Occupational exposure to chemicals and fetal growth: the Generation R Study

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BACKGROUND: Developmental diseases, such as birth defects, growth restriction and preterm delivery, account for >25% of infant mortality and morbidity. Several studies have shown that exposure to chemicals during pregnancy is associated with adverse birth outcomes. The aim of this study was to identify whether occupational exposure to various chemicals might adversely influence intrauterine growth patterns and placental weight.

METHODS: Associations between maternal occupational exposure to various chemicals and fetal growth were studied in 4680 pregnant women participating in a population-based prospective cohort study from early pregnancy onwards in the Netherlands (2002–2006), the Generation R Study. Mothers who filled out a questionnaire during mid-pregnancy (response: 77% of enrolment) were included if they conducted paid employment during pregnancy and had a spontaneously conceived singleton live born pregnancy (n = 4680). A job exposure matrix was used, linking job titles to expert judgement on exposure to chemicals in the workplace. Fetal growth characteristics were repeatedly measured by ultrasound and were used in combination with measurements at birth. Placental weight was obtained from medical records and hospital registries. Linear regression models for repeated measurements were used to study the associations between maternal occupational exposure to chemicals and intrauterine growth.

RESULTS: We observed that maternal occupational exposure to polycyclic aromatic hydrocarbons, phthalates, alkylphenolic compounds and pesticides adversely influenced several domains of fetal growth (fetal weight, fetal head circumference and fetal length). We found a significant association between pesticide and phthalate exposure with a decreased placental weight.

CONCLUSIONS: Our results suggest that maternal occupational exposure to several chemicals is associated with impaired fetal growth during pregnancy and a decreased placental weight. Further studies are needed to confirm these findings and to assess post-natal consequences.

Key words: chemical exposure / occupational exposure / phthalates / pesticides / fetal growth

Introduction

Developmental diseases, such as structural alterations (birth defects), functional alterations, growth restriction and preterm delivery, account for >25% of infant mortality and morbidity (Liu and Roth, 2008; Stillerman et al., 2008). Fetal growth is generally assessed by surrogate measures, including length of gestation and fetal size, and these endpoints are important determinants of later health and morbidity (McCormick, 1985; McIntire et al., 1999; Yanney and Marlow, 2004). Common risk factors for adverse fetal development include ethnicity (Thompson et al., 2001), smoking and alcohol use (Jaddoe et al., 2007), previous children with low birthweight or preterm birth, older maternal age and low socioeconomic status (Silva et al., 2010). Recently, it has been suggested that environmental risk factors and parental occupation may also play an important role (Windham and Fenster, 2008; Li et al., 2010a,b).
Women constitute a substantial part of the labour force in the European Union (EU). In 2010, ~58% of the women aged between 15 and 64 years had paid employment, which was a substantial increase from 54% in 2002 (Eurostat, 2011). With the increasing labour force participation among women in European countries, the likelihood that women will be exposed to a variety of chemical, physical and psychological risk factors at work during pregnancy will also increase (Linos and Kirch, 2008). Although women in paid employment have better pregnancy outcomes than those without paid jobs (Savitz et al., 1996; Jansen et al., 2010; Burdorf et al., 2011), certain work-related factors, such as exposure to chemicals (Mattison, 2010), physically demanding work (Mozurkewich et al., 2000) and psychological job strain (Vrijkotte et al., 2009) may adversely influence the pregnancy outcome.

Exposure to chemicals during fetal development may increase the risk of adverse health consequences, including adverse birth outcomes, childhood morbidity and adult disease and mortality (Gluckman and Hanson, 2004; Stillerman et al., 2008). Chemicals that have been associated with adverse fetal development are lead, other heavy metals (Llano and Ronco, 2009; Zhu et al., 2010), phthalates (Latini et al., 2006) and pesticides (Perera et al., 2005; Weselak et al., 2007; Gilden et al., 2010). Chemicals can cross the placenta and enter the fetus, and a number of chemicals measured in maternal urine and serum have also been found in amniotic fluid, cord blood and meconium (Barr et al., 2007). A recent study by Woodruff et al. (2011) showed that pregnant women in the USA were exposed to multiple chemicals. The mechanism by which chemicals affect reproductive events are not completely understood; direct toxic effects may occur when normal processes such as differentiation, mitosis, meiosis intracellular communication and DNA repair are altered. In this regard, the fetus is particularly vulnerable due to its fast growth, the process of cellular differentiation, the immaturity of its metabolic pathways and the stage of development of vital organs (Bruckner, 2000).

