

# Dust and chemical exposures, and miscarriage risk among women textile workers in Shanghai, China

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Accepted 28 June 2008  
Published Online First  
5 December 2008

## ABSTRACT

**Introduction:** To investigate possible associations between miscarriage and occupational exposures in the Shanghai textile industry.

**Methods:** A retrospective cohort study of miscarriages among 1752 women in the Shanghai textile industry was conducted. Reproductive history was self-reported by women and occupational work histories were collected from factory personnel records. Occupational exposures were assigned by linking work history information to an industry-specific job-exposure matrix informed by factory-specific textile process information and industrial hygiene assessments. Estimates of cotton dust and endotoxin exposure were also assigned. Odds ratios (OR) and 95% CI were estimated by multivariate logistic regression, with adjustment for age at pregnancy, educational level, smoking status of the woman and her spouse, use of alcohol, and woman's year of birth.

**Results:** An elevation in risk of a spontaneously aborted first pregnancy was associated with exposure to synthetic fibres (OR 1.89, 95% CI 1.20 to 3.00) and mixed synthetic and natural fibres (OR 3.31, 95% CI 1.30 to 8.42). No increased risks were observed for women working with solvents, nor were significant associations observed with quantitative cotton dust or endotoxin exposures.

Associations were robust and similar when all pregnancies in a woman's reproductive history were considered.

**Conclusions:** Occupational exposure to synthetic fibres may cause miscarriages, and this possibility should be the subject of further investigation.

As a growing number of women work outside the home during pregnancy, the role of occupational risk factors in adverse pregnancy and birth outcomes is of increasing importance. Work in the textile industry subjects employees to an array of exposures during the spinning, dyeing, weaving, sewing and finishing of garments. In a study from Finland,<sup>1</sup> textile spinning was associated with an increased risk of miscarriage (odds ratio (OR) 1.3, 95% CI 1.0 to 1.9), as has weaving (OR 1.4, 95% CI 1.1 to 1.9), fabric inspection (OR 1.5, 95% CI 1.0 to 2.4) and other textile work (OR 1.4, 95% CI 1.0 to 2.0). In a separate Finnish study, women working at a textile plant had an increased rate of miscarriage (miscarriage rates of 16.7% vs 11.4%),<sup>2</sup> but no significant increase in risk was found in a US study of maternal occupation in the textile industry overall.<sup>3</sup>

Textile workers may be exposed to cotton dust during fibre processing and spinning, to solvents in the dyeing, weaving and finishing of textile goods, and to bleaches and dyes during dyeing and

weaving processes. Elevated miscarriage risks have been found in several occupational groups of women exposed to solvents, including factory workers (toluene),<sup>4</sup> semiconductor industry workers (glycol ethers)<sup>5</sup> and laboratory workers (toluene and xylene).<sup>6</sup> Carbon disulfide is used in the manufacture of viscose rayon fibres in the textile industry, and an increased miscarriage risk has been identified for women viscose rayon workers.<sup>7-9</sup> Fibre dust exposure is widespread in the textile industry, with frequent exposure to cotton dust in the textile industry in Shanghai, China. Cotton textile workers are commonly exposed to endotoxin, a lipopolysaccharide component of the cell wall of Gram-negative bacteria present in these and other organic dusts. Endotoxin is an established respiratory toxicant and has been shown to induce miscarriage in animal studies.<sup>9-12</sup> Workers in other industries also experience the chemical and dust exposures seen in the textile industry; thus, findings from this study could have implications for exposures in other occupational settings.

A prior study of cancer risks in the Shanghai, China textile industry provided the opportunity to conduct a historical cohort study to examine associations between occupational exposures and self-reported history of miscarriage in a group of women textile workers.

## METHODS

### Study population

Subjects for the current study were selected from participants previously enrolled in a large randomised trial (n = 267 400) of breast self-examination conducted among workers from 526 factories affiliated with the Shanghai Textile Industry Bureau (STIB) in Shanghai, China. Enrolment in the trial occurred during 1988–91.<sup>13-14</sup> Women eligible for the randomised trial were Shanghai residents, born between 1925 and 1958 (aged 30–64 years at entry into the study), who were current or retired workers in any of the factories. Participation in the study was high with 98% of eligible women taking part.

As part of two case-control studies of breast diseases nested within the randomised trial, 1814 control women (women without a diagnosis of breast cancer or benign breast disease in 1994) were administered a questionnaire that inquired about the woman's pregnancy history.<sup>15-17</sup> These women form the cohort of women for the current study. This reproductive questionnaire elicited detailed information for each pregnancy, including end date

of pregnancy, outcome of each pregnancy, and length of gestation in an interview conducted by trained Chinese physicians and nurses. Also recorded was information on personal and spousal cigarette use, alcohol use, demographic data and gynaecological history (age at menarche, contraceptive use). The overall response rate was 81%. All procedures were approved by the relevant institutional review boards of the Fred Hutchinson Cancer Research Center (Seattle, USA) and the Shanghai Textile Industry Bureau (Shanghai, China).

