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ORIGINAL RESEARCH

Asthma-chronic obstructive pulmonary disease overlap syndrome in the urban Chinese population: prevalence and disease burden using the 2010, 2012, and 2013 China National Health and Wellness Surveys

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Background: Research has suggested a significant burden for patients with asthma-chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS). However, few studies have studied this population in the People's Republic of China, a region in the midst of rapid epidemiological change with respect to respiratory disease. The aim of this study was to assess the prevalence of ACOS and its association with patient outcomes in urban China.

Methods: Data from the 2010, 2012, and 2013 China National Health and Wellness Survey, an Internet-based survey of adults in urban China, were used (N=59,935). Respondents were categorized into one of four groups based on self-reported physician diagnoses: ACOS, asthma only, COPD only, or control (ie, no asthma or COPD). A propensity score matching procedure was conducted to cull the control group into a subgroup (ie, matched controls) who resembled patients with ACOS, asthma only, and COPD only. These four groups (ACOS, asthma only, COPD only, matched controls) were then compared with respect to health status (Short Form-12 version 2/Short Form-36 version 2), work productivity, and health care resource use using generalized linear models.

Results: Patients with ACOS (N=366) comprised 0.61% of the adult population, 30.73% of the asthma population, and 18.60% of the COPD population in the People's Republic of China. Patients with ACOS reported significantly worse health status (eg, health utilities =0.63, 0.66, 0.63, and 0.69 for ACOS, COPD only, asthma only, and matched controls, respectively) and significantly greater work impairment (eg, overall work impairment =43.65%, 35.19%, 48.55%, and 29.80%, respectively) and health care resource use (eg, physician visits in the past 6 months =5.13, 3.84, 4.65, and 2.39, respectively) compared with matched controls and patients with COPD only. Few significant differences were observed between patients with ACOS and asthma only.

Conclusion: Patients with ACOS have a greater comorbidity burden and significantly worse health outcomes compared with COPD only patients and matched controls. Better management of these patients may help to improve their outcomes.

Keywords: ACOS, quality of life, work productivity, healthcare resource use

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Background

Asthma is a chronic inflammatory condition that causes the airways to swell and narrow, leading to dyspnea, coughing, and tightening of the chest.[1,2] Asthma has been found to be quite common, though its prevalence varies significantly by region, ranging from

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1% to 18%.[3–5] Using data from 2010 to 2011, a recent epidemiological survey study conducted across eight provinces in the People's Republic of China estimated the prevalence of asthma in the population older than 14 years at 1.24%.[6] This figure has increased dramatically in the past 20 years, however. A study in Shanghai found that the prevalence of asthma among those 6 years and older increased from 0.4% in 1997 to 1.8% in 2007.[5] Evidence has also suggested increases in the prevalence of chronic obstructive pulmonary disease (COPD) over time.[7] A recent review, which extracted data from 80 studies, found that the prevalence of COPD ranged from 0.2% to 37%, with significant variation across countries, populations, and methods to diagnose and classify COPD.[7] In the People's Republic of China, the prevalence of COPD among those 40 years and older was estimated at 8.2% based on a recent large-scale, population-based epidemiological study on COPD prevalence in the People's Republic of China.[8] Additional studies have produced similar estimates.[9–11]

In part, the increases in the prevalence of these two respiratory conditions may be due to high rates of smoking and environmental pollutants, among other factors; however, some of the variation is currently difficult to explain.[8] Given the increasing incidence and prevalence of respiratory conditions in the People's Republic of China and the high mortality rate of these patients,[4,5] further research is necessary to understand the overlap between asthma and COPD (ie, asthma COPD overlap syndrome [ACOS]), which can be quite common.[12,13]

Research has suggested a significant burden for patients with ACOS. Pleasants et al[14] reported that patients with ACOS had significantly more comorbidities and impairment than those with individual conditions. Similarly, Kauppi et al[15] reported a significantly poorer quality of life among patients with ACOS. Studies have also found greater health care resource utilization and costs among these patients.[16]

The epidemiology of ACOS has not been studied in the People's Republic of China. The current study had two objectives. The first objective was to estimate the prevalence and profile (with respect to demographics, health characteristics, and disease history) of patients with ACOS among the adult population in urban China. The second objective was to investigate the association among ACOS and health status, work productivity, and health care resource use.

Methods

Data source

This study included data from the 2010 (N=19,954), 2012 (N=19,994), and 2013 (N=19,987) China National Health and Wellness Survey (NHWS; no China NHWS was fielded in 2011). All the 3 years were combined for the purposes of analysis to maximize sample size for those with ACOS. The total sample size for 2010–2013 China NHWS was N=59,935.

The NHWS is a cross-sectional, self-administered, Internet-based survey of adults (aged 18 or older) intended to represent the urban adult population in the People's Republic of China (ie, tier 1 and tier 2 cities). A comparison between the NHWS and the urban Chinese population with respect to age and sex distributions is shown in Table 1. Detailed information on the methods of the China NHWS is provided elsewhere.[17] To briefly summarize, potential respondents were recruited through a combination of Internet panels and offline recruiting (the latter implemented to ensure adequate representation among the elderly and those without Internet access) using a random stratified sampling framework. Strata were based on age, sex, and region to match these characteristics to the total urban China population.