Since several studies have shown that exposure to chemicals during pregnancy adversely influences fetal development, as demonstrated by an increased occurrence of low birthweight, small-for-gestational age and preterm delivery (Stillerman et al., 2008; Windham and Fenster, 2008; Wigle et al., 2008), we expect that exposure to chemicals might already influence fetal growth in the different trimesters during pregnancy. Although birth outcomes are important from an obstetric perspective, they are rather crude measures of fetal growth during pregnancy.

The aim of this study was to identify, within a population-based prospective birth cohort study, whether occupational exposure to various chemicals might adversely influence intrauterine growth patterns and placental weight.

**Materials and Methods**

**Study design**

The Generation R Study is a population-based prospective cohort study on growth, development and health from early fetal life until young adulthood in Rotterdam, the Netherlands. The study design has previously been described in detail (Jaddoe et al., 2006, 2010). Briefly, all pregnant women who had an expected delivery date between April 2002 and January 2006 and lived in the study area of Rotterdam were invited to participate. In total, 9778 pregnant women (response of 61%) were enrolled in the study, of which 8880 women were enrolled during pregnancy and another 898 at birth of their child. Extensive assessments were carried out during the first trimester (gestational age <18 weeks), second trimester (gestational age 18–25 weeks) and third trimester (gestational age >25 weeks), including physical examinations, questionnaires, interviews and biological samples. The study was approved by the Medical Ethics Committee at Erasmus University Medical Centre, Rotterdam, The Netherlands (MEC 198.782/2001/31).

The occupational information required for this study was gathered in the questionnaire completed during mid-pregnancy, which was filled out by 6830 women (77% of enrolment). For this study, we selected women who were prenatally enrolled, with paid employment before or during pregnancy, and with a spontaneously conceived singleton live born pregnancy. For each couple, we included the first pregnancy within the Generation R cohort in our study, since some women participated with more than one child in the study. Finally, the study population consisted of 4680 women; the flowchart of the study population is depicted in Fig. 1. Our results are based on the second and third trimester ultrasonography measures in combination with birth outcomes.

**Fetal ultrasounds**

For this study, we used the ultrasound measures of fetal head circumference (HC), femur length (FL) and estimated fetal weight (EFW), since these three measures are essential characteristics to describe fetal growth. Fetal ultrasound examinations were carried out in two dedicated research centres in each trimester of pregnancy. We measured fetal HC, abdominal circumference (AC) and FL to the nearest millimetre using standardized ultrasound procedures in the second (median, 20.5; minimum–maximum, 18.0–25.0 weeks) and third (median, 30.4; minimum–maximum, 25.8–37.0 weeks) trimester. Since the use of the last menstrual period for pregnancy dating has several limitations (Verburg et al., 2008a) and a large number of women in our study population did not know the exact date of their last menstrual period (76%), we used crown-rump length for pregnancy dating until a gestational age of 12 weeks (2308 women) and biparietal diameter for pregnancy dating thereafter (2372 women) in all women (Robinson et al., 1979; Altman and Chitty, 1997). First trimester measurements (3459 women) were primarily used to establish gestational age and therefore not included in the growth analysis. EFW was calculated using the formula by Hadlock et al. (1985).

Ultrasound examinations were performed using an Aloka model SSD-1700 (Tokyo, Japan) or the ATL-Philips Model HDI 5000 (Seattle, WA, USA). Customized growth curves for the entire study population were constructed, and standard deviation (SD) scores for each individual woman were calculated as a deviation from the ‘overall’ average at that gestational week, and represent the equivalent z-scores (Verburg et al., 2008a). The intraclass correlation coefficient of fetal growth measurements was 0.95, tested on 21 subjects, indicating a high reproducibility of fetal biometry measurements (Verburg et al., 2008b).

**Placenta and birth outcomes**

Placental weight was obtained from medical records and hospital registries. Information about gender at birth, gestational age, weight, length and HC at birth was obtained from medical records and hospital registries. For the analysis, we used birthweight, HC at birth and length of the infant at birth.

