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## **Cohort profile: The PELAGIE mother-child cohort**

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## **Key Features**

- The PELAGIE mother-child cohort was initially established to study the effect of prenatal exposure to chemicals on pregnancy outcomes and child health. The scope of the cohort has since expanded, and a broad number of health determinants are under study.
- PELAGIE was set up in 2002 in the Brittany region of western France, and included 3,421 pregnant women and their 3,460 newborns from the general population. Women were included in early pregnancy, and the children were followed up at birth and at the ages of 2, 6 and 12 years. A follow-up at ages 18-20 years is ongoing among the 2,336 mother-child pairs still enrolled in the cohort.
- To date, the PELAGIE cohort has collected a wealth of data on exposures (e.g. to pesticides, solvents or air pollution) and health (e.g. neurodevelopment, cardiometabolic and reproductive health), from life in utero through to young adulthood.
- The PELAGIE cohort ([www.pelagie-inserm.fr](http://www.pelagie-inserm.fr)) is part of the European mother-child cohort network and is open to collaborations. Data are available upon request from the PIs (CC and CW at [cecile.chevrier@inserm.fr](mailto:cecile.chevrier@inserm.fr) and [charline.warembourg@inserm.fr](mailto:charline.warembourg@inserm.fr); Inserm, Rennes, France), either through traditional data sharing or via a federated infrastructure (DataShield) without disclosing any individual data.

## **Why was the cohort set up?**

At the end of the twentieth century, there was widespread concern about the adverse effects of other environmental chemicals on human health. Meanwhile, there was growing worldwide interest and research activity in the field of developmental plasticity, formalising the Developmental Origins of Health and Disease (DOHaD) hypothesis. The first evidence of the adverse effect on child health of exposure to chemicals during pregnancy came from observational studies following accidental high-level exposure episodes, as well as from epidemiological studies performed in occupational settings in which exposure levels could be high. At that time, one of the main limitations of existing studies was that their assessment of exposure during pregnancy was both retrospective and indirect; this highlighted the need for longitudinal follow-up of women and their children that would begin in early pregnancy. Concerns were

also raised about the possible effects of chronic low-level exposure occurring within the general population.

In this context, the PELAGIE (*Perturbateurs Endocriniens: Étude Longitudinale sur les Anomalies de la Grossesse, l'Infertilité et l'Enfance*) mother-child cohort was set up to study the effects of prenatal exposure to environmental and occupational chemical contaminants on pregnancy outcomes and child development. The objective of the cohort was soon rapidly expanded, to take an interest in both postnatal exposures and various environmental hazards (e.g., air pollution). The PELAGIE cohort was established in Brittany, a region located in the north-west of France known both as one of the country's top agricultural regions and for its fishing and agri-food-industrial activities. Recruitment began in 2002, and the PELAGIE cohort was set up in close collaboration with another mother-child cohort (the EDEN cohort) conducted simultaneously (2003-2005) in other areas of France (Poitiers and Nancy cities), and which shared part of the data collection protocol.(1)

The baseline PELAGIE cohort set-up was supported by Inserm and various French ministries. Since then, public agencies and independent foundations supporting public research have awarded grants on an ad hoc basis for specific projects, such as the conduct or completion of cohort family follow-up, or to fund PhD students working on the PELAGIE data (see Funding section).

### **Who is in the cohort?**

The PELAGIE mother-child cohort includes 3,421 pregnant women and their offspring, enrolled between 2002 and 2006 from three departments (Ille-et-Vilaine, Côtes d'Armor and Finistère) in the region of Brittany, France. Women were recruited in early pregnancy (<19 weeks of gestation) in the course of their first prenatal appointments with gynaecologists, ultrasonographers, midwives or obstetricians. The inclusion criteria were the following: pregnant women who were i)  $\geq 18$  years old, ii) at <19 weeks of gestation, and iii) French speakers. The research team identified and informed the regional health practitioners about the study via the gynecologist's college. The interested professionals had to express their intention to participate, on a voluntary basis, to the research team; we estimated that less than 25% of the invited health professionals volunteered to participate. In practice, the health practitioners informed

