European Journal of Pediatrics
https://doi.org/10.1007/s00431-022-04733-z

RESEARCH

Determinants of incomplete vaccination in children at age two in France: results from the nationwide ELFE birth cohort

Marianne Jacques[1,2] · Fleur Lorton[1,2,3] · Marie-Noëlle Dufourg[4] · Corinne Bois[4] · Elise Launay[1,2,3] · Thierry Siméon[4] · Jocelyn Raude[5] · Christèle Gras-Le Guen[1,2,3] · Daniel Lévy-Brühl[6] · Marie-Aline Charles[4] · Martin Chalumeau[1,7] · Pauline Scherdel[1,2]

Received: 10 August 2022 / Revised: 18 November 2022 / Accepted: 23 November 2022

Abstract

Incomplete vaccination in the pediatric population is a growing public health issue in high-income countries, but its determinants are poorly understood. Their identification is necessary to design target actions that can improve vaccination uptake. Our aim was to assess the determinants of incomplete vaccination in two-year-old children in France. Among the 18,329 children included in the 2011 ELFE French nationwide population-based birth cohort, we selected those for whom vaccination status was available at age two years. Incomplete vaccination was defined as ≥ 1 missing dose of recommended vaccines. Potential determinants of incomplete vaccination were identified by using logistic regression, taking into account attrition and missing data. Of the 5,740 (31.3%) children analyzed, 46.5% (95% confidence interval [CI] 44.7–48.0) were incompletely vaccinated. Factors independently associated with incomplete vaccination were having older siblings (adjusted odds ratio 1.18, 95% CI [1.03–1.34] and 1.28 [1.06–1.54] for one and ≥ 2 siblings, respectively, vs. 0), residing in an isolated area (1.92 [1.36–2.75] vs. an urban area), parents not following health recommendations or using alternative medicines (1.81 [1.41–2.34] and 1.23 [1.04–1.46], respectively, vs. parents confident in institutions and following heath recommendations), not being visited by a maternal and child protection service nurse during the child's first two months (1.19 [1.03–1.38] vs. ≥ 1 visit), and being followed by a general practitioner (2.87 [2.52–3.26] vs. a pediatrician).

Conclusions: Incomplete vaccination was highly prevalent in the studied pediatric population and was associated with several socio-demographic, parental, and healthcare service characteristics. These findings may help in designing targeted corrective actions.

What is Known:
- *Incomplete vaccination in the pediatric population is a growing public health issue in high-income countries.*
- *The partial understanding of the determinants of incomplete vaccination precludes the design of effective targeted corrective actions.*

What is New:
- *High prevalence of incomplete vaccination at age two years in France.*
- *Incomplete vaccination was independently associated with several socio-demographic, parental, and healthcare service characteristics.*

Keywords (MeSH) Child · Cohort studies · France · Primary prevention · Socio-economic factors · Vaccination

Abbreviations

aOR	Adjusted odds ratio
aP	Acellular pertussis vaccine
CI	Confidence interval
DT-IPV	Diphtheria, tetanus, and inactivated poliomyelitis vaccine
ELFE	*Etude Longitudinale Française depuis l'Enfance*
GP	General practitioner
HepB	Hepatitis B vaccine
Hib	*Haemophilus influenzae* type b conjugate vaccine
HIC	High-income country
KAP	Knowledge, attitude, and practice

Communicated by Tobias Tenenbaum

✉ Martin Chalumeau
martin.chalumeau@inserm.fr

Extended author information available on the last page of the article

Published online: 21 December 2022

MCPS	Maternal and child protection service
MenC	Serogroup C meningococcal vaccine
MMR	Measles-mumps-rubella vaccine
PCV	Pneumococcal conjugate vaccine

Introduction

Vaccine hesitancy and incomplete vaccination issues were recently highlighted by the COVID-19 pandemic [1] but are a three-decade-old problem in high-income countries (HICs) [2] and primarily affect children. Depending on the age group considered, one-third to one-half of children aged two to six years living in HICs are incompletely vaccinated [3, 4], and 2% to 3% of two-year-old children are completely unvaccinated [5]. Among children living in HICs, vaccination coverage for most vaccines does not meet defined targets [5–7], with harmful consequences. For instance, outbreaks of vaccine-preventable diseases such as measles and pertussis continue to occur sporadically in France [8–10]. Moreover, 25% of childhood deaths and severe sequelae due to community-onset pneumococcal and meningococcal infections were found to be vaccine-preventable [11]. Thus, a better understanding of the main drivers of incomplete vaccination in the pediatric population is pivotal to design corrective actions, notably to identify priority targets and messages for future educational campaigns.

Some determinants of incomplete vaccination in HICs have been identified and are related to (i) child characteristics [3, 5, 12–14]; (ii) household socio-demographic characteristics [3, 5, 12–19]; (iii) parental knowledge, attitude, and practices (KAPs) such as lack of information or perception that natural disease is preferable to vaccination [3, 16]; (iv) healthcare system characteristics such as no usual provider [3, 13, 15, 18]; and (v) local vaccination schedule characteristics such as non-simultaneous vaccination [12, 16, 17] (eTable 1). However, the results of these studies are of limited interest to understand the current main drivers of incomplete vaccination in children because of the timing of data collection [3, 12, 13, 15, 16], their design exposing them to strong selection bias [13, 17], and the paucity of parental KAP [5, 14, 15, 18, 19] data analyzed.

France is a country of particular interest to study the determinants of incomplete vaccination because it hosts a strong and well-established phenomenon of vaccine hesitancy [14, 20] and also hosts one of the most recent European national population-based birth cohorts [21], the ELFE study (*Etude Longitudinale Française depuis l'Enfance*: French Longitudinal Study from childhood). This cohort allows for studying incomplete vaccination with a very large sample offering good statistical power, a population-based design that limits selection bias, and numerous and complementary data regarding household socio-demographic characteristics and parental KAPs. In this study, we aimed to use this database to assess the determinants of incomplete vaccination in two-year-old children in France.

Materials and methods

General methodology

We used the data from the ELFE prospective nationwide birth cohort, which intends to follow children from birth to adulthood to study the relation between socio-demographic context, behaviors, and overall health [22, 23]. The ELFE cohort enrolled 18,329 children born in 2011 in metropolitan France who were recruited in the 320 participating maternity units among 349 randomly selected hospitals. A stratified sampling according to the size of each maternity unit was used and patient recruitment took place during four inclusion periods of four to eight days spread over the year. The inclusion criteria were infant born alive, singleton or twins, term $\geq$ 33 weeks of gestation, mother aged 18 years or older, parent(s) able to provide informed consent in one of the established languages (French, English, Arabic, Turkish), and not living temporarily in France. A prospective follow-up of the children was performed by several surveys [22, 23]. The ELFE study was approved by the Advisory Committee for the Treatment of Information on Health Research (no. 13,004), the National Agency Regulating Data Protection (no. 913,074), and the National Statistics Council (visa 2013X719AU). All participating parents provided written consent for their own and their child's participation.

For the present study, we analyzed all children included in the ELFE cohort whose parents did not withdraw consent and had available data on the main vaccinations recommended before age two years according to the French vaccination schedule in 2011–2012. For twin pairs, only one infant was randomly selected. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to report this study (eTable 2) [24].

Vaccination status

Vaccination against 11 infectious pathogens was recommended before age two years in France at the time of the study [25]. This immunization program was normally to be achieved by four doses of diphtheria, tetanus, and inactivated poliomyelitis vaccine (DT-IPV); four doses of acellular pertussis vaccine (aP); four doses of *Haemophilus influenzae* type b conjugate vaccine (Hib); three doses of pneumococcal

conjugate vaccine (PCV); three doses of hepatitis B vaccine (HepB); two doses of measles-mumps-rubella vaccine (MMR); and one dose of serogroup C meningococcal vaccine (MenC) (eFigure 1). In France, vaccination for children is available from any primary care practitioner of the parents' choice. It includes general practitioners (GP) and pediatricians (whereby parents pay for the consultation and the vaccine then are reimbursed in full), as well as physicians working in maternal and child protection services (MCPSs), which are free-of-charge universal services in France offering prevention and health promotion services for pregnant women and children up to age six [26]. Only DT-IPV was mandatory at the time of the study, and MenC was introduced to the vaccination schedule in 2010 [27]. The number of doses received for each vaccine from birth until the visit and reported in the child health booklet was collected in 2013 by the child's referring physician during the mandatory medical consultation scheduled at the age of two. In France, vaccination during infancy is systematically noted in this booklet. Vaccination was considered incomplete when at least one recommended vaccine dose was missing because the failure to receive a single dose by age two years is considered potentially dangerous for most of the vaccines studied [28].

Potential determinant measurements

Child characteristics, household socio-demographic characteristics, parental KAPs, and healthcare system characteristics were collected by using the successive parent questionnaires of the ELFE study as described elsewhere [22]. The baseline assessment was achieved during the maternity hospital stay with a face-to-face interview with the mother and data collection from the mother's medical record. During the follow-up, computer-assisted telephone interviews were performed at two months, one and two years of age.

Statistical analyses

We first described the general characteristics of the analyzed children and compared them with those not analyzed (i.e., meeting the ELFE study inclusion criteria but without information on vaccination status at age two) and we estimated the vaccine coverage by vaccine. Then, we calculated the incomplete vaccination rate at age two years and studied crude and multi-variable associations with potential determinants by using a logistic regression model including candidate covariates previously identified as potential risk factors of incomplete vaccination in a literature review [3, 5, 12–19] (eTable 1), significantly associated with incomplete vaccination in the crude analyses or considered of interest by the co-authors.

