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Risk of pleural empyema in patients with schizophrenia: a nationwide propensity-matched cohort study in Taiwan

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ABSTRACT

Objective Thoracic infection and pneumonia are prevalent in patients with schizophrenia; however, it is unclear whether patients with schizophrenia are at an increased risk of developing pleural empyema.

Design A retrospective cohort study with propensity-matched cohorts with and without schizophrenia.

Setting Using the National Health Insurance Research Database of Taiwan.

Participants We identified 55 888 patients with schizophrenia newly diagnosed in 2000–2011 and same number of individuals without schizophrenia as the comparison cohort, frequency matched by propensity scores estimated using age, sex, occupation, income, urbanisation, year of diagnosis and comorbidities.

Primary outcome measures We assessed incident pleural empyema by the end of 2011 and used the Cox proportional hazards model to calculate the schizophrenia cohort to comparison cohort HR of pleural empyema.

Results The overall incidence of pleural empyema was 2.44-fold greater in the schizophrenia cohort than in the comparison cohort (4.39vs1.80 per 10 000 person-years), with an adjusted HR of 2.87(95% CI 2.14 to 3.84). Stratified analyses by age, sex, occupation, income, urbanisation and comorbidity revealed significant hazards for pleural empyema associated with schizophrenia in all subgroups.

Conclusions Patients with schizophrenia are at an increased risk of developing pleural empyema and require greater attention and appropriate support.

Strengths and limitations of this study

- This is the first nationwide propensity score-matched cohort study to evaluate the risk of pleural empyema in patients with schizophrenia.
- The National Health Insurance programme of Taiwan have covered >99% of 23.74 million people.
- Universal coverage reduces barriers to healthcare access for all citizens.
- The International Classification of Diseases, Ninth Revision, Clinical Modification algorithm was used to define diseases and an ad hoc committee was in charge to monitor the claims data to prevent errors and violation of confidentiality.
- The database does not provide detailed information on lifestyles and other psychosocial and environmental factors.
- Relevant clinical variables such as serum laboratory data and image reports were unavailable in the database.

INTRODUCTION

Patients with pleural empyema require prompt and timely treatments, such as antibiotic therapy, pleural space drainage, intrapleural fibrinolysis and/or surgery.[1 2] Approximately 60 000 cases of pleural empyema are diagnosed annually in the USA.[3] The condition is more prevalent in Taiwan, with the incidence rates ranging from 0.96 to 8.19 per 10 000 person-years.[4–6] Alcoholism, drug abuse, diabetes mellitus, immunocompromised status, neoplasm and pre-existent pulmonary disease or pleural effusion are risk factors for the development of pleural empyema.[7 8] Patients with pleural empyema and comorbid with chronic illness are at a poorer prognosis and a greater risk of mortality.[9 10]

Schizophrenia is a severe mental disorder, characterised by profound disruptions in thinking, affecting language, perception and the sense of self.[11] The hallmark symptom of schizophrenia is psychosis, such as experiencing auditory hallucinations and delusions.[12] Approximately 0.3%–0.7% of individuals are affected by schizophrenia during their lifetime, and thus, schizophrenia affects >21 million people worldwide.[13] People with schizophrenia are at a markedly increased risk of premature death. Despite elevated rates of suicide and other unnatural causes of death, most of the excess mortality

Table 1 Baseline characteristics compared between cohorts with and without schizophrenia

