ORIGINAL ARTICLE

Factors associated with length of hospital stay in children with respiratory disease

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Objectives To explore factors associated with length of stay, and secondarily to explore the potential of enhanced diagnostics to address respiratory disease burden in children.

Design Prospective study.

Setting A university teaching hospital in Hong Kong.

Patients Data from 475 children with respiratory tract symptoms or fever admitted to Prince of Wales Hospital, Hong Kong from November 2005 to April 2007.

Main outcome measures Aetiological diagnoses based on enhanced diagnostics and their association with clinical information.

Results Data from 469 subjects showed that major presentations were fever (84%), cough (72%), and runny nose (64%). The median length of stay was longest (3 days) for adenovirus, metapneumovirus and mycoplasma infections, while children with negative aetiological results had a median length of stay of 2 days. Fever duration during admission (P<0.001), the highest recorded temperature during admission (P<0.001), use of antibiotics during admission (P<0.001), ear pain before admission (P=0.019), and high white cell counts (P=0.021) were associated with increased length of stay (univariate analysis). Identifying an aetiological agent did not affect length of stay. Comparison of children with a positive immunofluorescence test result (rapidly available) with those in whom the test was negative though a positive multiplex polymerase chain reaction ensued (result not available to clinicians) also showed no association with length of stay.

Conclusion Although rapid enhanced diagnostics may not have a major influence on length of stay, these data form an integral part of enhanced sentinel surveillance systems.

Introduction

Safe and effective vaccines are available for influenza, avian influenza, pneumococcal disease, and haemophilus influenza. Avian influenza vaccines have recently become available and development of vaccines for other respiratory diseases (parainfluenza and respiratory syncytial virus infection) is progressing. Surveillance of respiratory disorders can establish reliable estimates of disease burdens and monitor circulating pathogens. Surveillance can also provide vital data for economic analyses to determine whether vaccines should be included in National Immunization Programmes. The World Health Organization has launched a new global framework for immunisation monitoring and surveillance (GFIMS).[1] The GFIMS principles advocate integration of programme monitoring and vaccine-preventable disease surveillance into the health systems context. This is achieved by building capacity at district and health facility levels and assuring quality data. It is deemed essential that these new surveillance activities link other monitoring and surveillance systems in a financially sustainable way.

Using passive surveillance data in Hong Kong, a primary diagnosis of a respiratory disorder was noted in 38% of all general paediatric hospital admissions in children younger than 15 years; in 43% it was the primary or secondary diagnosis.[2] The economic burden for these admissions must be substantial. One of the main drivers of economic evaluations is length of hospital stay (LOS), so reliably documenting LOS could be important in respiratory disease surveillance systems. In addition, a better understanding of the various factors that can influence LOS could be important, though relatively few studies

Key words
Influenza A virus; Length of stay; Nasopharyngeal diseases; Respiratory syncytial virus infections

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have assessed such possible predictive factors in children admitted with respiratory tract infections and/or febrile illness.[3] Potential factors that could influence LOS include: rapidly available results from nasopharyngeal aspirates (NPA), and antibiotic usage prior to admission. Children admitted to the Prince of Wales Hospital with respiratory symptoms and/or febrile illness undergo routine testing with NPA or throat swabs, to try and identify potential aetiological viral and bacterial pathogens. Such routine testing however, increases hospital costs, particularly if advanced polymerase chain reaction (PCR) tests are also undertaken.[4,5] Furthermore, it is common for Hong Kong children to receive antimicrobial therapy in primary care settings before they visit hospital emergency departments.[6,7]

As part of a study that used enhanced diagnostics to compare NPA and nasal swab (NS) specimens for diagnosis of acute respiratory infection (ARI), we collected detailed demographic and clinical data on children aged less than 5 years with respiratory symptoms and/or fever.[8,9] To explore factors associated with LOS, further analyses of these data were undertaken using variables available on admission together with the results of the detailed virological diagnostic tests. A secondary objective of this analysis was to explore the potential of enhanced diagnostics to provide high-quality sentinel respiratory disease burden surveillance data. Our previous review of admissions for respiratory disorders had emphasised that routinely collected passive hospital discharge data underestimate the true disease burden of conditions caused by specific viral pathogens.[2] To better understand the potential benefits of routine active surveillance with enhanced diagnostics, the ensuing detailed aetiological diagnoses were compared with the International Classification of Diseases (ICD) discharge codes entered into the hospital's routine health information system.