**Occupation and working conditions**

The mid-pregnancy questionnaire contained questions about work status, occupation and working conditions and focused on the periconception
and pregnancy period. The work status, based on a single question on the current economic status with seven categories such as paid labour, self-employed, unemployed, disabled, homemaker, student or other, was used to select women with paid employment. This question was followed by questions whether the mother had worked before conception in this current occupation, and the starting and (optional) closing date of this current occupation. We selected women who started working before conception and women who started working somewhere during the first trimester of pregnancy. Further questions on job title, type of business, name of the employer and activities in the job were used to classify jobs into the Dutch Classification of Occupations (Statistics Netherlands, 1992) and subsequently link these codes to a job exposure matrix (JEM) for chemical exposure (Brouwers et al., 2009). This new JEM was developed according to a general strategy, comprising a literature search to identify chemicals, information gathering on occupations at risk and literature on occupational settings in which the selected chemicals were encountered and exposure measurements were performed. This reference material served as a starting point for the expert assessment. Three experts were asked to estimate exposures based on their knowledge of tasks and working environment in various occupations. Finally, exposure probability scores were added based on the judgement of three experts. For various chemicals, subjects experience a certain level of exposure through diet, environment or widely used consumer products. The JEM exposure score refers to the probability of occupational exposure, which is assumed to exceed the background level in the general population. The exposure probability scores were assigned by means of consensus discussions in which the original scores were taken into account where possible, but no prior individual assessments were performed. The JEM comprises 10 categories of chemicals, namely polycyclic aromatic hydrocarbons (PAHs), polychlorinated organic compounds, pesticides, phthalates, organic solvents, bisphenol A, alkylphenolic compounds, flame retardants, metals and miscellaneous agents (Brouwers et al., 2009). For 353 job titles, probability scores were classified into three levels: ‘unlikely’ (0), ‘possible’ (1) and ‘probable’ (2). Different country-specific JEMs have been used in several studies, and the JEM is a valuable tool for exposure assessment in epidemiological studies on the health risks of chemical exposure (Vrijheid et al., 2003; Pierik et al. 2004; Burdorf et al., 2011; Snijder et al., 2011). For this study, we collated the last two categories into one category indicating the occurrence of exposure to chemicals.

**Potential confounders**

Information about maternal age, pre-pregnancy weight, educational level, ethnicity, parity and folic acid supplement use was obtained by questionnaire at enrolment in the study. Maternal smoking habits and alcohol use were assessed on the basis of three questionnaires (in early, mid- and late pregnancy) and classified as no, until pregnancy was known or during pregnancy (Jaddoe et al., 2008). Maternal height was measured at intake in the study. The questions on physical work load were obtained from the Dutch Musculoskeletal Questionnaire and concerned questions on long periods of standing, manually handling loads of 5 kg or more, manually handling loads of 25 kg or more and night shifts. The presence of doctor-diagnosed pre-eclampsia, pregnancy-induced hypertension and diabetes gravidarum was retrieved from medical records and was based on the criteria of the International Society for the Study of Hypertension in Pregnancy (Brown et al., 2001; Coolman et al., 2010).

**Statistical analysis**

We assessed the associations between maternal occupational exposure to various chemicals and longitudinally measured SD scores of HC, length (second and third trimester FL and birth length) and weight (second and third trimester EFW and birthweight) using a mixed model for repeated measurements with an unstructured error term. This is a commonly used method to analyse data from longitudinal studies (Twisk, 2004).

**Figure 1** Flowchart of the study population.
and child mortality in order to increase comparability of effects independent of underlying differences in distributions (Fishman et al., 2004). These gestational age-adjusted SD scores were used as parameters of fetal growth, the dependent variables in the statistical analyses. Second, a linear model was used to study the influence of occupational exposure to chemicals on these gestational age-adjusted SD scores. The final model can be written as (for example, for fetal weight): 

$$SD\ \text{score of fetal weight} = b_0 + b_1 \times \text{gawks} + b_2 \times \text{exposure group} + b_3 \times \text{gawks} \times \text{exposure group}$$