A large majority of the China NHWS sample accessed the survey from an email invitation received through their panel membership and completed the survey using a web-based format (response rates were as follows: 2010=16.46%, 2012=15.78%, and 2013=4.89%). In order to achieve an adequate sample of respondents aged 50 and over (and account for those without reliable Internet access), computer-assisted web interviewing was also conducted for ~15% of the sample in a given year. Computer-assisted web interviewing was conducted in ten of the largest urban regions: Beijing, Shenyang, Xi'an, Hefei, Changsha, Chengdu, Shanghai, Jinan, Guiyang, and Guangzhou. In these cases, respondents were recruited offline and asked to complete the survey (using a computer) in a centralized facility. Permission to use the NHWS data for this study was granted by Kantar Health (New York, NY). The 2010, 2012, and 2013 China NHWS was reviewed and approved by an independent institutional review board (Essex IRB) and participants provided written informed consent to be included in this study. All respondents were compensated

Table 1 Distribution of age and sex between the NHWS sample and the urban China population

Age (years)	NHWS sample		Urban China population[a]	
	Male (%)	Female (%)	Male (%)	Female (%)
18–29	13	13	13	12
30–39	13	10	10	9
40–49	12	8	12	11
50–59	8	8	8	7
60–69	5	5	5	5
70+	2	2	4	4

Note: [a]Based on the China Statistical Yearbook from the National Bureau of Statistics of the People's Republic of China (Accessed at: http://www.stats.gov.cn/).[24]
Abbreviation: NHWS, National Health and Wellness Survey.

for their participation. No ethical review was sought for the current analysis as it was limited to secondary analysis of de-identified patient survey data. All principles outlined in the Declaration of Helsinki were followed.

Measures

ACOS

The key independent variable of interest was a four-level categorical variable indicating ACOS status: ACOS versus asthma without COPD (asthma only) versus COPD without asthma (COPD only) versus no asthma or COPD (ie, the control group). Each respondent in NHWS was placed into one of the four categories based on self-reported physician diagnoses. All respondents in the NHWS were asked, "Which of the following conditions have you ever experienced?" with a list of conditions to select (eg, anxiety, COPD, high blood pressure). For patients who selected "asthma", "COPD", "chronic bronchitis", or "emphysema", they were then asked (for each condition separately) whether the condition has been diagnosed by a health care professional (Has your [CONDITION] ever been diagnosed by a health care professional?). Respondents who self-reported a diagnosis of asthma and a diagnosis of COPD, chronic bronchitis, or emphysema were classified as "ACOS". Respondents who self-reported a diagnosis of asthma but did not report a diagnosis of COPD, chronic bronchitis, or emphysema were classified as "asthma only". Respondents who did not self-report a diagnosis of asthma but self-reported a diagnosis of COPD, chronic bronchitis, or emphysema were classified as "COPD only". All remaining respondents (ie, those without a diagnosis of asthma, COPD, chronic bronchitis, or emphysema) were classified as "controls".

Demographics

Demographic variables assessed in the NHWS include the year of the survey (2010, 2012, 2013), sex (male vs female), age, monthly household income (renminbi [RMB] 2,500–5,999, RMB 6,000–9,999, RMB 10,000+, or declined to answer, vs ≤RMB 2,499), and education (university or beyond+ vs lower).

Health history

Health history variables include smoking habits (current smoker, former smoker, vs never smoker), alcohol consumption (current alcohol use vs no alcohol use), exercise (≥1 times in the past month, vigorously for 20+ minutes, vs no vigorous exercise), and body mass index category (coded as based on the World Health Organization recommendation for Asian populations: underweight [<18.5 kg/m^2], acceptable risk [18.5 to <23 kg/m^2], increased risk [23 to <27.5 kg/m^2], high risk [≥27.5 kg/m^2] or decline to provide weight).[18] The Charlson comorbidity Index (CCI), which represents a weighted sum of multiple comorbid conditions predictive of mortality, was also included.[19] Greater scores indicate a greater comorbid burden on the patient. Since the CCI includes COPD as one of its conditions, an "adjusted" CCI was calculated removing COPD from the index (otherwise, controlling for the CCI as a covariate would result in inadvertently controlling for COPD, which is part of the main predictor of interest).

Disease history

For respondents who reported a diagnosis of asthma, the following information was also available: number of years they have been diagnosed, diagnosing physician (internist, allergist, nurse practitioner, pediatrician, pulmonologist, other), self-reported severity, frequency of asthma problems (daily to once a month or less), Asthma Control Test,[20] the main causes of asthma attacks (allergic reactions, exercise/physical activity, illnesses, pollutants, secondhand smoke, stress/anxiety, weather/temperature, other), and current treatment (prescription medication and over-the-counter medication, prescription medication only, over-the-counter medication only, no treatment). For respondents who reported a diagnosis of COPD, the following information was also available: number of years they have been diagnosed, diagnosing physician specialty, self-assessed severity of COPD (mild, moderate, and severe), presence of exacerbations, duration of exacerbations in the past 6 months, main cause of episodes, frequency/severity of breathlessness, and current treatment (prescription medication and over-the-counter medication, prescription medication only, over-the-counter medication only, no treatment).

Health status

Health status was measured using the Short Form-36 version 2 in 2012 and 2013 and the Short Form-12 version 2 in 2010.[21,22] The Short Form-12 version 2 is a subset of the Short Form-36 version 2 and both produce a normed physical component summary and mental component summary score. Additionally, both the Short Form-12 version 2 and Short Form-36 version 2 can be used to generate health state utilities for economic analysis by applying the Short Form-6D algorithm (which conceptually varies between 0 and 1 with higher values equating to better health states).

Work productivity

Productivity impairment was measured using the Work Productivity and Activity Impairment questionnaire.[23] The Work

Productivity and Activity Impairment questionnaire includes the following metrics: absenteeism (% work time missed because of one's health in the past 7 days), presenteeism (% impairment experienced while at work in the past 7 days), overall work impairment (combination of absenteeism and presenteeism), and activity impairment (% impairment in daily activities in the past 7 days). Only respondents who reported being employed provided data for absenteeism, presenteeism, and overall work impairment. All respondents provided data for activity impairment.

Resource use

Health care utilization was defined by the number of health care provider visits, number of emergency room (ER) visits (How many times have you been to the ER for your own medical condition in the past 6 months?), and number of times hospitalized (How many times have you been hospitalized for your own medical condition in the past 6 months?) in the past 6 months.

