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Hospitalizations and severe complications following acute sinusitis in general practice: a registry-based cohort study

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Objectives: To investigate complication rates of acute sinusitis in general practice, and whether antibiotic prescribing had an impact on complication rate.

Methods: All adult patients diagnosed with sinusitis in Norwegian general practice between 1 July 2012 and 30 June 2019 were included. GP consultation data from the Norwegian Control and Payment for Health Reimbursements Database were linked with antibiotic prescriptions (Norwegian Prescription Database) and hospital admissions (Norwegian Patient Registry). Main outcomes were sinusitis-related hospitalizations and severe complications within 30 days. Logistic regression was used to estimate associations between antibiotic prescriptions, prespecified risk factors, individual GP prescribing quintile, and outcomes.

Results: A total of 711 069 episodes of acute sinusitis in 415 781 patients were identified. During the study period, both annual episode rate (from 30.2 to 21.2 per 1000 inhabitants) and antibiotic prescription rate (63.3% to 46.5%; $P<0.001$) decreased. Yearly hospitalization rate was stable at 10.0 cases per 10 000 sinusitis episodes and the corresponding rate of severe complications was 3.2, with no yearly change ($P=0.765$). Antibiotic prescribing was associated with increased risk of hospitalization [adjusted OR 1.8 (95% CI 1.5–2.1)] but not with severe complications. Individual GP prescribing quintile was not associated with any of the outcomes, whereas risk factors such as previous drug abuse, or head injury, skull surgery or malformations, and being immunocompromised were significantly associated with increased risk of both outcomes.

Conclusions: Severe complications of acute sinusitis were rare and no protective effect of high prescribing practice among GPs was found. Recommendations to further reduce antibiotic prescribing are generally encouraged, except for high-risk groups.

Introduction

Acute rhinosinusitis (sinusitis) is a common infection in general practice.[1] Most episodes of acute sinusitis are caused by viral infections, and only 0.5%–2% are bacterial infections.[1] GPs consider acute bacterial sinusitis challenging to differentiate from viral infections.[2,3] Regardless of aetiology, there is increasing evidence that antibiotics have a marginal effect, and should be avoided in the treatment of uncomplicated sinusitis.[4] However, prescribing antibiotics for self-limiting sinusitis in primary care is still common.[5,6]

Measures aiming for less antibiotic use must take into consideration that correct use of antibiotics is not necessarily the same as no use. At some point, increased morbidity may result from too-limited antibiotic use, leading to more complications and hospitalizations, and potentially also to fatal outcomes.[7,8]

In a previous study, we reported a decrease in antibiotic prescriptions for respiratory tract infections (RTIs) in Norway between 2012 and 2019.[9] Although most episodes of acute sinusitis do not benefit from antibiotics, severe complications such as orbital infections, osteomyelitis and even intracranial infections have been reported.[1,10] Some studies indicate that

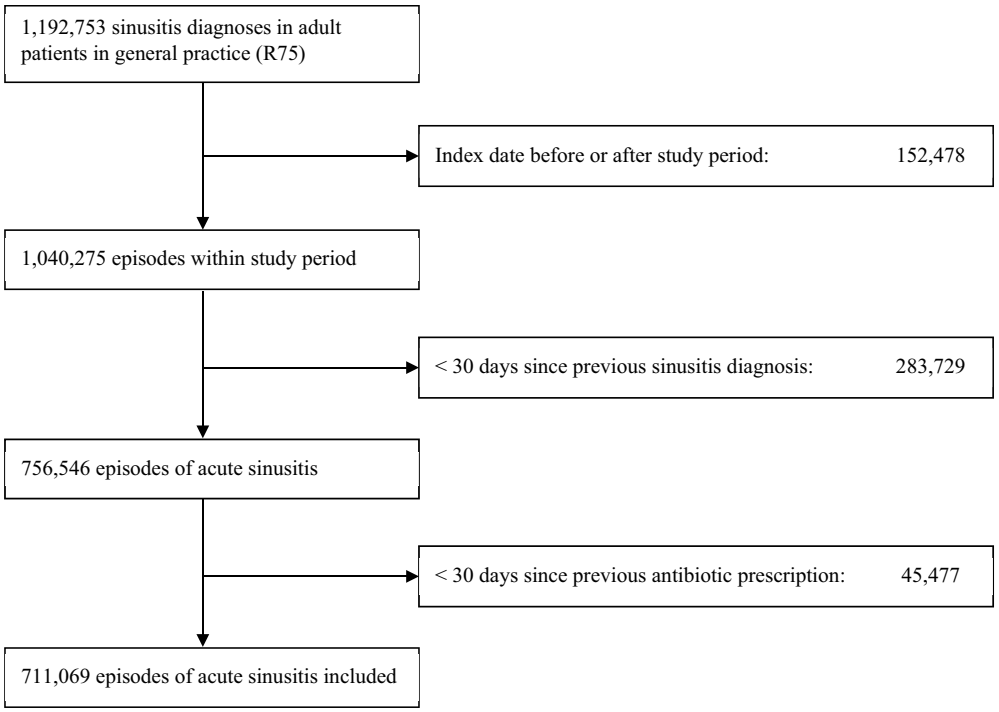

Figure 1. Flow chart of episode inclusion.

antibiotic use does not protect against severe complications, possibly due to a short prodromal phase from the debut of symptoms to the development of complications.[11,12] On the other hand, others have reported a slight protective effect of antibiotics regarding serious complications.[13]

In this study of adult patients diagnosed with acute sinusitis in Norwegian general practice, we examined hospital admissions following sinusitis diagnosis. We aimed to investigate whether the reduced antibiotic use in recent years has had any impact on the rate of hospital admissions and severe complications of acute sinusitis. We further aimed to explore potential risk factors and antibiotic prescribing practice in relation to the outcomes.

