ORIGINAL ARTICLE

Unexpected excessive chronic obstructive pulmonary disease mortality among female silk textile workers in Shanghai, China

Ling Cui,1 Lisa G Gallagher,1 Roberta M Ray,2 Wenjin Li,2,3 Daoli Gao,4 Yingzhe Zhang,5 Sverre Vedal,1 David B Thomas,2,3 Harvey Checkoway1,3

ABSTRACT

Objective To investigate chronic obstructive pulmonary disease (COPD) mortality among textile workers.

Methods A total of 267 400 Chinese female textile employees were monitored for COPD mortality from 1989 to 2000. Textile factories in the cohort were classified into 10 industrial sectors. Age-adjusted mortality, standardized mortality ratios (SMRs) and 95% CIs were calculated by sector. In addition, RRs (HRs) adjusted for smoking and age were calculated for exposure to cotton and silk textile work compared with the other sectors in the cohort.

Results A majority of textile sectors had lower or similar COPD mortality (age-adjusted SMRs=0.58–1.15) compared with the general female population in the city of Nanjing, China. SMRs for cotton and silk workers were, respectively, 1.02 (95% CI: 0.81 to 1.28) and 2.03 (95% CI: 1.13 to 3.34). Compared with all other textile sectors in the cohort, there was greater COPD mortality among cotton workers (HR=1.40, 95% CI: 1.03 to 1.89) and silk workers (HR=2.54, 95% CI: 1.47 to 4.39).

Conclusion Elevated COPD mortality among cotton workers is consistent with previous reports of adverse respiratory effects of cotton dust. The higher rate of COPD deaths among silk workers was unexpected.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a diverse group of lung disorders whose hallmark is airflow obstruction that impedes normal respiration. According to the latest available WHO estimates (2008), 210 million people worldwide have COPD and 3 million people died from COPD in 2005. WHO predicts that COPD will become the third leading cause of death worldwide by 2020. Cleaner indoor air and the use of antibiotics reduce the prevalence of COPD in the USA and the prevalence of COPD is 8.2% in people 40 years of age or older in China.

The primary known cause of COPD is exposure to tobacco smoke; however, air pollutants in the working environment may also increase the risk. Numerous previous studies indicate that cotton textile workers have a higher prevalence of respiratory symptoms and greater decline in lung function compared with the general population and compared with other textile workers, specifically, man-made fibre and silk workers. Historically, it was believed thatbyssinosis, whichever acute or chronic, could be associated with some impairment of ventilatory capacity, but the overall decline in lung function was small. However, emerging evidence indicates that cumulative exposure to cotton dust may cause a chronic decline in lung function, potentially resulting in COPD. The main occupational exposures of concern are cotton dust and endotoxin in the dust and both were found to be related to the decrease in FEV1. Other potential respiratory hazards in the textile industry include wool dust, silk dust, synthetic fibres, finishing agents, bleaches and highly acidic or basic chemicals.

To characterise the remaining uncertainty of risks for COPD among textile workers, we conducted a mortality study among a large cohort of female textile workers in Shanghai, China. The study was approved by the Institutional Review Boards of the University of Washington, the Fred Hutchinson Cancer Research Center in Seattle, WA and Zhong Shan Hospital in Shanghai.

METHODS

Study population

The cohort was composed of 267 400 female textile employees recruited from over 500 factories in the Shanghai Textile Industry Bureau (STIB). These women were born between 1st January 1925 and 31st December 1958 and had been previously enrolled in a randomised trial of breast self-examination. Although the participation in the study was not mandatory, almost all the women meeting the
eligibility criteria in the STIB were enrolled in the study. Baseline questionnaires were administered to subjects during the period from 1989 to 1991, with a response rate of 98%. Information regarding demographics, lifestyle, reproductive history, smoking and alcohol use were collected during enrolment through questionnaires.

### Outcome and exposure definition

All deaths were registered at each factory, and reported annually to a tumour and death registry operated by the STIB. Mortality in the cohort was analyzed using data from 1989 to 2000 by matching the cohort with the STIB registry. In addition, death in the cohort was analyzed using data from 1989 to 2000 by a tumour and death registry operated by the STIB. Mortality from COPD and allied conditions was defined when one or more causes of death was indicated by ICD-9 codes 490–496, which encompass bronchitis (not specified as acute or chronic); chronic bronchitis; emphysema; asthma; bronchiectasis; extrinsic allergic alveolitis and chronic airway obstruction (not elsewhere classified).