$$(\text{gawks} = \text{gestational age in weeks}).$$

In this model, $b_0$ reflects the intercept and $b_2$ expresses the systematic difference between the exposed and non-exposed groups. The coefficient $b_3$ reflects whether exposed and non-exposed fetus grow at the same rate over time. The later coefficient is the main interest of this analysis, since it represents the average decrease or increase in SD for fetal weight per gestational week for exposed women versus non-exposed women. Different beta coefficients of interaction were estimated for weight, HC and length, representing growth velocity for several domains of fetal growth. The regression models were adjusted for lifestyle and socioeconomic confounders used in previous studies on maternal occupational exposure (Burdorf et al., 2011; Snijder et al. 2011) and known determinants of fetal growth: maternal age, educational level, ethnicity, parity, pre-pregnancy weight, height at intake, smoking during pregnancy, alcohol use during pregnancy, folic acid use, parity, long periods of standing, handling loads of $> 5\ \text{kg}$, handling loads of $> 25\ \text{kg}$, night shifts, pre-eclampsia, pregnancy-induced hypertension and diabetes gravidarum.

Results

Table I shows the baseline characteristics of the study population. The mean age of the women at intake in the study was 31.1 years. Of all women, 30.3% had completed higher education and the largest group was from Dutch origin (64.0%). The majority of women were nulliparous (63.9%). A total of 11.7% of the mothers continued smoking and 39.4% of the mothers continued drinking alcohol after the pregnancy was known. According to the JEM, 1.3% of the women were exposed to PAHs, 0.5% to pesticides, 1.5% to phthalates, 4.7% to organic solvents, 3.3% to alkylphenolic compounds, 1.1% to metals and 6.7% to any chemicals. In total, 4197 (89.7%) women visited our clinic for second trimester ultrasonography and 4294 (91.8%) for third trimester ultrasonography. The median gestational age at birth was 40.1 weeks (minimum, 22.7; maximum, 43.4 weeks), while mean birthweight was 3450 g (SD 549 g). Slightly more than 50% of

![Figure 2](https://academic.oup.com/humrep/article-abstract/27/3/910/638826)
Figure 3  Adjusted relative differences in head circumference (HC) (SD scores) in various chemical groups compared with the non-exposed group. Values are based on repeated linear regression models and reflect the difference in the SD score of fetal HC measurements (based on 10 789 measurements) in the offspring of mothers occupationally exposed to various groups of chemicals compared with the offspring of non-exposed mothers. The reference value is an SD score of 0. *P < 0.05. Estimates are adjusted for the following confounders: maternal age, educational level, ethnicity, fetal gender, weight before pregnancy, height at intake, smoking during pregnancy, alcohol use during pregnancy, folic acid use, parity, long periods of standing, handling loads of >5 kg, handling loads of >25 kg, night shifts, pre-eclampsia, pregnancy-induced hypertension and diabetes gravidarum.

Figure 4  Adjusted relative differences in fetal length (SD scores) in various chemical groups compared with the non-exposed group. Values are based on repeated linear regression model and reflect the difference in the SD score of fetal length measurements (based on 11 401 measurements) in the offspring of mothers occupationally exposed to various groups of chemicals compared with the offspring of non-exposed mothers. The reference value is an SD score of 0. *P < 0.05. Estimates are adjusted for the following confounders: maternal age, educational level, ethnicity, fetal gender, weight before pregnancy, height at intake, smoking during pregnancy, alcohol use during pregnancy, folic acid use, parity, long periods of standing, handling loads of >5 kg, handling loads of >25 kg, night shifts, pre-eclampsia, pregnancy-induced hypertension and diabetes gravidarum.
the infants were boys. The three characteristics of fetal growth were interrelated with the highest association between fetal weight and length (Pearson correlation coefficient, $r = 0.59$, at birth) and the smallest association between HC and length ($r = 0.43$, at birth).

Table II shows the results of the linear regression analysis on occupational exposure to chemicals and placental weight. Women occupationally exposed to pesticides and phthalates showed a significantly lower placental weight compared with non-exposed women, respectively, 65.90 g for pesticides (95% CI: $-129.86$ to $-1.94$) and 45.88 g for phthalates (95% CI: $-85.15$; $-6.60$).

