ORIGINAL ARTICLE

Risk of pneumonia and pneumococcal disease in people with severe mental illness: English record linkage studies

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ABSTRACT

Background People with severe mental illness have a higher risk than others of some physical diseases. The risk of pneumococcal disease in people with mental disorders is unknown. This is potentially important because vaccines against the pneumococcus are available.

Methods We used two datasets of linked hospital admission and death records, the Oxford Record Linkage Study and all-England linked Hospital Episode Statistics, to estimate the risk of lobar pneumonia and other pneumococcal disease (here, all collectively termed pneumococcal disease) in people hospitalised with schizophrenia, bipolar disorder, depression or anxiety. We compared rates of pneumococcal disease in each cohort with rates in a comparison cohort of people without a record of hospitalisation for these psychiatric disorders.

Findings The risk of pneumococcal disease in each psychiatric group was significantly high in both datasets. In the English national dataset (spanning 1999–2011), the risk of pneumococcal disease in people hospitalised with schizophrenia, bipolar disorder, depression or anxiety was, respectively, 2.3 (95% CI 2.2 to 2.4), 2.3 (2.2 to 2.3), 2.1 (2.0 to 2.1) and 2.2 (2.1 to 2.2). The risk remained high for years after discharge, suggesting an association with the psychiatric disorder rather than with the event of hospitalisation.

Conclusions Severe mental illness is a risk factor for lobar pneumonia, pneumococcal pneumonia, pneumococcal septicaemia and meningitis. Possible explanations for the elevated risk include factors relating to lifestyle and health-risk activities. If our findings are replicated elsewhere, there would be a case for considering routine pneumococcal immunisation for people with severe mental illness.

Key messages

What is the key question?
▶ Is severe mental illness a risk factor for pneumococcal disease?

What is the bottom line?
▶ People with severe mental illness are at higher risk than others of pneumococcal disease, but are not yet recognised as a high-risk group in current immunisation policies.

Why read on?
▶ This is a new risk factor for pneumococcal disease. As we discuss, the risk is likely to be mediated by lifestyle factors associated with severe mental illness. Consideration should be given to routinely offering pneumococcal vaccine to people with severe mental illness.

INTRODUCTION

There is evidence that people with psychiatric disorders are at increased risk of common infectious diseases,[1] but to the best of our knowledge, there have been no large studies of the risk of pneumococcal disease in people with severe mental illness. Pneumococcal disease is the term used to describe infections caused by the bacterium *Streptococcus pneumoniae* when the pathogen is detected in normally sterile body fluids. *Streptococcus pneumoniae* is the main cause of community-acquired pneumonia, bacteraemia and bacterial meningitis in adults in developed countries.[2–4] Identification of people with an excess risk of pneumococcal disease is important because vaccines against the pneumococcus are now available. Immunisation for high-risk groups is routinely offered.

Current immunisation guidelines in the UK and the USA are designed to protect those at elevated risk of pneumococcal disease, including infants, adults aged 65 and over, and people with selected medical conditions.[5][6] However, patients with mental disorders are not specifically covered by the current guidelines. We used routine datasets of hospital admission and mortality data, enhanced by record linkage, to study the risk of pneumococcal disease in people admitted to hospital for schizophrenia, bipolar disorder, depression or anxiety.

METHODS

We analysed records from an English national dataset of linked Hospital Episode Statistics and mortality statistics (LHES), and from the Oxford Record Linkage Study (ORLS).[7][8] Both datasets comprise statistical records of all hospital admissions, and day cases, for all patients admitted for National Health Service (NHS) care in their respective geographical areas. The ORLS covers the former Oxford NHS region from 1963 to February 2011. The all-England dataset runs from 1999 to February 2011. The analysis of the ORLS dataset was undertaken in two periods, 1963–1998 (ORLS1) and 1999–2011

(ORLS2). Cross linkage between the pre-1999 and post-1999 data is not possible. Fortuitously for the current study, routine pneumococcal immunisation for susceptible groups of people became reasonably widespread in England from about 1999. We were interested in risk in pre-immunisation and post-immunisation populations, and in studying two available datasets, which is why we used the longstanding ORLS and the national English data.