Information on 503 factory profiles were collected, including date of commencement of operations, number of workers and primary and secondary fibres used in production. The primary fibre was defined as the material that was used most often or in the greatest quantity in the factory; the secondary fibre was the next most used material. Ten industry sectors of interest were identified according to the type of fibres used: cotton spinning, weaving and knitting (SWK); silk SWK; wool SWK; synthetic fibre SWK; mixed fibre SWK; assembly and sewing; bleaching, dyeing, printing; machine and manufacturing; combined and other services. Each factory was classified into one sector accordingly, and factories that had multiple production lines were designated to a combined sector. Every subject was assigned to only one of these sectors on the basis of employment status at baseline. Each cohort member contributed in person-years from their enrolment until death, or until severance of ties with STIB, or until the end of follow-up (31 December 2000), whichever occurred first.

### Data analysis

The number of deaths and person-years were calculated for each 5-year age category from 1989 to 2000. Age-adjusted mortality was computed using the 2000 World Standard Population as the standard population. The female general population in the city of Nanjing in China was used as an external reference group. This population was chosen because it, to our knowledge, the only female Chinese population with age-specific COPD mortality data available for 1997–2005. Standardized mortality ratios (SMRs) for 1989–2000 comparing the observed and expected numbers of COPD deaths were calculated for the entire cohort and for different sectors, and 95% CIs were calculated using the Byar method. HRs and associated 95% CIs were calculated using the Cox proportional hazard model, adjusting for age and smoking (ever/never) using PROC PHREG in SAS 9.2 (SAS Institute, Cary, North Carolina, USA).

### Table 1 Characteristics of the cohort for specific sectors and age

<table>
<thead>
<tr>
<th>Workplace</th>
<th>Cotton SWK</th>
<th>Silk SWK</th>
<th>Other sectors Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total number</strong></td>
<td>86265</td>
<td>11121</td>
<td>170014</td>
</tr>
<tr>
<td><strong>All COPD and allied conditions</strong></td>
<td>77</td>
<td>15</td>
<td>92</td>
</tr>
<tr>
<td>Bronchitis, NOS</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>25</td>
<td>32.5</td>
<td>5</td>
</tr>
<tr>
<td>Emphysema</td>
<td>26</td>
<td>33.8</td>
<td>5</td>
</tr>
<tr>
<td>Asthma</td>
<td>23</td>
<td>29.9</td>
<td>5</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>3</td>
<td>3.9</td>
<td>0</td>
</tr>
<tr>
<td>Extrinsic allergic alveolitis</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td>Chronic airway obstruction NOS</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Age at baseline (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–34</td>
<td>17051</td>
<td>19.8</td>
<td>2333</td>
</tr>
<tr>
<td>35–39</td>
<td>15613</td>
<td>18.1</td>
<td>2386</td>
</tr>
<tr>
<td>40–44</td>
<td>10805</td>
<td>12.5</td>
<td>1675</td>
</tr>
<tr>
<td>45–49</td>
<td>4084</td>
<td>4.7</td>
<td>438</td>
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<tr>
<td>50–54</td>
<td>5735</td>
<td>6.6</td>
<td>705</td>
</tr>
<tr>
<td>55–59</td>
<td>16090</td>
<td>18.7</td>
<td>1587</td>
</tr>
<tr>
<td>60–64</td>
<td>15574</td>
<td>18.1</td>
<td>1694</td>
</tr>
<tr>
<td>65+</td>
<td>1313</td>
<td>1.5</td>
<td>303</td>
</tr>
<tr>
<td><strong>Age at death or end of follow-up</strong></td>
<td></td>
<td></td>
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<tr>
<td>30–34</td>
<td>1530</td>
<td>1.8</td>
<td>220</td>
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<tr>
<td>35–39</td>
<td>3655</td>
<td>4.2</td>
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<td>14031</td>
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<tr>
<td>55–59</td>
<td>4288</td>
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<td>403</td>
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<tr>
<td>60–64</td>
<td>6592</td>
<td>7.6</td>
<td>858</td>
</tr>
<tr>
<td>65–69</td>
<td>16509</td>
<td>19.1</td>
<td>1662</td>
</tr>
<tr>
<td>70–74</td>
<td>14279</td>
<td>16.6</td>
<td>1597</td>
</tr>
<tr>
<td>75+</td>
<td>989</td>
<td>1.1</td>
<td>75</td>
</tr>
<tr>
<td>Retired</td>
<td>36856</td>
<td>42.5</td>
<td>3957</td>
</tr>
<tr>
<td>Ever smokers</td>
<td>3086</td>
<td>3.6</td>
<td>300</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease; NOS, not otherwise specified; SWK, spinning, weaving and knitting.
RESULTS

