Title page

Title: Population-based estimates of the burden of pneumonia hospitalizations in Hong Kong, 2011-2015

Authors and affiliations:

Xue Li, Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China. Email: <u>sxueli@hku.hk</u>

Joseph E Blais, Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China. Email: <u>jblais@hku.hk</u>

Ian CK Wong, 1. Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China; 2. Research Department of Practice and Policy, UCL School of Pharmacy, London, UK. Email: <u>wongick@hku.hk</u>

Anthony WY Tam, Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China. Email: <u>awtam@hku.hk</u>

Benjamin J Cowling, WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China. Email: <u>bcowling@hku.hk</u> Ivan FN Hung, 1.Carol Yu Centre for Infection and Division of Infectious Diseases, State Key Laboratory of Emerging Infectious Diseases, Department of Microbiology, University of Hong Kong, Queen Mary Hospital, Hong Kong Special Administrative Region, China; 2 Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong Special Administrative Region, China. Email: <u>ivanhung@hku.hk</u>

Esther WY Chan, Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong Special Administrative Region, China. Email: <u>ewchan@hku.hk</u>

Corresponding author:

Dr Esther WY Chan

Associate Professor

Centre for Safe Medication Practice and Research, Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, University of Hong Kong

2/F, 21 Sassoon Road, Li Ka Shing Faculty of Medicine, Laboratory Block, Hong Kong SAR, China

Tel: (852) 3917 9029

Fax: (852) 2817 0859

Email: ewchan@hku.hk

Abstract

Purpose: Up-to-date data on the burden of disease are important to identify patients with unmet needs and to optimize healthcare resources. We aimed to characterize the burden of pneumonia hospitalizations in Hong Kong and inform targeted healthcare policies for pneumonia control in the era of global ageing.

Methods: This was a population-based study using a territory-wide administrative electronic health record system that covers all public hospitals of Hong Kong. Patients admitted to public hospitals, from 2011 to 2015, with a diagnosis of pneumonia at discharge were identified based on the International Classification of Diseases-Ninth Revision-Clinical Modification codes (480-486 and 487.0). Incidence, inpatient case-fatality, all-cause fatality, 28-days readmission, hospital length of stay, and healthcare costs were assessed for seven age strata.

Results: We identified 323,992 patients (median age 80 years, 44.4% female) with hospitalized pneumonia (organism unspecified: 84.2%; bacterial pneumonia: 12.3%; viral pneumonia: 2.5%; others: 1.0%). Annual incidence was 955.1 per 100,000 population, with a 10.6% decrease from 2011 to 2015. Case-fatality, all-cause fatality and 28-days readmission risks were 13.8%, 21.6%, and 19.5% respectively. The average hospital length of stay was 14.1 days with corresponding direct costs of \$9348 USD per episode in the monetary value of 2015. Individuals aged \geq 65 years accounted for over 75% of pneumonia-related hospitalizations, 90% of deaths and the majority of healthcare costs.

Conclusions: Hospitalized pneumonia represents a considerable health and economic burden in Hong Kong, especially in older adults. The study provides a population-level baseline estimate for further cost-effective evaluation of targeted strategies for pneumonia control.

Key words: pneumonia admission, burden of disease, healthcare resource, elderly care, population ageing

BACKGROUND

Pneumonia, the most common type of lower respiratory infection, is the leading causes of death for children under five, and is associated with considerable morbidity and economic loss worldwide [1]. As one of the most densely populated places in the world located in a subtropical climate, Hong Kong faces a large threat from infectious diseases, including pneumonia [2]. From 2012 to 2016, pneumonia was the second leading cause of death in Hong Kong and pneumonia-related admissions have continued to increase during the last decade [3]. There are growing concerns from the public and healthcare professionals about antimicrobial resistance, pneumococcal serotype replacement, and antimicrobial treatment failure associated with the management of pneumonia [4, 5].

Immunization against pneumococcus, *Haemophilus influenzae* type b, and influenza are effective ways to prevent pneumonia. In Hong Kong, the Childhood Immunization Program was launched in 2009 to offer free pneumococcal conjugate vaccine (PCV) to children under two years of age (PCV7 in September 2009; PCV10 in October 2010; PCV13 in December 2011) [6]. Pneumococcal and seasonal influenza vaccines are provided at no charge to older adults (\geq 65 years) and persons with underlying medical conditions who attend public health clinics. Various high-risk groups, including children (6 months to 12 years), older adults (\geq 65 years) and individuals of all ages with underlying medical conditions, are eligible for governmentsubsidized pneumococcal and influenza vaccinations in private medical clinics. However, the

uptake of seasonal influenza vaccine in the general population is low and many physicians do not actively recommend pneumococcal vaccinations to older adults [7, 8].

