

Maternal employment and atopic dermatitis in children: a prospective cohort study

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Summary

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Conflicts of interest

None declared.

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Background Considering the early onset of atopic dermatitis (AD), which most often arises in the first year of life, risk factors occurring very early in life must be considered. Little is known about the effects of maternal occupational exposure on the development of atopic disorders in children.

Objectives The aim of this study was to evaluate associations between maternal employment and childhood AD.

Methods We used multistage stratified systematic sampling to recruit 24 200 mother–newborn pairs from the Taiwan national birth register. Information on maternal occupation categories, work stress, working time, shift work and potential confounders during pregnancy was gathered by questionnaires after birth. At 3 years of age, information on the development of AD was assessed by home interviews. Multiple logistic regression analysis was performed to estimate the association of maternal employment and AD.

Results Overall, 11 962 out of 19 381 mothers (61.7%) worked during pregnancy. The children of mothers who worked during pregnancy had an increased risk of AD compared with those whose mothers did not work [odds ratio (OR) 1.38, 95% confidence interval (CI) 1.25–1.53]. The children of mothers with a professional or technical occupation had a higher risk of AD (OR 1.64, 95% CI 1.44–1.87). The risk of AD was found to increase with maternal work stress during pregnancy in a dose–response manner ($P_{\text{trend}} < 0.01$). The mothers of children with AD had a longer working time than those without AD ($P < 0.0001$). However, no significant association between AD and maternal shift work was found.

Conclusions Working in professional or technical occupations increased the risk of childhood AD in addition to work stress during pregnancy.

The prevalence of allergic diseases appears to have increased dramatically over the past decade.¹ The pathogenesis of allergic diseases is complex and not entirely understood. Considering the early onset of many childhood allergic diseases, and in particular atopic dermatitis (AD), which most often arises in the first year of life, risk factors occurring very early in life must be

considered. The prenatal environment can affect the development of the fetus during critical periods of exposure, with a permanent effect in later years.² This condition is called fetal programming of adult diseases. Programming agents include growth factors, cytokines and hormones, all of which can be altered by stress.³ As a consequence, such stress-modified sys-

tems in the offspring are more susceptible to environmental exposure, leading to the development of diseases during later life.

The employment rate for married women and mothers with young children has risen sharply since the mid-1970s.⁴ Ever-increasing competition and occupational demands affect women to a growing extent. Women who remain in their jobs at childbearing age have an increased potential occupational exposure to chemical, physical and biological agents, as well as to physical exertion and psychosocial stress. Maternal working conditions during pregnancy are considered to be associated with birth outcome in the children.⁵ Furthermore, certain occupations with a high hapten and irritant chemical exposure during pregnancy are significantly associated with atopic disorders in the offspring.⁶ It has been reported that elevated risks of childhood asthma are related to occupational groups such as bakers, needleworkers and dental assistants, who may be exposed to agents commonly associated with occupational asthma.⁶ At present, over 250 work-related agents have been reported to cause allergies, a number of them by inducing IgE-mediated responses.⁷

Whether the increasing employment rate or occupational exposure for pregnant women is linked to the unfavourable trend of atopy prevalence in recent decades is not clear.⁸ Little is known about maternal occupational exposure occurring prenatally as a risk factor for childhood atopic disorders. Moreover, data obtained from women are scanty, because psychoneuroimmunological research has traditionally included more men than women. As AD is the first step of atopic march, we wanted to explore the effects of maternal employment during pregnancy on the development of AD in the offspring, based on the national Taiwan birth cohort.

Patients and methods

Study population and sampling strategy

The Taiwan Birth Cohort Study is a national prospective longitudinal cohort study. In this study, we used a multistage stratified systematic sampling design to obtain representative samples from the Taiwan national birth registration data from 2005. We categorized a total of 369 towns in Taiwan into 12 strata according to the administrative division (four strata) and the total fertility rate (three strata). Using the principle of probability proportional to size, we randomly sampled 90 out of the 369 towns. In total, 24 200 pairs of mothers and newborns from these 90 towns were recruited. We then conducted home interviews with the postpartum women 6 and 36 months after delivery using a structured questionnaire as previously described.^{9,10} After excluding subjects due to loss to follow-up, multiple gestations, inability to answer questions in Chinese and plans to move out of the area after delivery, 19 381 participants in total (80.1%) were included in this study (Fig. 1). All study participants provided written informed consent. The study protocol was approved by the institutional review board of the National Taiwan University and complied with the principles outlined in the Declaration of Helsinki.