Materials and methods

Ethics

The study was approved by the Regional Committee for Medical and Health Research Ethics, REC Southeast (ref. 2016/2283), and the Norwegian Data Protection Authority (ref. 282558). The study was conducted in accordance with the Declaration of Helsinki and institutional standards.

Data setting and material

The study design was a retrospective cohort based on prospectively collected data from three national health registries: the Norwegian Control and Payment of Health Reimbursement (KUHR) database; the Norwegian Patient Registry (NPR); and the Norwegian Prescription Database (NorPD). Demographics were collected from Statistics Norway (SSB). All databases were linked using (encrypted) unique personal identification numbers assigned to all Norwegian residents.

The KUHR database stores data on reimbursement claims from Norwegian GPs and GP-staffed out-of-hours services. We obtained date and diagnosis of all infection-related contacts in the years 2012 to 2019. Diagnoses were recorded using the second version of the International Classification of Primary Care (ICPC-2).[14] From the NorPD database, we collected all antibiotic prescriptions dispensed at Norwegian pharmacies in the same period. In NorPD, drugs are classified according to the Anatomical Therapeutic Chemical (ATC) system.[15] NPR stores information on all hospital contacts in Norway. We obtained information on infection-related admissions to hospital departments during the period. The hospital data included time and date of admission and discharge, with up to 20 discharge diagnoses according to the 10th revision of the International Classification of Disease (ICD-10) per contact, procedure codes, hospital department, and admission urgency. For demographic data, we used data from SSB.

Population

The population consisted of patients aged 18 years or older diagnosed with ICPC-2 code R75 sinusitis in general practice between 1 July 2012 and 30 June 2019. To only include patients with acute sinusitis, we used the period between 1 January 2012 to 30 June 2012 as a wash-out period. In doing so, we could exclude episodes in patients with a sinusitis diagnosis prior to the diagnosis in general practice and include risk factors from previous contacts in general practice and hospital services.

Episode definition

Each patient could contribute with multiple episodes during the study period. A new episode started at an index date. To be defined as index, the patient had to have a sinusitis diagnosis (ICPC-2 R75) from general practice, and in the previous 30 days no sinusitis diagnosis from general practice or from a hospital contact, as well as no antibiotic prescription (Figure 1).

For each episode, follow-up lasted for 30 days after GP consultation. If there were more relevant contacts within 30 days after the index date, the follow-up period lasted 30 days after the last consultation for the episode to a maximum of 90 days from the index date. The 90 days limit was used because the definition of chronic sinusitis is 12 weeks of symptoms.[1]

Antibiotic prescription

From the NorPD, we extracted prescriptions for antibiotics dispensed within 1 week after a sinusitis consultation. All oral antibiotics were included, except (piv)mecillinam, trimethoprim and nitrofurantoin, as these antibiotics are solely prescribed for urinary tract infections.[16] Antibiotic prescriptions were only included if there was no other consultation in general practice between diagnosis and prescription. Antibiotic prescriptions were not included for episodes with hospitalization occurring on the first day of the episode, as these were referred from the GP rather than treated by them.

Antibiotics were categorized into broad-spectrum antibiotics (tetracyclines, penicillins with β-lactamase inhibitors, second- and third-generation cephalosporins, trimethoprim/sulfamethoxazole, macrolides (except erythromycin), lincosamides, fluoroquinolones) and narrow-spectrum antibiotics (β-lactam penicillin without β-lactamase inhibitors, first-generation cephalosporins, erythromycin and fusidic acid), based on the definition by ECDC.[17]

GPs were divided into quintiles from low to high prescribers by estimating the number of dispensed prescriptions of predefined RTI antibiotics (doxycycline J01AA02, amoxicillin J01CA04, phenoxymethylpenicillin J01CE02, macrolides J01FA) per 1000 RTI-related consultations (ICPC-2 codes: R01–05, R07–29, R71–72, R74–78, R80–83, H01, H71–74), for each study year in our analyses. These definitions are similar to previous studies on antibiotic prescribing in Norwegian general practice.[18,19] For doctors with fewer than 100 total consultations during a study year, prescription rates were not calculated, and these doctors were characterized as 'unclassified'.

Risk factors

Potential risk factors were defined as previous diagnoses from KUHR or NPR for risk factors based on findings from previous literature,[20–23] including chronic sinusitis or previous sinus surgery, previous head trauma, skull surgery or congenital skull malformations, chronic reactive airway disease, malignancy or immunosuppression (see Table S1, available as Supplementary data at *JAC* Online, for all risk factors included). Malignancy was defined as any previous cancer diagnosis of any organ as registered in KUHR or NPR. Previous malignancy is associated with more frequent history of smoking and potentially also immunosuppression if in active treatment. Based on the authors' clinical experience, we also included previous abuse of opioids, reflecting a group of patients with lower general health status and an increased risk of serious morbidity.[24,25] For episodes resulting in hospital admissions, potential risk factors were additionally recorded from the diagnoses registered at discharge. Patients with recurring infections were defined as chronic sinusitis patients if there were at least three sinusitis episodes in the previous 12 month period.