Up-to-date data on the burden of disease is important for identifying individuals with unmet health needs, evaluating healthcare policies, and guiding evidence-based resource allocation decisions. The burden of pneumonia has been frequently reported in Western countries, but data are limited in Asia [9-12]. Previous research in Hong Kong has focused on the incidence of pneumonia in children under five years of age (published data current as of 2005) [13, 14], the mortality trends from pneumonia [15, 16], the emergence of resistant pathogens, pneumococcal serotype replacement, and the patient and environmental factors associated with pneumonia. Because Hong Kong has the world's highest life expectancy (male: 81.2 years; female: 87.3 years) and a rapidly ageing population, a current assessment of the disease burden and its implications for healthcare resource utilization is required. This study aimed to address the identified gaps regarding the burden of hospitalized pneumonia in Hong Kong from 2011 to 2015.

METHODS

Data source

The Clinical Data Analysis and Reporting System (CDARS) is a territory-wide electronic health record database managed by the Hospital Authority of Hong Kong. It contains the health records from all public hospitals, which serve the 7.3 million population of Hong Kong. Patient-specific data, including demographic and prescription information, diagnosis, procedures, laboratory tests, date of consultation, and admission and discharge information, are imported daily into CDARS

for research and audit purposes. A unique and anonymous identifier is assigned to each patient to protect patient privacy and facilitate data retrieval. CDARS has been used for a number of highquality population-based studies and data validation demonstrated high coding accuracy for cardiovascular, gastrointestinal, and pneumonia diagnoses [13, 17].

Study design and patient identification

This was a population-based cross-sectional study. Hospitalized patients with a discharge diagnosis of pneumonia (principal, secondary, or others) recorded in CDARS, between 1 January 2011 and 31 December 2015, were identified based on the International Classification of Diseases-Ninth Revision-Clinical Modification (ICD-9-CM) codes (480-486 and 487.0). Pneumonia cases included any type of pneumonia caused by a specified or an unspecified pathogen regardless of the source of infection (community- or hospital-acquired). The index date was the first date of hospital admission with a diagnosis code for pneumonia. All diagnoses recorded from ten years prior to or on the index date were used to define medical conditions (see Online Resource 1).

The Infectious Diseases Society of America/American Thoracic Society guidelines define community-acquired pneumonia (CAP) as pneumonia acquired outside a hospital or long-term care facility, occurring within 48 hours of hospital admission [18]. International and local guidelines recommend initiating appropriate antimicrobial therapy as soon as possible for patients with CAP [2, 18]. Based on the British National Formulary categories for relevant antimicrobials (see Online Resource 2), we analyzed antimicrobial prescriptions within 48 hours of hospital admission to estimate a patient's likelihood of CAP. Organisms cultured from blood, sputum and throat samples during the hospitalization were also analyzed to confirm the presence of positive pathogens.

Outcome measurements

The disease burden was estimated for the entire population and stratified into seven age groups (0-4, 5-19, 20-49, 50-64, 65-74, 75-84 and ≥85 years). Clinical burden measurements included cumulative incidence and inpatient case-fatality. Age-specific incidences were calculated as the total number of cases divided by the age-matched Hong Kong census population for each year. Patients with multiple hospital admissions were considered as separate cases if the admission intervals were greater than or equal to two days. Admission records from the same patient, but with admission interval less than two days, were considered a single case of pneumonia. To adjust for demographic changes, we standardized the crude incidence by direct method using the Hong Kong population in 2015 as the reference population. The case-fatality analysis was restricted to death from pneumonia within the same hospital admission, defined as International Classification of Diseases-Tenth Revision-Clinical Modification (ICD-10-CM) codes J12-J18. Measurements of healthcare resource utilization included inpatient all-cause fatality, 28-day readmission hospital length of stay (LOS) and direct costs par apisode [19, 20] All cause

readmission, hospital length of stay (LOS), and direct costs per episode.[19, 20] All-cause fatality was calculated as the number of inpatient deaths from any cause divided by the number of cases. Direct costs considered the costs associated with hospitalization and follow-up visits to a specialist outpatient clinic after discharge. Unit costs, including daily charges of hospitalization and specialist consultation fees per visit, were referenced from the public charges of health service in the Hospital Authority in the value of 2015. Based on local clinician practice, we assumed discharged patients would have one follow-up consultation attributable to pneumonia. Total costs were calculated by multiplying the unit cost with the duration or frequency of services used. Costs were first calculated in Hong Kong Dollars and converted to US dollars in 2015 (1USD = 7.8 HKD).