### Outcome ascertainment

Overall, 1752 (96.5%) of the women who answered a detailed reproductive health questionnaire had ever been pregnant and were included in the present study. The pregnancies as reported on the questionnaire occurred between 1942 and 2001. Most (92.6%) first pregnancies occurred between 1950 and 1989, with only 24 (1.4%) first pregnancies occurring between 1990 and 1996. A woman was considered to have had a miscarriage as a pregnancy outcome if she reported a miscarriage of less than 20 weeks' gestation. Live births, terminations of pregnancy (induced abortions), still births and ectopic pregnancies were also reported pregnancy outcomes.

### Exposure assessment

The STIB was an industry-wide governing body for all textile factories in Shanghai. Work in the factories included all textile processes from processing raw materials to completing the finished products. The STIB also employed women in jobs such as teaching, nursing and work in medical clinics, cafeteria work and daycare, resulting in a wide spectrum of occupational exposures.

Exposures for each woman were determined by collecting information on her work history and job assignments. These data were abstracted in 2005–2006 from factory personnel records using a standardised form and protocol by trained personnel who were all former medical workers employed at STIB factories. The factory in which a woman worked, the textile processes and fibres with which she worked, the woman's job tasks, and the dates of employment were collected beginning with the woman's first job and ending with her last STIB job. Information was ascertained from factory records for 89% of the job assignments held by the women. In cases where factory personnel records could not be found, supervisors were identified and completed the form (2.6% of job assignments), or the woman was contacted and interviewed (7.3% of job assignments).

Factory-level information was collected for each of the textile factories in the STIB using a standardised form. The data collection instrument was modelled after the exposure measurement forms routinely collected by the Shanghai Municipal Centers for Disease Control, district offices, or STIB industrial hygienists as part of their routine monitoring. Experienced industrial hygienists, trained in China, collected information from factories regarding factory demographics (date operation began, factory size currently and at peak, and fibre used in production) and the factory textile processes. The industrial hygienists also recorded every industrial workshop and process within the factory, excluding administrative and educational services. Within each textile process, the industrial hygienists detailed dates of operation, fibre, worker types, exposure to up to five hazardous agents, and any changes in the process (eg, introducing synthetic fibre into a cotton factory). The industrial hygienists assessed hazardous exposure based on their

experience, monitoring data and investigations by the STIB. Textile processes were classified using a combination of 18 major process codes, which usually represented the workshop name (eg, material handling, fibre processing, spinning, dyeing), and 149 specific process codes which identified one component of textile manufacturing within the major process (eg, carding, drawing, combing, roving). A list of potentially hazardous exposures within each textile process was also recorded by the industrial hygienists and included 14 dusts (eg, cotton, wool, synthetic fibres) and 239 chemicals (eg, ammonia, formaldehyde, xylene). Infrequent exposures (<2 exposed women) are not presented in the tables.

A job-exposure matrix (JEM) specific to the textile industry was developed using a combination of information recorded by the Shanghai industrial hygienists and a priori assessment by a team of experts from the University of Washington and the STIB.<sup>18</sup> Exposure was assigned if the experts agreed that workers in the process would be exposed during normal operation, or if more than 30% of the textile processes reviewed above reported exposure on the standardised factory data collection forms.<sup>18</sup> Woman-level information and factory-level information were then linked by fibre type, major textile process type, specific textile process type, type of work performed (eg, operator, floor supervisor) and year. Exposure to potentially hazardous agents was determined by linkage to the JEM. Further extensive details on exposure assessment, factory data collection and JEM development are detailed in Wernli *et al.*<sup>18</sup>

Quantitative exposure information was also available to determine cotton dust and endotoxin exposures. For cotton dust, historical industrial hygiene records from 56 factories between 1975 and 1999 were transcribed for use in this study to estimate exposure for each specific textile process. Endotoxin data for this industry from a study of respiratory health in three cotton products factories by Christiani *et al.*<sup>19–21</sup> and additional contemporary measurements of cotton dusts collected for this study<sup>22, 23</sup> were used in the development of predictive models for endotoxin exposure. For cotton dust and endotoxin, both exposures during the pregnancy alone and cumulative exposures from the beginning of the woman's textile employment were of interest. Quantitative cotton dust and endotoxin estimates were combined with each woman's job-duration information from the work history to determine cumulative exposures.

Only work periods in STIB factories were included as the extensive exposure characterisation was conducted solely for STIB factories. A total of 323 women were excluded from the analyses because their work history during their pregnancies could not be ascertained, leaving 1429 women included in the analyses.

### Statistical analysis

For this historical cohort, quantitative analyses were first conducted evaluating associations between established risk factors (eg, age at pregnancy, smoking status and educational attainment) and pregnancy outcome to allow comparison with other epidemiological studies. Then, analyses were conducted examining associations between pregnancy outcome(s) and textile industry exposures. Two separate analyses were conducted, the first utilising all pregnancies and the second using only each woman's first pregnancy. Analyses limited to the first pregnancy only were conducted to exclude biases from a woman's pregnancy history, including prior adverse outcomes and within-woman correlations among pregnancies, while avoiding bias associated with choosing the most recent