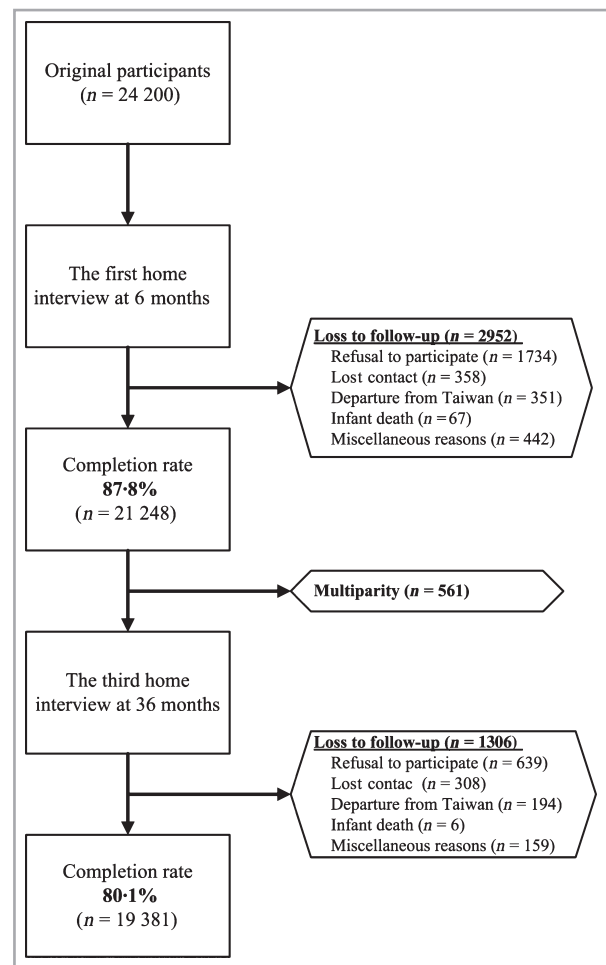


Fig 1. Flow chart of data collection.

Exposure

The characteristics of maternal employment during pregnancy included types of occupation and industry, work stress, work schedule, working days per week, working hours per day, and working hours per week. The type of occupation was classified into six groups: professional or technical; administrative or managerial; superintendents or clerical; sales; fabricators or operators, etc.; and others, according to the Taiwan Standard Occupational and Industrial Classification system.¹¹ The type of industry was divided into six groups: manufacturing, construction and mining; wholesale and retail trade; personal services; public administration and defence; professional services; and others.¹¹ Work stress was measured through the question, 'How much stress did you feel when working during pregnancy? Very high, high, intermediate, low, or not at all.'

Outcomes

Cases of AD were defined as physician-diagnosed AD through the question, 'Have you ever been informed by a doctor that your child has eczema?' The questionnaire-diagnosed AD was

determined by the question, 'Has your child ever had a recurrent itchy rash for at least six consecutive half-month periods over the elbows, knees, face, wrists, neck, periauricular and eyebrow areas during his/her lifetime?' according to the International Study of Asthma and Allergies in Childhood questionnaire via home interviews.¹⁰

Potential confounders

Questions about potential confounders and prenatal and postnatal risk factors were asked when the children were 6 months of age. These included maternal age at delivery, education, ethnicity, family income, maternal history of atopy, maternal smoking or drinking during pregnancy, diet and supplements during pregnancy, duration of breastfeeding, age of introduction of solid foods, number of siblings, day care, owning pets, carpets at home, environmental tobacco smoke, fungi on the walls of the residence, and place of residence. From the records of the collaborating hospitals, we collected neonatal health data at birth, including sex, head circumference, birth body weight, height, weeks of gestation, parity, type of delivery and vaccination history.