Statistical analysis

Results were reported according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for cross-sectional studies [21] and expressed as frequencies, proportions, means with standard deviation (SD), median with interquartile ranges, and estimates with 95% confidence intervals where appropriate. Two-way ANOVA was conducted to identify the high risk population among different age and sex groups. A 2-sided P value of less than 0.05 was considered as statistically significant. *R* version 3.3.1 (*R* Foundation for Statistical Computing, Vienna, Austria) and Microsoft Excel 2016 were used for data analysis and plots generations.

RESULTS

Patient characteristics

From 2011 to 2015, we identified 323,992 patients [median age: 80 (interquartile range: 22) years; female: 44.4%] hospitalized with any diagnosis of pneumonia at discharge, 69.4% (225 031/323 992) of which had pneumonia as the primary diagnosis (Table 1). When grouped according to age, the majority of the patients were older adults (\geq 65 years; 75.8%) followed by adults (20-64 years; 13.6%), and children (0-19 years; 10.6%). There were more males in most of the age groups, especially for the 50-84 years group. In the very old patient group (\geq 85 years), the majority of patients (59.2%) were females. Likely due to the longer life expectancy in females (87.3 vs. 81.3 years in 2016) and the sex differences in the age structure of the Hong Kong population (female : male ratio of 1.88 in 2016.)[22] The most prevalent medical conditions included chronic heart disease (26.8%), chronic lung disease (21.5%), diabetes

(21.0%), malignant neoplasms of solid organs (11.7%), and chronic renal failure (11.7%) (Table 1).

Based on ICD-9-CM diagnosis codes, 84.2% of patients had pneumonia with unspecified organism, 12.3% had bacterial pneumonia (pneumococcal pneumonia: 0.7%; other bacterial pneumonia: 11.6%) and 2.5% had viral pneumonia (viral pneumonia: 1.7%; influenza with pneumonia: 0.8%) (pneumonia type distribution is detailed in Online Resource 3). The proportion of patients with any immunocompromised condition (disease of white blood cells, human immunodeficiency infection, solid organ transplantation and peripheral blood and stem cell transplant, and malignant neoplasm of lymphatic and hematopoietic tissue) accounted for 1.5% or less of the overall cohort (Table 1).

Antimicrobial drugs were prescribed to 95.1% (308,257/323,992) of patients during their hospitalization period and 94.2% (290,381/308,257) of these patients were prescribed antimicrobial treatment within 48 hours of admission. Commonly prescribed antimicrobials were broad-spectrum penicillins (51.9%), macrolides (14.5%), cephalosporins (9.9%), antipseudomonal penicillins (7.5%), quinolones (4.4%) and antiviral drugs for influenza (4.1%). CDARS records indicated that 20.5% (66,502/323,992) of patients had at least one positive culture result obtained during hospitalization. Commonly isolated bacterial pathogens were *Pseudomonas aeruginosa* (18.4%), *Staphylococcus aureus* (13.2%) and *Haemophilus influenzae* (11.5%) (Fig. 1a), which closely matched the bacterial pathogens isolated in adults (20-64 years) and older adults (\geq 65 years) (Figs. 1c and 1d). In children, the top three isolated organisms were *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa* (Fig. 1b).