Hospitalization and severe complications

The main outcome was hospitalization, defined as hospital admissions lasting for more than 24 h,[26] with a discharge diagnosis of acute sinusitis (ICD-10 code J01), intracranial infection, orbital infection, osteomyelitis or sepsis (all codes in Table S1), within 30 days after GP consultation. Hospital contacts labelled as follow-up or elective admissions were not included, and admissions were only included if there was no general practice contact with infections other than sinusitis between sinusitis diagnosis and admission. The secondary outcome was severe complications. To be identified as a severe complication, the patient had to be discharged with a diagnosis of an intracranial infection, orbital infection, osteomyelitis or sepsis (Table S1). Patients with repeated admissions with the same complication were only counted at first registration. All hospitalizations meeting these requirements are reported. However, for the association analyses of antibiotic treatment and risk factors, we did not include hospitalizations where the patients were admitted on the first day of the episode. As a sensitivity analysis, all included hospital admissions were manually checked by the first author to exclude non-sinusitis-related admissions. The reasons for encounter in these excluded hospitalizations are listed in Table S2.

As a *post hoc* analysis, we extracted all hospital admissions from NPR with a primary discharge diagnosis of acute sinusitis in adults, as well as sinusitis-related intracranial abscesses and orbital infections, defined as a diagnosis of both the complication and acute sinusitis (ICD-10 code J01) at hospital discharge regardless of previous GP contact. This was done to report the complication rates in the whole Norwegian population in contrast to complication rates per sinusitis episode recorded in primary care.

Statistical methods

Descriptive statistics are presented with means and SDs. Each study year started 1 July and ended 30 June in the following calendar year. Differences between groups were analysed by *t*-test for mean age, and chi-squared test for categorical variables. Episode rates were calculated for each study year as number of episodes per 1000 adult inhabitants registered on 1 January. Antibiotic prescription rates were calculated as the percentage of episodes with at least one dispensed prescription within 7 days after any GP consultation during the episode. The proportion of narrow-spectrum antibiotics only included first prescription and were calculated as the percentage of antibiotics being defined as narrow-spectrum agents. Hospital admission rates and severe complication rates were calculated as proportions per 10 000 sinusitis episodes, and 95% CIs were calculated. For the population analysis, we calculated hospital admissions per million adult inhabitants aged 18 years and older on 1 January per study year. Linear regression was used to estimate change per study year for episode rates, antibiotic prescription rates and hospital admissions, and results are presented as regression coefficients with corresponding 95% CIs and *P* values.

The association between age, sex, potential risk factors, physicians' antibiotic prescribing quintile, antibiotic exposure, and outcomes were examined using logistic regression to calculate crude ORs. Hospitalizations occurring on the first day of the episode were not included in these analyses. Adjusted ORs were obtained separately for hospitalizations and severe complications, by adjusting for sex and age, as well as for the predefined risk factors. The significance level was set to 0.05. Stata version 16.1 (StataCorp, College station, TX, USA) was used for all analyses.

Results

We identified a total of 415 781 adult patients contributing 711 069 episodes of acute sinusitis. The mean age at diagnosis was 43.7 years (SD 15.4). Women contributed 68.8% of the episodes (Table 1) and 54.8% of episodes received an antibiotic prescription. The majority (78.6%) of episodes had no observed risk factor at the time of first consultation.

The yearly episode rate decreased during the study period (Table 2). The proportion of episodes with a dispensed antibiotic prescription was 63.3% in the first study year and 46.5% in the last study year ($P < 0.001$ for linear trend). The proportion of prescriptions being narrow-spectrum antibiotics increased from 66.1% to 75.7% during the study period ($P < 0.001$ for linear trend).

Table 1. Characteristics of acute sinusitis episodes in Norwegian general practice 2012–19

	Total[a]	Prescribed antibiotics	(%)	Not prescribed antibiotics	(%)	*P* value
Number of episodes	711 069	389 729	54.8	321 193	45.2	
Patient characteristics						
Age (years), mean (SD)	43.7 (15.4)	44.0 (15.4)		43.3 (15.4)		0.000
Male	221 697	118 533	53.5	103 101	46.5	0.000
Female	489 372	271 196	55.4	218 092	44.6	0.000
Risk factors						
No risk factors	558 667	312 713	56.0	245 954	44.0	0.000
Chronic or recurring sinusitis[b]	64 492	25 895	40.2	38 582	59.8	0.000
Other risk factors	106 659	59 342	55.6	47 317	44.4	0.000
Chronic lung disease[c]	60 112	32 628	54.3	27 465	45.7	0.007
Diabetes mellitus	24 116	14 201	58.9	9905	41.1	0.000
Immunocompromised[d]	4226	2469	58.5	1753	41.5	0.000
Previous cancer diagnosis[e]	26 700	15 131	56.7	11 560	43.3	0.000
Previous opioid abuse diagnosis	534	313	58.8	219	41.2	0.063
Head injury/skull malformation	955	501	52.5	454	47.5	0.143

[a]Total includes all episodes of acute sinusitis whereas 'Prescribed antibiotics' and 'Not prescribed antibiotics' do not include episodes where hospitalization occurred on the first day of the episode.
[b]Previous diagnosis of chronic sinusitis, nasal polyps, paranasal sinus surgery, or ≥3 episodes of acute sinusitis in the previous 12 months.
[c]Asthma/COPD/cystic fibrosis.
[d]Immunocompromised (HIV, asplenism, immunodeficiency, transplanted organ, end-stage kidney failure).
[e]Cancer diagnoses listed in Table S1.