All descriptive analyses performed on the total sample of children analyzed (rates and confidence intervals [CIs]) were weighted to take into account the inclusion procedure and the selection bias resulting from non-response and to provide representative results of births in 2011 in France. These statistical weights corrected by a calibration on margins were calculated for each child included in the analysis according to numerous covariates (eMethods 1). The parental KAP data were summarized in one latent variable, whose classes were identified by using clustering analysis including a latent class analysis and a selection of relevant variables (eMethods 2) [29, 30]. This parental KAP latent variable was integrated into the final multi-variable logistic regression model as a categorical covariate.

Several sensitivity analyses were performed to (i) repeat the descriptive analyses without weighting, (ii) repeat the multivariable analyses with weighting (eMethods 1), and (iii) modify the outcome (i.e., without MenC, the most recently recommended vaccine [27], or without HepB, the most controversial vaccine in France [31]). The rate of missing values for the potential determinants ranged from 0 to 5%. We performed multiple imputations with chained equations by applying logistic regression for binary variables, polytomous logistic regression for multinomial unordered qualitative variables, and a proportional odds model for ordinal qualitative variables (eMethods 3) [32]. The analyses involved using R v4.0.5 (R foundation for Statistical Computing, Vienna, Austria).

Results

Description of the population

Among the 18,329 newborns included in the initial ELFE study, 5,740 (31.3%) children were included in the present analyses (Fig. 1). Analyzed children differed from non-analyzed ones ($n = 11,844$) in several characteristics; notably, they were less often born prematurely, more often had a mother born in France, with a university degree, a higher household income, and more often resided in suburban areas (eTable 3).

Incomplete vaccination rate

Among 5,740 children analyzed, 46.5% (95% CI [44.7–48.0]) were incompletely vaccinated at age two years, and 0.4% [0.2–0.7] had never received a single vaccine dose (Table 1). The vaccination coverage was 82.6% [81.2–84.0] for the second dose of MMR, 71.1% [69.4–73.0] for MenC, and 89.6% [87.4–90.0] for HepB. Among the 2,550 incompletely vaccinated children, 46.0% ($n = 1,174$) were missing

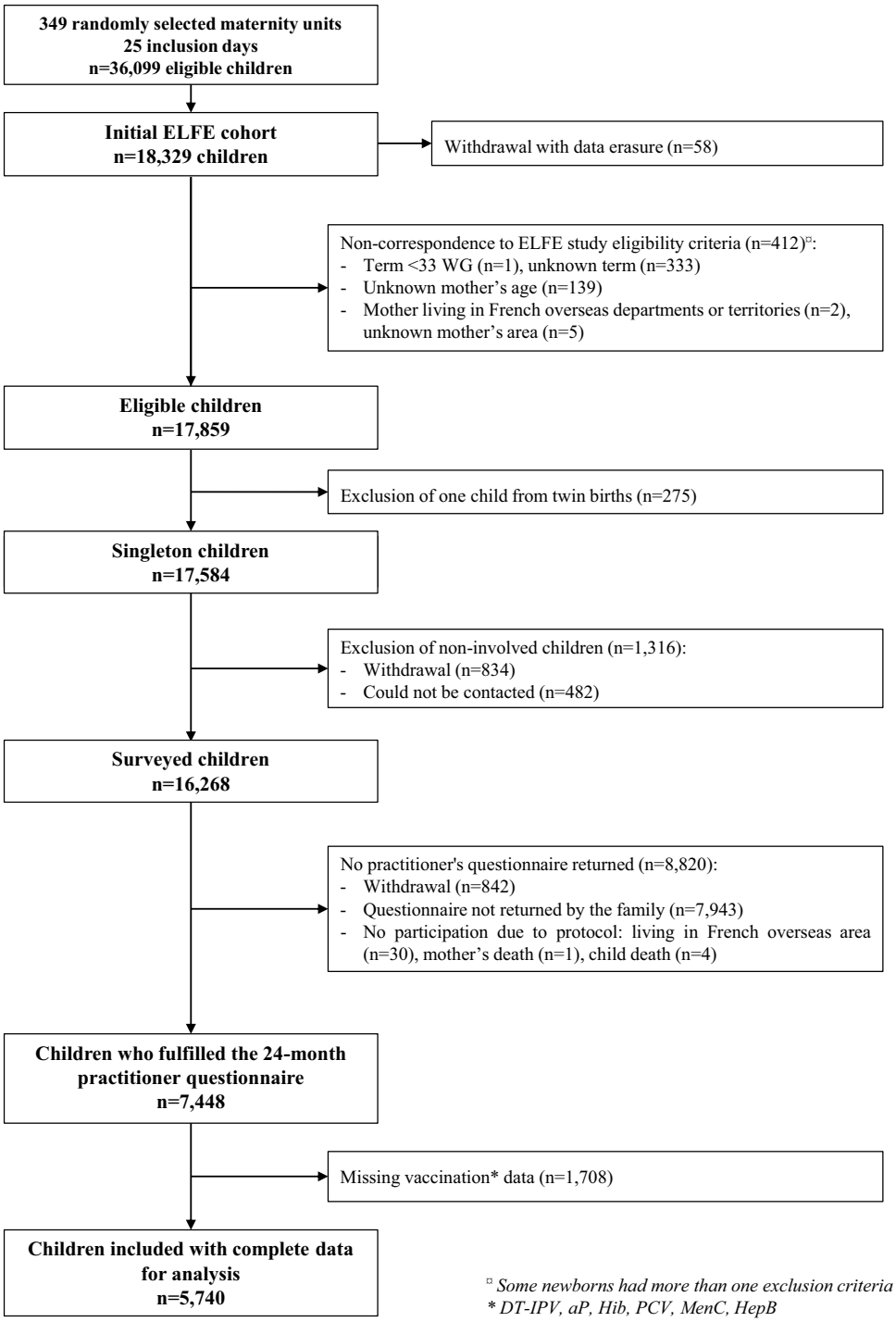


Fig. 1 Flowchart of participants in the study. aP: acellular pertussis vaccine, CI: confidence interval, DT-IPV: diphtheria, tetanus, and inactivated poliomyelitis vaccine, HepB: hepatitis B vaccine, Hib: *Haemophilus influenzae* type b conjugate vaccine, MenC: serogroup C meningococcal vaccine, PCV: pneumococcal conjugate vaccine, WG: weeks of gestation

one dose, 43.6% ($n = 1{,}111$) were missing two to five doses, and 10.4% ($n = 265$) were missing six or more doses.

Factors associated with incomplete vaccination

We found several significant crude associations between incomplete vaccination and potential determinants (eTable 4), and several independent ones after adjustment on all relevant covariates and on the parental KAP latent variable (eMethods 2). Regarding household socio-demographic characteristics, incomplete vaccination was independently associated with having older siblings (adjusted odds ratio [aOR] = 1.18, 95% CI [1.03–1.34] and 1.28 [1.06–1.54], for one and at least two siblings, respectively, vs. zero) and residing in an isolated area (1.92 [1.36–2.75] vs. an urban area) (Table 2). Regarding parental KAPs, incomplete

Table 1 Vaccination rate at age 2 years, by vaccine for the ELFE cohort and national 2013 data

Vaccine	ELFE children ($n = 5,740$)					National vaccination coverage data 2013 [e]
	Weighted[c] %	[95% CI][d]	Unweighted, *n*	%	[95% CI][d]	
DT-IPV						
Primo-vaccination [a]	98.5	[98.0–99.0]	5,666	98.7	[98.4–99.0]	98.5%
Booster [b]	90.4	[89.3–91.0]	5,202	90.6	[89.8–91.4]	91.0%
aP						
Primo-vaccination [a]	98.3	[97.8–99.0]	5,651	98.4	[98.1–98.7]	98.3%
Booster [b]	89.3	[88.1–90.0]	5,129	89.4	[88.5–90.1]	90.3%
Hib						
Primo-vaccination [a]	97.4	[96.7–98.0]	5,612	97.8	[97.3–98.1]	97.5%
Booster [b]	87.6	[86.3–89.0]	5,078	88.5	[87.6–89.3]	88.4%
PCV	94.2	[93.3–95.0]	5,392	93.9	[93.3–94.5]	89.2%
MenC	71.1	[69.4–73.0]	4,214	73.4	[72.2–74.6]	56.4%
MMR						
1 dose	97.5	[96.8–98.0]	5,601	97.6	[97.1–98.0]	90.3%
2 doses	82.6	[81.2–84.0]	4,782	83.3	[82.3–84.3]	74.5%
HepB	89.6	[87.4–90.0]	5,072	88.4	[87.5–89.2]	81.5%
Incompletely vaccinated	46.5	[44.7–48.0]	2,550	44.4	[43.1–45.7]	-
Completely unvaccinated	0.4	[0.2–0.7]	16	0.3	[0.2–0.5]	-

aP acellular pertussis vaccine, *CI* confidence interval, *DT-IPV* diphtheria, tetanus, and inactivated poliomyelitis vaccine, *HepB* hepatitis B vaccine, *Hib Haemophilus influenzae* type b conjugate vaccine, *MenC* serogroup C meningococcal vaccine, *MMR* measles-mumps-rubella vaccine, *PCV* pneumococcal conjugate vaccine

[a]"Primo-vaccination" refers to the administration of the first three doses of these vaccines

[b]"Booster" refers to the fourth dose

[c]Weighting is detailed in eMethods 1

[d]Calculated with the Wilson score method with continuity correction.