影響呼吸道疾病兒童患者住院期的因素

目的 探討影響呼吸道疾病兒童患者住院期的因素，並找出能增強診斷兒童呼吸道疾病的工具。

設計 前瞻性研究。

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患者 2005年11月至2007年4月期間因呼吸道症狀或發燒入住香港威爾斯親王醫院的475位兒童的資料。

主要結果測量 根據增強診斷工具得出的臨床診斷及其與臨床資料的關係。

結果 共469名兒童的資料顯示主要病發症狀為發燒（84%）、咳嗽（72%）和流鼻水（64%）。病因為腺病毒、副肺炎病毒和支原體病毒的患者，其住院期中位數最長（3天）。至於臨床結果呈陰性的兒童，住院期中位數為2天。單變量分析顯示以下因素與住院期增加有顯著關係：住院期內發燒時間的長短（P<0.001）、住院期內發燒的最高溫度（P<0.001）、住院期內曾接受抗生素治療（P<0.001）、入院前出現耳痛症狀（P=0.019），及白血球水平偏高（P=0.021）。能夠辨識致病原因並不影響住院期長短。免疫螢光（快速）測試呈陽性的兒童，與免疫螢光測試呈陰性但複合聚合連鎖反應呈陽性（未能提供結果）的兒童比較，均未能顯示與住院期長短有關。

結論 縱使快速增強診斷工具可能對住院期沒有顯著影響，但本研究的資料有助增強定點監測系統。

Methods

The study recruited children with either upper respiratory tract symptoms and/or fever, or ARI symptoms admitted to Prince of Wales Hospital during the period November 2005 to April 2007. Prince of Wales Hospital is a 1350-bed university hospital serving around 1 000 000 inhabitants in the New Territories East region of Hong Kong.

Active data collection

Details of data collection for this study have been previously reported.[8,9] All children younger than the age of 5 years with requisite presentation were eligible for inclusion, and those admitted on Monday (or Tuesday if Monday was a public holiday) were prospectively recruited after obtaining parental consent. After enrolment, children had both an NPA and a NS collected. Those with suspected asthma and allergic rhinitis were excluded. For each patient, after recruitment a standard form for demographic data, ethnicity and a detailed history was completed. Additional laboratory results, information on treatment, clinical course and variables, as well as the final diagnosis were retrieved from the medical records. Clinical variables included oxygen use, fever duration before and after admission, highest recorded temperature before and after admission, antibiotics use, chest radiograph findings, and the presence of any co-morbid conditions. Fever was defined as an axillary temperature of at least 38.5°C. White cell count and C-reactive protein test results were also recorded. Total LOS was measured in terms of days. The results of routine immunofluorescence for seven common respiratory viruses (adenovirus, influenza A, influenza B, parainfluenza 1,2,3, and respiratory syncytial virus) were available to clinicians within 1 working day. Additional multiplex PCR analyses were then performed for these seven viruses and for an additional six pathogens (metapneumovirus, mycoplasma, OC43 coronavirus, A229E coronavirus, rhinovirus, and enterovirus).[9] These PCR tests were undertaken separately in batches, and the results

TABLE 1. Demographic and clinical characteristics of the subjects (n=469)