There were 184 COPD deaths identified in the cohort during 12 years of follow-up (2,565,455 person-years). The distributions of age at baseline, age at the end of follow-up (or death) and the causes for 184 COPD deaths are summarised in table 1. For the entire cohort, mean (SD) age at baseline was 45.9 (11.1) and mean age at end of follow-up was 55.0 (11.6). Mean (SD) age at death from COPD was 65.5 (7.7). Approximately 3% of the textile workers had ever smoked and 37% of the subjects had retired at baseline.

By sectors, the highest age-standardised COPD mortality rates per 100,000 were found in silk SWK (9.21), assembly and sewing (4.57) and cotton SWK (3.19) (table 2). When stratifying by smoking habits, the mortality rate was 2.89 for cotton workers who never smoked and 8.11 for cotton workers who had smoked. No COPD deaths were observed among smokers in the silk SWK sector; the COPD mortality rate was 9.41 among non-smoker silk workers. Compared with the general female population of Nanjing (table 3), the entire cohort had lower or similar mortality from COPD compared with the female population in the cities of Nanjing and certain other chronic lung diseases among 282 employees of a cotton textile mill when compared with the non-textile worker population.21 However, it is difficult for these studies to fully compensate for the ‘healthy worker’ effect, resulting in an underestimation of the true risk.

In our cohort, excess COPD mortality was observed among cotton workers when compared with the remainder of the cohort. This finding corresponds to recent reports of a higher risk of COPD and chronic respiratory symptoms among cotton workers.22 23 However, this increased mortality was not seen among cotton workers when compared with the remainder of the cohort and the Nanjing female population. An increase in COPD mortality among silk workers was unexpected. In the series of lung function and symptom studies conducted by Christiani et al, cotton textile workers had more chronic cough and chronic bronchitis and greater decline in FEV₁ than silk workers.6 8 Silk workers in these studies were regarded as the non-exposed reference group, largely because silk dust had only background levels of endotoxin, compared with the
relatively high levels found in cotton dust.\textsuperscript{24} A recently published report from this study found both cotton and silk workers have improved FEV\textsubscript{1} and reduced prevalence of chronic respiratory symptoms after work cessation, suggesting that there may be respiratory hazards in silk factories as well.\textsuperscript{25}

The main components of silk dust are organic compounds, mostly protein, fats and carbohydrates. Contaminants of silk, such as silkworm larval proteins and constituents of fungal cell walls, could induce hypersensitivity pneumonitis and occupational asthma,\textsuperscript{26} which in turn could lead to COPD if exposure occurred over a prolonged period of time. Significantly, spirometric abnormalities (FVC, FEV\textsubscript{1}, MMF, V\textsubscript{50} and V\textsubscript{50}) were observed among 158 non-smoking female tussah (‘wild’) silk processing workers in Liaoning Province, China, compared with 20 non-smoking referent workers from an appliance assembling factory.\textsuperscript{27} Other studies in the Chinese literature reported an association between mulberry dust and cough, expectoration, and shortness of breath.\textsuperscript{28,29} Animal fibres, free silica, fungi and bacteria are all possible causes of these respiratory effects. Depending on the quality of the raw silk, pesticides and heavy metals such as lead may also be present in this dust. Other possible hazardous exposures include chemicals involved in processing, such as dyes and highly oxidative bleaching compounds. Previous studies have shown that humidifiers contaminated with microorganisms could cause byssinosis-like symptoms, and that this could be the mechanism by which the risk of COPD is increased among silk workers. A more extensive assessment of silk factory exposures is therefore suggested.