the pregnant women about the study objectives, obtained their written consent, gave them a study kit (questionnaire and material for urine sampling), and transmitted their personal contacts to the research team. At home, the women were asked to complete the questionnaire and to return it by mail to our laboratory (Inserm U1085), along with a 20-mL urine sample (first morning void). Of the pregnant women who accepted to take the study kit, more than 85% of them finally returned the inclusion questionnaire. At delivery, information about the pregnancy, delivery, and newborn health was collected at the maternity ward by midwives and paediatricians for 3,399 women (99.4%). Of the 22 families lost to follow-up at birth, one was retrieved via follow-up during childhood. Samples of umbilical cord blood, maternal hair and placental tissue were collected for 62%, 63%, and 58% of the participants respectively, and stored in our laboratory.

At baseline, the pregnant women were on average aged 30.1 years, and included at the 10<sup>th</sup> week of gestation: 44% were primiparous, most have a university degree (62%), and were of normal weight (74%) (Table 1). The newborns weighed on average 3,352g; 7% were small-for-gestational age and 6% were born preterm. In comparison to the national perinatal survey performed in 2003, the PELAGIE population is of similar age but has a higher level of education (62% vs. 43% educated beyond secondary school, respectively), smoked less during pregnancy (14% [at inclusion] vs 22% [during the third trimester of pregnancy], respectively), and had given birth to heavier newborns (3,352g vs 3,231g, respectively).(2)

### **How often have they been followed up?**

Figure 1 provides an overview of the study design. Of the 3,421 women included at baseline, 3,399 were followed at delivery, which resulted in 3,322 singleton livebirths. Of these, 1,506 children were followed up at the age of 2, 1,415 at age 6, and 1,212 at age 12, by means of self-administrated questionnaires completed by the parents (mainly the mothers), with additional questionnaire completed by the child at age 12. In addition, 1,635 mother-child pairs took part in an annual self-administrated questionnaire to assess pubertal development (from age 9 until reaching puberty). Compared to the baseline cohort, the mothers who took part in the follow-up at age 12, are slightly older, better educated and less likely to have smoked during pregnancy. Generally, this pattern of selection among participants has been consistently observed at each follow-up (Table 1). The participation rate for each follow-up is around 50%; the fact

that a mother has missed one follow-up does not mean that she cannot take part in any subsequent follow-up(s). The follow-up at age 12 ended in late 2018, and 2,336 families (68% of the baseline cohort) remain eligible to participate in the next follow-up at age 18-20.

Within the cohort, subgroups of children have taken part in a more in-depth follow-up at the ages of 6, 10 and/or 12 (Figure 1). At age 6, 287 children (participation rate = 67%) were visited at home by two psychologists, with the aim of performing neuropsychological and visual tests. They also collected biological samples (child urine and saliva) and house dust.<sup>(3–5)</sup> A subset of these children (n=101, participation rate = 44%) underwent additional neurological tests and a brain MRI between the ages of 10 and 12.<sup>(6)</sup> At age 12, 559 children (participation rate = 60%) were followed up in a hospital setting (the clinical investigation unit of *hôpital de Rennes*) for a clinical examination focused mainly on pubertal development, metabolic risk, and behavioural disorders. Biological samples were also collected (blood, hair, and buccal swab).

## **What has been measured?**

The data collected on child health, environmental exposures and maternal and child characteristics at each follow-up are summarized in Table 2.

### Child health

Routine data at delivery were collected at birth, including gestational age, weight, height, head circumference, and congenital anomalies. Additional data were collected retrospectively to confirm gestational age at birth and congenital anomalies. At each follow-up of the whole cohort (at the ages of 2, 6 and 12), child health data were collected by parental reports using self-administrated questionnaires that included data on growth, respiratory health (International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire), eczema and allergies, and child behaviour (Child Behaviour Checklist (CBCL) at age 2, the Strengths and Difficulties Questionnaire (SDQ) at ages 6 and 12).

