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Symptoms of respiratory tract infections and healthcare-seeking and antibiotics use: a cross sectional survey in rural Anhui, China

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Abstract

Objective: To investigated the occurrence and trajectory of RTI symptoms and their effects on use of self and professional care among patients in the community.

Design: A cross sectional retrospective household survey.

Setting: 12 administrative villages from rural Anhui, China.

Participants: 2160 rural adult residents aged ⩾18 years and registered rural residence or were actually living in the sampled villages when this study was conducted.

Method: It solicited information about social demographics, symptoms of last time RTI and healthcare-seeking following the RTI and performed descriptive and multi-regression analysis including: a) percentages of patients with a specific symptom by day on which the symptom occurred(DSO), reached its peak (DSP) and recovered(DSR); b) multivariate logistic regression models of healthcare-seeking and antibiotics use; and c) relationships between number of concurrent symptoms and healthcare-seeking and antibiotics use.

Results: The frequencies of DSO of specific symptoms all featured a steep peak followed by a long tail. The number of concurrent symptoms showed clear increasing trend with seeking help from clinics and being prescribed with antibiotics. Multivariate regression revealed statistically significant associations between: a) visiting clinics and education(OR=0.790), sore throat(OR=1.355), cough(OR=1.492), shortness of breath(OR=1.707) and fever(OR=2.142); b) buying medicine from shops without prescription and education(OR=1.230) and cough(OR=1.452); c) getting antibiotics at clinics and sore throat(OR=2.05) and earache and/or tinnitus(OR=4.884) and d) obtaining antibiotics at medicine shops and productive cough(OR=1.971).

Conclusions: RTI symptoms manifest featured trajectories and play an important role in shaping both the patient- and doctor-dominated responses toward the infections.

Strengths and limitations of this study

Contrasting contemporary focus on demand and supply side factors, this study centered on effects of symptoms on RTI-related care.

The study described detailed trajectory of common symptoms and analyzed collective effects of concurrent symptoms.

The study relied on subjective perceptions or self-reports and therefore may be biased by potential under or over reporting.

The study used a broad definition of RTIs and the occurrence and trajectory of symptoms may be distorted by part of the infections that were exceptionally high or low due to seasonal and other factors when the study was conducted.

Background

Respiratory tract infections (RTIs) are the most common diseases in humans. Studies have demonstrated that adults usually experience 1–3 times of upper respiratory tract infections per year,[1,2] whereas children have considerably greater chances of getting the infections (up to 11, depending on age) and experience more prolonged symptoms.[3] RTIs claim over 3 million lives annually and are the leading cause of death for children younger than 5 years.[4,5] Although many RTIs are mild and self-limiting, they are associated with significant burden in terms of medical visits as well as work and school absenteeism. It is estimated that the median duration of an episode of non-influenza-related viral respiratory tract infection (the most common but least serious kind of RTIs) is 7.4 days, with 25% of cases lasting for 2 weeks.[6] According to the 1996 report from the National Center for Health Statistics of US, viral RTIs alone caused approximately 20 million lost workdays in adults and 21 million lost school days in children annually.[7] While a study in 13 European countries in 2007 indicated that one case of acute cough and lower RTIs caused 3.08 lost workdays and €56.29 direct cost plus €287.09 indirect cost.[8] In addition to heavy burden on health systems and patients, RTIs are closely linked to antibiotics use and resistance. It is estimated that RTIs account for up to 60% of all antibiotic prescribing in primary care,[9,10] Irrational use or abuse of antibiotics is recognized as one of the most serious public health issues worldwide. Antibiotic abuse not only increases cost of care, exposes people to unnecessary side effects, but also accelerates antibiotic resistance.[11]

According to the 10th edition of the International Classification of Diseases, RTIs comprise as many as 34 kinds of infections. However their symptoms are relatively limited consisting of mainly sore throat, fever, cough, productive cough, rhinorrhea with or without pus, shortness of breath, headache and/or general discomfort, purulent sputum, earache and/or tinnitus.[12,13] When faced with symptoms, patients' responses vary greatly. Some patients manage their symptoms by simply having a rest, drinking warm water etc. without using any medicines;[14] others buy medicines from medicine shops or pharmacies or seek professional help from doctors;[15-17] still others opt to traditional remedies.[18, 19]A 2014 study of consumer attitudes on cough and cold in US indicated that 36.1% of those surveyed reported beginning OTC treatments at the first sign of cough/cold, 42.6% waited until cold symptoms 'get bad enough' (i.e. to cause distress) and another 20.2% waited until they have more than one symptom before beginning treatment. Putting together, 55% of them sought professional care eventually [20]. These varied responses may be attributed to a whole range of reasons including: 'diseases features', e.g., severity of symptoms and their patterns of progress (aggravating versus, diminishing symptoms);[2]and 'demand side' issues such as age, gender, education,[21] knowledge and attitudes about RTIs and RTI-related services,[22,23] cultural expectations and social norms; [24,25] and 'supply side' factors such as perverse financial incentives, systemic pressures on healthcare providers and professional standards.[24,26,27] Previous studies on determinants of health service utilization following RTIs have been focused mainly on the demand and supply side factors with little attention been paid to the occurrence and trajectory of RTI symptoms among patients in the community and their effects on decisions about self or professional care.

RTIs are also very common in China with an incidence rate ranging from 84.13% to 120.831% in 2006.[28] These translate into 2 to 4 times of RTIs per person per year and 16 billion person-times of RTIs annually in the whole country. Data about service use for RTIs among China residences are scarce. But limited researches reported huge discrepancies between different populations and very high use of antibiotics at various medical settings. An earlier study at rural primary care settings of 10 provinces in Western China showed that nearly 50% of all the patients were prescribed antibiotics.[29]Another recent study found that antibiotics were prescribed for 78% of colds and 93.5% for acute bronchitis.[30]Studies exploring reasons for the varied service use and prevalent antibiotic prescription in China are also lacking. According to our systemic literature review, there is little publication that focuses primarily on factors affecting service and antibiotics use following RTIs. Although a number of papers on reasons of general service utilization did include RTIs as a subcomponent, they again addressed only demand and supply side factors.

Methods

Study sites and population

The study adopted a stratified-clustered randomized sampling in recruiting site villages and participating residents. Selection of site villages proceeded in 4 steps. Step 1 divided all counties in Anhui province into north, middle and south regions. Step 2 randomly selected 4 counties from each of the three regions and 1 township from each of the counties selected and then 1 administrative village from each of the site township selected above. Step 3 randomly selected 1 household from the village selected as the starting household and then recruited 180 households being geographically most close to the starting household. Step 4 randomly selected one household member from each of the households according to preset eligibility criteria, i.e., men and women who: a) had registered rural residence and were actually living in the sampled villages when this study was conducted; b) aged 18 years and plus; c) were willing to participate and able to answer the survey questions.

Questionnaire

The study used a structured questionnaire consisting of questions about four categories of variables: a) social demographics (e.g., gender, age and education); b) last time symptomatic RTI, including symptoms experienced (e.g., sore throat, fever, dry cough, productive cough, rhinorrhea without pus, rhinorrhea with pus, shortness of breath, headache and/or general discomfort, earache and/or tinnitus) and day on which a specific symptom occurred (DSO), reached its peak or became most serious (DSP) and recovered (DSR); c) responses toward the RTI, including taking leftover medicines, buying medicine(s) from medicine shops (hereafter referred to as buying medicine) and seeking help from clinics; d) antibiotics obtained from clinics and medicine shops.

Data collection

Filed data collection took place during 30 April to 12 May 2016 via face-to-face interviews using the structured questionnaire mentioned above. Twenty-six under graduate students from Anhui Medical University performed the interview. Measures taken to ensure data quality included: a) training and examination of the filed data collector; b) daily checks, by quality supervisor, of all the questionnaires completed during the day; c) retest of 5% randomly selected subjects; d) feedback of errors found via the daily checks and retests; e) elimination of disqualified field data collectors.

Data analysis

The data collected were doubled-entered using EPI DATA 3.1 and analyzed via SPSS 10.01 and Microsoft Excel 2010. Data analysis included: a) distribution of respondents by gender, age and education; b) percentages and accumulative percentages of patients by DSO, DSP and DSR for different RTI symptoms in total and by different demographics; c) multivariate logistic regression models of healthcare-seeking and antibiotics use using the social demographics and common symptoms as the independent variables; d) the relationships between number of symptoms experienced by single patient and his or her healthcare-seeking and antibiotics use. Cases with missing data were excluded from the data analyses.

Ethical review

The study involved recruitment and assessment of a sample of rural residents and thus adhered to rigorous human subject production principles and procedures. The study protocol had been reviewed and approved by the Biomedical Ethics Committee of Anhui Medical University (reference number: 201500800) study commence. Participation of rural residents was voluntary and written informed consent was sought from all participants.

Results

Overview of participants, symptoms and healthcare-seeking

As shown in Figure 1, a total of 2160 residents were accessed and 1968 completed the survey, resulting in a response rate of 91.1%. The mean age of these respondents was 50.39 years (SD=13.04 years). The majority (68.0%) of them was females and around one third (29.6%) had no formal school education (For details, see the appendix). Dry cough (58.9%, 1159), rhinorrhea without pus (51.7%, 1017), sore throat (49.8%, 980) and shortness of breath (18.3%, 360) were the most frequent symptoms. Following RTIs, 55.7% of the patients sought professional help from clinics, 13.4% bought medicine from medicine shops, 23.1% used leftover medicine from previous illnesses and 20.8% did nothing. Putting together, 81.3% of them used antibiotics.

Development of symptoms

Figure 2 displays common symptoms the respondents had experienced due to their last time RTIs. The lines representing DSO of specific symptoms all featured a skewed peak, i.e., they increased rapidly at the beginning, reached a sharp peak on day 1 or day 2, and then followed by a long tail reaching over 15 days. The height of the peaks varied greatly across symptoms ranging from 28.3% for rhinorrhea with pus to 56.8% for sore throat. The curves representing DSP of specific symptoms mimicked the shape of DSO in general, but showed a delayed (for 2 to 3 days) and lower (by 22.0% to 33.8%) peak. The DSR curves deviated a step further from DSO curves. They had 2 to 3 peaks centered on day 3, day 5 , day 10 and especially day 7. The lines depicting accumulative rates of symptom occurrence (ARSO), symptom peak (ARSP) and symptom recovery (ARSR) by different days following onset of RTIs all showed an atypical "S-shape". In terms of ARSO lines, the one representing dilute snivel displayed the fastest increase followed by the lines for sore throat, fever, headache/general discomfort, dry cough, productive cough, shortness of breath, rhinorrhea with pus, earache and/or tinnitus. Looking at the differences between the lines of ARSO, ARSP and ARSR for a same symptom, ARSP was much more close to ARSO than ARSR. The time lag between ARSO and ARSR was the biggest for cough followed by that of sore throat, shortness of breath, rhinorrhea with pus, headache and soreness, rhinorrhea without pus, rhinorrhea with pus, earache and/or tinnitus, fever.

Figure 3 shows the distribution of DSO, DSP and DSR of three selected symptoms (including dry cough, rhinorrhea without pus, sore throat) by different demographic characteristics (more information about symptom trajectories by different subgroups is given in Appendix 2 and 4). There was no statistical difference in these distributions between different social demographic subgroups for almost all of the symptoms studied except rhinorrhea without pus, headache and soreness, shortness of breath. The respondents with over 10 years of education tended to report earlier occurrence of headache and soreness, shortness of breath but later rhinorrhea without pus; while those aged over 60 years were more likely to experience earlier rhinorrhea without pus.

Individual symptoms and service use

Table 1 provides selected statistics of logistic regression modeling between service use and individual symptoms and socio-demographics. Education was negatively associated with seeking help from clinics (OR= 0.790[0.697-0.896]), but positively related with buying medicine (OR=1.230[1.068-1.417]) and using leftover medicine (OR=1.283[1.073-1.535]); Females were more likely to use leftover medicine than males (OR=2.016[1.411-2.881]); while age had no effects on all the behaviors. When controlled for social demographics, buying medicine was positively related with cough (OR=1.452[1.124-1.875]); while taking leftover medicine, with headache and soreness (OR=1.581[1.169-2.138]); and. seeking help from clinics, with sore throat (OR=1.355[1.109-1.654]), cough (OR=1.492[1.198-1.859]), shortness of breath (OR=1.707[1.287-2.265]) and fever (OR=2.142[1.654-2.775]). As for getting antibiotics at clinics, it only witnessed positive relation with earache and/or tinnitus (OR=4.884[1.162-20.522]); while buying antibiotics from medicine shops was only positively linked with productive cough (OR=1.971[1.125-3.453]). Rhinorrhea with pus and Rhinorrhea without pus have no associations with all the behaviors.

Concurrent symptoms and service use

Figure 4 displays the relationships between service-seeking and number of concurrent symptoms in total and by demographics. Putting together, seeking help from clinics and getting antibiotics at clinics witnessed a clear increase trend with number of symptoms. Only 37.5% of the respondents who had experienced one symptom had sought help from clinics; while 75.0% those who had experienced over seven symptoms had done so. Similarly, the use of antibiotics at clinics increased from 77.7% for patients with one symptom to 96.4% for those with over seven symptoms. However buying medicine from shops，taking leftover medicine and getting antibiotics from shops showed no statistically significant trend as the number of symptoms increased. Looking at social demographics, the increasing relationships between the number of symptoms and service-seeking were consistent across all gender, age and education subgroups. This inter-subgroup consistency was also observed in the null trend of getting antibiotics at clinics or at medicine shops by patients with increasing number of symptoms.

Discussion

This study uncovered useful data for better understanding RTIs among patients in the community and their relations with healthcare seeking and antibiotics use. It described detailed trajectories of the occurrence, peak and disappearance of common RTI symptoms. Such data are essential for both clinicians and patients, as they set expectations and let them know when the illness is deviating from the expected [6, 31]. Commonly used estimates of the expected time course of RTI symptoms are highly variable and not always evidence-based but reflects expert opinions.[32] Although a number of studies have documented onset and duration of cough, earache etc. in terms of median days or days of interquartile range,[20, 33-35]the current study is the first to portrait the course of common RTI symptoms using curves of frequencies by days following onset of RTIs. These featured curves (a sharp increase and peak followed by a long tail) provide intuitive and detailed information. This study also revealed that most of the RTI symptoms did not show statistically significant differences between socio-demographic subgroups except for education and age. The more educated tended to report earlier occurrence of headache and soreness, shortness of breath but later rhinorrhea without pus; while those aged over 60 years, more likely to experience rhinorrhea without pus. The difference between education groups may be explained by: a) the more educated may be more sensitive to their health; [22,23,36] b) the more educated may have greater chance, due to better health and environment conditions, of avoiding part of the less virulent RTIs. Similar difference in susceptibility to RTIs may also apply to the under versus over 60 years. In addition, the over 60 years may have different immunological responses as compared with that of the under 60 years [37].

The study showed selective associations between service use and socio-demographics. More specifically, education was negatively related to seeking help from clinics but positively linked to taking leftover medicine and buying medicine from shops; while females are more likely than males to take leftover medicine. However using antibiotics at clinics and medicine shops did not show any statistically significant difference between socio-demographic subgroups. These findings suggest that the decision on whether or not to seek help from clinics, to take leftover medicine or to buy medicine from a shop is made by the patients themselves and is thus amenable to the influence of the patients' socio-demographics; while the decision on whether or not to give antibiotics to patients is determined mainly by the doctors at clinics or staff at medicine shops and thus is not affected by the patients' socio-demographics. Therefore the claim that antibiotic overuse is driven by patient demand and/or expectations may be a misperception on the part of healthcare providers, or a rationalization of their own antibiotic prescribing practices. [25,38]

The study documented strong and consistent relations between symptoms and service-seeking. As the number of concurrent symptoms increased from 1 to 7 or more, the proportion of patients who had sought help from clinics increased from 37.5% to 75.0% and the proportion of service seekers who had been prescribed antibiotics increased from 77.7% to 96.4%. These findings suggest that symptoms affect both patient- and doctor-dominated behaviors and thus merit particular attention in future interventions. Interestingly, the difference in the percentage of service-seeking for patients with 1 symptom (37.5%) versus that for those with 7+ symptoms (75.0%) is substantially greater than that of antibiotics prescribing (77.7% versus 96.4%). This may be explained by: a) patients had real sufferings from the symptoms while professionals were only indirectly told about the symptoms and so patient dominated behaviors (e.g., health service-seeking) may be more sensitive to symptoms than professional-dominated ones (e.g., antibiotics prescribing); [39,40] b) as lay persons, patients may not be as capable as doctors in distinguishing important from non-important symptoms, and so numbers of symptoms have closer links with percept urgency among patients than professionals. As for the non-significant relations between number of symptoms and buying medicines from shops, it may reflect the combined effects of two drivers. On the one hand, more symptoms serve as a greater driver for the patients to seek professional help from clinics as well as medicine shops. On the other, seeking help from clinics and shops are competitive behaviors and as patients experience more symptoms they feel greater urgency to visit clinics than shops. Looking at the relations between specific symptoms and service-seeking, all those with statistical significance were positive. Seeking help from clinics was linked to, in order of magnitude of logistic regression coefficient, fever (B=0.76), shortness of breath (B=0.54), cough (B=0.40) and soreness (B=0.30).

These coefficients and their rank order reveal useful information about the perceived importance, suffering and urgency of each of the corresponding symptoms for patients. Compared with seeking help from clinics, the driving symptoms for buying medicine from shops may be relatively milder in nature and fewer in number. The former showed significant relations with 4 symptoms; while the latter, only 1 symptom, dry cough. This indicates that patients with equal access to the two kinds of help tend to choose clinics than shops if they have more and severer symptoms and vice versa. In addition, being given antibiotics at clinics was linked with earache and/or tinnitus and at medicine shops, productive cough. These seem to be consistent with published evidences.[41]

The study also has limitations. First, it relied heavily on subjective perceptions or self-reports. Individuals are poor at accurately reporting certain health behaviors and feelings. They are particularly prone to under- or over-estimations because of the inherent tendency to respond in a way that makes them appear healthier or more confirm to social standards. However, these demand characteristics are typically apparent across the board, reducing the effects of this threat to internal validity. Second, the study used a broad definition of RTIs by enumerating all common symptoms and included various infections, e.g., common cold, influencing, sore throat. So the occurrence and trajectory of symptoms may be distorted by part of the infections that were exceptionally high or low due to seasonal and other factors when the study was conducted. Third, the study was undertaken in one province of a vast and diverse country and readers are cautioned about potential risks in generalizing the findings to other parts of China.

Abbreviations

RTI(S) respiratory tract infection(s)

DSO day on which symptom occurred

DSP day on which symptom reached its peak or became most serious

DSR day on which symptom recovered

ARSO Accumulative rate of symptom occurrence

ARSP Accumulative rate of symptom peak

ARSR Accumulative rate of symptom recovery

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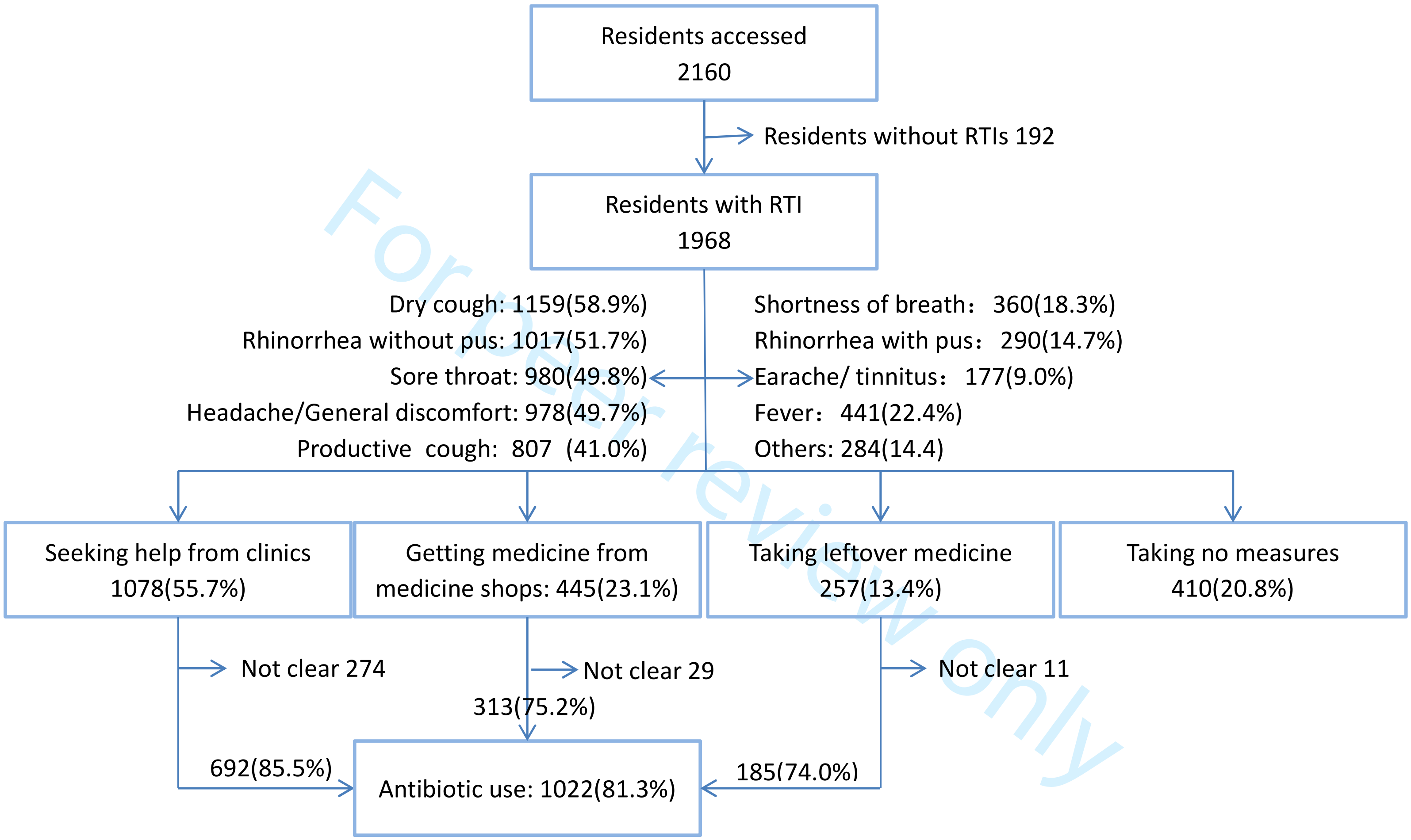


Figure 1 Flow chart describing symptoms, healthcare-seeking and antibiotics use among study population

