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Marie Tartaglia, Nathalie Costet, Sabyne Audignon-Durand, Camille Carles, Alexis d'Escatha, et al.. Profiles of the maternal occupational exposome during pregnancy and associations with intrauterine growth: analysis of the French Longitudinal Study of Children – ELFE study. Environmental Research, 2024, pp.120669. 10.1016/j.envres.2024.120669. hal-04870799

HAL Id: hal-04870799 https://hal.science/hal-04870799v1

Submitted on 7 Jan 2025

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Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres





Profiles of the maternal occupational exposome during pregnancy and associations with intrauterine growth: Analysis of the French Longitudinal Study of Children – ELFE study

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ARTICLE INFO

Keywords:
Occupational exposome
Multi-exposure
Pregnancy
Small for gestational age
Birthweight
Head circumference

ABSTRACT

Background: Numerous agents in the workplace are suspected of impairing fetal growth. To date, no epidemiological studies have specifically described the occupational exposome during pregnancy.

Objective: The objectives were to determine maternal occupational exposome profiles and study their associations with intrauterine growth characteristics measured by small for gestational age (SGA), birthweight (BW), and head circumference (HC).

Methods: We used data from the French national ELFE cohort. Occupational exposures to 47 agents (chemical, physical, biological, biomechanical, organizational and psychosocial), were identified using job exposure matrices. Mothers were classified as occupationally not exposed, uncertainly exposed, or exposed depending on their probability of exposure. Outcomes of interest were BW, SGA and HC. Maternal profiles of the occupational exposome were determined using hierarchical clustering of principal components. Associations between profiles and intrauterine growth outcomes were studied using linear or logistic regression models adjusted for potential confounders. Analyses were carried out depending on whether mothers stopped working during pregnancy.

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Results: The 12,851 included women were exposed to a median of 6 factors. Four occupational exposome profiles were identified, characterized by "low exposure, stress at work"; "strenuous, high organization, low decision"; "postural constraints, psychosocial factors", "postural and strength constraints, chemical and biological factors". In multivariate analyses, and among women who stopped working during the third trimester of pregnancy, analyses found associations between the profile "postural constraints, psychosocial factor" and SGA, and HC. None of the other exposure profiles were statistically significantly associated with foetal growth outcomes. Conclusion: The results show that the specific profile "postural constraints, psychosocial factors" may increase the risk of foetal growth retardation. Although these results need to be replicated, this study provides a first better understanding of the exposome of pregnant women at the workplace which may help to better adapt prevention strategies.

1. Introduction

Although pregnancy is a physiological process, adverse effects especially intra-uterine growth retardation including small for gestational age (SGA), reduced birthweight (BW) and decreased head circumference (HC), may occur. Reduced BW and SGA are of particular interest, as these are associated with short-to-longer term effects (Cinelli et al., 2021; Birks et al., 2016). Short-term effects include increased neonatal mortality (term or preterm), anoxoischemia in term newborns, poor adaptation to extrauterine life, hypothermia and hypoglycemia, bronchopulmonary dysplasia, pulmonary hypertension and enteropathy in preterm newborns. The longer-term consequences of SGA are a lower neurodevelopmental score at two years of age, an increased risk of hyperactivity and/or inattention at age five, and academic difficulties at age eight (Sentilhes et al., 2022). In addition, HC is also an important parameter to consider, as it reflects brain volume and in-utero brain development (Barbier et al., 2013).

A study conducted in 13 European birth cohorts showed that 80.2% of women worked during pregnancy (Casas et al., 2015). It's nearly 70% in France in 2011 and thus could be exposed to various occupational factors, such as chemical, physical, biological, biomechanical, organizational or psychosocial agents (Cinelli et al., 2021). Some of these occupational exposures during pregnancy could put women at risk (Delva et al., 2020; Teysseire et al., 2019). To date, the literature for SGA and reduced BW reported significant adverse associations with occupational exposures to solvents (Ahmed and Jaakkola, 2007; Enderle et al., 2023), ultrafine particles (UFP) (Manangama et al., 2019, 2020) pesticides (Shirangi et al., 2020; Mayhoub et al., 2014), polycyclic aromatic hydrocarbons (PAHs) (Langlois et al., 2014), electromagnetic fields (Migault et al., 2020), standing (Croteau et al., 2006), carrying loads (Kwegyir-Afful et al., 2018), and intensity of physical effort (Vrijkotte et al., 2009; Bonzini et al., 2007) whereas inconsistent results were reported with other occupational exposures such as noise (Selander et al., 2019; Nurminen and Kurppa, 1989), shift work, night work (Croteau et al., 2006; Davari et al., 2018; Suzumori et al., 2020), and job strain (Croteau et al., 2006; Niedhammer et al., 2009; Arafa et al., 2007; Loomans et al., 2013). Some other factors, such as sitting (Shirangi et al., 2020; Vrijkotte et al., 2009; Pompeii et al., 2005), endocrine disruptors (Shirangi et al., 2020), and vibrations (Skröder et al., 2021), have been studied, but no significant association were found with SGA. Regarding HC, far fewer studies have been published, showing that UFP (Manangama et al., 2020), solvents (Enderle et al., 2023), standing (Bonzini et al., 2009; Snijder et al., 2012a) and number of hours worked per week at 11 or 19 weeks of gestation were associated with a decreased HC (Bonzini et al., 2009). Carrying loads (Bonzini et al., 2009; Snijder et al., 2012b; Croteau, 2020) and night work (Bonzini et al., 2009) were also studied but no significant association were found.

Most previous studies have only considered one exposure at a time. Some studies tried to take co-exposures into account although only partially, by adjusting their analyses for other occupational factors when studying a specific class of exposures (Shirangi et al., 2020; Croteau et al., 2006; Selander et al., 2019; Skröder et al., 2021; Snijder et al.,

2012a; Norlén et al., 2019a, 2019b; Vaktskjold et al., 2007); and only one study was interested in co-exposure of job strain and load handling for SGA, by integrating an interaction term in the analysis (Sejbaek et al., 2018). Current approaches have generally not considered the issue of multiple exposures which nevertheless represents the reality of occupational situations. However, to understand the complexity of exposures at the workplace, it is necessary to better characterize the occupational exposome during pregnancy (Roquelaure et al., 2022; Pronk et al., 2022). Indeed, there is a lack of comprehensive data providing an overview of current occupational exposures among pregnant women especially considering mixed exposure in the workplace (Grossesse et travail).

The first objective of our study was to determine the profiles of the maternal occupational exposome during pregnancy, including various factors, such as chemical, physical, biological, biomechanical, organizational and psychosocial factors during pregnancy, without any a priori hypothesis on these occupational exposures studied. The second objective was to study the association between these profiles and intrauterine growth especially SGA, BW, and HC.

2. Methods

2.1. Population study

The ELFE (French Longitudinal Study of Children) cohort is the first French national study dedicated to monitoring children, from birth to adulthood. The methodology of the ELFE cohort was previously described in detail (Charles et al., 2020). Briefly, a stratified sampling approach was employed, considering the size of each maternity facility, to facilitate oversampling in large maternity units. Maternity hospitals were selected based on a two-stage stratified random sampling plan. First, maternity wards located in metropolitan France were randomly selected at the national level from a sampling base stratified by the institution's status (private/public) and according to the number of births per year and region. After excluding maternity hospitals with fewer than 365 births per year, 349 wards were randomly selected from a total of 542 across France. Among the 349 selected, 320 wards agreed to participate in the study (Charles et al., 2020). Recruitment took place in the following periods in 2011: 1 to 4 April, 27 June to 4 July, 27 September to 4 October, 28 November to 5 December. Single or multiple live births >33 weeks of gestation, mothers whose age was >18 years, who did not plan to leave France within three years, and who had signed an informed consent, were included in the study. Because 59 families requested the destruction of their data, 18,270 children were included in the ELFE cohort follow-up.

The population of this study excluded multiple pregnancies (n=574), major congenital malformation (n=377), as defined by the European surveillance of congenital anomalies ("European Platform on Rare Disease Registration"), and mothers who did not work during their pregnancies (n=4,137).

The ELFE study was approved by the Consultative Committee for the Treatment of Information in Health Research (CCTIRS), the National Commission for Data Protection and Liberties (CNIL), and the

Committee for the Protection of Persons (CPP). The study was also endorsed by the National Council for Statistical Information (CNIS).

2.2. Data collection

Socio-demographic data were collected at the maternity facility through face-to-face interviews, while medical data were collected from medical records. Information on women's occupation during pregnancy, including job title, was collected in the face-to-face interviews at the maternity stay and also completed with a two-month questionnaire. More details are available at: https://www.elfe-france.fr/en.

2.3. Assessment of occupational exposures

Occupational exposures examined here were characterized with jobexposure matrices (JEM) linked to maternal jobs on the basis of a common job coding system. All mothers included in this study held only one job during their pregnancy. They were coded to the 4-digit level, by one expert, according to the International Standard Classification of Occupations (ISCO-1968 and ISCO-1988) and the French classification of professions and socioprofessional categories (PCS-2003). Industry activities were coded according to the International Standard Industrial Classification of All Economic Activities (ISIC-1975) and the French nomenclature of activities (NAF-2003). We used 13 JEMs to assess the occupational exposure of pregnant women (Table 1). Occupational exposures that can be characterized by JEMs constructed in the general population, preferably in the French (or European) population, and for which hypotheses exist about impact on pregnancy, were chosen. Specifically, we evaluated: 1) chemical factors (solvents (chlorinated (Dananché and Févotte, 2009), oxygenated (Dananché et al., 2015) and petroleum solvents (Pilorget et al., 2007)), detergents (Kauppinen et al., 2014), pesticides (Carles et al., 2018), heavy metals (arsenic, cadmium, chromium, iron, lead, nickel (Kauppinen et al., 2014)), ultrafine particles (Audignon-Durand et al., 2021), welding fumes (Kauppinen et al., 2014), polycyclic aromatic hydrocarbons (benzo(a)pyrene (Kauppinen et al., 2014)), gas (carbon monoxide (Kauppinen et al., 2014)), endocrine disruptor and other chemicals (Brouwers et al., 2009)), 2) physical factors (ionizing radiation (Sauvé et al., 2018), low frequency magnetic fields (Kauppinen et al., 2014), intermediate frequency (IFELF, IFRF), radiofrequency (RF) (Migault et al., 2019), ultraviolet (Kauppinen et al., 2014), 3) biological factors (airborne germs (Descatha et al., 2021), cytomegalovirus, parvovirus B19, hepatitis A, E, B, C, human immunodeficiency virus (Base de données EFICATT)), 4) strenuous factors (strength: intensity of physical efforts, carrying loads 10-25 kg, load handling >4 kg; posture: arms in the air above the shoulders, standing, to kneel or squat, to lean forward or sideways, to repeat the same actions; vibration: to use vibrating tools, to drive construction machinery, to drive a vehicle; to use of a computer screen or control panel (Evanoff et al., 2019)), 5) organizational factors (night work (Houot et al., 2022), interruption of tasks, work outdoors (Evanoff et al., 2019)) and 6) psychosocial factors (low decision authority, high job demands, high strain (Almroth et al., 2021)). For each exposure we built a categorical exposure variable in three categories mainly according to probability, since it was the most frequently used metric in the literature and in the JEMs used in the present work. If probability was not available, we used intensity or frequency of exposure to assess exposure (Table 1).

