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OVERVIEW

AT A GLANCE

- > Health, health environment & social sciences
- > Perinatal period, growth, development, accidents and injuries, asthma, respiratory disease & allergies, mental health, infectious disease, sleep, healthcare consumption
- > Track children from birth to adulthood
- > Coordinator: Marie-Aline Charles
- > Coordinated by the National Institute for Demographic Studies (INED) in collaboration with the National Institute for Health and Medical Research (Inserm), and the French National Blood Service (EFS)
- > Funding: TGIR-IRESP, ANR

KEY FACTS & FIGURES

- > Inclusion closed; follow-up on-going
- > 18,329 enrolled children in 2011
- > Followed from birth to adulthood
- > 320 maternity units in France in 2011
- > Biobank: cord blood, maternal urine, breast milk, maternal hair
- > Administrative linkage to death certificates, hospital information system, health insurance database planned

Elfe is the first longitudinal study of this kind in France, tracking children from birth to adulthood. It will examine every aspect of these children's lives from the perspectives of health, social sciences and environmental health. Elfe will offer a unique opportunity to identify the factors that help or hinder children development.



Positioning

- > Elfe cohort works in close collaboration with the Epipage 2 cohort (children born premature) launched at the same time as Elfe
- > Elfe cohort is also committed in the European Child Cohort Network (Euconet), I4C (International Childhood Cancer Cohort Consortium) and the FP7 ENRIECO projects
- > Elfe is the first French national birth cohort combining multiple disciplines such as health, social science and environmental sciences

LEADERSHIP

Marie-Aline Charles, an epidemiologist at Inserm, is the director of the «Elfe» INED-Inserm-EFS mixed unit. She is helped by a deputy director, Bertrand Geay, Professor at the University of Picardy.

Marie-Aline Charles, M.D., MPH

- █ Epidemiologist and research director at Inserm
- █ Team leader of “Early origin of the child’s health and development”, Centre of Research in Epidemiology and Statistics Sorbonne Paris Cité
- █ Expertise: growth, obesity, metabolism, nutrition
- █ Committee membership: scientific committee of the French diabetes society, founding member of the French DOHAD Society, Aviesan research in public health group
- █ Current collaborations: environment and children international birth cohort group (Japan, China, Germany)

Bertrand Geay, Ph.D.

- █ Sociologist and professor at the University of Picardy
- █ Director of the CNRS-Picardie University mixed research center on public action and politics (CURAPP)
- █ Expertise: education & socialization
- █ Committee membership: early childhood national observatory
- █ Current collaborations: National institute for education of young handicapped people (INS-HEA), German national educational panel (NEPS)

SCIENTIFIC NETWORK & MANAGEMENT

- █ European Child Cohort Network (Eucconet) (2008-2012)
 - > Funded by the European Science Foundation
 - > Jointly directed by Henri Leridon and Heather Joshi from the Center for Longitudinal Studies in London, UK
 - > Eucconet has provided an opportunity to exchange ideas about the best way of managing longitudinal and multidisciplinary studies, and to develop common tools for undertaking Europe-wide comparisons
- █ I4C (International Childhood Cancer Cohort Consortium) coordinated by Terry Dwyer from The George Institute for Global Health, UK
- █ Environment and children international birth cohort group
 - > Funded by the German and Japanese ministries of environment
 - > Coordination Ruth Etzel, Office of children health protection, US Environment Protection Agency
 - > Aim: develop international collaborations between large birth cohorts on chemical contaminants affecting children health
- █ Funded European projects
 - > FP7 ENRIECO (Environmental Health Risks in European Birth Cohorts) coordinated by Prof. M. Kogevinas and Dr. M. Vassilaki from the Department of Social Medicine, Medical School, University of Crete, Greece
- █ Elfe has direct links with several major foreign cohorts, notably:
 - > the Millennium Cohort Study in the United Kingdom coordinated by Emla Fitzsimons, Professor of Economics, Institute of Education, London
 - > National Educational Panel Study (NEPS) in Germany coordinated by Hans-Günther Roßbach, Director of Leibniz Institute for Educational Trajectories
 - > Japan Environment and Children’s Study (JECS) coordinated by Toshihiro Kawamoto, Japan Environment and Children’s Study (JECS) Programme Office
 - > Shanghai birth cohort coordinated by Jim Zhang, Shanghai Jiao Tong University School of Medicine, China
- █ The study’s scientific aspects are monitored by a scientific council made up of independent experts from France and abroad:

<ul style="list-style-type: none"> > Health: <ul style="list-style-type: none"> >> Frédéric Villebrun >> Juliane Léger >> Serge Herberg >> Fred Paccaud >> Anne Cambon-Thomsen >> Anne-Marie Nybo-Andersen > Health environment: <ul style="list-style-type: none"> >> Sylvaine Cordier 	<ul style="list-style-type: none"> > Social sciences: <ul style="list-style-type: none"> >> Alain Chenu >> Michel Fayol >> Cécile Lefèvre >> Gérard Mauger >> Agnès van Zanten >> Heather Joshi
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PROJECT DESCRIPTION

SCIENTIFIC OBJECTIVES

- Observing children born within the same year over a period of two decades will offer a unique opportunity to identify the factors that help or hinder their health, development and school achievements
- Allow to analyze how these children find their place in society. Their health and schooling, what they eat and where they live, as well as their family and social life, will be examined by one hundred fifty researchers involved in the study
- By crossing the children collected data, it will be possible to answer to the questions addressing by parents and scientists notably about early development, how promoting the well-being of children's physical health and psychological

INNOVATIVE SCIENTIFIC FEATURES

- First longitudinal study of this nature in France
- Involve 150 researchers from more than 80 research teams
- Quality:
 - > Every stage of the project and each separate procedure is approved by the label Committee of the National Council for Statistical Information (CNIS), the consultative committee for health data treatment (CCTIRS) and the French data protection authority (CNIL), the committee for protection of persons engaged in research (CPP)
 - > Elfe team had launched a pilot survey in 2007 in 62 maternity units to check the study's feasibility and validate the methodology before scaling it up to cover the whole of the country

METHODOLOGY QUALITY

- Representative of mainland French population and territories
- Data collected by computer combined telephone interviews carried out by trained interviewers or parents completed web/paper questionnaires
- Health data collected from medical file at the maternity, general practitioner at 2 years (subgroup: 7,600), school doctor at 4-5 years (subgroup) and matching with health insurance and hospital data bases (SNIIRAM: planned)
- Cognitive and visuo-motor tests performed at 3 years during a home visit (subgroup: 9,300)

DESIGN, METHODOLOGY & TIMELINE



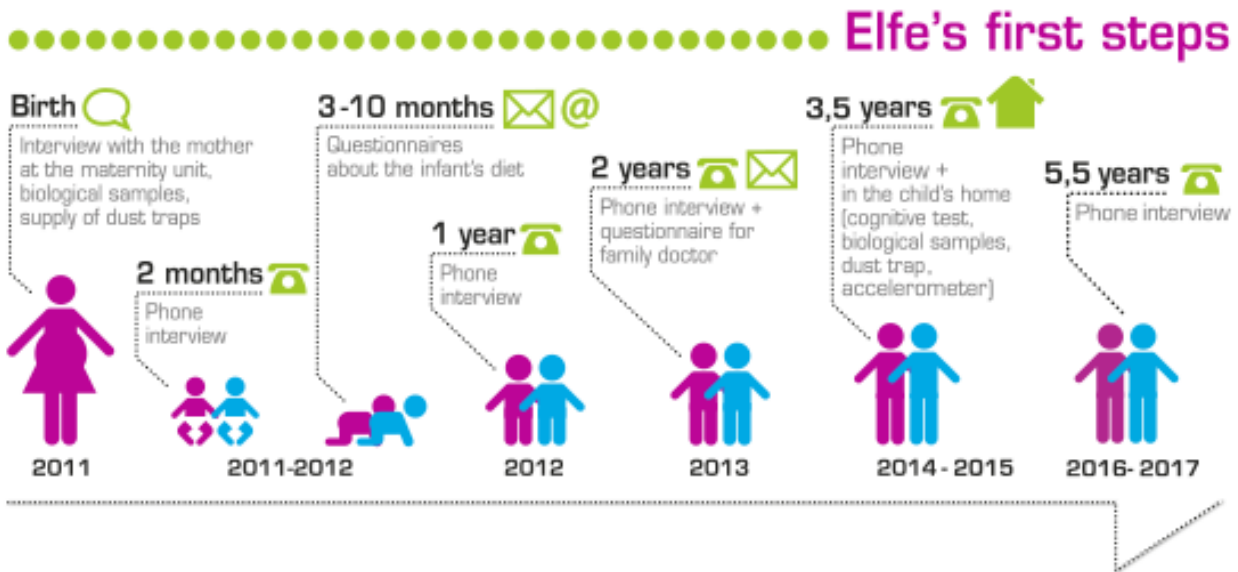
Recruitment objectives:	18,329 children (51% participation rate)
Sites:	Random sample of 349 maternity units in France
Inclusion criteria:	Children whose parents ≥ 18 yrs have consented to their inclusion All selected purely on the basis of their date and place of birth, able to speak French, English, Arabic or Turkish
Exclusion criteria:	Stillbirth, birth <33 weeks of gestation, or planning to moving out of metropolitan France in the following 3 years