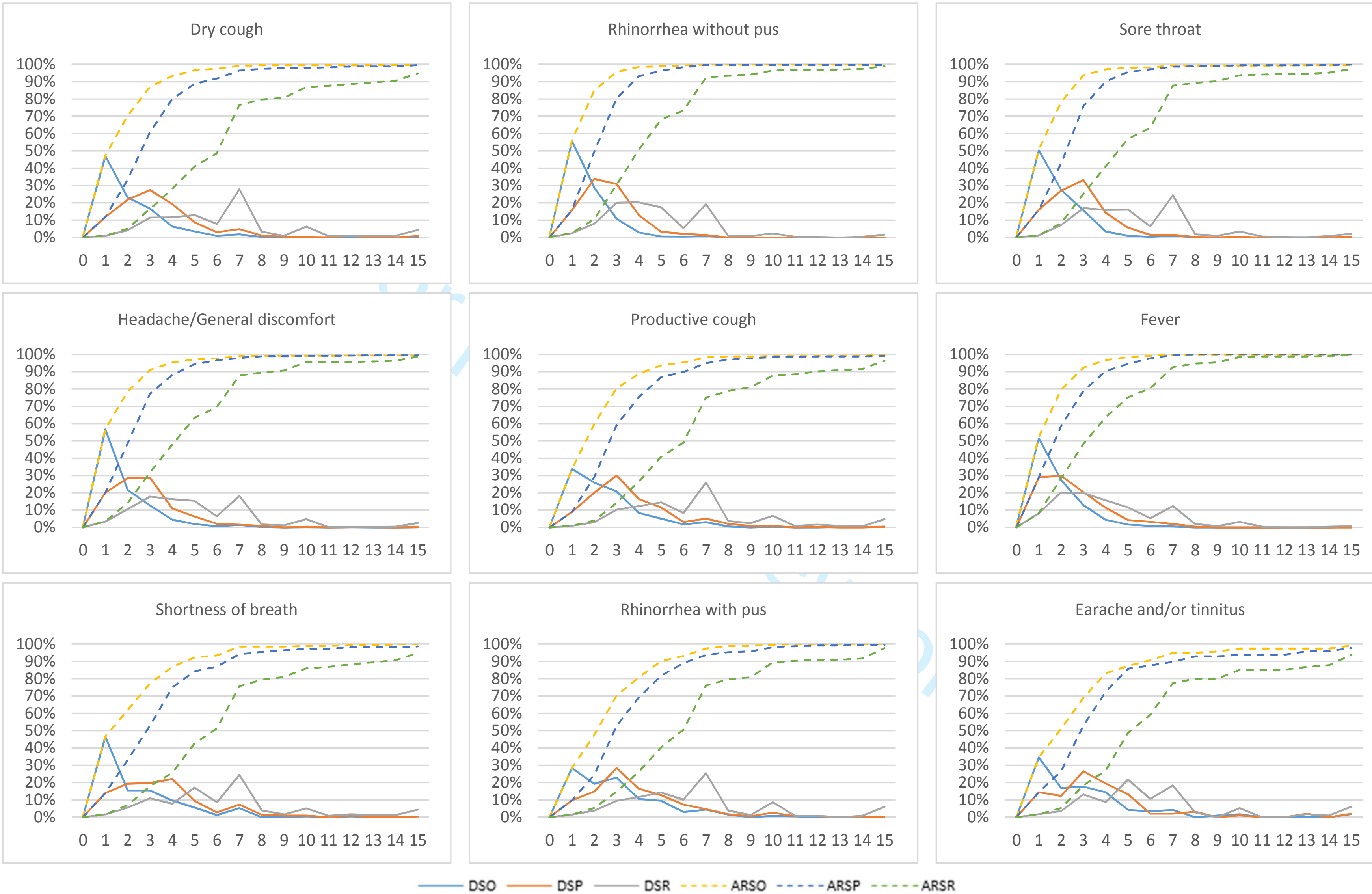


Figure2 Trajectory of common symptoms experienced in the last time RTIs (DSO: day on which symptom occurred; DSP: day on which symptom reached its peak or became most serious; DSR: day on which symptom recovered; ARSO: Accumulative rate of symptom occurrence; ARSP: Accumulative rate of symptom peak; ARSR: Accumulative rate of symptom recovery.

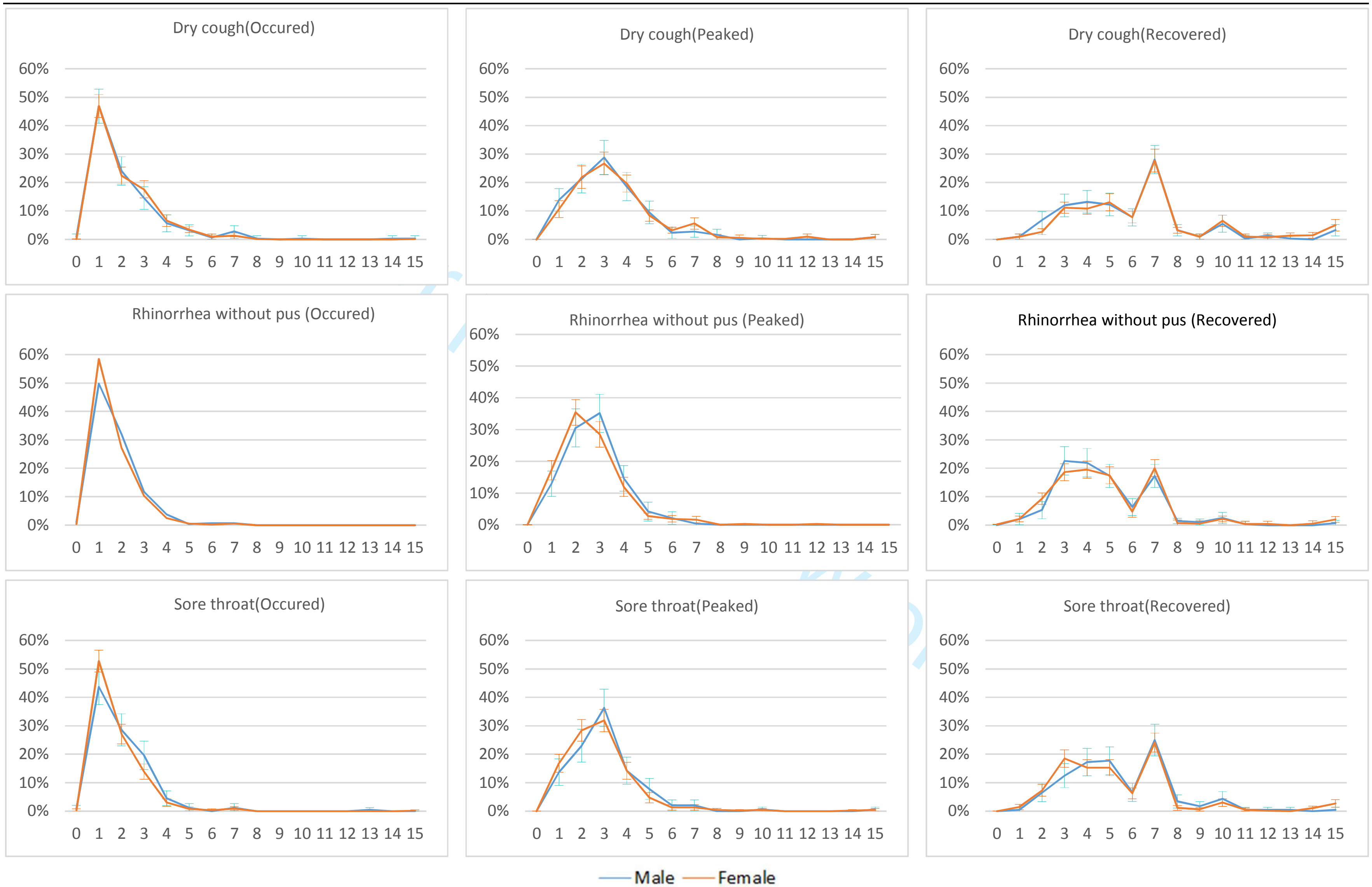


Figure 3 Symptom occurrence, peak and recovery by gender and days following onset of infection

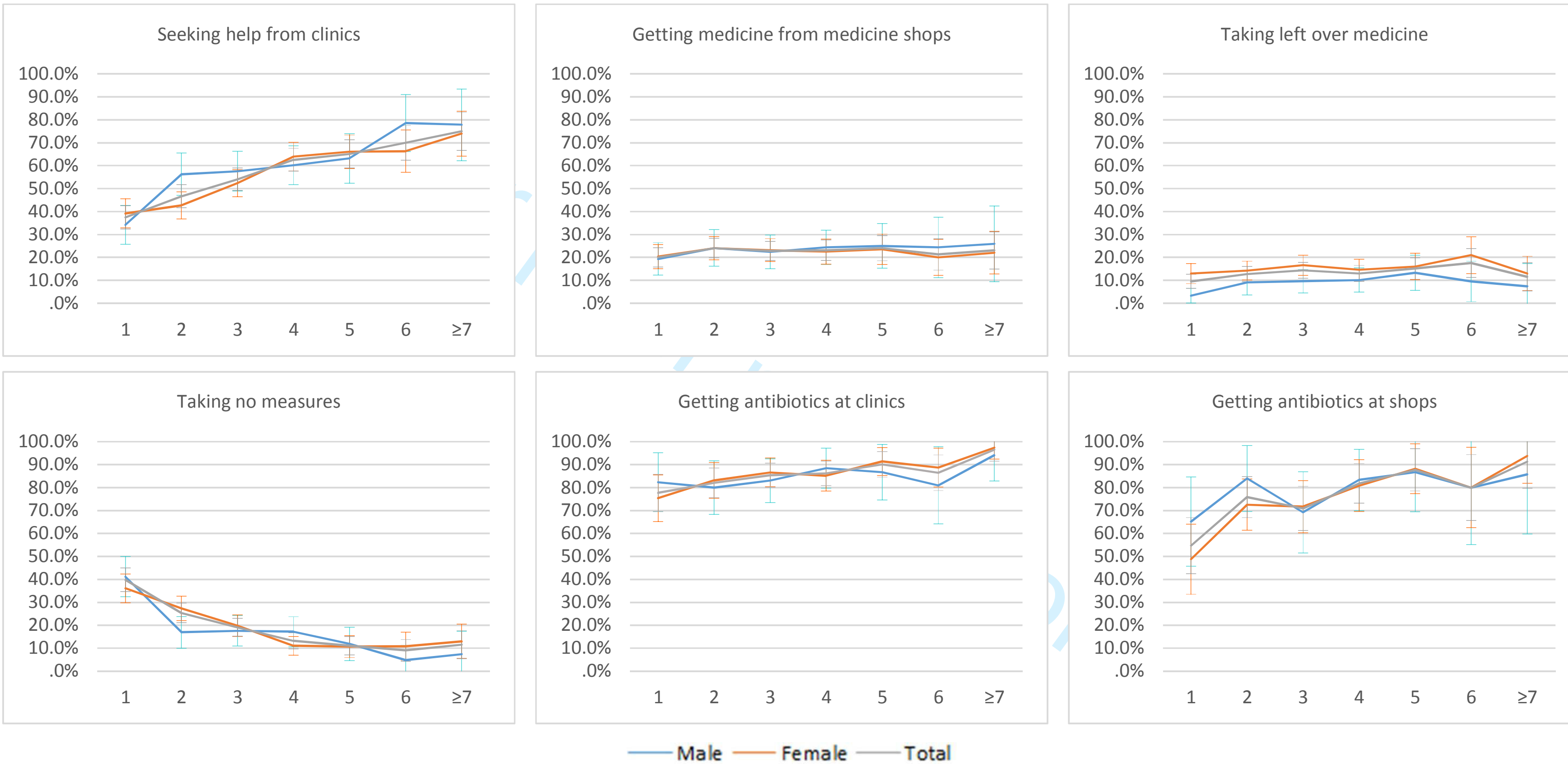


Figure 4 Service-seeking by number of symptoms in total and by genders

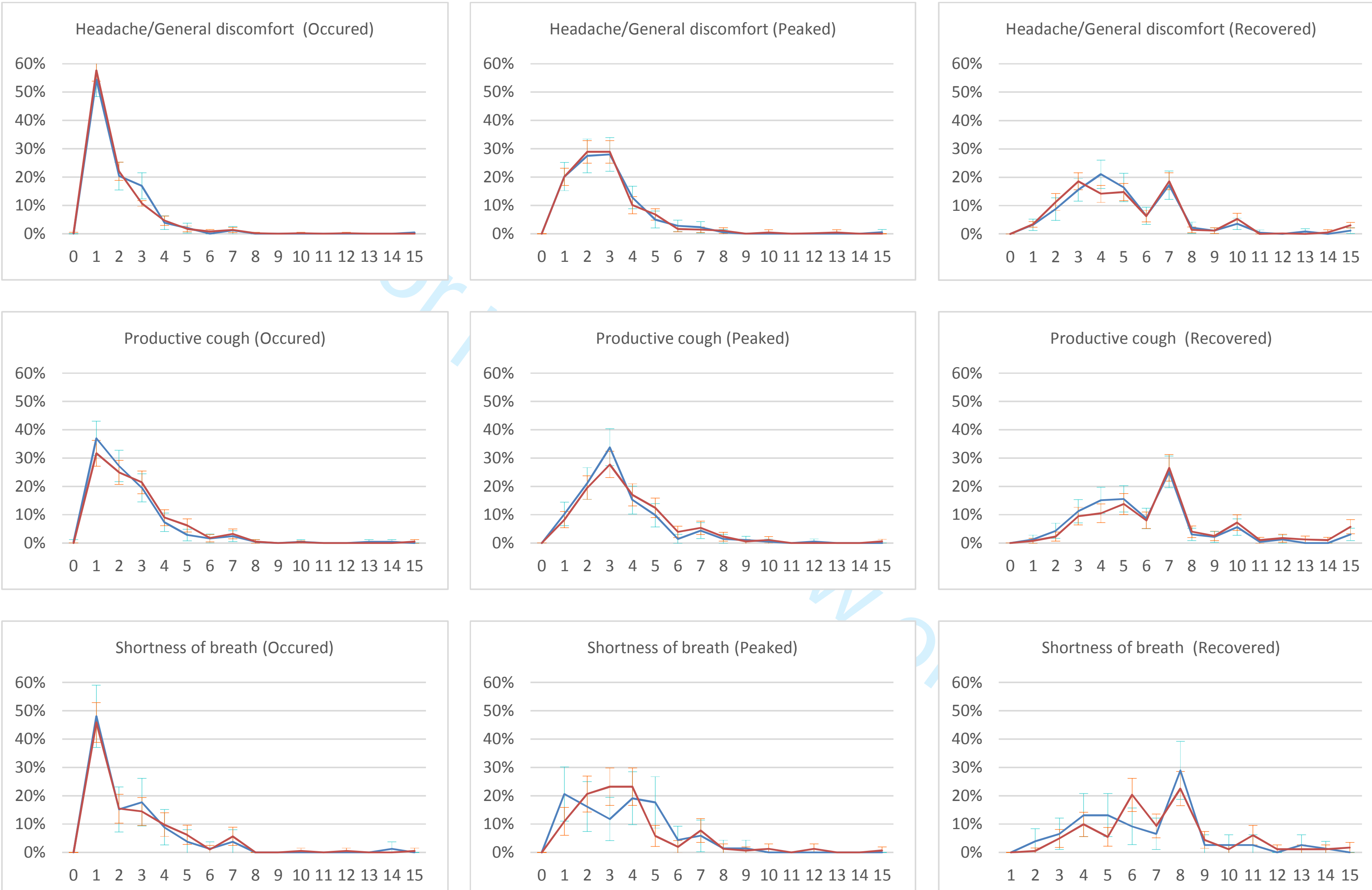
Table1 Multivariate logistic regression models between service-seeking and specific symptoms

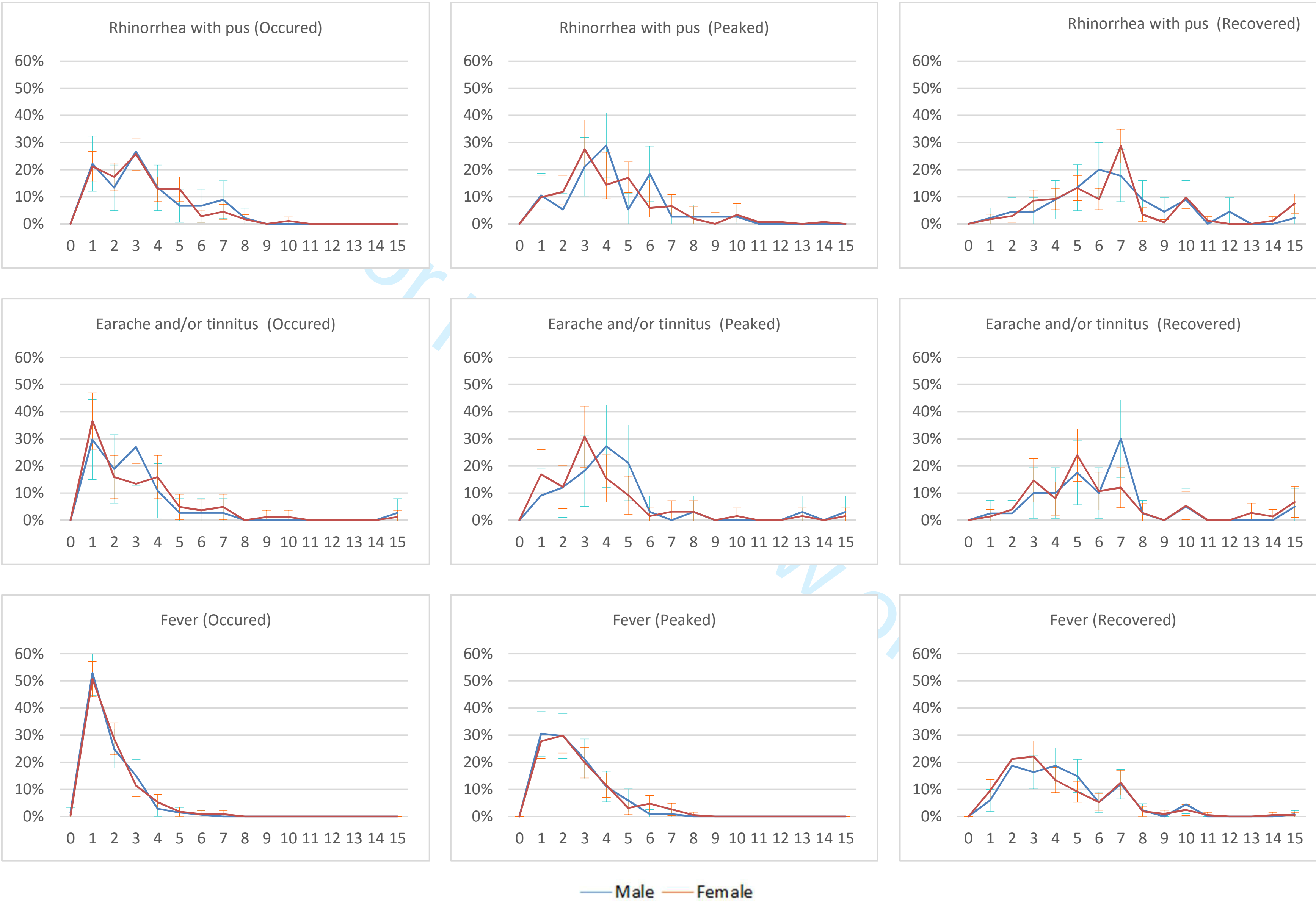
	buying medicine from shops (n1=1484,n2=445)			taking leftover medicine (n1=1668, n2=257)			Seeking help from clinics (n1=857,n2=1078)			Getting antibiotics at clinics (n1=117，n2=692)			Getting antibiotics at shops (n1=103，n2=313)		
	B	Exp(B)	95%CI	B	Exp(B)	95%CI	B	Exp(B)	95%CI	B	Exp(B)	95%CI	B	Exp(B)	95%CI
Gender	0.081	1.085	0.840-1.400	0.701	2.016	1.411-2.881	-0.200	0.819	0.653-1.027	-0.049	0.952	0.592-1.532	-0.147	0.863	0.497-1.498
Age	-0.016	0.984	0.873-1.109	-0.144	0.866	0.742-1.011	0.099	1.104	0.993-1.227	-0.119	0.887	0.704-1.118	0.022	1.022	0.789-1.324
Education	0.207	1.230	1.068-1.417	0.249	1.283	1.073-1.535	-0.235	0.790	0.697-0.896	-0.164	0.849	0.646-1.114	0.124	1.133	0.842-1.523
Sore throat	0.016	1.016	0.810-1.275	0.264	1.303	0.971-1.748	0.303	1.355	1.109-1.654	0.718	2.050	1.337-3.143	0.472	1.604	0.990-2.599
Rhinorrhea without pus	-0.176	0.838	0.669-1.051	0.055	1.057	0.791-1.411	0.044	1.045	0.856-1.276	0.223	1.250	0.816-1.915	-0.233	0.792	0.486-1.290
Rhinorrhea with pus	-0.040	0.960	0.714-1.292	-0.249	0.780	0.531-1.145	0.044	1.045	0.804-1.359	0.013	1.013	0.566-1.813	0.585	1.796	0.869-3.711
Dry cough	0.373	1.452	1.124-1.875	-0.213	0.809	0.587-1.114	0.400	1.492	1.198-1.859	0.276	1.318	0.812-2.140	0.284	1.328	0.777-2.269
Productive cough	0.025	1.026	0.798-1.318	0.247	1.280	0.926-1.770	0.109	1.115	0.891-1.395	-0.097	0.907	0.561-1.466	0.678	1.971	1.125-3.453
Shortness of breath,	-0.246	0.782	0.571-1.071	-0.365	0.695	0.458-1.054	0.535	1.707	1.287-2.265	-0.075	0.927	0.533-1.613	0.048	1.049	0.488-2.255
Earache/tinnitus	0.351	1.421	0.979-2.063	0.266	1.305	0.825-2.063	-0.278	0.757	0.535-1.072	1.586	4.884	1.162-20.522	0.398	1.489	0.608-3.648
Headache general discomfort	0.098	1.102	0.875-1.389	0.458	1.581	1.169-2.138	0.164	1.178	0.962-1.443	0.168	1.184	0.765-1.831	0.026	1.026	0.623-1.690
Fever	-0.251	0.778	0.583-1.037	0.201	1.223	0.866-1.725	0.762	2.142	1.654-2.775	0.285	1.330	0.791-2.236	0.554	1.740	0.833-3.633
Constant	-1.891	0.151		-3.737	0.024		0.052	1.054		1.699	5.466		0.215	1.239	

Note: n1 and n2 stands for the number of no and yes response respectively to each service use behavior; for each service use behavior, no (n1) was coded as 0 and yes(n2), as 1. Gender: 1=male,2=female; Age group: 1= ≤40y, 2=41-50y, 3=51-60y,4= ≥61y；Educatio:1=0 years,2=1-6 years ,3=7-9 years ,4=≥10 years. Symptoms: no= 0 and yes= 1.