Statistical analysis

The prevalence for ACOS among the total adult population, adult asthma population, and adult COPD population was calculated across sex and age group strata. These estimates were made both on the raw data and weighted data (the latter incorporated sampling weights). To calculate the sampling weights, the age, sex, and region distribution of our combined 2010, 2012, and 2013 China NHWS study sample was produced. We then examined the age, sex, and region distribution for the total adult urban China population as reported by the 2012 National Bureau of Statistics of China.[24] A ranking procedure was then used to calculate a sample weight for each age by sex by region cell.[25] These weights were then assigned to reach respondent based on their cell membership (ie, which sex, age group, and region they belonged to) and applied in relevant analyses.

The overall intent of this analysis was to compare those with ACOS versus those with asthma only versus those with COPD only versus controls. Given the anticipated sample size imbalance as it relates to the control group (which would have statistical implications including, but not limited to, overpowering the analyses), a preliminary propensity score match was undertaken to create a matched control group which is similar to those with COPD and/or asthma but do not have either condition.

Demographic and health history differences among groups (ACOS vs asthma only vs COPD only vs controls) were examined using chi-square tests and one-way analysis of variance tests for categorical and continuous variables, respectively ("prepropensity score matching" differences). Variables which differed between asthma/COPD and no asthma or COPD (ie, controls) at $P<0.20$ were considered as candidates for inclusion in the propensity score model to identify a matched control group. This list included the following variables: survey year, age, sex, education, household income, body mass index, alcohol use, exercise behavior, smoking habits, and the "adjusted" CCI (ie, the CCI excluding COPD as explained earlier). These variables were then all entered into a logistic regression model to predict asthma/COPD versus no asthma or COPD (ie, controls). Propensity score values were saved from this model. For each case (ie, respondent with asthma or COPD), a single control was identified whose propensity score value was closest using a greedy-matching algorithm.[26]

Upon completion of the match, two equally sized groups remained: asthma/COPD versus matched controls. The asthma/COPD group was then split into three groups: ACOS, those with asthma only and those with COPD only. The four groups (ACOS, asthma only, COPD only, and matched controls) were then compared with respect to demographic and health history variables (using chi-square tests and one-way analysis of variance tests for categorical and continuous variables, respectively) to identify covariates ("postpropensity score matching" differences).

A regression model approach was then undertaken to compare the four groups (ACOS vs asthma only vs COPD only vs matched controls) with respect to health status, work productivity, and health care resource use controlling for survey year, age, education, household income, body mass index, alcohol use, exercise behavior, smoking habits, and the adjusted CCI. Generalized linear models were used that specified the appropriate distribution (normal for health status variables, negative binomial for all other variables) and link function (identity for health status variables, log for all other variables) according to the best fit to the data.

Results

A total of N=59,935 respondents completed the 2010, 2011, and 2013 China NHWS. These respondents who represent the total urban population were 54.65% male and had a mean age of 41.52 years (standard deviation =14.99). A total of N=1,968 respondents met the definition of COPD (3.28% of the total adult population, 95% confidence interval [CI]: 3.14%, 3.43%), with the majority of respondents reporting a diagnosis of chronic bronchitis (Table 2). A total N=1,191 respondents met the definition of asthma (1.99% of

Table 2 Overlap of COPD conditions among patients with COPD (N=1,968)

COPD phenotype	n	%
Chronic bronchitis only	1,689	85.82
Emphysema only	166	8.43
COPD only	42	2.13
Emphysema + chronic bronchitis	32	1.63
COPD + chronic bronchitis	18	0.91
COPD + emphysema + chronic bronchitis	14	0.71
COPD + emphysema	7	0.36

Abbreviation: COPD, chronic obstructive pulmonary disease.

the total adult population, 95% CI: 1.88%, 2.10%) and N=366 respondents met the definition for ACOS (0.61% of the total population [95% CI: 0.55%, 0.67%], 30.73% of those with asthma [95% CI: 28.11%, 33.35%], and 18.60% of those with COPD [95% CI: 16.88%, 20.32%]). The prevalence of these conditions by age and sex is reported in Table 3.

Demographic and health history differences among the groups prior to the matching process were examined in Table 4 (prepropensity score matching). Although several differences between control respondents and the asthma/COPD groups were found, few significant differences were observed between patients with ACOS and those patients with asthma only or COPD only. Patients with ACOS were more likely to regularly exercise compared with patients with COPD only (67.76% vs 57.55%, $P<0.05$) and had a greater comorbidity burden (as measured using the "adjusted" CCI, which did not include COPD) compared with patients with COPD only (1.60 vs 0.42, $P<0.05$) and patients with asthma only (1.60 vs 0.71, $P<0.05$). No other significant differences were observed.

With respect to differences in asthma history, patients with ACOS have been diagnosed for longer (11.5 vs 9.9 years for ACOS and asthma only, respectively), reported themselves as more severe when not using their medication (28.69% vs