[e]National vaccination coverage at age 2 years in 2013 calculated by the French national public health agency [45]

vaccination was independently associated with having parents not following health recommendations or parents using alternative medicines (1.81 [1.41–2.34] and 1.23 [1.04–1.46], respectively, vs. parents confident in institutions and following heath recommendations). Regarding healthcare system characteristics, incomplete vaccination was independently associated with not receiving any visit from an MCPS nurse during the child's first two months (1.19 [1.03–1.38] vs. at least one visit) and being medically followed by a GP (2.87 [2.52–3.26] vs. a pediatrician or an MCPS physician).

Sensitivity analyses

On sensitivity analyses, the same associations as above were found except for (i) the number of siblings when analyses were weighted, (ii) the area of residence and a visit from an MCPS nurse when MenC was removed from the outcome, and (iii) younger maternal age, which became significantly associated with incomplete vaccination (0.98 [0.97–1.00]) when MenC or HepB was removed from the outcome (eTables 5 and 6).

Discussion

Main results and interpretation

In this national-scale population-based prospective study, incomplete vaccination at age two years was frequent, with more than 45% of children incompletely vaccinated. This finding is consistent with the study of Bailly et al., which found 47% of children with at least one delayed vaccination for their age among 443 French children under age two followed by primary-care pediatricians in 2014 [14]. In other HICs, incomplete vaccination rates seemed lower, about 20% to 30% of children aged two to three years [15, 17, 33]. This observation could be explained by differences in the organization of vaccine delivery and administration in different countries, discrepancies in mandatory vaccination, and the strong phenomenon of vaccine hesitancy in France

Table 2 Multi-variable associations between main characteristics and incomplete vaccination (adjusted logistic regression, reference group: children with full vaccination)

	aOR	[95% CI]	p[a]
Household socio-demographic characteristics			
Number of older siblings			0.02
Zero	1	-	
One	1.18	[1.03–1.34]	
≥ Two	1.28	[1.06–1.54]	
Area of residence [b]			< 0.001
Urban	1	-	
Suburban	1.10	[0.98–1.24]	
Isolated	1.92	[1.36–2.75]	
Parental KAPs			
Parental KAP latent variable [c]			< 0.001
Compliant with health recommendations and confident in institutions	1	-	
Alternative medicine user	1.23	[1.04–1.46]	
Low compliant with recommendations during pregnancy	1.15	[0.95–1.39]	
Low compliant for child care	1.81	[1.41–2.34]	
Healthcare system characteristics			
No visit of an MCPS nurse during the first two months (ref = ≥ 1)	1.19	[1.03–1.38]	0.02
Specialty of child's physician during the first two years			< 0.001
Pediatrician or MCPS physician alone	1	-	
GP and either pediatrician or MCPS physician	1.10	[0.94–1.28]	
GP alone	2.87	[2.52–3.26]	

No multi-collinearity problem was detected (overall VIF < 1.21)

aOR adjusted odds ratio, *CI* confidence interval, *GP* general practitioner, *KAP* knowledge, attitude, and practice, *MCPS* maternal and child protection service, *ref* reference group, *VIF* variance inflation factor

[a]Calculated with likelihood ratio test, adjusted on preterm birth, child's health, mother's country of birth, mother's age, marital status of parents, mother's level of education, parental difference of education level, mother's employment, household income, type of mother's health insurance, type of mother's complementary insurance, and childcare providers

[b]Defined according to the French National Institute of Statistics and Economic Studies (INSEE) 2010 classification [36]

[c]Clusters within the parental KAP latent variable were identified with latent class analysis (eMethods 2)

[34]. Incomplete vaccination rates were worrying in view of the resurgence of some vaccine-preventable diseases and their severity in a particularly vulnerable population whose age is close to the peak incidence of many of these diseases [28]. This high rate also emphasizes the need for quantitative evidence-based studies to identify risk factors of incomplete vaccination.

We identified several independent factors associated with incomplete vaccination at age two years, and some were previously identified in the literature. The strength of these associations, from modest (having older siblings, having parents using alternative medicine, and never having received a visit from an MCPS nurse) to more substantial (residing in an isolated area, and being followed by a GP), could be useful in prioritizing targets for corrective actions. Regarding household socio-demographic characteristics, having older siblings was significantly associated with incomplete vaccination, as was found in previous studies [3, 15, 17]. This could be related to an increase in parental self-confidence regarding the absence of visible immediate health consequences of non-vaccination, as found with other preventive attitudes [35], and a restriction of parenting availability associated with the competing needs of each child in the household. Thus, families with a high number of children should probably be targeted by vaccine programs, and vaccines being available in the physician's office could improve vaccination uptake by allowing immediate vaccination during the consultation.

Consistently with the Cotter et al.'s study in the United States in 2002 [13], we found incomplete vaccination strongly associated with residing in an isolated versus an urban area [36]. Thus, geographic distance to healthcare facilities seems to remain a barrier for families to access vaccination in HICs in the twenty-first century [3]. Suggested solutions to simplify access to vaccination included allowing vaccination in alternative settings such as pharmacies, schools, or by private nurses [37]. Vaccination of children directly in childcare settings during French targeted

vaccination campaigns following local outbreaks (e.g., MenC) has been successful [38].

Contrary to previous findings [5, 39], we did not find any association between vaccination status and the socio-economic level of the family, which could be explained by the free access to vaccination for all children under age six in the MCPSs and the French state-funded health coverage for precarious people, which aim to reduce health inequalities.

Regarding the parental socio-cognitive profiles defined according to their KAPs, parents with low compliance for child care and those who used alternative medicine were over-represented among children with incomplete vaccination. These profiles were similar to those associated with the phenomenon of vaccine hesitancy [39–41]. The individual decision-making process of vaccination, more generally health-related decisions, is a complex phenomenon that rests on social, cultural, and historical foundations [40]. In particular, the relationship between a favorable opinion of alternative medicine and skepticism about vaccination can be explained by common attitudes and beliefs, especially magical beliefs about health [42]. Moreover, it was shown in other studies that some parents belonging to an educated environment tend to control their health and have a greater awareness of the risks produced by science and industry, which can lead them to turn to alternative medicine or to refuse some preventive care procedures [39]. We identified a high education level as a risk factor for incomplete vaccination in crude analysis but not adjusted, possibly in relation with the adjustment strategy [5, 15, 17, 18]. So parental health education should probably be adapted to each target profile, in particular, alternative medicine users who accounted for almost half of the parents (eFigure 2). Information should be delivered using messengers who share their worldview to better communicate prevention messages.

Regarding healthcare system characteristics, never having received a visit from an MCPS nurse during the child's first two months was associated with incomplete vaccination regardless of parental education level, household income, or area of residence and seems particularly relevant for recently recommended vaccines (eTable 6). This result is consistent with the known positive impact of the MCPSs on other aspects of health prevention [26]. Increasing the territorial coverage of preventive health centers such as the MCPSs could be an effective measure to reduce health inequalities in vaccination; indeed, the prevalence of families that did not receive support from an MCPS nurse during the first months was high (over 80%). Moreover, we found a substantially higher incomplete vaccination rate when the child's medical follow-up was only assured by a GP as compared with a follow-up by a pediatrician or an MCPS physician regardless of the child's health status at age two or area of residence. Medical follow-up by a GP alone rather than a pediatrician was previously found associated with increased drug prescriptions, lower preventive attitudes, and lower vaccination coverage [18, 43]. The phenomenon of vaccine hesitancy is also present among some GPs and may affect their attitude toward the vaccination advice given to parents [20]. Improving GPs' awareness of preventive measures for children seems a key measure for improving vaccine coverage.

Strengths and limitations

This population-based study was the first nationwide prospective study to investigate overall vaccination status in HICs. Its unique design allowed for an estimation of the findings to the general national population of two-year-olds. The large sample size allowed for studying many covariates from a variety of research fields [23]. Moreover, the use of latent class analysis to constitute the parental KAP latent variable facilitated the interpretation of parental behaviors [30]. Finally, in this study, missing data for covariates were ≤ 5%, which probably had a limited impact on our results.

However, the main limitation was a selection bias resulting from two phenomena. First, although participation in this study was proposed to almost all eligible mothers at the maternity ward, only 51% agreed to participate [22]. Additionally, the ELFE study did not include children born extremely and very preterm who are more sensitive to infections, including vaccine-preventable ones, and usually benefit from a specific medical follow-up that improves their vaccination status [12]. However, these births represented less than 2% of French live births, and children born with moderate to late prematurity, who account for 5.5% of life births [44], displayed no significant difference in vaccination status at age two in our study (eTable4). Second, the number of patients was further limited by a significant rate of lost to follow-up at age two years and lack of complete information on vaccination status. This attrition bias led to an over-representation of social categories with high income and a high education level (eTable 3) [22]. Such selection bias was expected because the association between high socio-economic level and compliance with follow-up in cohort has been well described in this cohort and others [35]. After a careful weighting, the characteristics of our population were close to those of the reference population of women who gave birth in 2011 known by the National Perinatal Survey [22]. Also, the calculated rates and multivariable analyses were not significantly altered, so the impact of selection bias on the external validity of our study seemed limited. Moreover, vaccination coverages per vaccine were consistent with those calculated by the French national public health agency in 2013 for DT-IPV, aP, and Hib based on the 24-month medical certificates (Table 1) [45]. In practice, these three vaccines are almost always combined in a single injection, so a similar vaccine coverage is expected even though some vaccines are not mandatory. Vaccination coverage for other vaccines was slightly higher overall than the French national public health

agency estimates, so the rate of incomplete vaccination may be slightly underestimated in our study.