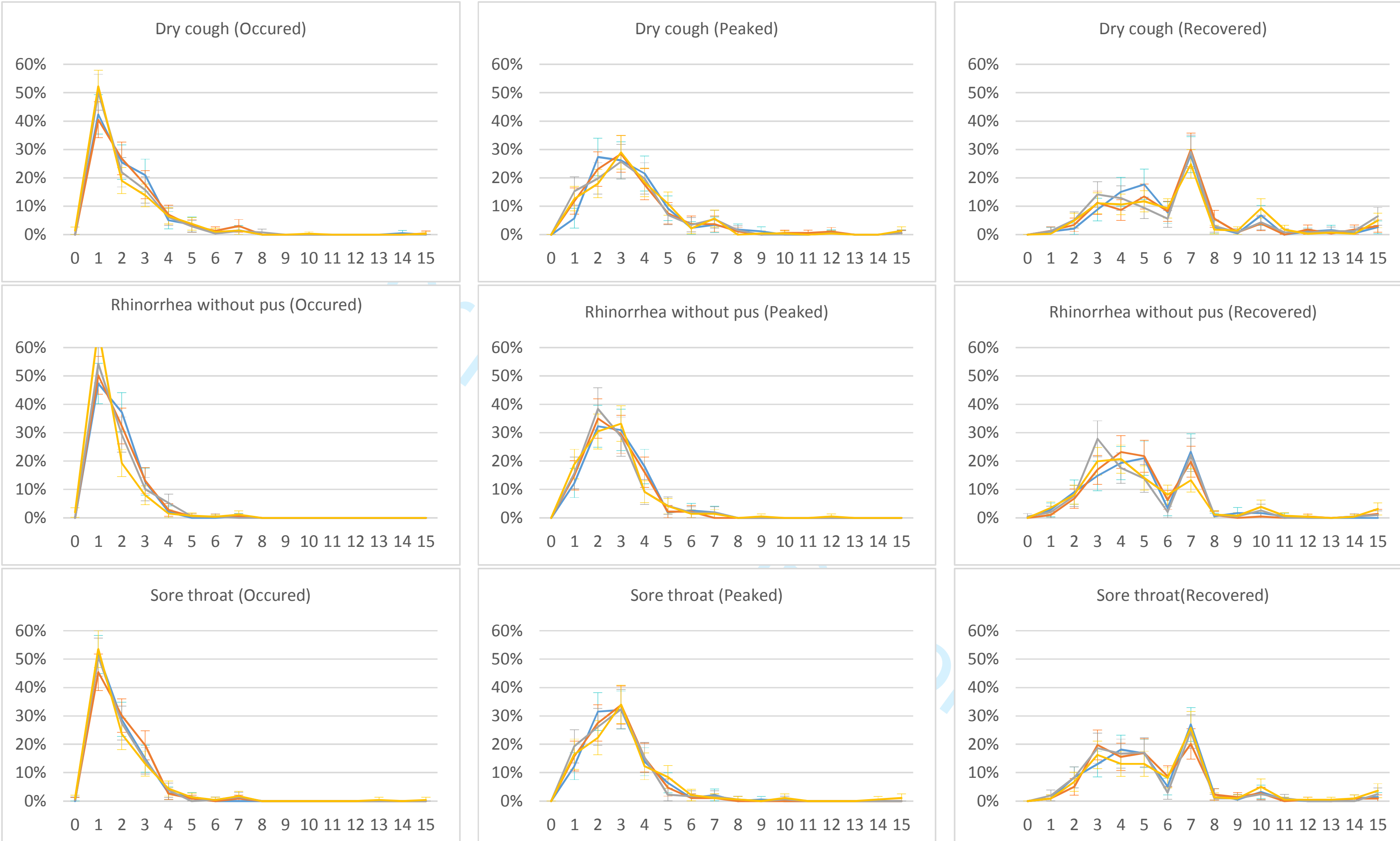
Appendix 1 Characteristics of 1968 adults with respiratory tract infection

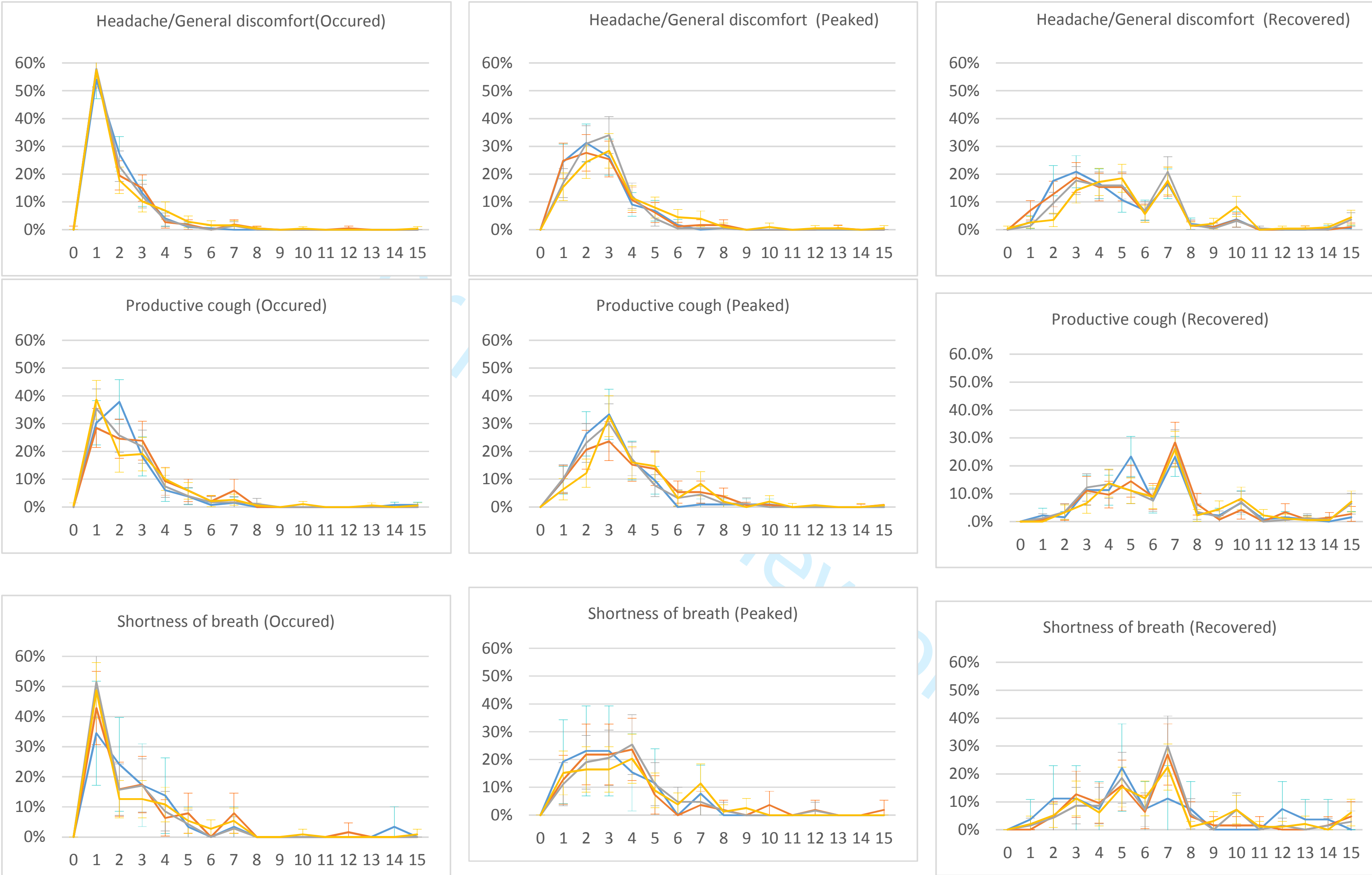
	Male	Female	Total
Age			
18-40y	128(20.3)	317(23.7)	445(22.6)
41-50y	152(24.1)	360(26.9)	512(26.0)
51-60y	134(21.3)	323(24.1)	457(23.3)
≥61y	216(34.3)	338(25.3)	554(28.2)
Education			
0y	95(15.1)	487(36.4)	582(29.6)
1-6y	195(31.0)	390(29.1)	585(29.7)
7-9y	269(42.7)	360(26.9)	629(32.0)
≥10y	71(11.3)	101(7.5)	172(8.7)
Total	630	1338	1968

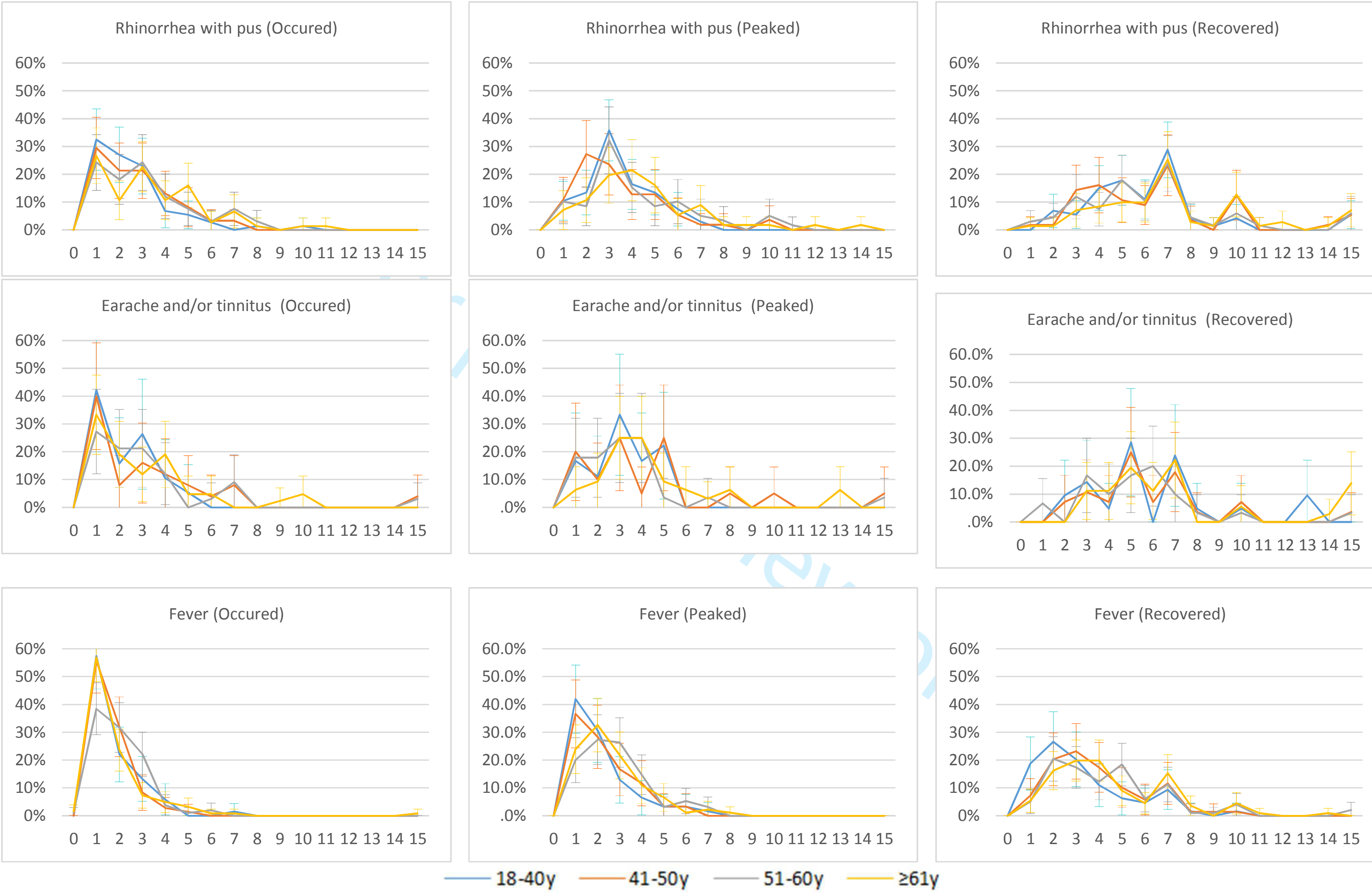

Headache/General discomfort (Occured)
Headache/General discomfort (Peaked)
Headache/General discomfort (Recovered)
Productive cough (Occured)
Productive cough (Peaked)
Productive cough (Recovered)
Shortness of breath (Occured)
Shortness of breath (Peaked)
Shortness of breath (Recovered)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15



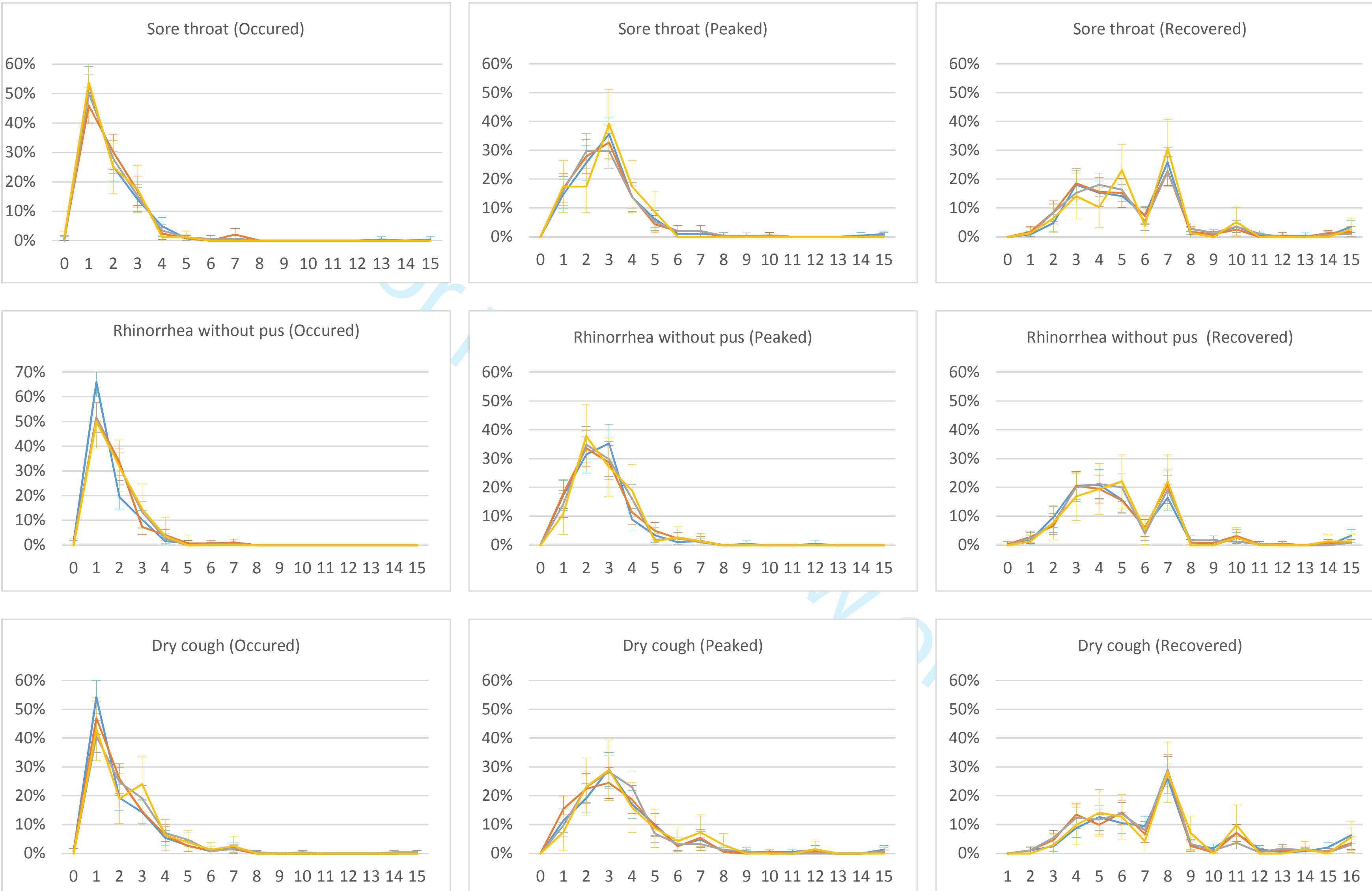
Appendix 2 Symptom occurrence, peak and recovery by gender and days following onset of infection


Dry cough (Occured)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Dry cough (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Dry cough (Recovered)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Rhinorrhea without pus (Occured)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Rhinorrhea without pus (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Rhinorrhea without pus (Recovered)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Sore throat (Occured)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Sore throat (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Sore throat(Recovered)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

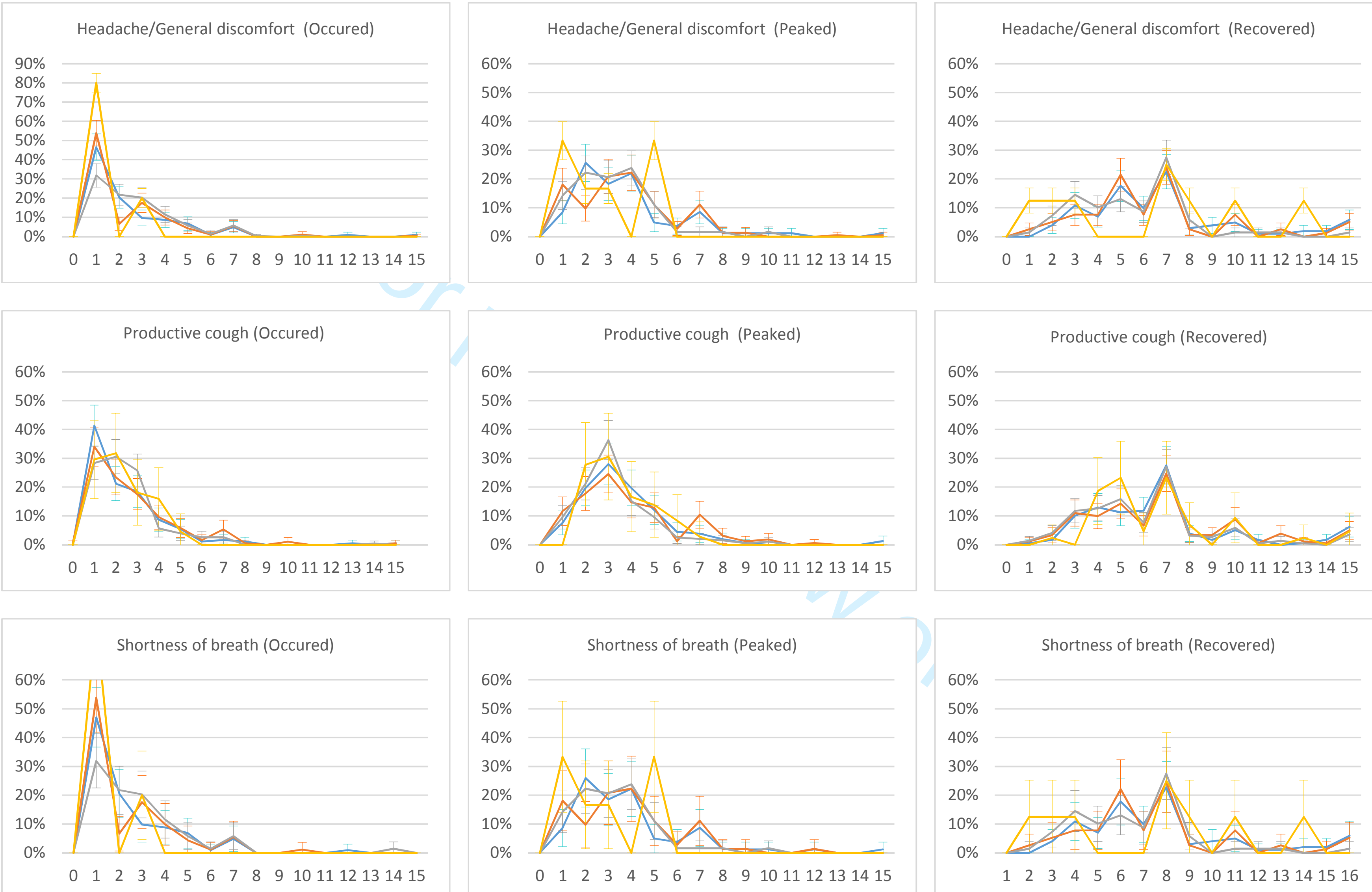

Headache/General discomfort(Occured)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Headache/General discomfort (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Headache/General discomfort (Recovered)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Productive cough (Occured)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Productive cough (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Productive cough (Recovered)
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
.0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Shortness of breath (Occured)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Shortness of breath (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Shortness of breath (Recovered)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

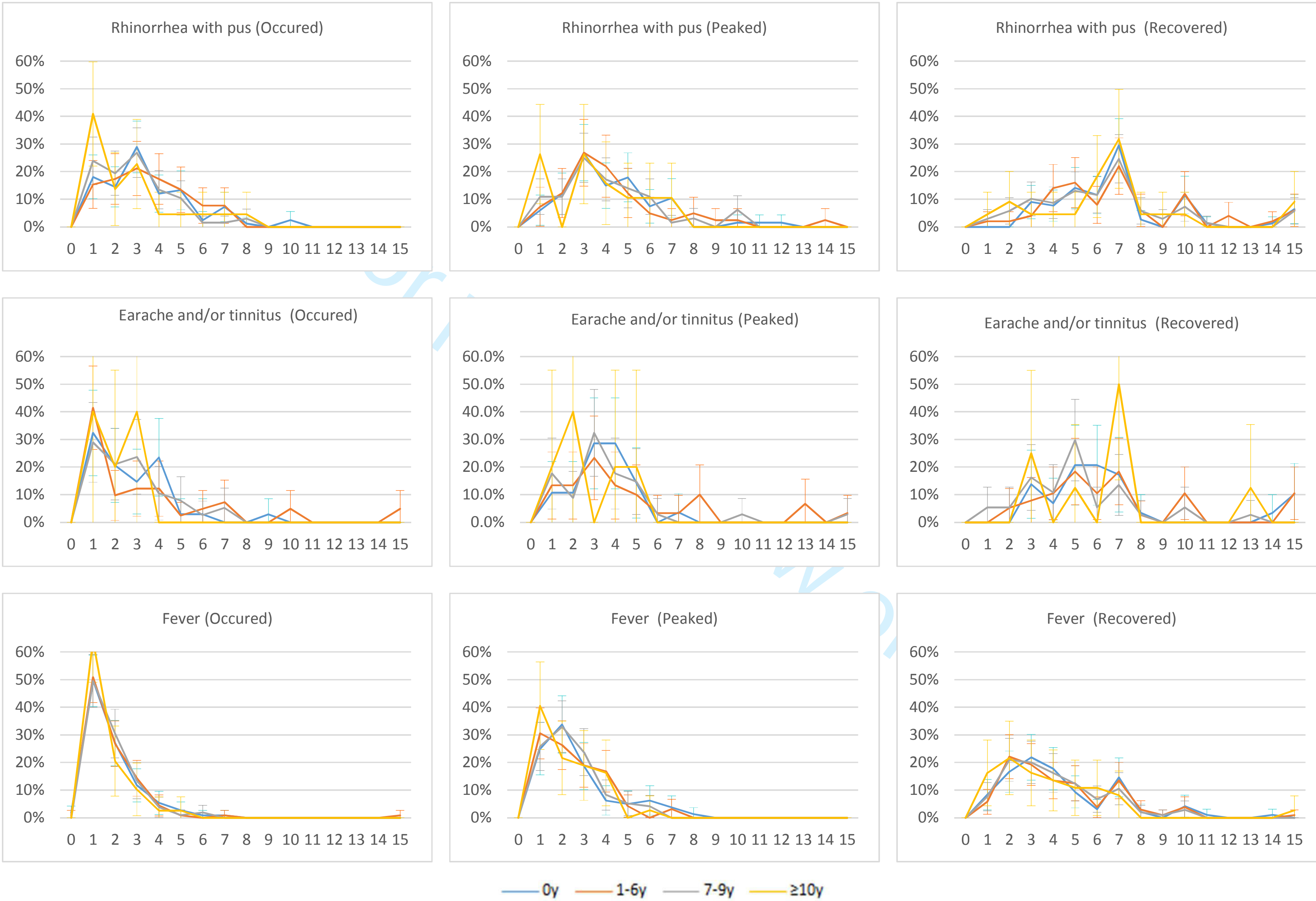


Appendix 3 Symptom occurrence, peak and recovery by age and days following onset of infection



Sore throat (Occured)
Sore throat (Peaked)
Sore throat (Recovered)
Rhinorrhea without pus (Occured)
Rhinorrhea without pus (Peaked)
Rhinorrhea without pus (Recovered)
Dry cough (Occured)
Dry cough (Peaked)
Dry cough (Recovered)
0% 10% 20% 30% 40% 50% 60% 70%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16


Headache/General discomfort (Occured)
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Headache/General discomfort (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Headache/General discomfort (Recovered)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Productive cough (Occured)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Productive cough (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Productive cough (Recovered)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Shortness of breath (Occured)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Shortness of breath (Peaked)
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Shortness of breath (Recovered)
60%
50%
40%
30%
20%
10%
0%
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16



Appendix 4 Symptom occurrence, peak and recovery by education and days following onset of infection

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	P4
Methods			
Study design	4	Present key elements of study design early in the paper	P4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P4-5
Bias	9	Describe any efforts to address potential sources of bias	P4-5
Study size	10	Explain how the study size was arrived at	P4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P17
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P4
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	P5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	P4
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P4，14
		(b) Give reasons for non-participation at each stage	P14
		(c) Consider use of a flow diagram	P14
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P5
		(b) Indicate number of participants with missing data for each variable of interest	P14
Outcome data	15*	Report numbers of outcome events or summary measures	P5-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P5-7
		(*b*) Report category boundaries when continuous variables were categorized	P17
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	P17
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	P7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P7-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	P9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P9

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

How patients' experiences of respiratory tract infections affect healthcare seeking and antibiotic use: Insights from a cross sectional survey in rural Anhui, China

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Primary Subject Heading:	Health services research
Secondary Subject Heading:	Public health, Epidemiology, Health services research
Keywords:	Respiratory tract infection, Healthcare-seeking behavior, Rural residents, Antibiotics

How patients' experiences of respiratory tract infections affect healthcare seeking and antibiotic use: Insights from a cross sectional survey in rural Anhui, China

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Debin Wang: School of Health Service Management, Anhui Medical University, Hefei, Anhui, China.