Population

The ORLS commenced in part of the former NHS region of Oxford (covering about 850 000 people) and gradually expanded over time until it covered the whole region (from 1987) with a population of about 2.5 million. It covers a relatively affluent part of England and comprises towns, but no large cities (the city of Oxford had a population of 134 000 at the 2001 census), and rural populations. The great majority of this population, particularly in the early years of the ORLS, were born in southern England. It is demographically more homogeneous than England as a whole. England has a population of about 52 million.

Exclusion and inclusion criteria

We excluded anyone aged under 15 years. We assembled statistical cohorts of the records of people with day case care or hospital admission for schizophrenia, defined as International Classification of Diseases, 10th revision (ICD-10) codes F20–F21, bipolar disorder (F31, F32.3, F33.3, F39), depression (F32.0–F32.2, F32.8, F32.9, F33.0–F33.2) and phobic anxiety disorders (F41). We termed these the 'exposure' conditions. The 'outcomes' of interest were lobar pneumonia, without further specification (J18.1), which is considered to be generally caused by *Streptococcus pneumoniae*,[3] pneumonia specified as *S pneumoniae* (J13), septicaemia due to *S pneumoniae* (A40.3) and pneumococcal meningitis (G00.1). Although lobar pneumonia without further specification can only be considered 'presumed' pneumococcal disease, for simplicity we refer to these conditions collectively as pneumococcal disease. The same codes have been used by other researchers in studies of pneumococcal disease.[9] The corresponding diagnostic codes were selected from the seventh, eighth and ninth revisions of ICD. There was no separate code for pneumococcal pneumonia in the earlier versions of ICD because pneumococcal pneumonia and lobar pneumonia 'organism unspecified' had the same ICD code (481 in ICD-9 and ICD-8, 490 in ICD-7).

Analytical design

The same methods were used for each mental illness and are described for schizophrenia. The schizophrenia cohort was constructed by identifying the first record of hospital care for schizophrenia for each individual, recorded as the principal diagnostic reason for admission or day care. We excluded those with a record of pneumococcal disease before or at the same time as admission for schizophrenia. We did this, first, to ensure as best as possible the likely temporal relationship between prior mental illness and subsequent pneumococcal infection; and second, to avoid the 'surveillance bias' that people might have been diagnosed with mental disease as a result of having in-hospital care for pneumococcal disease. We included subsequent pneumococcal disease, as an outcome, when recorded in any diagnostic position. In a sensitivity analysis, we varied the selection criteria (eg, pneumococcal disease in any diagnostic position or as the principal diagnosis) to check whether our choices made any appreciable difference to the results. They did not.

We constructed a comparison cohort using hospital controls and the standard epidemiological practice of selecting a wide range of conditions. The majority were minor medical or surgical conditions or injuries (see footnotes to table 2). As a check, for each condition in the reference cohort we estimated the risk of pneumococcal disease to ensure that the reference cohort did not include conditions with atypically high or low rates. In line with our work elsewhere, we term this the reference cohort.[10] Anyone with one of the mental illnesses and a reference cohort condition was assigned only to the mental illness cohort. All patients aged 15 and over who were eligible for the reference cohort were included. During analysis, patients in the exposure and reference cohorts were stratified by age (in 5-year groups), sex, district of residence in ORLS (eight districts) and region of residence in LHES (of which there are nine in England), calendar year of first hospitalisation, and Index of Multiple Deprivation quintile (only available in LHES) to ensure that, following stratified analysis (see below), the results comparing the cohorts were equivalent in these respects. The assumptions made in the design are that the rates of pneumococcal disease in the reference cohort are representative of the general population while allowing for inward and outward migration (data on migration of individuals were not available).