During the specific follow-up of a subgroup of children at age 6, their cognitive abilities were assessed using the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV) as well as several subtests of the Developmental Neuropsychological Assessment (NEPSY) battery. The children's inhibitory capacity

was also assessed, as well as the children's visual function (sensitivity to contrasts). Maternal IQ was assessed using the Wechsler Adult Intelligence Scale, 3rd revision (WAIS-III), and the quality and extent of stimulation available to the child in the home environment was assessed using the HOME (Home Observation for Measurement of the Environment) inventory.

At age 10-11, brain imaging was based on an Magnetic Resonance Imaging (MRI) protocol that included several types of sequences for joint structural and functional exploration.(6) Functional brain imaging (using BOLD-MRI) was acquired in the course of three specific tasks involving motor inhibition, attention and working memory. This brain imaging protocol was combined with cognitive assessment (using the WISC and NEPSY tests)

Data on the children's pubertal status (Tanner stage) was obtained across the whole cohort via repeated self-questionnaires completed by child and mother between ages 9 and 16. For a sub-cohort, this data was also obtained via a clinical examination carried out by trained health professionals at age 12. In addition, data on child adiposity, blood pressure, self-reported mental health (Dominique Interactive) and visual function were collected during this clinical examination, which ended with a specific oral examination conducted by a dentist.

Biological samples collected during pregnancy or at birth were used to measure biomarkers of effects, including hormone levels (steroids, adiponectin, insulin) from the cord blood samples, and untargeted metabolomics from both urine and cord blood samples. At age 12, various biological markers were measured in non-fasting blood samples collected during the clinical examination; these included steroid and thyroid hormones, lipids, transaminases, inflammatory markers and markers of renal function.

A follow-up at ages 18-20 is underway (2022-2025), using questionnaires at home and clinical examination at the hospital focusing specifically on cardiovascular and metabolic health, as well as female reproductive disorders.

### Environmental exposures

During pregnancy, the environmental and occupational exposures were assessed using questionnaires, biomarkers, job-exposure matrices (JEM), or GIS modelling. Exposures of interest included exposure to solvents, pesticides (mainly organophosphorus/pyrethroid insecticides, triazine herbicides), persistent organic pollutants (organochlorine pesticides, polychlorobiphenyls, polybromodiphenylethers, per- and polyfluorinated compounds), air pollution, noise and various other chemicals. Exposure data derived from questionnaires, JEM and GIS are available for almost all the women included at baseline (n=3,421), while exposure biomarkers were measured in sub-cohorts of participants only.

Postnatal exposures to pesticides and solvents at ages 2, 6 and 12 were assessed by means of questionnaires sent to the mothers (n=1,505, 1,415, and 1,212, respectively) containing detailed questions on frequency of use, user, and product type. For those children included in the visit at age 6 (n=287), biomarkers of exposure to pesticides and solvents were measured in child urine (first morning void sample), and the contamination of homes by numerous persistent organic pollutants and pesticides was also assessed on the basis of house dust samples. Biomarkers of exposure to numerous persistent organic pollutants were measured in blood samples collected at age 12.

### Maternal and child characteristics

A great deal of additional data was collected from the self-administrated questionnaires, with several questions being repeated at each follow-up. Data collected included maternal characteristics at baseline (age, body mass index, parity, chronic and gestational pathologies, education level, smoking status, diet, etc.), child habits from age 2 to 12 (physical activity, diet, TV/video games, sleep, etc.), and housing characteristics at ages 6 and 12 (residential history from birth, building characteristics, frequency of cleaning, etc.).

### **What has it found?**

#### Early-life exposure to organic solvents

The PELAGIE mother-child cohort has made a major contribution to current knowledge of the effects on child health of prenatal exposure to solvents. Maternal occupational exposure to solvents (assessed by



self-reports and the job-exposure matrix) has been associated with higher risk of congenital anomalies,(7) higher levels of hyperactivity, attention deficit, and aggressiveness in children at age 2,(8) and increased externalizing behaviour at ages 2 and 6.(9) Prenatal exposure to glycol ethers specifically, assessed by exposure biomarkers, has been associated with a higher risk of congenital anomaly,(10,11) variations in steroid hormone levels at birth,(12) lower neurocognitive abilities at age 6,(13) and lower visual functioning at age 6.(14) Postnatal exposure to solvents has been associated with a higher risk of wheezing at age 2.(15)