Word count: 3562

Abstract

Objective: To investigate the occurrence and trajectory of reported RTI symptoms and their effects on use of self and professional care among patients in the community.

Design: A cross sectional retrospective household survey.

Setting: 12 administrative villages from rural Anhui, China.

Participants:2160 rural adult residents aged ≥18 years registered as rural residents and actually living in the sampled villages when this study was conducted.

Method: The respondents were recruited using stratified-clustered randomized sampling. A structured questionnaire was deployed to solicit information about social demographics, symptoms of last respiratory tract infection (RTI) and healthcare-seeking following the RTI. Descriptive analyses were performed to investigate the perceived trajectory of reported symptoms and multivariate logistic regression models were developed to identify relationships between number of concurrent symptoms and healthcare-seeking and antibiotics use.

Results: A total of 1968 residents completed the survey, resulting in a response rate of 91.1%.The frequencies of day on which the symptom occurred of specific symptoms all featured a steep peak followed by a long tail. The number of concurrent symptoms showed a clear increasing trend with seeking help from clinics and being prescribed antibiotics. Multivariate regression revealed statistically significant associations between: a) visiting clinics and education(OR=0.790), sore throat(OR=1.355), cough(OR=1.492), shortness of breath(OR=1.707) and fever(OR=2.142); b) buying medicine from shops without prescription and education(OR=1.230) and cough(OR=1.452); c) getting antibiotics at clinics and sore throat(OR=2.05) and earache and/or tinnitus(OR=4.884) and d) obtaining antibiotics at medicine shops and productive cough(OR=1.971).

Conclusions: Reported RTI symptoms manifest specific trajectories and play an important role in shaping both patient- and doctor-led responses. Patients' retrospective recall of the course of prior RTI episodes and their associated actions may guide future responses to similar infections. Knowledge of these trajectories may help to inform doctors about patient expectations, enabling them better to manage shared decision-making around antibiotic treatment.

Strengths and limitations of this study

- This study demonstrates relationships between patient-reported symptoms and RTI-related healthcare-seeking.
- The study is the first to describe detailed trajectories of common symptoms and the collective effects of concurrent symptoms as perceived by patients experiencing them.
- The study relies on subjective retrospective perceptions or self-reports and therefore may be biased by potential under- or over-reporting and recall bias.
- The study used a broad definition of RTIs and the occurrence and trajectory of symptoms may be distorted by seasonal and other variations when the study was conducted.

Background

Respiratory tract infections (RTIs) are the most common diseases in humans. Studies have demonstrated that adults usually experience 1–3episodes of upper respiratory tract infection per year.[1,2] RTIs claim over 3 million lives annually and are the leading cause of death for children under 5 years.[3,4] Although many RTIs are mild and self-limiting, they are associated with a significant burden in terms of medical visits as well as work and school absenteeism.[5,6] The median duration of an episode of non-influenza-related viral respiratory tract infection (the most common but least serious kind of RTIs) is estimated to be 7.4 days, with 25% of cases lasting for 2 weeks.[7] In addition to the heavy burden on patients and health systems, RTIs are closely linked to antibiotic use and hence the development of antibiotic resistance. RTIs account for up to 60% of all antibiotic prescribing in UK primary care.[8,9] Excessive use of antibiotics is recognized as one of the most serious public health issues worldwide.[10]

According to the 10th edition of the International Classification of Diseases, RTIs comprise as many as 34 kinds of infections. However their symptoms are relatively limited, consisting mainly of sore throat, fever, cough, productive cough, rhinorrhea with or without pus, shortness of breath, headache and/or general discomfort, earache and/or tinnitus.[11,12] When faced with symptoms, patients' responses vary greatly. Some patients manage their symptoms by simply resting, drinking warm water etc. without using any medicines;[13]others buy medicines from medicine shops or pharmacies or seek professional help from doctors;[14-16] still others opt for traditional remedies.[17,18] A 2014 study of consumer attitudes on cough and cold in USA indicated that 36.1% of those surveyed reported beginning over-the-counter (OTC) treatment at the first sign of a cough or cold, 42.6% waited until cold symptoms 'get bad enough' (i.e. to cause distress) and another 20.2% waited until they had more than one symptom before beginning treatment. Altogether, 55% sought professional care eventually [19]. These varied responses have been attributed to a wide range of reasons including: features of the disease, such as severity of symptoms and their patterns of progression;[2] 'demand side' issues such as age, gender, education,[20] knowledge and attitudes about RTIs and RTI-related services,[21-25] cultural expectations and social norms;[26,27] and 'supply side' factors such as perverse financial incentives, systemic pressures on healthcare providers and professional standards.[26,28,29]

RTIs are very common in China with an incidence rate ranging from 84.13% to 120.83% in 2006.[30] This translates to 1.16 to 1.67 billion person-times of RTIs annually in the whole country. Data about service use for RTIs among China residents are scarce, but the limited research available reports huge discrepancies between different populations and very high use of antibiotics in various medical settings. An earlier study in rural primary care settings of 10 provinces in Western China found that nearly 50% of patients were prescribed antibiotics.[31] Another recent study found that antibiotics were prescribed for 78% of colds and 93.5% of

acute bronchitis cases.[32] According to our systemic literature review, few studies focus on factors affecting service and antibiotics use for RTIs or investigate reasons for variations in service use and antibiotic prescribing for RTIs in China. Although a number of papers on reasons for health service utilization in general did include RTIs as a subcomponent, they addressed only demand and supply side factors, with little attention being paid to the occurrence and trajectory of RTI symptoms among patients in the community and their effects on decisions about self or professional care. This study therefore aimed to investigating the occurrence and trajectory of self-reported RTI symptoms and their effects on use of self and professional care among patients in the community.

Methods

Sites and population

The study used across a sectional retrospective household survey design and adopted a stratified-clustered randomized sampling approach in recruiting site villages and participating residents. Selection of site villages proceeded in 4 steps. Step 1 divided all counties in Anhui province into north, middle and south regions. Step 2 randomly selected 4 counties from each of the three regions and 1 township from each of the counties selected and then 1 administrative village from each of the site townships selected above. Step 3 randomly selected 1 household from the village selected as the starting household and then recruited 180 households that were geographically closest to the starting household. Step 4 randomly selected one household member from each of these households according to preset eligibility criteria, i.e., men and women who were aged 18 years and over, were registered as rural residents and were actually living in the sampled villages when this study was conducted, and were willing and able to participate in the survey.

Questionnaire

The study used a structured questionnaire consisting of questions about four categories of variables: a) social demographics (e.g., gender, age and education); b) last episode of symptomatic RTI, including symptoms experienced and day on which each specific symptom occurred (DSO), reached its peak or became most serious (DSP) and recovery (DSR); c) responses to the RTI, including taking leftover medicines, buying any type of medicine OTC from medicine shops(here after referred to as buying medicine) and seeking treatment from clinics; d) antibiotics obtained from clinics and medicine shops. In China, a pharmacy generally refers to a department within a hospital or clinic that dispenses medicines to patients according to prescriptions by the clinicians working for the same hospital/clinic; while a medicine shop is an independent business that sells medicines to customers with or without prescriptions from clinicians. 'Seeking help from clinics' refers to visiting a local health facility staffed by a qualified health professional and is thus largely equivalent to 'seeking professional care' in western countries. Conversely, the use of antibiotics does not necessarily mean that professional care was sought. Antibiotics may be purchased from medicine shops directly without prescription or kept at home for subsequent use. Almost all medicine shops in China sell both OTC and non-OTC medicines, including antibiotics. Although they may be displayed in separate cabinets, in practice non-OTC medicines may be purchased directly without prescription and customers generally do not distinguish these two types of medicines.

Data collection

Field data collection took place from 30 April-12 May 2016 via face-to-face interviews using the structured questionnaire. Twenty-six under graduate students from Anhui Medical University performed the interviews. Measures taken to ensure data quality included: a) training and examination of the data collectors; b) daily checks by a quality control supervisor of all questionnaires completed each day; c) retest of 5% randomly selected subjects; d) feedback of errors found via daily checks and readministering of the questionnaire; e) elimination of disqualified field data collectors.

Data analysis

Data were double-entered using EPI DATA 3.1 and SPSS 10.01 and Microsoft Excel 2010 were used to analyze the data. Data analysis included: a) distribution of respondents by gender, age and education; b) percentages and accumulative percentages of patients by DSO, DSP and DSR for different RTI symptoms in total and by different demographics; c) multivariate logistic regression of healthcare-seeking and antibiotics use using social demographics and common symptoms as the independent variables; d) relationships between number of symptoms experienced by a single patient and his or her healthcare-seeking and antibiotics use. Cases with missing data were excluded from the data analyses.

Ethical review

The study protocol was reviewed and approved by the Biomedical Ethics Committee of Anhui Medical University (reference number: 201500800) prior to the study commencing. Participation of rural residents was voluntary and written informed consent was obtained from all participants.

Results

Overview of participants, symptoms and healthcare-seeking

As shown in Figure 1 and Appendix 1, a total of 2160 residents were accessed and 1968 completed the survey, resulting in a response rate of 91.1%. The mean age of respondents was 50.39 years (SD=13.04 years). The majority (68.0%) were females and around one third (29.6%) had no formal school education (for details, see Appendix). The high proportion of female respondents in this random sample results from the fact that in this rural area the majority of male residents have moved to cities to obtain temporary work [33]. Over 80% of reported infections had occurred within nine months prior to the survey. Dry cough (58.9%, 1159), rhinorrhea without pus (51.7%, 1017) and sore throat (49.8%, 980) were the most common symptoms. 55.7% of respondents reported seeking professional help from clinics, 13.4% bought medicine from medicine shops, 23.1% used leftover medicine from previous illnesses and 20.8% did nothing. Altogether, 81.3% of respondents reported having used antibiotics to treat their RTI. As shown in Table 1, Time interval between onset of infection and when the data were collected was not associated with any statistical differences between in healthcare-seeking behavior except use of leftover medicines, suggesting that recall bias had limited effects (see also Discussion and Limitations sections).

Development of symptoms

Figure 2 displays common symptoms reported by respondents for their most recent episode of RTI. Day of onset of specific symptoms (DSO) all feature a skewed peak; that is, they increased rapidly at the beginning, reached a sharp peak on day 1 or 2 and then tailed off over 15 days. The height of symptom peaks varied across symptoms, ranging from 46.5% for shortness of breath to 56.8% for sore throat. The curves representing the most acute experience of the symptom (DSP) for specific symptoms mimic the shape of DSO in general, but are delayed (by 2-3 days) and lower (by 22.0% to 40.1%) peak. The DSR curves deviate a step further from DSO curves, with 2-3 peaks centered on days 3, 5, 10 and especially day 7. The lines depicting accumulative rates of symptom occurrence (ARSO), symptom peak (ARSP) and symptom recovery (ARSR) by different days following onset of RTIs all show an atypical "S-shape". Accumulative rates of symptom occurrence for rhinorrhea display the fastest increase followed by sore throat, fever, headache/general discomfort, cough and shortness of breath. For the same symptom, accumulative rates of symptom peak (ARSP) are much closer to those for symptom occurrence (ARSO) than symptom recovery (ARSR). The time lag between symptom occurrence (ARSO) and recovery (ARSR) was longest for cough, followed by that of sore throat, shortness of breath, rhinorrhea headache/general discomfort and fever.

Figure 3 shows the distribution of DSO, DSP and DSR of three selected symptoms (dry cough, rhinorrhea without pus, sore throat) by gender (more information about symptom trajectories by different subgroups is given in Appendices2 to 4). Statistical differences in these distributions between different social demographic groupings are apparent only for the symptoms rhinorrhea without pus, headache and soreness, and shortness of breath. Respondents with over 10 years of education tended to report earlier occurrence of headache and soreness, and shortness of breath but later occurrence of rhinorrhea; while those aged over 60 years were more likely to report earlier occurrence of rhinorrhea.

Individual symptoms and treatment-seeking

Table 2 displays logistic regression modeling of service use individual symptoms and socio-demographic characteristics. Education was negatively associated with seeking help from clinics (OR=0.790[0.697-0.896]), but positively related with buying medicine (OR=1.230[1.068-1.417]) and using leftover medicine (OR=1.283[1.073-1.535]); Females were more likely to use leftover medicine than males (OR=2.016[1.411-2.881]), while age had no effects on any treatment-seeking behavior. When controlled for social demographic characteristics, buying medicine was positively related with cough (OR=1.452[1.124-1.875]); taking leftover medicine, with headache and soreness (OR=1.581[1.169-2.138]); and. seeking help from clinics, with sore throat (OR=1.355[1.109-1.654]), cough (OR=1.492[1.198-1.859]), shortness of breath (OR=1.707[1.287-2.265]) and fever (OR=2.142[1.654-2.775]). Being prescribed antibiotics at clinics was related positively only to with earache and/or tinnitus (OR=4.884[1.162-20.522]), while purchasing antibiotics OTC from medicine shops was positively linked with productive cough (OR=1.971[1.125-3.453]). Rhinorrhea with or without pus are not associated with any specific treatment-seeking behavior.

As shown in Figure 4, over 60.5% of healthcare-seeking happened between two days before and one day after symptoms peaked. Less than 7% of healthcare-seeking occurred two or more days after symptoms had peaked. The timing of healthcare-seeking showed varied extent of clustering on different symptom peaks, being most narrowly centered for Fever followed by Headache/General discomfort and Rhinorrhea without pus.

Concurrent symptoms and service use

Figure 5 and Appendices 5-6 display the relationships between service-seeking and number of concurrent symptoms in total and by demographic characteristics. Overall, seeking help from clinics and getting antibiotics at clinics show a clear increasing trend with number of symptoms. Only 37.5% of respondents who had experienced one symptom had sought help from a clinic, while 75.0% those who had experienced over seven symptoms had done so. Similarly, the use of antibiotics at clinics increased from 77.7% for patients with one symptom to 96.4% for those with over seven symptoms. However buying medicine from shops，taking leftover medicine and getting antibiotics from shops showed no statistically significant trend as the number of symptoms increased. The relationships between number of symptoms and service-seeking were consistent across all gender, age and education subgroups. This inter-subgroup consistency was also observed in the null trend of getting antibiotics at clinics or at medicine shops by patients with increasing number of symptoms.

Discussion

This study has uncovered useful data for better understanding the experience of RTIs among patients in the community and their relations with healthcare seeking and antibiotics use. Since the respondents' reports of RTI symptoms are retrospective and relate to experiences of illness and its treatment occurring up to nine months previously, our data provide insights into their perceptions of symptom trajectories rather than actual trajectories. However, self-reported disease courses are of equal (if not greater) significance than actual ones in terms of healthcare-seeking. When faced with an RTI, a patient's experiences and recollections of previous similar symptoms may affect his/her prediction of the current infection and thus inform decisions about whether or what type of healthcare to use; while perceptions leading to inappropriate treatment imply education and counseling needs.

Knowledge of patients' perceptions of RTI symptom trajectories is valuable for both clinicians and patients, as they set expectations and facilitate recognition of when an illness is deviating from the expected course [34]. Commonly used estimates of the expected time course of RTI symptoms are highly variable and not always evidence-based but reflect expert opinion. [35] Although a number of studies have documented onset and duration of cough, earache etc. in terms of median days or days of inter quartile range,[19, 36-38] the current study is the first to portray the course of common RTI symptoms as experienced and reported by patients, using frequency curves by days following onset. Our interpretation of the featured curves (a sharp increase and peak followed by a long tail) is that they reflect the joint effects of not only the pathology of RTIs, but also health service use and psycho-social factors, as well as memory/self-report biases. Comparison of such curves for different symptoms and from different populations may yield new insights. Our study found that multiple peaks occurred only in the curves of symptom recovery days and that different symptom peaked after different days rather than together. While the length of time between RTI episode and data collection could lead to 'wild guessing' the peaks on day 7 and 10 are more likely to be attributable to 'rough reporting', since in China people customarily plan activities and measure time periods in terms of 'Zhou (a week)' or 'Xun (ten days)'.

Interestingly, our symptom trajectories did not show statistically significant differences between socio-demographic characteristics except for education and age. Education-based differences in symptom reporting may be attributable to those with more education being more conscious of their health; [22,23,39] and by them having greater likelihood, due to better health and environment conditions, of avoiding some of the less virulent RTIs. Similar differences in susceptibility to RTIs may also apply to the observed difference between those under versus over 60 years.

The study showed selective associations between service use and socio-demographic characteristics. Education was negatively related to seeking help from clinics but positively associated with taking leftover medicine and buying medicine from shops; while females are more likely than males to take leftover medicine. However, specifically using antibiotics obtained from clinics and medicine shops did not show any statistically significant socio-demographic differences. These findings may suggest that decisions on whether or not to visit a clinic, take leftover medicine or buy medicine from a shop is made by patients themselves and is thus amenable to the influence of patients' socio-demographic characteristics; while the decision on whether or not to provide antibiotics to patients is determined mainly by the doctors at clinics or staff at medicine shops and thus is not affected by these characteristics.

The study documented strong and consistent relations between symptoms and service-seeking. As the number of concurrent symptoms increased from 1 to 7 or more, the proportion of patients who had sought help from clinics increased from 37.5% to 75.0% and the proportion of service seekers who had been prescribed antibiotics increased from 77.7% to 96.4%. These findings suggest that clustering of symptoms affect both patient- and doctor-led behavior and thus merit particular attention in future interventions. Interestingly, the difference in the percentage of service-seeking for patients with 1 symptom (37.5%) versus that for those with 7+ symptoms (75.0%) is substantially greater than that of antibiotics prescribing (77.7% versus 96.4%). One possible explanation for this difference is that patients directly suffer from symptoms while professionals are only told about them by their patients, so patient-led behaviors (i.e. health service-seeking) may be more sensitive to symptoms than professional-led ones (i.e. antibiotics prescribing). [40,41] In addition, as lay persons, patients may not be as capable as doctors of distinguishing important from non-important symptoms, and so numbers of symptoms have closer links with perceptions of acute or serious illness among patients than among health professionals. As for the lack of correlation between number of symptoms and purchase of medicines from shops, this may reflect the combined effects of two drivers. On the one hand, more symptoms serve as a greater driver for patients to seek professional help from clinics as well as medicine shops. On the other, seeking help from clinics and shops are competitive behaviors and as patients experience more symptoms they are more likely to visit clinics than shops.

Positive relationships were found between a number of specific symptoms and service-seeking. Seeking help from clinics was linked to, in order of magnitude of logistic regression coefficient, fever (B=0.76), shortness of breath (B=0.54), cough (B=0.40) and soreness (B=0.30). These coefficients and their rank order reveal useful information about the perceived importance, suffering and urgency of each of the corresponding symptoms for patients. Compared with seeking help from clinics, the driving symptoms for buying medicine from shops may be milder in nature and fewer in number, with only 1 symptom, dry cough, being positively associated with the latter behavior. This indicates that patients with equal access to the two kinds of help tend to choose clinics rather than shops if they have more and severer symptoms and vice versa. In addition, being given antibiotics at clinics was linked with earache and/or tinnitus and at medicine shops, with productive cough. These findings are consistent with published evidence.[42]

Study Limitations

The study has a number of limitations. First, prior care may have affected the symptom trajectories reported in this paper. Given that over 80% of patients had used antibiotics, the curves of RTI symptoms derived in this study may differ from 'natural' trajectories without any treatment and in western communities where antibiotics use is much lower. Unfortunately, we were unable to find similar trajectory data from western populations. However, although antibiotic use is much higher in China than in US, data about RTI duration from our populations seem to be close to that from US. [19,43].This suggests that the effect of antibiotics on RTI trajectory in the community may not be particularly important, since the majority of RTIs are caused by viruses rather than bacteria.

Secondly, the study relied on subjective perceptions and self-reports. Individuals are poor at accurately reporting certain health behaviors and feelings and inherent tendencies to respond in ways that make them appear healthier or otherwise confirm to social norms may introduce bias. However, these characteristics are typically apparent across the board, reducing the effects of this threat to internal validity. More importantly, the long recall period between last experienced episode and survey data collection is likely to have led to recall bias; milder RTIs in particular, exact patterns of symptom experience and details of associated treatment-seeking behavior may have been forgotten. Our findings do suggest some extent of recall/memory bias, but Table 1 shows that there was no statistical relationship between time interval from onset of infection and data collection for any healthcare-seeking behavior except for use of leftover medicines, which was reported as 9.6% among patients with a time interval of over 9 months compared with 16.2% among patients with a less than 3 months time interval. Moreover, as described in the discussion, our analysis treats these data as proxy evidence of patients' typical perceptions of the course of infection rather than of the actual course of infection.

Third, given the broad symptom-based definition of RTIs used in the study, seasonal and other influences on symptom occurrence may have affected the frequency and trajectory of symptoms. Fourth, the overrepresentation of females may raise concerns about selection biases. However, our analysis revealed no significant differences by gender in terms of symptom-related treatment-seeking except for taking leftover medicines, which was more commonly reported by females.