Moreover, although we investigated numerous potential determinants previously highlighted [3, 5, 12–19], some were not collected, and these included move before or shortly after birth [46] or delay in the first vaccinations [12, 16]. Because age at vaccination was not recorded, we could not assess whether completely vaccinated children experienced potentially dangerous vaccination delays [28]. Moreover, the exact age of data collection was not precisely known, so delayed vaccination of some children may have been reported when they may have been vaccinated shortly after data collection [28], notably for the second dose of MMR scheduled at 24 months of age and the first dose of MenC which could be given up to 24 months of age.

In addition, totally unvaccinated children were included in the incompletely vaccinated group, but these two situations could share different risk factors [5]. A specific analysis of the determinants associated with complete lack of vaccination is planned.

Finally, the findings of this study were limited by the timing of data collection. France has introduced mandatory vaccination for all newborns since 2018, which has improved vaccine coverage per vaccine for children at age two years [7, 8]. This move has probably resulted in a decrease in the current rate of incompletely vaccinated children and potentially a change in the determinants associated with incomplete vaccination in children under two years of age. However, this obligation is not intended to be permanent, and some vaccinations recently recommended by the French National Authority for Health are not mandatory for children or adolescents, such as vaccination against meningococcal B [47], human papillomavirus [48], and SARS-CoV-2 [1]. Thus, our results may guide the implementation strategy for these non-mandatory vaccines and to reach children that are not vaccinated despite the 2018 mandatory vaccination law.

Conclusions

The rate of incompletely vaccinated children at age two was very high in France in the studied population. The risk factors we identified could guide corrective actions such as campaigns promoting vaccination among parents with large families and those with specific socio-cognitive profiles; the strengthening of the vaccination forces by a better territorial coverage of the MCPSs, the removal of logistic and territorial barriers by the prescriber delivering the vaccines and the implementation of alternative vaccination settings; and an active medical education of GPs regarding vaccines and vaccine hesitancy.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00431-022-04733-z.

Author contribution Conception of study: Corinne Bois, Marie-Aline Charles, and Marie-Noëlle Dufourg. Collection of the data: Corinne Bois, Marie-Aline Charles, and Marie-Noëlle Dufourg. Design of study: Corinne Bois, Martin Chalumeau, Marie-Aline Charles, Marie-Noëlle Dufourg, Christèle Gras-Le Guen, Elise Launay, Daniel Lévy-Brühl, Fleur Lorton, and Jocelyn Raude. Data management: Marianne Jacques, Fleur Lorton, Pauline Scherdel, and Thierry Siméon. Data analysis: Marianne Jacques, Fleur Lorton, Pauline Scherdel, and Thierry Siméon. Drafting of the manuscript: Martin Chalumeau, Marianne Jacques, Fleur Lorton, and Pauline Scherdel. Revising of the manuscript: Corinne Bois, Marie-Aline Charles, Marie-Noëlle Dufourg, Christèle Gras-Le Guen, Elise Launay, Daniel Lévy-Brühl, Jocelyn Raude, and Thierry Siméon. Final approval of the version to be published: All.

Funding The ELFE birth cohort is a joint project between the French Institute for Demographic Studies (INED, Institut national d'études démographiques) and the National Institute of Health and Medical Research (INSERM, Institut national de la santé et de la recherche médicale), in partnership with the French blood transfusion service (EFS, Etablissement français du sang), the French National Public Health Agency (Santé publique France), the National Institute for Statistics and Economic Studies (INSEE, Institut national de la statistique et des études économiques), the French Ministry of Health (DGS, Direction générale de la santé), the Ministry for the Environment (DGPR, Direction générale de la prévention des risques), the Ministry of Health and Social Affairs (DREES, Direction de la recherche, des études, de l'évaluation et des statistiques), the Ministry of Culture (DEPS, Département des études, de la prospective et des statistiques), and the National Family Allowance Fund (CNAF, Caisse nationale des allocations familiales), with the support of the Ministry of Higher Education and Research (INJEP, Institut national de la jeunesse et de l'éducation populaire). Via the RECONAI platform, it receives a government grant managed by the National Research Agency under the investments for the future programs (ANR-11-EQPX-0038).

Availability of data and materials Access to participant data with identifiers, data dictionary, and code is available only once approval has been obtained through the constituent entities controlling access to the data. The crude data can be requested to the ELFE Data Access Committee (https://pandora-elfe.inserm.fr/public/).

Declarations

Ethics approval and consent to participate The ELFE study was approved by the Advisory Committee for the Treatment of Information on Health Research (no. 13,004), the National Agency Regulating Data Protection (no. 913,074), and the National Statistics Council (visa 2013X719AU). All participating parents provided written consent for their own and their child's participation.

Competing interests The authors declare no competing interests.

References

1. Eberhardt CS, Siegrist CA (2021) Is there a role for childhood vaccination against COVID-19? Pediatr Allergy Immunol 32(1):9–16
2. The Editors of the Lancet (2010) Retraction-Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. Lancet 375(9713):445

3. Danis K, Georgakopoulou T, Stavrou T, Laggas D, Panagiotopoulos T (2010) Socioeconomic factors play a more important role in childhood vaccination coverage than parental perceptions: a cross-sectional study in Greece. Vaccine 28(7):1861–1869
4. Luman ET, Barker LE, Shaw KM, McCauley MM, Buehler JW, Pickering LK (2005) Timeliness of childhood vaccinations in the United States: days undervaccinated and number of vaccines delayed. JAMA 293(10):1204–1211
5. Gilbert NL, Gilmour H, Wilson SE, Cantin L (2017) Determinants of non-vaccination and incomplete vaccination in Canadian toddlers. Hum Vaccin Immunother 13(6):1–7
6. Anello P, Cestari L, Baldovin T, Simonato L, Frasca G, Caranci N et al (2017) Socioeconomic factors influencing childhood vaccination in two northern Italian regions. Vaccine 35(36):4673–4680
7. Martinot A, Leboucher B, Cohen R, Stahl JP, Subtil D, Pujol P et al (2021) Evolution between 2008 and 2018 of mothers' perception regarding vaccination and infant vaccine coverage in France. Infect Dis Now 51(2):153–158
8. Lévy-Bruhl D, Fonteneau L, Vaux S, Barret AS, Antona D, Bonmarin I et al (2019) Assessment of the impact of the extension of vaccination mandates on vaccine coverage after 1 year, France. Eurosurveillance 24(26):1900301
9. Robert A, Kucharski AJ, Funk S (2022) The impact of local vaccine coverage and recent incidence on measles transmission in France between 2009 and 2018. BMC Med 20(1):77
10. Bouchez V, Guillot S, Landier A, Armatys N, Matczak S, Toubiana J et al (2021) Evolution of Bordetella pertussis over a 23-year period in France, 1996 to 2018. Euro Surveill 26(37)
11. Lorton F, Chalumeau M, Assathiany R, Martinot A, Bucchia M, Roué JM et al (2018) Vaccine-preventable severe morbidity and mortality caused by meningococcus and pneumococcus: a population-based study in France. Paediatr Perinat Epidemiol 32(5):442–447
12. Fiks AG, Alessandrini EA, Luberti AA, Ostapenko S, Zhang X, Silber JH (2006) Identifying factors predicting immunization delay for children followed in an urban primary care network using an electronic health record. Pediatrics 118(6):e1680–e1686
13. Cotter JJ, Bramble JD, Bovbjerg VE, Pugh CB, McClish DK, Tipton G et al (2002) Timeliness of immunizations of children in a Medicaid primary care case management managed care program. J Natl Med Assoc 94(9):833–840
14. Bailly AC, Gras P, Lienhardt JF, Requillart JC, Vié-le-Sage F, Martinot A et al (2018) Timeliness of vaccination in infants followed by primary-care pediatricians in France. Hum Vaccin Immunother 14(4):1018–1023
15. Dombkowski KJ, Lantz PM, Freed GL (2004) Risk factors for delay in age-appropriate vaccination. Public Health Rep 119(2):144–155
16. Boulianne N, Deceuninck G, Duval B, Lavoie F, Dionne M, Carsley J et al (2003) Why are some children incompletely vaccinated at the age of 2? Can J Public Health 94(3):218–223
17. O'Donnell S, Dubé E, Tapiero B, Gagneur A, Doll MK, Quach C (2017) Determinants of under-immunization and cumulative time spent under-immunized in a Quebec cohort. Vaccine 35(43):5924–5931
18. Guthmann JP, Ragot M, Ben Boutieb M, Bois C, Dufourg MN, Lévy-Bruhl D (2016) Vaccination coverage and socioeconomic determinants of BCG vaccination in children before 3 months: results of the Elfe cohort study, 2011. Rev Epidemiol Sante Publique 64(4):271–280
19. Hill HA, Yankey D, Elam-Evans LD, Singleton JA, Pingali SC, Santibanez TA (2020) Vaccination coverage by age 24 months among children born in 2016 and 2017 - national immunization survey-child, United States, 2017–2019. MMWR Morb Mortal Wkly Rep 69(42):1505–1511
20. Verger P, Fressard L, Collange F, Gautier A, Jestin C, Launay O et al (2015) Vaccine hesitancy among general practitioners and its determinants during controversies: a national cross-sectional survey in France. EBioMedicine 2(8):891–897
21. Pansieri C, Pandolfini C, Clavenna A, Choonara I, Bonati M (2020) An inventory of European birth cohorts. Int J Environ Res Public Health 17(9):3071
22. Charles MA, Thierry X, Lanoe JL, Bois C, Dufourg MN, Popa R et al (2020) Cohort profile: the French national cohort of children (ELFE): birth to 5 years. Int J Epidemiol 49(2):368–369
23. Vandentorren S, Bois C, Pirus C, Sarter H, Salines G, Leridon H (2009) Rationales, design and recruitment for the Elfe longitudinal study. BMC Pediatr 9:58
24. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP (2007) The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 370(9596):1453–1457
25. Institut de Veille Sanitaire (2011) vaccination schedule and recommendations from the "Haut conseil de la santé publique" in France. Bull Epidemiol Hebd 10–11:101–156
26. Saïas T, Clavel C, Dugravier R, Bonnard A, Bodard J (2018) Maternal and child protection services at home. Results from a national study. Sante Publique 30(4):477–87.
27. Gaudelus J, Cohen R, Leboucher B, Stahl JP, Denis F, Pujol P et al (2019) Meningococcal C vaccine coverage in France in infants, children, and adolescents. Med Mal Infect 49(3):180–186
28. Gras P, Bailly AC, Lagrée M, Dervaux B, the GPIP Infovac-France partners et al (2016) What timing of vaccination is potentially dangerous for children younger than 2 years? Hum Vaccin Immunother 12(8):2046–52
29. Marbac M, Sedki M (2017) Variable selection for model-based clustering using the integrated complete-data likelihood. Stat Comput 27:1049-63
30. Nylund-Gibson K, Choi AY (2018) Ten frequently asked questions about latent class analysis. Translational Issues in Psychological Science 4(44P):461
31. Killian M, Detoc M, Berthelot P, Charles R, Gagneux-Brunon A, Lucht F et al (2016) Vaccine hesitancy among general practitioners: evaluation and comparison of their immunisation practice for themselves, their patients and their children. Eur J Clin Microbiol Infect Dis 35(11):1837–1843
32. Little RJ, Rubin DB (2019) Statistical analysis with missing data: John Wiley & Sons
33. Schneider R, Reinau D, Schur N, Blozik E, Früh M, Signorell A et al (2020) Coverage rates and timeliness of nationally recommended vaccinations in Swiss preschool children: a descriptive analysis using claims data. Vaccine 38(6):1551–1558
34. de Figueiredo A, Simas C, Karafillakis E, Paterson P, Larson HJ (2020) Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study. The Lancet 396(10255):898–908
35. Sacri AS, de Lauzon-Guillain B, Dufourg MN, Bois C, Charles MA, Chalumeau M (2019) Iron-fortified formula use in young children and association with socioeconomic factors in the French nationwide ELFE cohort. Acta Paediatr 108(7):1285–1294
36. ELFE team (2014) Variables d'urbanisation (INSEE 2010). Available from: https://pandora-elfe.inserm.fr/doc/variables_Pandora_Codes_Urbanisation_2014.pdf
37. Hofstetter AM, Schaffer S (2021) Childhood and adolescent vaccination in alternative settings. Acad Pediatr 21(4s):S50–S6
38. Fokoun C (2018) Strategies implemented to address vaccine hesitancy in France: a review article. Hum Vaccin Immunother 14(7):1580–1590
39. Bocquier A, Ward J, Raude J, Peretti-Watel P, Verger P (2017) Socioeconomic differences in childhood vaccination in developed countries: a systematic review of quantitative studies. Expert Rev Vaccines 16(11):1107–1118
40. Dubé E, Gagnon D, Zhou Z, Deceuninck G (2016) Parental vaccine hesitancy in Quebec (Canada). PLoS Curr 8