**Table 1** Descriptive statistics of women and pregnancies

	n
Women	1429
Total number of pregnancies	4258
Number of women contributing to each pregnancy number	
1	1429
2	1192
3	744
4	454
5 or more	235
Number of pregnancies per woman	
1st quartile	1
Median	2
3rd quartile	3
Maximum number of pregnancies	10
Outcome of first pregnancy	
Live birth	1278 (89.4%)
Termination of pregnancy	46 (3.2%)
Miscarriage	84 (5.9%)
Still birth	13 (0.9%)
Ectopic pregnancy or other outcome	8 (0.6%)

pregnancy.<sup>24</sup> The most meaningful result to present from our data was a summary measure of the average risk ratio, hence the use of logistic regression analysis methods. In most analyses, we considered exposure only during pregnancy ("current exposure") to evaluate the effects of acute exposures during pregnancy. A woman was considered to have current exposure during the pregnancy if she was exposed between the estimated date of conception and the earlier of either her 20th week of pregnancy or the end date of the pregnancy. As prior mechanistic data supported a model of chronic exposure<sup>25–28</sup> potentially leading to miscarriage for endotoxin, cumulative exposure up to the first pregnancy was also analysed for cotton dust and endotoxin exposure. Cumulative occupational exposure was accumulated from the beginning of a woman's first employment in the STIB up until the earlier of either the 20th week of the pregnancy or the end date of the pregnancy, excluding periods of non-exposure if the woman changed jobs. Analyses were conducted evaluating associations with specific potentially hazardous agents of interest as assigned using the JEM and with employment in a textile manufacturing process as a surrogate of potential exposure. Quantitative cotton dust and endotoxin exposures were analysed by quartile of exposure among exposed women.

Analyses considering all pregnancies in a woman's reproductive history were conducted. In order to consider the within-woman correlations between pregnancies, analyses considering all pregnancies utilised generalised estimating equations to estimate the OR and 95% CI.<sup>29</sup> Terminated pregnancy (induced abortions, n = 1122), ectopic pregnancy (n = 22) or other unspecified outcomes (n = 4) were excluded. Our analyses thus compare pregnancies that ended in miscarriage with the comparison group of pregnancies that could have ended in miscarriages, still births and live births. Analyses were adjusted for gravidity, age at pregnancy (in 5-year age groups), woman's year of birth, highest level of education completed (never went, elementary school, middle and high school, college or more), woman's smoking status during pregnancy (yes/no), spouse's smoking status during the pregnancy (yes/no), and woman's alcohol use (never, ≤1/month, ≤1/week, >1/week).

**Table 2** Demographic characteristics of women working in the Shanghai textile industry studied for risk of miscarriage, based on the outcome of the first pregnancy

	First pregnancy outcome		OR (95% CI)
	Miscarriage (n = 84), n (%)	Other* (n = 1291), n (%)	
Age at first pregnancy			
15–19	5 (6.0)	41 (3.2)	3.23 (1.05 to 9.93)
20–24	16 (19.0)	287 (22.2)	1.00 (ref)
25–29	46 (54.8)	736 (57.0)	0.81 (0.40 to 1.61)
30–34	14 (16.7)	200 (15.5)	0.89 (0.39 to 2.08)
35+	3 (3.6)	27 (2.1)	1.35 (0.32 to 5.64)
Alcohol consumption			
Never	79 (94.0)	1164 (90.2)	1.00 (ref)
≤1/month	2 (2.4)	37 (2.9)	0.79 (0.18 to 3.38)
≤1/week	1 (1.2)	33 (2.6)	0.36 (0.05 to 2.83)
>1/week	2 (2.4)	55 (4.3)	0.49 (0.11 to 2.06)
Smoking status during pregnancy			
Did not smoke	82 (97.6)	1287 (99.7)	1.00 (ref)
Smoked	2 (2.4)	4 (0.3)	12.23 (1.87 to 79.76)
Spouse's smoking status during pregnancy			
Did not smoke	63 (75.0)	770 (59.6)	1.00 (ref)
Smoked	21 (25.0)	521 (40.4)	0.40 (0.23 to 0.69)
Education completed (years completed)			
None (<5 years)	6 (7.1)	131 (10.1)	1.00 (ref)
Elementary (5 years)	7 (8.3)	181 (14.0)	0.96 (0.30 to 3.00)
Middle school (8 years)	68 (81.0)	931 (72.1)	2.06 (0.65 to 6.51)
College or over (11 or more)	3 (3.6)	48 (3.7)	1.58 (0.32 to 7.78)
Year first pregnancy ended			
1942–1949	5 (6.0)	41 (3.2)	
1950–1954	3 (3.6)	114 (8.8)	
1955–1959	7 (8.3)	126 (9.8)	
1960–1964	4 (4.8)	87 (6.7)	
1965–1969	5 (6.0)	92 (7.1)	
1970–1974	6 (7.1)	78 (6.0)	
1975–1979	11 (13.1)	130 (10.1)	
1980–1984	29 (34.5)	396 (30.7)	
1985–1989	13 (15.5)	204 (15.8)	
1990–2002	1 (1.2)	23 (1.8)	
Woman's year of birth			
1925–1929	5 (6.0)	98 (7.6)	
1930–1934	10 (11.9)	181 (14.0)	
1935–1939	3 (3.6)	101 (7.8)	
1940–1944	8 (9.5)	67 (5.2)	
1945–1949	9 (10.7)	152 (11.8)	
1950–1954	24 (28.6)	240 (18.6)	
1955–1958	25 (29.8)	452 (35.0)	

\*Other outcomes include still births and live births.  
OR, odds ratio.