Statistical methods

Rates of pneumococcal disease were calculated using person-years. The 'date of entry' into either the schizophrenia or reference cohort was that of first admission for schizophrenia or the reference condition. The 'date of exit' was that of first admission for pneumococcal disease, death or the end of the data-file (December 1998 for ORLS1, February 2011 for ORLS2 and LHES), whichever was the earliest. In comparing the schizophrenia cohort with the reference cohort, we first calculated the rates stratified, and then standardised, according to age at entry to the cohort (in 5-year age groups) and by the other stratification variables described above.

We applied the indirect method of standardisation, using the schizophrenia cohort and the reference cohort, combined, as the standard population, and applied the stratum-specific rates in the combined population to the number of people in each stratum in, first, the schizophrenia cohort, and second, the reference cohort. We calculated the ratio of the rate of pneumococcal disease in the schizophrenia cohort relative to that in the reference cohort, using the formula (O^s/E^s) divided by (O^r/E^r), where O^s and E^s are the observed and expected numbers of pneumococcal disease in the schizophrenia cohort and O^r and E^r are the equivalents in the reference cohort. We calculated the 95% CI for the rate ratio (RR) and χ^2 statistics for its significance, with continuity corrections for small numbers, as described elsewhere.[11]

RESULTS

In the England dataset there were 85 769 people with schizophrenia, 83 951 with bipolar disorder, 138 963 with depression and 58 816 with anxiety. Basic population characteristics are shown in table 1. In the ORLS2 dataset there were 3616 people with schizophrenia, 3699 with bipolar disorder, 8252 people with depression, and 1970 with anxiety. The corresponding figures in ORLS1 were 5451 people with schizophrenia, 8193 with bipolar disorder, 20 842 with depression and 16 538 with anxiety. The great majority of the pneumococcal disease outcomes were lobar pneumonia.

Tables 2 and 3 show the RRs for the association between the mental disorders and pneumococcal disease in the three

Table 1 Age and sex distribution of people admitted to hospital with mental conditions: number of people, percentage who were men, and ratio of people in the reference cohort in each stratum for each case in the mental illness cohort in the same stratum*, England

Age group (years)	Schizophrenia			Bipolar disorder			Depression			Anxiety		
	N in exposure cohort (% men)	% of total	Stratum ratio*	N in exposure cohort (% men)	% of total	Stratum ratio*	N in exposure cohort (% men)	% of total	Stratum ratio*	N in exposure cohort (% men)	% of total	Stratum ratio*
15–24	13490 (78.5)	16	60	6099 (49.7)	8	133	12835 (43.0)	9	62	5291 (39.3)	9	153
25–34	21832 (73.1)	25	42	13205 (44.0)	15	69	20847 (45.9)	15	43	7034 (43.4)	12	129
35–44	19771 (64.0)	23	47	16748 (40.2)	20	55	25477 (44.8)	19	35	9164 (41.6)	16	100
45–59	17987 (55.4)	21	76	21353 (38.4)	26	64	27778 (45.4)	20	47	12629 (39.6)	21	107
60–74	9085 (41.4)	11	153	16249 (36.5)	19	86	24099 (39.9)	17	56	12233 (32.9)	21	113
75+	3604 (25.5)	4	185	10297 (29.4)	12	65	27927 (32.3)	20	23	12465 (23.2)	21	53
Total	85769 (62.8)	100	74	83951 (39.0)	100	75	138963 (41.5)	100	44	58816 (35.6)	100	106

The equivalent data are not shown for people in the ORLS1 and ORLS2 datasets, and are available from the authors.

*In the analysis we included all people eligible to be in each stratum in the reference cohort in calculating the stratum-specific 'expected' numbers of people with subsequent pneumococcal disease (there was no benefit in excluding people to get equal numbers in each stratum). For example, in the schizophrenia analysis, there were 809 400 people in the reference cohort aged 15–24 compared with 13 490 people in the schizophrenia cohort.

datasets. In the England and ORLS2 datasets there was about a twofold elevation of risk of pneumococcal disease in each of the four psychiatric groups: for example, the RRs in England were 2.3 in people with schizophrenia and bipolar disorder, 2.1 for depression and 2.2 for anxiety (all significant, see table 2 for CIs). When the analysis was restricted to people aged under 60 years, the association strengthened: for example, the RRs in England were 2.8 in people with schizophrenia, 2.6 for bipolar disorder, 2.9 for depression and 2.8 for anxiety (all significant, see table 3). RRs in the ORLS1 cohorts were also all high, though less elevated than those in the England and ORLS2 cohorts (tables 2 and 3). RRs were very similar for lobar pneumonia and for pneumococcal pneumonia specified as such (tables 2 and 3).