This study has several strengths. First, COPD is rarely seen in non-smokers. Patients diagnosed with COPD are expected to have smoked the equivalent of about 20 cigarettes per day for more than 20 years.\textsuperscript{30} The prevalence of smoking is less than 5% in our cohort and none of the silk workers who developed COPD were smokers. Although the confounding effects of secondhand smoke outside the workplace cannot be completely discounted, it is unlikely that this exposure would differ among women working in other sectors of the textile industry or the general female population in Nanjing. The textile workers in this study were relatively homogeneous with regard to residence, religion, race, marital status and social-economic status. Also, the vast majority of the women in this study had held only one job and worked in the same factory for their entire career. During the follow-up period, only 1.14% (n=3056) of the entire cohort transferred to a different sector. Among textile workers, 0.05% (n=50) transferred from cotton to silk and 0.04% (n=5) transferred from silk to cotton. None of the women who died from COPD had a factory transfer. Therefore, it is unlikely that changes in exposures due to job transfers influenced our results.

One limitation of this study is the possible misclassification of COPD using death certificate data. We included asthma as one of the underlying or contributing causes of death from COPD for several reasons. COPD and asthma share many clinical characteristics. In order to distinguish severe asthma from COPD, we would require more detailed clinical data than was available. It has been noted that chronic illnesses, COPD in particular, are prone to misdiagnosis and misclassification on death certificates in China. In an independent review of death certificates in China, 178 (73.5%) of 242 actual deaths due to COPD were correctly coded as such and 50 (20.1%) of 228 deaths coded as COPD were actually due to other causes.\textsuperscript{31} Under the reasonable assumption that misclassification of cause of death in our study was not associated with any of the possible risk factors considered, misclassification of this order of magnitude would have biased our OR estimates towards unity, but would not have resulted in spurious associations. Indeed, both conditions might be present simultaneously in an individual patient to variable degrees. In our study, 35 of the 184 COPD deaths had COPD listed as a secondary cause of death. The first causes listed were primarily heart failure, chronic cor pulmonale (pulmonary heart disease) or other respiratory illnesses. Those deaths were kept in the final analysis as COPD deaths because we believe COPD was an important contributing cause. Similar results were found when those deaths were excluded. We did not have complete employment history record and exposure for each individual worker. Complete work history information was available only for a subset (n=3199) of the cohort who were recruited for a series of cancer case-cohort studies.\textsuperscript{32,33} and there were six COPD deaths in the subcohort. Future work will assess complete work history and exposures of COPD cases compared with controls from this cohort.

Already a common cause of death in developed countries, COPD is an increasingly important cause of death and disability in the developing world.\textsuperscript{34} Much of this increased prevalence is likely due to cigarette smoking, but occupational exposures, particularly among non-smokers, are also driving this increase. Recent studies from Nicaragua,\textsuperscript{35} Turkey,\textsuperscript{36} India,\textsuperscript{37} Pakistan,\textsuperscript{38} Nigeria\textsuperscript{39} and Ethiopia all report on byssinosis in textile workers and several authors also describe chronic and irreversible changes in lung function in these workers.\textsuperscript{40} These chronic changes may go by the term ‘chronic bronchitis,’ ‘chronic declines in FEV\textsubscript{1}’ or ‘chronic respiratory symptoms,’ but all are likely equivalent terms for what we term COPD. Epidemiologic assessments of COPD in developing countries should therefore be a high priority to identify preventable causes of disease.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Human Subjects Division, University of Washington.

Contributors Each author has participated sufficiently in the work and takes responsibility for appropriate portions of the content. LC was responsible for writing the first draft, each component of the cited research and interpreting and reporting the data. LGG and RMF designed the study’s analytic strategy and conducted the data analysis. WL designed the study, coordinated and directed its implementation. DG helped supervise the field activities and data acquisition from corresponding agency. YZ helped conduct the literature review for the Introduction and the Discussion sections of the text. SV revised drafts, particularly for important clinical content. DBT conceived and designed the study, and orchestrated funding. HG is chiefly responsible for the scientific integrity of the whole paper, designed the study and coordinated the efforts of the collaborators and orchestrated funding.

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