Abbreviations

RTI(S) respiratory tract infection(s)
DSO day on which specific symptom occurred
DSP day on which symptom reached its peak or became most serious
DSR day on which symptom recovery
ARSO Accumulative rate of symptom occurrence
ARSP Accumulative rate of symptom peak
ARSR Accumulative rate of symptom recovery

Contributors

Mengjie Diao participated in data collection and drafted the manuscript. Xingrong Shen and Rui Feng designed the instruments and performed data analysis. Jing Cheng and Jing Chai implemented field data collection, trained data collectors and controlled data quality. Rongyao Zhou and Panpan Zhang implemented the data collection. Debin Wang and Helen Lambert provided expertise for overall design of the study and revised and finalized the manuscript. All authors approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Figure 1 Flow chart describing symptoms, healthcare-seeking and antibiotics use among study population

Figure2 Trajectory of common symptoms experienced in the last time RTIs

Figure 3 Symptom occurrence, peak and recovery by gender and days following onset of infection

Table1 Service use by time interval in between onset of infection and data collection

Table2 Multivariate logistic regression models between service-seeking and specific symptoms

Figure 4 distribution of healthcare-seeking by time difference between day on which patient sought healthcare and day on which symptom peaked

Figure 5 Service-seeking by number of symptoms in total and by genders

Table 1 Service use by time interval between onset of infection and data collection

Time interval (Days)	Total	Buying medicine from medicine shops	Taking leftover medicine	Seeking help from clinics	Getting antibiotics at clinics	Getting antibiotics at medicine shops
≤90	844(44.6%)	196(23.3%)	136(16.2%)	475(56.3%)	315(86.1%)	144(77.4%)
91-180	494(26.1%)	107(21.8%)	60(12.2%)	276(55.9%)	177(85.9%)	67(67.0%)
181-270	192(10.2%)	51(26.6%)	18(9.4%)	110(57.3%)	72(85.7%)	38(80.9%)
≥271	361(19.1%)	80(22.2%)	34(9.6%)	198(54.8%)	116(84.7%)	59(78.7%)
χ^2		1.907	13.438	0.355	0.165	5.409
P		0.592	**0.004**	0.949	0.983	0.144

Table 2 Multivariate logistic regression models between service-seeking and specific symptoms

	buying medicine from shops (n1=1484,n2=445)		taking leftover medicine (n1=1668, n2=257)		Seeking help from clinics (n1=857,n2=1078)		Getting antibiotics at clinics (n1=117， n2=692)		Getting antibiotics at shops (n1=103，n2=313)	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Gender	1.085	0.840-1.400	**2.016**	**1.411-2.881**	0.819	0.653-1.027	0.952	0.592-1.532	0.863	0.497-1.498
Age	0.984	0.873-1.109	0.866	0.742-1.011	1.104	0.993-1.227	0.887	0.704-1.118	1.022	0.789-1.324
Education	**1.23**	**1.068-1.417**	**1.283**	**1.073-1.535**	**0.79**	**0.697-0.896**	0.849	0.646-1.114	1.133	0.842-1.523
Sore throat	1.016	0.810-1.275	1.303	0.971-1.748	**1.355**	**1.109-1.654**	**2.05**	**1.337-3.143**	1.604	0.990-2.599
Rhinorrhea without pus	0.838	0.669-1.051	1.057	0.791-1.411	1.045	0.856-1.276	1.25	0.816-1.915	0.792	0.486-1.290
Rhinorrhea with pus	0.96	0.714-1.292	0.78	0.531-1.145	1.045	0.804-1.359	1.013	0.566-1.813	1.796	0.869-3.711
Dry cough	**1.452**	**1.124-1.875**	0.809	0.587-1.114	**1.492**	**1.198-1.859**	1.318	0.812-2.140	1.328	0.777-2.269
Productive cough	1.026	0.798-1.318	1.28	0.926-1.770	1.115	0.891-1.395	0.907	0.561-1.466	**1.971**	**1.125-3.453**
Shortness of breath,	0.782	0.571-1.071	0.695	0.458-1.054	**1.707**	**1.287-2.265**	0.927	0.533-1.613	1.049	0.488-2.255
Earache/tinnitus	1.421	0.979-2.063	1.305	0.825-2.063	0.757	0.535-1.072	**4.884**	**1.162-20.522**	1.489	0.608-3.648
Headache general discomfort	1.102	0.875-1.389	1.581	1.169-2.138	1.178	0.962-1.443	1.184	0.765-1.831	1.026	0.623-1.690
Fever	0.778	0.583-1.037	1.223	0.866-1.725	**2.142**	**1.654-2.775**	1.33	0.791-2.236	1.74	0.833-3.633

Note: n1 and n2 stands for the number of no and yes response respectively to each service use behavior; for each service use behavior, no (n1) was coded as 0 and yes(n2), as 1. Gender: 1=male,2=female; Age group: 1= ≤40y, 2=41-50y, 3=51-60y,4= ≥61y；Educatio:1=0 years,2=1-6 years ,3=7-9 years ,4=≥10 years. Symptoms: no= 0 and yes= 1； Medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines.

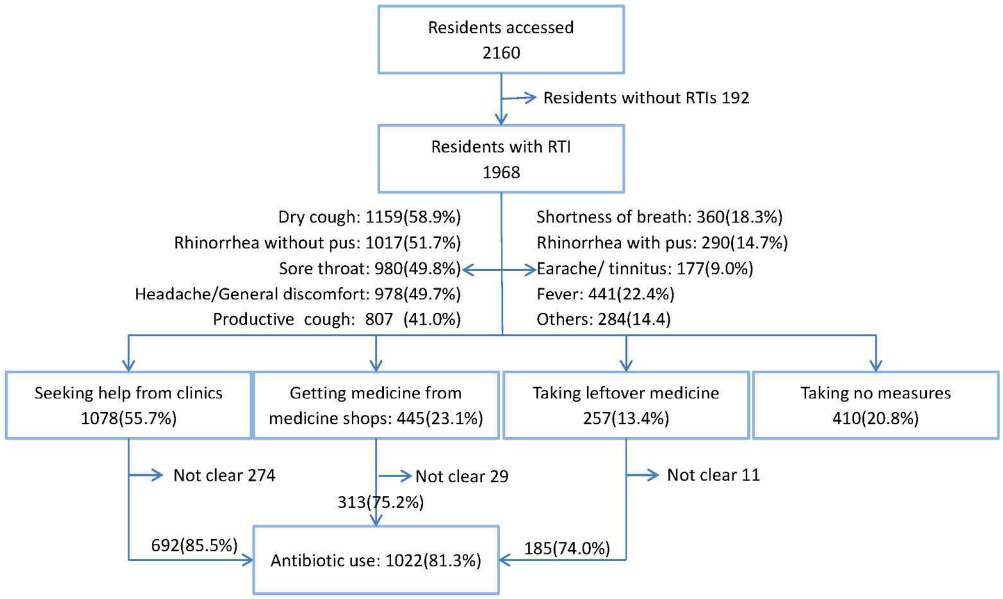


Figure 1 Flow chart describing symptoms, healthcare-seeking and antibiotics use among study population

224x136mm (300 x 300 DPI)

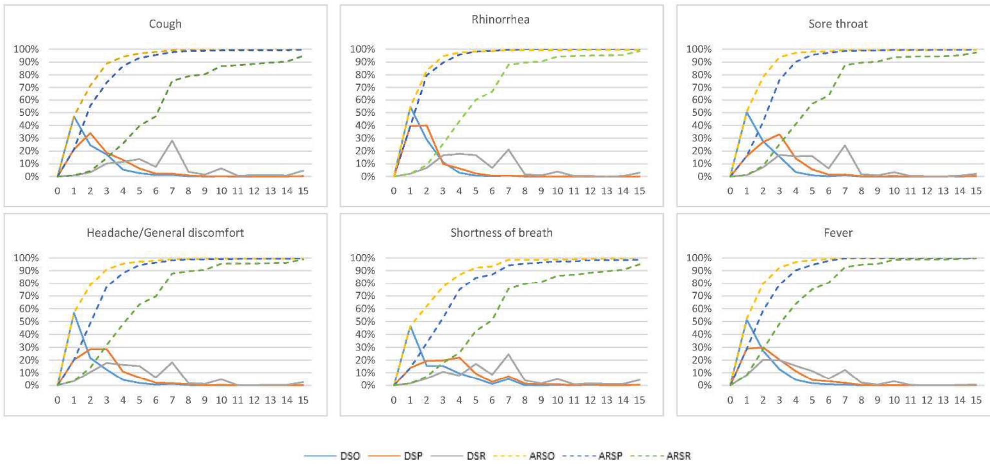


Figure 2 Trajectory of common symptoms experienced in the last time RTIs
Note: DSO, day on which symptom occurred; DSP, day on which symptom reached its peak or became most serious; DSR, day on which symptom remitted; ARSO, Accumulative rate of symptom occurrence; ARSP, Accumulative rate of symptom peak; ARSR, Accumulative rate of symptom remitted.

248x116mm (300 x 300 DPI)

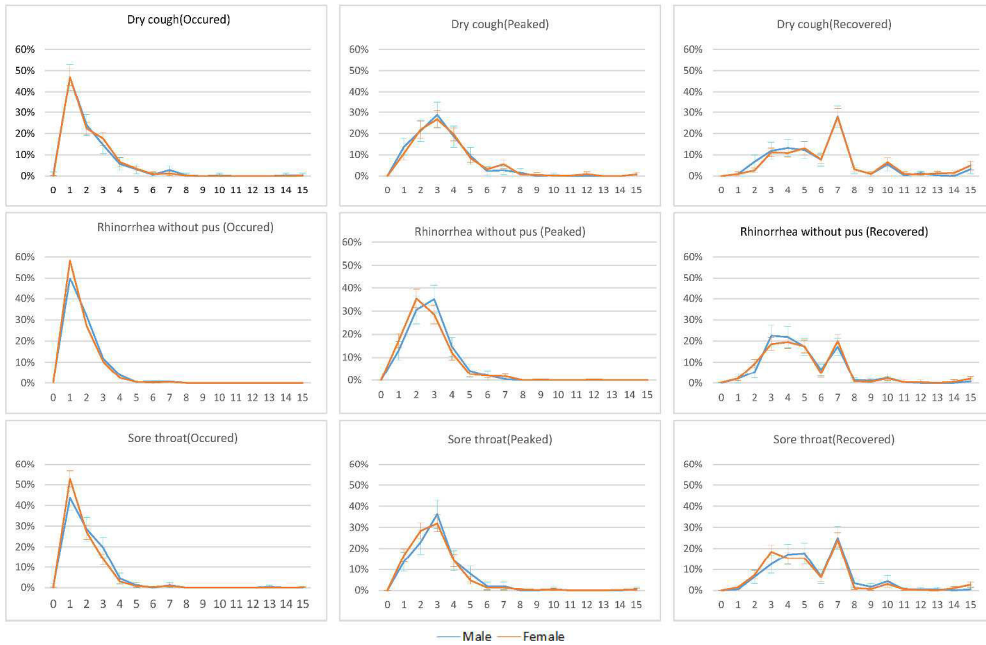


Figure 3 Symptom occurrence, peak and recovery by gender and days following onset of infection

249x161mm (300 x 300 DPI)

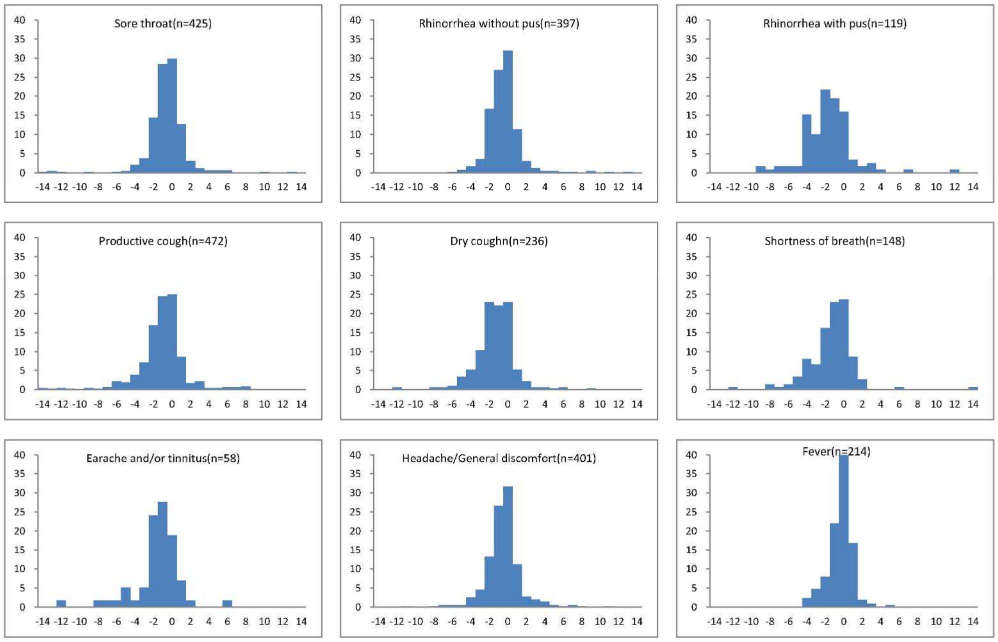


Figure 4 distribution of healthcare-seeking by time difference between day on which patient sought healthcare and day on which symptom peaked
Note: the numbers along "Y" axis stand for percentages of healthcare-seeking happened on a given day. The negative numbers along the "X" axis stand for days of healthcare-seeking before the day symptom peaked; while the positive numbers along the "X" axis, days of healthcare-seeking after the day symptom peaked.

252x163mm (300 x 300 DPI)

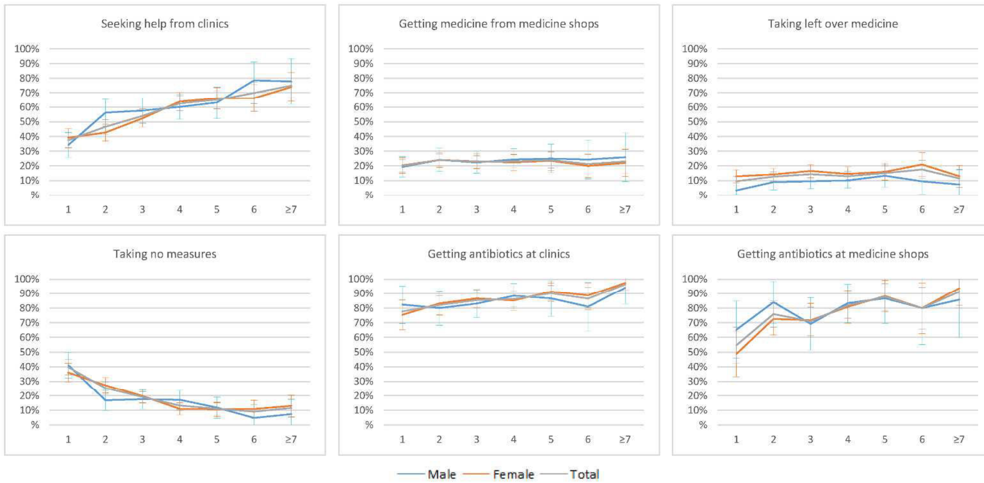


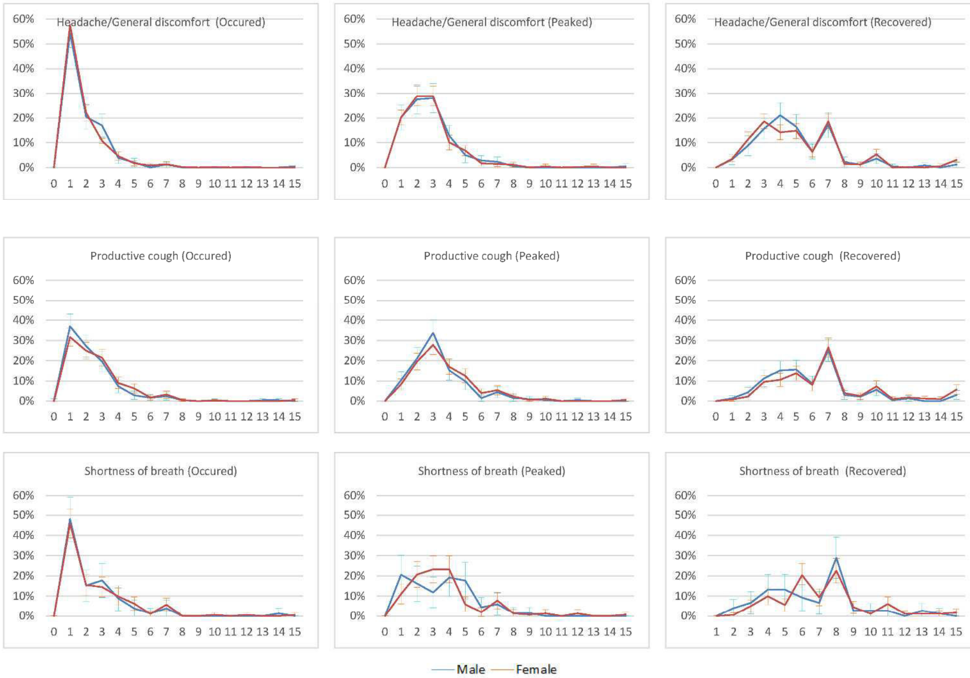
Figure 5 Healthcare-seeking by number of symptoms in total and by genders
Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines

249x121mm (300 x 300 DPI)

Appendix 1 Characteristics of 1968 adults with respiratory tract infection

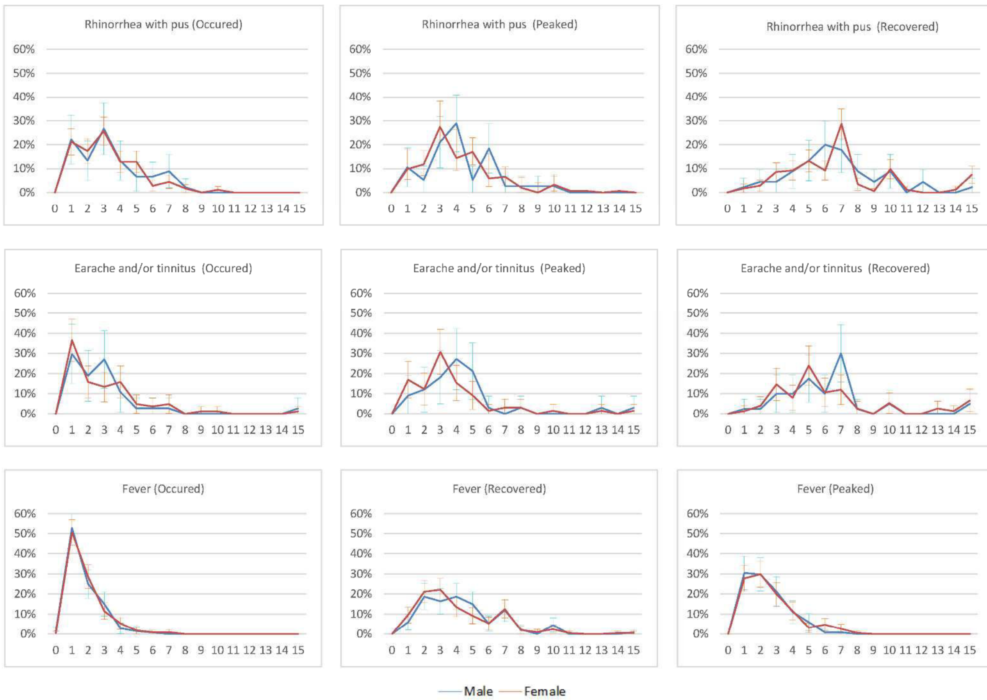
	Male	Female	Total
Age			
18-40y	128(20.3)	317(23.7)	445(22.6)
41-50y	152(24.1)	360(26.9)	512(26.0)
51-60y	134(21.3)	323(24.1)	457(23.3)
⩾61y	216(34.3)	338(25.3)	554(28.2)
Education			
0y	95(15.1)	487(36.4)	582(29.6)
1-6y	195(31.0)	390(29.1)	585(29.7)
7-9y	269(42.7)	360(26.9)	629(32.0)
⩾10y	71(11.3)	101(7.5)	172(8.7)
Total	630	1338	1968

242x75mm (300 x 300 DPI)



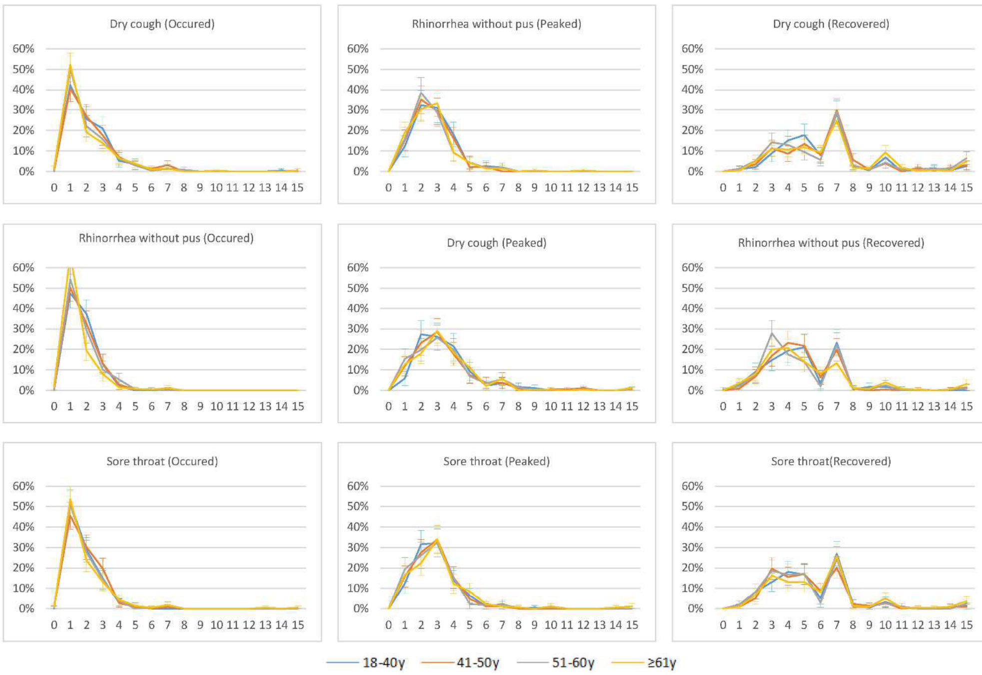
Appendix 2-1 Symptom occurrence, peak and recovery by gender and days following onset of infection

254x183mm (300 x 300 DPI)