Cases of pneumococcal septicaemia and meningitis were uncommon (72 and 24 cases, respectively, across the psychiatric cohorts in the all-England analysis), but, when numbers were large enough to make judgements, people in the psychiatric cohorts had an elevated risk of both. Because of small numbers, we combined the four psychiatric disorders: overall, the RR for pneumococcal septicaemia in people with severe mental disorder was 1.9 (95% CI 1.5 to 2.4) and the RR for pneumococcal meningitis was 1.8 (95% CI 1.1 to 2.7).

Table 2 Number of observed (O) and expected (E) cases, rate ratios* (RRs) with upper and lower 95% CIs for pneumococcal disease (including pneumonia, septicaemia and meningitis) in people with selected mental disorders compared with the reference cohort†

Diagnosis	Dataset	Lobar pneumonia and pneumococcal disease, combined				Lobar pneumonia				Pneumococcal pneumonia			
		O	E	RR	95% CI	O	E	RR	95% CI	O	E	RR	95% CI
Schizophrenia	LHES	1922	827.7	2.3	2.2 to 2.4	1859	791.8	2.4	2.3 to 2.5	75	36.5	2.1	1.6 to 2.6
	ORLS2	67	27.1	2.5	1.9 to 3.2	66	26.1	2.6	2.0 to 3.3	‡			
	ORLS1	50	30.9	1.6	1.2 to 2.2	48	29.0	1.7	1.2 to 2.2	‡			
Bipolar disorder	LHES	2811	1259.9	2.3	2.2 to 2.3	2729	1217.9	2.3	2.2 to 2.4	97	45.4	2.2	1.8 to 2.6
	ORLS2	94	42.7	2.2	1.8 to 2.7	91	41.4	2.2	1.8 to 2.7	‡			
	ORLS1	84	59.2	1.4	1.1 to 1.8	82	56.6	1.5	1.2 to 1.8	‡			
Depression	LHES	4973	2444.5	2.1	2.0 to 2.1	4845	2369.8	2.1	2.0 to 2.1	158	78.7	2.1	1.7 to 2.4
	ORLS2	229	117.2	2.0	1.7 to 2.3	226	114.0	2.0	1.8 to 2.3	9	3.3	2.9	1.3 to 5.6
	ORLS1	174	121.8	1.5	1.2 to 1.7	165	115.3	1.5	1.2 to 1.7	7	3.1	2.3	0.9 to 4.9
Anxiety	LHES	2122	997.0	2.2	2.1 to 2.2	2069	969.3	2.2	2.1 to 2.3	74	31.2	2.4	1.9 to 3.0
	ORLS2	61	29.2	2.1	1.6 to 2.7	61	28.3	2.2	1.7 to 2.8	‡			
	ORLS1	129	92.0	1.4	1.2 to 1.7	123	86.7	1.4	1.2 to 1.7	‡			

The numbers in the columns for lobar pneumonia and for pneumococcal pneumonia exceed those in the column for 'pneumococcal disease, combined' because some people had a diagnosis of each of the first two conditions on different occasions; and because the 'pneumococcal disease, combined' totals also include cases of pneumococcal septicaemia and meningitis.

*Adjusted for sex, age in 5-year bands, time period in single calendar years in the ORLS1 and LHES datasets, and also adjusted for district of residence in ORLS1 and ORLS2, and for region of residence and deprivation score associated with patient's area of residence, in quintiles, in the LHES dataset.