Statistical analysis

For the association between maternal employment status and AD in children, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated by logistic regression models. For the effect of working time during pregnancy on AD in children, the β -value $\pm$ SE was also calculated by logistic regression models. Analyses were performed in both univariate and multivariate models. Potential confounders were taken into

consideration. Variables were included in the model if they changed the univariate point estimate by at least 10%. All hypothesis testing was two sided at a significance level of 0.05, and was performed using JMP statistical software version 5.0.1 (SAS Institute Inc., Cary, NC, U.S.A.).

Results

In total, 11 962 mothers (61.7%) worked during pregnancy. The prevalence rates of having questionnaire-diagnosed AD and physician-diagnosed AD during the child's lifetime were 6.9% (1340) and 10.5% (2033), respectively. Among the mothers who were employed during pregnancy, 2276 (19.0%) were in the professional and technical group, 1456 (12.2%) in administrative and managerial, 5036 (42.1%) in superintendents and clerical, 948 (7.9%) in sales, 1346 (11.3%) in fabricators and operators, and 888 (7.4%) in others, when classified by occupation. When classified by type of industry, 3355 (28.0%) were in the manufacturing, construction and mining group, 3135 (26.2%) in wholesale and retail trade, 1502 (12.6%) in personal services, 406 (3.4%) in public administration and defence, 3191 (26.7%) in professional services, and 359 (3.0%) in others. As to the scale of the workplace, 5288 employers (44.2%) had fewer than 30 employees and 6620 (55.3%) had more than 30 employees.

The children of mothers who were employed tended more often to have questionnaire- and physician-diagnosed AD, to have been delivered via caesarean section, to have fewer siblings, to live in urban areas, and to have a higher family income. The mothers who were employed were older at the birth of their baby, received a higher education and had a higher atopy history, but a lower prevalence of smoking and

Table 1 Characteristics of the study subjects by maternal employment during pregnancy (n = 19 381)

Characteristic	Total	Not employed	Employed	P-value
Total number	19 381	7396	11 962	
Boys, n (%)	10 174 (52.5)	3859 (52.2)	6304 (52.7)	NS
Gestation age (weeks), mean $\pm$ SD	38.5 $\pm$ 1.5	38.5 $\pm$ 0.02	38.5 $\pm$ 0.01	NS
Birth weight (g), mean $\pm$ SD	3127.0 $\pm$ 426.1	3123.7 $\pm$ 5.0	3129.4 $\pm$ 3.9	NS
Delivery via caesarean section, n (%)	6299 (32.5)	2330 (31.5)	3965 (33.1)	< 0.05
Number of siblings $\geq$ 1, n (%)	2675 (13.8)	1284 (17.4)	1390 (11.6)	< 0.0001
Maternal age at baby's birth (years), mean $\pm$ SD	28.8 $\pm$ 4.8	27.6 $\pm$ 0.06	29.6 $\pm$ 0.04	< 0.0001
Maternal education, n (%)				
> 12 years	8799 (45.4)	1853 (25.1)	6942 (58.0)	< 0.0001
$\leq$ 12 years	10 550 (54.4)	5531 (74.8)	5003 (41.8)	
Maternal smoking, n (%)	1207 (6.2)	639 (8.6)	567 (4.7)	< 0.0001
Maternal atopy, n (%)	3567 (18.4)	1203 (16.3)	2365 (19.8)	< 0.0001
Foreign maternal nationality, n (%)	3786 (19.5)	2354 (31.8)	1427 (11.9)	< 0.0001
Family income, n (%)				
High	11 231 (57.9)	2362 (32.0)	8859 (74.1)	< 0.0001
Low	8090 (41.7)	4992 (67.5)	3088 (25.8)	
Live in an urban area, n (%)	11 056 (57.0)	3823 (51.7)	7220 (60.4)	< 0.0001
Questionnaire-diagnosed AD, n (%)	1340 (6.9)	453 (6.1)	885 (7.4)	< 0.001
Physician-diagnosed AD, n (%)	2033 (10.5)	627 (8.5)	1405 (11.7)	< 0.0001

NS, not significant; AD, atopic dermatitis. Some numbers do not add up to the total n because of missing values.