Table 3 Prevalence of ACOS by age and sex

Demographic stratum	Unweighted				
	Within total population (N=59,935)			Within COPD (N=1,968)	Within asthma (N=1,191)
	COPD (n=1,968)	Asthma (n=1,191)	ACOS (n=366)	ACOS (n=366)	ACOS (n=366)
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Total	3.28 (3.14, 3.43)	1.99 (1.88, 2.10)	0.61 (0.55, 0.67)	18.60 (16.88, 20.32)	30.73 (28.11, 33.35)
Males	3.58 (3.38, 3.79)	2.11 (1.95, 2.26)	0.66 (0.57, 0.74)	18.31 (16.1, 20.53)	31.16 (27.7, 34.62)
Females	2.92 (2.72, 3.12)	1.84 (1.68, 2.00)	0.56 (0.47, 0.64)	19.02 (16.29, 21.75)	30.14 (26.12, 34.16)
18–29	2.79 (2.53, 3.05)	1.46 (1.27, 1.65)	0.44 (0.33, 0.54)	15.63 (12.22, 19.05)	29.82 (23.88, 35.77)
30–39	3.5 (3.19, 3.81)	2.1 (1.86, 2.34)	0.74 (0.60, 0.88)	21.12 (17.47, 24.76)	35.17 (29.67, 40.68)
40–49	3.46 (3.14, 3.78)	2.1 (1.85, 2.35)	0.60 (0.47, 0.74)	17.41 (13.8, 21.02)	28.68 (23.16, 34.21)
50–59	3.6 (3.22, 3.97)	2.5 (2.18, 2.81)	0.74 (0.57, 0.91)	20.52 (16.26, 24.78)	29.58 (23.8, 35.37)
60–69	3.5 (3.03, 3.97)	2.17 (1.79, 2.54)	0.63 (0.43, 0.83)	18.05 (12.78, 23.32)	29.13 (21.22, 37.05)
70+	2.67 (2.07, 3.27)	1.73 (1.25, 2.22)	0.51 (0.24, 0.77)	18.92 (9.99, 27.85)	29.17 (16.29, 42.04)
	Weighted				
	Within total population (N=444,643,405)			Within COPD (N=14,777,846)	Within asthma (N=8,958,717)
	COPD (N=14,777,846)	Asthma (N=8,958,717)	ACOS (N=2,733,141)	ACOS (N=2,733,141)	ACOS (N=2,733,141)
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Total	3.32 (3.17, 3.47)	2.01 (1.9, 2.13)	0.61 (0.55, 0.68)	18.49 (16.71, 20.28)	30.51 (27.78, 33.24)
Males	3.71 (3.5, 3.93)	2.12 (1.96, 2.28)	0.68 (0.58, 0.77)	18.27 (15.97, 20.58)	31.98 (28.32, 35.64)
Females	2.92 (2.71, 3.12)	1.9 (1.73, 2.08)	0.55 (0.46, 0.64)	18.79 (15.98, 21.6)	28.78 (24.71, 32.86)
18–29	2.76 (2.49, 3.02)	1.46 (1.27, 1.66)	0.43 (0.33, 0.54)	15.71 (12.19, 19.22)	29.62 (23.53, 35.7)
30–39	3.55 (3.23, 3.87)	2.1 (1.85, 2.35)	0.73 (0.58, 0.87)	20.45 (16.8, 24.1)	34.53 (28.92, 40.15)
40–49	3.54 (3.2, 3.88)	2.14 (1.87, 2.41)	0.64 (0.49, 0.79)	18.02 (14.19, 21.85)	29.77 (23.91, 35.62)
50–59	3.64 (3.25, 4.03)	2.45 (2.13, 2.76)	0.73 (0.55, 0.9)	20 (15.67, 24.33)	29.76 (23.74, 35.78)
60–69	3.35 (2.88, 3.81)	2.08 (1.71, 2.45)	0.55 (0.37, 0.73)	16.46 (11.41, 21.51)	26.48 (18.78, 34.18)
70+	2.68 (2.06, 3.3)	1.69 (1.2, 2.18)	0.55 (0.26, 0.84)	20.52 (10.81, 30.24)	32.53 (18.49, 46.57)

Notes: All weighted results were generated using a survey sample procedure (PROC SURVEYFREQ), including a sample weight generated through a raking procedure to match the sample to the total urban population with respect to age, sex, and region.
Abbreviations: ACOS, asthma COPD overlap syndrome; CI, confidence interval; COPD, chronic obstructive pulmonary disease.

Table 4 Demographic and health history differences among asthma and COPD groups, both before and after propensity score matching