†Conditions used in reference cohort, with Office of Population, Censuses and Surveys (OPCS) code edition 4 for operations and International Classification of Diseases, 10th revision (ICD-10) code for diagnosis (with equivalent codes used for other coding editions): adenoidectomy (OPCS4 E20), appendectomy (H01–H03), dilation and curettage (Q10–Q11), hip replacement (W37–W39), knee replacement (W40–W42), squint (ICD10 H49–H51), cataract (H25), varicose veins (I83), haemorrhoids (I84), deflected septum (J34.2), nasal polyp (J33), impacted tooth and other disorders of teeth (K00–K03), inguinal hernia (K40), in-growing nail, toenail and other diseases of nails (L60), bunion (M20.1), internal derangement of knee (M23), dislocations, sprains and strains (S03, S13, S23, S33, S43, S53, S63, S73, S83, S93), head injury (S06 excluded from analysis of meningitis), selected limb fractures (S42, S52, S62, S82, S92), superficial injury and contusion (S00, S10, S20, S30, S40, S50, S60, S70, S80, S90), contraceptive management (Z30).

‡Data not shown for pneumonia and pneumococcal disease with non-significant results and five or fewer observed cases.

LHES, linked Hospital Episode Statistics and mortality statistics; ORLS, Oxford Record Linkage Study.

Table 3 Number of observed (O) and expected (E) cases, rate ratios* (RRs) with upper and lower 95% CIs for pneumococcal disease (including pneumonia, septicaemia and meningitis) in people aged under 60 years with selected mental disorders, compared with the reference cohort†

Diagnosis	Dataset	Lobar pneumonia and pneumococcal disease, combined				Lobar pneumonia				Pneumococcal pneumonia			
		O	E	RR	95% CI	O	E	RR	95% CI	O	E	RR	95% CI
Schizophrenia	LHES	1144	420.1	2.8	2.6 to 3.0	1092	395.0	2.9	2.7 to 3.0	60	24.7	2.5	1.9 to 3.2
	ORLS2	40	15.0	2.7	1.9 to 3.7	39	14.3	2.8	2.0 to 3.9	‡			
	ORLS1	25	19.2	1.3	0.8 to 1.9	24	17.7	1.4	0.9 to 2.0	‡			
Bipolar disorder	LHES	968	378.2	2.6	2.5 to 2.8	931	357.5	2.7	2.5 to 2.9	42	20.4	2.1	1.5 to 2.8
	ORLS2	33	14.0	2.4	1.6 to 3.4	32	13.3	2.4	1.7 to 3.5	‡			
	ORLS1	39	21.3	1.9	1.3 to 2.6	39	20.2	2.0	1.4 to 2.7	‡			
Depression	LHES	1431	513.4	2.9	2.8 to 3.1	1360	484.2	2.9	2.8 to 3.1	70	27.9	2.6	2.0 to 3.3
	ORLS2	77	26.8	3.0	2.4 to 3.8	74	25.6	3.0	2.4 to 3.8	7	1.2	6.6	2.5 to 14.8
	ORLS1	73	51.7	1.4	1.1 to 1.8	51	33.8	1.5	1.1 to 2.0	‡			
Anxiety	LHES	516	187.3	2.8	2.6 to 3.1	498	177.5	2.8	2.6 to 3.1	25	9.7	2.6	1.7 to 3.9
	ORLS2	19	5.5	3.5	2.1 to 5.5	19	5.3	3.7	2.2 to 5.8	‡			
	ORLS1	65	48.7	1.4	1.0 to 1.7	51	45.2	1.4	1.0 to 1.8	‡			