	Schizophrenia				
	No		Yes		
	n=55 888		n=55 888		Standardised difference
	n	%	n	%	
Age (years)					
20–49	43 651	78.1	44 679	79.9	0.045
50–64	7083	12.7	8654	15.5	0.081
≥65	5154	9.22	2555	4.57	0.18
Mean (SD)	38.7	16.2	38.9	13.4	0.015
Sex					
Women	27 036	48.4	26 796	48.0	0.009
Men	28 852	51.6	29 092	52.1	0.009
Occupation*					
Office worker	24 539	43.9	24 844	44.5	0.011
Labourer	17 604	31.5	17 499	31.3	0.004
Other	13 745	24.6	13 545	24.2	0.008
Monthly income†					
<15 000	25 221	45.1	24 985	44.7	0.008
15 000–19 999	23 266	41.6	23 696	42.4	0.016
≥20 000	7401	13.2	7207	12.9	0.01
Urbanisation level‡					
City	29 894	53.5	30 151	54.0	0.009
Rural area	25 994	46.5	25 737	46.1	0.009
Comorbidity					
Diabetes	2442	4.37	2485	4.45	0.004
Asthma	2204	3.94	2245	4.02	0.004
COPD	3168	5.67	3262	5.84	0.007
CLD	7134	12.8	7249	13.0	0.006
Cancer	430	0.77	417	0.75	0.003
SLE/RA/immune disorders	32	0.06	31	0.06	0.001
Organ transplant	7	0.01	7	0.01	0.000
Malnutrition	362	0.65	331	0.59	0.007
Obesity	719	1.29	724	1.30	0.001
Alcohol abuse	2922	5.23	2884	5.16	0.003
Drug abuse	1818	3.25	1986	3.55	0.017
Tobacco use disorder	843	1.51	789	1.41	0.008

*Other occupations include primarily retired, unemployed and low-income populations.
†1 new Taiwan dollar is equal to 0.03 US dollar.
‡The urbanisation level is categorised by the population density of the residential area into two levels: city and rural area.
CLD, chronic liver disease and cirrhosis; COPD, chronic obstructive pulmonary disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

has been attributed to cardiovascular disease, respiratory disease and other natural causes.[14]

Patients with schizophrenia have been associated with a higher risk of thoracic infections.[15–17] The risk of having pneumonia is threefold greater in patients with schizophrenia than in general population.[16 18] Unhealthy lifestyle, lack of self-care, poorer physical circumstances and health-risk activities may contribute to this condition.[13] Furthermore, patients with schizophrenia suffering from these infections may have poorer clinical outcomes, such as acute respiratory failure, the use of mechanical ventilation, intensive care unit admission and hospital death.[16 19] Thoracic infection and pneumonia greatly increase morbidity and mortality in patients with schizophrenia and seriously threaten the health of these patients. However, the association between schizophrenia and the occurrence of pleural empyema, an advanced and specific thoracic infection, remains unclear.

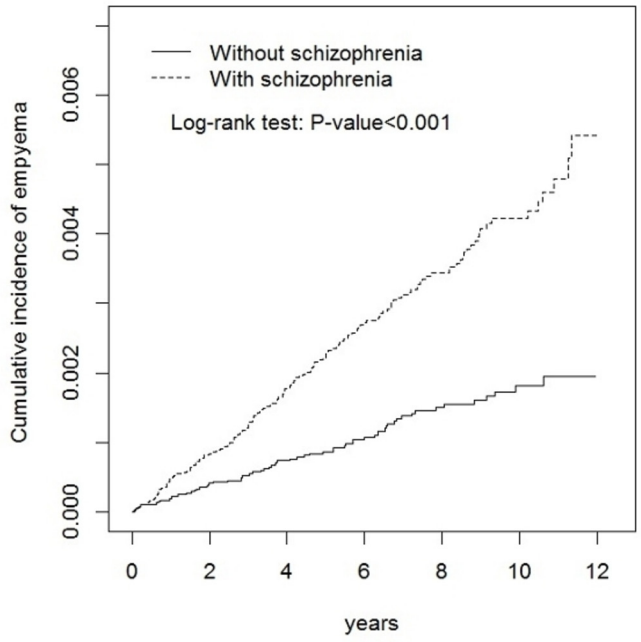

Figure 1 Cumulative incidence of pleural empyema in the schizophrenia cohort (dashed line) and the comparison cohort (solid line).