Variable	Prepropensity score matching					Postpropensity score matching				
	ACOS (A) (N=366)	Asthma only (B) (N=825)	COPD only (C) (N=1,602)	Control (D) (N=57,142)	*P*-value	ACOS (A) (N=350)	Asthma only (B) (N=822)	COPD only (C) (N=1,598)	Matched control (D) (N=2,770)	*P*-value
Survey year					*<0.001*					*<0.001*
2010 (%)	124 (33.88) BC	202 (24.48) ACD	678 (42.32) ABD	18,950 (33.16) BC		123 (35.14) B	202 (24.57) ACD	677 (42.37) BD	1,031 (37.22) BC	
2012 (%)	123 (33.61)	297 (36.00)	496 (30.96)	19,078 (33.39)		114 (32.57)	295 (35.89)	494 (30.91)	890 (32.13)	
2013 (%)	119 (32.51)	326 (39.52) CD	428 (26.72) BD	19,114 (33.45) BC		113 (32.29)	325 (39.54) CD	427 (26.72) BD	849 (30.65) BC	
Age (years)					*<0.001*					*0.002*
N	366	825	1,602	57,142		350	822	1,598	2,770	
Mean ± SD	42.79±14.30	43.45±14.63 D	42.10±14.71	41.47±15.01 B		43.11±14.42	43.47±14.65 C	42.07±14.69 BD	43.83±15.11 C	
Sex					*<0.001*					*0.263*
Male (%)	215 (58.74)	475 (57.58)	959 (59.86) D	31,105 (54.43) C		205 (58.57)	473 (57.54)	957 (59.89)	1,695 (61.19)	
Female (%)	151 (41.26)	350 (42.42)	643 (40.14) D	26,037 (45.57) C		145 (41.43)	349 (42.46)	641 (40.11)	1,075 (38.81)	
Education					*<0.001*					*<0.001*
Less than University degree (%)	150 (40.98)	319 (38.67) CD	720 (44.94) B	26,707 (46.74) B		145 (41.43)	319 (38.81) CD	719 (44.99) B	1,295 (46.75) B	
University degree (%)	216 (59.02)	506 (61.33) CD	882 (55.06) B	30,435 (53.26) B		205 (58.57)	503 (61.19) CD	879 (55.01) B	1,475 (53.25) B	
Household income					*<0.001*					*0.001*
Renminbi (RMB) <2,500 (%)	24 (6.56)	64 (7.76)	130 (8.11) D	6,088 (10.65) BC		24 (6.86)	64 (7.79)	130 (8.14)	243 (8.77)	
RMB 2,500 to <6,000 (%)	86 (23.50)	179 (21.70)	397 (24.78%) BD	15,943 (27.90) BC		83 (23.71)	179 (21.78)	396 (24.78)	722 (26.06)	
RMB 6,000 to <10,000 (%)	108 (29.51)	270 (32.73)	488 (30.46)	16,987 (29.73)		101 (28.86)	267 (32.48)	485 (30.35)	931 (33.61)	
RMB 10,000+ (%)	145 (39.62)	299 (36.24)	565 (35.27)	16,238 (28.42) ABC		139 (39.71) D	299 (36.37) D	565 (35.36) D	826 (29.82) ABC	
Declined to answer (%)	3 (0.82)	13 (1.58)	22 (1.37)	1,886 (3.30) ABC		3 (0.86)	13 (1.58)	22 (1.38)	48 (1.73)	
Body mass index (kg/m^2)					*<0.001*					*0.009*
Underweight (%)	28 (7.65)	59 (7.15)	110 (6.87)	4,701 (8.23)		27 (7.71)	59 (7.18)	109 (6.82)	159 (5.74)	
Acceptable risk (%)	155 (42.35)	354 (42.91)	761 (47.50)	26,744 (46.80)		149 (42.57)	353 (42.94)	759 (47.50) D	1,186 (42.82) C	
Increased risk (%)	132 (36.07)	277 (33.58)	506 (31.59)	18,280 (31.99)		126 (36.00)	277 (33.70)	505 (31.60)	911 (32.89)	
High risk (%)	49 (13.39)	129 (15.64) D	213 (13.30)	6,546 (11.46) B		46 (13.14)	127 (15.45)	213 (13.33) D	484 (17.47) C	
Decline to provide weight (%)	2 (0.55)	6 (0.73)	12 (0.75)	871 (1.52)		2 (0.57)	6 (0.73)	12 (0.75)	30 (1.08)	
Alcohol use					*<0.001*					*0.002*
Do not drink (%)	73 (19.95) D	180 (21.82) D	396 (24.72) D	20,814 (36.43) ABC		72 (20.57) D	180 (21.90) D	395 (24.72)	756 (27.29) AB	
Drink alcohol (%)	293 (80.05) BD	645 (78.18) BD	1,206 (75.28) D	36,328 (63.57) ABC		278 (79.43) D	642 (78.10) D	1,203 (75.28)	2,014 (72.71) AB	
Exercise behavior					*<0.001*					*<0.001*
Do not exercise (%)	118 (32.24) CD	282 (34.18) CD	680 (42.45) ABD	26,311 (46.04) ABC		115 (32.86) CD	282 (34.31) CD	679 (42.49) AB	1,141 (41.19) AB	
Regularly exercise (%)	248 (67.76) CD	543 (65.82) CD	922 (57.55) ABD	30,831 (53.96) ABC		235 (67.14) CD	540 (65.69) CD	919 (57.51) AB	1,629 (58.81) AB	

Smoking habits					<0.001				<0.001
Never smoked (%)	164 (44.81)	381 (46.18)	833 (52.00) BD	37,960 (66.43) ABC		163 (46.57)	381 (46.35)	831 (52.00) D	1,303 (47.04) C	
Former smoker (%)	64 (17.49)	108 (13.09)	248 (15.48) D	7,390 (12.93) C		62 (17.71)	108 (13.14) D	248 (15.52)	481 (17.36) B	
Current smoker (%)	138 (37.70)	336 (40.73) CD	521 (32.52) BD	11,792 (20.64) ABC		125 (35.71)	333 (40.51) C	519 (32.48) B	986 (35.60)	
Charlson Comorbidity Index (CCI) – adjusted[a]					<0.001					<0.001
N	366	825	1,602	57,142		350	822	1,598	2,770	
Mean ± SD	1.60±4.25 BCD	0.71±1.26 ACD	0.42±0.94 ABD	0.18±0.50 ABC		0.87±1.62 BCD	0.68±1.07 ACD	0.40±0.87 ABD	0.58±1.12 ABC	

Notes: Letters beside values indicate which groups are significantly different from this value using a post hoc comparison (with a Tukey adjustment). For example, the letters "CD" below a value would suggest the mean/percentage is significantly different from the COPD only (group C) and the control (group D) groups. [a]The adjusted CCI removes COPD conditions from the calculation. The *P*-values in this table are based on a chi-square test (for categorical variables) or a one-way ANOVA test (for continuous variables).

Abbreviations: ACOS, asthma COPD overlap syndrome; COPD, chronic obstructive pulmonary disease; SD, standard deviation.

22.91% self-reported themselves as moderately or severely persistent), and were more likely to attribute the cause of their asthma to allergies, illness, pollutants, stress, and weather than patients with only asthma (all $P<0.05$; Table 5). Patients with ACOS also reported significantly higher levels of asthma control based on the ACT (18.8 vs 18.3, $P<0.05$; though both mean less than adequate control).

With respect to differences in COPD history, patients with ACOS were more likely to have been diagnosed by a pulmonologist (33.61% vs 23.28%), reported a greater severity (25.14% vs 24.41% self-reported as either moderate or severe), and experienced more frequent exacerbations and more severe breathlessness (all $P<0.05$; Table 6). Patients with ACOS were significantly more likely to be treated overall (88.80% vs 52.68%, $P<0.05$) and were more likely to use a prescription medication (either alone or in combination with a nonprescription treatment; 65.30% vs 52.55%, $P<0.05$).