The numbers in the columns for lobar pneumonia and for pneumococcal pneumonia exceed those in the column for 'pneumococcal disease, combined' because some people had a diagnosis of each of the first two conditions on different occasions; and because the 'pneumococcal disease, combined' totals also include cases of pneumococcal septicaemia and meningitis.
*Adjusted for sex, age in 5-year bands, time period in single calendar years in the ORLS1 and LHES datasets, and also adjusted for district of residence in ORLS1 and ORLS2, and for region of residence and deprivation score associated with patient's area of residence, in quintiles, in the LHES dataset.
†Conditions used in reference cohort, with Office of Population, Censuses and Surveys (OPCS) code edition 4 for operations and International Classification of Diseases, 10th revision (ICD10) code for diagnosis (with equivalent codes used for other coding editions): adenoidectomy (OPCS4 E20), appendectomy (H01–H03), dilation and curettage (Q10–Q11), hip replacement (W37–W39), knee replacement (W40–W42), squint (ICD10 H49–H51), cataract (H25), varicose veins (I83), haemorrhoids (I84), deflected septum (J34.2), nasal polyp (J33), impacted tooth and other disorders of teeth (K00–K03), inguinal hernia (K40), in-growing nail, toenail and other diseases of nails (L60), bunion (M20.1), internal derangement of knee (M23), dislocations, sprains and strains (S03, S13, S23, S33, S43, S53, S63, S73, S83, S93), head injury (S06 excluded from analysis of meningitis), selected limb fractures (S42, S52, S62, S82, S92), superficial injury and contusion (S00, S10, S20, S30, S40, S50, S60, S70, S80, S90), contraceptive management (Z30).
‡Data not shown for pneumonia and pneumococcal disease with non-significant results and five or fewer observed cases.
LHES, linked Hospital Episode Statistics and mortality statistics; ORLS, Oxford Record Linkage Study.

All analyses were repeated excluding cases of pneumonia and pneumococcal disease that occurred within the first year of hospitalisation for each of the psychiatric disorders (see online appendix). The results were almost unchanged: for example, in the England dataset, the RR for pneumonia and pneumococcal disease in people with schizophrenia excluding cases in the first year was 2.3 (95% CI 2.2 to 2.5), similar to the RR overall (RR=2.3) (online appendix and Table 2). Thus, the increased risk of pneumococcal infection was not just a risk of having been in hospital recently with a psychiatric disorder.

To assess the risk of pneumococcal infection in people with mental disorders in the context of diseases that are well known to be associated with a high risk of infection, we undertook the same analysis as described in the Methods section to estimate risks in patients with chronic obstructive pulmonary disease (COPD) and diabetes mellitus (DM). The risk of pneumococcal disease associated with COPD was 4.0 (95% CI 4.0 to 4.1) in the English dataset and 3.6 (95% CI 3.3 to 3.9) in ORLS1. The risk of pneumococcal disease associated with DM was 2.1 (95% CI 2.0 to 2.2) in the England dataset and 1.9 (95% CI 1.6 to 2.2) in ORLS1.

Absolute risk
We can only calculate absolute risk approximately because we do not have data on migration. The number of people in the schizophrenia cohort in England was 85 769, and of those, 1922 (2.2%) had a hospital admission for pneumococcal disease. The equivalent percentages for people with bipolar disorder, depression or anxiety were 3.3% (2811/83 951), 3.6% (4973/138 963) and 3.6% (2122/58 816), respectively. In those under 60 years old, the approximate absolute risk of hospitalisation for pneumococcal disease was 1.6% (1144/73 080) in the schizophrenia cohort, 1.7% (968/57 405) in those with bipolar disorder, 1.6% (1431/86 937) in those with depression and 1.5% (516/34 118) in those with anxiety. These are incomplete enumerations of lifetime risk as they include only a mean follow-up of approximately 6 years.

DISCUSSION
Principal findings
People admitted to hospital for schizophrenia, bipolar disorder, depression or anxiety had an increased risk of subsequent pneumococcal disease. The RR was higher in people younger than 60 years than in others. The risk was associated with the psychiatric disorder rather than with the event of hospitalisation: it remained high for years after discharge. It seems unlikely that the mechanism of the association is specific to any biological characteristics of the disorders studied, particularly as similarly high RRs were found in all four mental conditions.