The National Health Insurance Research Database (NHIRD) in Taiwan is a nationwide database containing the medical claims data of 23 million residents. These reliable data have been used in studies on various disorders, including schizophrenia and pleural empyema.[6 20–22] The present study aims to investigate whether patients with schizophrenia are at an increased risk of subsequent occurrence of pleural empyema. In addition to estimate the incidence of pleural empyema in persons with and without schizophrenia, we also compared the 30-day mortality from pleural empyema between the two cohorts.

MATERIALS AND METHODS

Data source

The universal health insurance of Taiwan covers >99% of the Taiwanese population. Information on demographic status of insured people and their medical services received were available in the NHIRD obtained from the National Health Research Institutes. Patient identifiers were re-encoded before the release of NHIRD to protect the patient privacy.

Study population

Pleural empyema is one of the diseases among 30 categories of catastrophic illnesses classified in the insurance system, requiring long-term and/or extensive care, similar to cancers, end-stage major organ diseases, systemic autoimmune diseases and major mental disorders. After a careful peer-review process, patients registered with a catastrophic illness certificate are eligible for reduced financial burden for healthcare.

For the present study, we used a subset data of NHIRD, the Longitudinal Health Insurance Database 2000 (LHID2000), which contains health data of 1 million people randomly selected from 23 million people. From the database, we identified patients with schizophrenia aged 20 years and older newly diagnosed in 2000–2011 (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 295), without the history of pleural empyema (ICD-9-CM code 510) as the schizophrenia cohort. The comparison cohort were randomly selected from individuals without schizophrenia and pleural empyema from the LHID2000 file, using a 1:1 ratio, frequency matched by propensity scores. The propensity score was estimated to reduce bias from baseline variables, including age, sex, occupation, monthly income, urbanisation level and comorbidities of diabetes (ICD-9-CM code 250), asthma (ICD-9-CM code 493), chronic obstructive pulmonary disease (COPD) (ICD-9-CM code 496), chronic liver disease and cirrhosis (CLD) (ICD-9-CM code 571), cancer (ICD-9-CM codes 140–208), systemic lupus erythematosus (SLE)/rheumatoid arthritis (RA)/immune diseases (ICD-9-CM codes 710.0, 714.0, 279), organ transplant (ICD-9-CM code V42), malnutrition (ICD-9-CM codes 260–269), obesity (ICD-9-CM code 278.0), alcohol abuse (ICD-9-CM codes 291, 303, 305.0), drug abuse (ICD-9-CM codes 292, 304, 305.2, 305.9) and tobacco use disorder (ICD-9-CM code 305.1).

Patient and public involvement

This retrospective cohort study used the secondary data of insurance claims with anonymised identifications. Therefore, we considered that patients and public were not involved.

Outcome

The main outcome of this study was pleural empyema. Person-years indicated the sum of the follow-up time for all participants, and the follow-up time was defined as the time from the index date to the diagnosis of pleural empyema, death, withdrawal from the insurance or the end of 2011.

Statistical analysis

The two study groups were matched by the propensity scores, and the standardised difference was used to quantify differences in means or prevalence rates between schizophrenia and comparison cohorts for continuous or categorical variables, respectively. A standardised difference of 0.1 or less indicated a negligible difference between two cohorts.[23] The incidence rate of pleural empyema was estimated per 10 000 person-years. We used Poisson regression analysis to calculate the patients with schizophrenia to controls incidence rate ratio (IRR). The Kaplan-Meier method was then used to calculate and plot the cumulative incidence of pleural empyema for each cohort and the difference between the two curves was examined using log-rank test. Multivariable Cox proportional hazards regression analysis was used to estimate the adjusted HR (aHR) and 95% CI for the

Table 2 Incidence of pleural empyema, IRR and aHR measured for pooled study population by study cohort, sociodemographic status and comorbidities