Characteristic	No. of patients
Gender	
Female	219 (47%)
Male	250 (53%)
Age (years)	
<1	143 (30%)
1 to <3	171 (36%)
3 to 5	155 (33%)
Runny nose at admission	301 (64%)
Cough at admission	339 (72%)
Shortness of breath at admission	43 (9%)
Sore throat at admission	34 (7%)
Ear pain at admission	10 (2%)
Convulsion	32 (7%)
Previous admission	27 (6%)
Fever at admission	392 (84%)
Fever duration before admission (days)	3 (1-4)*
Highest temperature before admission (°C)	39.2 (0.8)†
Fever duration during admission (days)	1 (1-2)*
Highest temperature during admission (°C)	38.6 (1.1)†
Chest X-ray taken	380 (81%)
Antibiotic given	99 (21%)
Oxygen given	7 (1%)
Admitted to Intensive Care Unit	0
White cell count (x 10^9 / L)	11.5 (6.1)†
Length of hospital stay (days)	2 (1-3)*
≤1	122 (26%)
2	130 (28%)
3	108 (23%)
4	45 (10%)
5	32 (7%)
≥6	32 (7%)

* Median (interquartile range)
† Mean (standard deviation)

were not available for clinical decision-making.

Passive data collection

From 1996, standardised discharge data on all patients admitted to Hong Kong's publicly funded government hospitals system (Hospital Authority) were stored on a central computerised database known as the Clinical Management System (CMS). The information collected included: patient identifiers, date of birth, sex, a maximum of 15 diagnoses and 15 procedures (classified according to the ICD9-CM codes), and admission and discharge dates. These ICD discharge codes were grouped into different categories of respiratory disorders as previously described.[2]

Statistical analyses

Simple descriptive tabulations were undertaken to show the demographic details of the subjects and the causes of admission based on both the ICD discharge codes and the results of the detailed virological investigations. Skewed continuous variables and near normally distributed variables were respectively presented as medians (interquartile ranges [IQRs]) and means (standard deviations). Categorical data were presented as counts and percentages. Univariate comparisons were made using non-parametric Kruskal-Wallis test, one-way analysis of variance, Pearson Chi squared or exact Chi squared tests, as appropriate. All statistical analyses were performed using the Statistical Package for the Social Sciences (Windows version 16.0; SPSS Inc, Chicago [IL], US); a two-sided P value of less than 0.05 was considered statistically significant.

Results

Descriptive data

During the study period, 475 eligible children were enrolled, and data on LOS were available for 469. Their demographic and clinical features—including major presenting complaints and less common presentations on admission, as well as investigative and treatment interventions—are shown in Table 1. The median fever duration before hospital admission was 3 (IQR, 1-4) days, while the median fever duration during their admission was 1 (IQR, 1-2) day. The mean of the highest reported temperature before admission was 39.2°C, while that during admission was 38.6°C. Approximately 77% of the children were admitted for 3 days or less. None of the patients received intensive care or ventilatory support.

Diagnoses and aetiological causes of admission

Based on the ICD codes recorded in the CMS, 62% had either a primary or secondary diagnosis associated with the respiratory disorder (Table 2). Upper respiratory tract infection codes were most common (31%), followed by pneumonia (10%) and influenza (5%). Half (n=234) of the NPA or NS samples analysed by both immunofluorescence and multiplex PCR identified a potential pathogen (Table 3). The most common pathogens identified were influenza A and B (23%), respiratory syncytial virus (20%), and parainfluenza 1,2,3 (18%). Median LOS was longest (3 days) for patients tested positive for adenovirus, parainfluenza, metapneumovirus, and mycoplasma (Table 3). Children in whom diagnostic testing turned out to be negative for any aetiological agent had a median LOS of 2 days. Co-infection with aetiological

