



## Prevalence of Chronic Obstructive Pulmonary Disease in Southwestern Taiwan: A Population-Based Study

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### Abstract

**Objectives:** Chronic obstructive pulmonary disease (COPD) poses a substantial burden of illness in the Asia-Pacific region, as it does worldwide. However large-scale and community-based epidemiology studies of COPD in Taiwan are limited. This paper conducted a population-based study to investigate the prevalence of COPD in southwestern Taiwan.

**Methods:** Data were conducted using a subset of medical claims data from the National Health Insurance Research database (NHIRD) from 2008 to 2010. The prevalence of COPD was calculated for the population aged 40 years and older in southwestern Taiwan. The relative risks (RRs) of prevalence for COPD was estimated using a multiple linear regression model.

**Results:** The overall average annual prevalence of COPD was 2.80%. Men had slightly higher COPD prevalence than women (3.18% vs. 2.42%), with the male-to-female ratio and the relative risks (RRs) were 1.31 and 1.42 (95% CI: 0.07-2.77), respectively. For the population aged 40 to 49 years, female had slightly higher COPD prevalence than male (1.25% vs. 1.02%). Prevalence increased with age, with the highest prevalence of 6.97% for those aged 70 and above. There were significantly increased RRs of 2.50 (95% CI: 0.59-4.41) and 6.53 (95% CI: 4.63-8.44) for those aged 60-69 years and aged  $\geq 70$  years, respectively.

**Conclusions:** This population-based study revealed the COPD is still a major cause of morbidity in Taiwan. Prevalence of COPD for men is consistently higher than women. The results of this study would provide valuable information for the government concerning in COPD management.

### Keywords

Chronic obstructive pulmonary disease, Prevalence, Population-based

### Introduction

Chronic obstructive pulmonary disease (COPD) is a leading and increasingly major cause of morbidity and mortality worldwide [1]. COPD results in a substantial and increasing burden in terms of prevalence, incidence and mortality, and is predicted to be the third leading cause of global mortality by 2030 (WHO, 2013) [2]. Results of the Burden of Obstructive Lung Disease (BOLD) study—a multinational investigation of the prevalence of COPD showed that Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage II COPD range from 5.9% in Hannover, Germany, to 19.1% in Cape Town, South Africa [3]. The findings from the five sites in the Latin American Project for the Investigation of Obstructive Lung Disease (PLATINO) study indicated that adjusted prevalence of COPD ranged from 11.9% in Mexico City to 19.4% in Montevideo [4].

COPD poses a major health and socioeconomic burden in the Asia-Pacific region, as it does worldwide [5]. The estimated prevalence of moderate to severe COPD among adults aged  $\geq 30$  years was 6.3% in the 12 Asia-Pacific countries, and the COPD prevalence in Taiwan was 5.4% [6]. Recent research of the impact of COPD in the Asia-Pacific region: the Epidemiology and Impact of COPD (EPIC) Asia population-based survey, indicated that the overall prevalence of COPD was 6.2%, ranging from 4.5% (Indonesia) to 9.5% (Taiwan) in 2012 [7]. According to a government report, chronic lower respiratory diseases was the 7th-leading cause of death in Taiwan, accounting for the standard mortality was 15.3 deaths per 100,000 population in 2014 [8]. Chan et al. explored the COPD mortality among the Taiwan population found that the COPD age-adjusted mortality rates for males and females were 19.67 and 5.70 deaths per 100,000, respectively [9]. An earlier analysis for chronic airway obstruction (CAO) in Taiwan based on national health insurance medical reimbursement claims pointed out that average annual

prevalence of CAO for the population aged  $\geq 40$  years old from 1996 to 2002 were 2.48% [10]. Chen et al. conducted a telephone sampling and interviews survey to determine the prevalence of COPD in Taiwan, and pointed out the national prevalence of COPD in adults aged 40 years and older to be 6.1% in 2013 [11]. However, Chen et al. used a telephone-base survey to estimate the prevalence of COPD in Taiwan had several limitations with low response rate (below the level of 60%). In addition, a telephone sampling survey can't ensure a representative population sample and may be subject to a selection bias toward urban populations. A further limitation was that the assessment of COPD subjects relies on respondents' self-reported recall of prior symptoms or diagnosis, which is less accurate than clinical assessment, and would lead the prevalence of COPD to be biased.