Differences after propensity score matching in demographics and health history are also reported in Table 4 (postpropensity score matching). The intent of the matching process was to create a matched control group similar to the patients with asthma and/or COPD; the intent was not to eliminate any differences between ACOS and patients with asthma only/COPD only. As a result, the demographic and health history differences between ACOS and patients with asthma only/COPD only were largely the same as the prematch results. Patients with ACOS were more likely to exercise regularly compared with patients with COPD only and had a greater comorbidity burden compared with both patients with COPD only and asthma only. No other significant differences were observed.

The ACOS, asthma only, COPD only, and matched control cohorts were then compared among one another with respect to health outcomes, using a regression approach (Table 7). Patients with ACOS reported significantly worse mental component summary and physical component summary scores and worse health utilities compared with matched controls (adjusted mean =40.47 vs 44.85; 44.99 vs 49.86; and 0.63 vs 0.69, respectively; all $P<0.05$) and patients with COPD only (adjusted mean =40.47 vs 42.88; 44.99 vs 47.66; and 0.63 vs 0.66, respectively; all $P<0.05$). No significant differences were observed between patients with ACOS and patients with asthma only.

The pattern of results was very similar when examining work and activity impairment outcomes. Patients with ACOS reported significantly greater absenteeism, presenteeism, overall work impairment, and activity impairment compared with matched controls and compared with patients with

Table 5 Asthma history differences between patients with asthma only and ACOS

Variable	ACOS (N=366)	Asthma only (N=825)	*P*-value
Years diagnosed (asthma)			*0.039*
n	312	667	
Mean ± SD	11.5±12.6	9.9±10.7	
Diagnosing physician (asthma)			*0.129*
General internist (%)	154 (42.08)	285 (34.55)	
Allergist (%)	46 (12.57)	105 (12.73)	
Pediatrician (%)	18 (4.92)	43 (5.21)	
Pulmonologist (%)	87 (23.77)	199 (24.12)	
Other (%)	7 (1.91)	35 (4.24)	
Asthma severity (with medication)			*0.164*
Mild intermittent (%)	188 (51.37)	395 (47.88)	
Mild persistent (%)	79 (21.58)	161 (19.52)	
Moderate persistent (%)	19 (5.19)	59 (7.15)	
Severe persistent (%)	2 (0.55)	2 (0.24)	
Asthma severity (without medication)			*<0.001*
Mild intermittent (%)	152 (41.53)	362 (43.88)	
Mild persistent (%)	109 (29.78)	274 (33.21)	
Moderate persistent (%)	89 (24.32)	163 (19.76)	
Severe persistent (%)	16 (4.37)	26 (3.15)	
Asthma treatment			*<0.001*
Untreated (%)	33 (9.02)	71 (8.61)	
OTC only (%)	95 (25.96)	211 (25.58)	
Rx only (%)	88 (24.04)	209 (25.33)	
OTC and Rx (%)	150 (40.98)	334 (40.48)	
Causes of asthma			
Allergies/allergic reaction (%)	190 (51.91)	373 (45.21)	*0.013*
Exercise/physical activity (%)	69 (18.85)	176 (21.33)	*0.485*
Illnesses/conditions (eg, colds, flu) (%)	188 (51.37)	334 (40.48)	*0.003*
Pollutants/airborne irritants (%)	156 (42.62)	296 (35.88)	*<0.001*
Secondhand smoke (%)	82 (22.40)	153 (18.55)	*0.149*
Stress/anxiety/emotional states (%)	97 (26.50)	168 (20.36)	*0.036*
Weather/temperature (%)	166 (45.36)	290 (35.15)	*0.010*
None of these (%)	3 (0.82)	16 (1.94)	*<0.001*
ACT score			*<0.001*
N	366	825	
Mean ± SD	18.8±4.6	18.3±4.7	

Note: The *P*-values in this table are based on a chi-square test (for categorical variables) or a one-way ANOVA test (for continuous variables).
Abbreviations: ACT, asthma control test; ACOS, asthma COPD overlap syndrome; COPD, chronic obstructive pulmonary disease; OTC, over-the-counter; SD, standard deviation; Rx, prescription medication.

COPD only. Indeed, levels of overall work impairment and activity impairment for those with ACOS were ~50% higher than matched controls and 25% higher than patients with COPD only. No differences were observed between patients with ACOS and patients with asthma only with the exception of presenteeism, which was actually higher among those with asthma only (adjusted mean =42.69% vs 37.07%, $P<0.05$).

With respect to health care resource utilization, patients with ACOS reported significantly more physician visits, ER visits, and hospitalizations in the past 6 months compared with matched controls and patients with COPD only. Patients with ACOS reported more than double the number of physician visits (adjusted mean =5.13 vs 2.39) and ER visits (adjusted mean =1.09 vs 0.46) and triple the number of hospitalizations (adjusted mean =0.32 vs 0.11) compared with matched controls (all $P<0.05$). Although no differences were observed between patients with ACOS and asthma only patients with respect to physician visits and ER visits, asthma only patients reported significantly more hospitalizations compared with ACOS patients (adjusted mean =0.48 vs 0.32, $P<0.05$).

Discussion

Several studies have documented a significant overlap between asthma and COPD.[12,13] Our results suggest that ~30% of adults with asthma also have COPD and ~18% of adults with COPD also have asthma. Overall, 0.61% of the adult population in the People's Republic of China have ACOS. It is important to note that these prevalence figures were