Burden of disease

The crude incidences of hospitalized pneumonia fluctuated between 831.8-926.6 per 100,000 population over the study period. Standardized by the 2015 Hong Kong population, the average incidence per 100,000 population was 955.1 with a decrease from 1024.4 to 915.8 from 2011 to 2015 (Fig. 2a). In children aged 5-19 years, the annual incidence was consistently below 250 per 100,000 population; however, the estimates for children 0-4 years was higher, reaching 1,579 per 100,000 population in 2014 (Fig. 2b). The annual incidence for adults aged 20-49 years and 50-64 years was stable at 100 and 400 per 100,000 population (Fig. 2c). Adults aged 65-74 years had a similar incidence (1,312-1,740 per 100,000 population) as that for children aged 0-4 years. Adults aged 75-84 and \geq 85 years had the highest incidence among all age groups; 3-4 times (75-84 years) and 10-12 times (\geq 85 years) higher than the estimate for children aged 0-4 years (Fig. 2d). Two-way ANOVA showed significant differences in the incidence of hospitalized pneumonia among age groups (P < 0.01), sex groups (P < 0.01) and their interactions (age*sex, P<0.01). For patients aged more than 50 years old, males are at higher risk of hospitalized pneumonia, particularly for the very old male patients (\geq 85 years) (Online Resource 4).

Case-fatality risk increased with age (Fig. 3). The risk of in-hospital death from pneumonia was 13.8% in adults aged ≥ 65 years, and this group accounted for 93.4% of deaths from pneumonia in the study. No pneumonia deaths were recorded in children aged 0-4 years and the case-fatality was less than 0.5% in children aged 5-19 years. In younger adults, case-fatality risks ranged from 3-7%. In older adults, case-fatality was generally above 10%. Notably, the case-fatality risk was 14.1-16.1% for adults aged 75-84 years and it rose to 19.2-22.6% for individuals aged ≥ 85 years.

The overall risk of inpatient death from any cause was 21.6%, with 89.7% of deaths occurring in older adults (Table 2). The 28-days readmission was 19.5% with a similar contribution from older adults. Both all-cause fatality and readmission risks increased with age. Overall, the

average LOS was 14.1 days with corresponding direct costs of \$9,348 per episode. Mean hospital LOS was longest in patients aged 50-64 years (16.4 days), followed by patients aged 65-74 years (15.9 days). LOS in patients aged ≥75 years decreased slightly, likely due to more deaths while admitted. By summing up the individual costs, annual healthcare expenditure for the management of hospitalized pneumonia was estimated to be \$605.4 million (Table 2). In general, no apparent increasing or decreasing trend of average hospital LOS and readmission were observed for all the age groups in 2011-2015 (Online Resource 5 and 6). Given the average LOS is sensitive to outliers, we also plotted the median LOS as the indicator of healthcare quality. We found a stable median hospital LOS for pneumonia hospitalization over five years that implied the consistent quality of healthcare during the study period.

DISCUSSION

In the era of targeted pneumococcal and influenza vaccination, the burden of hospitalized pneumonia remains high in Hong Kong, with a standardized incidence of 955.1 per 100,000 population and a stable case-fatality close to 14%. In contrast to global data which places pneumonia as the leading cause of death in children under five [23], we did not identify any deaths from pneumonia for children under five years during the study period. Instead, the major disease burden was among older adults, as has been reported in other developed countries [9-11, 24]. Incidence, case-fatality, all-cause fatality and readmission risks all increased with age. In the US, the PCV vaccine has contributed to a sustained decrease in pneumonia-related hospitalizations in children and adults since its introduction in 2000 through 2009 [11]. However, our estimates in Hong Kong showed no apparent decline in the overall crude incidence of pneumonia-related hospitalizations in the post-PCV period. Rather, the absolute total number of

patients diagnosed with pneumonia increased from 64,312 in 2011 to 66,872 in 2015. Individuals aged \geq 65 years accounted for over 75% of pneumonia-related hospitalizations and 90% of deaths. The incidence of pneumonia admission was alarmingly high in the very old adults (\geq 85 years) – tenfold greater than the estimates for children under five years.

Moreover, the clinical burden of pneumonia translates into a correspondingly large economic cost. The disease-attributable direct costs are 4.5 times the average per capita healthcare expenditure in Hong Kong (\$2014). At the population-level, annual healthcare expenditure on pneumonia accounted for 7.8% of the total public expenditure on health (\$6.8 billion) [25]. Driven by older adults, approximately 20% of patients in our analysis died while in hospital and another 20% were readmitted within 28 days of discharge. Compared with other studies, the longer pneumonia-related LOS (14.1 vs. 6-12 days) may be explained by the older median age of our study population (80 years) –a reflection of longer life expectancy in Hong Kong [12, 26]. Although describing the cause of readmission was not an objective of this study, the high readmission rates align with the literature describing the complexities of pneumonia management and the increased frailty in older adults after a diagnosis of pneumonia [27, 28].