2.4. Outcomes

We studied three outcomes, available in the ELFE cohort, that reflect the health of newborn at birth: BW, SGA and HC. BW corresponds to the weight of the newborn at birth, expressed in grams. SGA was defined as a birthweight under the 10th percentile for gestational age and sex, by using the WHO curves (de Onis et al., 2007; Verspyck et al., 2022). Severe small for gestational age, was defined as a birthweight under the third percentile for gestational age and sex. HC is the fronto-occipital

circumference measured at birth, expressed in centimetres.

2.5. Statistical analysis

Clustering can be used to identify specific population subgroups that share a similar exposure profile (Gibson et al., 2019; Stafoggia et al., 2017). To answer the first objective, Hierarchical Clustering on Principal Components (HCPC) was performed using Multiple Correspondence Analysis (MCA) as a pre-processing step before performing clustering. By retaining only the first dimensions of the factor analysis, the classification provided more statistical stability and robustness to the clustering process, thus minimizing the risk of individual misclassification. The partition of HCPC was performed according to the Euclidean distance between observations, and Ward's algorithm which maximizes inter-class inertia (at each aggregation) to obtain the most homogeneous classes possible. The decision was made to use the partition with the highest relative inertia loss. Initially, the algorithm considers each individual as a separate class, and iteratively groups the most similar subjects pairwise until a certain number of homogeneous classes of individuals is achieved. Since these profiles are unstable, the partition was consolidated using k-means to increase the homogeneity of the profiles.

Missing data on occupational exposures were imputed using a 10-dimensional MCA factor. The imputation model contains occupations, ISCO-1968 code and NAF-2003 code, all the occupational exposure variables, and education level.

To answer the second objective, logistic regression models were performed to study the association between occupational profiles and SGA; and linear regression for BW and HC. The profile with the least exposure was chosen as the reference profile. Based on a directed acyclic graph (DAG) (Appendix A), models were adjusted for pre-pregnancy BMI (<18.5 kg/m², 18.5-<25.0 kg/m², 25.0-<30.0 kg/m², \geq 30 kg/m²), tobacco (yes, no) and alcohol (continuous, number of glasses per day) consumption during pregnancy for analysis on SGA. In addition, for analysis on BW and HC we additionally adjusted for gestational age (continuous) and infant's sex (female, male) strong determinants of intrauterine growth. These variables were not included for SGA analysis since these factors are already considered in the construction of this outcome variable. Results were presented as Odds Ratios (OR) and their 95% confidence interval (95%CI) for logistic regressions; and beta (95% CI) for linear regression.

We performed additional analysis stratifying on maternal leave: depending on whether mothers stopped working during pregnancy (first, second or third trimester). We also performed sensitivity analysis adjusted, in addition, for educational level (low, high school, university), as suggested in the study of Richiardi et al. (2008), another one for the HC adjusted in addition on mode of delivery (vaginal delivery, caesarean), and finally, one excluding mothers with gestational diabetes and gestational hypertension.

The analyses were performs using R Core Team (2023) software, using the packages FactoMineR (Lê et al., 2008), missMDA (Josse and Husson, 2016) and epiDisplay (Chongsuvivatwong, 2022).

3. Results

3.1. Population

Among the 18,329 women who participated in the ELFE cohort, 12,851 constituted our study population (Appendix B). Comparisons between included and excluded participants are presented in Appendix C. The mean maternal age at inclusion was 31.1 years (SD = 4.7). The majority of mothers were French (n = 12,161; 95.5%), and over two-thirds had higher education degrees (n = 8,863; 69.2%). Before their pregnancy, the women mostly had a normal BMI (n = 8,604; 67.9%) and a small proportion presented with a history of diabetes (n = 115; 0.9%) or chronic hypertension (n = 284; 2.3%). Just under 20% of mothers were smokers (n = 2,279; 17.9%) or consumed alcohol (n = 2,077;

 Table 1

 Assessment of maternal occupational exposures in the French National ELFE cohort.

Factors	Job exposure matrices or database	Construction	Occupations nomenclatures	Industry activities nomenclatures	Metrics	Temporal axis/Gender specific	Categorical exposure variable
1) Chemical factors							
Solvents Chlorinated solvents ^a	Matgéné – chlorinated solvents (JEM) France (Dananché and Févotte, 2009)	Experts	ISCO-1968 PCS-1994	NAF-2000° CITI-1975	Probability Frequency Intensity	Yes 1950–2007/ No	Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability
Oxygenated solvents ^b	Matgéné – oxygenated solvents (JEM) France (Dananché et al., 2015)	Experts	ISCO-1968 PCS-1994	NAF-2000°	Probability Frequency Intensity	Yes 1950–2012/ No	>50% Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50%
Petroleum solvents	Matgéné – petroleum solvents (JEM) France (Pilorget et al., 2007)	Experts	ISCO-1968 PCS-1994	CITI-1975 NAF-2000 ^c	Probability Frequency Intensity	Yes 1947–2005/ No	Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50%
Detergents	FinJEM (JEM) Finland (Kauppinen et al., 2014)	Experts	ISCO-1988	-	Probability Intensity	Yes 1945–2015/ No	Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50%
Pesticides	Pestipop (JEM) France (Carles et al., 2018)	Experts Questionnaires	PCS-2003	NAF-2003	Probability Frequency	No/No	Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50%
Heavy metals Arsenic Cadmium Chromium Iron Lead Nickel	FinJEM (JEM) Finland (Kauppinen et al., 2014)	Experts	ISCO-1988	-	Probability Intensity	Yes 1945–2015/ No	Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50%
Ultrafine particles	MatPUF (JEM) France (Audignon-Durand et al., 2021)	Experts	ISCO-1968	NAF-2000°	Probability Frequency	Yes 1950–2014/ No	Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50%
Welding fumes	FinJEM (JEM) Finland (Kauppinen et al., 2014)	Experts	ISCO-1988	-	Probability Intensity	Yes 1945–2015/ No	Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50%
Polycyclic aromatic polycarbon Benzo a pyrene	FinJEM (JEM) Finland (Kauppinen et al., 2014)	Experts	ISCO-1988	-	Probability Intensity	Yes 1945–2015/ No	Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50%
Gas Carbon monoxide	FinJEM (JEM) Finland (Kauppinen et al., 2014)	Experts	ISCO-1988	-	Probability Intensity	Yes 1945–2015/ No	Not exposed: probability 0% Uncertain: probability between 0 and 50% (continued on next page)

Table 1 (continued)

DC (JEM) nited Kingdom (rouwers et al., 2009) ANJEM (JEM) anada (Sauvé et al., 018) inJEM (JEM) inland (Kauppinen et al., 014) F-JEM (JEM) rance, UK, New Zealand, ermany, Israel, USA and anada (Migault et al., 019)	Experts Experts Experts Literature-based measurement data and study participant questionnaire information	ISCO-1988 ISCO-1968 CCDO-1971 NOC-2011 SOC-2010 ISCO-1988	-	Probability Probability Intensity Frequency Probability Intensity Probability Intensity	Yes 1920-2005/ No Yes 1945-2015/ No	Exposed: probability >50% Not exposed: probability 0% Uncertain: probability between 0 and 10% Exposed: probability >10% Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50% Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50% Not exposed: probability between 0 and 50% Exposed: probability >50% Not exposed:
anada (Sauvé et al., 2018) in JEM (JEM) inland (Kauppinen et al., 2014) F-JEM (JEM) rance, UK, New Zealand, 2019, 2019 in JEM (JEM) rance, UK, New Zealand, 2019)	Experts Literature-based measurement data and study participant questionnaire	CCDO-1971 NOC-2011 SOC-2010	_	Intensity Frequency Probability Intensity Probability	1920–2005/ No Yes 1945–2015/ No	probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50% Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50% Not exposed:
anada (Sauvé et al., 2018) in JEM (JEM) inland (Kauppinen et al., 2014) F-JEM (JEM) rance, UK, New Zealand, 2019, 2019 in JEM (JEM) rance, UK, New Zealand, 2019)	Experts Literature-based measurement data and study participant questionnaire	CCDO-1971 NOC-2011 SOC-2010	-	Intensity Frequency Probability Intensity Probability	1920–2005/ No Yes 1945–2015/ No	probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50% Not exposed: probability 0% Uncertain: probability between 0 and 50% Exposed: probability >50% Not exposed:
inland (Kauppinen et al., 014) F-JEM (JEM) rance, UK, New Zealand, ermany, Israel, USA and anada (Migault et al., 019)	Literature-based measurement data and study participant questionnaire		-	Intensity Probability	1945–2015/ No Yes	Not exposed: probability 0% Uncertain: probability betweer 0 and 50% Exposed: probability >50% Not exposed:
rance, UK, New Zealand, ermany, Israel, USA and anada (Migault et al., 019)	measurement data and study participant questionnaire	ISCO-1988	-	•		Not exposed:
**************************************					No	probability 0% Uncertain: probability between 0 and 50% Exposed: probabilit >50%
inJEM (JEM) inland (Kauppinen et al., 014)	Experts	ISCO-1988	-	Probability Intensity	Yes 1945–2015/ No	Not exposed: probability 0% Uncertain: probability betwee 0 and 50% Exposed: probabilit >50%
lat O Covid (JEM) rance (Descatha et al., 021)	Experts	PCS-2003 ISCO-2008	-	Probability	No/No	Not exposed: probability 5% Uncertain: probability betwee 5 and 50% Exposed: probability 50%
ficatt (database) rance (Base de données FICATT)	Experts	ISCO-1968	_	Exposed/ Not exposed	No/No	Not exposed Exposed
EM Constances (JEM) rance (Evanoff et al., 019)	Questionnaires	PCS-2003	-	Bias corrected mean	No/No	For intensity of physical efforts: Not exposed: no physical effort Uncertain: extreme light, very light, lig Exposed: slightly difficult, challengin very difficult, extremely difficult, exhausting For others factors: Not exposed: almosnever Uncertain: rarely Exposed: often, almost always
fi Fi EE	catt (database) ance (Base de données ICATT) M Constances (JEM) ance (Evanoff et al.,	catt (database) cate (Base de données ICATT) Experts M Constances (JEM) cate (Evanoff et al.,	catt (database) Experts ISCO-1968 ance (Base de données ICATT) M Constances (JEM) Questionnaires PCS-2003 ance (Evanoff et al.,	catt (database) Experts ISCO-1968 – ance (Base de données ICATT) M Constances (JEM) Questionnaires PCS-2003 – ance (Evanoff et al.,	ance (Descatha et al., 21) catt (database) Experts ISCO-1968 - Exposed/ Not exposed ICATT) M Constances (JEM) Questionnaires PCS-2003 - Bias corrected	ISCO-2008 ISCO-2008 ISCO-2008 ISCO-2008 ISCO-2008 ISCO-2008 ICATT ISCO-2008 ISCO-