Table III shows the results of the univariable and multivariable longitudinal models for the associations between occupational exposure to various chemicals and fetal weight, HC and fetal length. The average decline in SD per gestational week is graphically illustrated in Figs 2–4. Maternal occupational exposure to several chemicals showed similar trends with lower growth rates for all three parameters. Women occupationally exposed to PAHs and phthalates showed significant lower fetal weight growth rates (average decline in SD per gestational week: 0.01660 for PAHs and 0.01691 for phthalates) compared with non-exposed mothers, adjusted for potential confounders. In the fully adjusted model, the following covariates statistically significantly influenced fetal growth in order of decreasing importance: weight, height, parity, smoking, ethnicity and diabetes gravidarum, but adjustments did not change the effect estimates of chemical exposure on fetal growth (Supplementary data, SI). No interaction for exposure with ethnicity and educational level was observed in the multivariate models, indicating that ethnicity and education do not moderate or explain the observed associations between occupational exposure and fetal growth parameters.

For fetal HC, only maternal occupational exposure to alkylphenolic compounds showed a statistically significant lower growth rate ($-0.01752$ SD per gestational week) compared with non-exposed mothers, adjusted for potential confounders. For fetal length, we observed statistically significant lower growth rates between mothers occupationally exposed to pesticides and phthalates ($-0.0361$ and $-0.0185$ SD per gestational week, respectively) compared with non-exposed mothers, with a much steeper decline during the course of pregnancy for pesticides than for other occupational chemicals.

In total, 4177 (89.3%) women filled out the question concerning the starting date of their current occupation, 4068 women (97.4%) started working before conception, whereas 109 (2.6%) women started working somewhere during their first trimester of pregnancy. In the sensitivity analyses, no differences in effect estimates were observed between women who started working before conception compared with women who started working during the first trimester of pregnancy. The differences in SD scores for all fetal growth characteristics for the unadjusted model, the adjusted model, and for the five imputation models are shown in Supplement I. Supplement II and III show the individual data points of exposed and non-exposed women for fetal weight and fetal head circumference in the second trimester, third trimester and at birth.

**Discussion**

This large population-based prospective cohort study showed that maternal occupational exposure to several chemicals, such as PAHs, phthalates, alkylphenolic compounds and pesticides during pregnancy,
adversely influenced their fetal growth rates of weight, HC and length. These differences in fetal growth rates could already be demonstrated during pregnancy, and were partly reflected in a decreased placental weight. These findings suggest that early exposure during the critical window of fetal development is crucial.

In this study, we used ultrasound measurements for pregnancy dating (Robinson et al., 1979; Altman and Chitty, 1997); this method appears to be superior to dating based on the last menstrual period (Verburg et al., 2008a). A disadvantage of pregnancy dating by ultrasound is that growth variations in crown-rump length and biparietal diameter in early pregnancy are assumed to be zero, impairing detailed analysis on fetal growth in the first trimester. In a sensitivity analyses on the subset of women with a certain last menstrual period and regular cycle (n = 1221), the direction of the effect estimates did not change. Reference curves for fetal growth were constructed for our cohort, which enables linear analyses of fetal growth characteristics. These curves are based on a large, urban, non-hospital-based population, which makes these curves generalizable to normal fetal development in industrialized countries (Verburg et al., 2008a). For the repeated measurements concerning fetal length, we used the SD score of birth length in combination with SD scores of FL in second and third trimester in order to assess relative changes in fetal skeletal growth. However, the results should be interpreted with caution, since these measurements reflect different body parts. The repeated measurements based on gestational age-adjusted SD scores were used in previous studies within the same cohort (Jaddoe et al., 2007; Bakker et al., 2010). This method enables us to identify pathological smallness instead of constitutional smallness, which may be normal intrauterine growth. The advantage of SD scores as relative measure of difference is that the SD scores can be used in linear regression models, whereas absolute differences in fetal growth were highly skewed since growth curves during pregnancy have a typical parabolic shape that must be described by fractional polynomials instead of normal distributions.

We demonstrated two of these curves with absolute differences in Supplementary data, SII and SIII.