TABLE 2. Reported diagnoses derived from the Clinical Management System*

Reported diagnosis	ICD-CM codes	Primary diagnosis, No. (%)	Any diagnosis, No. (%)†	Female:male (%:%)	Mean (SD) age (years)	Median (IQR) length of hospital stay (days)
Upper respiratory tract infections	460-461.9, 465-465.9, 786.2	134 (29)	145 (31)	50:50	2.5 (1.7)	2 (1-3)
Pharyngitis and tonsillitis	462-463.9, 034.0, 474.11	5 (1)	7 (1)	0:100	3.9 (1.7)	2 (1-4)
Croup and laryngitis	464-464.9, 786.1	6 (1)	7 (1)	50:50	1.1 (0.6)	2 (2-5)
Otitis media	381-382.9	5 (1)	5 (1)	40:60	3.7 (0.6)	3 (1-4)
Bronchitis and non-specific chest infection	466-466.09, 490-490.9, 519.8	3 (0.6)	3 (0.6)	0:100	2.6 (0.2)	5 (2-5)
Bronchiolitis	466.1-466.9	13 (3)	15 (3)	31:69	0.9 (0.8)	3 (2-5)
Bronchiolitis due to respiratory syncytial virus infection	466.11	18 (4)	18 (4)	44:56	1.1 (1.0)	4 (2-5)
Pneumonia	480-486.9, 507.0	48 (10)	49 (10)	46:54	3.3 (1.2)	3 (2-4)
Influenza	487-487.9	21 (4)	23 (5)	62:38	3.0 (1.7)	3 (2-3)
Asthma and allergic rhinitis	493-493.9, 477-477.9	16 (3)	18 (4)	62:38	4.0 (1.3)	2 (2-3)
Total respiratory		**269 (57)**	**290 (61)**	**48:52**	**2.6 (1.7)**	**2 (1-3)**
All other diseases		200 (43)	179 (38)	45:55	1.9 (1.5)	2 (2-4)
Likely infectious cause		126 (27)	112 (24)	48:52	1.8 (1.5)	3 (2-4)
Gastroenteritis		55 (12)	51 (11)	38:62	2.1 (1.5)	2 (2-4)
Likely non-infectious cause		19 (4)	16 (3)	47:53	2.1 (2.0)	3 (1-4)

* ICD-CM denotes International Classification of Diseases–Clinical Modification, SD standard deviation, and IQR interquartile range

† Any of 15 possible diagnosis codes, with category selected hierarchically when more than one respiratory-related code was used, that is, first diagnostic code would take precedence over the second and so on

TABLE 3. Grouping based on aetiological agent identified*

Aetiological agent	No. (%)	Female:male (%:%)	Mean (SD) age (years)	Median (IQR) length of hospital stay (days)
Adenovirus	26 (5.5)	42:58	3.5 (1.4)	3 (1-4)
Influenza A	37 (7.9)	38:62	3.1 (1.6)	2 (2-3)
Influenza B	16 (3.4)	69:31	3.5 (1.9)	2 (1-3)
Paraflu group (1,2,3)	41 (8.7)	51:49	1.8 (1.4)	3 (2-4)
Respiratory syncytial virus	46 (9.8)	52:48	1.8 (1.4)	2 (1-4)
Metapneumovirus	7 (1.5)	57:43	2.3 (1.5)	3 (2-3)
Mycoplasma	7 (1.5)	43:57	2.0 (1.2)	3 (1-4)
OC43	15 (3.2)	33:67	1.7 (0.8)	2 (1-3)
Rhinovirus	17 (3.6)	24:76	2.6 (1.4)	2 (1-3)
A229E	1 (0.2)	0:100	5.0 (0.0)	0 (0-0)
Enterovirus	2 (0.4)	50:50	0.7 (0.7)	2 (2-3)
Co-infection	19 (4.1)	58:42	2.4 (1.6)	2 (1-3)
None of the above	235 (50.1)	47:53	2.2 (1.7)	2 (1-4)

* SD denotes standard deviation, and IQR interquartile range

agents was not associated with a longer median LOS.