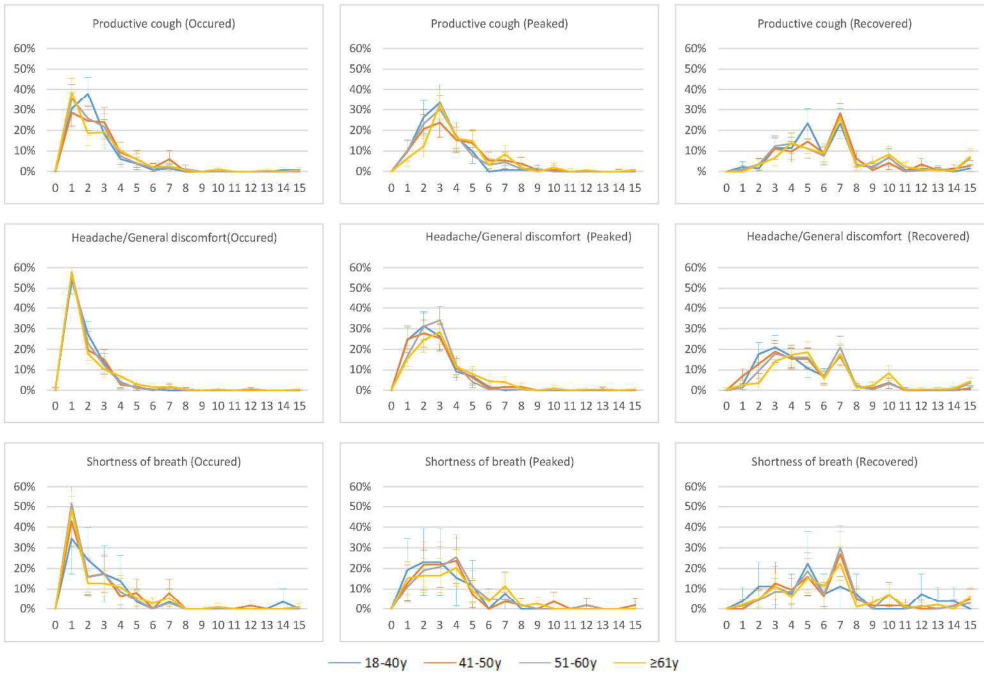
Appendix 2-2 Symptom occurrence, peak and recovery by gender and days following onset of infection

250x185mm (300 x 300 DPI)



Appendix 3-1 Symptom occurrence, peak and recovery by age and days following onset of infection

251x176mm (300 x 300 DPI)



Appendix 3-2 Symptom occurrence, peak and recovery by age and days following onset of infection

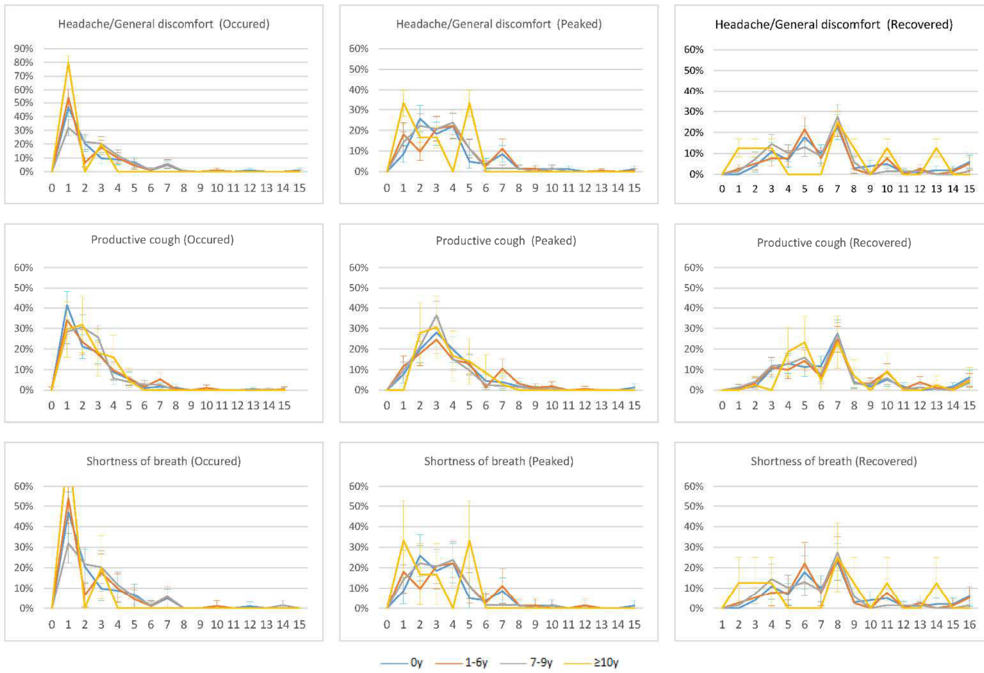
251x176mm (300 x 300 DPI)

Appendix 3-3 Symptom occurrence, peak and recovery by age and days following onset of infection

251x175mm (300 x 300 DPI)

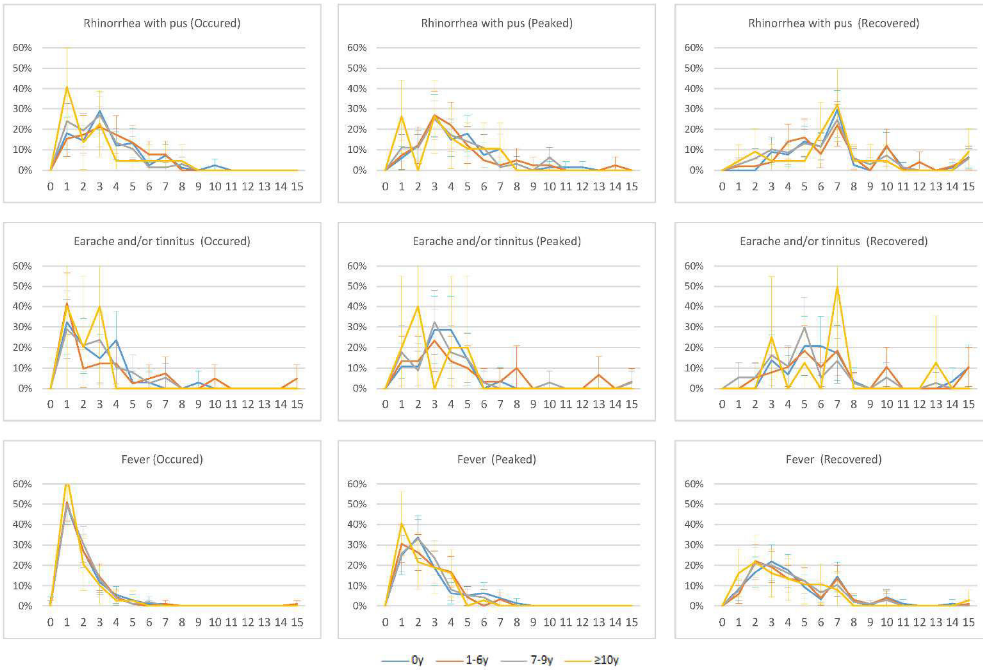
Appendix 4-1 Symptom occurrence, peak and recovery by education and days following onset of infection

252x175mm (300 x 300 DPI)



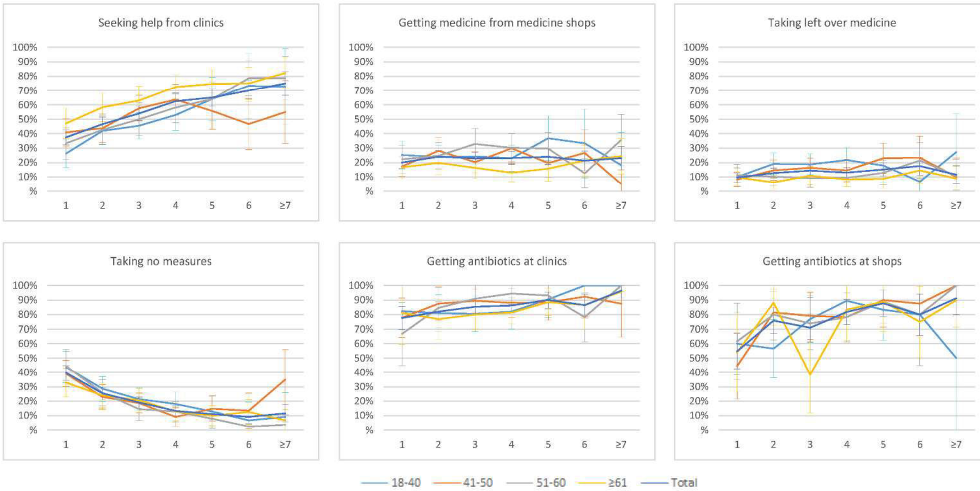
Appendix 4-2 Symptom occurrence, peak and recovery by education and days following onset of infection

251x176mm (300 x 300 DPI)



Appendix 4-3 Symptom occurrence, peak and recovery by education and days following onset of infection

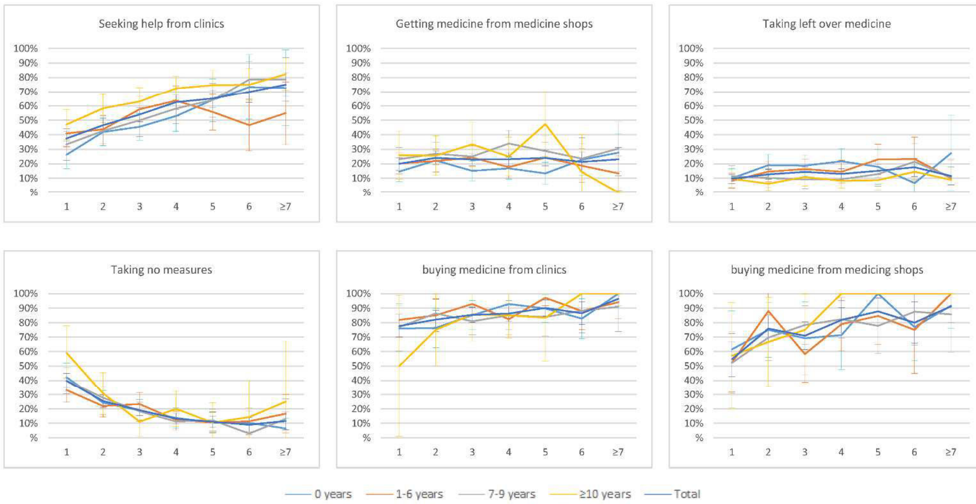
252x175mm (300 x 300 DPI)



Appendix 5 Service-seeking by number of symptoms in total and by age

Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines

253x143mm (300 x 300 DPI)



Appendix 6 Healthcare-seeking by number of symptoms in total and by education

Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines

254x148mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	P4
Methods			
Study design	4	Present key elements of study design early in the paper	P4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P4-5
Bias	9	Describe any efforts to address potential sources of bias	P4-5
Study size	10	Explain how the study size was arrived at	P4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P17
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P4
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	P5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	P4
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P4，15
		(b) Give reasons for non-participation at each stage	P15
		(c) Consider use of a flow diagram	P15
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P6
		(b) Indicate number of participants with missing data for each variable of interest	P5,15
Outcome data	15*	Report numbers of outcome events or summary measures	P6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P18,21
		(*b*) Report category boundaries when continuous variables were categorized	P16-19
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	P19
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	P7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P7-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	P10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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How patients' experiences of respiratory tract infections affect healthcare seeking and antibiotic use: Insights from a cross sectional survey in rural Anhui, China

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How patients' experiences of respiratory tract infections affect healthcare seeking and antibiotic use: Insights from a cross sectional survey in rural Anhui, China

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Word count: 2869

Abstract

Objective: To investigate the occurrence and trajectory of reported RTI symptoms and their effects on use of self and professional care among patients in the community.

Design: A cross sectional retrospective household survey.

Setting: 12 administrative villages from rural Anhui, China.

Participants: 2160 rural adult residents aged ≥18 years registered as rural residents and actually living in the sampled villages when this study was conducted.

Method: The respondents were recruited using stratified-clustered randomized sampling. A structured questionnaire was deployed to solicit information about social demographics, symptoms of last respiratory tract infection (RTI) and healthcare-seeking following the RTI. Descriptive analyses were performed to investigate the reported symptoms and multivariate logistic regression models were developed to identify relationships between number of concurrent symptoms and healthcare-seeking and antibiotics use.

Results: A total of 1968 residents completed the survey, resulting in a response rate of 91.1%. The number of concurrent symptoms showed a clear increasing trend with seeking help from clinics and being prescribed antibiotics. Multivariate regression revealed statistically significant associations between: a) visiting clinics and education(OR=0.790), sore throat(OR=1.355), cough(OR=1.492), shortness of breath(OR=1.707) and fever(OR=2.142); b) buying medicine from shops without prescription and education(OR=1.230) and cough(OR=1.452); c) getting antibiotics at clinics and sore throat(OR=2.05) and earache and/or tinnitus(OR=4.884) and d) obtaining antibiotics at medicine shops and productive cough(OR=1.971).

Conclusions: Reported RTI symptoms play an important role in shaping both patient- and doctor-led responses.

Strengths and limitations of this study

- This study demonstrates relationships between patient-reported symptoms and RTI-related healthcare-seeking.
- The study is the first to describe the collective effects of concurrent symptoms as perceived by patients experiencing them.
- The study relies on subjective retrospective perceptions or self-reports and therefore may be biased by potential under- or over-reporting and recall bias.
- The study used a broad definition of RTIs and the occurrence of symptoms may be distorted by seasonal and other variations when the study was conducted.

Background

Respiratory tract infections (RTIs) are the most common diseases in humans. Studies have demonstrated that adults usually experience 1–3episodes of upper respiratory tract infection per year.[1,2] RTIs claim over 3 million lives annually and are the leading cause of death for children under 5 years.[3,4] Although many RTIs are mild and self-limiting, they are associated with a significant burden in terms of medical visits as well as work and school absenteeism.[5,6] The median duration of an episode of non-influenza-related viral respiratory tract infection (the most common but least serious kind of RTIs) is estimated to be 7.4 days, with 25% of cases lasting for 2 weeks.[7] In addition to the heavy burden on patients and health systems, RTIs are closely linked to antibiotic use and hence the development of antibiotic resistance. RTIs account for up to 60% of all antibiotic prescribing in UK primary care.[8,9] Excessive use of antibiotics is recognized as one of the most serious public health issues worldwide.[10]

According to the 10th edition of the International Classification of Diseases, RTIs comprise as many as 34 kinds of infections. However their symptoms are relatively limited, consisting mainly of sore throat, fever, cough, productive cough, rhinorrhea with or without pus, shortness of breath, headache and/or general discomfort, earache and/or tinnitus.[11,12] When faced with symptoms, patients' responses vary greatly. Some patients manage their symptoms by simply resting, drinking warm water etc. without using any medicines;[13]others buy medicines from medicine shops or pharmacies or seek professional help from doctors;[14-16] still others opt for traditional remedies.[17,18] A 2014 study of consumer attitudes on cough and cold in USA indicated that 36.1% of those surveyed reported beginning over-the-counter (OTC) treatment at the first sign of a cough or cold, 42.6% waited until cold symptoms 'get bad enough' (i.e. to cause distress) and another 20.2% waited until they had more than one symptom before beginning treatment. Altogether, 55% sought professional care eventually [19]. These varied responses have been attributed to a wide range of reasons including: features of the disease, such as severity of symptoms and their patterns of progression;[2] 'demand side' issues such as age, gender, education,[20] knowledge and attitudes about RTIs and RTI-related services,[21-25] cultural expectations and social norms;[26,27] and 'supply side' factors such as perverse financial incentives, systemic pressures on healthcare providers and professional standards.[26,28,29]

RTIs are very common in China with an incidence rate ranging from 84.13% to 120.83% in 2006.[30] This translates to 1.16 to 1.67 billion person-times of RTIs annually in the whole country. Data about service use for RTIs among China residents are scarce, but the limited research available reports huge discrepancies between different populations and very high use of antibiotics in various medical settings. An earlier study in rural primary care settings of 10 provinces in Western China found that nearly 50% of patients were prescribed antibiotics.[31] Another recent study found that antibiotics were prescribed for 78% of colds and 93.5% of

acute bronchitis cases.[32] According to our systemic literature review, few studies focus on factors affecting service and antibiotics use for RTIs or investigate reasons for variations in service use and antibiotic prescribing for RTIs in China. Although a number of papers on reasons for health service utilization in general did include RTIs as a subcomponent, they addressed only demand and supply side factors, with little attention being paid to RTI symptoms among patients in the community and their effects on decisions about self or professional care. This study aims to investigate reported RTI symptoms and their effects on use of self and professional care among patients in the community.

Methods

Sites and population

The study used a retrospective cross-sectional household survey design and adopted a stratified-clustered randomized sampling approach in recruiting site villages and participating residents. Selection of site villages proceeded in 4 steps. Step 1 divided all counties in Anhui province into north, middle and south regions. Step 2 randomly selected 4 counties from each of the three regions and 1 township from each of the counties selected and then 1 administrative village from each of the site townships selected above. Step 3 randomly selected 1 household from the village selected as the starting household and then recruited 180 households that were geographically closest to the starting household. Step 4 randomly selected one household member from each of these households according to preset eligibility criteria, i.e., men and women who were aged 18 years and over, were registered as rural residents and were actually living in the sampled villages when this study was conducted, and were willing and able to participate in the survey.

Questionnaire

The study used a structured questionnaire consisting of questions about four categories of variables: a) social demographics (e.g., gender, age and education); b) last episode of symptomatic RTI, including symptoms experienced and day on which each specific symptom occurred (DSO), reached its peak or became most serious (DSP) and recovery (DSR); c) responses to the RTI, including taking leftover medicines, buying any type of medicine OTC from medicine shops(here after referred to as buying medicine) and seeking treatment from clinics; d) antibiotics obtained from clinics and medicine shops. In China, a pharmacy generally refers to a department within a hospital or clinic that dispenses medicines to patients according to prescriptions by the clinicians working for the same hospital/clinic; while a medicine shop is an independent business that sells medicines to customers with or without prescriptions from clinicians. ‘Seeking help from clinics’ refers to visiting a local health facility staffed by a qualified health professional and is thus largely equivalent to ’seeking professional care’ in western countries. Conversely, the use of antibiotics does not necessarily mean that professional care was sought. Antibiotics may be purchased from medicine shops directly without prescription or kept at home for subsequent use. Almost all medicine shops in China sell both OTC and non-OTC medicines, including antibiotics. Although they may be displayed in separate cabinets, in practice non-OTC medicines may be purchased directly without prescription and customers generally do not distinguish these two types of medicines.

Data collection

Field data collection took place from 30 April-12 May 2016 via face-to-face interviews using the structured questionnaire. Twenty-six under graduate students from Anhui Medical University performed the interviews. Measures taken to ensure data quality included: a) training and examination of the data collectors; b) daily checks by a quality control supervisor of all questionnaires completed each day; c) retest of 5% randomly selected subjects; d) feedback of errors found via daily checks and readministering of the questionnaire; e) elimination of disqualified field data collectors.

Data analysis

Data were double-entered using EPI DATA 3.1 and SPSS 10.01 and Microsoft Excel 2010 were used to analyze the data. Data analysis included: a) distribution of respondents by gender, age and education; b) multivariate logistic regression of healthcare-seeking and antibiotics use using social demographics and common symptoms as the independent variables; c) relationships between number of symptoms experienced by a single patient and his or her healthcare-seeking and antibiotics use. Cases with missing data were excluded from the data analyses.

Ethical review

The study protocol was reviewed and approved by the Biomedical Ethics Committee of Anhui Medical University (reference number: 201500800) prior to the study commencing. Participation of rural residents was voluntary and written informed consent was obtained from all participants.

Results

Overview of participants, symptoms and healthcare-seeking

As shown in Figure 1 and Table 1, a total of 2160 residents were accessed and 1968 completed the survey, resulting in a response rate of 91.1%. The mean age of respondents was 50.39 years (SD=13.04 years). The majority (68.0%) were females and around one third (29.6%) had no formal school education. The high proportion of female respondents in this random sample results from the fact that in this rural area the majority of male residents have moved to cities to obtain temporary work [33]. Over 80% of reported infections had occurred within nine months prior to the survey. Dry cough (58.9%, 1159), rhinorrhea without pus (51.7%, 1017) and sore throat (49.8%, 980) were the most common symptoms. 55.7% of respondents reported seeking professional help from clinics, 13.4% bought medicine from medicine shops, 23.1% used leftover medicine from previous illnesses and 20.8% did nothing. Altogether, 81.3% of respondents reported having used antibiotics to treat their RTI. As shown in Table 2, Time interval between onset of infection and when the data were collected was not associated with any statistical differences between in healthcare-seeking behavior except use of leftover medicines, suggesting that recall bias had limited effects (see also Discussion and Limitations sections).

Individual symptoms and treatment-seeking

Table 3 displays logistic regression modeling between service use and individual symptoms and socio-demographic characteristics. Education was negatively associated with seeking help from clinics (OR=0.790[0.697-0.896]), but positively related with buying medicine (OR=1.230[1.068-1.417]) and using leftover medicine (OR=1.283[1.073-1.535]); Females were more likely to use leftover medicine than males (OR=2.016[1.411-2.881]), while age had no effects on any treatment-seeking behavior. When controlled for social demographic characteristics, buying medicine was positively related with cough (OR=1.452[1.124-1.875]); taking leftover medicine, with headache and soreness (OR=1.581[1.169-2.138]); and. seeking help from clinics, with sore throat (OR=1.355[1.109-1.654]), cough (OR=1.492[1.198-1.859]), shortness of breath (OR=1.707[1.287-2.265]) and fever (OR=2.142[1.654-2.775]). Being prescribed antibiotics at clinics was related positively only to with earache and/or tinnitus (OR=4.884[1.162-20.522]), while purchasing antibiotics OTC from medicine shops was positively linked with productive cough (OR=1.971[1.125-3.453]). Rhinorrhea with or without pus are not associated with any specific treatment-seeking behavior.

Concurrent symptoms and service use

Figure 2 and Appendices 1-2 display the relationships between service-seeking and number of concurrent symptoms in total and by demographic characteristics. Overall, seeking help from clinics and getting antibiotics at clinics show a clear increasing trend with number of symptoms. Only 37.5% of respondents who had experienced one symptom had sought help from a clinic, while 75.0% those who had experienced over seven symptoms had done so. Similarly, the use of antibiotics at clinics increased from 77.7% for patients with one symptom to 96.4% for those with over seven symptoms. However buying medicine from shops，taking leftover medicine and getting antibiotics from shops showed no statistically significant trend as the number of symptoms increased. The relationships between number of symptoms and service-seeking were consistent across all gender, age and education subgroups. This inter-subgroup consistency was also observed in the null trend of getting antibiotics at clinics or at medicine shops by patients with increasing number of symptoms.

Discussion

This study has uncovered useful data for better understanding the experience of RTIs among patients in the community and their relations with healthcare seeking and antibiotics use. The study showed selective associations between service use and socio-demographic characteristics. Education was negatively related to seeking help from clinics but positively associated with taking leftover medicine and buying medicine from shops; while females are more likely than males to take leftover medicine. However, specifically using antibiotics obtained from clinics and medicine shops did not show any statistically significant socio-demographic differences. These findings may suggest that decisions on whether or not to visit a clinic, take leftover medicine or buy medicine from a shop is made by patients themselves and is thus amenable to the influence of patients' socio-demographic characteristics; while the decision on whether or not to provide antibiotics to patients is determined mainly by the doctors at clinics or staff at medicine shops and thus is not affected by these characteristics.