Table 1 (continued)

Factors	Job exposure matrices or database	Construction	Occupations nomenclatures	Industry activities nomenclatures	Metrics	Temporal axis/Gender specific	Categorical exposure variable
Arms in the air above the shoulders Standing To kneel or squat To lean forward or sideways To repeat the same actions	JEM Constances (JEM) France (Evanoff et al., 2019)	Questionnaires	PCS-2003	-	Bias corrected mean	No/No	Not exposed: almost never Uncertain: rarely Exposed: often, almost always
Vibration To use vibrating tools To drive construction machinery To drive a vehicle	JEM Constances (JEM) France (Evanoff et al., 2019)	Questionnaires	PCS-2003	-	Bias corrected mean	No/No	Not exposed: almost never Uncertain: rarely Exposed: often, almost always
To use of a computer screen or control panel	JEM Constances (JEM) France (Evanoff et al., 2019)	Questionnaires	PCS-2003	-	Bias corrected mean	No/No	Not exposed: almost never Uncertain: rarely Exposed: often, almost always
5) Organizational fac	tors						
Night work	Matgéné – night work (JEM) France (Houot et al., 2022)	Questionnaires	PCS-1982 PCS-2003	NAF-1993 NAF-2003 NAF-2008	Probability	Yes 1993–2017/ Yes	Not exposed: no or 0% Exposed: yes (ELFE data) or >50% (JEM data when missing data)
Interruption of tasks Work outdoors	JEM Constances (JEM) France (Evanoff et al., 2019)	Questionnaires	PCS-2003	-	Bias corrected mean	No/No	For others factors: Not exposed: almost never Uncertain: rarely Exposed: often, almost always
6) Psychosocial factor	rs						
Low decision authority High job demands High strain	Swedish psychosocial JEM (JEM) Sweden (Almroth et al., 2021; Solovieva et al., 2022)	Questionnaires	SSYK-1996	-	Intensity	No/Yes	For low decision authority, high job demands: Not exposed: low Uncertain: medium, medium low Exposed: high, medium high For high strain: Not exposed: low Uncertain: passive Exposed: high, active Exposed: high, active

^a Chlorinated solvents: at least one of these five factors (trichloroethylene, tetrachloroethylene, dichloromethane, tetrachloromethane, and trichloromethane).

18.7%). The average duration of work during pregnancy was 27 weeks (SD = 7.9 weeks), with 57.3% (n = 7,179) of mothers stopping work in the third trimester, 32.5% (n = 4,074) in the second trimester, and 10.2% (n = 1,283) in the first trimester. Workplace adjustments were made for 15.1% (n = 1,663) of them. Mean gestational age at birth was 39.3 weeks (SD = 1.4). The mean birthweight was 3,338.8 g (SD = 471.3), and 8.6% of infants were SGA. The mean HC was 34.4 cm (SD = 1.4) (Table 2).

3.2. Occupational characteristics during pregnancy

The occupation groups of the mothers during pregnancy were predominantly professional, technical and related workers (41.2%), followed by clerical and related workers (23.9%), service workers (16.6%), sales workers (11.1%), managerial workers (3.6%), production workers (3.1%), and agricultural workers (0.8%) (Appendix D, Table 1).

Mothers were exposed to a median of 6 occupational exposure factors (min = 1, max = 17). Virtually all (99.9%) of mothers were multi-exposed, with all mothers exposed to at least one postural factor, 70.6% to at least one psychosocial factor, 47.4% to at least one strength factor,

^b Oxygenated solvents: at least one of these five factors (alcohols, ethylene glycol, ketones/esters, diethyl ether, and tetrahydrofuran).

^c Fuels and petroleum based solvents: at least one of these five factors (benzene, special petroleum products and other aliphatic petroleum based solvents, gasoline, white spirit and aliphatic petroleum based solvents, and kerosene/fuels oils/diesel oil).

^d Endocrine disrupters and other chemicals: at least one of these factors (polycyclic aromatic hydrocarbons, polychlorinated organic compounds, pesticides, phthalates, organic solvents, bisphenol A, alkylphenolic compounds, brominated flame retardants, metals (arsenic, cadmium, copper, lead, and mercury), and others (benzophenones, parabens, and siloxanes)).

^e This is the 2000 version of NAF, which was introduced in 1993.

 $^{^{\}mathrm{f}}$ For night work, exposure data were collected from ELFE questionnaires. Where data was missing (n = 3,194), it was replaced by data from the JEM.

Table 2 Characteristics of the population. ELFE study, France, n=12,851.

	N = 12,851	
	n (%)	Mean (SD ^a)
Socio economic		
Maternal age (years)		31.1 (4.7)
< 27	2,464 (19.3)	, ,
[27–30[2,897 (22.6)	
[30–34[4,043 (31.6)	
≥ 34	3,395 (26.5)	
Unknown	52	
Mother's nationality		
French	12,161 (95.5)	
Foreign	571 (4.5)	
Stateless	4 (0.0)	
Unknown	115	
Maternal education level ^b		
Low	249 (1.9)	
High school	3,692 (28.8)	
University	8,863 (69.2)	
Unknown	47	
In a relationship	12,287 (96.5)	
Unknown	120	
Marital status		
Celibate	4,474 (35.6)	
Partner	2,221 (17.7)	
Married	5,733 (45.7)	
Divorced	116 (0.9)	
Widow	13 (0.1)	
Unknown	294	
Monthly household income (euros)		
< 2500	2,289 (18.9)	
2500-4000	6,713 (55.5)	
> 4000	3,095 (25.6)	
Unknown	754	
efore pregnancy		
Body mass index (kg/m ²) <18.5	932 (7.4)	
[18.5–25.0[
[25.0–30.0[8,573 (67.6)	
≥30	2,116 (16.7)	
_	1,052 (8.3) 178	
Unknown		
Diabetes (type 1 or 2) Unknown	115 (0.9) 371	
Chronic high blood pressure	284 (2.3)	
Unknown	268	
	200	
During pregnancy		
Parity		
Primiparous	6,153 (48.3)	
Multiparous	6,587 (51.7)	
Unknown	111	
Number of deliveries		1.4 (0.7)
Unknown	6,857	
Hypertensive disorders	405 (3.2)	
Unknown	360	
Preeclampsia	149 (1.2)	
Unknown	360	
Smoking	2,279 (17.9)	
Unknown	136	
Alcohol consumption		
No	9,024 (81.3)	
< 1 glass per month	1,637 (14.7)	
≥ 1 glass per month	440 (4.0)	
Unknown	1,750	
Stopping the professional activity	-	
	1,283 (10.2)	
First trimester		
First trimester Second trimester		
First trimester Second trimester Third trimester	4,074 (32.5)	
Second trimester Third trimester		
Second trimester Third trimester Unknown	4,074 (32.5) 7,179 (57.3)	27,4 (7.9)
Second trimester Third trimester Unknown Duration of work (weeks)	4,074 (32.5) 7,179 (57.3) 315	27.4 (7.9)
Second trimester Third trimester Unknown Duration of work (weeks) Unknown	4,074 (32.5) 7,179 (57.3) 315 376	27.4 (7.9)
Second trimester Third trimester Unknown Duration of work (weeks) Unknown Hospitalization	4,074 (32.5) 7,179 (57.3) 315 376 1,857 (14.6)	27.4 (7.9)
Second trimester Third trimester Unknown Duration of work (weeks) Unknown	4,074 (32.5) 7,179 (57.3) 315 376	27.4 (7.9)

Table 2 (continued)

	N = 12,851	
	n (%)	Mean (SD ^a)
Unknown	1,828	
Childbirth		
Gestational age (weeks of gestation)		39.3 (1.4)
Unknown	200	
Mode of delivery		
Caesarean	2,141 (17.1)	
Vaginal delivery	10,376 (82.9)	
Unknown	334	
Infant's sex		
Female	6,283 (49.3)	
Male	6,458 (50.7)	
Unknown	110	
Birthweight (in grams)		3,338.8 (471.3
Unknown	272	
Small for gestational age ^c	1,084 (8.6)	
Severe small for gestational age ^c	407 (3.2)	
Unknown	287	
Head circumference (in centimetres)		34.4 (1.4)
Unknown	1,439	

^a SD: standard deviation.

39.5% to at least one biological factor, 33.2% to at least one chemical factor, 12.6% to at least one physical factor, and 8.5% to at least one vibration factor.

The chemical factors to which mothers were most exposed during pregnancy were oxygenated solvents (20.3%) and detergents (17.7%). Concerning the physical factors, 10% of women were exposed to lowfrequency electromagnetic fields. Among the biological factors to which mothers were exposed, a third of population were exposed to airborne germs (33.3%). We also found frequent exposure to cytomegalovirus/parvovirus B19 (17.3%) and hepatitis B/C (15.4%). Concerning postural factors, using a computer screen or control panel (66.6%) and standing (58.5%) were the factors to which mothers were most exposed. For strength factors, the most frequent factor was intensity of physical efforts (47.5%). Regarding organizational factors, 57.8% were exposed to interruption of tasks and less than 10% to night work. Finally, concerning psychosocial factors, 51.8% were exposed to high strain, 40% to high job demands, and 40.1% to low decision authority (Table 3). Correlations between occupational exposures studied are presented in Appendix E.

3.3. Clustering

The MCA allowed for reduction of the number of data dimensions. HCPC was carried out on the 25 first dimensions of MCA, explaining 73.9% of variability. Dendrogram, projection of the profiles on the factorial plane formed by the first two axes, as well as the representation of the hierarchical tree on the factorial plane, are presented in appendix F. Characteristics of the four profiles identified are presented in Table 4 and Appendix G.

The first profile "low exposure, stress at work" included 51.4% (n = 6,602) of the mothers in the population studied. Mothers in this profile have mostly attended university (85.1%), and 22.1% were office workers. They were exposed to five categories of factors: physical, biological, postural, organizational and psychosocial factors. Nearly all mothers were exposed to use of a computer screen or a control panel (94.7%), interruption of task (82.3%), low decision authority (67.3%),

^b Lower defined as never attended school, primary and middle school; High school defined as certificate of vocational aptitude, professional qualifications, high school; University defined as higher education.

^c Small for gestational age defined as a birthweight under the 10th percentile for gestational age and sex, by using the WHO curves. Severe small for gestational age, was defined as a birthweight under the third percentile for gestational age and sex.