Table 2 The effect of maternal employment status and work stress during pregnancy on questionnaire- and physician-diagnosed atopic dermatitis (AD) in 3-year-old children (*n* = 19 381)

Factor (<i>n</i>)	Questionnaire-diagnosed AD		Physician-diagnosed AD	
	<i>n</i> (%)	OR (95% CI) ^a	<i>n</i> (%)	OR (95% CI) ^a
Employed				
Yes (11 962)	885 (7.4)	1.18 (1.05–1.33)**	1405 (11.7)	1.38 (1.25–1.53)***
No (7396)	453 (6.1)	Reference	627 (8.5)	Reference
Occupation				
Professional, technical (2276)	198 (8.7)	1.34 (1.13–1.60)**	322 (14.1)	1.64 (1.42–1.90)***
Administrative, managerial (1456)	120 (8.2)	1.32 (1.07–1.63)**	185 (12.7)	1.52 (1.27–1.81)***
Superintendents, clerical (5036)	394 (7.8)	1.26 (1.09–1.45)**	663 (13.2)	1.59 (1.42–1.79)***
Sales (948)	49 (5.2)	0.81 (0.59–1.08)	80 (8.4)	0.96 (0.75–1.22)
Fabricators, operators, etc. (1346)	79 (5.9)	0.95 (0.74–1.21)	98 (7.3)	0.84 (0.67–1.05)
Others (888)	45 (5.1)	0.81 (0.58–1.10)	57 (6.4)	0.73 (0.55–1.00)
Not employed (7396)	453 (6.1)	Reference	627 (8.5)	Reference
Industry				
Manufacturing, construction, mining (3355)	234 (7.0)	1.14 (0.96–1.34)	336 (10.0)	1.19 (1.03–1.37)*
Wholesale and retail trade (3135)	230 (7.3)	1.17 (0.99–1.38)	375 (12.0)	1.42 (1.24–1.63)***
Personal service (1502)	100 (6.7)	1.06 (0.85–1.33)	145 (9.7)	1.12 (0.93–1.36)
Professional service (3191)	271 (8.5)	1.31 (1.12–1.54)***	450 (14.1)	1.64 (1.44–1.87)***
Public administration and defence (406)	27 (6.7)	1.06 (0.69–1.56)	57 (14.0)	1.72 (1.27–2.28)***
Others (359)	22 (6.1)	1.01 (0.63–1.54)	41 (11.4)	1.41 (0.99–1.95)*
Not employed (7396)	453 (6.1)	Reference	627 (8.5)	Reference
Work schedule				
Day (8825)	687 (7.8)	1.25 (1.01–1.41)*	1093 (12.4)	1.47 (1.33–1.63)*
Night (308)	19 (6.2)	1.04 (0.62–1.66)	30 (9.7)	1.04 (0.68–1.52)
Shift/all day (2815)	177 (6.3)	0.98 (0.82–1.18)	281 (10.0)	1.14 (0.99–1.33)
Not employed (7396)	453 (6.1)	Reference	627 (8.5)	Reference
Work stress				
Very high/high (4386)	382 (8.7)	1.43 (1.20–1.70)***	581 (13.2)	1.34 (1.16–1.54)***
Intermediate (3941)	286 (7.3)	1.20 (1.00–1.45)*	469 (11.9)	1.22 (1.05–1.41)**
Low/not at all (3629)	217 (6.0)	Reference	355 (9.8)	Reference

^aAdjusted for sex, maternal atopy, maternal education level, maternal smoking, family income, number of siblings, and residence location.
 P* < 0.05, *P* < 0.01, ****P* < 0.001. OR, odds ratio; CI, confidence interval. Some numbers do not add up to the total *n* because of missing values.

foreign nationality than those who were not employed (Table 1).