Hong Kong now faces a demographic challenge with a rapidly ageing population. The proportion of the population aged \geq 65 years increased from 8 to 16% in the last three decades, and is expected to double to 32% by 2036 [29]. However, there is limited regional emphasis on maintaining population health and well-being to tackle the challenge of ageing. The current disease burden of pneumonia is likely to increase significantly in the coming decades if no effective preventative interventions are taken. Regions with an ageing population similar to Hong Kong may face a soaring demand for health services and policy-makers should develop an adequate response plan [30, 31].

Avoiding pneumonia-related hospitalization is crucial for saving healthcare costs. Our results underline the importance of pneumonia control in older adults as key to improving clinical and economic outcomes associated with the disease. Among our target patient cohort aged 50-74 years, approximately 20% of them had a disease history of malignant neoplasm of solid organs. This fact further supports that patients with an immunocompromising health condition are at higher risk of pneumonia admission that need appropriate preventive and therapeutic interventions and close clinical monitoring while in hospital.

Preventative interventions have the potential to save health resources in the long-term. Pneumococcal and seasonal influenza vaccines are available to the Hong Kong public and are funded or subsidized by the government for high-risk populations. However, none of these vaccine programs are universally subsidised, which may contribute to low vaccine uptake among the general public [8]. In addition to the longest life expectancy in the world, Hong Kong is also well-known for its high population density and subtropical climate, both of which potentially exacerbate the emergence and transmission of infectious diseases. Considering this distinct sociodemographic and geographic environment, whether current vaccine policies are adequate for pneumonia control in Hong Kong should be carefully evaluated. An immunization strategy with extended target populations needs to be discussed when immunogenicity and vaccine effectiveness in older adults is confirmed. Developing multidimensional strategies for targeted pneumonia control is warranted in the era of epidemiological transitions.

Only 20.5% of the patients with a pneumonia-related hospitalization had a bacterial pathogen identified by a laboratory culture result. This is consistent with routine clinical practice in that a microbiological diagnosis of CAP occurs about 20% of the time [32] and also roughly matches patient identification based on ICD-9-CM codes in the current analysis (84.5% of patients were

diagnosed with pneumonia with unspecified organism). Interpretation of these results needs to be taken cautiously. Clearly, the results contain several organisms implicated in nosocomial pneumonia, as suggested by the proportion of isolates for *Pseudomonas aeruginosa* and *Staphylococcus aureus* (inclusive of methicillin-resistant *Staphylococcus aureus*). However, the results do not represent the overall etiological profiles of the targeted patients given the majority is unknown. Commonly identified pathogens may be resistant to several antimicrobials, and future research into real-time and cost-effective diagnostic tests in public hospital inpatient settings could help clinicians rapidly determine the causal pathogen and guide appropriate antimicrobial therapy, thereby ensuring treatment success [33]. Improving the microbiologic diagnosis of pneumonia is another strategy for optimal disease control and could reduce unwarranted antimicrobial exposure.

We acknowledge the study limitations. First, our target population is hospitalized patients using the public healthcare system, so we may have underestimated the true disease burden of all-cause pneumonia given the lack of data from outpatient, nursing home, and private hospital settings. However, it is well recognized that inpatient care utilizes the majority of healthcare resources associated with pneumonia [12] and the database used in this study covers more than 70% of the total hospital beds in Hong Kong [25] which suggests that the major burden of pneumonia was captured. Secondly, we confronted the challenges of differentiating various types of pneumonia (CAP, hospital-acquired pneumonia, aspiration pneumonia and pneumonia in immunocompromised hosts) from the ICD-9-CM diagnosis codes. In our analysis, patients with immunocompromised conditions represented a very small subset ($\leq 1.5\%$) of the cohort, and approximately 90% of patients initated antimicrobial therapy within 48 hours of hospital admission. Based on this fact, we suspect that most of the included patients are representative of

hospitalizations for CAP rather than other types of pneumonia. Thirdly, the study period was relatively short, thus we did not conduct a time-trend analysis to statistically test the incidence changes in response to time. We were further limited by the fact that the vaccination status of each individual was unknown and bacterial pathogens were confirmed in only 20% of the patients. Future studies with a longer duration, detailed laboratory results, and vaccination status among the representative population are warranted to estimate the pattern of changes in disease burden, and to elucidate the distribution of pneumonia etiologies.