The study documented strong and consistent relations between symptoms and service-seeking. As the number of concurrent symptoms increased from 1 to 7 or more, the proportion of patients who had sought help from clinics increased from 37.5% to 75.0% and the proportion of service seekers who had been prescribed antibiotics increased from 77.7% to 96.4%. These findings suggest that clustering of symptoms affect both patient- and doctor-led behavior and thus merit particular attention in future interventions. Interestingly, the difference in the percentage of service-seeking for patients with 1 symptom (37.5%) versus that for those with 7+ symptoms (75.0%) is substantially greater than that of antibiotics prescribing (77.7% versus 96.4%). One possible explanation for this difference is that patients directly suffer from symptoms while professionals are only told about them by their patients, so patient-led behaviors (i.e. health service-seeking) may be more sensitive to symptoms than professional-led ones (i.e. antibiotics prescribing). [34,35] In addition, as lay persons, patients may not be as capable as doctors of distinguishing important from non-important symptoms, and so numbers of symptoms have closer links with perceptions of acute or serious illness among patients than among health professionals. As for the lack of correlation between number of symptoms and purchase of medicines from shops, this may reflect the combined effects of two drivers. On the one hand, more symptoms serve as a greater driver for patients to seek professional help from clinics as well as medicine shops. On the other, seeking help from clinics and shops are competitive behaviors and as patients experience more symptoms they are more likely to visit clinics than shops.

In addition, positive relationships were found between a number of specific symptoms and service-seeking. Seeking help from clinics was linked to, in order of magnitude of logistic regression coefficient, fever (B=0.76), shortness of breath (B=0.54), cough (B=0.40) and soreness (B=0.30). These coefficients and their rank order reveal useful information about the perceived importance, suffering and urgency of each of the corresponding symptoms for patients. Compared with seeking help from clinics, the driving symptoms for buying medicine from shops may be milder in nature and fewer in number, with only 1 symptom, dry cough, being positively associated with the latter behavior. This indicates that patients with equal access to the two kinds of help tend to choose clinics rather than shops if they have more and severer symptoms and vice versa. In addition, being given antibiotics at clinics was linked with earache and/or tinnitus and at medicine shops, with productive cough. These findings are consistent with published evidence.[36]

Study Limitations

The study has a number of limitations. First, the study relied on subjective perceptions and self-reports. Individuals are poor at accurately reporting certain health behaviors and feelings and inherent tendencies to respond in ways that make them appear healthier or otherwise conform to social norms may introduce bias. However, these characteristics are typically apparent across the board, reducing the effects of this threat to internal validity. More importantly, the long recall period between last experienced episode and survey data collection is likely to have led to recall bias; milder RTIs in particular, exact patterns of symptom experience and details of associated treatment-seeking behavior may have been forgotten. Our findings do suggest some extent of recall/memory bias, but Table 1 shows that there was no statistical relationship between time interval from onset of infection and data collection for any healthcare-seeking behavior except for use of leftover medicines, which was reported as 9.6% among patients with a time interval of over 9 months compared with 16.2% among patients with a less than 3 month time interval. Second, given the broad symptom-based definition of RTIs used in the study, seasonal and other influences on symptom occurrence may have affected the frequency of symptoms. Third, the overrepresentation of females may raise concerns about selection biases. However, our analysis revealed no significant differences by gender in terms of symptom-related treatment-seeking except for taking leftover medicines, which was more commonly reported by females.

Contributors Mengjie Diao participated in data collection and drafted the manuscript. Xingrong Shen and Rui Feng designed the instruments and performed data analysis. Jing Cheng and Jing Chai implemented field data collection, trained data collectors and controlled data quality. Rongyao Zhou and Panpan Zhang implemented the data collection. Debin Wang provided expertise for overall design of the study and revised and finalized the manuscript. Helen Lambert contributed to the interpretation of data and revised and finalized the manuscript. All authors approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data sharing statement Anonymised participant data used in the preparation of this article will be made available on request from the lead author.

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Table 1 Characteristics of 1968 adults with respiratory tract infection

Figure 1 Flow chart describing symptoms, healthcare-seeking and antibiotics use among study population

Table2 Service use by time interval in between onset of infection and data collection

Table3 Multivariate logistic regression models between service-seeking and specific symptoms

Figure 2 Service-seeking by number of symptoms in total and by genders

Table 1 Characteristics of 1968 adults with respiratory tract infection

	Male	Female	Total
Age			
18-40y	128(20.3)	317(23.7)	445(22.6)
41-50y	152(24.1)	360(26.9)	512(26.0)
51-60y	134(21.3）	323(24.1)	457(23.3)
≥61y	216(34.3)	338(25.3)	554(28.2)
Education			
0y	95(15.1)	487(36.4)	582(29.6)
1-6y	195(31.0)	390(29.1)	585(29.7)
7-9y	269(42.7)	360(26.9)	629(32.0)
≥10y	71(11.3)	101(7.5)	172(8.7)
Total	630	1338	1968

Table 2 Service use by time interval between onset of infection and data collection

Time interval (Days)	Total	Buying medicine from medicine shops	Taking leftover medicine	Seeking help from clinics	Getting antibiotics at clinics	Getting antibiotics at medicine shops
≤90	844(44.6%)	196(23.3%)	136(16.2%)	475(56.3%)	315(86.1%)	144(77.4%)
91-180	494(26.1%)	107(21.8%)	60(12.2%)	276(55.9%)	177(85.9%)	67(67.0%)
181-270	192(10.2%)	51(26.6%)	18(9.4%)	110(57.3%)	72(85.7%)	38(80.9%)
≥271	361(19.1%)	80(22.2%)	34(9.6%)	198(54.8%)	116(84.7%)	59(78.7%)
χ^2		1.907	13.438	0.355	0.165	5.409
P		0.592	**0.004**	0.949	0.983	0.144

Table 3 Multivariate logistic regression models between service-seeking and specific symptoms

	buying medicine from shops (n1=1484,n2=445)		taking leftover medicine (n1=1668, n2=257)		Seeking help from clinics (n1=857,n2=1078)		Getting antibiotics at clinics (n1=117， n2=692)		Getting antibiotics at shops (n1=103，n2=313)	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Gender	1.085	0.840-1.400	**2.016**	**1.411-2.881**	0.819	0.653-1.027	0.952	0.592-1.532	0.863	0.497-1.498
Age	0.984	0.873-1.109	0.866	0.742-1.011	1.104	0.993-1.227	0.887	0.704-1.118	1.022	0.789-1.324
Education	**1.23**	**1.068-1.417**	**1.283**	**1.073-1.535**	**0.79**	**0.697-0.896**	0.849	0.646-1.114	1.133	0.842-1.523
Sore throat	1.016	0.810-1.275	1.303	0.971-1.748	**1.355**	**1.109-1.654**	**2.05**	**1.337-3.143**	1.604	0.990-2.599
Rhinorrhea without pus	0.838	0.669-1.051	1.057	0.791-1.411	1.045	0.856-1.276	1.25	0.816-1.915	0.792	0.486-1.290
Rhinorrhea with pus	0.96	0.714-1.292	0.78	0.531-1.145	1.045	0.804-1.359	1.013	0.566-1.813	1.796	0.869-3.711
Dry cough	**1.452**	**1.124-1.875**	0.809	0.587-1.114	**1.492**	**1.198-1.859**	1.318	0.812-2.140	1.328	0.777-2.269
Productive cough	1.026	0.798-1.318	1.28	0.926-1.770	1.115	0.891-1.395	0.907	0.561-1.466	**1.971**	**1.125-3.453**
Shortness of breath,	0.782	0.571-1.071	0.695	0.458-1.054	**1.707**	**1.287-2.265**	0.927	0.533-1.613	1.049	0.488-2.255
Earache/tinnitus	1.421	0.979-2.063	1.305	0.825-2.063	0.757	0.535-1.072	**4.884**	**1.162-20.522**	1.489	0.608-3.648
Headache general discomfort	1.102	0.875-1.389	1.581	1.169-2.138	1.178	0.962-1.443	1.184	0.765-1.831	1.026	0.623-1.690
Fever	0.778	0.583-1.037	1.223	0.866-1.725	**2.142**	**1.654-2.775**	1.33	0.791-2.236	1.74	0.833-3.633

Note: n1 and n2 stands for the number of no and yes response respectively to each service use behavior; for each service use behavior, no (n1) was coded as 0 and yes(n2), as 1. Gender: 1=male,2=female; Age group: 1= ≤40y, 2=41-50y, 3=51-60y,4= ≥61y；Educatio:1=0 years,2=1-6 years ,3=7-9 years ,4=≥10 years. Symptoms: no= 0 and yes= 1； Medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines.

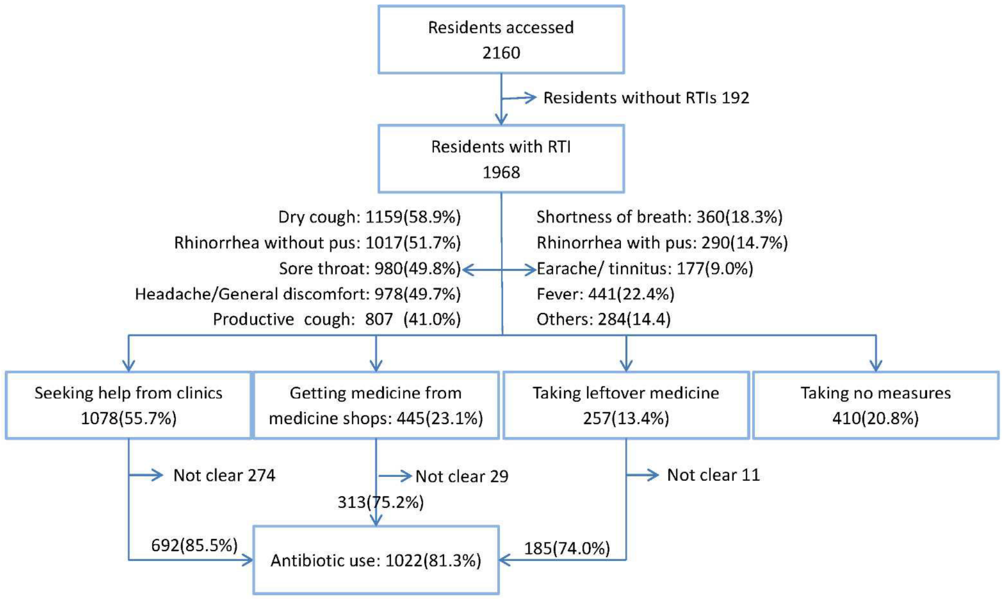


Figure 1 Flow chart describing symptoms, healthcare-seeking and antibiotics use among study population

224x136mm (300 x 300 DPI)

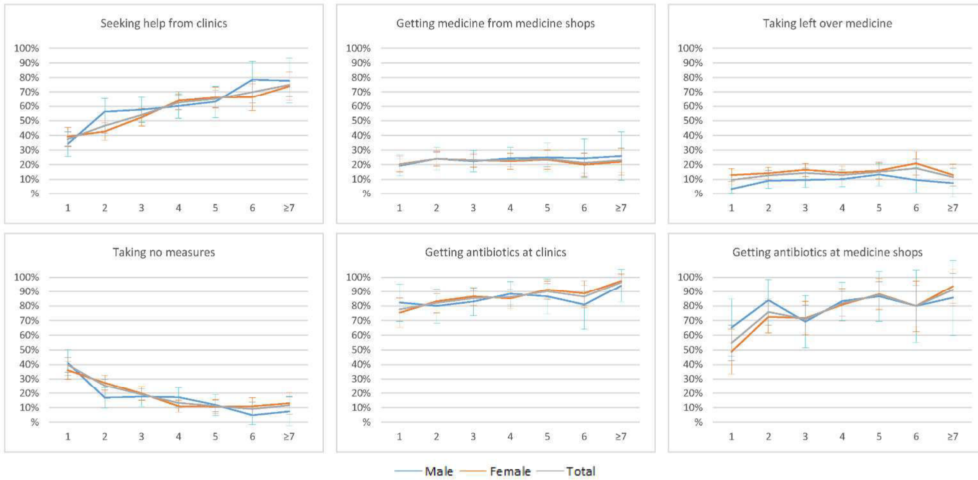
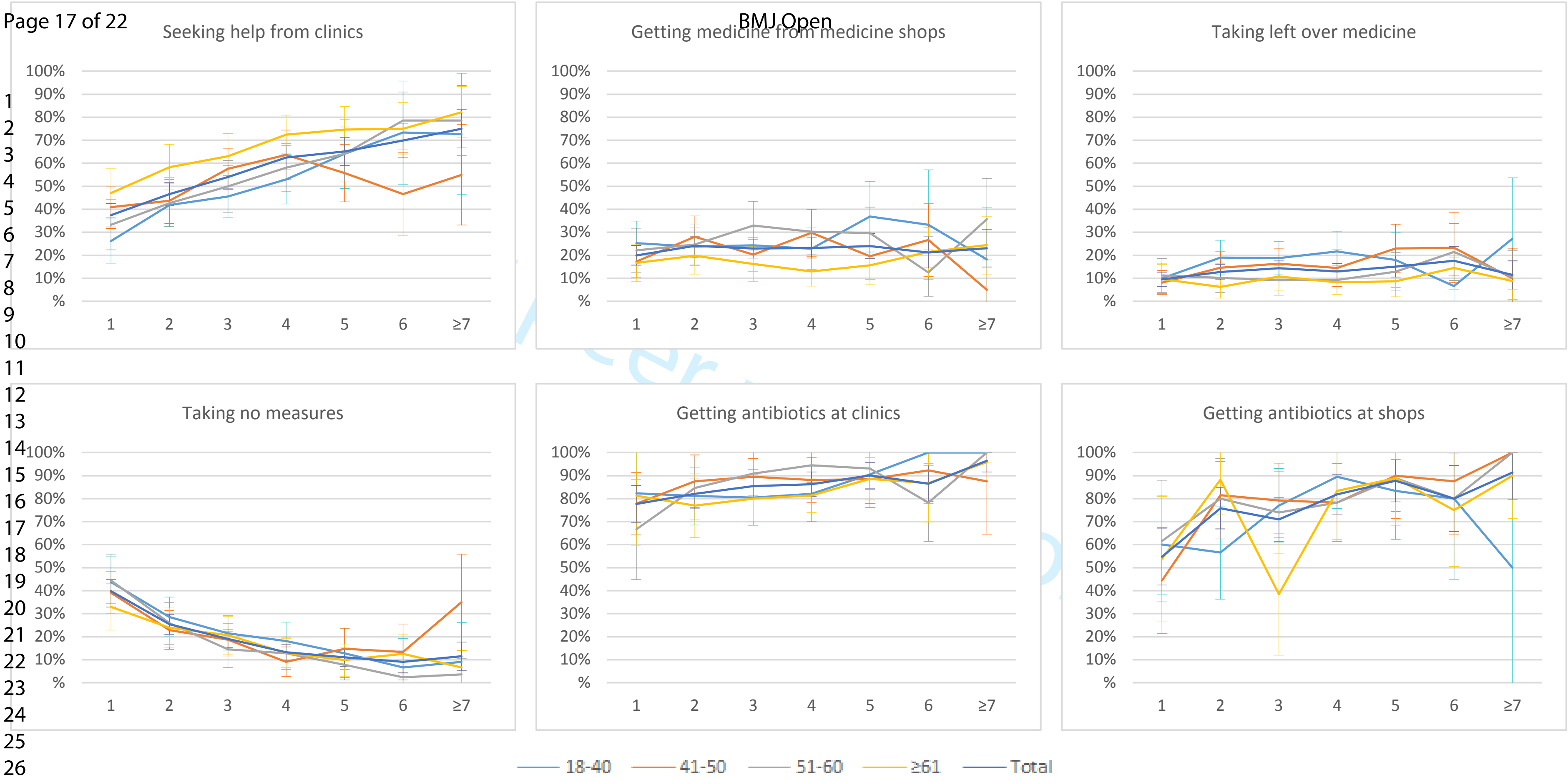


Figure 2 Healthcare-seeking by number of symptoms in total and by genders
Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines.

251x121mm (300 x 300 DPI)



Appendix 1 Service-seeking by number of symptoms in total and by age

(Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines)

Appendix 2 Healthcare-seeking by number of symptoms in total and by education

(Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	P4
Methods			
Study design	4	Present key elements of study design early in the paper	P4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P5-6
Bias	9	Describe any efforts to address potential sources of bias	P8
Study size	10	Explain how the study size was arrived at	P4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P4
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	P5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	P4
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P5
		(b) Give reasons for non-participation at each stage	P5
		(c) Consider use of a flow diagram	P5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P5
		(b) Indicate number of participants with missing data for each variable of interest	P5
Outcome data	15*	Report numbers of outcome events or summary measures	P5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P6
		(*b*) Report category boundaries when continuous variables were categorized	P5,6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	P6
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	P7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P7-8
Generalisability	21	Discuss the generalisability (external validity) of the study results	P8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P9

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	P4
Methods			
Study design	4	Present key elements of study design early in the paper	P4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P4-5
Bias	9	Describe any efforts to address potential sources of bias	P4-5
Study size	10	Explain how the study size was arrived at	P4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P17
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P4
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	P5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	P4
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P4，15
		(b) Give reasons for non-participation at each stage	P15
		(c) Consider use of a flow diagram	P15
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P6
		(b) Indicate number of participants with missing data for each variable of interest	P5,15
Outcome data	15*	Report numbers of outcome events or summary measures	P6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P18,21
		(*b*) Report category boundaries when continuous variables were categorized	P16-19
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	P19
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	P7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P7-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	P10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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How patients' experiences of respiratory tract infections affect healthcare seeking and antibiotic use: Insights from a cross sectional survey in rural Anhui, China

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How patients' experiences of respiratory tract infections affect healthcare seeking and antibiotic use: Insights from a cross sectional survey in rural Anhui, China

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Abstract

Objective: To investigate the occurrence of reported RTI symptoms and their effects on use of self and professional care among patients in the community.

Design: A cross sectional retrospective household survey.

Setting: 12 administrative villages from rural Anhui, China.

Participants: 2160 rural adult residents aged ≥18 years registered as rural residents and actually living in the sampled villages when this study was conducted.

Method: The respondents were recruited using stratified-clustered randomized sampling. A structured questionnaire was deployed to solicit information about social demographics, symptoms of last respiratory tract infection (RTI) and healthcare-seeking following the RTI. Descriptive analyses were performed to investigate the reported symptoms and multivariate logistic regression models were developed to identify relationships between number of concurrent symptoms and healthcare-seeking and antibiotics use.

Results: A total of 1968 residents completed the survey, resulting in a response rate of 91.1%. The number of concurrent symptoms showed a clear increasing trend with seeking help from clinics and being prescribed antibiotics. Multivariate regression revealed statistically significant associations between: a) visiting clinics and education(OR=0.790), sore throat(OR=1.355), cough(OR=1.492), shortness of breath(OR=1.707) and fever(OR= 2.142); b) buying medicine from shops without prescription and education(OR=1.230) and cough(OR=1.452); c) getting antibiotics at clinics and sore throat(OR=2.05) and earache and/or tinnitus(OR=4.884) and d) obtaining antibiotics at medicine shops and productive cough(OR=1.971).

Conclusions: Reported RTI symptoms play an important role in shaping both patient- and doctor-led responses.

Strengths and limitations of this study

- This study demonstrates relationships between patient-reported symptoms and RTI-related healthcare-seeking.
- The study is the first to describe the collective effects of concurrent symptoms as perceived by patients experiencing them.
- The study relies on subjective retrospective perceptions or self-reports and therefore may be biased by potential under- or over-reporting and recall bias.
- The study used a broad definition of RTIs and the occurrence of symptoms may be distorted by seasonal and other variations when the study was conducted.

Background

Respiratory tract infections (RTIs) are the most common diseases in humans. Studies have demonstrated that adults usually experience 1–3episodes of upper respiratory tract infection per year.[1,2] RTIs claim over 3 million lives annually and are the leading cause of death for children under 5 years.[3,4] Although many RTIs are mild and self-limiting, they are associated with a significant burden in terms of medical visits as well as work and school absenteeism.[5,6] The median duration of an episode of non-influenza-related viral respiratory tract infection (the most common but least serious kind of RTIs) is estimated to be 7.4 days, with 25% of cases lasting for 2 weeks.[7] In addition to the heavy burden on patients and health systems, RTIs are closely linked to antibiotic use and hence the development of antibiotic resistance. RTIs account for up to 60% of all antibiotic prescribing in UK primary care.[8,9] Excessive use of antibiotics is recognized as one of the most serious public health issues worldwide.[10]

According to the 10th edition of the International Classification of Diseases, RTIs comprise as many as 34 kinds of infections. However their symptoms are relatively limited, consisting mainly of sore throat, fever, cough, productive cough, rhinorrhea with or without pus, shortness of breath, headache and/or general discomfort, earache and/or tinnitus.[11,12] When faced with symptoms, patients' responses vary greatly. Some patients manage their symptoms by simply resting, drinking warm water etc. without using any medicines;[13]others buy medicines from medicine shops or pharmacies or seek professional help from doctors;[14-16] still others opt for traditional remedies.[17,18] A 2014 study of consumer attitudes on cough and cold in USA indicated that 36.1% of those surveyed reported beginning over-the-counter (OTC) treatment at the first sign of a cough or cold, 42.6% waited until cold symptoms 'get bad enough' (i.e. to cause distress) and another 20.2% waited until they had more than one symptom before beginning treatment. Altogether, 55% sought professional care eventually [19]. These varied responses have been attributed to a wide range of reasons including: features of the disease, such as severity of symptoms and their patterns of progression;[2] 'demand side' issues such as age, gender, education,[20] knowledge and attitudes about RTIs and RTI-related services,[21-25] cultural expectations and social norms;[26,27] and 'supply side' factors such as perverse financial incentives, systemic pressures on healthcare providers and professional standards.[26,28,29]

RTIs are very common in China with an incidence rate ranging from 84.13% to 120.83% in 2006.[30] This translates to 1.16 to 1.67 billion person-times of RTIs annually in the whole country. Data about service use for RTIs among China residents are scarce, but the limited research available reports huge discrepancies between different populations and very high use of antibiotics in various medical settings. An earlier study in rural primary care settings of 10 provinces in Western China found that nearly 50% of patients were prescribed antibiotics.[31] Another recent study found that antibiotics were prescribed for 78% of colds and 93.5% of

acute bronchitis cases.[32] According to our systemic literature review, few studies focus on factors affecting service and antibiotics use for RTIs or investigate reasons for variations in service use and antibiotic prescribing for RTIs in China. Although a number of papers on reasons for health service utilization in general did include RTIs as a subcomponent, they addressed only demand and supply side factors, with little attention being paid to RTI symptoms among patients in the community and their effects on decisions about self or professional care. This study aims to investigate reported RTI symptoms and their effects on use of self and professional care among patients in the community.

Methods

Sites and population

The study used a retrospective cross-sectional household survey design and adopted a stratified-clustered randomized sampling approach in recruiting site villages and participating residents. Selection of site villages proceeded in 4 steps. Step 1 divided all counties in Anhui province into north, middle and south regions. Step 2 randomly selected 4 counties from each of the three regions and 1 township from each of the counties selected and then 1 administrative village from each of the site townships selected above. Step 3 randomly selected 1 household from the village selected as the starting household and then recruited 180 households that were geographically closest to the starting household. Step 4 randomly selected one household member from each of these households according to preset eligibility criteria, i.e., men and women who were aged 18 years and over, were registered as rural residents and were actually living in the sampled villages when this study was conducted, and were willing and able to participate in the survey.