Table 3 Description of occupational exposure of women during pregnancy. ELFE study, France, n=12.851.

	Not exposed n (%)	Uncertain n (%)	Exposed n (%)	Missing
Chemical factors				
Solvents				
Chlorinated	12,275	178 (1.4)	10 (0.1)	388
Oxygenated	(98.5) 9,592	289 (2.4)	2,520	450
Petroleum	(77.3) 11,573	778 (6.3)	(20.3) 37 (0.3)	463
Detergents	(93.4) 9,024	1,202 (9.6)	2,193	432
Pesticides	(72.7)	545 (5.2)	(17.7)	2,461
	9,765 (94.0)	343 (3.2)	80 (0.8)	2,401
Heavy metals				
Arsenic	12,624	16 (0.1)	0	211
	(99.9)			
Cadmium	12,505	115 (0.9)	0	231
	(99.1)			
Chromium	12,438	199 (1.6)	0	214
	(98.4)	100 (1.4)	0 (0 0)	010
Iron	12,456	180 (1.4)	2 (0.0)	213
Lead	(98.6) 12,315	291 (2.3)	0	245
Lead	(97.7)	291 (2.3)	O	243
Nickel	12,450	186 (1.5)	0	215
	(98.5)	()	-	
Ultrafine particles	9,527	1,610	689 (5.8)	1,025
•	(80.6)	(13.6)	, ,	,
Welding fumes	12,456	180 (1.4)	2 (0.0)	213
	(98.6)			
Polycyclic aromatic	12,612	25 (0.2)	0	214
hydrocarbons	(99.8)			
Benzo(a)pyrene	12,628	16 (0.1)	0	214
	(99.9)			
Gas			_	
Carbon monoxide	11,039	1,231	0	578
Endonino diamentos and	(89.9)	(10.1)	E40 (4.4)	226
Endocrine disruptor and other chemicals	11,673 (93.3)	293 (2.3)	549 (4.4)	336
Physical factors	(93.3)			
Ionizing radiations	10,059	2,008	75 (0.6)	709
iomzing radiations	(82.8)	(16.5)	70 (0.0)	,0,
Low frequency magnetic	9,279	1,379	1,277	916
fields	(77.7)	(11.6)	(10.7)	
Non-thermal	10,511	972 (8.5)	0	1,368
intermediate frequency	(91.5)			-
Radiofrequency (E field)	1,299	10,161	23 (0.2)	1,368
	(11.3)	(88.5)		
Radiofrequency (H field)	1,700	9,775	8 (0.1)	1,368
	(14.8)	(85.1)		
Thermal intermediate	9,734	1,749	0	1,368
frequency (E field)	(84.8)	(15.2)		
Thermal intermediate	9,828	1,655	0	1,368
frequency (H field)	(85.6)	(14.4)	00 (0.7)	664
Ultraviolet	11,509	589 (4.9)	89 (0.7)	664
Biological factors	(94.4)			
Airborne germs	87 (0.7)	7,975	4,019	770
Amborne germs	07 (0.7)	(66.0)	(33.3)	770
Cytomegalovirus,	10,280	0	2,145	426
parvovirus B19	(82.7)		(17.3)	
Hepatitis A, E	11,512	0	919 (7.4)	420
* *	(92.6)		, ,	
Hepatitis B, C, human	10,517	0	1,914	420
immunodeficiency virus	(84.6)		(15.4)	
Strenuous factors				
Strength				
Intensity of physical	1,626	4,690	5,716	819
effort	(13.5)	(39.0)	(47.5)	
Carrying loads 10–25 kg	10,004	1,200 (9.9)	897 (7.4)	750
	(82.7)			

Table 3 (continued)

	Not exposed n (%)	Uncertain n (%)	Exposed n (%)	Missing
Load handling > 4 kg	7,628	2,199	2,222	802
	(63.3)	(18.3)	(18.4)	
Posture				
Arms in the air above the	8,861	1,763	1,631	596
shoulders	(72.3)	(14.4)	(13.3)	
Standing	2,632	2,354	7,037	818
	(21.9)	(19.6)	(58.5)	
To kneel or squat	6,572	2,526	3,054	699
	(54.1)	(20.8)	(25.1)	
To lean forward or	6,059	2,361	3,834	597
sideways	(49.4)	(19.3)	(31.3)	
To repeat the same	6,419	1,413	4,375	644
actions	(52.6)	(11.6)	(35.8)	
Vibration				
To use vibrating tools	11,945	427 (3.5)	105 (0.8)	374
_	(95.7)			
To drive construction	12,316	146 (1.1)	150 (1.2)	239
machinery	(97.7)			
To drive a vehicle	10,492	896 (7.3)	828 (6.8)	635
	(85.9)			
To use of a computer screen	2,187	1,862	8,073	729
or control panel	(18.0)	(15.4)	(66.6)	
Organizational factors				
Night work	9,046	0	876 (7.5)	1,172
Ü	(92.5)			,
Interruption of tasks	2,740	2,348	6,979	784
1	(22.7)	(19.5)	(57.8)	
Work outdoors	9,321	1,874	923 (7.6)	733
	(76.9)	(15.5)	- \	
Psychosocial factors	Ç	,		
Low decision authority	2,986	3,965	4,651	1,249
	(25.7)	(34.2)	(40.1)	,
High job demands	2,555	4,407	4,642	1,247
	(22.0)	(38.0)	(40.0)	-,- 17
High strain	2,504	3,092	6,008	1,247
	(21.6)	(26.6)	(51.8)	-,,

and high strain (56.6%). Mothers' exposure was uncertain regarding radiofrequency electric fields (88.1%), radiofrequency magnetic fields (83.2%), airborne germs (92.7%), and intensity of physical effort (73.1%). Approximately half were uncertainly exposed to demand (53.7%). Also, 60.9% of mothers who stopped working during the third trimester of pregnancy were in this profile.

The second profile "strenuous, high organization, low decision" comprised 1.5% (n = 199) of the mothers in the study population. Mothers in this profile have attended both high school (49.7%) and university (49.2%); they were primarily saleswomen (76.9%). They accumulated exposures across six categories: chemical, physical, biological, strenuous, organizational and psychosocial factors. Almost all mothers were exposed to standing posture (96.5%), intensity of physical effort (72.9%), repetition of tasks (65.8%), interruption of tasks (89.4%), leaning posture (69.3%), kneeling or squatting posture (58.3%), using a computer screen or a control panel (86.9%), arms above shoulders posture (68.3%), and low decision authority (91.0%). Mothers' exposure was uncertain regarding iron (90.5%), chromium (99.5%), lead (100.0%), nickel (92.0%), fumes (90.5%), low frequency electromagnetic fields (85.9%), radiofrequencies (99.0%), airborne germs (63.3%), load handling (57.8%), and demand (82.4%). Moreover, 53.7% of mothers stopped working during the third trimester of pregnancy.

The third profile "postural constraints, psychosocial factors" comprised 34.7% (n = 4,460) of the mothers in the study population. Most mothers in this profile had a high school education (50.3%), and 16.8% were teachers, 16.0% were cleaners and helpers, and 12.2% were saleswomen or shops assistants. They were exposed to six categories of factors: chemical, physical, biological, force, postural, and psychosocial factors. Almost all were exposed to intensity of physical effort (96.8%),

 $\label{eq:conditional} \textbf{Table 4} \\ \textbf{Occupational profiles characteristics of women during pregnancy. ELFE study, France, } n = 12,851. \\ \\ \textbf{Study}, \textbf{S$