Pneumococcal vaccine is now offered routinely to people aged 65 and over in England. Accordingly, we thought that we might find a lower risk in the ORLS2 and England datasets than in the earlier period of ORLS1. We did not; RRs were actually higher, rather than lower, in the later cohorts. We cannot account for the difference between the periods, but admission rates for psychiatric care were much lower in recent years than they were in the period covered by ORLS1. It is likely that patients in the recent era who are admitted for psychiatric care are more severely ill or less able to care for themselves than those in earlier times.

Speculative mechanisms of association
Unhealthy lifestyle, lack of self-care, physical circumstances including poor housing and homelessness, and health-risk activities are common in people with mental illness, and these are associated with adverse health outcomes.[12–14] Compared with the general population, the prevalence of smoking,[15 16] alcohol[17] and

substance abuse,[18] which are known risk factors for lung infections,[19][20] are higher in patients with mental disorders than in the general population. Whether independently or in combination, these factors are likely to increase the risk of pneumococcal disease. We had no data on smoking, but other studies have shown that the risk of respiratory infection was high in people with mental disorders even after controlling for smoking.[1][21]

The effect of psychiatric conditions, especially active psychosis, on cognitive function may compromise patients' ability to adequately recognise health problems, to actively look for help, and to communicate effectively with care providers.[13][22][23] Altered perception of pain and atypical presentation of pain-related symptoms are widely reported in people with severe mental diseases, affecting their healthcare-seeking behaviour and clinical presentation.[24][25] If pain thresholds are high in people with psychiatric conditions, the earlier and milder symptoms of pneumococcal infection, such as chest pain or headache, might not be recognised by the patient until the infection progresses. Patients with mental illness may require continuous treatment with antipsychotics, some of which are known to have side effects that include a reduction of white blood cells and worsened respiratory muscle functioning.[26–29] These factors, too, may increase the risk of infection, including pneumonia. It is also possible that staff caring for patients with severe mental illness may not always readily recognise symptoms and signs of physical illness.

Strengths and limitations
The strengths include the use of a large, current, nationwide population-based dataset and of a historical 'baseline' for pneumococcal infection in the ORLS1.

We were wholly dependent on the reliability of coded diagnostic data in the datasets. Most of the cases of pneumococcal disease were coded as lobar pneumonia. Until the most recent revision, the ICD classification regarded lobar pneumonia and pneumococcal pneumonia as synonymous and they had the same code. We had to accept this and, even after 2001 when they became distinguishable by code, lobar pneumonia was a much more common diagnosis than pneumococcal pneumonia. In fact, the RRs for lobar and pneumococcal pneumonia were very similar. Further, although the numbers were small, the risks of pneumococcal septicaemia and meningitis (unlikely to be misdiagnosed) were also elevated.

We had no data on pneumococcal vaccination, laboratory confirmation of pneumococcal infection or pathology reports, microbiological information on serotypes, information on prescribed treatment or antibiotic sensitivity. The study population was limited to people who had a record of hospital admission or day care for the mental disorders and may not necessarily apply to people with mental disorders that are less severe.

Our estimates of the absolute risk of pneumococcal disease are approximate. They do not take account of population migration, or of cases of pneumococcal infection treated outside hospital. Nonetheless, the estimated absolute risk of 2.2% in the schizophrenia cohort and above 3% in the other three groups of patients with mental disorders indicates that pneumococcal disease is a common enough risk for immunisation to be considered.

Implications of the study
Our findings should be regarded as hypothesis generating rather than definitive. They need confirmation or refutation. If confirmed, national guidance on pneumococcal vaccination might need revision to include people with severe mental disorders.

The level of risk of pneumococcal disease in people with severe mental illness, at about a twofold excess, is similar to that for pneumococcal disease in people with diabetes (for which immunisation is generally recommended). If the high-risk group is mainly those with severe enough mental illness to warrant hospitalisation for psychiatric care, opportunistic immunisation of these patients while in hospital could be part of the policy.