Table 6 COPD history differences between patients with COPD only and ACOS

Variable	ACOS (N=366)	COPD only (N=1,602)	*P*-value
Years diagnosed (COPD)			*0.395*
n	327	1,347	
Mean ± SD	10.1±11.2	9.5±10.6	
Diagnosing physician (COPD)			*<0.001*
General internist (%)	168 (45.90)	826 (51.56)	
Allergist (%)	20 (5.46)	36 (2.25)	
Pulmonologist (%)	123 (33.61)	373 (23.28)	
Other (%)	16 (4.37)	112 (6.99)	
COPD severity			*<0.001*
Mild (%)	274 (74.86)	1,211 (75.59)	
Moderate (%)	84 (22.95)	366 (22.85)	
Severe (%)	8 (2.19)	25 (1.56)	
COPD treatment			*<0.001*
Untreated (%)	41 (11.20)	758 (47.32)	
OTC only (%)	86 (23.50)	2 (0.12)	
Rx only (%)	80 (21.86)	836 (52.18)	
OTC and Rx (%)	159 (43.44)	6 (0.37)	
Presence of exacerbations			
Episodes when my COPD symptoms become markedly worse (%)	68 (18.58)	198 (12.36)	*0.025*
The need for antibiotics to treat my COPD (%)	111 (30.33)	425 (26.53)	*<0.001*
The need for oral steroids to treat my COPD (%)	61 (16.67)	144 (8.99)	*<0.001*
COPD symptoms requiring unexpected hospitalization (%)	30 (8.20)	66 (4.12)	*0.001*
Worsening COPD symptoms lasting for days or weeks (%)	17 (4.64)	94 (5.87)	*0.041*
None of the above (%)	51 (13.93)	260 (16.23)	*<0.001*
Duration of exacerbations (days)			*0.580*
N	8	54	
Mean ± SD	25.8±16.6	30.3±14.9	
Breathlessness severity			*<0.001*
I only get breathless after strenuous exercise (%)	102 (27.87)	416 (25.97)	
I get breathless after moderate exercise (%)	52 (14.21)	212 (13.23)	
I get breathless when hurrying on level ground or walking up a slight incline (%)	34 (9.29)	92 (5.74)	
I walk slower than most people my age due to my breathing (%)	25 (6.83)	49 (3.06)	
I sometimes have to stop for breath even when walking on level ground at my own pace (%)	9 (2.46)	30 (1.87)	
I stop for breath every few minutes while walking, even on level ground (%)	3 (0.82)	9 (0.56)	
I am too breathless to leave the house (%)	1 (0.27)	3 (0.19)	
None of the above (%)	16 (4.37)	113 (7.05)	

Note: The *P*-values in this table are based on a chi-square test (for categorical variables) or a one-way ANOVA test (for continuous variables).
Abbreviations: ACOS, asthma COPD overlap syndrome; COPD, chronic obstructive pulmonary disease; OTC, over-the-counter; SD, standard deviation.

generated purely from patient self-report. As COPD may not be well recognized in the People's Republic of China and lung function tests may be performed less frequently than in the West, the prevalence of COPD and ACOS may be underrepresented.

The general demographic and health history profile of patients with ACOS was no different between patients with asthma only and COPD only. The major exception was a greater comorbidity burden, as assessed using the CCI. This finding is consistent with Pleasants et al[14] who reported that patients with ACOS had significantly more comorbidities than those with asthma or COPD only. However, we did find some additional disease-specific differences. Patients with ACOS had more severe disease than patients with asthma only and patients with COPD only (eg, greater self-reported severity, breathlessness, and more frequent exacerbations).

After creating a matched control group and further adjusting for demographic and health history differences, there was a significant burden for patients with ACOS relative to matched controls and those with COPD only. Patients with ACOS reported significantly worse mental and physical health status and health utilities, to a clinically relevant degree

Table 7 Adjusted mean health outcomes among patients with ACOS, COPD only, asthma only, and propensity score matched controls

Dependent variable	ACOS group	Adjusted mean	SE	95% LCL	95% UCL	*P*-value*	*P*-value**	*P*-value***
SF-12v2/36v2: Mental component summary	ACOS	40.47	0.44	39.60	41.33	<0.0001	0.5947	<0.0001
SF-12v2/36v2: Mental component summary	COPD only	42.88	0.21	42.48	43.29	<0.0001	<0.0001	–
SF-12v2/36v2: Mental component summary	Asthma only	40.75	0.29	40.18	41.32	<0.0001	–	–
SF-12v2/36v2: Mental component summary	Matched control	44.85	0.16	44.54	45.16	–	–	–
SF-12v2/36v2: Physical component summary	ACOS	44.99	0.36	44.29	45.70	<0.0001	0.9896	<0.0001
SF-12v2/36v2: Physical component summary	COPD only	47.66	0.17	47.32	47.99	<0.0001	<0.0001	–
SF-12v2/36v2: Physical component summary	Asthma only	44.99	0.24	44.53	45.45	<0.0001	–	–
SF-12v2/36v2: Physical component summary	Matched control	49.86	0.13	49.61	50.11	–	–	–
SF-6D: Health state utility score	ACOS	0.63	0.01	0.62	0.64	<0.0001	0.5311	<0.0001
SF-6D: Health state utility score	COPD only	0.66	0.00	0.65	0.66	<0.0001	<0.0001	–
SF-6D: Health state utility score	Asthma only	0.63	0.00	0.62	0.63	<0.0001	–	–
SF-6D: Health state utility score	Matched control	0.69	0.00	0.68	0.69	–	–	–
Absenteeism %	ACOS	14.28	1.62	11.43	17.83	<0.0001	0.7998	<0.0001
Absenteeism %	COPD only	8.71	0.47	7.84	9.68	0.0008	<0.0001	–
Absenteeism %	Asthma only	13.79	1.02	11.93	15.95	<0.0001	–	–
Absenteeism %	Matched control	6.93	0.28	6.39	7.51	–	–	–
Presenteeism %	ACOS	37.07	1.85	33.63	40.87	<0.0001	0.0178	0.0014
Presenteeism %	COPD only	31.07	0.74	29.65	32.56	<0.0001	<0.0001	–
Presenteeism %	Asthma only	42.69	1.40	40.04	45.52	<0.0001	–	–
Presenteeism %	Matched control	26.30	0.48	25.38	27.26	–	–	–
Overall work impairment %	ACOS	43.65	2.17	39.59	48.12	<0.0001	0.0732	<0.0001
Overall work impairment %	COPD only	35.19	0.83	33.61	36.85	<0.0001	<0.0001	–
Overall work impairment %	Asthma only	48.55	1.58	45.56	51.74	<0.0001	–	–
Overall work impairment %	Matched control	29.80	0.53	28.77	30.86	–	–	–
Activity impairment %	ACOS	40.08	1.76	36.78	43.68	<0.0001	0.4529	<0.0001
Activity impairment %	COPD only	31.38	0.65	30.13	32.69	<0.0001	<0.0001	–
Activity impairment %	Asthma only	41.69	1.20	39.40	44.11	<0.0001	–	–
Activity impairment %	Matched control	25.83	0.41	25.04	26.63	–	–	–
Health care provider visits in past 6 months	ACOS	5.13	0.41	4.39	5.99	<0.0001	0.2961	0.0010
Health care provider visits in past 6 months	COPD only	3.84	0.15	3.56	4.14	<0.0001	0.0035	–
Health care provider visits in past 6 months	Asthma only	4.65	0.24	4.20	5.15	<0.0001	–	–
Health care provider visits in past 6 months	Matched control	2.39	0.07	2.25	2.54	–	–	–
ER visits in the past 6 months	ACOS	1.09	0.13	0.87	1.38	<0.0001	0.2337	0.0006
ER visits in the past 6 months	COPD only	0.70	0.04	0.62	0.79	<0.0001	<0.0001	–
ER visits in the past 6 months	Asthma only	1.29	0.10	1.11	1.49	<0.0001	–	–
ER visits in the past 6 months	Matched control	0.46	0.02	0.42	0.51	–	–	–
Hospitalizations in the past 6 months	ACOS	0.32	0.05	0.24	0.44	<0.0001	0.0205	0.0003
Hospitalizations in the past 6 months	COPD only	0.17	0.02	0.14	0.21	0.0004	<0.0001	–
Hospitalizations in the past 6 months	Asthma only	0.48	0.04	0.41	0.58	<0.0001	–	–
Hospitalizations in the past 6 months	Matched control	0.11	0.01	0.10	0.13	–	–	–