	Event	PY	Rate†	IRR (95% CI)	aHR‡ (95% CI)
Schizophrenia					
No	67	371 984	1.80	1.00	1.00
Yes	164	373 435	4.39	2.44 (1.83 to 3.24)***	2.87 (2.14 to 3.84)***
Age (years)					
20–49	126	604 297	2.09	1.00	1.00
50–64	65	97 993	6.63	3.19 (2.36 to 4.30)***	2.86 (2.09 to 3.93)***
≥65	40	43 129	9.27	4.46 (3.13 to to 6.37)***	3.45 (2.29 to 5.19)***
Sex					
Women	52	360 369	1.44	1.00	1.00
Men	179	385 050	4.65	3.22 (2.37 to 4.39)***	3.52 (2.57 to 4.82)***
Occupation§					
Office worker	79	328 927	2.40	1.00	1.00
Labourer	75	232 762	3.22	1.34 (0.98 to 1.84)	0.94 (0.67 to 1.33)
Other	77	183 730	4.19	1.75 (1.28 to 2.39)***	1.19 (0.82 to 1.71)
Monthly income¶					
<15 000	113	328 597	3.44	2.00 (1.20 to 3.33)**	1.92 (1.10 to 3.33)*
15 000–19 999	101	318 118	3.17	1.84 (1.10 to 3.08)*	1.97 (1.15 to 3.36)*
≥20 000	17	98 704	1.72	1.00	1.00
Urbanisation level††					
City	97	399 858	2.43	1.00	1.00
Rural area	134	345 561	3.88	1.60 (1.23 to 2.08)***	1.46 (1.12 to 1.90)**
Comorbidity					
Diabetes					
No	197	718 779	2.74	1.00	1.00
Yes	34	26 641	12.8	4.67 (3.24 to 6.73)***	2.62 (1.77 to 3.87)***
Asthma					
No	202	719 903	2.81	1.00	1.00
Yes	29	25 516	11.4	4.06 (2.75 to 5.99)***	1.98 (1.27 to 3.07)**
COPD					
No	182	707 738	2.57	1.00	1.00
Yes	49	37 681	13.0	5.07 (3.69 to 6.95)***	2.01 (1.38 to 2.95)***
CLD					
No	186	655 200	2.84	1.00	1.00
Yes	45	90 219	4.99	1.76 (1.27 to 2.43)***	1.00 (0.71 to 1.42)
Cancer					
No	228	741 180	3.08	1.00	
Yes	3	4239	7.08	2.30 (0.74 to 7.19)	
SLE/RA/immune disorders					
No	231	745 075	3.10	1.00	
Yes	0	345	0.00	–	
Organ transplant					
No	231	745 312	3.10	1.00	
Yes	0	107	0.00	–	

Continued

Table 2 Continued

	Event	PY	Rate†	IRR (95% CI)	aHR‡ (95% CI)
Malnutrition					
No	223	741 266	3.01	1.00	1.00
Yes	8	4154	19.3	6.38 (3.15 to 12.9)***	3.60 (1.76 to 7.36)***
Obesity					
No	229	737 942	3.10	1.00	
Yes	2	7478	2.67	0.86 (0.21 to 3.46)	
Alcohol abuse					
No	209	714 370	2.93	1.00	1.00
Yes	22	31 049	7.09	2.42 (1.56 to 3.77)***	1.74 (1.10 to 2.74)*
Drug abuse					
No	220	724 902	3.03	1.00	
Yes	11	20 517	5.36	1.77 (0.96 to 3.24)	
Tobacco use disorder					
No	227	739 856	3.07	1.00	
Yes	4	5564	7.19	2.37 (0.88 to 6.39)	

*p<0.05, **p<0.01, ***p<0.001.
†Incidence rate per 10 000 PY.
‡Multivariable analysis controlling for age, sex, occupation, income, urbanisation and comorbidities of diabetes, asthma, COPD, CLD, malnutrition and alcohol abuse.
§Other occupations include primarily retired, unemployed and low-income populations.
¶1 new Taiwan dollar is equal to 0.03 US dollar.
††The urbanisation level is categorised by the population density of the residential area into two levels: city and rural area.
CLD, chronic liver disease and cirrhosis; COPD, chronic obstructive pulmonary disease; IRR, incidence rate ratio; PY, person-years; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

two groups. The multivariable model included variables of age, sex, occupation, monthly income, urbanisation level and comorbidities of diabetes, asthma, COPD, CLD, malnutrition and alcohol abuse. Data analysis for this study was performed using SAS statistical software (V.9.4 for Windows; SAS Institute Cary, North Carolina, USA). Statistical significance was determined at p<0.05.