### Early-life exposure to pesticides

Another area of expertise derived from the PELAGIE cohort study is that of environmental exposure to pesticides. The PELAGIE cohort has contributed to several research articles aimed at studying the effect on child health and development of early-life exposure to various classes of pesticides: 1) prenatal exposure to atrazine and residential proximity to agricultural fields was associated with lower birth weight and head circumference,(16,17) 2) prenatal exposure to organophosphate pesticides was associated with higher insulin levels at birth,(18) a higher risk of otitis media at age 2,(19) lower visual contrast sensitivity at age 6, (20) an altered pattern of brain activity in regions associated with inhibition among children aged 10-12,(6) and an increase in autistic traits at age 11,(21) 3) pre- and post-natal exposure to pyrethroids was associated with a higher risk of behavioural disorders at age 6,(22) and 4) postnatal exposure to organophosphate pesticides and pyrethroids was associated with lower cognitive abilities at age 6 (though prenatal exposure was not).(3,4)

### Early-life exposure to persistent organic pollutants

Exposure to some persistent organic pollutants measured in cord blood was associated with longer time-to-pregnancy,(23) lower birth weight,(24,25) higher risk of being small for gestational age,(26) variations in several cord blood hormone levels (including insulin, adiponectin and steroids),(18,27) as well as higher risk of wheezing before the age of 18 months,(28) and with child growth and body mass index up to age 12.(29,30) No association was observed with hyperactivity,(31) while postnatal (though not

prenatal) exposure to PBDEs was associated with lower cognitive functions at age 6.(5) Several of these results have been obtained thanks to the participation of PELAGIE in the European birth cohort consortia.

### **What are the main strengths and weaknesses?**

The main strengths of the PELAGIE cohort include i) population-based regional recruitment, allowing heterogeneity in the living areas of the pregnant women (urban and rural populations) and consequently, in their exposure levels; ii) recruitment performed early in pregnancy – a sensitive window for development – followed by longitudinal follow-up of the children, including the pubertal stages, through to young adulthood; iii) collection of biological samples for assessment of both exposure and outcome data, and iv) the use of standardized and validated methods to assess child health.

The PELAGIE cohort also has some weaknesses, notably the fact that the recruitment depended on the involvement of health practitioners, which was on a voluntary and free basis, and fluctuated over time according to their own constraints. It was thus impossible to determine the total number of invited pregnant (i.e., including the women who refused to take the study kit) and to compare the characteristics of respondents and non-respondents. According to the national perinatal survey(2), a selection of the cohort has been observed at baseline towards more highly-educated women than are found in the general population, which was slightly accentuated in subsequent follow-ups. This selection did however lead to a homogenous study population that might avoid certain confounding factors. Because of logistical and financial constraints, clinical examination of the children and biomarker measurements were limited to subgroups of the baseline cohort. Although a wide range of environmental exposures were assessed to cover the prenatal period, we have so far covered only limited data on postnatal exposures. We should also acknowledge a risk of measurement error in assessment of the exposures measured in a single urine sample, when the collection of multiple biospecimens is now recommended for the assessment of exposure to certain non-persistent chemicals.

### **Can I get hold of the data? Where can I find out more?**

The PELAGIE cohort is already involved in national and international collaborations and is open to new collaborations. Enquiries can be submitted either by completing the contact form available on the

PELAGIE website (<http://www.pelagie-inserm.fr/index.php/nous-contacter>) or by emailing the cohort PIs (Dr. Cécile Chevrier, [cecile.chevrier@inserm.fr](mailto:cecile.chevrier@inserm.fr) and Dr. Charline Warembourg, [charline.warembourg@inserm.fr](mailto:charline.warembourg@inserm.fr)). Data transfer agreement will be obtained according to French and European Union legislation. Data use through the DataShield platform can also be allocated;(32) a number of variables have been harmonized in the framework of European consortia (the list of variables is available at <https://data-catalogue.molgeniscloud.org>).