Notes: All models adjusted for survey year, age, education, household income, BMI, alcohol use, exercise behavior, smoking habits, and the Charlson Comorbidity Index. *Statistical significance of comparing to the control group. **Statistical significance of comparing to the asthma only group. ***Statistical significance of comparing to the COPD only group. The *P*-values in this table are based on a Wald chi-square test as part of the generalized linear regression model.

Abbreviations: ACOS, asthma COPD overlap syndrome; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ER, emergency room; SE, standard error; SF-12v2/SF-36v2, Short Form-12 version 2/Short Form-36 version 2; SF-6D, Short Form-6D; LCL, lower confidence limit; UCL, upper confidence limit.

(ie, mental component summary and physical component summary differences exceeded 3 points and health utility differences exceeded 0.03 points), compared with matched controls. Levels of health status were also worse for patients with ACOS compared with patients with COPD only. Additionally, patients with ACOS reported significantly greater impairment and health care resource utilization compared with matched controls and those with COPD only. Indeed, the overall work impairment and activity impairment for patients with ACOS were 50% greater than matched controls and ~25% greater than patients with COPD only. These findings were consistent with studies conducted in other geographies.[14,16]

However, despite these effects, there was a lack of differences in health outcomes between patients with ACOS

and patients with asthma only. This might suggest that the burden of ACOS is primarily a function of asthma as both patients with ACOS and asthma only had similar health outcomes. Framed differently, it is possible that the burden of COPD (both in isolation and as part of ACOS) is weaker in the present study than might be observed in other data sources, which could be a result of our focus on the urban population of the People's Republic of China (which has a mean age of ~40 years). Many of the patients with COPD in our study are also young. Indeed, when compared with literature from the West using similar methods, the patients with COPD in the present study are between 10 and 20 years younger and diagnosed ~5 years more recently.[27] Therefore, the disease may still be in a relatively early stage of progression (though without clinical data, such as forced expiratory volume in 1 second, it is difficult to confirm this post hoc hypothesis).

Although not possible in our present study due to sample size, future research replicating this study among the elderly or those who have been diagnosed with their condition for a certain period of time may be warranted. With such stratification, the pattern of results might be slightly different. For example, focusing on slightly more older patients (with a more comparable distribution of COPD severity as reported elsewhere),[27] those with ACOS and those with only COPD may have a greater burden than reported here even though the burden of the asthma only group may be the same. As a result, it is possible our findings are slightly conservative as they produced effects that include an underestimated contribution of COPD (both in the ACOS and COPD only groups).

Limitations

There are a few additional limitations to note. All data were self-reported and there was no verification of diagnosis or disease history for patients with asthma or COPD (or ACOS). This could have resulted in misclassification of patients in the analysis. In particular, as noted earlier, patients with COPD may have been classified as controls and patients with ACOS may have been classified as asthma only patients due to the underreporting of COPD and infrequency of using the lung function test in a clinical setting. With respect to estimating the burden of ACOS, although an attempt was made to rule out alternative explanations for the findings using both a propensity score matching and a regression approach, there may have been other relevant factors which we neglected to include (or were not assessed in the NHWS). Patients with a particularly poor health profile may be underrepresented in the data. As a result, the prevalence and burden estimates may be conservative (given elderly respondents with COPD, asthma, and other comorbidities may be disproportionately less likely to participate). It is also important to note that our sample is intended to represent the entire urban population of the People's Republic of China which, as shown in Table 1, is a young demographic. Studies focusing on the prevalence and burden of ACOS in a more rural or clinic-based population, both of which may be older and less healthy populations, would likely identify different estimates.

Conclusion

ACOS occurs in 0.61% of the total adult population, ~30% of the asthma population, and ~18% of the COPD population in the People's Republic of China. Our results suggest patients with ACOS have a greater comorbidity burden and significantly worse health outcomes compared with patients with COPD only and matched controls. Better management of these patients may help in improving their outcomes.

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Disclosure

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