41. Thomire A, Raude J (2021) The role of alternative and complementary medical practices in vaccine hesitancy among nurses: a cross-sectional survey in Brittany. Infect Dis Now 52(2):159–163
42. Bryden GM, Browne M, Rockloff M, Unsworth C (2018) Anti-vaccination and pro-CAM attitudes both reflect magical beliefs about health. Vaccine 36(9):1227–1234
43. Bocquet A, Chalumeau M, Bollotte D, Escano G, Langue J, Virey B (2005) Comparison of prescriptions by pediatricians and general practitioners: a population-based study in Franche-Comté from the database of regional health insurance fund. Arch Pediatr 12(12):1688–1696
44. Cinelli H, Lelong N, Le Ray C, ENP 2021 Study Group (2022) [National perinatal survey - 2021 report. Situation and evolution since 2016.] Paris
45. Santé Publique France (2020) [BCG, diphtheria, tetanus, poliomyelitis, pertussis, Hib, pneumococcal, hepatitis B, MMR and meningococcal C vaccination coverage at age 24 months, France, 1998–2018]. Available from: https://www.santepubliquefrance.fr/determinants-de-sante/vaccination/articles/synthese-des-couvertures-vaccinales-chez-l-enfant-de-2-ans
46. Dunn AC, Black CL, Arnold J, Brodine S, Waalen J, Binkin N (2015) Childhood vaccination coverage rates among military dependents in the United States. Pediatrics 135(5):e1148–e1156
47. Haute Autorité de Santé (2021) [Vaccination strategy for the prevention of invasive meningococcal disease: serogroup B and the place of BEXSERO®. Vaccine Recommendation.] Saint-Denis La Plaine
48. Dalon F, Majed L, Belhassen M, Jacoud F, Bérard M, Lévy-Bachelot L et al (2021) Human papillomavirus (HPV) vaccine coverage rates (VCRs) in France: a French claims data study. Vaccine 39(36):5129–5137

Authors and Affiliations

Marianne Jacques[1,2] · Fleur Lorton[1,2,3] · Marie-Noëlle Dufourg[4] · Corinne Bois[4] · Elise Launay[1,2,3] · Thierry Siméon[4] · Jocelyn Raude[5] · Christèle Gras-Le Guen[1,2,3] · Daniel Lévy-Brühl[6] · Marie-Aline Charles[4] · Martin Chalumeau[1,7] · Pauline Scherdel[1,2]

Marianne Jacques
marianne.jacques@inserm.fr

Fleur Lorton
fleur.lorton@chu-nantes.fr

Marie-Noëlle Dufourg
marie-noelle.dufourg@ined.fr

Corinne Bois
bois.dardel@free.fr

Elise Launay
elise.launay@chu-nantes.fr

Thierry Siméon
thierry.simeon@ined.fr

Jocelyn Raude
jocelyn.raude@ehesp.fr

Christèle Gras-Le Guen
christele.grasleguen@chu-nantes.fr

Daniel Lévy-Brühl
daniel.levy-bruhl@santepubliquefrance.fr

Marie-Aline Charles
marie-aline.charles@inserm.fr

Pauline Scherdel
pauline.scherdel@inserm.fr

[1] Obstetrical Perinatal and Pediatric Epidemiology Research Team (EPOPé), Université Paris Cité, Inserm, Center for Research in Epidemiology and StatisticS (CRESS), 75004 Paris, France

[2] Inserm 1413 CIC FEA, Nantes University Hospital, Nantes, France

[3] Department of Pediatric Emergency Care, Nantes University Hospital, Nantes, France

[4] French Institute for Demographic Studies (Ined), Inserm, French Blood Agency, ELFE Joint Unit, Aubervilliers, France

[5] EHESP-School of Public Health, Rennes, France

[6] Santé Publique France, French National Public Health Agency, Saint-Maurice, France

[7] Department of General Pediatrics and Pediatric Infectious Diseases, AP-HP, Necker-Enfants malades hospital, Université Paris Cité, Paris, France

SUPPLEMENTAL MATERIALS

eTable 1 Determinants of incomplete vaccination already identified in high-income countries.

Articles	**Child characteristics**	**Household socio-demographic characteristics**	**Parental KAPs**	**Healthcare system characteristics**	**Vaccination schedule characteristics**
Bailly (14)	Older child	Mother's employment			
Boulianne (16)		Single parenthood; number of children in the household	Lack of information; disagreement with vaccine recommendations; refusal of simultaneous injections		No simultaneous vaccination; first vaccine delayed
Cotter (13)	Ethnic minorities*	Younger maternal age; rural residing		Private provider	
Danis (3)	Born outside the country	Number of children in the household; younger maternal age; low parental education level	Perception that natural disease is preferable to vaccination	Long distance to immunization site	
Dombkowski (15)		Single parenthood; number of children in the household; lack of health insurance or state-funded health insurance; low parental education level		No usual provider	
Fiks (12)	Full term birth	Nonparent caregiver; lack of health insurance			First vaccine delayed
Gilbert (5)	Born outside the country	Single parenthood; low parental education level; low income			
Guthmann (18)		Non immigrant parents, high parental education level		General practitioner follow-up	
Hill (19)		Lack of health insurance or state-funded health insurance			
O'Donnell (17)		Younger maternal age; number of children in the household; high parental education level; high income			First vaccine delayed; no simultaneous vaccination

KAP: knowledge, attitude and practice

* African American

eTable 2 STROBE Statement (24) — checklist of items that should be included in reports of observational studies.

	Item No	Recommendation	page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	3
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	3
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3
Bias	9	Describe any efforts to address potential sources of bias	3
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	-
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	3
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	3/supp
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	3
		(*e*) Describe any sensitivity analyses	3
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	3
		(b) Give reasons for non-participation at each stage	3
		(c) Consider use of a flow diagram	4

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	3
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	-
		Cross-sectional study—Report numbers of outcome events or summary measures	-
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	4/supp
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarize key results with reference to study objectives	5
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7-8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	5-7
Generalizability	21	Discuss the generalizability (external validity) of the study results	7-8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	8

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

eTable 3 Comparison of characteristics of analysed and non-analysed children.