### **Ethics approval**

Adults participating in this study provided their written informed consent, and the children provided written assent at age 12. Written informed consent was obtained from parents/legal guardians for all participants aged under 18. The study has been approved by the Advisory Committee on Information Processing in Health Research (CCTIRS; 2015; no. 15.326bis), the Committee for the Protection of Persons (CPP; 2015; no.15/23-985) and the French National Commission for Information Technology and Civil Liberties (CNIL;2002, 2015; no. 915420/2015-456).

### **Data availability**

See ‘Can I get hold the data?’ above.

### **Supplementary data**

None

### **Author contributions**

SC, CC, CW, FR, RG, NC, CM, and FP conceptualized the cohort and/or specific follow-ups. SC, CC, CW are the subsequent PI of the cohort. CM is responsible for cohort logistic, data management and quality control. NC is the statistical referent for all statistical analyses of the cohort. CW wrote the original draft, with editing by CC. All authors approved the final version of the manuscript.

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## **Conflict of Interest**

None declared

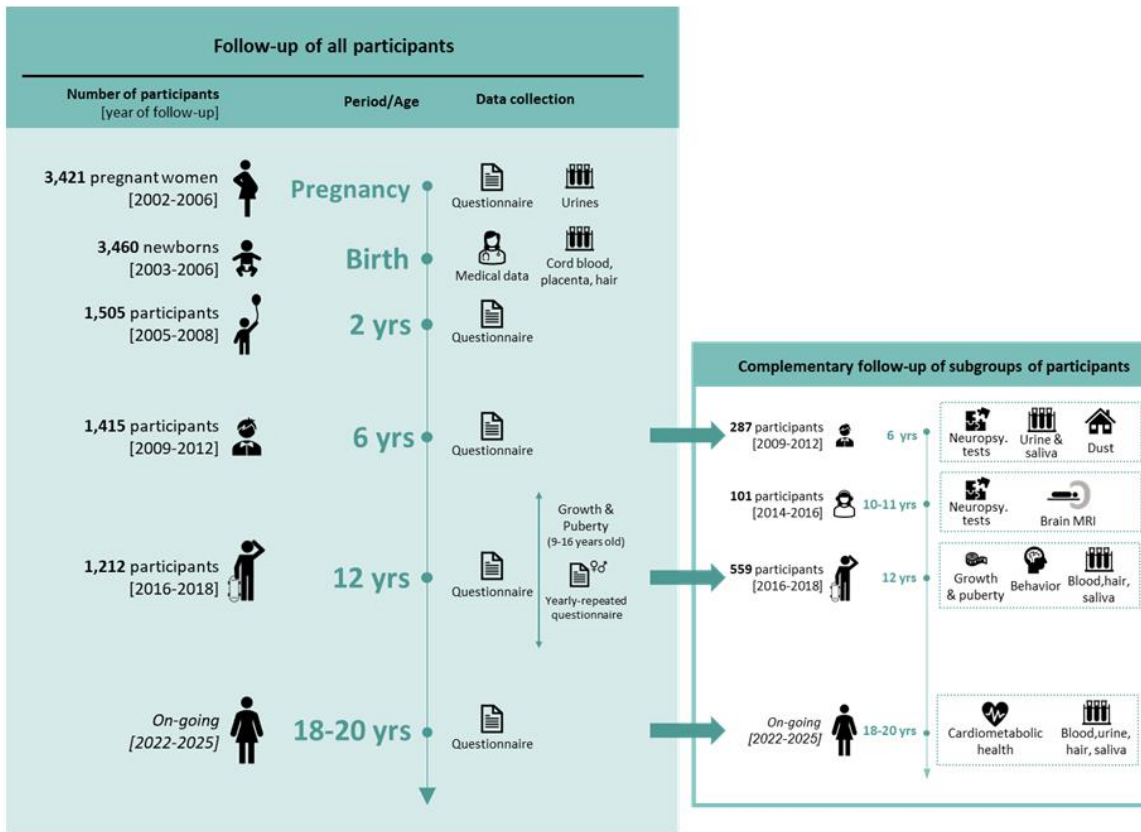
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**Figure 1. Overview of the PELAGIE mother-child cohort.**