Characteristics	Low exposure, stress at work $N = 6,602 \text{ n (}\%^{\text{a}}/$ $\%^{\text{b}})$	Strenuous, high organization, low decision $N=199~n~(\%^{a}/\%^{b})$	Postural constraints, psychosocial factors $N=4,460~n~(\%^a/\%^b)$	Postural and strength constraints, chemical, and biological factors $N=1{,}590~n~(\%^a/\%^b)$	Overall N = 12,851 n (%)
Childbirth					
Maternal age (years)	31.9 (4.3)	31.6 (5.0)	30.0 (5.0)	30.6 (4.6)	31.1 (4.7)
Unknown	29	0	15	8	52
Gestational age (weeks of	39.3 (1.4)	39.2 (1.5)	39.3 (1.4)	39.2 (1.4)	39.3 (1.4)
gestation)					
Unknown Birth weight (g)	120 3,342.8 (463.3)	1 3,327.6 (469.9)	60 3,337.1 (484)	19 3,328.5 (468.4)	200 3,338.8
bittii weigiit (g)	3,342.6 (403.3)	3,327.0 (409.9)	3,337.1 (404)	3,326.3 (406.4)	(471.3)
Unknown	140	3	102	27	272
Small for gestational age ^c	510 (7.9/47.0)	13 (6.7/1.2)	418 (9.6/38.6)	143 (9.1/13.2)	1,084 (8.6)
Severe small for	196 (3.0/48.2)	5 (2.6/1.2)	159 (3.7/39.1)	47 (3.0/11.5)	407 (3.2)
gestational age					
Unknown	149	5	106	27	287
Head circumference (cm) Unknown	34.5 (1.4) 769	34.3 (1.3) 21	34.4 (1.4) 496	34.4 (1.4) 153	34.4 (1.4) 1,439
	709	21	490	133	1,439
Occupational exposures					
Chemical factors Solvents					
Chlorinated					
Not exposed	6,548 (99.2/51.7)	198 (99.5/1.6)	4,327 (97.0/34.2)	1,590 (100.0/12.6)	12,663
	== (0.0 (0.0 0)	4 (0 = 10 5)	404 (0.0 (0.0 =)	0.00.00	(98.5)
Uncertain	53 (0.8/29.8)	1 (0.5/0.6)	124 (2.8/69.7)	0 (0.0/0.0)	178 (1.4)
Exposed Oxygenated	1 (0.0/10.0)	0 (0.0/0.0)	9 (0.2/90.0)	0 (0.0/0.0)	10 (0.1)
Not exposed	6,480 (98.2/64.8)	183 (92.0/1.8)	3,327 (74.6/33.3)	3 (0.2/0.0)	9,993 (77.8)
Uncertain	25 (0.4/8.6)	14 (7.0/4.8)	251 (5.6/86.6)	0 (0.0/0.0)	290 (2.3)
Exposed	97 (1.5/3.8)	2 (1.0/0.1)	882 (19.8/34.3)	1,587 (99.8/61.8)	2,568 (20.0)
Petroleum					
Not exposed	6,484 (98.2/53.9)	183 (92.0/1.5)	3,769 (84.5/31.3)	1,590 (100.0/13.2)	12,026
					(93.6)
Uncertain	117 (1.8/14.8)	3 (1.5/0.4)	668 (15.0/84.8)	0 (0.0/0.0)	788 (6.1)
Exposed Detergents	1 (0.0/2.7)	13 (6.5/35.1)	23 (0.5/62.2)	0 (0.0/0.0)	37 (0.3)
Not exposed	6,086 (92.2/65.4)	193 (97.0/2.1)	2,834 (63.5/30.5)	189 (11.9/2.0)	9,302 (72.4)
Uncertain	308 (4.7/25.4)	4 (2.0/0.3)	900 (20.2/74.2)	1 (0.1/0.1)	1,213 (9.4)
Exposed	208 (3.2/8.9)	2 (1.0/0.1)	726 (16.3/31.1)	1,400 (88.1/59.9)	2,336 (18.2)
Pesticides					
Not exposed	6,511 (98.6/53.3)	198 (99.5/1.6)	3,927 (88.0/32.1)	1,590 (100.0/13.0)	12,226
		4 (0 = (0 0)	1616010=1	0 (0 0 (0 0)	(95.1)
Uncertain	80 (1.2/14.7)	1 (0.5/0.2)	464 (10.4/85.1)	0 (0.0/0.0)	545 (4.2)
Exposed	11 (0.2/13.8)	0 (0.0/0.0)	69 (1.5/86.3)	0 (0.0/0.0)	80 (0.6)
Heavy metals Arsenic					
Not exposed	6,601 (100.0/51.4)	194 (97.5/1.5)	4,450 (99.8/34.7)	1,590 (100.0/12.4)	12,835
-					(99.9)
Uncertain	1 (0.0/6.3)	5 (2.5/31.3)	10 (0.2/62.5)	0 (0.0/0.0)	16 (0.1)
Cadmium	(500 (00 0 /51 0)	177 (00 4 (1 4)	4 447 (00 7 (04 0)	1 500 (100 0 (10 5)	10.706
Not exposed	6,523 (98.8/51.2)	176 (88.4/1.4)	4,447 (99.7/34.9)	1,590 (100.0/12.5)	12,736 (99.1)
Uncertain	79 (1.2/68.7)	23 (11.6/20.0)	13 (0.3/11.3)	0 (0.0/0.0)	115 (0.9)
Chromium	7 5 (1.2/00.7)	20 (11.0/20.0)	10 (0.0/11.0)	0 (0.0/ 0.0)	113 (0.5)
Not exposed	6,602 (100.0/52.2)	1 (0.5/0.0)	4,459 (100.0/35.2)	1,590 (100.0/12.6)	12,652
					(98.5)
Uncertain	0 (0.0/0.0)	198 (99.5/99.5)	1 (0.0/0.5)	0 (0.0/0.0)	199 (1.5)
Iron	((00 (100 0 /50 1)	17 (0.5 (0.1)	4.460.(100.0.(05.0)	1 500 (100 0 (10 6)	10.660
Not exposed	6,602 (100.0/52.1)	17 (8.5/0.1)	4,460 (100.0/35.2)	1,590 (100.0/12.6)	12,669 (98.6)
Uncertain	0 (0.0/0.0)	180 (90.5/100.0)	0 (0.0/0.0)	0 (0.0/0.0)	180 (1.4)
Exposed	0 (0.0/0.0)	2 (1.0/100.0)	0 (0.0/0.0)	0 (0.0/0.0)	2 (0.0)
Lead					•
Not exposed	6,589 (99.8/52.5)	0 (0.0/0.0)	4,381 (98.2/34.9)	1,590 (100.0/12.7)	12,560
	40.000.44	400 (400 0 (60))	== (1 = 10 = 1)	0.40.0.40.03	(97.7)
	13 (0.2/4.5)	199 (100.0/68.4)	79 (1.8/27.1)	0 (0.0/0.0)	291 (2.3)
Uncertain			4,457 (99.9/35.2)	1,590 (100.0/12.6)	12,665
Nickel	6 602 (100 0 /52 1)	16 (8 0/0 1)			
	6,602 (100.0/52.1)	16 (8.0/0.1)	4,437 (99.9/33.2)	1,000 (10010, 1210)	
Nickel	6,602 (100.0/52.1) 0 (0.0/0.0)	16 (8.0/0.1) 183 (92.0/98.4)	3 (0.1/1.6)	0 (0.0/0.0)	(98.6)
Nickel Not exposed					

(continued on next page)

Table 4 (continued)

Characteristics	Low exposure, stress at work $N = 6,602 \text{ n (}\%^{\text{a}}/$ $\%^{\text{b}})$	Strenuous, high organization, low decision $N=199~n~(\%^a/\%^b) \label{eq:N}$	Postural constraints, psychosocial factors $N=4,460~n~(\%^a/\%^b)$	Postural and strength constraints, chemical, and biological factors $N=1{,}590~n~(\%^{\text{a}}/\%^{\text{b}})$	Overall N = 12,851 n (%)
Uncertain	249 (3.8/15.1)	1 (0.5/0.1)	1,305 (29.3/79.0)	97 (6.1/5.9)	1,652 (12.9)
Exposed Welding fumes	278 (4.2/39.5)	22 (11.1/3.1)	380 (8.5/54.1)	23 (1.4/3.3)	703 (5.5)
Not exposed	6,602 (100.0/52.1)	17 (8.5/0.1)	4,460 (100.0/35.2)	1,590 (100.0/12.6)	12,669 (98.6)
Uncertain Exposed	0 (0.0/0.0) 0 (0.0/0.0)	180 (90.5/100.0) 2 (1.0/100.0)	0 (0.0/0.0) 0 (0.0/0.0)	0 (0.0/0.0) 0 (0.0/0.0)	180 (1.4) 2 (0.0)
Polycyclic aromatic hydrocai Not exposed	rbons 6,601 (100.0/51.5)	177 (88.9/1.4)	4,458 (100.0/34.8)	1,590 (100.0/12.4)	12,826
Uncertain	1 (0.0/4.0)	22 (11.1/88.0)	2 (0.0/8.0)	0 (0.0/0.0)	(99.8) 25 (0.2)
Benzo(a)pyrene Not exposed	6,601 (100.0/51.4)	194 (97.5/1.5)	4,450 (99.8/34.7)	1,590 (100.0/12.4)	12,835 (99.9)
Uncertain Gas	1 (0.0/6.3)	5 (2.5/31.3)	10 (0.2/62.5)	0 (0.0/0.0)	16 (0.1)
Carbon monoxide					
Not exposed	5,732 (86.8/49.3)	193 (97.0/1.7)	4,103 (92.0/35.3)	1,589 (99.9/13.7)	11,617 (90.4)
Uncertain	870 (13.2/70.7)	6 (3.0/0.5)	354 (7.9/28.8)	1 (0.1/0.1)	1,231 (9.6)
Exposed	0 (0.0/0.0)	0 (0.0/0.0)	3 (0.1/100.0)	0 (0.0/0.0)	3 (0.0)
Endocrine disruptor and othe Not exposed		170 (85.4/1.4)	3,728 (83.6/31.3)	1,555 (97.8/13.0)	12,002
Uncertain	31 (0.5/10.6)	13 (6.5/4.4)	243 (5.4/82.9)	6 (0.4/2.0)	(93.4) 293 (2.3)
Exposed	22 (0.3/4.0)	16 (8.0/2.9)	489 (11.0/87.9)	29 (1.8/5.2)	556 (4.3)
Physical factors Ionizing radiations		, , ,		, , ,	
Not exposed	6,216 (94.2/58.0)	199 (100.0/1.9)	4,053 (90.9/37.8)	243 (15.3/2.3)	10,711 (83.3)
Uncertain	384 (5.8/18.6)	0 (0.0/0.0)	383 (8.6/18.5)	1,298 (81.6/62.9)	2,065 (16.1)
Exposed Low frequency magnetic field	2 (0.0/2.7) ds	0 (0.0/0.0)	24 (0.5/32.0)	49 (3.1/65.3)	75 (0.6)
Not exposed	4,804 (72.8/47.5)	21 (10.6/0.2)	3,697 (82.9/36.6)	1,583 (99.6/15.7)	10,105 (78.6)
Uncertain Exposed	700 (10.6/47.7) 1,098 (16.6/86.0)	171 (85.9/11.6) 7 (3.5/0.5)	591 (13.3/40.2) 172 (3.9/13.5)	7 (0.4/0.5) 0 (0.0/0.0)	1,469 (11.4) 1,277 (9.9)
Non-thermal intermediate fro Not exposed	6,506 (98.5/54.8)	195 (98.0/1.6)	4,450 (99.8/37.5)	725 (45.6/6.1)	11,876 (92.4)
Uncertain Radiofrequency E field	96 (1.5/9.8)	4 (2.0/0.4)	10 (0.2/1.0)	865 (54.4/88.7)	975 (7.6)
Not exposed Uncertain	764 (11.6/58.8) 5,817 (88.1/50.5)	2 (1.0/0.2) 197 (99.0/1.7)	512 (11.5/39.4) 3,946 (88.5/34.2)	22 (1.4/1.7) 1,568 (98.6/13.6)	1,300 (10.1) 11,528 (89.7)
Exposed Radiofrequency H field	21 (0.3/91.3)	0 (0.0/0.0)	2 (0.0/8.7)	0 (0.0/0.0)	23 (0.2)
Not exposed Uncertain	1,103 (16.7/64.7) 5,491 (83.2/49.3)	2 (1.0/0.1) 197 (99.0/1.8)	578 (13.0/33.9) 3,882 (87.0/34.9)	22 (1.4/1.3) 1,568 (98.6/14.1)	1,705 (13.3) 11,138
Exposed	8 (0.1/100.0)	0 (0.0/0.0)	0 (0.0/0.0)	0 (0.0/0.0)	(86.7) 8 (0.1)
Thermal intermediate freque Not exposed	6,459 (97.8/57.7)	195 (98.0/1.7)	3,992 (89.5/35.7)	546 (34.3/4.9)	11,192 (87.1)
Uncertain Thermal intermediate freque	143 (2.2/8.6)	4 (2.0/0.2)	468 (10.5/28.2)	1,044 (65.7/62.9)	1,659 (12.9)
Not exposed	6,373 (96.5/57.4)	195 (98.0/1.8)	3,984 (89.3/35.9)	546 (34.3/4.9)	11,098 (86.4)
Uncertain Ultraviolet	229 (3.5/13.1)	4 (2.0/0.2)	476 (10.7/27.2)	1,044 (65.7/59.6)	1,753 (13.6)
Not exposed	6,265 (94.9/51.5)	187 (94.0/1.5)	4,214 (94.5/34.6)	1,507 (94.8/12.4)	12,173 (94.7)
Uncertain	293 (4.4/49.7)	10 (5.0/1.7)	214 (4.8/36.3)	72 (4.5/12.2)	589 (4.6)
Exposed Biological factors	44 (0.7/49.4)	2 (1.0/2.2)	32 (0.7/36.0)	11 (0.7/12.4)	89 (0.7)
Airborne germs					
Not exposed	87 (1.3/100.0)	0 (0.0/0.0)	0 (0.0/0.0)	0 (0.0/0.0)	87 (0.7)
Uncertain	6,121 (92.7/70.5)	126 (63.3/1.5)	2,317 (52.0/26.7)	120 (7.5/1.4)	8,684 (67.6)
Exposed Cytomegalovirus, parvovirus	394 (6.0/9.7) B19	73 (36.7/1.8)	2,143 (48.0/52.5)	1,470 (92.5/36.0)	4,080 (31.7)
Not exposed	6,512 (98.6/60.8)	199 (100.0/1.9)	3,988 (89.4/37.3)	5 (0.3/0.0)	10,704 (83.3)
Exposed	90 (1.4/4.2)	0 (0.0/0.0)	472 (10.6/22.0)	1,585 (99.7/73.8)	2,147 (16.7)