Factors associated with length of stay

Univariate analysis showed that fever duration during admission (P<0.001), the highest recorded temperature (P<0.001) during admission, antibiotic use during admission (P<0.001), ear pain before admission (P=0.019), and high white cell counts (P=0.021) during the admission were all associated with an increased LOS (Table 4). The reported primary CMS diagnosis and the aetiological agent identified were not associated with LOS. Comparison of children with a positive immunofluorescence (positive result available within 1 day for clinical decision-making) with those with a negative result

TABLE 4. Clinical and laboratory characteristics associated with length of hospital stay

Characteristic*	Length of hospital stay (days)			P value
	≤2 (n=252)	3-4 (n=153)	≥5 (n=64)	
Background and clinical characteristics				
Male gender	135 (54%)	81 (32%)	34 (14%)	0.992†
Age (years), mean (SD)	2.4 (1.7)	2.2 (1.6)	2.3 (1.6)	0.546‡
Runny nose before admission	164 (55%)	97 (32%)	40 (13%)	0.901†
Cough before admission	187 (55%)	105 (31%)	47 (14%)	0.466†
Shortness of breath before admission	22 (51%)	12 (28%)	9 (21%)	0.329†
Sore throat before admission	19 (56%)	12 (35%)	3 (8.8%)	0.708§
Ear pain before admission	2 (20%)	4 (40%)	4 (40%)	0.019§
Convulsion	21 (66%)	10 (31%)	1 (3.1%)	0.161§
Previous admission	11 (41%)	10 (37%)	6 (22%)	0.276§
Fever at admission	210 (54%)	132 (34%)	50 (13%)	0.331†
Fever duration before admission (days), median (IQR)	3 (1-4)	2 (2-4)	2 (2-5)	0.935¶
Highest temperature before admission (°C), mean (SD)	39.2 (0.8)	39.2 (0.7)	39.2 (0.7)	0.967‡
Fever duration during admission (days), median (IQR)	1 (0-2)	2 (1-3)	3 (2-5)	<0.001¶
Highest temperature during admission (°C), mean (SD)	38.4 (1.1)	38.8 (1.1)	39.0 (1.2)	<0.001‡
Chest X-ray taken	203 (53%)	127 (33%)	50 (13%)	0.678†
Antibiotic given	38 (38%)	38 (38%)	23 (23%)	<0.001†
Oxygen given	3 (43%)	2 (29%)	2 (29%)	0.581§
Abnormal C-reactive protein	3 (43%)	2 (29%)	2 (29%)	0.581§
White cell count (x 10^9 / L), mean (SD)	10.7 (5.4)	11.8 (6.6)	13.7 (6.4)	0.021‡
Reported primary diagnosis				-
Upper respiratory tract infections	89 (66%)	40 (30%)	5 (3.7%)	
Pharyngitis and tonsillitis	3 (60%)	1 (20%)	1 (20%)	
Croup and laryngitis	3 (50%)	1 (17%)	2 (33%)	
Otitis media	2 (40%)	2 (40%)	1 (20%)	
Bronchitis and non-specific chest infection	1 (33%)	0 (0%)	2 (67%)	
Bronchiolitis	6 (46%)	3 (23%)	4 (31%)	
Bronchiolitis due to respiratory syncytial virus infection	6 (33%)	6 (33%)	6 (33%)	
Pneumonia	22 (46%)	17 (35%)	9 (19%)	
Influenza	9 (43%)	9 (43%)	3 (14%)	
Asthma and allergic rhinitis	10 (63%)	4 (25%)	2 (13%)	
Total respiratory	**151 (56%)**	**83 (31%)**	**35 (13%)**	**0.480‖**
All other diseases	101 (51%)	70 (35%)	29 (15%)	
Likely infectious cause	62 (49%)	45 (36%)	19 (15%)	
Gastroenteritis	30 (55%)	19 (35%)	6 (11%)	
Likely non-infectious cause	9 (47%)	6 (32%)	4 (21%)	
Aetiological agent identified				-
Single infection				
Adenovirus	12 (46%)	10 (39%)	4 (15%)	
Influenza A	20 (54%)	15 (41%)	2 (5.4%)	
Influenza B	9 (56%)	6 (38%)	1 (6.3%)	
Paraflu group (1,2,3)	20 (49%)	14 (34%)	7 (17%)	
Respiratory syncytial virus	28 (61%)	10 (22%)	8 (17%)	
Metapneumovirus	3 (43%)	3 (43%)	1 (14%)	
Mycoplasma	3 (43%)	3 (43%)	1 (14%)	
OC43	11 (73%)	3 (20%)	1 (6.7%)	
Rhinovirus	11 (65%)	6 (35%)	0	
A229E	1 (100%)	0	0	
Enterovirus	1 (50%)	1 (50%)	0	
Co-infection	11 (58%)	6 (32%)	2 (11%)	-
None of the above	122 (52%)	76 (32%)	37 (16%)	0.402**
The above aetiological agents identified				
Positive by IF but negative by PCR	4 (67%)	0	2 (33%)	0.083§
Negative by IF but positive by PCR	63 (54%)	44 (38%)	9 (7.8%)	
Positive by both IF and PCR	62 (57%)	31 (29%)	15 (14%)	