INCLUSION COLLECTION
Database: face-to-face interview with the new mother (at the maternity unit) & medical file data collection
Biobank: (in a sub-group of 154 maternity units): maternal blood, various maternal material (urine, hair, breast milk)
 Child: cord blood, cord fragment, meconium, & faeces

FOLLOW-UP:
Database: telephone interview at 2 months, 1 year and 2 years
 3 to 10 months: postal or Internet questionnaires on child's diet
 At 2 years: questionnaire filled out by the family doctor
 At 3 ½ years: in-home survey (mother) and phone survey (father)
Biobank: at 3 ½ years: collection of child's hair, urine and stools + dust

DATABASE & BIOBANK CONTENTS

DATABASE



Retrospective data on exposure during pregnancy and a prospective follow-up of the child:

- > **Exposures:** medication, air pollution, occupation, tobacco, alcohol, diet, chemical and physical agents, social position
- > **Outcomes:** birth defects, infections, growth/obesity, neurodevelopment, asthma/allergies, pubertal development, sleep, mental health
- > **Data available in medical files at the time of delivery:** characteristics of the newborn child (weight, size, gestational age, birth defects, circumstances of delivery, infections...)
- > **Medical examinations:** vaccination, hearing, vision, weight/height, asthma, allergies, anemia, genital and neuro-psycho-motor testing at various ages
- > **Dust collection** at home for microbiology or chemical contaminants
- > **Register-based follow-up:** death certificates, hospital information system, Health Insurance Data Base

BIOBANK

Originality

- > **A biobank with more than 2,500 mothers and 2,500 children sampled at enrollment** associated to a longitudinal child biobanking

Scientific objective

- > Biobank aims to carry out future studies investigating the association between biomarkers (nutrition, inflammation, metabolism, hormones, environmental exposures...) or to understand the interactions between the environment and the genome
- > A call for proposal is currently on-going to access to biobank for Elfe researchers in a first step. A larger opening is scheduled after this first round

Samples

- > Mother & child sampling at birth. Additional child sampling at 3-year follow-up
- > A large variety of biospecimens with numerous aliquots per participants

Associated resources

- > The samples can be linked to all the other data collected by questionnaires, medical examinations, matching with external files such as the National Health Insurance files
- > At 2 months, dust sample from the infant bedroom on which microbiological contamination has been assessed
- > At 3 ½ years, bank of dust sample collected during the home visit for a subgroup of 830 families with biological samples at enrollment

TECHNICAL MODALITIES & SPECIFICATIONS

ORGANIZATION

- Biological samples collection, treatment, and storage is organized and performed in collaboration with the **EFS (Etablissement Français du Sang)**
- Three EFS Biological Ressources Center (in Annemasse, Bois-Guillaume and Dijon) represent the Elfe biobank
- Biological samples are **stored at -80°** in labellized Biological Ressources Centers
- Each biological sample is identified with unique and common label with sample tracking sheets. Theses IDs are different from the patient ID in the database. A secondary ID has been generated for the correspondence between both and is stocked in biobank database

SPECIFICATIONS

- Mothers who have consented from themselves and their child to participate to the Elfe study and to biological sampling in 209 from the initial sample out of the 349 maternities selected at the Elfe cohort inception
- Date of the first sampling: 07/06/2011
- Protocol for the biological sample collection exists
- The information system associated to the Elfe biobank, based on the ModulBio software, is an online multisite solution hosted in the Elfe information center. The Elfe coordination team as well as the three EFS biological Resource Centers have access to the data files
- Label of quality: ELFE biobank received a bio-collection authorization from the French Ministry of Research, CODECOH n° AC-2011-1367 based on the EFS quality standard
- Biobank procedures were developed by the ELFE biobank coordination team in order to apply standardized methods for sample collection, treatment and conservation (Standard Operating Procedure)
- ELFE biological samples are available through response to periodical calls for proposals