Tobacco smoking remains the most important risk factor for COPD in high-income countries [12,13]. Evidences from recent studies suggest that other non-smoking related risk factors (indoor and outdoor air pollution, use of biomass fuels, and occupation exposure to dust and fumes) are also major causes of COPD, especially in low-income and middle-income countries [12-16]. The prevalence of smoking is rising in developing countries, especially in Asia [17]. Approximately half of male adults in East Asia are cigarette smokers in 2010 (36.7% in Japan, 52.9% in China, 35.0% in Taiwan, and 48.3% in South Korea) [18,19].

In Taiwan, smoking rate peaked in 1990 among men (59.4%) and in 2002 among female (5.3%) [19], moreover, air pollution is a growing concern in Taiwan. Particulate matter (PM) concentrations in Taiwan often exceed the recommended World Health Organization's Air Quality guidelines [20]. According to the Air Quality Report of R.O.C. (Taiwan), it was indicated that the concentrations of PM in southwestern Taiwan were higher than those in other areas in Taiwan [20]. Recent studies in Taiwan have indicated that exposure to fine particulate matter (PM<sub>2.5</sub>) is associated with increased respiratory disease hospitalizations and mortality [21-23]. However, community-based epidemiology studies of COPD in Taiwan are limited. The objective of this study was to investigate the prevalence of COPD among residents in southwestern Taiwan, over a 3-year period, 2008-2010, based on a population-based study.

## Methods

### Database

This study has been approved by the Institutional Review Board (IRB) of Chang Gung Medical Foundation (IRB no. 102-2492B and 104-6146C). A population-based study was conducted using a subset of medical claims data from the National Health Insurance Research Database (NHIRD) obtained from the National Health Insurance (NHI) program in Taiwan (Registered number: NHI-NHIRD 102-261). The NHI program has reimbursed nearly all of the costs of medical services for Taiwanese inhabitants since 1995 [24]. Furthermore, at the end of 2010, this insurance covered approximately 99.89% of the total population in Taiwan [25]. The NHIRD appears to be a valid resource for epidemiological research, with the information on prescription use, diagnosis and hospitalizations has been shown to be of high quality [26,27].

### Study population

Cases of COPD were ascertained by the service claim for patients who had at least two ambulatory visits or one inpatient record with compatible diagnosis of COPD (International Classification of Diseases, 9<sup>th</sup> revision, Clinical Modification (ICD-9-CM) Code 490, 491 and 496). Prevalence for population aged  $\geq 40$  years were estimated and adjusted by annual age-specific population. The analyses covered 4 municipalities (Chiayi City, Chiayi County, Tainan City and Tainan County), which are located in southwestern Taiwan.

### Statistics

The COPD prevalence from 2008 to 2010 for the population were estimated and adjusted by annual age-specific population with the same temporal and geographic characteristics in southwestern

**Table 1:** Distribution of chronic obstructive pulmonary disease (COPD) and Male-to-Female case by age in southwestern Taiwan, 2008-2010.