Table 4 (continued)

Characteristics	Low exposure, stress at work $N = 6,602 \text{ n (}\%^{\text{a}}/$ $\%^{\text{b}})$	Strenuous, high organization, low decision $N=199~n~(\%^{\text{a}}/\%^{\text{b}})$	Postural constraints, psychosocial factors $N=4,460~n~(\%^a/\%^b)$	Postural and strength constraints, chemical, and biological factors $N=1{,}590~n~(\%^{\circ}/\%^{\circ})$	Overall N = 12,851 n (%)
Hepatitis A, E	70 J				
Not exposed	6,585 (99.7/55.2)	199 (100.0/1.7)	4,051 (90.8/34.0)	1,097 (69.0/9.2)	11,932 (92.8)
Exposed Hepatitis B, C, Human immu	17 (0.3/1.8)	0 (0.0/0.0)	409 (9.2/44.5)	493 (31.0/53.6)	919 (7.2)
Not exposed	6,476 (98.1/59.2)	199 (100.0/1.8)	4,260 (95.5/39.0)	0 (0.0/0.0)	10,935 (85.1)
Exposed Biomechanical factors	126 (1.9/6.6)	0 (0.0/0.0)	200 (4.5/10.4)	1,590 (100.0/83.0)	1,916 (14.9)
Strength Intensity of the physical of	forte				
Intensity of the physical ef Not exposed	1,626 (24.6/100.0)	0 (0.0/0.0)	0 (0.0/0.0)	0 (0.0/0.0)	1,626 (12.7)
Uncertain	4,823 (73.1/92.1)	54 (27.1/1.0)	143 (3.2/2.7)	214 (13.5/4.1)	5,234 (40.7)
Exposed	153 (2.3/2.6)	145 (72.9/2.4)	4,317 (96.8/72.1)	1,376 (86.5/23.0)	5,991 (46.6)
Carrying loads 10–25 kg					
Not exposed	6,602 (100.0/61.4)	133 (66.8/1.2)	2,994 (67.1/27.9)	1,016 (63.9/9.5)	10,745
Uncertain	0 (0.0/0.0)	49 (24.6/4.1)	1,155 (25.9/95.9)	1 (0.1/0.1)	(83.6) 1,205 (9.4)
Exposed	0 (0.0/0.0)	17 (8.5/1.9)	311 (7.0/34.5)	573 (36.0/63.6)	901 (7.0)
Load handling >4 kg	0 (0.0/ 0.0)	17 (0.5/1.5)	011 (7.0701.0)	373 (30.07 03.07	301 (7.0)
Not exposed	6,509 (98.6/78.1)	59 (29.6/0.7)	1,501 (33.7/18.0)	266 (16.7/3.2)	8,335 (64.9)
Uncertain	93 (1.4/4.1)	115 (57.8/5.1)	1,368 (30.7/60.4)	689 (43.3/30.4)	2,265 (17.6)
Exposed	0 (0.0/0.0)	25 (12.6/1.1)	1,591 (35.7/70.7)	635 (39.9/28.2)	2,251 (17.5)
Posture					
Arms in the air above the s					
Not exposed	6,257 (94.8/66.7)	60 (30.2/0.6)	1,979 (44.4/21.1)	1,078 (67.8/11.5)	9,374 (72.9)
Uncertain	345 (5.2/19.4)	3 (1.5/0.2)	921 (20.7/51.7)	511 (32.1/28.7)	1,780 (13.9)
Exposed Standing	0 (0.0/0.0)	136 (68.3/8.0)	1,560 (35.0/91.9)	1 (0.1/0.1)	1,697 (13.2)
Not exposed	2,942 (44.6/99.6)	0 (0.0/0.0)	10 (0.2/0.3)	1 (0.1/0.0)	2,953 (23.0)
Uncertain	2,364 (35.8/97.4)	7 (3.5/0.3)	26 (0.6/1.1)	30 (1.9/1.2)	2,427 (18.9)
Exposed	1,296 (19.6/17.3)	192 (96.5/2.6)	4,424 (99.2/59.2)	1,559 (98.1/20.9)	7,471 (58.1)
To kneel or squat					
Not exposed	6,426 (97.3/90.7)	57 (28.6/0.8)	363 (8.1/5.1)	241 (15.2/3.4)	7,087 (55.1)
Uncertain Exposed	110 (1.7/4.1) 66 (1.0/2.1)	3 (1.5/0.1) 139 (69.8/4.5)	2,353 (52.8/88.6) 1,744 (39.1/56.1)	191 (12.0/7.2) 1,158 (72.8 /37.3)	2,657 (20.7) 3,107 (24.2)
To lean forward or sideway		137 (07.0/ 4.3)	1,7 44 (33.1/30.1)	1,130 (72.0 / 37.3)	3,107 (24.2)
Not exposed	6,191 (93.8/95.7)	59 (29.6/0.9)	113 (2.5/1.7)	109 (6.9/1.7)	6,472 (50.4)
Uncertain	404 (6.1/16.6)	24 (12.1/1.0)	1,846 (41.4/75.8)	160 (10.1/6.6)	2,434 (18.9)
Exposed	7 (0.1/0.2)	116 (58.3/2.9)	2,501 (56.1/63.4)	1,321 (83.1/33.5)	3,945 (30.7)
To repeat the same actions					
Not exposed	4,689 (71.0/68.0)	63 (31.7/0.9)	1,120 (25.1/16.2)	1,025 (64.5/14.9)	6,897 (53.7)
Uncertain	759 (11.5/53.7)	5 (2.5/0.4)	625 (14.0/44.2)	24 (1.5/1.7)	1,413 (11.0)
Exposed Vibration	1,154 (17.5/25.4)	131 (65.8/2.9)	2,715 (60.9/59.8)	541 (34.0/11.9)	4,541 (35.3)
To use vibrating tools					
Not exposed	6,594 (99.9/53.5)	175 (87.9/1.4)	3,984 (89.3/32.4)	1,562 (98.2/12.7)	12,315 (95.8)
Uncertain	0 (0.0/0.0)	3 (1.5/0.7)	426 (9.6/99.3)	0 (0.0/0.0)	429 (3.3)
Exposed To drive construction mach	8 (0.1/7.5)	21 (10.6/19.6)	50 (1.1/46.7)	28 (1.8/26.2)	107 (0.8)
Not exposed	6,549 (99.2/52.2)	191 (96.0/1.5)	4,223 (94.7/33.6)	1,590 (100.0/12.7)	12,553 (97.7)
Uncertain	31 (0.5/20.9)	7 (3.5/4.7)	110 (2.5/74.3)	0 (0.0/0.0)	148 (1.2)
Exposed	22 (0.3/14.7)	1 (0.5/0.7)	127 (2.8/84.7)	0 (0.0/0.0)	150 (1.2)
To drive a vehicle	•				
Not exposed	5,721 (86.7/51.5)	136 (68.3/1.2)	3,858 (86.5/34.7)	1,395 (87.7/12.6)	11,110 (86.5)
Uncertain	441 (6.7/48.5)	13 (6.5/1.4)	322 (7.2/35.4)	133 (8.4/14.6)	909 (7.1)
Exposed To use of a computer screen	440 (6.7/52.9)	50 (25.1/6.0)	280 (6.3/33.7)	62 (3.9/7.5)	832 (6.5)
To use of a computer screen Not exposed	or control panel 15 (0.2/0.7)	18 (9.0/0.8)	2,177 (48.8/97.4)	26 (1.6/1.2)	2,236 (17.4)
Uncertain	334 (5.1/17.7)	8 (4.0/0.4)	974 (21.8/51.7)	569 (35.8/30.2)	1,885 (14.7)
Exposed	6,253 (94.7/71.6)	173 (86.9/2.0)	1,309 (29.3/15.0)	995 (62.6/11.4)	8,730 (67.9)
Organizational factors					
Night work					
Not exposed	6,436 (97.5/53.7)	195 (98.0/1.6)	4,188 (93.9/35.0)	1,156 (72.7/9.7)	11,975 (93.2)
Exposed (yes or >50) Interruption of tasks	166 (2.5/18.9)	4 (2.0/0.5)	272 (6.1/31.3)	434 (27.3/49.5)	876 (6.8)
Not exposed	943 (14.3/33.0)	3 (1.5/0.1)	1,813 (40.7/63.5)	97 (6.1/3.4)	2,856 (22.2)
Uncertain	228 (3.5/9.7)	18 (9.0/0.8)	936 (21.0/39.7)	1,174 (73.8/49.8)	2,356 (18.3)
Exposed	5,431 (82.3/71.1)	178 (89.4/2.3)	1,711 (38.4/22.4)	319 (20.1/4.2) (cc	7,639 (59.4) ontinued on next page)

Table 4 (continued)

Characteristics	Low exposure, stress at work $N = 6,602 \text{ n } (\%^a/$	Strenuous, high organization, low decision $N=199~n~(\%^a/\%^b)$	Postural constraints, psychosocial factors $N = 4,460 \text{ n } (\%^a/\%^b)$	Postural and strength constraints, chemical, and biological factors $N=1{,}590~n~(\%^a/\%^b)$	Overall N = 12,851 n (%)
	% ^b)				
Work outdoors					
Not exposed	5,832 (88.3/58.6)	128 (64.3/1.3)	2,471 (55.4/24.8)	1,528 (96.1/15.3)	9,959 (77.5)
Uncertain	415 (6.3/21.2)	54 (27.1/2.8)	1,427 (32.0/72.9)	61 (3.8/3.1)	1,957 (15.2)
Exposed	355 (5.4/38.0)	17 (8.5/1.8)	562 (12.6/60.1)	1 (0.1/0.1)	935 (7.3)
Psychosocial factors					
Low decision authority					
Not exposed	435 (6.6/13.8)	1 (0.5/0.0)	1,191 (26.7/37.9)	1,517 (95.4/48.3)	3,144 (24.5)
Uncertain	1,721 (26.1/40.9)	17 (8.5/0.4)	2,402 (53.9/57.1)	69 (4.3/1.6)	4,209 (32.8)
Exposed	4,446 (67.3/80.9)	181 (91.0/3.3)	867 (19.4/15.8)	4 (0.3/0.1)	5,498 (42.8)
High job demands					
Not exposed	775 (11.7/30.0)	9 (4.5/0.3)	698 (15.7/27.0)	1,100 (69.2/42.6)	2,582 (20.1)
Uncertain	3,547 (53.7/70.8)	164 (82.4/3.3)	1,296 (29.1/25.9)	3 (0.2/0.1)	5,010 (39.0)
Exposed	2,280 (34.5/43.4)	26 (13.1/0.5)	2,466 (55.3/46.9)	487 (30.6/9.3)	5,259 (40.9)
High strain					
Not exposed	2,072 (31.4/81.8)	164 (82.4/6.5)	295 (6.6/11.6)	2 (0.1/0.1)	2,533 (19.7)
Uncertain	790 (12.0/25.0)	8 (4.0/0.3)	1,266 (28.4/40.0)	1,101 (69.2/34.8)	3,165 (24.6)
Exposed	3,740 (56.6/52.3)	27 (13.6/0.4)	2,899 (65.0/40.5)	487 (30.6/6.8)	7,153 (55.7)

^a % in column.

standing posture (99.2%), repetition of tasks (60.9%), leaning posture (56.1%), demand (55.3%), and high strain (65.0%). Mothers' exposure was uncertain regarding radiofrequency electric fields (88.5%), radiofrequency magnetic fields (87.0%), airborne germs (52.0%), kneeling or

squatting posture (52.8%), and low decision authority (53.9%). In total, 48.7% of mothers stopped working during the third trimester of pregnancy.