RESULTS

Table 1 shows that schizophrenia and comparison cohorts were similar in distributions of baseline demographics and comorbidities with mean ages of 38.9 and 38.7 years, respectively.

After a mean follow-up time of 6.7 years in both cohorts, figure 1 shows that the cumulative incidence of pleural empyema was 0.34% higher in the schizophrenia cohort than in the comparison cohort. The incidence was 2.4-fold greater in patients with schizophrenia than in comparisons (4.39 vs 1.80 per 10 000 person-years), with an IRR of 2.44 (95% CI 1.83 to 3.24) or an aHR of 2.87 (95% CI 2.14 to 3.84) (table 2). The pooled data showed that the overall incidence increased with age, and higher in men than in women. Study population of low income and living in rural area were at higher risk of empyema. Individuals with comorbidities are also at increased risk of pleural empyema, including those with diabetes (aHR 2.62, 95% CI 1.77 to 3.87), asthma (aHR 1.98, 95% CI 1.27 to 3.07), COPD (aHR 2.01, 95% CI 1.38 to 2.95), malnutrition (aHR 3.60, 95% CI 1.76 to 7.36) and alcohol abuse (aHR 1.74, 95% CI 1.10 to 2.74).

Table 3 shows the incident empyema developed in the two cohorts by demographic status and comorbidity status. The incidence rates in each stratum were greater in the schizophrenia subgroups than in the comparison subgroups. The schizophrenia group to the comparison group IRRs and aHRs were significant for all strata. Significant IRRs ranged from 1.51 to 3.63 and significant aHRs ranged from 2.45 to 3.70. Comorbidity increased the incidence of pleural empyema in both cohorts for 3.74 and 3.51 per 10 000 person-years, respectively. The schizophrenia group to comparison group aHR showed a relatively greater impact for study individuals without comorbidities than those with comorbidity.

Table 4 shows a lower 30-day mortality rate from pleural empyema for the schizophrenic cohort than for the comparison cohort (6.71% vs 8.96%), with an adjusted OR of 0.95 (95% CI 0.30 to 3.01).

DISCUSSION

To the best of our knowledge, this is the first propensity-matched cohort study using population data to evaluate the risk of developing pleural empyema in patients

Table 3 Incidence of pleural empyema and schizophrenia cohort to comparison cohort IRR and aHR