For secondary analyses considering the first pregnancy only, women whose first pregnancy resulted in a termination of pregnancy (n = 46) or other pregnancy outcome (ectopic pregnancy (n = 5) and other unspecified outcome (n = 3)) were excluded from the comparison group. Analyses examining the outcome of the first pregnancy were conducted using logistic regression to estimate the OR and 95% CI. As before, all analyses were adjusted for age at pregnancy, woman's year of birth, level of education, smoking status of the woman and her spouse, and alcohol use. All analyses were conducted in Stata v 9.0 (StataCorp, College Station, TX).

**Table 3** Risk of miscarriage for those exposed ( $\geq 1$  day) versus not ( $< 1$  day) exposed during pregnancy by employment in textile process, adjusted for age, education, smoking, alcohol use, spousal smoking and woman's year of birth

Exposure	First pregnancy only			All pregnancies		
	Other outcome, n (%)	Miscarriage, n (%)	OR (95% CI)	Other outcome, n (%)	Miscarriage, n (%)	OR (95% CI)
Warehouse/packing/quality control						
Unexposed	1169 (93.6)	80 (6.4)	1.00 (ref)	2584 (93.6)	178 (6.4)	1.00 (ref)
Exposed	122 (96.8)	4 (3.2)	0.43 (0.15 to 1.22)	242 (94.2)	15 (5.8)	0.82 (0.49 to 1.38)
Cotton fibre-material handling, fibre processing, spinning						
Unexposed	1122 (93.7)	76 (6.3)	1.00 (ref)	2425 (93.7)	164 (6.3)	1.00 (ref)
Exposed	169 (95.5)	8 (4.5)	0.70 (0.32 to 1.52)	401 (93.3)	29 (6.7)	1.20 (0.71 to 2.01)
Wool fibre-material handling, fibre processing, spinning						
Unexposed	1260 (93.8)	83 (6.2)	1.00 (ref)	2750 (93.6)	188 (6.4)	1.00 (ref)
Exposed	31 (96.9)	1 (3.1)	0.52 (0.07 to 3.90)	76 (93.8)	5 (6.2)	1.01 (0.42 to 2.47)
Synthetic fibre-material handling, fibre processing, spinning						
Unexposed	1266 (93.9)	82 (6.1)	1.00 (ref)	2773 (93.6)	189 (6.4)	1.00 (ref)
Exposed	25 (92.6)	2 (7.4)	0.98 (0.21 to 4.65)	53 (93.0)	4 (7.0)	0.97 (0.35 to 2.70)
Mixed fibre-material handling, fibre processing, spinning						
Unexposed	1142 (93.9)	74 (6.1)	1.00 (ref)	2476 (93.7)	167 (6.3)	1.00 (ref)
Exposed	149 (93.7)	10 (6.3)	1.12 (0.56 to 2.25)	350 (93.1)	26 (6.9)	1.18 (0.72 to 1.93)
Weaving						
Unexposed	925 (94.2)	57 (5.8)	1.00 (ref)	1923 (93.3)	137 (6.65)	1.00 (ref)
Exposed	366 (93.1)	27 (6.9)	1.32 (0.81 to 2.16)	903 (94.2)	56 (5.84)	1.00 (0.71 to 1.42)
Cutting/sewing						
Unexposed	1190 (94.0)	76 (6.0)	1.00 (ref)	2647 (93.6)	182 (6.43)	1.00 (ref)
Exposed	101 (92.7)	8 (7.3)	1.20 (0.55 to 2.62)	179 (94.2)	11 (5.79)	0.75 (0.39 to 1.43)
Administration/non-production						
Unexposed	1111 (94.2)	68 (5.8)	1.00 (ref)	2465 (93.8)	163 (6.20)	1.00 (ref)
Exposed	180 (91.8)	16 (8.2)	1.51 (0.82 to 2.79)	361 (92.3)	30 (7.67)	1.06 (0.68 to 1.66)
Other manufacturing						
Unexposed	1226 (94.0)	78 (6.0)	1.00 (ref)	2702 (93.6)	185 (6.41)	1.00 (ref)
Exposed	65 (91.5)	6 (8.5)	1.23 (0.51 to 2.97)	124 (93.9)	8 (6.06)	0.83 (0.39 to 1.78)

OR, odds ratio.

## RESULTS

A total of 4258 pregnancies were experienced by the 1429 women in the study. Table 1 shows the numbers of pregnancies contributed by the women. Women had a median of two pregnancies, ranging from one to 10 pregnancies per woman. As regards first pregnancies only, approximately 6% were miscarriages, 0.9% still births, 0.4% ectopic pregnancies, 3.2% terminations of pregnancy and 89.4% live births. When considering all pregnancies, 4.4% were miscarriages and 59% were live births, with a much higher percentage of pregnancy outcomes compared with first pregnancies being terminations of pregnancy. The gestational durations differed by outcome of pregnancy, with live births having a mean of 40 weeks, miscarriage a mean of 10.1 weeks and termination of pregnancy a mean of 6.7 gestational weeks.