BIOLOGICAL SAMPLE COLLECTION & ACCESS

Biospecimens	Origin	Quantity available	No. of aliquots	No. of subjects available	Storage conditions
At Baseline in 2011					
Hair	Mother	-	-	1477	Envelop; RT
Breast milk	Mother	1 mL	5	1616	Cryotube; -80°C
Serum	Mother	2 mL	3	588	Cryotube; -80°C
Serum	Mother	0.5 mL	9	1735	Frozen stick; LN
DNA	Mother	Extraction in progress			
Plasma	Mother	0,5 mL	4	2740	Frozen stick; LN
Whole blood	Mother	0,5 mL	2	2800	Frozen stick; LN
Urine	Mother	19,5 mL	Not available	2019	
Meconium	Infant	40 mL	Not available	1380	Coprology pot; -80°C
Stools	Infant	40 mL	Not available	1209	Coprology pot; -80°C
Tissues	Umbilical cord	2 mL	2	981	Cryotube; -80°C
Cord DNA	Cord blood	Extraction in progress			
Red blood cells	Cord blood	1 mL	6	1686	Cryotube; -80°C
Plasma	Cord blood	0,5 mL	6	2481	Frozen stick; LN
Whole blood	Cord blood	6 mL	-	286	Paxgene; -80°C
Whole blood	Cord blood	0,5 mL	2	2748	Frozen stick; LN
Serum	Cord blood	0,5 mL	10	2803	Frozen stick; LN
During the follow-up at 3 ½ years (in 2014-2015)					
Urine	Children	1 ml	20	2100	Cryotube; -80°C
Stools	Children			830	Cryotube; -80°C
Hair	Children			2100	Envelop; RT

RT: room temperature, LN: liquid nitrogen

BIOBANK SAMPLE ACCESS MODALITIES

- A document specifying biobank access is available
- To date, biological samples are accessible to Elfe public research teams only. In a second time, biobank will be available to public research teams or public-private partnership
- Access to biological samples is possible for an industrial research team through a public-private partnership on the basis of a specific research project proposal
- Specific biological samples access is granted on the research project proposal basis selected through a Elfe project call. Fundings for the project can be sought only after the project has been selected by the Elfe call

BIOLOGICAL SAMPLE ANALYSES

- Research team proposing a project needs to identify the laboratory able to perform sample analyses and find the specific funding for biological measurements
- The results generated from sample analysis through a specific research project will be made available to the whole research community from the Elfe database
- The first analyses performed on the samples were done in the context of the perinatal part of the first French national biomonitoring plan and concerned a set of environmental contaminants. They will be made available in 2016

COST

- Costs related to sample release, sample transport and eventually sample re-aliquoting are in charge of requesting research team
 - > Costs related to sample release and transport: €0,98HT per sample (in 2015)
 - > Cost to process aliquoting samples: on a quotation basis provided by EFS
- Access right to Elfe data is also mandatory in order to contribute to cohort management and sustainability. The pricing principles are currently under development

RESEARCH COLLABORATION OPPORTUNITIES

Phase IV Product approval Phase III Phase II Phase I Pre-clinical Proof of concept

Translational research

- > Vaccine coverage and determinants of vaccine refusals
- > Recourse to care of French children
- > Growth of French children

Clinical development

- > Recourse to care of French children
- > Medication use in French children

Outcomes research

- > Long-term consequences of early exposure to environmental contaminants
- > Family, economic and sociocultural factors that determine children's long-term educational outcomes
- > Long-term consequences of head trauma in children
- > Folate supplementation in pregnancy and long-term child development and health
- > Early determinants of food allergies
- > Quality of sleep of French children
- > Determinants of precocious puberty
- > Determinants and phenotype of respiratory diseases in children
- > Production of social health inequalities in French children

BIBLIOGRAPHY

Design

- > Vandentorren S *et al.*, **Rationales, design and recruitment for the Elfe longitudinal study**, *BMC Pediatrics* 2009, 9:58
- > Pirus C *et al.*, **La construction d'une cohorte : l'expérience du projet français Elfe**, *Population* 2010, 65(4), 637-670
- > Oleko A, *et al.*, **A Pilot Study of the ELFE Longitudinal Cohort: Feasibility and Preliminary Evaluation of Biological Collection**. *Biopreserv Biobank*. 2011; 9:223-227

Environment

- > Zeman FA, *et al.*, **Exposure assessment of phthalates in French pregnant women: results of the ELFE pilot study**. *International journal of hygiene and environmental health* 2013; 216(3):271-9
- > Rocchi S *et al.*, **Microbiological characterization of 3193 French dwellings of Elfe cohort children**. *The Science of the total environment* (2014) 505C, 1026-1035

Nutrition

- > Kersuzan C *et al.*, **Prévalence de l'allaitement à la maternité selon les caractéristiques des parents et les conditions de l'accouchement**. Résultats de l'enquête Elfe maternité, France métropolitaine, 2011, BEH 2014, n° 27, p. 440-449.

Health

- > Bales M, *et al.*, **Prenatal psychological distress and access to mental health care in the ELFE cohort**. *Eur Psychiatry*. 2015 Feb; 30(2):322-8.
- > Richaud-Eyraud E., *et al.*, **Dépistage des maladies infectieuses en cours de grossesse, résultats de l'enquête Elfe en maternités**, France métropolitaine, 2011, BEH 2015, N°15-16 pp 254-263