	Schizophrenia							
	No			Yes				
	Event	PY	Rate†	Event	PY	Rate†	IRR (95% CI)	aHR‡ (95% CI)
Age (years)								
20–49	30	297 238	1.01	96	307 059	3.13	3.10 (2.06 to 4.67)***	2.77 (1.84 to 4.18)***
50–64	17	45 162	3.76	48	52 831	9.09	2.41 (1.39 to 4.19)**	2.55 (1.45 to 4.49)**
≥65	20	29 584	6.76	20	13 546	14.8	2.15 (1.16 to 3.99)*	2.68 (1.43 to 5.05)**
Sex								
Women	12	182 640	0.66	40	177 729	2.25	3.43 (1.80 to 6.53)***	3.70 (1.93 to 7.11)***
Men	55	189 345	2.90	124	195 706	6.34	2.18 (1.59 to 2.99)***	2.63 (1.90 to 3.65)***
Occupation§								
Office worker	20	164 783	1.21	59	164 144	3.59	2.99 (1.80 to 4.96)***	3.05 (1.83 to 5.11)***
Labourer	28	115 910	2.42	47	116 852	4.02	1.67 (1.04 to 2.66)*	2.50 (1.53 to 4.08)***
Other	19	91 291	2.08	58	92 439	6.27	3.01 (1.79 to 5.05)***	3.41 (1.97 to 5.93)***
Monthly income¶								
<15 000	28	162 081	1.73	85	166 516	5.10	2.95 (1.93 to 4.53)***	3.20 (2.07 to 4.94)***
15 000–19 999	35	158 330	2.21	66	159 788	4.13	1.87 (1.24 to 2.82)**	2.49 (1.62 to 3.82)***
≥20 000	4	51 573	0.78	13	47 131	2.76	3.63 (1.18 to 11.1)*	3.64 (1.17 to 11.4)*
Urbanisation level††								
City	24	199 255	1.20	73	200 604	3.64	3.03 (1.91 to 4.80)***	3.67 (2.29 to 5.90)***
Rural area	43	172 729	2.49	91	172 832	5.27	2.11 (1.47 to 3.04)***	2.45 (1.69 to 3.56)***
Comorbidity‡‡								
No	26	283 934	0.92	96	276 098	3.48	3.81 (2.47 to 5.87)***	3.73 (2.42 to 5.76)***
Yes	41	88 050	4.66	68	97 338	6.99	1.51 (1.02 to 2.22)*	2.27 (1.50 to 3.42)***

*p<0.05, **p<0.01, ***p<0.001.
†Incidence rate per 10 000 PY.
‡Multivariable analysis controlling for age, sex, occupation, income, urbanisation and comorbidities of diabetes, asthma, chronic obstructive pulmonary disease, chronic liver disease and cirrhosis, malnutrition and alcohol abuse.
§Other occupations include primarily retired, unemployed and low-income populations.
¶1 new Taiwan dollar is equal to 0.03 US dollar.
††The urbanisation level is categorised by the population density of the residential area into two levels: city and rural area.
‡‡Individuals with any comorbidity of diabetes, asthma, chronic obstructive pulmonary disease, chronic liver disease and cirrhosis, cancer, systemic lupus erythematosus/rheumatoid arthritis/immune disorders, organ transplant, malnutrition, obesity, alcohol abuse, drug abuse and tobacco use disorder were classified into the comorbidity group.
IRR, incidence rate ratio; PY, person-years.

with schizophrenia. The risk of pleural empyema is more than twofold greater than those without schizophrenia. Stratified analyses by age, sex, occupation, income, urbanisation and presence of comorbidities also showed that the incidence rates of pleural empyema were consistently higher in the schizophrenia cohort than in comparisons, and the aHRs for pleural empyema associated with schizophrenia were significant for all subgroups. In addition, the incidences of pleural empyema were higher in older people than in young people, higher in men than in women and in individuals with comorbidities than in those without comorbidities. These findings are in accordance with the general concepts.

Table 4 30-day mortality from pleural empyema in cohorts with and without schizophrenia and OR of mortality

	Schizophrenia	
	No	Yes
Deaths/events	6/67	11/164
Mortality per 100	8.96	6.71
Crude OR (95% CI)	1 (reference)	0.73 (0.26 to 2.06)
Adjusted OR* (95% CI)	1 (reference)	0.95 (0.30 to 3.01)

*Multivariable analysis controlling for age, sex, occupation, income, urbanisation and comorbidities of diabetes, asthma, chronic obstructive pulmonary disease, chronic liver disease and cirrhosis, malnutrition and alcohol abuse.