The strength of this study is the population-based approach with recruitment during the prenatal period and the availability of a large number of potential confounders. A limitation of this study is the selective participation with mothers from ethnic minorities and with lower socioeconomic status less represented in the study population (Jaddoe et al., 2006). This selection may have influenced the prevalence of exposure to chemicals at the workplace, but bias is unlikely since exposure status was assessed independently from and prior to the fetal growth characteristics by a recently updated JEM. This approach assured that exposure status was blinded to participants and researchers, both aspects which avoid information bias. The characterization of exposure in the JEM must be interpreted as exposure probabilities, which are only a crude measure of exposure, which have to be interpreted with caution. Background exposure to various chemicals through diet and environment may occur. Previous research within the Generation R Study (Ye et al., 2008), but also within the NHANES national survey, showed that almost all pregnant women are exposed to chemicals, and that levels are comparable between pregnant and non-pregnant women (Woodruff et al., 2011). However, there is a reason to believe that occupational exposure is generally much higher than background exposure through diet and environment (Nieuwenhuijsen, 2003). For example, for phthalates, Hines et al. (2009) showed that for several occupations the urinary phthalate concentrations exceeded the levels of the general population. However, biomonitoring data comparing occupational exposures with exposure from non-occupational sources are scarce. In the current study, we did not assess background exposure and, thus, it is not possible to distinguish the importance of different routes of exposure. Since it is unlikely that the widespread environmental exposure is associated with occupational exposure in specific jobs, background exposure will most likely not confound the observed relation between occupational chemical exposure and fetal growth.

### Table II Associations between occupational exposure to chemicals and placental weight among pregnant women participating in a birth cohort study.

<table>
<thead>
<tr>
<th>Occupational chemical exposure</th>
<th>Crudea</th>
<th>Adjustedb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAH</td>
<td>−21.21 (−65.17 to 22.75)</td>
<td>−7.64 (−52.03 to 36.76)</td>
</tr>
<tr>
<td>Pesticides</td>
<td>−74.84 (−138.34 to −11.35)*</td>
<td>−65.90 (−129.86 to −1.94)*</td>
</tr>
<tr>
<td>Phthalates</td>
<td>−59.55 (−98.11 to −21.00)*</td>
<td>−45.88 (−85.15 to −6.60)*</td>
</tr>
<tr>
<td>Organic solvents</td>
<td>−17.74 (−39.21 to 3.74)</td>
<td>−10.00 (−32.36 to 12.36)</td>
</tr>
<tr>
<td>Alkylphenolic compounds</td>
<td>−15.81 (−41.01 to 9.39)</td>
<td>−5.43 (−32.03 to 21.16)</td>
</tr>
<tr>
<td>Metals</td>
<td>−37.14 (−80.53 to 6.26)</td>
<td>−35.22 (−78.54 to 8.09)</td>
</tr>
<tr>
<td>Any chemicals</td>
<td>−18.71 (−37.20 to −0.22)*</td>
<td>−11.03 (−30.28 to 8.23)</td>
</tr>
</tbody>
</table>

Results from simple and multiple linear regression analysis. Values are regression coefficients (95% CIs) and reflect the difference in grams for placental weight between women exposed to chemicals in the workplace compared with non-exposed women. Based on 3185 measurements of placental weight.

*aAdjusted for gestational age at birth.

*bAdjusted for gestational age at birth, maternal age, educational level, ethnicity, fetal gender, weight before pregnancy, height at intake, smoking during pregnancy, alcohol use during pregnancy, folic acid use, parity, long periods of standing, handling loads of >5 kg, handling loads of >25 kg, night shifts, pre-eclampsia, pregnancy-induced hypertension and diabetes gravidarum.

*P < 0.05.
### Table III  Association between occupational chemical exposure and fetal weight, fetal HC, and fetal length among pregnant women participating in a birth cohort study.