	Non-analysed children (n = 11,844)	**Analysed children (n = 5,740)**		***p*** [b]
		Unweighted, n (%)	Weighted [a], (%)	
Child characteristics				
Sex				0.8
Boy	6,084 (51.4)	2,936 (51.1)	(50.7)	
Girl	5,759 (48.6)	2,804 (48.9)	(49.3)	
Twinship				0.3
Twin	193 (1.6)	82 (1.4)	(1.4)	
Singleton	11,651 (98.4)	5,658 (98.6)	(98.6)	
Term of birth				<0.001
Preterm birth	655 (5.5)	211 (3.7)	(3.8)	
Term birth	11,189 (94.5)	5,529 (96.3)	(96.2)	
Household socio-demographic characteristics				
Mother's country of birth				<0.001
France	9,920 (83.8)	5,338 (93.0)	(84.8)	
Abroad	1,908 (16.1)	402 (7.0)	(15.2)	
Mother's age, years [c]	30.00 (26.30-33.80)	31.20 (28.60-34.40)	30.50 (27.51-34.10)	
	30.17 (5.31)	31.57 (4.34)	30.87 (4.83)	<0.001
Marital status of parents				<0.001
Together	9,596 (81.0)	5,578 (97.2)	(94.6)	
Separated	691 (5.8)	102 (1.8)	(3.9)	
Number of older siblings				<0.001
Zero	4,465 (37.7)	2,633 (45.9)	(40.6)	
One	3,671 (31.0)	2,169 (37.8)	(38.2)	
≥ Two	2,151 (18.2)	877 (15.3)	(19.7)	
Mother's level of education				<0.001
University degree	6,053 (51.1)	4,513 (78.6)	(62.6)	
High school	2,874 (24.3)	809 (14.1)	(22.9)	
None or primary/secondary school	2,915 (24.6)	418 (7.3)	(14.5)	
Parental difference of education level				
Same level	4,513 (38.1)	2,846 (49.6)	(46.7)	<0.001
Father with higher level	1,817 (15.3)	932 (16.2)	(21.4)	
Mother with higher level	3,002 (25.3)	1,875 (32.7)	(29.0)	
Mother's employment				<0.001
Unemployed	3,476 (29.3)	1,043 (18.2)	(30.0)	
Employed	6,682 (56.4)	4,635 (80.7)	(68.4)	
Parents' employment				<0.001

Both employed	6,156 (52.0)	4,374 (76.2)	(62.9)	
One unemployed	3,548 (30.0)	1,173 (20.4)	(30.5)	
Both unemployed	704 (5.9)	129 (2.2)	(5.2)	
Income amount per consumption unit, Euros				<0.001
≥ 1,905	1,872 (15.8)	1,886 (32.9)	(22.5)	
1,501-1,905	2,003 (16.9)	1,566 (27.3)	(22.6)	
1,112-1,500	2,729 (23.0)	1,447 (25.2)	(28.4)	
<1,111	2,864 (24.2)	649 (11.3)	(21.7)	
Mother's health insurance				<0.001
State funded or none	1,260 (10.6)	106 (1.8)	(5.2)	
General scheme or equivalent	10,432 (88.1)	5,585 (97.3)	(94.0)	
Mother's complementary insurance				<0.001
Personal	9,318 (78.7)	5,283 (92.0)	(87.5)	
State funded	811 (6.8)	72 (1.3)	(3.0)	
None	1,136 (9.6)	215 (3.7)	(6.0)	
Area of residence [d]				<0.001
Urban	8,201 (69.2)	3,588 (62.5)	(62.1)	
Suburban	3,306 (27.9)	2,000 (34.8)	(34.0)	
Isolated	336 (2.8)	152 (2.6)	(3.9)	

[a] Clusters within the parental KAP latent variable were identified with latent class analysis (**eMethods 2**); [b] Chi-squared test or Student's *t* test between included and excluded children (unweighted data); [c] Data are median (interquartile range) and mean (SD); [d] Defined according to the French National Institute of Statistics and Economic Studies (INSEE) 2010 classification (36).

eTable 4 Crude associations between incomplete vaccination and main characteristics (logistic regression, reference group: children with full vaccination).

	Incomplete vaccination (n=2,550)	Full vaccination (n=3,190)	OR	[95% CI]	*p* [a]
Child characteristics					
Female sex (ref = Boy)	1,256 (49.3)	1,548 (48.5)	1.03	[0.93-1.14]	0.58
Twinship (ref = Singleton)	35 (1.4)	47 (1.5)	0.93	[0.60-1.45]	0.75
Preterm birth (ref = Term birth)	85 (3.3)	126 (3.9)	1.19	[0.90-1.58]	0.22
Child's health					0.89
Good health	2,279 (89.4)	2,850 (89.3)	1	-	
Ear nose and throat repetitive diseases	210 (8.2)	269 (8.4)	0.98	[0.81-1.18]	
Chronic disease	61 (2.4)	71 (2.2)	1.07	[0.76-1.52]	
Household socio-demographic characteristics					
Mother born in France (ref = Abroad)	2,390 (93.7)	2,948 (92.4)	1.23	[1.00-1.51]	0.05
Mother's age at birth, years					0.22
≥ 35	520 (20.4)	701 (22.0)	1	-	
30-34	1,053 (41.3)	1,331 (41.7)	1.07	[0.93-1.23]	
25-29	834 (32.7)	1,007 (31.6)	1.12	[0.96-1.29]	
< 25	143 (5.6)	151 (4.7)	1.28	[0.99-1.65]	
Marital status of parents (ref = Separated)	2,499 (98.0)	3,133 (98.2)	0.89	[0.61-1.31]	0.55
Number of older siblings					<0.001
Zero	1,091 (42.8)	1,569 (49.2)	1	-	
One	1,017 (39.9)	1,179 (37.0)	1.24	[1.11-1.39]	
≥ Two	442 (17.3)	442 (13.9)	1.44	[1.23-1.68]	
Mother's level of education					0.002
University degree	1,951 (76.5)	2,562 (80.3)	1	-	
High school	399 (15.6)	410 (12.9)	1.28	[1.10-1.48]	
None or primary/secondary school	200 (7.8)	218 (6.8)	1.20	[0.99-1.47]	
Parental difference of education level					0.43

Same level	1,256 (49.6)	1,628 (51.0)	1	-	
Father with higher level	422 (16.5)	533 (16.7)	1.02	[0.88-1.18]	
Mother with higher level	863 (33.8)	1,029 (32.3)	1.08	[0.96-1.21]	
Mother unemployed (ref = Employed)	505 (19.8)	558 (17.5)	1.16	[1.02-1.33]	0.03
Parent's employment					0.08
Both employed	1,935 (75.9)	2,482 (77.8)	1	-	
One unemployed	562 (22.0)	630 (19.7)	1.14	[1.01-1.30]	
Both unemployed	53 (2.1)	78 (2.4)	0.87	[0.61-1.24]	
Household income per consumption unit, euros					<0.001
> 1,905	763 (29.9)	1,178 (36.9)	1	-	
1,501-1,905	724 (28.4)	877 (27.5)	1.27	[1.11-1.46]	
1,112-1,500	720 (28.2)	781 (24.5)	1.42	[1.24-1.63]	
≤ 1,111	343 (13.5)	354 (11.1)	1.50	[1.26-1.78]	
Mother's state funded health insurance or lack (ref = General scheme)	44 (1.7)	65 (2.0)	0.84	[0.57-1.24]	0.41
Mother's complementary insurance					0.26
Personal	2,413 (94.6)	3,024 (94.8)	1	-	
State funded	30 (1.2)	50 (1.6)	0.75	[0.48-1.18]	
No	107 (4.2)	116 (3.6)	1.16	[0.88-1.51]	
Area of residence [a]					<0.001
Urban	1,491 (58.5)	2,097 (65.7)	1	-	
Suburban	963 (37.8)	1,037 (32.5)	1.31	[1.17-1.46]	
Isolated	96 (3.8)	56 (1.8)	2.41	[1.72-3.37]	
Childcare providers					0.004
Day-care centre	436 (17.1)	616 (19.3)	1	-	
Family child care homes	1,249 (49.0)	1,615 (50.6)	1.09	[0.95-1.26]	
Child's family	865 (33.9)	959 (30.1)	1.27	[1.09-1.49]	
Parental KAPs					
No folic acid supplementation during pregnancy (ref = Yes)	1,316 (51.6)	1,494 (46.8)	1.21	[1.09-1.34]	<0.001
Tobacco consumption during pregnancy (ref = No)	357 (14.0)	404 (12.7)	1.12	[0.96-1.31]	0.14
Alcohol consumption during pregnancy (ref = No)	540 (21.2)	608 (19.1)	1.14	[1.00-1.30]	0.05
No birth preparation sessions (ref = Follow-up)	773 (30.3)	897 (28.1)	1.11	[0.99-1.25]	0.07