CONCLUSIONS

In summary, hospitalized pneumonia, especially in adults aged 65 years or above, represents a considerable disease burden in Hong Kong. Developing multidimensional cost-effective strategies for the prevention and management of pneumonia in older adults should be an important public health priority in this era of global ageing. Findings from this study provide a baseline estimate of the burden of pneumonia hospitalizations for further evaluation of targeted strategies for pneumonia control.

DECLARATIONS

Ethical approval and consent to participate

The study was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster (reference number: UW16-327). Informed patient consent was waived as the data used in this study were de-identified.

Consent for publication

Not applicable.

Availability of data and material

The study protocol is available online from the website of the Centre for Safe Medication Practice and Research, the University of Hong Kong (<u>http://www.pharma.hku.hk/sweb/CSMPR/</u>). The datasets used and analyzed in the study are available from the corresponding author upon on reasonable request, and up to the approval from the University of Hong Kong and the Hong Kong Hospital Authority.

Competing interests

EWC has received the Early Career Scheme and the General Research Fund from the Hong Kong Research Grants Council; Health and Medical Research Fund from the Food and Health Bureau of Hong Kong; internal funding from The University of Hong Kong; and research funding from Bristol-Myers Squibb, Pfizer, and Janssen, all unrelated to the current work. BJC has received research funding from Sanofi Pasteur, and consulting fees from Roche, all unrelated to the current work. The other co-authors declare no conflict of interest.

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Authors' contributions

Conception and design of the work: ICW, BJC, IFH and EWC; data collection and analysis: XL and AWT; results interpretation: all authors; drafting the article: XL; critical revision of the article: XL, JB, BJC, IFH, EWC; study supervision: EWC. Final approval of the version to be published: all authors.

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Online Resources

File name: ESM_1

File format: .docx

Title of data: ICD-9-CM Diagnostic/Procedure Codes for Identifying Medical Conditions

Description of data: List of International Classification of Diseases-Ninth Revision-Clinical

Modification (ICD-9-CM) codes used for identifying the medical conditions of target patients

File name: ESM_2

File format: .docx

Title of data: British National Formulary Categories for Relevant Antimicrobials (5.1-5.3)

Description of data: List of British National Formulary Categories for identifying the

antimicrobial treatments of target patients

File name: ESM_3

File format: .docx

Title of data: Pneumonia Type Distribution Based on ICD9-CM Code

Description of data: Detailed pneumonia type distribution among the overall all-cause pneumonia

File name: ESM_4

File format: .tiff

Title of data: Incidence of hospitalized pneumonia by age and sex

Figure legend:

Middle line in the box: median value; Upper and lower line of the box: interquartile ranges

File name: ESM_5

File format: .tiff

Title of data: Average length of stay of hospitalized pneumonia by age, 2011-2015

File name: ESM_6

File format: .tiff

Title of data: Readmission of hospitalized pneumonia by age, 2011-2015

Age group (years)	0-4	5-19	20-49	50-64	65-74	75–84	85+	Total
Demographics [number (%)]								
Number of patients	18 321	11 337	16 207	32 873	39 072	94 768	111 414	323 992
	(5.6)	(3.5)	(5.0)	(10.1)	(12.1)	(29.3)	(34.4)	(100)
Female	8313	5829	7420	10 827	10 893	34 745	65 970	143 997
	(45.4)	(51.4)	(45.8)	(32.9)	(27.9)	(36.7)	(59.2)	(44.4)
Medical conditions [number (%)]								
Chronic heart disease	493	204	891	4843	9444	30 264	40 743	86 882
	(2.7)	(1.8)	(5.5)	(14.7)	(24.2)	(31.9)	(36.6)	(26.8)
Chronic liver disease	5	15	344	1466	1392	2382	1735	7339
	(0)	(0.1)	(2.1)	(4.5)	(3.6)	(2.5)	(1.6)	(2.3)
Chronic lung disease	1 017	783	893	4999	9614	26 213	25 981	69 500
	(5.6)	(6.9)	(5.5)	(15.2)	(24.6)	(27.7)	(23.3)	(21.5)
Chronic renal failure	70	114	965	3368	4849	13 530	14 940	37 836
	(0.4)	(1.0)	(6.0)	(10.2)	(12.4)	(14.3)	(13.4)	(11.7)
Congenital heart disease	893	417	180	188	166	205	160	2209
	(4.9)	(3.7)	(1.1)	(0.6)	(0.4)	(0.2)	(0.1)	(0.7)
Congenital immunodeficiency	33	38	70	89	41	30	36	337