The children of the mothers who worked during pregnancy had an increased risk of physician-diagnosed AD compared with those whose mothers did not work (OR 1.38, 95% CI 1.25–1.53), after adjusting for sex, maternal atopy, maternal education level, maternal smoking, family income, number of siblings and residence location (Table 2). Within the occupational category, the children of mothers with professional or technical, administrative or managerial, and superintendent and clerical occupations had a higher risk of childhood physician-diagnosed AD (OR 1.64, 95% CI 1.42–1.90; OR 1.52, 95% CI 1.27–1.81; OR 1.59, 95% CI 1.42–1.79, respectively) and questionnaire-diagnosed AD (OR 1.34, 95% CI 1.13–1.60; OR 1.32, 95% CI 1.07–1.63; OR 1.26, 95% CI 1.09–1.45, respectively) (Table 2). As for the category of industry, an increased risk of questionnaire- and physician-diagnosed AD was found for the children whose mothers' work involved professional services (OR 1.31, 95% CI 1.12–1.54; OR 1.64, 95% CI 1.44–1.87, respectively). The risk of questionnaire- and physician-diagnosed AD was found to increase with

maternal work stress during pregnancy in a dose–response manner, after adjusting for potential confounders ($P_{\text{trend}} < 0.01$) (Table 2). However, no significant association between AD and maternal night or shift work during pregnancy was found.

The mothers of children with physician-diagnosed AD had longer working days per week and more working hours per day than those without AD ($P < 0.0001$) (Table 3). The same results were found for children with questionnaire-diagnosed AD, although not all factors were statistically significant. After adjusting for potential confounders, working days per week and working hours per day were positively associated with the risk of physician-diagnosed AD [β (SE) = 0.0428 (0.009) and 0.0308 (0.006), respectively].

Pregnant women with professional or technical occupations and administrative or managerial occupations had higher work stress than other fields (OR 2.95, 95% CI 2.49–3.49) (Table 4). More working days per week and more working hours per day were also correlated with higher work stress (OR 2.58, 95% CI 1.95–3.42; and OR 3.00, 95% CI 2.54–3.54, respectively). As maternal professional occupation, high work stress and long

Table 3 The effect of working time during pregnancy on questionnaire- and physician-diagnosed atopic dermatitis (AD) in 3-year-old children (n = 19 381)

	Working days per week, mean $\pm$ SE	Working hours per day, mean $\pm$ SE
Physician-diagnosed AD		
With (n = 2032)	3.62 $\pm$ 0.06	5.80 $\pm$ 0.10
Without (n = 17 323)	3.28 $\pm$ 0.02	5.16 $\pm$ 0.03
P-value	< 0.0001	< 0.0001
β value $\pm$ SE ^a	0.0428 $\pm$ 0.009***	0.0308 $\pm$ 0.006***
Questionnaire-diagnosed AD		
With (n = 1340)	3.46 $\pm$ 0.07	5.58 $\pm$ 0.12
Without (n = 18 041)	3.31 $\pm$ 0.02	5.20 $\pm$ 0.03
P-value	0.0514	0.0017
β -value $\pm$ SE ^a	0.0151 $\pm$ 0.01	0.0165 $\pm$ 0.007*

^aAdjusted for sex, maternal atopy, maternal education level, maternal smoking, family income, number of siblings, and residence location.
*P < 0.05, ***P < 0.001. Some numbers do not add up to the total n because of missing values.

Table 4 The effect of maternal occupation and working time during pregnancy on work stress

Variable	Work stress		OR (95% CI)
	Yes, n (%)	No, n (%)	
Occupation			
Professional, technical	1832 (80.5)	443 (19.5)	2.95 (2.49–3.49)***
Administrative, managerial	1070 (73.6)	383 (26.4)	1.99 (1.67–2.38)***
Superintendents, clerical	3524 (70.0)	1510 (30.0)	1.66 (1.44–1.92)***
Sales	575 (60.7)	373 (39.4)	1.10 (0.91–1.32)
Fabricators, operators, etc.	797 (59.3)	547 (40.7)	1.04 (0.87–1.23)
Others	518 (58.4)	369 (41.6)	Reference
Working days per week ^a			
≥ 3.32	8233 (70.0)	3525 (30.0)	2.58 (1.95–3.42)***
< 3.32	94 (47.5)	104 (52.5)	Reference
Working hours per day ^a			
≥ 5.22	8056 (71.0)	3292 (29.0)	3.00 (2.54–3.54)***
< 5.22	266 (44.9)	326 (55.1)	Reference

^aThe cut-off value was the mean working time. ***P < 0.001. OR, odds ratio; CI, confidence interval. Some numbers do not add up to the total n because of missing values.

working times were related to an increased risk of childhood atopic disorders, and as work stress may be correlated with the other two risk factors, we further investigated whether work stress alone could account for all of the effect on atopic disorders. After stratification by work stress, the effect of job category on AD still existed (OR 3.05, 95% CI 1.83–5.34 for those without work stress). However, the effect of longer working times on AD disappeared (Table 5).