The mechanism associating schizophrenia with the risk of developing pleural empyema remains largely unknown. Smoking is a well-known behaviour prevalent in patients with schizophrenia and has association with the development of pleural empyema. In addition, an unhealthy lifestyle, lack of self-care, poorer physical circumstances and health-risk activities may contribute to

this condition.[15] Frequent medical visits and a prolonged hospital stay may also be contributing factors.[18] Moreover, patients with schizophrenia may reside in a long-term care facility. Pneumonia in these residents has been defined as a specific type, healthcare-associated pneumonia (HCAP).[24] The pathogens of HCAP are often multidrug-resistant bacteria, which is a potential risk factor for developing pleural empyema. Furthermore, patients with schizophrenia are at a higher risk of developing swallowing disorders, leading to aspiration pneumonia.[25] Pleural empyema is easily caused by the aspiration of mixed bacterial flora and other materials from the oropharyngeal cavity and even from the upper gastrointestinal tract. In addition, previous studies have suggested that the use of second-generation antipsychotics, such as clozapine, may increase the risk of pneumonia in patients with schizophrenia.[26–28] Clozapine has been associated with agranulocytosis, sialorrhea and impaired swallowing function; patients with this medication may thus have a greater risk for pneumonia.[29]

Patients with schizophrenia are at a markedly increased risk of premature death, particularly from thoracic infection and pneumonia. A large-scale study in the USA showed that the overall mortality rate was 3.7 times higher in patients with schizophrenia than in the general population.[30] The increased mortality was mainly from respiratory diseases: 9.9 times higher from COPD and 7.0 times higher from influenza and pneumonia. A study in Taiwan showed that patients with schizophrenia experienced a 3.09-fold increased risk of developing pneumonia, with an aHR of 1.39 for deaths from pneumonia.[16] In a Romanian study, autopsy findings in sudden unexpected deaths in inpatients with schizophrenia revealed that the top three specific causes were myocardial infarction (52.9%), pneumonia (11.8%) and airway obstruction (7.8%).[31] However, the present study showed no significant disparity in the 30-day mortality between the schizophrenic and comparison cohorts.

The strength of this study was using a large nationwide data to perform the propensity-matched evaluation assessing the pleural empyema risk for patients with schizophrenia. Confounding bias has been thus reduced in this inexpensive retrospective cohort study. The National Health Insurance programme has covered >99.0% of the Taiwanese population. The universal health coverage reduces barriers to healthcare access for all citizens, regardless of their socioeconomic background and/or residential location.[32] The present study reflected a 'real-world' scenario by using the claims data, as schizophrenia, pleural empyema and comorbidities were diagnosed at clinics during medical consultations.

There are several limitations that should be considered when interpreting the study findings. First, we used the ICD-9-CM algorithm to define schizophrenia, pleural empyema and comorbidities. The diagnosis of schizophrenia is mostly accurate because it is a disease with catastrophic certificate. All other diagnoses depended on the competence of clinical physicians. An ad hoc committee established by the insurance authority was in charge of evaluating the claims data to prevent errors and violations. In addition, only the disease with at least two diagnosis codes identified within a year was included to increase the validity and accuracy. Second, the information on smoking, drinking, nutrition and other psychosocial and environmental factors were unavailable, which may affect the risk of pulmonary infections and consequent complications. Instead, we used the tobacco use disorder and alcohol abuse to substitute smoking and drinking, respectively, in the multivariable analysis for adjustment. Similarly, malnutrition is a crucial factor for pleural empyema development; however, it is unlikely to be identified adequately by relying on recorded diagnoses. In addition, institutional residence is a possible source of multiple-resistant infection, but the relevant data were unavailable. Furthermore, other clinical variables such as serum laboratory data, image reports and culture results were not available to our study.[33]

CONCLUSION

This study provides evidence that patients with schizophrenia are at an elevated risk of developing pleural empyema. The risk increases further for those with comorbidity. Patients with schizophrenia suffering from pneumonia or other thoracic infection need close surveillance for potential risk of development of pleural empyema and disease-related mortality.

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Contributors T-CS, C-HC, Y-JH, T-CC, C-YT and C-MS conceived and designed the study. T-CH, C-MS and W-HH provided administrative support. T-CS, C-LL, C-MS and F-CS analysed and interpreted the data. T-CS, C-LL, C-MS and F-CS developed and revised the manuscript. All authors were involved in collection and assembly of data. All authors approved the final version of the manuscript to be published.

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