**Table 1. Characteristics of the study population**

	Pregnant women At baseline N=3,421 <sup>a</sup>	2-year-old follow-up (questionnaire) N=1506	6-year-old follow-up (questionnaire) N=1,415	12-year-old follow-up (questionnaire) N=1,212	12-year-old follow-up (clinical examination) N=559
Year of inclusion					
2002	407 (12)	32 (2)	171 (12)	183 (15)	90 (16)
2003	1270 (37)	595 (40)	518 (37)	452 (37)	234 (42)
2004	1229 (36)	609 (40)	520 (37)	421 (35)	165 (30)
2005-2006	515 (15)	270 (18)	206 (15)	156 (13)	70 (13)
Department of residence					
Ille-et-Vilaine	2144 (62)	853 (57)	911 (64)	811 (67)	427 (76)
Côtes d'Armor	949 (28)	494 (33)	373 (26)	301 (25)	117 (21)
Finistère	200 (6)	101 (7)	81 (6)	61 (5)	0 (0)
Other neighbouring departments	128 (4)	58 (4)	50 (4)	39 (3)	15 (3)
Gestational age at inclusion (week)	10.0 (2.6)	9.9 (2.5)	9.8 (2.6)	9.8 (2.6)	9.9 (2.4)
Maternal age at inclusion (years)					
<25	381 (11)	141 (9)	103 (7)	74 (6)	34 (6)
25-30	1361 (40)	587 (39)	555 (39)	475 (39)	218 (39)
30-35	1202 (35)	554 (37)	547 (39)	477 (39)	222 (40)
>35	477 (14)	224 (15)	210 (15)	186 (15)	85 (15)
Mean +/- sd	30.1 (4.3)	30.4 (4.2)	30.6 (4.0)	30.7 (4.0)	30.7 (3.9)
Maternal education					
Primary/secondary school	648 (19)	221 (15)	199 (14)	130 (11)	61 (11)
Baccalaureate	635 (19)	278 (18)	242 (17)	198 (16)	91 (16)
University degree	2130 (62)	1003 (67)	972 (69)	881 (73)	406 (73)
Maternal pre-pregnancy body mass index (kg/m <sup>2</sup> )					
<18.5	257 (8)	98 (7)	99 (7)	91 (8)	45 (8)
18.5-25	2540 (74)	1139 (76)	1067 (75)	925 (76)	432 (77)
25-30	432 (13)	193 (13)	181 (13)	140 (12)	62 (11)
>30	166 (5)	71 (5)	63 (4)	53 (4)	17 (3)
Mean +/- sd	22.4 (4.1)	22.5 (4.1)	22.4 (4.0)	22.2 (3.8)	22.1 (3.7)
Smoking status at inclusion					
Non-smoker	1631 (48)	742 (49)	730 (52)	640 (53)	304 (54)