No vitamin D administration (ref = Administration)	100 (3.9)	80 (2.5)	1.59	[1.18-2.14]	0.002
Sleeping in other position (ref = Supine)	462 (18.1)	470 (14.7)	1.28	[1.11-1.47]	<0.001
Organic food consumption (ref = No)	826 (32.4)	1,042 (32.7)	0.99	[0.88-1.10]	0.83
Breast feeding duration, months					0.25
No	809 (31.7)	1,023 (32.1)	1	-	
< 2	727 (28.5)	972 (30.5)	0.95	[0.83-1.08]	
2-12	951 (37.3)	1,127 (35.3)	1.07	[0.94-1.21]	
> 12	63 (2.5)	68 (2.1)	1.17	[0.82-1.67]	
No iron-rich formula administration (ref = Administration)	900 (35.3)	788 (24.7)	1.66	[1.48-1.86]	<0.001
Osteopathy consultation (ref = No)	1,332 (52.2)	1,686 (52.9)	0.98	[0.88-1.08]	0.64
Homeopathy use (ref = No)	330 (12.9)	393 (12.3)	1.06	[0.90-1.24]	0.48
Phytotherapy use (ref = No)	35 (1.4)	45 (1.4)	0.97	[0.62-1.51]	0.90
Relationship with health practitioners					<0.001
Friendly	1,693 (66.4)	1,975 (61.9)	1	-	
Professional	815 (32.0)	1,170 (36.7)	0.81	[0.73-0.91]	
Sometimes strained	42 (1.6)	45 (1.4)	1.09	[0.71-1.67]	
Source of advice about child's health					0.29
No advice	657 (25.8)	842 (26.4)	1	-	
Only from physician	804 (31.5)	937 (29.4)	1.10	[0.96-1.26]	
Only from entourage or book/internet/media	72 (2.8)	105 (3.3)	0.88	[0.64-1.20]	
From both	1,017 (39.9)	1,306 (40.9)	1.00	[0.88-1.14]	
No trust in political institutions (ref = Trust)	2,050 (80.4)	2,450 (76.8)	1.24	[1.09-1.41]	<0.001
No trust in media (ref = Trust)	1,596 (62.6)	1,885 (59.1)	1.16	[1.04-1.29]	0.007
Importance of religion					0.20
Week	1,072 (42.0)	1,293 (40.5)	1	-	
Medium	803 (31.5)	985 (30.9)	0.98	[0.87-1.11]	
Strong	675 (26.5)	912 (28.6)	0.89	[0.79-1.01]	
Healthcare system characteristics					
No visit of an MCPS nurse during the first two months (ref = ≥ 1)	2,119 (83.1)	2,567 (80.5)	1.19	[1.04-1.37]	0.01
Specialty of child's physician during the first two years					<0.001
Paediatrician or MCPS physician alone	646 (25.3)	1,349 (42.3)	1	-	

GP and either paediatrician or MCPS physician	440 (17.3)	822 (25.8)	1.12	[0.99-1.26]
GP alone	1,464 (57.4)	1,019 (31.9)	3.00	[2.65-3.39]

CI: confidence interval, GP: general practitioner, KAP: knowledge, attitude and practice, MCPS: maternal and child protection service, OR: odds ratio, ref: reference group.

Data are n (%) otherwise stated.

[a] Calculated with likelihood ratio test; [b] Defined according to the French National Institute of Statistics and Economic Studies (INSEE) 2010 classification (36).

eTable 5 Weighted multivariable associations between incomplete vaccination and main characteristics (weighted adjusted logistic regression, reference group: children with full vaccination).

	aOR	[95% CI]	*p* [a]
Household socio-demographic characteristics			
Area of residence [b]			<0.001
Urban	1	-	
Suburban	1.03	[0.99-1.07]	
Isolated	1.21	[1.11-1.33]	
Parental KAPs			
Parental KAP latent variable [c]			0.003
Compliant with health recommendations and confident in institutions	1	-	
Alternative medicine user	1.07	[1.01-1.12]	
Low compliant with recommendations during pregnancy	1.05	[0.99-1.11]	
Low compliant for child care	1.14	[1.06-1.23]	
Healthcare system characteristics			
No visit of an MCPS nurse during the first two months (ref = ≥ 1)	1.06	[1.01-1.10]	0.02
Specialty of child's physician during the first two years			<0.001
Paediatrician or MCPS physician alone	1	-	
GP and either paediatrician or MCPS physician	1.01	[0.96-1.05]	
GP alone	1.29	[1.24-1.35]	

aOR: adjusted odds ratio CI: confidence interval, GP: general practitioner, KAP: knowledge, attitude and practice, MCPS: maternal and child protection service, ref: reference group.

[a] Calculated with likelihood ratio test, adjusted on preterm birth, child's health, mother's country of birth, mother's age, marital status of parents, number of children in the household, mother's level of education, parental difference of education level, mother's employment, household income, type of mother's health insurance, type of mother's complementary insurance, childcare providers; [b] Defined according to the French National Institute of Statistics and Economic Studies (INSEE) 2010 classification (36); [c] Clusters within the parental KAP latent variable were identified with latent class analysis (**eMethods 2**).

eTable 6 Multivariable associations between incomplete vaccination i) without MenC and ii) without HepB and main characteristics (adjusted logistic regression, reference group: children with full vaccination).

	Without MenC			Without HepB		
	aOR	**[95% CI]**	***p*** [a]	**aOR**	**[95% CI]**	***p*** [a]
Household socio-demographic characteristics						
Number of older siblings			0.004			0.007
Zero	1	-		1	-	
One	1.19	[1.03-1.38]		1.20	[1.05-1.37]	
≥ Two	1.39	[1.14-1.70]		1.31	[1.08-1.58]	
Area of residence [b]			0.43			0.004
Urban	1	-		1	-	
Suburban	1.00	[0.88-1.14]		1.06	[0.94-1.20]	
Isolated	1.26	[0.88-1.78]		1.78	[1.26-2.53]	
Mother's age	0.98	[0.97-1.00]	0.03	0.98	[0.97-1.00]	0.03
Parental KAPs						
Parental KAP latent variable [c]			<0.001			<0.001
Compliant with health recommendations and confident in institutions	1	-		1	-	
Alternative medicine user	1.33	[1.10-1.62]		1.22	[1.03-1.46]	
Low compliant with recommendations during pregnancy	1.19	[0.97-1.48]		1.17	[0.97-1.42]	
Low compliant for child care	2.02	[1.54-2.65]		1.91	[1.48-2.47]	
Healthcare system characteristics						
No visit of an MCPS nurse during the first two months (ref = ≥ 1)	1.00	[0.85-1.17]	0.99	1.22	[1.05-1.41]	0.009
Specialty of child's physician during the first two years			<0.001			<0.001
Paediatrician or MCPS physician alone	1	-		1	-	

GP and either paediatrician or MCPS physician	1.00	[0.89-1.27]	1.20	[1.03-1.41]
GP alone	2.15	[1.86-2.47]	3.27	[2.87-3.72]

aOR: adjusted odds ratio CI: confidence interval, GP: general practitioner, KAP: knowledge, attitude and practice, MCPS: maternal and child protection service, ref: reference group.

[a] Calculated with likelihood ratio test, adjusted on preterm birth, child's health, mother's country of birth, marital status of parents, mother's level of education, parental difference of education level, mother's employment, household income, type of mother's health insurance, type of mother's complementary insurance, childcare providers; [b] Defined according to the French National Institute of Statistics and Economic Studies (INSEE) 2010 classification; [c] Clusters within the parental KAP latent variable were identified with latent class analysis (**eMethods 2**).

eMethods 1 Statistical weighting.

A statistical weight was calculated for each child for the maternity survey according to the inclusion procedure and the initial non-response, called maternity weight. The maternity weight for each infant were obtained in three steps (**equation 1**). First, each maternity unit was weighted (P1) by the inverse of probability of inclusion according to their size (defined by strata), then by an adjustment coefficient for the non-participation of maternity units using variables common to participants and non-participant units (maternity unit size, area, level of medical care, legal status). Second, each inclusion period was weighted (P2) according to maternity unit size (defined by strata), inclusion periods and number of days of inclusion periods. Third, each participating newborn was weighted (P3) according to an adjustment coefficient for mother's non-response using variables common to respondents and non-respondents (mother's year of birth, gestational age, area of residence, socio-professional category, mother's employment during pregnancy, twinship and primiparity). Then an under-coverage coefficient, which takes into account that some eligible mothers were not contacted (number of eligible infants/number of infants included in the survey), was applied.

$$Weight_{maternity} = P1 \times P2 \times P3 \quad (1)$$

For our study population, the fitted weight for each child was calculated by multiplying the maternity weight for each child with an adjustment coefficient for the non-response of the child (**equation 2**). This adjustment coefficient was calculated from estimated probabilities of response obtained by logistic regression including variables common to respondents and non-respondents (birth preparation sessions, father's employment at birth, father's age, mother's marital status at birth, alcohol consumption during pregnancy, twinship, mother's employment at birth). These probabilities were ordered to obtain sorted scores used to constitute homogeneous response groups in which the non-response was considered to be

random. Thus, the maternity weight of respondents with a low probability of responding and uncommon characteristics was increased.

$$Weight_{study\ pop} = Weight_{maternity} \times adjustment\ coefficient\ for\ non-response \quad (2)$$

Finally, a calibration on margins was performed on the study population weights by using auxiliary variables (mother's age, region, life in couple, migration status, level of education and primiparity) obtained from the 2011 state register's statistical data and the 2010 French National Perinatal study. Because of a specific attrition due to the low rate of respondents in our population study, the weights considered as extreme were truncated, which induced a bias but decreased the variance and the range of weights (22). Weighting fitted to the study population was calculated by the ELFE team.

eMethods 2 Clustering analysis for parental KAP data.