The distribution of the study subjects by age at first pregnancy is shown in table 2. Overall, 79% of the women in the study had their first pregnancy in their 20s, and only 2% of women had a first pregnancy at age 35 years or later. Table 2 also shows that 76% of the women completed at least middle school education (completed 8 years of education), all women had been married, smoking was infrequent (but spousal smoking was much more frequent) and alcohol use was also infrequent. Risk of a miscarriage was increased in teen pregnancies and in women who smoked, and was lower than

expected in women married to smokers. Women were more likely to have been born after the Second World War, with 53% born between 1950 and 1958.

No statistically significant associations between miscarriages and employment in a specific textile process during pregnancy were identified when considering all pregnancies or when analyses were restricted to the first pregnancy (table 3).

An increased risk of miscarriages was found for women with exposure to synthetic fibres and mixed synthetic and natural fibres, both when analyses were limited to the first pregnancy and when all pregnancies were considered (table 4). Among those few women who were exposed to synthetic or a mixture of natural and synthetic fibres, but not during their pregnancies, no elevation in risk was observed (for synthetic fibres,  $n = 3$  cases, OR 1.16, 95% CI 0.35 to 3.88; and for mixed synthetic and natural fibres,  $n = 1$  case, OR 0.90, 95% CI 0.12 to 6.97). Results for synthetic fibre exposures for first or all pregnancies were not appreciably changed when adjustments were made for exposures to other fibre types (OR 1.93, 95% CI 1.21 to 3.08).

No statistically significant elevations in risk were found for women exposed to solvents, or any of the other exposures considered. No statistically significant elevations in risk of a miscarriage were observed with any of the measures of exposure to endotoxin or cotton dust that were utilised (table 5).

**Table 4** Risk of miscarriage for those ever/never exposed during pregnancy to dusts and hazardous agents, adjusted for age, education, smoking, alcohol use, spousal smoking and woman's year of birth

Exposure	First pregnancy only			All pregnancies		
	Other outcome, n (%)	Miscarriage, n (%)	OR (95% CI)	Other outcome, n (%)	Miscarriage, n (%)	OR (95% CI)
Cotton dust						
Unexposed	596 (93.6)	41 (6.4)	1.00 (ref)	1220 (93.3)	88 (6.7)	1.00 (ref)
Exposed	695 (94.2)	43 (5.8)	0.98 (0.62 to 1.56)	1606 (93.9)	105 (6.1)	1.02 (0.74 to 1.40)
Wool dust						
Unexposed	1152 (93.8)	76 (6.2)	1.00 (ref)	2512 (93.6)	173 (6.4)	1.00 (ref)
Exposed	139 (94.6)	8 (5.4)	0.87 (0.40 to 1.87)	314 (94.0)	20 (6.0)	0.90 (0.53 to 1.55)
Silk dust						
Unexposed	1235 (94.1)	78 (5.9)	1.00 (ref)	2681 (93.7)	180 (6.3)	1.00 (ref)
Exposed	56 (90.3)	6 (9.7)	1.66 (0.67 to 4.08)	145 (91.8)	13 (8.2)	1.45 (0.70 to 3.00)
Synthetic fibre dust						
Unexposed	885 (95.1)	46 (4.9)	1.00 (ref)	1925 (94.4)	114 (5.6)	1.00 (ref)
Exposed	406 (91.4)	38 (8.6)	1.89 (1.20 to 3.00)	901 (91.9)	79 (8.1)	1.46 (1.07 to 1.99)
Mixed fibre, not otherwise specified (mix of synthetic/natural)						
Unexposed	1260 (94.2)	78 (5.8)	1.00 (ref)	2740 (93.8)	181 (6.2)	1.00 (ref)
Exposed	31 (83.8)	6 (16.2)	3.31 (1.30 to 8.42)	86 (87.8)	12 (12.2)	1.99 (0.95 to 4.18)
Solvents						
Unexposed	1127 (93.6)	77 (6.4)	1.00 (ref)	2516 (93.4)	177 (6.6)	1.00 (ref)
Exposed	164 (95.9)	7 (4.1)	0.54 (0.24 to 1.21)	310 (95.1)	16 (4.9)	0.63 (0.37 to 1.08)
Acids and bases						
Unexposed	1204 (93.8)	80 (6.2)	1.00 (ref)	2657 (93.6)	181 (6.4)	1.00 (ref)
Exposed	87 (95.6)	4 (4.4)	0.60 (0.21 to 1.71)	169 (93.4)	12 (6.6)	0.98 (0.46 to 2.08)
Resins						
Unexposed	1261 (94.0)	80 (6.0)	1.00 (ref)	2772 (93.6)	188 (6.4)	1.00 (ref)
Exposed	30 (88.2)	4 (11.8)	1.91 (0.64 to 5.68)	54 (91.5)	5 (8.5)	1.20 (0.44 to 3.31)
Lubricants						
Unexposed	595 (93.0)	45 (7.0)	1.00 (ref)	1182 (92.6)	94 (7.4)	1.00 (ref)
Exposed	696 (94.7)	39 (5.3)	0.78 (0.49 to 1.24)	1644 (94.3)	99 (5.7)	0.87 (0.62 to 1.22)
Metals						
Unexposed	1204 (93.7)	81 (6.3)	1.00 (ref)	2661 (93.5)	185 (6.5)	1.00 (ref)
Exposed	87 (96.7)	3 (3.3)	0.44 (0.13 to 1.45)	165 (95.4)	8 (4.6)	0.63 (0.32 to 1.25)

OR, odds ratio.