Non-smoker but smoker at conception	1280 (37)	581 (39)	536 (38)	463 (38)	196 (35)
Smoker at inclusion	475 (14)	170 (11)	137 (10)	100 (8)	56 (10)
Alcohol consumption during pregnancy					
Never	2873 (84)	1262 (84)	1191 (84)	1014 (84)	474 (85)
Occasionally	505 (15)	228 (15)	213 (15)	188 (16)	83 (15)
Parity					
Primiparous	1521 (44)	646 (43)	599 (42)	513 (42)	222 (40)
Multiparous	1888 (55)	852 (57)	814 (58)	695 (57)	336 (60)
Pregnancy number					
Singleton	3360 (99)	1506 (100)	1415 (100)	1212 (100)	559 (100)
Multiple pregnancy	39 (1)	-	-	-	-
Unknown	22	-	-	-	-
Delivery					
Vaginal	2717 (82)	1221 (81)	1143 (81)	990 (84)	475 (88%)
C-section	590 (18)	258 (19)	239 (19)	187 (16)	63 (12%)
Pregnancy outcome					
Live birth	3399 (98)	1506 (100)	1415 (100)	1212 (100)	559 (100)
Miscarriages (<12 weeks)	7 (0.2)	-	-	-	-
Stillbirth (>12 weeks)	21 (0.6)	-	-	-	-
Abortion for medical reason	19 (0.5)	-	-	-	-
Unknown	22 (0.6)	-	-	-	-
Newborn sex					
Male	1728 (50)	768 (51)	709 (50)	605 (50)	281 (50)
Female	1705 (50)	738 (49)	706 (50)	607 (50)	278 (50)
Small for gestational age (<10th percentile)					
No	3156 (93)	1407 (93)	1322 (93)	1134 (94)	536 (96)
Yes	241 (7)	97 (6)	90 (6)	77 (6)	23 (4)
Birth weight (g)	3352 (557)	3411 (484)	3412 (487)	3410 (498)	3436 (483)
Preterm birth (<37 weeks)					
No	3220 (94)	1453 (96)	1366 (97)	1162 (96)	540 (97)
Yes	162 (6)	49 (3)	42 (3)	44 (4)	17 (3)
Gestational age at delivery	39.2 (2.4)	39.4 (1.5)	39.4 (1.5)	39.4 (1.6)	39.5 (1.5)

<sup>a</sup> Newborn characteristics (Pregnancy outcome, sex, small for gestational age and preterm birth) are expressed for the total number of newborns (n=3460) including twins and non-live births.

**Table 2. Summary of data collected at each follow-up<sup>a</sup>**

		Pregnancy or birth	2 years	6 years	12 years
		✓ n ≈ 3,421 ✓ n ≈ 250 to 1000	✓ n ≈ 1506	✓ n ≈ 1415 ✓ n ≈ 287	✓ n ≈ 1212 ✓ n ≈ 559
<b>Health outcomes</b>					
Time to pregnancy	Self-reported	✓			
Gestational age	Medical record	✓			
Congenital anomaly	Clinical examination	✓			
	Self-reported		✓	✓	
Anthropometric measures					
Weight, height, head circumference	Clinical examination or medical records at birth	✓			✓
	Self-reported		✓	✓	✓
Skinfolds, waist circumference, bioimpedance	Clinical examination				✓
Blood pressure	Clinical examination				✓
Neurodevelopment					
Strengths and difficulties questionnaire (SDQ)	Self-reported			✓	✓
CBCL	Self-reported		✓		
Other neuropsychological testing (part of ELDEQ, RT-CPT, CAST, ...)	Self-reported or Clinical examination		✓	✓	✓
WISC-IV	Psychologist			✓	
NEPSY	Psychologist			✓	
Dominic interactive	Computer				✓
MRI	Clinical examination (10- 12 years old)				✓ (n=101)
Wheezing, Asthma (ISAAC)	Self-reported		✓	✓	✓
Allergy, eczema (ISAAC)	Self-reported		✓	✓	✓
Dental health	Self-reported			✓	✓
	Clinical examination				✓
Pubertal development (Tanner stage, age at menarche)	Self-reported (repeated between 9-16 years old)				✓
	Clinical examination				✓
Visual function (contrast sensitivity, color)	Clinical examination			✓	✓
Biological markers					
Steroid hormones (n=14 steroids)	Cord and child serum	✓			✓
Lipids (cholesterol, HDL, LDL, TG)	Cord and child serum	✓			✓
Creatinine	Urine	✓		✓	✓ (serum)
Leptin, Adiponectin	Serum	✓			✓
Glucose	Serum				✓
Thyroid hormones	Serum				✓
Inflammatory markers (IL6, TNFα, C-reactive protein)	Serum				✓
Transaminases (ALT, AST, GGT)	Serum				✓
Untargeted metabolomics	Cord serum and urine	✓			
<b>Environmental exposures</b>					