Discussion

Associations between mothers who work and atopic diseases among their offspring have not been previously reported, and thus merit further investigation. In our study, significant associations between childhood AD and maternal employment status and occupational category were found. In addition, the risk of AD was found to increase with maternal work stress

and working time during pregnancy. After stratification by maternal work stress, the effect of occupational category on AD still existed; however, the effect of working time on AD disappeared. Therefore, maternal occupational category was a risk factor for childhood AD in addition to work stress. This study adds important weight to the fact that maternal occupational exposure during pregnancy has significant effects on the development of atopic disorders in the offspring.

We found that the children of mothers who worked during pregnancy had an increased risk of AD compared with those whose mothers did not work. With the increasing participation of fertile women in working life, this increase may be due to working conditions having an impact on reproductive health. The general stress of combining family life and household responsibilities with a full-time job can also have a negative impact on daily well-being, particularly during pregnancy. Several studies have reported that the children of

Table 5 The effect of maternal occupation and working time during pregnancy on questionnaire- and physician-diagnosed atopic dermatitis (AD) in 3-year-old children after stratification by maternal work stress

Variable	Work stress					
	No			Yes		
	With AD, n (%)	Without AD, n (%)	OR (95% CI)	With AD, n (%)	Without AD, n (%)	OR (95% CI)
Occupation						
Professional, technical	63 (14.2)	380 (85.8)	3.05 (1.83–5.34)***	259 (14.1)	1573 (85.9)	2.08 (1.48–3.01)***
Administrative, managerial	41 (10.7)	342 (89.3)	2.21 (1.27–3.96)**	144 (13.5)	926 (86.5)	1.96 (1.37–2.89)***
Superintendents, clerical	170 (11.3)	1340 (88.7)	2.34 (1.47–3.93)***	493 (14.0)	3031 (86.0)	2.05 (1.48–2.94)***
Sales	27 (7.2)	346 (92.8)	1.44 (0.79–2.67)	53 (9.2)	522 (90.8)	1.28 (0.83–1.99)
Fabricators, operators, etc.	35 (6.4)	512 (93.6)	1.26 (0.72–2.28)	63 (7.9)	734 (92.1)	1.08 (0.72–1.66)
Others	19 (5.2)	350 (94.8)	Reference	38 (7.3)	480 (92.7)	Reference
Working days per week^a						
≥ 3.32	343 (9.7)	3182 (90.3)	0.83 (0.47–1.60)	1038 (12.6)	7195 (87.4)	0.99 (0.56–1.91)
< 3.32	12 (11.5)	92 (88.5)	Reference	12 (12.8)	82 (87.2)	Reference
Working hours per day^a						
≥ 5.22	313 (9.5)	2979 (90.5)	0.73 (0.52–1.05)	1017 (12.6)	7039 (87.4)	1.02 (0.71–1.50)
< 5.22	41 (12.6)	285 (87.4)	Reference	33 (12.4)	233 (87.6)	Reference

^aThe cut-off value was the mean working time. ***p* < 0.01, ****p* < 0.001. OR, odds ratio; CI, confidence interval. Some numbers do not add up to the total *n* because of missing values.

working women have a higher risk of developing asthma, which may result from a high physical workload and psychological stress.^{3,12,13}

Consistent with a survey from Statistics Canada, which reported that most employed women work in traditionally female jobs, including nursing and health-related occupations, we found that the two most common maternal occupation groups were the superintendent or clerical group and the professional or technical group.⁴ Interestingly, we observed that the children of the mothers with professional or technical occupations had a higher risk of AD. A possible explanation is that these mothers may have an increased exposure to certain allergens or chemicals, leading to atopic disorders in their offspring.^{6,8} This is consistent with the 'haptent-atopy' hypothesis, which postulates that increased haptent and irritant chemical exposure during maternal pregnancy, when there is already a natural tendency to Th2 immunological bias, contributes to the subsequent development of atopic disorders in children.¹⁴ Work-related exposures were reported to be associated with AD.¹⁵ Occupational exposure to gas, dust or fumes appeared to be a strong risk factor for AD.¹⁶ It is interesting that cooking with wood and biomass has also been associated with an increased risk of AD, further emphasizing the influence of environmental exposures.¹⁷ In addition, more and more studies have reported associations between prenatal exposure to environmental chemicals and childhood atopic disorders.^{18,19} Prenatal exposure to organic solvents may confer immune modulation or programme the immune function, and increase the risk of allergic manifestations.²⁰ Therefore, it is reasonable that maternal occupational exposures may contribute to a Th1/Th2 imbalance in pregnancy and lead to the development of atopic diseases.²¹