## DISCUSSION

An elevated risk of miscarriage was found in women with exposure to synthetic fibres and a mix of synthetic and natural fibres. No elevations in risk were identified with exposure to cotton dust, endotoxin or solvents.

Synthetic fibres used in the Shanghai textile industry to which the women were exposed include polyester, lastrile, nylon and rayon. The specific hazardous agents potentially responsible for the observed associations with synthetic fibre exposures are not known. Carbon disulfide, a major ingredient in rayon manufacturing, has been previously found to have reproductive effects in female viscose rayon workers.<sup>7 8 30</sup> Although carbon disulfide has been detected in historical measurement data in this industry, all measurements were conducted in synthetic fibre manufacturing factories, and no women in the current study were employed during pregnancy in factories manufacturing synthetic fibres. Only 15 of the 500 STIB factories produced synthetic fibres and men may have been preferentially employed in the manufacturing processes. Women working in manufacturing processes were not preferentially selected for inclusion in this study. In this study, women with exposure to synthetic fibre dusts encountered these dusts in non-manufacturing factories which used synthetic fibres to make finished products, and carbon disulfide exposure would not be expected in these processes. Textile processes associated with synthetic fibre dust exposure outside of manufacturing included applying coatings, spooling, weaving, knitting, printing,

laminating, cutting, sewing and packing of synthetic fibre products. It is also possible that the elevated risks associated with synthetic fibre exposure are surrogates of an exposure we were not able to fully characterise using our semi-quantitative JEMs.

Exposure to other solvents has also been associated with elevations in risk of a miscarriage. In a cohort of 3105 non-smoking, 20–24-year-old female petrochemical workers in Beijing, the relative risk of a first pregnancy ending in a miscarriage was 2.7 (95% CI 1.8 to 3.9) for exposure to any petrochemical and 2.5 (95% CI 1.7 to 3.7) for exposure to benzene.<sup>31</sup> In a population based cohort of 15–29-year-old pregnant women in the San Jose, CA area of the USA, elevated risks of miscarriage were found in relation to self-reported jobs likely involving solvent exposures (OR 4.4, 95% CI 1.5 to 12.7) and self-reported solvent exposures (OR 2.8, 95% CI 1.1 to 7.0).<sup>32</sup> In this study, women classified as having exposure to solvents were likely exposed to a mixture of solvents, and we were not able to identify exposures to specific solvents. No elevation in risk with exposure to solvents as a class was found. In the Shanghai textile industry, commonly used solvents included carbon disulfide, toluene, benzene and xylene. Although historical industrial hygiene data were available, inconsistent data quality and lack of consistent monitoring did not allow for a quantitative JEM of solvent exposure.

In the textile industry, exposure to cotton and other dusts is widespread, and exposures occur at exceptionally high levels in

**Table 5** Risk of miscarriage with exposure during the pregnancy only and cumulative exposure beginning from the start of employment, using quantitative cotton and endotoxin measurements

	Other outcome, n (%)	Miscarriage, n (%)	OR (95% CI)	p Trend
Exposure during first pregnancy				
Endotoxin (EU/m <sup>3</sup> ×years)				
None	659 (92.7)	52 (7.3)	1.00 (ref)	0.46
0–64.9	235 (95.5)	11 (4.5)	0.62 (0.31 to 1.23)	
65.0–123	228 (95.4)	11 (4.6)	0.63 (0.32 to 1.25)	
124–252	221 (90.6)	23 (9.4)	1.57 (0.92 to 2.68)	
253 or more	232 (95.1)	12 (4.9)	0.79 (0.40 to 1.55)	
Cotton dust (mg/m <sup>3</sup> ×years)				
None	659 (92.7)	52 (7.3)	1.00 (ref)	0.73
0–2.25	194 (94.2)	12 (5.8)	0.81 (0.41 to 1.60)	
2.26–4.65	254 (92.0)	22 (8.0)	1.20 (0.71 to 2.05)	
4.66–8.87	232 (95.5)	11 (4.5)	0.68 (0.34 to 1.34)	
8.88 or more	236 (95.2)	12 (4.8)	0.74 (0.37 to 1.47)	
Exposure during all pregnancies				
Endotoxin (EU/m <sup>3</sup> ×years)				
None	1387 (93.5)	96 (6.5)	1.00 (ref)	0.22
0–92.5	516 (94.7)	29 (5.3)	0.76 (0.47 to 1.24)	
92.6–168	453 (91.5)	42 (8.5)	1.37 (0.92 to 2.03)	
169–319	551 (94.3)	33 (5.7)	1.00 (0.62 to 1.61)	
320 or more	598 (93.4)	42 (6.6)	1.24 (0.81 to 1.92)	
Cotton dust (mg/m <sup>3</sup> ×years)				
None	1387 (93.5)	96 (6.5)	1.00 (ref)	0.09
0–3.36	505 (94.0)	32 (6.0)	0.85 (0.53 to 1.36)	
3.37–6.57	473 (92.6)	38 (7.4)	1.17 (0.77 to 1.78)	
6.58–11.84	535 (94.4)	32 (5.6)	0.97 (0.60 to 1.55)	
11.85 or more	605 (93.2)	44 (6.8)	1.36 (0.88 to 2.11)	
Cumulative exposure for first pregnancy				
Endotoxin (EU/m <sup>3</sup> ×years)				
None	792 (93.3)	57 (6.7)	1.00 (ref)	0.37
0–338	197 (93.8)	13 (6.2)	0.97 (0.52 to 1.83)	
339–629	199 (95.2)	10 (4.8)	0.72 (0.36 to 1.46)	
630–1086	196 (93.8)	13 (6.2)	1.04 (0.55 to 1.98)	
1087 or more	191 (92.3)	16 (7.7)	1.12 (0.60 to 2.09)	
Cotton dust (mg/m <sup>3</sup> ×years)				
None	792 (93.3)	57 (6.7)	1.00 (ref)	0.98
0–12.7	191 (92.3)	16 (7.7)	1.23 (0.69 to 2.21)	
12.8–24.5	197 (94.7)	11 (5.3)	0.83 (0.42 to 1.63)	
24.6–42.0	202 (95.3)	10 (4.7)	0.71 (0.35 to 1.43)	
42.1 or more	193 (92.8)	15 (7.2)	1.08 (0.57 to 2.05)	