The last profile "postural and strength constraints, chemical, and

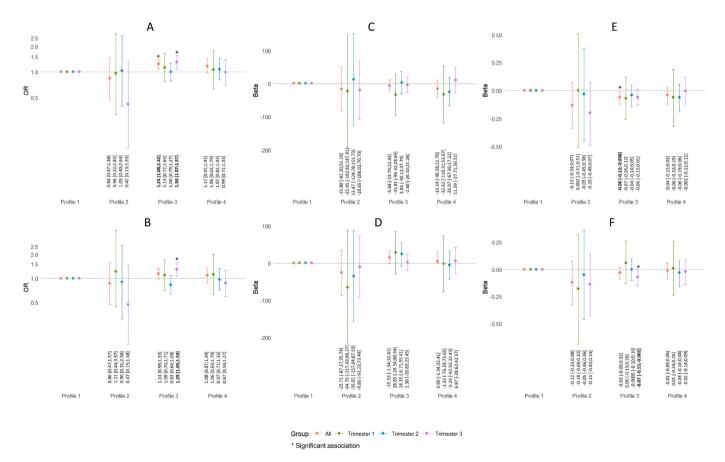


Fig. 1. Association between maternal occupational exposure profiles (Profile 1: Low exposure, stress at work, Profile 2: Strenuous, high organization, low decision, Profile 3: Postural constraints, psychosocial factors, Profile 4: Postural and strength constraints, chemical, and biological factors) and SGA (Fig. 1A crude OR, Fig. 1B adjusted OR for tobacco use, alcohol consumption, and BMI), BW (Fig. 1C crude Beta, Fig. 1D adjusted Beta for tobacco use, alcohol consumption, BMI, gestational age, and infant's sex), HC (Fig. 1E crude Beta, Fig. 1F adjusted Beta for tobacco use, alcohol consumption, BMI, gestational age, and infant's sex), and according to the trimester when mothers stopped working during pregnancy. ELFE study, France, n = 12,851.

^b % in line.

^c Small for gestational age defined as a birthweight under the 10th percentile for gestational age and sex, by using the OMS curves. Severe small for gestational age, was defined as a birthweight under the third percentile for gestational age and sex.

biological factors" included 12.4% (n = 1,590) of the mothers in the study population. Mothers in this profile predominantly attended university (72.7%) and worked in paramedical (54.7%) and medical (14.2%) professions; 31.0% were nurses' aides. They were exposed to six categories of factors: chemical, physical, biological, force, postural, and psychosocial factors. Most mothers were exposed to oxygenated solvents (99.8%), detergents (88.1%), airborne germs (92.5%), cytomegalovirus, parvovirus B19 (99.7%), hepatitis B, C, HIV (100.0%), intensity of physical efforts (86.5%), standing posture (98.1%), kneeling or squatting posture (72.8%), leaning posture (83.1%), and screen work (62.6%). Mothers' exposure was uncertain regarding radiofrequencies (98.6%), non-thermal intermediate frequencies (54.4%), thermal intermediate frequencies (65.7%), interruption of tasks (73.8%), and high strain (69.2%). Only 38.0% of mothers in this profile stopped working during the third trimester of pregnancy.

3.4. Relation between maternal occupational profiles and intra-uterine growth

The multivariate analyses showed no significant associations (Fig. 1B), but the risk of SGA tended to be increased in profile "Postural constraints, psychosocial factors" for all women (aOR = 1.14, 95% CI = 0.98; 1.33). Depending on whether mothers stopped working during pregnancy, this risk was driven by women who stopped working during the third trimester of pregnancy (aOR = 1.29, 95% CI = 1.05; 1.59 in profile "Postural constraints, psychosocial factors", compared to profile "Low exposure, stress at work") (Fig. 1B).

Regarding BW, the multivariate analyses showed no significant associations either (Fig. 1D), but BW seemed to be increased in profile "Postural constraints, psychosocial factors" compared to profile "Low exposure, stress at work" (a β = 15.53, 96% CI = -1.34; 32.41) among all women. Depending on whether mothers stopped working during pregnancy, the risk remained insignificant (Fig. 1D).

The multivariate analyses showed no significant association between the occupational profiles and HC among all women (Fig. 1F). The results were consistent when we additionally adjusted our analysis for mode of delivery (Appendix F, Table 2). Depending on whether mothers stopped working during pregnancy, we observed a significant decreased of HC only when women stopped working during the third trimester of pregnancy (a $\beta=-0.07,\,95\%$ CI $=-0.15;\,-0.002$ in profile "Postural constraints, psychosocial factors" compared to profile "Low exposure, stress at work") (Fig. 1F).

For severe SGA, the multivariate analyses no showed significant associations (Appendix I, Table 3), independent on when mothers stopped working during pregnancy (Appendix I, Table 4).

Finally, we performed a sensitivity analysis with adjustment for educational level, which showed associations going in the same direction as in the main analyses (Appendix J, Table 7). The sensitivity analysis excluding women with gestational diabetes and gestational hypertension showed that profile "Postural constraints, psychosocial factors" is significantly associated with SGA (Appendix K).

4. Discussion

Our study reported a median of six occupational exposures among pregnant women and identified four profiles of maternal occupational exposome during pregnancy: "Low exposure, stress at work", "Strenuous, high organization, low decision", "Postural constraints, psychosocial factors", "Postural constraints, chemical and biological factors". One of these profiles "Postural constraints, psychosocial factors" was associated with higher risk of SGA and reduced HC especially in women who worked until the third trimester of pregnancy.

To the best of our knowledge, this is the first study that presents multiple occupational exposures in pregnant women. A study published in 2014, in France, revealed that 43.1% of pregnant women were exposed to at least 3 occupational factors at risk for pregnancy; 27.2% to

at least 5 occupational factors at risk for pregnancy; and only 27.7% had no exposure (Henrotin et al., 2018). Also, the French SUMER survey, a cross sectional study of multiple occupational exposure, described all workstation-related exposures evaluated by occupational physicians in more than 26,000 employees (Anses et al., 2021). If we compare our results to SUMER, with some precautions since there was no specific analysis on women of childbearing age in that study and the exposure assessment methods differed, mothers in our study being exposed to a comparable median number of exposure factors: 6 factors (min = 1, max = 17) in ELFE vs 7.3 factors (min = 0, max = 25) in SUMER (Anses et al., 2021), with 99.9% of mothers were multi-exposed in ELFE and 97.1% in SUMER. We found more exposure to strenuous factors (100% to at least one in ELFE vs 45% in SUMER), less to physical factors (13 % in ELFE vs 45% in SUMER), which can be explained by the types of occupations in our study compared to SUMER; and less to organizational factors (64.6% in ELFE vs 95% in SUMER). In the United States, the Occupational Requirements Survey (ORS) realized in 2023, showed that strenuous factors were also common with reaching at or below the shoulder for 75.9% of civilian workers whereas only 13.3% were exposed in our study for arms above the shoulders, standing for 56.3%, similar to 58.5% in our study and sitting for 43.7% (Occupational Requirements Survey). The Danish Work Environment Cohort Study (DWECS) in 2000, identified that some sectors were more exposed than others, especially the health care and service sectors, which can be compared with our profile "postural and strength constraints, chemical, and biological factors". These women were exposed to chemical factors, and in particular cleaning agents (88.1% of women were exposed to detergents in this profile in our study) and solvents (99.8% of women were exposed to oxygenated solvents in this profile in our study). Strenuous and psychosocial factors were also present in this sector (Danish Work Environment Cohort Study, 2000), like in our study, in which this profile contained 86.5% of women exposed to intensity of physical efforts, 98.1% to standing posture, 72.8% to kneeling or squatting posture, and 83.1% to leaning posture. In addition, the SUMER study identified 12 profiles of exposome with similarities to several of ours. For example, one profile in SUMER characterized by low exposure work, low social support (Anses et al., 2021) with higher socio-professional categories exposed only to psychosocial factors is close to our profile "Low exposure, stress at work". Moreover, they identified another profile characterized by an accumulation of constraints linked to health professions (Anses et al., 2021), like our profile "Postural and strength constraints, chemical, and biological factors".

Interestingly, we observed that although duration of work during pregnancy was similar in our study to that in the national perinatal survey, we observed several differences between profiles. Mothers in profile "Low exposure, stress at work" worked for a longer duration (approximately 29 weeks) compared to those in the other profiles (around 24–26 weeks) and they had the fewest workplace adjustments (approximately 11% in contrast to the other profiles around 16%–21%). Women with less stable jobs and lower-skilled professions tended to stop working earlier (Vigoureux et al., 2016) and the perception of the need to change jobs was higher when jobs had high physical demands and low substantive complexity (Tannis et al., 2023).