<table>
<thead>
<tr>
<th>Occupational exposure</th>
<th>Fetal weight</th>
<th></th>
<th></th>
<th>Fetal HC</th>
<th></th>
<th></th>
<th>Fetal length</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted estimate</td>
<td>Adjusted estimate</td>
<td>Standard error</td>
<td>Unadjusted estimate</td>
<td>Adjusted estimate</td>
<td>Standard error</td>
<td>Unadjusted estimate</td>
<td>Adjusted estimate</td>
</tr>
<tr>
<td>PAH</td>
<td>-0.01647*</td>
<td>-0.01660*</td>
<td>0.00798</td>
<td>-0.01053</td>
<td>-0.01056</td>
<td>0.01114</td>
<td>-0.00328</td>
<td>-0.003139</td>
</tr>
<tr>
<td>Pesticides</td>
<td>-0.01892</td>
<td>-0.01891</td>
<td>0.01274</td>
<td>-0.02619</td>
<td>-0.02603</td>
<td>0.01703</td>
<td>-0.03610*</td>
<td>-0.035071*</td>
</tr>
<tr>
<td>Phthalates</td>
<td>-0.01675*</td>
<td>-0.01691*</td>
<td>0.00744</td>
<td>-0.01632</td>
<td>-0.01553</td>
<td>0.00982</td>
<td>-0.01845*</td>
<td>-0.018183</td>
</tr>
<tr>
<td>Organic solvents</td>
<td>-0.00411</td>
<td>-0.00410</td>
<td>0.00424</td>
<td>-0.00975</td>
<td>-0.00902</td>
<td>0.00560</td>
<td>-0.00743</td>
<td>-0.007048</td>
</tr>
<tr>
<td>Alkylphenolic compounds</td>
<td>-0.00757</td>
<td>-0.00766</td>
<td>0.00500</td>
<td>-0.01834*</td>
<td>-0.01752*</td>
<td>0.00661</td>
<td>-0.00954</td>
<td>-0.008890</td>
</tr>
<tr>
<td>Metals</td>
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<td>-0.00649</td>
<td>0.00872</td>
<td>-0.00937</td>
<td>-0.00888</td>
<td>0.01163</td>
<td>-0.01246</td>
<td>-0.012172</td>
</tr>
<tr>
<td>Any chemicals</td>
<td>-0.00712</td>
<td>-0.00710</td>
<td>0.00363</td>
<td>-0.00912</td>
<td>-0.00861</td>
<td>0.00482</td>
<td>-0.00520</td>
<td>-0.004850</td>
</tr>
</tbody>
</table>

The beta coefficients represent the average decline in SD per gestational week for fetal weight, HC and fetal length. Estimates are adjusted for the following confounders: maternal age, educational level, ethnicity, fetal gender, weight before pregnancy, height at intake, smoking during pregnancy, alcohol use during pregnancy, folic acid use, parity, long periods of standing, handling loads of >5 kg, handling loads of >25 kg, night shifts, pre-eclampsia, pregnancy-induced hypertension and diabetes gravidarum.*

*P < 0.05.
horticultural trades must be informed about the risks of pesticide exposure in the workplace. However, the underlying mechanism is largely unclear, and results from earlier studies are conflicting, warranting further research into this important topic.

This study supports existing evidence from human studies regarding occupational exposures and adverse pregnancy outcomes (Wigle et al., 2008). Although the chemicals in our study were considered to be potential endocrine disrupters, it remains to be established whether the mode of action is through endocrine disruption. A recent review by Caserta et al. (2011) summarizes the literature regarding exposure to endocrine-disrupting chemicals on the pregnancy outcome. They conclude that epidemiological studies on endocrine disrupters are not always consistent. This is further illustrated by occupational studies, for example, in hairdressers, that show conflicting results (Rylander and Kallen, 2005; Zhu et al., 2006; Axmon and Rylander, 2009). Further studies are urgently needed to identify the molecular basis of the effects, to study the epigenetic effects of these exposures and to develop strategies to prevent exposure to these agents to improve birth outcomes (Robins et al., 2011).

Our results suggest that maternal occupational exposure to several chemicals adversely influence fetal growth patterns. Further studies are needed to confirm these findings and to identify potential targets for prevention.

**Supplementary data**

Supplementary data are available at http://humrep.oxfordjournals.org/.

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**Authors’ roles**

C.S. wrote the first draft of the manuscript and was responsible for the statistical analyses and interpretation of the data, and the revisions of the manuscript. E.S., H.R., A.H. and V.J. initiated and designed the study, were responsible for the infrastructure in which the study is conducted, contributed to the original data collection, critically revised the manuscript and approved the final version of the manuscript. N.R. and E.V. contributed to the interpretation of the data and critically revised the manuscript for important intellectual content. A.B. contributed to all revisions of the manuscript, supervised the data analysis and critically revised the manuscript for important intellectual content. All authors have read the manuscript and agree that the work is ready for submission and accept the responsibility for the manuscript’s contents.

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**Conflict of interest**

None declared.

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