Exposure by quartiles and analyses adjusted for age, education, smoking, alcohol use, spousal smoking and woman's year of birth. EU, endotoxin units; OR, odds ratio.

certain processes. Endotoxin is a lipopolysaccharide component of the cell wall of Gram-negative bacteria and is commonly found in cotton dusts. In animal studies, injections of endotoxin have led to miscarriages,<sup>9–11 35</sup> possibly as a result of a systemic inflammatory response which has been fairly consistently documented between studies and has been observed following either injection or inhalation exposure routes.<sup>34</sup> Occupational exposure to dusts has been previously associated with reproductive effects.<sup>1 35</sup> Self-reported exposure to dusts was associated with a 2.7 (95% CI 1.2 to 6.1) fold increase in risk of infertility, specifically ovulatory causes (3.0, 95% CI 1.2 to 7.5) and tubal causes (2.9, 95% CI 1.1 to 7.9).<sup>35</sup> In contrast, another epidemiological study found no association when using job titles to identify dust exposure (OR 1.1, 95% CI 0.9 to 1.2).<sup>1</sup> A strength of our current study was the ability to test the association of miscarriage with quantitative measurements of cotton dust and endotoxin exposure.<sup>25</sup> However, no significant elevations in risk of miscarriages with either endotoxin or cotton dust exposure were identified in the current study when

examining the outcome of all pregnancies, when assessing cumulative exposures, or with concurrent exposure during the first pregnancy.

This study has several limitations that should be acknowledged. One is the potential for exposure misclassification that may have reduced our ability to detect true associations with miscarriage. Exposures were assigned based on linking employment history with a JEM which was based on fibre type, major textile process type, specific process type, type of work and year. The JEM was supplemented by historical industrial hygiene monitoring data, some of which did not span full years of the cohort's employment and were sparse in other years. The cotton dust and endotoxin data were based on considerably larger numbers of quantitative samples than were available for other agents.

Another potential limitation is the accuracy of pregnancy outcome data. All pregnancy outcomes of women in this study were determined via self-report a mean of 26 years (range 3–55 years) after occurrence. Self-reported miscarriages have been shown to be imperfectly recalled and the recall accuracy to

## Main messages

- ▶ Among a group of women working in the textile industry who had low rates of alcohol use and smoking, elevations in risk of miscarriage were identified for women whose jobs entailed exposure to synthetic fibres and a mixture of synthetic and natural fibres.
- ▶ No elevations in miscarriage risk were identified for women textile workers whose jobs included exposure to cotton dust or endotoxin.
- ▶ Exposure levels of solvents experienced by women in the textile industry do not appear to be associated with risk of miscarriage.

decrease with time.<sup>36</sup> However, in that study,<sup>36</sup> recall of miscarriages was over 80% within 10 years of the event, and 72% even after 30 years. Recall in our study may have decreased with time. Although validation of miscarriage is not possible with our available data, comparisons can be made with live births, which are likely recalled with a high degree of accuracy. The percentage of first pregnancies ending in miscarriage remained at 6.0–7.7% for 3–29 years of recall decreasing to 5% for 30–49 years of recall. However, 11.5% of first pregnancies were miscarriages after 50 years of recall. Rates of miscarriage in this report are similar to those in another Chinese women textile industry population that utilised daily biomarkers to identify pregnancies and losses,<sup>37</sup> suggesting that sociocultural factors in this population and time period support accurate recall of reproductive history, although our rates of miscarriage are lower due to lack of biomarker pregnancy identification. Under the one-child family planning policy and previous family planning policies, pregnancy occurrence was closely monitored and therefore care-seeking patterns did not play a role in the identification of pregnancies or pregnancy loss; and because all women in the study had routine access to medical care within their factory,<sup>38</sup> inadequate access to care is not a likely factor leading to under-reporting of pregnancy outcomes. Furthermore, it is unlikely that any under-reporting of outcome of pregnancy would be related to any of the occupational exposures of interest, so any effect of underascertainment of miscarriage would only obscure true associations but would not lead to false relationships. It is possible that higher industrial exposures and more frequent under-reporting of miscarriage may have occurred in the earlier study period years. Exposures were not found to vary significantly by decade of time, and thus time-dependent exposures were not included in the JEMs.<sup>18</sup> Underascertainment of miscarriage is possible due to the self-reported nature of these data. The current study found a miscarriage rate of 6% for the first pregnancy. A much lower miscarriage rate in subsequent pregnancies is due to the high rate of termination of pregnancy, in which some of those pregnancies would have gone on to become miscarriages. Although information on timing and dates was collected, self-reported pregnancy outcome data did not allow for a main analysis using a survival time approach. When sensitivity analyses were conducted using survival analysis techniques, no differences in conclusions were found.