Table 2. Episode rate and complication rates for acute sinusitis diagnosed in Norwegian general practice by study year

	2012–13	2013–14	2014–15	2015–16	2016–17	2017–18	2018–19	Coef[a]	95% CI
Episodes	118 447	103 520	109 019	99 844	100 075	91 166	88 998		
per 1000 adult inhabitants[b]	30.2	26.0	27.0	24.4	24.2	21.9	21.2	−1.4	**−1.9 to −0.8**
Prescription rate	63.3	59.7	58.5	54.1	50.8	47.1	46.5	−3.0	**−3.5 to −2.5**
proportion narrow antibiotics[c]	66.1	67.2	68.5	69.7	73.0	75.1	75.7	1.8	**1.4 to 2.1**
Hospitalizations (cases)	113	104	118	84	97	97	95		
per 10 000 episodes	9.5	10.0	10.8	8.4	9.7	10.6	10.7	0.1	−0.3 to 0.6
Severe complications (cases)	38	29	41	34	24	24	37		
per 10 000 episodes	3.2	2.8	3.8	3.4	2.4	2.6	4.2	0.0	−0.3 to 0.4
Intracranial complications (cases)	6	6	3	3	5	8	6		
per 10 000 episodes	0.5	0.6	0.3	0.3	0.5	0.9	0.7	0.0	−0.1 to 0.1
Orbital complications (cases)	2	7	7	3	2	4	7		
per 10 000 episodes	0.2	0.7	0.6	0.3	0.2	0.4	0.8	0.0	−0.1 to 0.2

[a]Coef, coefficient from linear regression of variables over study year.
[b]Adult inhabitants aged 18 years or older registered in Norway on 1 January during the study year.
[c]Narrow-spectrum antibiotics (β-lactam penicillins without β-lactamase inhibitors, first-generation cephalosporins, erythromycin, fusidic acid) as proportion of all antibiotic prescriptions.
Bold numbers indicate statistical significance at 0.05 level.

There were 13 956 individual doctors diagnosing acute sinusitis in general practice during the study period.

Infectious complications following sinusitis diagnosed in general practice

During the study period, 708 episodes of acute sinusitis resulted in a hospitalization within 30 days. The majority of the hospitalizations resulted in a discharge diagnosis of acute sinusitis, whereas 227 cases were identified as severe complications. All complications are listed in Table 3. Of the 708 hospitalizations, 150 (21.2%) were admitted on the first day of the episode.

The mean age at admission was 47.3 years (SD 17.8). Female patients contributed to 63.4% of hospitalizations, and 57.7% of the severe complications. Sixty percent (428/708) of hospitalized patients had no observed risk factor before admission.

Table 3. Complications following acute sinusitis diagnosed in Norwegian general practice 2012–19

Complication	No antibiotic prescription	(%)	Antibiotic prescription	(%)	Admitted first day of episode	(%)	Total
Hospitalized with acute sinusitis	97	20.2	267	55.5	117	24.3	481
Severe complications							
Intracranial complications							
Encephalitis	0	0.0	0	0.0	1	100.0	1
Intracranial abscess	2	16.7	10	83.3	0	0.0	12
Meningitis	3	17.6	9	52.9	5	29.4	17
Venous sinus thrombosis	3	42.9	3	42.9	1	14.3	7
Orbital complications							
Periorbital cellulitis	11	52.4	8	38.1	2	9.5	21
Orbital infection	4	36.4	4	36.4	3	27.3	11
Other complications							
Osteomyelitis	2	66.7	1	33.3	0	0.0	3
Sepsis	56	36.1	78	50.3	21	13.5	155
All hospital admissions following acute sinusitis	178	25.1	380	53.7	150	21.2	708

Figure 2 illustrates the yearly rates of hospitalizations and severe complications. The total incidence of hospitalization was 10.0 cases per 10 000 episodes of acute sinusitis (95% CI 9.3–10.7) and did not change during the study period (Table 2). The incidence rate of severe complications was 3.2 cases per 10 000 episodes (95% CI 2.8–3.6), with no change over time (*P* for linear trend = 0.765).

Antibiotics, risk factors and risk of hospitalization and severe complications

For the 558 hospitalizations not occurring on the same day as the first GP consultation, antibiotics had been dispensed in 380 (68.1%) episodes prior to admission. As a result, antibiotics were associated with increased risk of hospitalization with adjusted OR 1.8 (95% CI 1.5–2.1). For severe complications not occurring on the first day, the corresponding ratio was 58.2% (113/194) and antibiotic treatment was not associated with risk of severe complications, adjusted OR 1.1 (95% CI 0.9–1.5).

The risk of both hospitalization (Table 4) and severe complication (Table 5) increased with increasing age. Compared with female patients, male patients were associated with higher risk of severe complications but not hospitalization. Chronic or recurring sinusitis was associated with increased risk of hospitalization but not for severe complications, whereas immunocompromised patients, previous drug abuse, and previous head injury, skull surgery or malformations were associated with increased risk of both hospitalization and severe complications. These risk factors were the only ones significantly associated with severe complications after manually excluding admissions with urinary tract infections, orthopaedic admissions, heart disease and other possible non-sinusitis-related admissions.