Regarding the association with intrauterine growth, we observed an increased risk of SGA in profile "Postural constraints, psychosocial factors", compared to profile "Low exposure, stress at work" (aOR = 1.14, 95% CI = 0.98; 1.33). This increase became significant (aOR = 1.29, 95% CI = 1.05; 1.59) among mothers who stopped working during the third trimester of pregnancy. When we looked at literature on occupational exposures and SGA, previous studies found contradictory results. Associations were found for certain exposures identified in this profile, that is standing (Croteau et al., 2006), intensity of physical effort (Vrijkotte et al., 2009), and job strain (Vrijkotte et al., 2009). Certain biological mechanisms may explain these results. Indeed, intense movements divert blood from the fetoplacental unit to the active muscles. Standing can reduce venous return and blood volume. In addition,

heavy physical work reduces blood flow to the uterus and placenta and reduces the availability of oxygen and nutrients for the fetus (Dickute et al., 2002). Finally, concerning high strain, the release of stress hormones, such as norepinephrine, cortisol, harm the growth of the fetus due to dysregulation of the hypothalamic pituitary adrenal axis (Vrijkotte et al., 2009). Regarding HC, there is a decrease ($\beta = -0.07$, 95% CI = -0.15; -0.002) in HC within profile "Postural constraints, psychosocial factors", among mothers who stopped working during the third trimester of pregnancy, in comparison to profile "Low exposure, stress at work". The limited data available in the literature indicates a decrease in HC with standing; no associations were found regarding kneeling or squatting (Bonzini et al., 2009). More surprisingly, we observed a trend to increase birthweight within profile "Postural constraints, psychosocial factors", in comparison to profile "Low exposure, stress at work". However, this result was not confirmed in analysis by trimester. The results of the analysis on mothers who stopped working during the third trimester of pregnancy suggest that this is a period of higher risk, considering that the development of fetus, in particular weight gain is greater during this period.

In our study, we chose to exclude mothers who did not work during pregnancy to limit the healthy worker effect since non-working pregnant women tend to be in poorer health than those who work, potentially carrying a higher risk of adverse pregnancy outcomes. The study by Casas et al., in 2015 reported that non-employed women indeed had an increased risk of adverse pregnancy outcomes (Casas et al., 2015). In addition, women who do not work are predominantly at home compared to working women who are predominantly at their work-Non-working women are thus mostly exposed non-occupational exposures that are not well known. We chose to not adjust our main analysis for educational level. Indeed, educational level is often discussed in occupational epidemiology. For example, the article of Richiardi et al. (2008) suggests adjusting by educational level when the socio-economic status causes the outcome and the occupation under study. In this case, only one exposure factor was studied; whereas in our study, many exposures were studied simultaneously. Moreover, we were interested in patterns of multi-exposures, so educational level can be considered as already taken into account by the profiles. However, we also performed a sensitivity analysis with an adjustment for educational level and results were consistent.

Regarding the assessment of occupational exposure, the data regarding tasks and occupational activities carried out during pregnancy enabled a precise job coding by a single expert using both a national and an international classification. This permitted the assessment of 47 occupational exposures even if we recognized that others could have been studied such as exposure to noise (Ulin et al., 2024) and heat (Rekha et al., 2024) at work for example recently associated with adverse pregnancy outcomes. The application of numerous internationally well recognized job-exposure matrices ensure a specific evaluation of numerous exposures. Although we must acknowledge that the use of JEMs will not consider individual differences since all workers with the same job are classified identically. However, the evaluation between individuals is more homogeneous (Ge et al., 2018). JEMs used in our study have been constructed by expert (CANJEM, MatPUF, Pestipop, endocrine disruptor, Matgéné solvents, Mat-O-Covid, FinJEM, Eficatt), self-administered questionnaires (Matgéné night work, JEM Constances, Swedish psychosocial JEM), or literature-based measurements data combined with questionnaire data (RF-JEM). Although the declaration of subjects can be judged as less reliable than expertises, we have chosen to limit the use of JEMs based on questionnaires to those targeting strenuous and psychosocial factors for which the declaration of subjects can be considered more valid than for chemical exposures. Additionally, some of the JEMs used were constructed with data from the French population (Matgéné, MatPUF, Pestipop, Mat-O-Covid, JEM Constances) and others with data from international populations (Endocrine disruptor, FinJEM, Swedish psychosocial JEM, RF-JEM, CANJEM), which may lead to measurement error. We hypothesized,

however, that any differences in the context would be minimal for high-income countries. Moreover, we incorporated only two JEMs (Matgéné night work and Swedish psychosocial JEM) that were gender specific. The JEMs are often constructed using male populations, which can result in either underestimation or overestimation of exposure-related parameters (probability, frequency, intensity). In addition, we used several JEMs with a temporal axis, covering the period 2011 or the closest period of the pregnancy considered in our study. This allowed taking into account temporal developments in work activities, and in regulations that may be important, especially for chemical exposures. Other JEMs concerning biological, strenuous, and psychosocial factors have no temporal axis in our study even if we think that for these exposures, the change over time is less pronounced than for chemical exposures. Finally, JEMs may have different internal/external validity, according to the agents studied, for example, there are less JEMs for strenuous and psychosocial factors than for chemical and physical factors. Moreover, we mainly used probability to define exposure status with an a priori threshold (to assess exposure of 0%/0-50%/>50%). All of these characteristics may lead to non-differential measurement error that may be more or less pronounced depending to the exposure considered and consequently may impact our results.

Our study had several strengths. We used data from a large national prospective cohort with detailed data available that allowed consideration of the most important confounding factors. Using a large number of well recognized JEMs we were able to characterize a wide range of occupational exposures (n = 47). In addition, the statistical approach used, hierarchical clustering on principal components, takes into consideration the simultaneous exposure of mothers to a range of diverse factors, without establishing a hierarchy among the different categories of exposures.

However, our study had also several limitations including f the evaluation of professional exposures which has already been discussed above. The classification methods employed to determine profiles were based on certain decisions and assumptions that can be subject to discussion, particularly the number of dimensions retained in the multiple correspondence analysis (MCA), or the cut-off point of the dendrogram obtained from the hierarchical clustering on principal components (HCPC). Moreover, we must acknowledge that the use of hierarchical clustering on principal components methods, is guided by the frequency of exposure that cannot consider exposures which are rare but have a real impact on pregnancy and intrauterine growth. Finally, a large number of statistical tests were performed. This multiplicity of testing may have increased the risk of incorrectly identifying a statistically significant difference; but results were confirmed in sensitivity analyses. The identification of profiles of multiple occupational exposure make it possible to draw general observations on work environments favouring exposure to a group of constraints, further inviting us to consider prevention from a more global angle, by targeting certain areas or professional activities, reflecting a set of particular constraints experienced by employees. It is necessary to consider occupational exposures simultaneously, representing the reality but also the complexity of occupational situations. Indeed, occupational factors can act independently, synergistically, or antagonistically. Over the past thirty years, significant progress has been made in the field of health and safety at work, leading to a reduction in chemical and physical risks. However, the accumulation of work-related pressures has been accompanied by an increase in psychosocial risks (Roquelaure et al., 2022). From a broader perspective, these analyses enable us to better characterize the occupational sectors that are particularly exposed to multiple stressors, and thus to get closer to the concerns of prevention in the field. Thus, it seems necessary to carry out an assessment of the working environment of pregnant women, in order to propose preventive measures to reduce exposure to these risk factors, and, if necessary, consider adapting the work circumstances. Also, given the results of this study, early cessation of work (during the second trimester of pregnancy), among women identified as being at higher risk: teachers, cleaners, saleswomen, could be

considered. The observation made by Henrotin et al., in 2018, as well as the elements of this study show that maintaining employment through workplace adjustment or changes in the work are still insufficient and that it is necessary to promote contact between employees and occupational health services (Henrotin et al., 2018). A study carried out in Norway in 1998 already showed that assessment of working conditions during the first prenatal visit rapidly predicted the need for occupational adaptation during pregnancy (Wergeland and Strand, 1998). Another study, carried out in the United States recommend the implementation of pre-conceptual visits that would enable the evaluation of professional and extraprofessional exposure (McDiarmid and Gehle, 2006).

5. Conclusion

This study offers an overview of exposome during pregnancy. By identifying profiles of multiple occupational exposures, this study provides a better understanding of the factors to which women are exposed during pregnancy. In terms of research perspectives, it would be worthwhile to further develop tools to better understand the risks associated with occupational exposures such as strenuous and psychosocial factors that represent a major challenge for occupational prevention. It would also be useful to examine interactions between the various exposures and the associated effects on mothers working during pregnancy. These necessary advances in the comprehension of potential impact of multiple occupational exposures on pregnancy are important to better adapt prevention strategies.

CRediT authorship contribution statement

Marie Tartaglia: Writing - original draft, Visualization, Methodology, Formal analysis, Conceptualization. Nathalie Costet: Writing review & editing, Methodology. Sabyne Audignon-Durand: Writing – review & editing, Resources. Camille Carles: Writing - review & editing, Resources. Alexis Descatha: Writing – review & editing, Resources. Daniel Falkstedt: Writing – review & editing, Resources. Marie-Tülin Houot: Writing - review & editing, Resources. Katarina Kjellberg: Writing - review & editing, Resources. Corinne Pilorget: Writing review & editing, Resources. Nel Roeleveld: Writing - review & editing, Resources. Jack Siemiatycki: Writing – review & editing, Resources. Michelle C. Turner: Writing - review & editing, Resources. Maxime Turuban: Writing – review & editing, Resources. Sanni Uuksulainen: Writing – review & editing, Resources. Marie Noëlle Dufourg: Writing – review & editing, Resources. Ronan Garlantézec: Writing – review & editing, Supervision, Methodology, Conceptualization. Fleur Delva: Writing review & editing, Supervision, Conceptualization.

Contributors

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The Elfe survey is a joint project between the French Institute for

Demographic Studies (INED) and the National Institute of Health and Medical Research (INSERM), in partnership with the French blood transfusion service (Etablissement français du sang, EFS), Santé publique France, the National Institute for Statistics and Economic Studies (INSEE), the Direction générale de la santé (DGS, part of the Ministry of Health and Social Affairs), the Direction générale de la prévention des risques (DGPR, Ministry for the Environment), the Direction de la recherche, des études, de l'évaluation et des statistiques (DREES, Ministry of Health and Social Affairs), the Département des études, de la prospective et des statistiques (DEPS, Ministry of Culture), and the Caisse nationale des allocations familiales (CNAF), with the support of the Ministry of Higher Education and Research and the Institut national de la jeunesse et de l'éducation populaire (INJEP). Via the RECONAI platform, it receives a government grant managed by the National Research Agency under the "Investissements d'avenir" programme (ANR-11-EQPX-0038 and ANR-19-COHO-0001).

We thank Jérôme Lavoué and Elisabeth Cardis for sharing JEM.

MCT is funded by a Ramón y Cajal fellowship (RYC-2017-01892) from the Spanish Ministry of Science, Innovation and Universities and co-funded by the European Social Fund. ISGlobal acknowledges support from the the grant CEX2018-000806-S funded by MCIN/AEI/10.13039/501100011033, and support from the Generalitat de Catalunya through the CERCA Program. The conduct of the INTEROCC study was funded by the National Institutes for Health (NIH) (grant no. 1R01CA124759-01). Funding for the OccRF Health Study is provided by ANSES No. EST-2018 RF-35.

We thank The Language Room for proofreading the English version of this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2024.120669.

Data availability

The authors do not have permission to share data.

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