In recent years people aged 65 years and over in the general population in England have routinely been offered immunisation against the pneumococcus. If people with severe mental illness had been protected either directly, or by an increase in herd immunity in the general population resulting from routine pneumococcal immunisation, a decline in the relative risk of pneumococcal disease in our study might have been expected. We did not find a decline. However, there are questions about the effectiveness of the vaccine used in the UK (Pneumovax, PPV-23) in preventing pneumonia. Reports on effectiveness of pneumococcal vaccine PPV-23 in adults are inconclusive and consideration should be given to conjugate vaccines, with greater efficacy in preventing pneumonia and other invasive forms of pneumococcal disease in high-risk groups.[30][31]

Unanswered questions
Although people with mental disorders have an increased risk of pneumococcal disease, it is not known whether they would benefit from pneumococcal immunisation. There is a chance that the association reported by us might be mediated by confounders or other factors that would not be affected by immunisation. One possible approach to taking this work forward would be to undertake a randomised controlled trial of pneumococcal vaccine in people with severe mental illness.

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Appendix Number of observed (O) and expected (E) cases, rate ratios[1] (RR) with upper and lower 95% CI for pneumococcal disease (including pneumonia, septicaemia and meningitis) in people with selected mental disorders, after excluding cases of pneumococcal disease within one year of first admission for each mental disorder, compared with the control cohort[2], England

Diagnosis	Data set	Lobar pneumonia and pneumococcal disease combined				Lobar pneumonia				Pneumococcal pneumonia				Pneumococcal septicaemia				Pneumococcal meningitis			
		O	E	RR	95% CI	O	E	RR	95% CI	O	E	RR	95% CI	O	E	RR	95% CI	O	E	RR	95% CI
Schizophrenia	LHES	1671	718.7	2.3	2.2–2.5	1612	688.2	2.4	2.3–2.5	71	31.8	2.3	1.8–2.9	8	6.6	1.2	0.5–2.4	7	3.1	2.2	0.9–4.8
	ORLS2	57	22.2	2.6	2.0–3.4	56	21.4	2.6	2.0–3.4	†				†				†			
	ORLS1	45	28.2	1.6	1.2–2.2	43	26.5	1.6	1.2–2.2	†				†				†			
Bipolar disorder	LHES	2343	1062.5	2.2	2.1–2.3	2282	1027.9	2.2	2.2–2.3	76	38.4	2.0	1.6–2.5	7	8.6	0.8	0.3–1.7				
	ORLS2	69	34.2	2.0	1.6–2.6	67	33.2	2.0	1.6–2.6	†				†				†			
	ORLS1	76	51.5	1.5	1.2–1.9	74	49.0	1.5	1.2–1.9	†				†				†			
Depression	LHES	4032	2048.5	2.0	1.9–2.1	3930	1987.9	2.0	2.0–2.1	134	65.8	2.1	1.7–2.5	31	15.4	2.1	1.4–2.9	6	4.7	1.3	0.5–2.9
	ORLS2	186	93.3	2.0	1.8–2.4	183	90.9	2.1	1.8–2.4	9	2.7	3.6	1.6–7.0	†				†			
	ORLS1	141	102.3	1.4	1.2–1.7	134	96.6	1.4	1.2–1.7	6	2.9	2.1	0.8–4.8	†				†			
Anxiety	LHES	1626	786.0	2.1	2.0–2.2	1589	764.5	2.1	2.0–2.2	56	24.9	2.3	1.7–3.0	12	5.7	2.1	1.1–3.7	4	1.6	2.6	0.7–6.8
	ORLS2	42	21.7	1.9	1.4–2.6	42	21.1	2.0	1.5–2.7	†				†				†			
	ORLS1	108	80.6	1.4	1.1–1.6	102	75.8	1.4	1.1–1.7	†				†				†			

[1] Adjusted for sex, age in 5-year bands, time period in single calendar years in the ORLS1 and HES data sets; for district of residence in ORLS1, and for region of residence and deprivation score associated with patient's area of residence, in quintiles, in the HES data set.
† Data not shown for pneumococcal disease with non-significant results and five or fewer observed cases.
For conditions used in reference cohort, see footnote to Table 2.