A doctor's RTI antibiotic prescribing rate, or being registered as a GP specialist, was not associated with risk of hospitalizations or severe complications.

In total, 83 individuals died within 30 days after a GP consultation for sinusitis; 35 died in hospital. Three of these were included in our outcome (two meningitis, one sepsis); the rest died from with other diagnoses, mainly cancer (11 cases) or acute myocardial infarction (6 cases). Another 19 were declared dead by a GP, and the remaining 32 patients most likely died in nursing homes or abroad as no registration in the included registries occurred.

Hospitalizations on population level

Between 1 July 2012 and 30 June 2019, there were 2415 admissions with acute sinusitis as primary diagnosis, of which 42 underwent sinus surgery. The mean yearly hospitalization rate was 84.6 (95% CI 78.9–90.3) admissions per million adult inhabitants per study year, with no yearly change during the study period (*P* for linear trend = 0.417). Both sinusitis-related orbital infections and intracranial abscesses were rare throughout the study period, with an incidence of 1.2 (95% CI 0.8–1.5) and 0.9 (95% CI 0.5–1.4) cases per million adult inhabitants, respectively, with no changing trend over time.

A GP contact had been recorded on the same date as the admission in 52.7% (1273/2415) of all hospital admissions, whereas 15.2% (367/2.415) had a recorded GP contact within 30 days preceding admission. No change in proportion of hospitalizations with a preceding GP contact was seen during the study period (*P* for linear trend = 0.097).

Discussion

Main findings

In this retrospective observational study, we found 708 hospitalizations following acute sinusitis diagnosed in general practice. Thirty-two percent (227) of these were due to severe complications. Linear regression showed stable hospitalization rates at 10.0 cases per 10 000 episodes. For severe complications, the rates were stable at approximately 3.2 cases per 10 000 episodes. This was observed even with a significant decrease in

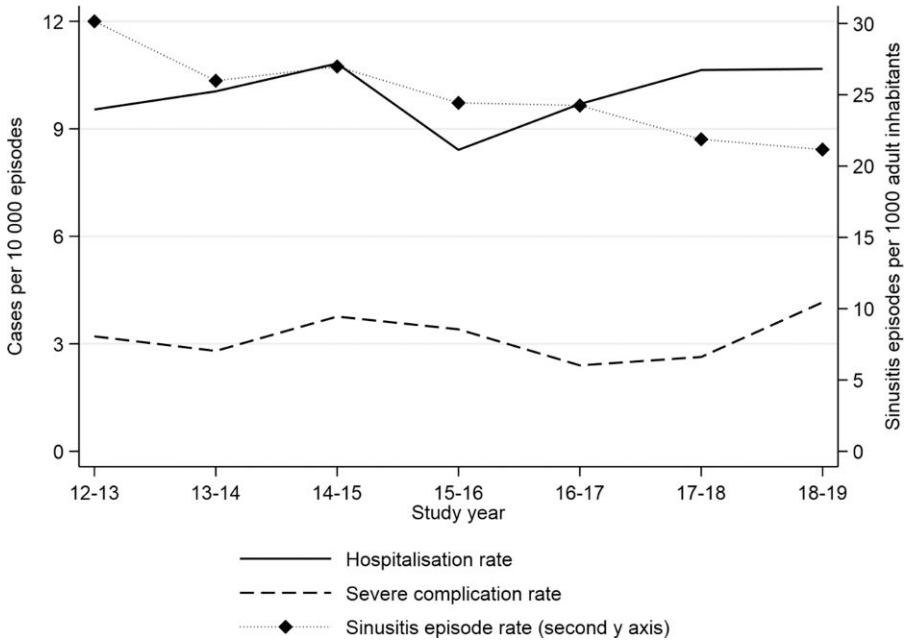

Figure 2. Hospitalization rate per 10 000 episodes of acute sinusitis in adult patients diagnosed in Norwegian general practice. Severe complications (dashed line) include intracranial infections, orbital infections, and sepsis.

GP-diagnosed sinusitis episodes, reduced antibiotic prescribing, and increased proportion of narrow-spectrum antibiotics during the study period.

In one-fifth (21%) of the hospitalizations, the patients were admitted on the first day of the episode. For those not immediately admitted, 68% had an antibiotic prescription dispensed prior to admission. For the severe intracranial, orbital and systemic complications, 15% were admitted on the first day, and 58% of those not immediately admitted had antibiotics dispensed prior to admission.

We could not find a protective effect of antibiotics for severe complications, and logistic regression showed that antibiotic treatment was associated with an increased risk of hospitalization. We were able to identify several significant risk factors for severe complications (immunocompromised patients, previous opioid abuse and previous head injury, skull surgery or malformations). The overall antibiotic prescribing practice of the GPs did not affect the risk of complications following acute sinusitis.

