 986 (9.9)        | 1.65 (1.48 to 1.84) | <0.001 |
| 3                 | 7777            | 867 (11.1)       | 1.76 (1.58 to 1.97) | <0.001 |
| 4                 | 5096            | 634 (12.4)       | 1.90 (1.82 to 2.14) | <0.001 |
| ≥5                | 7685            | 1014 (13.2)      | 2.00 (1.79 to 2.23) | <0.001 |
| Comorbidities     |                 |                  |                  |         |
| COPD              | 11 798          | 1810 (15.3)      | 1.77 (1.65 to 1.89) | <0.001 |
| Asthma            | 13 347          | 1471 (11.0)      | 1.11 (1.03 to 1.18) | 0.004 |
| Chronic lung disease* | 896         | 106 (11.8)       | 1.56 (1.29 to 1.90) | <0.001 |
| Congestive cardiac failure | 5648 | 705 (12.5) | 1.12 (1.02 to 1.23) | 0.016 |
| Myocardial infarction | 5268 | 614 (11.7) | 1.03 (0.94 to 1.13) | 0.496 |
| Other cardiac diseases† | 23 326 | 2344 (10.1) | 1.05 (0.98 to 1.12) | 0.149 |
| Malignancy        | 12 397          | 1402 (11.3)      | 1.17 (1.10 to 1.25) | <0.001 |
| Chronic renal disease | 10 974    | 1343 (12.2)     | 1.16 (1.09 to 1.24) | <0.001 |
| Cerebrovascular disease | 6377 | 768 (12.0) | 1.05 (0.97 to 1.12) | 0.228 |
| Diabetes mellitus | 9390            | 996 (10.6)       | 1.14 (1.05 to 1.23) | 0.001 |
| Cognitive impairment | 5383          | 660 (11.3)       | 1.11 (1.02 to 1.21) | 0.017 |
| Liver disease     | 531             | 53 (10.0)        | 1.24 (0.94 to 1.62) | 0.128 |

The 2015 English IMD was used as a composite measure of material deprivation at the patient level. Two multivariate models were conducted: model 1: all variables+Charlson Comorbidity Index (without individual comorbidities) and model 2: all variables+individual comorbidities (without Charlson Comorbidity Index). Results are presented from model 1, except for individual comorbidities from model 2 as estimates for other variables in both models were similar. See online supplemental file 3 for factors associated with death within a year of discharge.

*Chronic lung disease excluding COPD and asthma.
†Other cardiac diseases excluding CCF and MI (eg, hypertension, arrhythmias, valvular heart disease, conduction disorder of the heart, pericarditis and myocarditis).

CCF, congestive cardiac failure; CRR, competing-risks regression; IMD, Index of Multiple Deprivation; MI, myocardial infarction; sHR, subhazard ratio.

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type of tobacco smoked were only available in about half of the patients, with most consuming cigarettes and few consuming cigars (<5%).

In conclusion, our findings confirm a high and rising incidence of recurrent hospitalisation for pneumonia in England, and that current smoking status at index admission is associated with an increased risk of recurrent pneumonia. These findings support smoking cessation interventions as a key component of pneumonia management, in accordance with the NHS Long Term Plan.

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**ORCID ID** Vadsala Baskaran http://orcid.org/0000-0002-6470-5726

**REFERENCES**

1. García-Vidal C, Viasus D, Roset A, et al. Low incidence of multidrug-resistant organisms in patients with healthcare-associated pneumonia requiring hospitalization. *Clin Microbiol Infect* 2011;17:1659–65.
2. Hedlund J, Kalin M, Ortvist A. Recurrence of pneumonia in middle-aged and elderly adults after hospital-treated pneumonia: aetiology and predisposing conditions. *Scand J Infect Dis* 1997;29:387–92.
3. Ishifuji T, Sando E, Kaneko N, et al. Recurrent pneumonia among Japanese adults: disease burden and risk factors. *BMC Pulm Med* 2017;17:12.
4. Dang TT, Majumdar SR, Marrie TJ, et al. Recurrent pneumonia: a review with focus on clinical epidemiology and modifiable risk factors in elderly patients. *Drugs Aging* 2015;32:13–19.
5. Baskaran V, Murray RL, Hunter A, et al. Effect of tobacco smoking on the risk of developing community acquired pneumonia: a systematic review and meta-analysis. *Plos One* 2019;14:e0220204.
6. El Solh AA, Brewer T, Okada M, et al. Indicators of recurrent hospitalization for pneumonia in the elderly. *J Am Geriatr Soc* 2004;52:2010–5.
7. Dang TT, Eurich DT, Weir DL, et al. Rates and risk factors for recurrent pneumonia in patients hospitalized with community-acquired pneumonia: population-based prospective cohort study with 5 years of follow-up. *Clin Infect Dis* 2014;59:74–80.
8. García-Vidal C, Carratalà J, Fernández-Sable N, et al. Aetiology of, and risk factors for, recurrent community-acquired pneumonia. *Clin Microbiol Infect* 2009;15:1053–8.
9. Ek Dahl K, Braconier JH, Roloff J. Recurrent pneumonia: a review of 90 adult patients. *Scand J Infect Dis* 1992;24:71–6.
10. Lim WS, Lawrence H. National audit report: adult community acquired pneumonia audit 2018-2019. *Br Thorac Soc Reports* https://www.brit-thoracic.org.uk/quality-improvement/clinical-audit/national-adult-community-acquired-pneumonia-audit-201819/