* SD denotes standard deviation, IQR interquartile range, IF immunofluorescence, and PCR polymerase chain reaction
† Pearson Chi squared test
‡ One-way analysis of variance
§ Exact Chi squared test
¶ Kruskal-Wallis test
‖ Pearson Chi squared test on dichotomised as whether the listed respiratory diseases or all other diseases
** Pearson Chi squared test on dichotomised as whether infected with any of the listed virus or none of them

but a positive multiplex PCR test result also showed no association with LOS (Table 4).

Discussion

Length of hospital stay is an outcome that can be used to compare quality of care among health care institutions. It is also a key variable in economic evaluations of health care costs and interventions. These data may provide information for better use of resources for the management of children hospitalised with ARI, which comprises about one third of general paediatric admissions in Hong Kong. These data could also drive policy decisions on the use of routine vaccines for haemophilus influenza, pneumococcal disease, and seasonal influenza. Many clinical and non-clinical factors may affect LOS. Financial and other incentives to encourage early discharge and use of practice guidelines may be important. The latter factors are likely to remain constant over any given short period of time and should not have affected the results of the present study, in which neither the clinical discharge diagnoses nor the detailed aetiological (viral) diagnoses were associated with LOS.

It was hypothesised that timely viral aetiological results might influence clinical decision-making and encourage earlier hospital discharge. However in the subgroup analysis comparing subjects with a positive aetiological result on immunofluorescence (available for clinical decision-making) with those with a positive result only obtained from PCR (not available for clinical decision-making), there was no difference in LOS (Table 4). Even if timely, comprehensive aetiological results do not influence LOS, they may have other benefits and could influence other treatments. Conceivably, a positive viral aetiology may make it easier for the physician to explain to the family that antibiotic therapy was not needed. In this study however, the use of antibiotics during admission was similar in those with and without a viral aetiological result (13% vs 19% respectively, P=0.353).

Highest recorded temperature and the duration of an elevated temperature during the admission, use of antibiotics, and high white cell counts were significantly associated with a longer LOS. These associations are not surprising, given that they are used as markers of more serious clinical illness. Parents in Hong Kong are often very concerned about fever and its persistence, and frequently prefer that their child stay in hospital for closer observations until it subsides. It could be argued that finding therapies that result in earlier resolution of fever might result in earlier hospital discharges and potential cost-savings to the health care system. However, this proposition could be countered with the argument that fever is an important part of the body's response to infection, and that its unnecessary and over-zealous suppression may result in adverse clinical outcomes.[10,11]