Variables	Cases in 3 Years				
			Male/Female		
	No.	(%)	Gender, No.	Gender, (%)	
Age, yr					
	40-49	14,957	14.1	6,949/8,008	46.5/53.5
	50-59	21,124	20.0	10,893/10,231	51.6/48.4
	60-69	20,866	19.7	11,803/9,063	56.6/43.4
	$\geq 70$	48,878	46.2	30,426/18,452	62.3/37.7
	all	105,825	100	60,071/45,754	56.8/43.2

**Table 2:** Prevalence of chronic obstructive pulmonary disease (COPD) in southwestern Taiwan, 2008-2010.

Variables	Prevalence, /100				
	Total	Male	Female	Male/Female, Prevalence ratio	
Year					
	2008	3.01	3.40	2.63	1.29
	2009	2.64	3.00	2.28	1.32
	2010	2.76	3.16	2.37	1.33
	2008-2010 (average)	2.80	3.18	2.42	1.31
Age, yr					
	40-49	1.13	1.02	1.25	0.82
	50-59	1.86	1.86	1.85	1.01
	60-69	3.37	3.91	2.86	1.37
	$\geq 70$	6.97	9.46	4.86	1.95
	all	2.80	3.18	2.42	1.31

**Table 3:** Relative risks (with 95% CI) for COPD prevalence in southwestern Taiwan, 2008-2010.

Variables	COPD Prevalence	
	RR	95% CI
Gender		
	Male	1.42** (0.07, 2.77)
	Female *	
Age, yr		
	40-49 *	
	50-59	0.80 (-1.11, 2.71)
	60-69	2.50** (0.59, 4.41)
	$\geq 70$	6.53** (4.63, 8.44)

Abbreviation: RR: relative risk; \*: Reference group; \*\*:  $p < 0.01$

Taiwan. Additionally, a multiple linear regression was performed to assess the relationships between COPD prevalence and gender and age using the relative risk (RR) and their 95% confidence intervals (95% CI). The criterion for statistical significance was  $p < 0.05$ . Statistical analysis was performed using statistical software (SAS version 8.2; SAS Institute; Cary, NC).

## Results

As shown in table 1, a total of 105,825 diagnosed COPD patients were identified from the NHIRD during the study period for the population aged 40 years and older in this study. Cases claimed for COPD were in patients predominantly aged 70 and above (46.2%) (male: 62.3%; female: 37.7%). From 2008 to 2010, the overall average annual prevalence of COPD was 2.80% (Table 2). Men had slightly higher COPD prevalence than women (3.18% vs. 2.42%), with the male-to-female ratio was 1.31. For the population aged 40 to 49 years, female had slightly higher COPD prevalence than men (1.25% vs. 1.02%). Furthermore, the COPD prevalence increased with age, with the lowest prevalence of 1.13% for those aged 40-49 years; and the highest prevalence of 6.97% for those aged 70 and above.

Table 3 shows the result of multiple linear regression analysis. The relative risk of prevalence for COPD was higher for male than female, with the relative risks (RRs) was 1.42 (95% CI = 0.07-2.77). There were significantly increased RRs for the population aged 60-69 and  $\geq 70$  years, with the RRs were 2.50 (95% CI: 0.59-4.41) and 6.53 (95% CI: 4.63-8.44), respectively.

## Discussion

This present population-based study estimated the COPD prevalence in southwestern Taiwan. The results showed that the average annual COPD prevalence of adults aged 40 years and older was 2.80% during a 3-year period from 2008 to 2010. The estimated COPD prevalence in this study is similar to a previously reported figure of 2.48% based on national health insurance claims in Taiwan [10]. However, the estimated COPD prevalence in present study is lower than a previously reported figure of 6.1% based on telephone sampling cross-sectional survey in Taiwan [11]. Moreover, the estimated COPD prevalence in the current study is lower than previous other studies in Asia [6,7]. Tan et al. who used a mathematical model to estimate the prevalence of COPD in the 12 Asia countries, revealed higher COPD estimates (Taiwan 5.4%) compared with our study [6]. In addition, Lim et al. conducted a cross-sectional, household screening study to examine the prevalence of COPD in the participating nine Asia-Pacific territories (the EPIC Asia population-based survey), and showed higher prevalence of COPD in Taiwan (9.5%) [7].