We used a finite mixture modelling latent class analysis, which allowed us to define subgroups of individuals (classes) among our population without prior identification (30), by using the R package "VarSellCM" v2.1.3.1. With this approach, we postulated that *p* explanatory observed variables were reflective measures of an underlying unordered categorical latent variable with *k* modalities (called the latent classes) (30). The latent class analysis assumes local independence for the set of observed variables conditional on class membership in the latent variable that we called here "parental KAPs" (30). According to the observed variables of individuals, the model allowed us to obtain posterior individual probabilities of membership at each latent class and to calculate the average posterior latent class probabilities for most likely latent class membership by latent class, to assign each individual in the most probable class (30). The meaning of each class was interpreted by the conditional probabilities of response to each observed variables within each class (30).

The joint probability of all the observed variables in the latent class variable, under the conditional independence model is expressed as (30):

$$\Pr(u_1, u_2, \dots, u_M) = \sum_{k=1}^{K}[\pi_k \,.\, (\prod_{m=1}^{M} \Pr(u_m|c = k))] \quad (3)$$

Where:

- $u_1, u_2, \dots, u_M$ are observed variables
- c is the underlying unordered categorical latent variable
- k is the number of latent classes in the underlying unordered latent variable c
- $\pi_k = \Pr(c = k)$ is the proportion of individuals in a given latent class k

We used the approach proposed by Marbac and Sedki that allowed us to simultaneously detect and select relevant variables for clustering and to find the most likely number of latent classes according to minimization of information criterion (e.g., Bayesian information

criterion [BIC]) (29). Variable selection facilitated the interpretation of the results and increased the precision of the estimators (29). The relevance of a given variable for the constitution of classes was measured by its discriminating power, which was defined as the logarithm of the ratio between the probability that the variable was relevant for the clustering and that the variable was irrelevant for the clustering. This index was presented for each relevant observed variable as a percentage of total discriminative power. The larger the index, the more this variable determined the classes, and a variable was irrelevant for the constitution of classes if its distribution parameters were the same in the different classes (29). For a defined number of classes, the variable selection and maximum likelihood inference was performed simultaneously by an iterative algorithm called Expectation-Maximization for considering missing data (29). We tested several latent class models ranging from one to a maximum of five classes (so that no class represents less than 5% of the sample) and selected the most relevant observed variables. The number of latent classes retained by the model was four. The following variables were retained as relevant for clustering: trust in political institutions, birth preparation sessions follow-up, trust in media, exclusive or predominant breast feeding duration, organic food consumption by parents, osteopathy consultations for the child, iron milk administration at age 2 years, folic acid consumption during pregnancy, child's bedding position at 2 months, tobacco consumption during pregnancy, religion importance for the parents and homeopathy use for the child. The irrelevant variables were alcohol consumption during pregnancy, vitamin D administration, phytotherapy use, relationship with health practitioners and source of advice about child's health. The probabilities of response to each observed variable within each parental KAP latent class are described in **eFigure 2**.

The first parental profile (49.8% of children) was characterized by a high use of alternative medicines but following health preventive recommendations during pregnancy

and for child's health. The second profile (26.8%) was characterized by a low compliance of health recommendations especially during pregnancy and a lack of breast feeding. The third profile (8.2%) was characterized by poor follow-up with health recommendations especially for child's health, a high importance of religion and prolonged exclusive or predominant breast feeding. The fourth profile (15.2%) was characterized by a high follow-up with health preventive recommendations during pregnancy and a trust in political institutions and media. The average posterior probabilities of membership to the assigned class varied from 0.68 to 0.78, suggesting a correct separation within parental KAP latent classes.

eMethods 3 Multiple imputation of missing data.

We performed multiple imputations with chained equations (MICE), using the R package "mice" v3.13.0. Analyses were repeated in each dataset (with a number of iterations set to ten, because it was considered sufficient for a low average missing data number) and estimations were pooled by using Rubin's rules (32). The convergence of the MICE algorithm was checked graphically by investigating the appearance of the means and standard deviation curves of the imputed values. The plots confirmed that there was no trend and that the trace lines intermingled well. The distributions of imputed and observed values were compared graphically and showed no significant change between imputed and observed values. The fit of the imputation model was considered good.

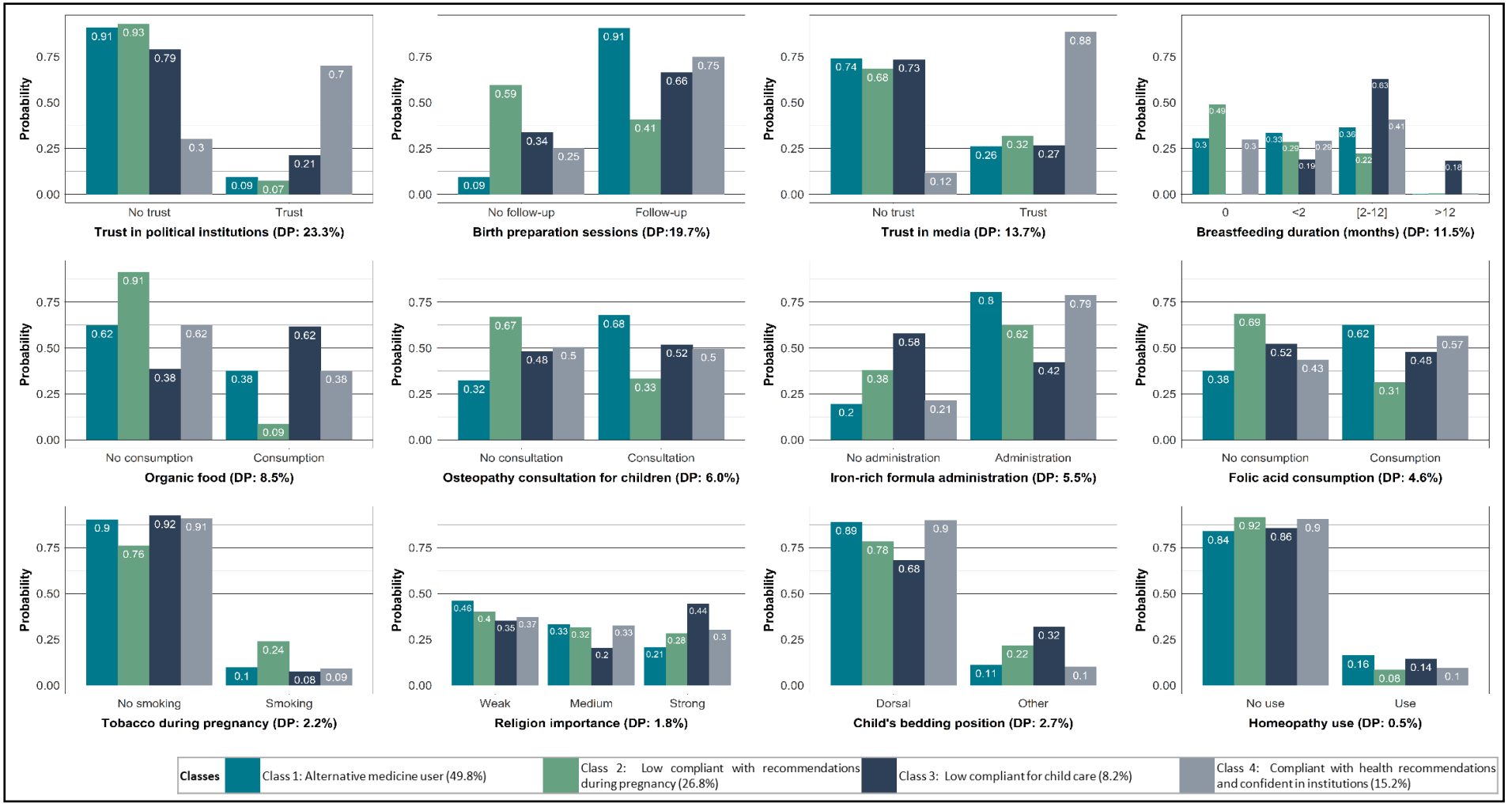
HBsAg: hepatitis B surface antigen, aP: acellular pertussis vaccine, DT-IPV: diphtheria, tetanus, and inactivated poliomyelitis vaccine, HepB: hepatitis B vaccine, Hib: Haemophilus influenzae type b conjugate vaccine, MenC: meningococcal C vaccine, MMR: measles – mumps – rubella vaccine, PCV: pneumococcal conjugate vaccine.

	Birth	1 month	2 months	3 months	4 months	6 months	9 months	11 months	12 months	16-18 months	24 months
DT-IPV											
aP											
Hib											
HepB	*if HBsAg + mother* *if HBsAg + mother* *if HBsAg + mother*	*if HBsAg + mother* *if HBsAg + mother* *if HBsAg + mother*				*if HBsAg + mother* *if HBsAg + mother* *if HBsAg + mother*					
PCV				*if high-risk* *if high-risk* *if high-risk*							
MenC			*if high-risk : 2 doses between 2 and 11 months and 1 between 12 and 24 months* *if high-risk : 2 doses between 2 and 11 months and 1 between 12 and 24 months* *if high-risk : 2 doses between 2 and 11 months and 1 between 12 and 24 months*								
MMR							*if collective childcare* *if collective childcare*				

Year Schedule	2011	2012	2013

eFigure 1 French vaccination schedule at age two years in 2011-2012-2013**.**

DP: discriminative power.



eFigure 2 Conditional probabilities and discriminative power of relevant observed variables by four classes of parental KAP latent variable**.**