<b>Pesticides</b>					
Pesticides use at home	Self-reported	✓	✓	✓	✓
Agricultural proximity	GIS-based	✓	✓	✓	✓
Organophosphate pesticides	Urine	✓		✓	
Pyrethroid pesticides	Urine	✓		✓	
Other pesticides of interest in the Brittany area (atrazine, carbamate, bromoxynil, ...)	Urine	✓			
	House dust			✓	
<b>Solvents</b>					
Occupational exposure	Self-reported and JEM	✓			
Recreational exposure	Self-reported	✓	✓	✓	✓
Glycol ethers	Urine	✓		✓	
Occupational exposure to endocrine disruptors	Self-reported and JEM	✓			
<b>Water disinfection by products</b>					
Trihalomethanes	Regulatory water surveillance coupled with self-reported use	✓			
Haloacetic acid	Urine	✓			
Air pollution (PM, NO2)	GIS-based	✓	✓	✓	✓
Traffic and noise	GIS-based	✓	✓	✓	✓
Meteorology	GIS-based	✓	✓	✓	✓
Built environment and natural spaces	GIS-based	✓	✓	✓	✓
Light-at-night	GIS-based	✓	✓	✓	✓
<b>Persistent organic pollutants</b>					
Organochlorine pesticides	Serum (cord, child blood)	✓			✓
	House dust			✓	
Polychlorinated biphenyls (PCB)	Serum (cord, child blood)	✓			✓
	House dust			✓	
Polybrominated diphenyl ethers (PBDE)	Serum (cord)	✓			
	House dust			✓	
Per- and polyfluoroalkyl substances (PFASs)	Serum (cord, child blood)	✓			✓
Phthalate metabolites	Urine	✓			
Phenols	Urine	✓			
Cotinine	Urine	✓		✓	
Mercury	Maternal hair	✓			
Lead	House dust			✓	
<b>Maternal and child characteristics</b>					
Chronic or gestational pathology	Medical records	✓			
Parental occupation & education	Self-reported	✓	✓	✓	✓
Smoking/passive smoking	Self-reported	✓	✓	✓	✓
Alcohol consumption	Self-reported	✓			
Physical activity	Self-reported	✓	✓	✓	✓
Breastfeeding	Self-reported		✓	✓	
Diet and eating behaviour	Self-reported	✓	✓	✓	✓
TV and video games	Self-reported			✓	✓
Sleep	Self-reported		✓	✓	✓

Pets	Self-reported		✓	✓	✓
Medicine intake	Self-reported	✓	✓	✓	✓
Water consumption (drink and bath)	Self-reported	✓	✓	✓	✓
Residential address	Self-reported	✓	✓	✓	✓
House characteristics	Self-reported			✓	✓
Family composition (marital, status, siblings, ...)	Self-reported	✓	✓	✓	✓
Deprivation index	GIS-based	✓	✓	✓	✓
HOME inventory	Psychologist			✓	
Maternal WAIS score	Psychologist			✓	
Parental disease antecedents	Self-reported		✓	✓	✓

✓ assessed in the whole cohort; ✓ assessed in a specific subsample of the cohort

<sup>a</sup> As much as possible, we utilised the same protocol and methods for measuring the variables across the various PELAGIE follow-ups (e.g., standardised self-reported questionnaire) and we maintained stable collaboration with laboratories in charge of measuring the biomarkers. As part of the European mother-child cohort consortium, several variables have been harmonised following specific protocols to facilitate joint analyses with other cohorts.

Abbreviations: CBCL, Child behaviour checklist; ELDEQ, Étude longitudinale du développement des enfants du Québec; RT-CPT, Continuous performance task reaction time; CAST, Childhood Autism Spectrum Test; WISC-IV, Wechsler Intelligence Scale for Children, 4th edition; NEPSY, Developmental Neuropsychological Assessment; MRI, Magnetic resonance imaging; ISAAC, International Study of Asthma and Allergies in Childhood; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; TG, Triglycerides; IL6, Interleukin-6; TNF $\alpha$ , Tumor Necrosis Factor alpha; ALT, alanine transaminase; AST, aspartate transaminase; GGT, Gamma-glutamyltransferase; GIS, Geographic information system; JEM, Job-exposure matrix; PM, Particulate matter; NO<sub>2</sub>, Nitrogen dioxide; HOME, Home Observation for Measurement of the Environment; WAIS, Wechsler Adult Intelligence Scale.