The differences in measurement methodology, study population, and criteria for definition of COPD, such as symptoms of chronic bronchitis, physician-diagnosed COPD, or spirometric airflow limitation might influence the estimates of COPD prevalence. There are several possible reasons why the estimate in the present study varies from the Taiwan and Asian studies of Chen et al., Tan et al. and Lim et al. [6,7,11]. First, the estimates of COPD prevalence in 12 Asia countries and regions by Tan et al. were derived from a mathematical model, which might have been overestimated the prevalence. Second, the EPIC Asia population-based survey involved only 207 subjects in Taiwan; moreover, the identification of COPD in subjects was based on subject-reported physician diagnosis and subjects' perception of their condition and symptoms, these are likely to have response bias, selection bias, and diagnostic bias. This may also lead to less reliability of COPD prevalence estimations. Moreover, for Chen et al., a telephone sampling survey cannot ensure a representative population sample and may be subject to a selection bias [11]. Third, for Tan et al. in particular, estimated prevalence for the population aged over 30 years using data generated from mathematical model [6]. However, this present study estimated the prevalence of COPD for the population  $\geq 40$  years old. The differences in the age range of people who were enrolled in different studies could be introduced as another source of heterogeneity.

This present study revealed that female had slightly higher COPD prevalence than male for the population aged 40 to 49 years. Recent evidence suggests that men and women may have differential susceptibility to tobacco smoke and other pollutants, possibly related to biologic and hormonal mechanisms [28-30]. Female sex hormone, estrogen, does not modify detoxifying enzymes, and contributes to oxidative stress and greater airway injury [31]. Therefore, the female sex hormone estrogen may play a role in worsening the lung damage among the population aged 40 to 49 years in the current study.

A health-care based study in Taiwan indicated that exposure to second-hand smoke (SHS) is a major risk for chronic bronchitis in Taiwanese women [32]. According to the Adult Smoking Behavior Surveillance System Survey conducted by the Taiwan Bureau of Health Promotion of the Department of Health, 24.6% females live in homes where others smoke in their presence, and 6.9% of females are frequently exposed to secondhand smoking in public in 2010 [33]. Passive smoking or environmental tobacco smoke (ETS) as a risk factor for COPD among non-smokers has been demonstrated in a number of studies [34-35]. Result from a population-based study in Northern Sweden reported that COPD prevalence was associated with increased ETS exposure: 4.2% (no ETS), 8.0% (ETS ever at home), 8.3% (ETS at previous work) and 14.7% (ETS ever at home and at both previous and current work) [35]. Therefore, the decreased male-to-female ratios for COPD prevalence in current study, possibly because both the decreasing male/female smoking rate ratio and increasing SHS exposure among women.

This study has several strengths. First, this study was a large-scale and population-based study to estimate the prevalence of COPD in Taiwan. The NHIRD can represent the whole population, and thus reduces the potential for selection bias. Second, the recall bias is minimized by analyzing the database with comprehensive information on medical records. Still, this study has several potential limitations. First, this study analyzed medical claims data during 2008-2010, and it is too relative short-term to observe the temporal trend of COPD prevalence. Second, information on other risk factors contributing to COPD, such as smoking habit, occupation, and income were unavailable for retrieval from the National Health Insurance Research database (NHIRD). Third, the claims database did not include individual data of pulmonary function tests (PFTs). Therefore, studies of the diagnostic accuracy of COPD will be criticized. Fourth, the ICD-9 codes used for COPD diagnosis have been extensively employed in other studies [21,22,36,37], but haven't been clinically validated in NHIRD. Therefore, the reliance on the disease coding in the medical claims might be subject to disease misclassification bias.

In conclusion, the analysis for this population-based study has revealed that COPD remains a major cause of morbidity in Taiwan. Men had slightly higher COPD prevalence than women. Female hormonal (i.e., estrogen) might to explain female had slightly higher COPD prevalence than male for the population aged 40 to 49 years in present study. Moreover, increased smoking rates and second-hand smoke inhalation in female might explain the decreased male-to-female ratios for COPD prevalence in the current study. Further studies are need and will be helpful to clarify the temporal trends of morbidity and mortality for COPD in Taiwan.

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