Comparison with previous literature

It is well established that severe complications of acute sinusitis are rare. Nevertheless, the fear of complications is frequently reported as an explanation for the widespread use of antibiotics for self-limiting RTIs.[27] Studies on complication frequency following reduced antibiotic use are scarce and have been requested by both professional communities and health authorities.[1,28]

Our numbers of serious complications of acute sinusitis in general practice align well with previous European studies. We observed an incidence for intracranial abscess of 0.17 per 10 000, which is comparable to 0.12 per 10 000 episodes reported from UK general practice,[13] and 0.10 to 0.16 per 10 000 acute sinusitis episodes in Swedish general practice.[29] For orbital infections, our incidence of 0.16 per 10 000 episodes was similar to the Swedish numbers of 0.05 to 0.16 cases per 10 000, but substantially lower than the UK numbers of 1.28 per 10 000 episodes. The differences might be due to our stricter criteria for hospitalization duration of at least 24 h, as well as using a 30 day limit instead of the 90 and 180 days used in the respective studies. Therefore, as a sensitivity analysis, we investigated complications within 90 days after index consultations, which resulted in three more cases of intracranial abscess (incidence of 0.2 per 10 000 episodes), but no more cases of orbital infections.

We found no increased incidence of severe complications despite reduced antibiotic prescribing including less use of broad-spectrum agents. This is in line with a Swedish study,[29] where no associations were found between antibiotic use and incidence of bacterial complications of RTIs, despite declining antibiotic prescribing in the study period.[29] Another Swedish study found a slight decrease in sinusitis complications (meningitis/brain abscess) in 2020 compared with 2019,[30] despite a sharp decrease in antibiotic prescribing during the same period.

We found that antibiotic use did not protect against hospitalizations or severe complications, consistent with findings from previous studies that sinusitis complications occur sporadically in both the antibiotic and the non-antibiotic treated groups.[10,31,32] The association between antibiotic treatment and increased risk of hospitalization in our material probably reflects that multimorbid and more severely ill patients are more likely to be prescribed antibiotics and to be hospitalized. However, our results contrast with two larger studies from the UK and Sweden showing increased risk of brain abscess in untreated sinusitis patients compared with patients treated with antibiotics.[13,33] In both studies, the number of intracranial abscesses were rare (five and eight cases, respectively).

Table 4. Logistic regression of patient and doctor characteristics and hospitalizations for infectious-related complications following acute sinusitis

						Adjusted[a]		Full model[b]		Full model + manual check[c]	
Characteristics	*N*	Cases	Per 10 000	Crude OR	95% CI	Adjusted OR	95% CI	Adjusted OR[b]	95% CI	Adjusted OR[b]	95% CI
Patient characteristics											
Male sex	221 634	196	8.8	ref							
Female sex	489 285	362	7.4	0.84	0.70–1.00			0.87	0.73–1.03	0.91	0.74–1.13
Age				**1.02**	**1.01–1.02**			**1.01**	**1.01–1.02**	1.00	0.99–1.01
Antibiotic (AB) treatment	389 729	380	9.8	**1.76**	**1.47–2.10**	**1.74**	**1.46–2.08**	**1.79**	**1.50–2.15**	**1.90**	**1.53–2.37**
No AB prescription	321 190	178	5.5	ref							
Broad-spectrum AB	116 620	81	6.9	1.25	0.96–1.63	1.20	0.92–1.56	1.20	0.93–1.57	1.21	0.88–1.68
Narrow-spectrum AB	273 109	299	10.9	**1.98**	**1.64–2.38**	**1.98**	**1.65–2.39**	**2.07**	**1.72–2.50**	**2.22**	**1.78–2.79**
Risk factors											
No risk factors	558 515	325	5.8								
Chronic or recurring sinusitis	64 477	83	12.9	**1.75**	**1.39–2.21**	**1.64**	**1.30–2.07**	**1.60**	**1.26–2.04**	**1.83**	**1.38–2.43**
Other risk factors[d]	106 838	192	18.0	**2.97**	**2.49–3.54**	**2.63**	**2.19–3.15**	**2.51[d]**	**2.09–3.02**	**2.02[d]**	**1.60–2.56**
Chronic lung disease[e]	60 092	82	13.6	**1.87**	**1.48–2.36**	**1.69**	**1.34–2.14**	**1.48**	**1.16–1.89**	1.28	0.94–1.75
Diabetes mellitus	24 106	41	17.0	**2.26**	**1.65–3.11**	**1.80**	**1.30–2.48**	**1.58**	**1.14–2.20**	1.25	0.79–1.99
Immunocompromised[f]	4 222	17	40.3	**5.28**	**3.25–8.56**	**4.76**	**2.93–7.73**	**3.26**	**1.98–5.35**	**3.52**	**1.91–6.50**
Previous cancer diagnosis[g]	26 691	72	27.0	**3.81**	**2.97–4.88**	**3.01**	**2.31–3.91**	**2.67**	**2.05–3.48**	**1.94**	**1.33–2.83**
Previous opioid abuse	532	4	75.2	**9.71**	**3.62–26.05**	**10.24**	**3.81–27.51**	**6.99**	**2.55–19.14**	**7.91**	**2.50–25.06**
diagnosis											
Head injury/skull	955	17	178.0	**27.08**	**16.13–45.46**	**21.74**	**13.34–35.44**	**19.94**	**12.21–32.59**	**19.84**	**10.82–36.37**
malformation											
Doctor characteristics											
Doctor's prescription rate (quintiles)[h]											
1st	114 877	89	7.7	ref							
2nd	145 718	110	7.5	0.97	0.74–1.29	0.99	0.75–1.31				
3rd	156 549	125	8.0	1.03	0.79–1.35	1.04	0.79–1.36				
4th	159 321	107	6.7	0.87	0.65–1.15	0.87	0.66–1.15				
5th	119 116	95	8.0	1.03	0.77–1.37	1.03	0.77–1.38				
Unclassified[i]	15 338	32	20.9	2.70	1.80–4.04	2.82	1.88–4.23				
Doctor's specialization as GP	356 277	245	6.9	1.02	0.83–1.27	1.00	0.81–1.24				