Questionnaire

The study used a structured questionnaire consisting of questions about four categories of variables: a) social demographics (e.g., gender, age and education); b) last episode of symptomatic RTI, including symptoms experienced; c) responses to the RTI, including taking leftover medicines, buying any type of medicine OTC from medicine shops(here after referred to as buying medicine) and seeking treatment from clinics; d) antibiotics obtained from clinics and medicine shops. In China, a pharmacy generally refers to a department within a hospital or clinic that dispenses medicines to patients according to prescriptions by the clinicians working for the same hospital/clinic; while a medicine shop is an independent business that sells medicines to customers with or without prescriptions from clinicians. ‘Seeking help from clinics’ refers to visiting a local health facility staffed by a qualified health professional and is thus largely equivalent to ’seeking professional care’ in western countries. Conversely, the use of antibiotics does not necessarily mean that professional care was sought. Antibiotics may be purchased from medicine shops directly without prescription or kept at home for subsequent use. Almost all medicine shops in China sell both OTC and non-OTC medicines, including antibiotics. Although they may be displayed in separate cabinets, in practice non-OTC medicines may be purchased directly without prescription and customers generally do not distinguish these two types of medicines.

Data collection

Field data collection took place from 30 April-12 May 2016 via face-to-face interviews using the structured questionnaire. Twenty-six under graduate students from Anhui Medical University performed the interviews. Measures taken to ensure data quality included: a) training and examination of the data collectors; b) daily checks by a quality control supervisor of all questionnaires completed each day; c) retest of 5% randomly selected subjects; d) feedback of errors found via daily checks and readministering of the questionnaire; e) elimination of disqualified field data collectors.

Data analysis

Data were double-entered using EPI DATA 3.1 and SPSS 10.01 and Microsoft Excel 2010 were used to analyze the data. Data analysis included: a) distribution of respondents by gender, age and education; b) multivariate logistic regression of healthcare-seeking and antibiotics use using social demographics and common symptoms as the independent variables; c) relationships between number of symptoms experienced by a single patient and his or her healthcare-seeking and antibiotics use. Cases with missing data were excluded from the data analyses.

Ethical review

The study protocol was reviewed and approved by the Biomedical Ethics Committee of Anhui Medical University (reference number: 201500800) prior to the study commencing. Participation of rural residents was voluntary and written informed consent was obtained from all participants.

Results

Overview of participants, symptoms and healthcare-seeking

As shown in Figure 1 and Table 1, a total of 2160 residents were accessed and 1968 completed the survey, resulting in a response rate of 91.1%. The mean age of respondents was 50.39 years (SD=13.04 years). The majority (68.0%) were females and around one third (29.6%) had no formal school education. The high proportion of female respondents in this random sample results from the fact that in this rural area the majority of male residents have moved to cities to obtain temporary work [33]. Over 80% of reported infections had occurred within nine months prior to the survey. Dry cough (58.9%, 1159), rhinorrhea without pus (51.7%, 1017) and sore throat (49.8%, 980) were the most common symptoms. 55.7% of respondents reported seeking professional help from clinics, 13.4% bought medicine from medicine shops, 23.1% used leftover medicine from previous illnesses and 20.8% did nothing. Altogether, 81.3% of respondents reported having used antibiotics to treat their RTI. As shown in Table 2, Time interval between onset of infection and when the data were collected was not associated with any statistical differences between in healthcare-seeking behavior except use of leftover medicines, suggesting that recall bias had limited effects (see also Discussion and Limitations sections).

Individual symptoms and treatment-seeking

Table 3 displays logistic regression modeling between service use and individual symptoms and socio-demographic characteristics. Education was negatively associated with seeking help from clinics (OR=0.790[0.697-0.896]), but positively related with buying medicine (OR=1.230[1.068-1.417]) and using leftover medicine (OR=1.283[1.073-1.535]); Females were more likely to use leftover medicine than males (OR=2.016[1.411-2.881]), while age had no effects on any treatment-seeking behavior. When controlled for social demographic characteristics, buying medicine was positively related with cough (OR=1.452[1.124-1.875]); taking leftover medicine, with headache and soreness (OR=1.581[1.169-2.138]); and. seeking help from clinics, with sore throat (OR=1.355[1.109-1.654]), cough (OR=1.492[1.198-1.859]), shortness of breath (OR=1.707[1.287-2.265]) and fever (OR=2.142[1.654-2.775]). Being prescribed antibiotics at clinics was related positively only to with earache and/or tinnitus (OR=4.884[1.162-20.522]), while purchasing antibiotics OTC from medicine shops was positively linked with productive cough (OR=1.971[1.125-3.453]). Rhinorrhea with or without pus are not associated with any specific treatment-seeking behavior.

Concurrent symptoms and service use

Figure 2 and Appendices 1-2 display the relationships between service-seeking and number of concurrent symptoms in total and by demographic characteristics. Overall, seeking help from clinics and getting antibiotics at clinics show a clear increasing trend with number of symptoms. Only 37.5% of respondents who had experienced one symptom had sought help from a clinic, while 75.0% those who had experienced over seven symptoms had done so. Similarly, the use of antibiotics at clinics increased from 77.7% for patients with one symptom to 96.4% for those with over seven symptoms. However buying medicine from shops，taking leftover medicine and getting antibiotics from shops showed no statistically significant trend as the number of symptoms increased. The relationships between number of symptoms and service-seeking were consistent across all gender, age and education subgroups. This inter-subgroup consistency was also observed in the null trend of getting antibiotics at clinics or at medicine shops by patients with increasing number of symptoms.

Discussion

This study has uncovered useful data for better understanding the experience of RTIs among patients in the community and their relations with healthcare seeking and antibiotics use. The study showed selective associations between service use and socio-demographic characteristics. Education was negatively related to seeking help from clinics but positively associated with taking leftover medicine and buying medicine from shops; while females are more likely than males to take leftover medicine. However, specifically using antibiotics obtained from clinics and medicine shops did not show any statistically significant socio-demographic differences. These findings may suggest that decisions on whether or not to visit a clinic, take leftover medicine or buy medicine from a shop is made by patients themselves and is thus amenable to the influence of patients' socio-demographic characteristics; while the decision on whether or not to provide antibiotics to patients is determined mainly by the doctors at clinics or staff at medicine shops and thus is not affected by these characteristics.

The study documented strong and consistent relations between symptoms and service-seeking. As the number of concurrent symptoms increased from 1 to 7 or more, the proportion of patients who had sought help from clinics increased from 37.5% to 75.0% and the proportion of service seekers who had been prescribed antibiotics increased from 77.7% to 96.4%. These findings suggest that clustering of symptoms affect both patient- and doctor-led behavior and thus merit particular attention in future interventions. Interestingly, the difference in the percentage of service-seeking for patients with 1 symptom (37.5%) versus that for those with 7+ symptoms (75.0%) is substantially greater than that of antibiotics prescribing (77.7% versus 96.4%). One possible explanation for this difference is that patients directly suffer from symptoms while professionals are only told about them by their patients, so patient-led behaviors (i.e. health service-seeking) may be more sensitive to symptoms than professional-led ones (i.e. antibiotics prescribing). [34,35] In addition, as lay persons, patients may not be as capable as doctors of distinguishing important from non-important symptoms, and so numbers of symptoms have closer links with perceptions of acute or serious illness among patients than among health professionals. As for the lack of correlation between number of symptoms and purchase of medicines from shops, this may reflect the combined effects of two drivers. On the one hand, more symptoms serve as a greater driver for patients to seek professional help from clinics as well as medicine shops. On the other, seeking help from clinics and shops are competitive behaviors and as patients experience more symptoms they are more likely to visit clinics than shops.

In addition, positive relationships were found between a number of specific symptoms and service-seeking. Seeking help from clinics was linked to, in order of magnitude of logistic regression coefficient, fever (B=0.76), shortness of breath (B=0.54), cough (B=0.40) and soreness (B=0.30). These coefficients and their rank order reveal useful information about the perceived importance, suffering and urgency of each of the corresponding symptoms for patients. Compared with seeking help from clinics, the driving symptoms for buying medicine from shops may be milder in nature and fewer in number, with only 1 symptom, dry cough, being positively associated with the latter behavior. This indicates that patients with equal access to the two kinds of help tend to choose clinics rather than shops if they have more and severer symptoms and vice versa. In addition, being given antibiotics at clinics was linked with earache and/or tinnitus and at medicine shops, with productive cough. These findings are consistent with published evidence.[36]

Study Limitations

The study has a number of limitations. First, the study relied on subjective perceptions and self-reports. Individuals are poor at accurately reporting certain health behaviors and feelings and inherent tendencies to respond in ways that make them appear healthier or otherwise conform to social norms may introduce bias. However, these characteristics are typically apparent across the board, reducing the effects of this threat to internal validity. More importantly, the long recall period between last experienced episode and survey data collection is likely to have led to recall bias; milder RTIs in particular, exact patterns of symptom experience and details of associated treatment-seeking behavior may have been forgotten. Our findings do suggest some extent of recall/memory bias, but Table 1 shows that there was no statistical relationship between time interval from onset of infection and data collection for any healthcare-seeking behavior except for use of leftover medicines, which was reported as 9.6% among patients with a time interval of over 9 months compared with 16.2% among patients with a less than 3 month time interval. Second, given the broad symptom-based definition of RTIs used in the study, seasonal and other influences on symptom occurrence may have affected the frequency of symptoms. Third, the overrepresentation of females may raise concerns about selection biases. However, our analysis revealed no significant differences by gender in terms of symptom-related treatment-seeking except for taking leftover medicines, which was more commonly reported by females.

Contributors Mengjie Diao participated in data collection and drafted the manuscript. Xingrong Shen and Rui Feng designed the instruments and performed data analysis. Jing Cheng and Jing Chai implemented field data collection, trained data collectors and controlled data quality. Rongyao Zhou and Panpan Zhang implemented the data collection. Debin Wang provided expertise for overall design of the study and revised and finalized the manuscript. Helen Lambert contributed to the interpretation of data and revised and finalized the manuscript. All authors approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data sharing statement Anonymised participant data used in the preparation of this article will be made available on request from the lead author.

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Table 1 Characteristics of 1968 adults with respiratory tract infection

Figure 1 Flow chart describing symptoms, healthcare-seeking and antibiotics use among study population

Table2 Service use by time interval in between onset of infection and data collection

Table3 Multivariate logistic regression models between service-seeking and specific symptoms

Figure 2 Service-seeking by number of symptoms in total and by genders

1 Table 1 Characteristics of 1968 adults with respiratory tract infection

	Male	Female	Total
Age			
18-40y	128(20.3)	317(23.7)	445(22.6)
41-50y	152(24.1)	360(26.9)	512(26.0)
51-60y	134(21.3）	323(24.1)	457(23.3)
⩾61y	216(34.3)	338(25.3)	554(28.2)
Education			
0y	95(15.1)	487(36.4)	582(29.6)
1-6y	195(31.0)	390(29.1)	585(29.7)
7-9y	269(42.7)	360(26.9)	629(32.0)
⩾10y	71(11.3)	101(7.5)	172(8.7)
Total	630	1338	1968

Table 2 Service use by time interval between onset of infection and data collection

Time interval (Days)	Total	Buying medicine from medicine shops	Taking leftover medicine	Seeking help from clinics	Getting antibiotics at clinics	Getting antibiotics at medicine shops
⩽90	844(44.6%)	196(23.3%)	136(16.2%)	475(56.3%)	315(86.1%)	144(77.4%)
91-180	494(26.1%)	107(21.8%)	60(12.2%)	276(55.9%)	177(85.9%)	67(67.0%)
181-270	192(10.2%)	51(26.6%)	18(9.4%)	110(57.3%)	72(85.7%)	38(80.9%)
⩾271	361(19.1%)	80(22.2%)	34(9.6%)	198(54.8%)	116(84.7%)	59(78.7%)
χ^2		1.907	13.438	0.355	0.165	5.409
P		0.592	**0.004**	0.949	0.983	0.144

Table 3 Multivariate logistic regression models between service-seeking and specific symptoms

	buying medicine from shops (n1=1484,n2=445)		taking leftover medicine (n1=1668, n2=257)		Seeking help from clinics (n1=857,n2=1078)		Getting antibiotics at clinics (n1=117，n2=692)		Getting antibiotics at shops (n1=103，n2=313)	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Gender	1.085	0.840-1.400	**2.016**	**1.411-2.881**	0.819	0.653-1.027	0.952	0.592-1.532	0.863	0.497-1.498
Age	0.984	0.873-1.109	0.866	0.742-1.011	1.104	0.993-1.227	0.887	0.704-1.118	1.022	0.789-1.324
Education	**1.23**	**1.068-1.417**	**1.283**	**1.073-1.535**	**0.79**	**0.697-0.896**	0.849	0.646-1.114	1.133	0.842-1.523
Sore throat	1.016	0.810-1.275	1.303	0.971-1.748	**1.355**	**1.109-1.654**	**2.05**	**1.337-3.143**	1.604	0.990-2.599
Rhinorrhea without pus	0.838	0.669-1.051	1.057	0.791-1.411	1.045	0.856-1.276	1.25	0.816-1.915	0.792	0.486-1.290
Rhinorrhea with pus	0.96	0.714-1.292	0.78	0.531-1.145	1.045	0.804-1.359	1.013	0.566-1.813	1.796	0.869-3.711
Dry cough	**1.452**	**1.124-1.875**	0.809	0.587-1.114	**1.492**	**1.198-1.859**	1.318	0.812-2.140	1.328	0.777-2.269
Productive cough	1.026	0.798-1.318	1.28	0.926-1.770	1.115	0.891-1.395	0.907	0.561-1.466	**1.971**	**1.125-3.453**
Shortness of breath,	0.782	0.571-1.071	0.695	0.458-1.054	**1.707**	**1.287-2.265**	0.927	0.533-1.613	1.049	0.488-2.255
Earache/tinnitus	1.421	0.979-2.063	1.305	0.825-2.063	0.757	0.535-1.072	**4.884**	**1.162-20.522**	1.489	0.608-3.648
Headache general discomfort	1.102	0.875-1.389	1.581	1.169-2.138	1.178	0.962-1.443	1.184	0.765-1.831	1.026	0.623-1.690
Fever	0.778	0.583-1.037	1.223	0.866-1.725	**2.142**	**1.654-2.775**	1.33	0.791-2.236	1.74	0.833-3.633

Note: n1 and n2 stands for the number of no and yes response respectively to each service use behavior; for each service use behavior, no (n1) was coded as 0 and yes(n2), as 1. Gender: 1=male,2=female; Age group: 1= ≤40y, 2=41-50y, 3=51-60y,4= ≥61y；Educatio:1=0 years,2=1-6 years ,3=7-9 years ,4=≥10 years. Symptoms: no= 0 and yes= 1； Medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines.

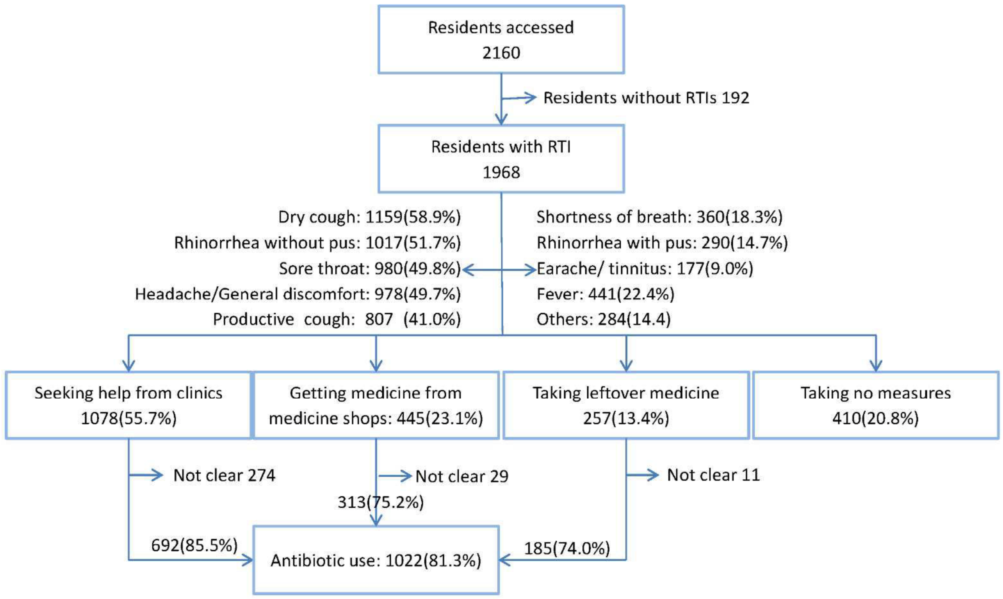


Figure 1 Flow chart describing symptoms, healthcare-seeking and antibiotics use among study population

224x136mm (300 x 300 DPI)

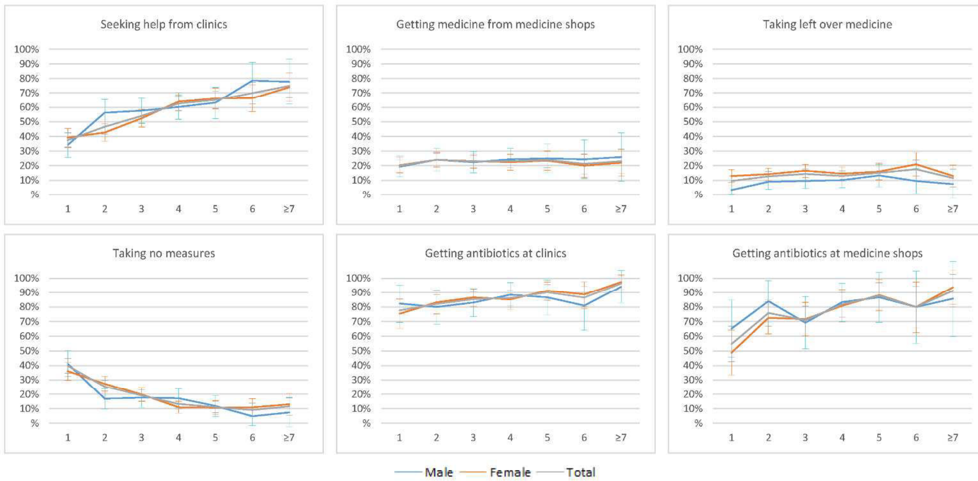
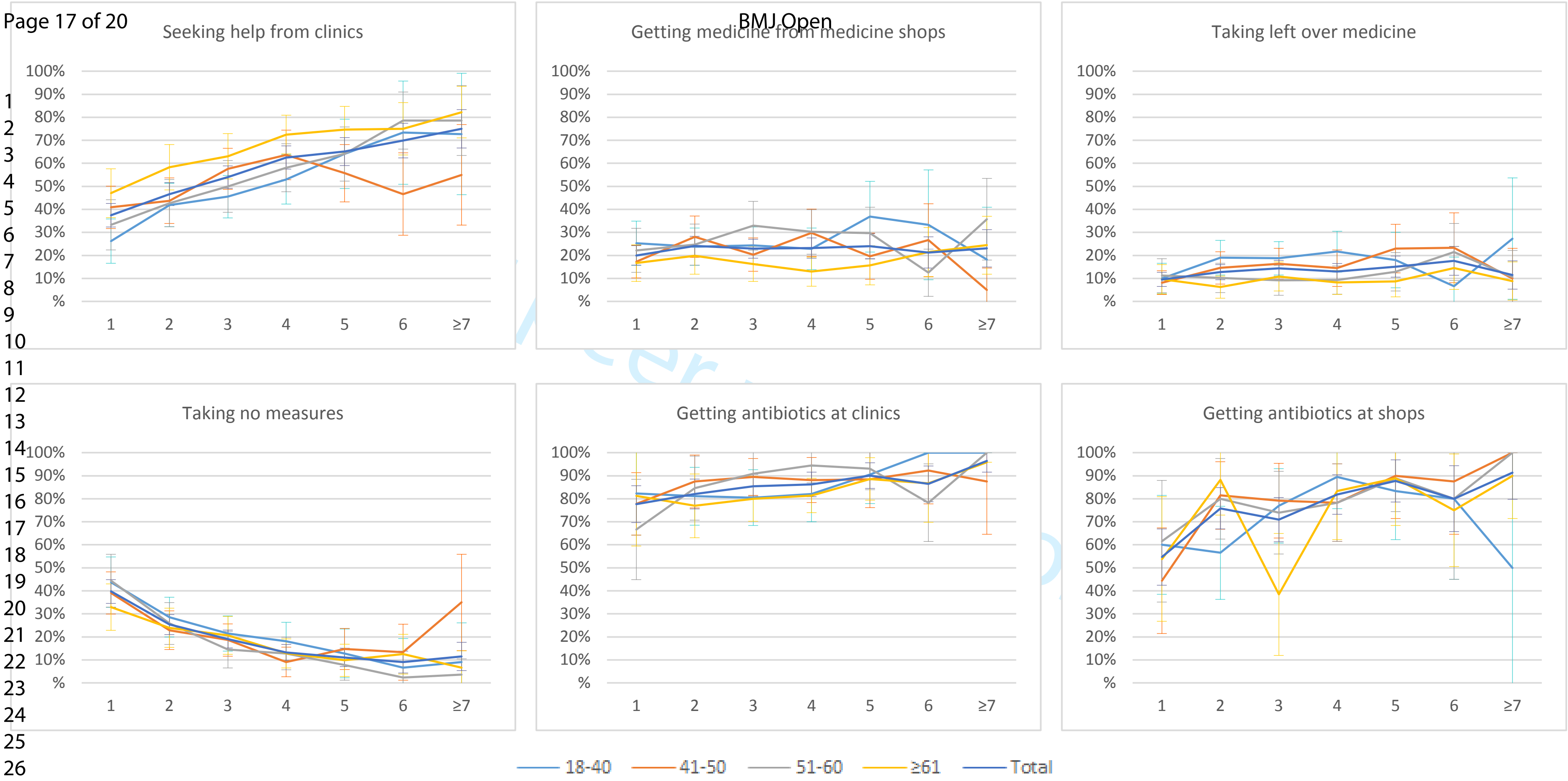


Figure 2 Healthcare-seeking by number of symptoms in total and by genders
Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines.

251x121mm (300 x 300 DPI)



Appendix 1 Service-seeking by number of symptoms in total and by age

(Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines)

Appendix 2 Healthcare-seeking by number of symptoms in total and by education

(Note: The numbers along the horizontal axis stand for numbers of symptoms; medicines comprise all kinds of drugs used for treating illnesses and antibiotics are one kind of medicines)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	P1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	P2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	P4
Methods			
Study design	4	Present key elements of study design early in the paper	P4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P4-5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	P4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	P5-6
Bias	9	Describe any efforts to address potential sources of bias	P8
Study size	10	Explain how the study size was arrived at	P4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	P4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	P4
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	P5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	P4
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P5
		(b) Give reasons for non-participation at each stage	P5
		(c) Consider use of a flow diagram	P5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P5
		(b) Indicate number of participants with missing data for each variable of interest	P5
Outcome data	15*	Report numbers of outcome events or summary measures	P5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	P6
		(*b*) Report category boundaries when continuous variables were categorized	P5,6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	P6
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	P7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P7-8
Generalisability	21	Discuss the generalisability (external validity) of the study results	P8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	P9

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.