High rates of termination of pregnancy were identified in this cohort of women. Termination of pregnancy is common among primiparous women in China, particularly after the implementation of family planning policies in 1979. Termination of pregnancy occurred at a mean of 6.7 gestational weeks, while

## Policy implications

- ▶ Occupational exposures in the textile industry may increase risk of miscarriages and other occupationally-exposed women may also experience these risks.
- ▶ Exposure to synthetic fibres may increase risk of miscarriages; this possibility needs to be corroborated by independent investigations, and the specific agents in synthetic fibres that may be responsible for these possible elevations in risk need to be identified.

miscarriage occurred at a mean of 10.1 weeks. The analysis considering all reproductive events may have some bias due to the high rates of termination of pregnancy in primiparous women. However, the analyses considering the first pregnancy alone are not limited by this bias yet have similar results, supporting the conclusions from our primary analyses considering all pregnancies.

Our results associated with spousal smoking are unexpected. Spousal (male) smoking status was determined retrospectively by asking the woman and thus may be under-reported. Study participants and their spouses were considered smokers if they had had more than 100 cigarettes in their lifetime. As expected, prevalence of spousal smoking is lowest for the earlier study years and increased over time.

Women in this current study were control subjects from prior nested case-control studies of breast disease within the larger cohort of 267 400 women textile workers. The response rates for both this study and the parent study were high, reducing the potential for biased participation by infertility status. The high participation rate was due to extensive partnership with the textile industry, thus allowing the researchers access to women and records, cultural norms supporting participation, and hiring of retired nurses and physician assistants who formerly worked in these factories as study recruiters. These control subjects completed a detailed reproductive history questionnaire for each pregnancy; this level of detail was not available on the baseline questionnaire for all randomised trial participants. However, using available information from the baseline questionnaire on outcome of the first pregnancy and total number of miscarriages experienced, no increased risk of breast cancer was identified with miscarriage history among these 267 400 women (OR 1.08, 95% CI 0.87 to 1.34) compared to women who never had a miscarriage, nor was a trend with increasing number of miscarriages identified ( $p = 0.90$ ).<sup>17</sup> Thus bias in the results examining associations between miscarriage outcome and textile industry exposures due to the selection method of this cohort is not expected.

This study also had some notable strengths, including the availability of detailed reproductive history data for each woman and complete data on work history in the textile industry, and data on potential confounders. Exposures were assigned by using written STIB personnel records for each woman, and very little misclassification is expected to have occurred because work history in STIB factories was found for 99% of women. Women also tended to be stable in a job position, with 19% of women ever holding only one job and 86% holding three or fewer jobs over their entire career. Confidence in the validity of the observed elevated risks in relation to synthetic fibres is enhanced by the lack of an elevated risk in women exposed to the same substances only while not pregnant. As use of personal protective equipment

was uncommon historically, personal exposures did not vary significantly from the process area sampling used to inform the JEMs.

One of the most important features of this group of women is the virtual lack of potential bias due to more fertile workers preferentially leaving the workplace (infertile worker bias). Because of the government's universal employment policy, all pregnant women worked until shortly before their due date and then returned to the same job position after maternity leave. Thus, the cohort enabled analyses of workplace exposures and miscarriage risks free of the potential biases found in most other occupational settings.

This study of occupational miscarriage risks in the textile industry identified elevations in risk with exposure to synthetic fibres and a mix of synthetic and natural fibres. This study offered an opportunity to study exposures that are relatively widespread worldwide and which occur with particularly high frequency and intensity in this industry. In conjunction with extensive health and exposure information, this study was able to quantitatively evaluate associations between miscarriage and occupational exposures and enable inference to other occupationally-exposed women. Specific causative agents were not readily identifiable and should be the subject of additional studies.

**Acknowledgements:** The authors would like to thank Drs Fan Liang Chen, Yong Wei Hu, Guan Lin Zhao and Lei Da Pan for their ongoing support. The authors thank Wen Wan Wang for project management; Drs He Lian Dai, Zhu Ming Wang, A Zhen Qi, Zia Ming Wang, Wei Ping Xiang and Yu Fang Li for their diligence in collecting factory information; the 30 field workers for the collection of women's personnel records; and Georgia Green, Shirley Zhang, Richard Gandolfo and Ted Grichuhin for technical and administrative support.

**Funding:** This research was supported by grants R01 CA80180 from the US National Cancer Institute, R01 OH008149 from the US National Institute for Occupational Safety and Health, and by training grant T32ES07262 from the US National Institute of Environmental Health Sciences.

**Competing interests:** None.

All procedures in this study were approved by the relevant institutional review boards of the Fred Hutchinson Cancer Research Center (Seattle, USA) and the Shanghai Textile Industry Bureau (Shanghai, China).

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