[a]Adjusted for age and sex.
[b]Adjusted for age, sex, antibiotic treatment, and risk factors.
[c]Manual check, not including cases with non-sinusitis-related hospitalizations (see Table S2 for excluded admissions).
[d]Other risk factors were specified as occurrence of any of the specified risk factors (except chronic or recurring sinusitis) versus no registered risk factors. This model did not include the individual risk factors due to collinearity.
[e]Asthma/COPD/cystic fibrosis.
[f]Immunocompromised (HIV, asplenism, immunodeficiency, transplanted organ, end-stage kidney failure).
[g]Cancer diagnoses listed in Table S1.
[h]GP prescribing rate quintile for all respiratory tract infections.
[i]Doctors with fewer than 100 consultations during a study year.
Bold numbers indicate statistical significance at 0.05 level.

Table 5. Logistic regression of patient and doctor characteristics and severe complications of acute sinusitis

						Adjusted[a]		Full model[b]		Full model + manual check[c]	
Characteristics	N	Cases	Per 10 000	Crude OR	95% CI	Adjusted OR	95% CI	Adjusted OR[b]	95% CI	Adjusted OR[b]	95% CI
Patient characteristics											
Male sex	221 634	83	3.7	ref							
Female sex	489 285	111	2.3	**0.61**	**0.46–0.80**			**0.64**	**0.48–0.85**	0.77	0.50–1.19
Age				**1.03**	**1.02–1.04**			**1.02**	**1.01–1.03**	1.01	0.99–1.02
Antibiotic (AB) treatment	389 729	113	2.9	1.15	0.86–1.53	1.14	0.85–1.51	1.14	0.85–1.51	1.13	0.74–1.72
No AB prescription	321 190	81	2.5								
Broad-spectrum AB	116 620	32	2.7	1.09	0.72–1.64	1.02	0.68–1.54	1.00	0.66–1.50	0.85	0.44–1.62
Narrow-spectrum AB	273 109	81	3.0	1.18	0.86–1.60	1.19	0.87–1.62	1.20	0.88–1.64	1.26	0.80–1.98
Risk factors											
No risk factors	558 515	103	1.8								
Chronic or recurring sinusitis	64 477	24	3.7	1.42	0.92–2.17	1.26	0.82–1.93	1.05	0.68–1.63	1.50	0.82–2.75
Other risk factors[d]	106 838	83	7.8	**4.23**	**3.18–5.62**	**3.37**	**2.50–4.54**	**3.36**	**2.48–4.54**	**2.45**	**1.53–3.91**
Chronic lung disease[e]	60 092	39	6.5	**2.73**	**1.92–3.87**	**2.34**	**1.64–3.34**	**2.16**	**1.50–3.11**	1.40	0.75–2.62
Diabetes mellitus	24 106	13	5.4	**2.05**	**1.17–3.59**	1.35	0.77–2.40	1.14	0.64–2.04	1.22	0.48–3.07
Immunocompromised[f]	4 222	8	18.9	**7.21**	**3.55–14.64**	**5.96**	**2.93–12.13**	**4.01**	**1.93–8.33**	**4.11**	**1-26–13.44**
Previous cancer diagnosis[g]	26 691	33	12.4	**5.26**	**3.62–7.65**	**3.45**	**2.31–5.15**	**3.00**	**2.00–4.50**	1.54	0.68–3.47
Previous opioid abuse diagnosis	532	3	56.4	**21.09**	**6.72–66.17**	**22.85**	**7.26–71.94**	**14.83**	**4.59–47.88**	**22.55**	**5.37–94.66**
Head injury/skull malformation	955	8	83.8	**32.24**	**15.84–65.61**	**26.49**	**12.96–54.12**	**24.04**	**11.72–49.30**	**29.46**	**10.69–81.14**
Doctor characteristics											
Doctor's prescription rate (quintiles)[h]											
1st	114 877	32	2.8	ref							
2nd	145 718	42	2.9	1.03	0.65–1.64	1.06	0.67–1.68				
3rd	156 549	37	2.4	0.85	0.53–1.36	0.86	0.53–1.37				
4th	159 321	37	2.3	0.83	0.52–1.34	0.84	0.52–1.34				
5th	119 116	31	2.6	0.93	0.57–1.53	0.93	0.57–1.52				
Unclassified[i]	15 338	15	9.8	**3.51**	**1.90–6.49**	**3.73**	**2.02–6.89**				
Doctor's specialization as GP	356 277	83	2.3	0.95	0.66–1.35	0.92	0.64–1.31				

[a]Adjusted for age and sex.
[b]Adjusted for age, sex, antibiotic treatment, and risk factors.
[c]Manual check, not including cases with non-sinusitis-related hospitalizations (see Table S2 for excluded admissions).
[d]Other risk factors were specified as occurrence of any of the specified risk factors (except chronic or recurring sinusitis) versus no registered risk factors. This model did not include the individual risk factors due to collinearity.
[e]Asthma/COPD/cystic fibrosis.
[f]Immunocompromised (HIV, asplenism, immunodeficiency, transplanted organ, end-stage kidney failure).
[g]Cancer diagnoses listed in Table S1.
[h]GP prescribing rate quintile for all respiratory tract infections.
[i]Doctors with fewer than 100 consultations during a study year.
Bold numbers indicate statistical significance at 0.05 level.