This study confirmed our previous observation that the ICD discharge codes entered into the passive health information system (CMS) provide a poor reflection of the aetiological diagnoses.[2] For example using the ICD codes alone, influenza was diagnosed in 23 subjects (any diagnosis in Table 2). However based on the detailed aetiological results, influenza A and B were identified in 37 and 16, respectively. As previously suggested, establishing designated sentinel hospitals to undertake detailed virological diagnostics on all patients with respiratory and other infections, and linking such data to the passive CMS discharge database could provide timely and reliable disease burden estimates for a range of specific pathogens.[2,9]

An important limitation of this study was the definition of LOS. The calculated hospital stay using admission and discharge dates may not reflect actual hospital stay. A common practice in Hong Kong is for parents to be given 'home leave' for observation during the child's hospital admission. This practice allows the family to return to the ward at any time they have concerns and effectively reserves the bed for the child. This practice appears to be practically and administratively easier than the alternative (discharging the child and arranging a follow-up on the ward). The practice of 'home leave' over-estimates actual LOS. The LOS was also estimated in whole days and may not reflect the difference between a child admitted at 11 pm and one admitted at 1 am, since discharge will usually occur after a morning or evening ward round. Ideally LOS should be estimated in hours rather than days.

Although this study failed to show any association between LOS and the viral aetiology, or the timely availability of results, detailed viral aetiological data can provide important information for clinicians and public health policy makers. In Hong Kong many hospitalisations for ARI often reflect societal practices and parental concerns, rather than actual medical need. Use of practice guidelines, improved out-patient follow-up facilities, and continued parental education could possibly reduce and avoid unnecessary hospital stays. More data are required before it can be determined whether multiplex PCR testing of routine NPA specimens might be cost-effective in routine sentinel surveillance systems. Nevertheless, both the clinical and public benefits of extending the use of such testing need to be explored

further.

Declaration

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References

1. Dabbagh A, Eggers R, Cochi S, Dietz V, Strebel P, Cherian T. A new global framework for immunization monitoring and surveillance. Bull World Health Organ 2007;85:904-5.
2. Nelson EA, Tam JS, Yu LM, Li AM, Chan PK, Sung RY. Assessing disease burden of respiratory disorders in Hong Kong children with hospital discharge data and linked laboratory data. Hong Kong Med J 2007;13:114-21.
3. Woo PC, Chiu SS, Seto WH, Peiris M. Cost-effectiveness of rapid diagnosis of viral respiratory tract infections in pediatric patients. J Clin Microbiol 1997;35:1579-81.
4. Lambert SB, Whiley DM, O'Neill NT, et al. Comparing nose-throat swabs and nasopharyngeal aspirates collected from children with symptoms for respiratory virus identification using real-time polymerase chain reaction. Pediatrics 2008;122:e615-20.
5. Syrmis MW, Whiley DM, Thomas M, et al. A sensitive, specific, and cost-effective multiplex reverse transcriptase-PCR assay for the detection of seven common respiratory viruses in respiratory samples. J Mol Diagn 2004;6:125-31.
6. Bertino JS. Cost burden of viral respiratory infections: issues for formulary decision makers. Am J Med 2002;112 Suppl 6A:42S-49S.
7. Nyquist AC, Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. JAMA 1998;279:875-7. Erratum in: JAMA 1998;279:1702.
8. Sung RY, Chan PK, Choi KC, et al. Comparative study of nasopharyngeal aspirate and nasal swab specimens for diagnosis of acute viral respiratory infection. J Clin Microbiol 2008;46:3073-6.
9. Sung RY, Chan PK, Tsen T, et al. Identification of viral and atypical bacterial pathogens in children hospitalized with acute respiratory infections in Hong Kong by multiplex PCR assays. J Med Virol 2009;81:153-9.
10. Russell FM, Shann F, Curtis N, Mulholland K. Evidence on the use of paracetamol in febrile children. Bull World Health Organ 2003;81:367-72.
11. Shann F. Antipyretics in severe sepsis. Lancet 1995;345:338.