Table 1. Characteristics of patients hospitalized with pneumonia in Hong Kong, 2011-15

	(0.2)	(0.3)	(0.4)	(0.3)	(0.1)	(0)	(0)	(0.1)
Diabetes	1	19	913	5572	10 440	26 518	24 470	67 933
	(0)	(0.2)	(5.6)	(17.0)	(26.7)	(28.0)	(22.0)	(21.0)
Disease of white blood cells	163	159	323	792	562	562	340	2901
	(0.9)	(1.4)	(2.0)	(2.4)	(1.4)	(0.6)	(0.3)	(0.9)
Human immunodeficiency virus	2	3	135	89	44	35	9	317
infection	(0)	(0)	(0.8)	(0.3)	(0.1)	(0)	(0)	(0.1)
Malignant neoplasm of lymphatic and	34	95	340	987	984	1439	896	4775
hematopoietic tissue	(0.2)	(0.8)	(2.1)	(3.0)	(2.5)	(1.5)	(0.8)	(1.5)
Malignant neoplasm of solid organs	61	155	1593	7014	7180	12 424	9496	37 923
	(0.3)	(1.4)	(9.8)	(21.3)	(18.4)	(13.1)	(8.5)	(11.7)
Nephrotic syndrome	8	22	180	558	587	699	434	2488
	(0)	(0.2)	(1.1)	(1.7)	(1.5)	(0.7)	(0.4)	(0.8)
Sickle cell diseases and other	189	241	430	957	1157	2943	3618	9535
hemoglobinopathies	(1.0)	(2.1)	(2.7)	(2.9)	(3.0)	(3.1)	(3.2)	(2.9)
Solid organ transplantation and	17	66	383	771	286	82	8	1613
peripheral blood and stem cell transplant	(0.1)	(0.6)	(2.4)	(2.3)	(0.7)	(0.1)	(0)	(0.5)

Age groups	0-4	5-19	20-49	50-64	65-74	75-84	+85	Total
Number of patients (%)	18 321	16 207	11 337	32 873	39 072	94 768	111 414	323 992
	(5.6)	(5.0)	(3.5)	(10.1)	(12.0)	(29.2)	(34.4)	(100)
Inpatient all-cause fatality	83 (0.4)	98 (0.6)	1334	5706	8353	22 300	32 070	69 944
[Number (%)]			(11.8)	(17.4)	(21.4)	(23.5)	(28.8)	(21.6)
28-days readmission	1319 (7.2)	683 (6.0)	1691	5198	7587	20 160	26 563	63 201
[Number (%)]			(10.4)	(15.8)	(19.4)	(21.3)	(23.8)	(19.5)
Length of stay	7.7 ±	7.8 ±	13.9 ±	16.4 ±	15.9 ±	15.1 ±	13.7 ±	14.1 ±
(days, mean ± SD)	32.4	37.4	45.8	45.1	35.7	31.9	28.0	33.8
Direct cost (\$ per episode,	$5178 \pm$	5246 ±	9242 ±	$10\;847\;\pm$	$10\ 536\ \pm$	$9983 \pm$	9064 ±	$9348~\pm$
mean \pm SD)	21 153	24 359	29 861	29 394	23 273	20 823	18 241	22 067
Annual healthcare expenditure (\$ million)	18.9	11.9	29.9	71.2	82.3	189.2	202.0	605.4

Figure Legends

Fig. 1 Commonly isolated bacterial pathogens from patients hospitalized with pneumonia

The six most commonly identified bacterial pathogens in the overall population (A), children 0-19 years (B), adults 20-64 years (C), and older adults \geq 65 years (D). Percentage refers to the proportion of patients with a culture result for the corresponding organism among all the patients with positive culture results.

Fig. 2 Cumulative incidence of hospitalized pneumonia in Hong Kong 2011-2015, by age

Shaded area: 95% confidence interval; age-standardized incidence referenced from Hong Kong population in 2015.

Fig. 3 Case-fatality of hospitalized pneumonia in Hong Kong, 2011-2015, by age

Shaded area: 95% confidence interval; no deaths from pneumonia were recorded for patients aged 0-4 years.