Although current guidelines for antibiotic prescribing in primary care advise against antibiotic prescribing for self-limiting infections, GPs' prescribing patterns vary between practices.[6,34,35] It has been shown that high GP consultation rates have larger impact on the variation in antibiotic prescribing than patient comorbidities.[36,37] Our study finds that GPs' overall prescribing practices of antibiotics for RTIs were not associated with occurrence of sinusitis complications or hospitalizations following sinusitis. These results are supported by several previous studies from general practice.[27,38,39]

It has previously been reported that a significant share of patients do not report sinusitis symptoms before they are admitted for complications.[10] As a measure to ensure that our cohort study did not overlook a trend of increased complications, we conducted a *post hoc* analysis investigating all hospital admissions for acute sinusitis. We could not observe any significant change in the proportion of patients consulting their GP prior to the sinusitis admissions. In the *post hoc* analysis, we observed stable rates of hospital admissions for acute sinusitis, sinusitis-related intracranial abscesses and sinusitis-related orbital infections during the study period. In the same time period, the total antibiotic consumption in Norway decreased.[40] This supports our results, showing that complications of sinusitis are rare, and do not increase, despite less frequent antibiotic use.

Strengths and limitations

To our knowledge, our study is the first to estimate associations between clinical risk factors and severe complications of acute sinusitis in a community setting. Few have so far reported a trustworthy frequency of infectious complications of acute sinusitis, and a major strength in the present study is that it benefits from complete national data for everyone treated in the public healthcare system. The unique personal identification number of all Norwegian residents enables database linkage and tracking of patient courses across the different levels in the healthcare system. The longitudinal design allowed us to present data and estimate trends for 7 years.

Another strength is the strong position of the public healthcare system in Norway, where 99% of the population is assigned a regular GP.[41] In Norway, commercial for-profit healthcare providers are still very few in number. Due to their limited role, we do not consider it to represent a limitation that they do not report their activities to national registries. All reported diagnoses were based on codes recorded by GPs or hospital departments. The data were gathered for administrative purposes, and may be associated with some uncertainty.[42] Norwegian GPs have a relatively high coding precision.[43] However, their use of the ICPC-2 code R75 for sinusitis remains to be validated. Potential misclassifications include other upper respiratory tract symptoms or infections being coded as sinusitis or vice versa. We have previously shown that Norwegian GPs increasingly used symptom codes and non-specific diagnosis codes for RTIs during our study period.[9] As antibiotic prescriptions are even rarer in individuals coded with other sinus symptoms, any misclassification here would probably not significantly alter our results. This is further supported by our *post hoc* analysis including all hospitalizations regardless of previous GP contact or coding not revealing any trend of increased hospitalization or severe complications missed by our inclusion strategy.

Limited clinical information in administrative health databases makes the relationship uncertain between sinusitis diagnosed at index and the reason for later hospitalization. In this study, sepsis was by far the most common severe complication, several cases of which could possibly have been caused by infections other than acute sinusitis. By manually excluding admissions with diagnoses indicating causes other than sinusitis, we aimed to improve the precision of our association analyses.

Other limitations of the study include lack of data on potential residual confounding factors such as severity of the infection and associated symptoms like fever and general health status. Further limitations are lack of data on risk factors such as smoking and anatomical sinus abnormalities. However, we used chronic lung disease as a proxy for smoking, and if the anatomical variations mandated surgery, they would be captured in our high-risk group if the surgery occurred between 2012 and 2019. Previous surgery, head trauma, and other risk factors such as opioid abuse are likely underreported in this material, yielding high specificity but low sensitivity for these diagnoses.

Another strength is the reporting of novel risk factors and their impact, both in terms of relative and absolute risks. However, for rare complications, risk factor groups with few episodes yielded broad confidence intervals in the bivariate analysis, and the adjustment for other risk factors with small outcome numbers must therefore be interpreted with caution. However, the incidence rate per 10 000 episodes shows that at least 'previous head injury, skull surgery or malformations' is probably an important risk factor clinicians should be mindful of, as unadjusted risk of serious infection is actually as high as 0.4% to 0.8% in this small group.

Conclusions

Complications of acute sinusitis are rare and rates remain stable, despite a significant decrease in antibiotic use and a shift to more narrow-spectrum antibiotics. We found no protective effect of high prescribing practices among GPs, but immunocompromised patients, and those with previous head injury and skull malformations emerged as important risk factors for serious complications. General recommendations in favour of limited antibiotic prescribing for acute sinusitis should be encouraged, except for high-risk patient groups.

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Transparency declarations

The authors declare that they have no competing interests. The data were provided by the Norwegian Directorate of Health, the Norwegian Institute of Public Health (NIPH) and Statistics Norway by permission. NIPH linked and anonymized the data, which cannot be shared publicly due to restrictions by the Norwegian Data Protection Authority.

Author contributions

G.H.F. and S.H. selected and applied for the data. M.S. and L.E. analysed the data and wrote the manuscript. G.H.F contributed to analysis and writing of manuscript. A.M.B., S.H. and J.S. contributed to conception of the work and interpretation of data, and revised the manuscript.

Supplementary data

Tables S1 and S2 are available as Supplementary data at *JAC* Online.

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