We found that the risk of AD increased with maternal work stress during pregnancy in a dose-response manner. It has been reported that exposure to stress during pregnancy is associated with an increased risk of respiratory and skin diseases in the offspring, and is related to elevated cord blood IgE and a change of Th1/Th2 balance.^{22,23} In our previous study, on maternal nerve growth factor levels during pregnancy, levels of a type of stress-related neuropeptide were significantly higher in children with AD compared with controls.²⁴ Maternal stress may affect fetal immune development either through hormonal regulation of fetal genes or through modification of placental and uterine functions.²⁵

Long working hours have been found to be a marker for ergonomic stress. It has been reported that women who work more than 50 h per week without taking antenatal leave from work tend to have small-for-gestational-age births.²⁶ However, in our study the effect of maternal working time on childhood AD disappeared after stratification by work stress. Shift work is associated with hormonal disturbances through changes in circadian rhythm and stress, affecting fetal development.²⁷ However, most studies investigating the effect of work schedule on the reproductive health of women have reached equivocal conclusions.²⁸ Although no associations between work schedules and AD in children were established in our study, public health concerns and the previously reported data warrant continued research.

There are limitations to our study. Firstly, we used occupational groups to assess exposure. This probably resulted in nondifferential misclassification of job exposure due to differences in work tasks within the groups. A classification of occupations according to allergen or chemical exposure would have been of interest; however, occupational grouping by ex-

posure was not feasible for such a large epidemiological study. Furthermore, a standard occupational and industrial classification system of occupational grouping for exposure assessment has previously been used in many epidemiological studies.^{5,29,30} Secondly, our study was limited by the use of questionnaires for ascertaining AD, which may not be as accurate as the standard diagnostic criteria used by a dermatologist. Nevertheless, maternal reports of physician-diagnosed AD with typical morphology and atopic distribution have been validated vs. clinical examinations in studies performed in the U.S.A. and Denmark, and have been used by many epidemiological studies.^{9,10,31,32}

The strengths of our study include the large sample size and the population-based prospective cohort design. Because of the large sample size, we were able to control for numerous potential confounders in the statistical analysis. The consistency across different outcome measures (questionnaire- and physician-diagnosed AD) and the evidence for a dose-response relationship between work stress severity and AD raises the possibility that this association may be causal. Therefore, we are fairly confident about our results. In addition, this is the first contribution to the literature linking the association between different characteristics of prenatal maternal employment exposure and subsequent AD development during childhood. Moreover, the multistage stratified systematic sampling, including urban, suburban and rural populations, may enhance the generality. As the follow-up rate was high, selection bias was not a major problem in our study. Finally, there were no significant differences in most of the variables in those lost to follow-up and in those who completed the follow-up.

In summary, working in professional or technical occupations increased the risk of childhood AD in addition to work stress during pregnancy. As the intrauterine environment plays a pivotal role for health throughout life, transferring pregnant women to a safe working environment is important. As worldwide fertility rates continue to decrease, action must be taken by governments to ease working conditions and prevent exposure to occupational hazards for female workers, particularly during pregnancy. There is an urgent need to further clarify which environmental exposures during pregnancy will influence the subsequent development of allergic diseases in children.

What's already known about this topic?

- Whether maternal occupations affect the development of atopic disorders in children remains to be elucidated.

What does this study add?

- In addition to work stress during pregnancy, working in professional or technical occupations increased the risk of childhood atopic dermatitis.
- Avoiding occupational exposure for pregnant women is important for prevention of atopic disorders in children.

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