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This is a French study of non-nutritive sucking habits among very preterm children at age 2 years and their association with familial, social, cultural background, health condition during neonatal hospitalization and specified developmental care practices.

Synopsis

Study question

Very preterm children have not achieved maturation of sucking reflexes *in utero*, and pacifiers are widely used in neonatal units to enhance sucking abilities. Therefore, very preterm children are probably more prone to have non-nutritive sucking habits (NNSHs). This study aimed to identify factors associated with NNSHs among very preterm children.

What's already known

Prolonged NNSHs have been associated with maxillofacial growth anomalies in the general population; factors associated with NNSHs include maternal age, maternal country of birth, child sex and duration of breast feeding.

What this study adds

NNSHs in very preterm children at age 2 years were more frequent among girls, children born in multiple pregnancies (*e.g.,* twins/triplets), children fed by nasogastric tube and those who benefitted from development care programs.

Abstract

Background: The association between prolonged non-nutritive sucking habits (NNSHs, *i.e.,* sucking pacifiers or fingers) and maxillofacial growth anomalies in the general population has been widely described. Because maturation of sucking abilities is not fully achieved in very preterm infants (<32 weeks' gestation), neonatal services worldwide rely on the use of pacifiers to promote the development of adequate sucking reflexes, possibly prolonging NNSHs during infancy.

Objective: We aimed to describe the frequency and to identify factors associated with NNSHs at age 2 years in very preterm children.

Methods: The study was based on data from EPIPAGE-2, a French national prospective cohort study of preterm births during 2011 that included 2593 children born between 24 and 31 weeks' gestation. The primary outcome was NNSHs at 2 years. Multivariable log-linear regression models with generalized estimation equations were used to study the association between the characteristics studied and NNSHs. Multiple imputations were used to take into account missing data.

Results: The frequency of NNSHs was 69% in the overall sample but higher among girls (adjusted risk ratio [RR] 1.12, 95% confidence interval [CI] 1.05, 1.17), children born from multiple pregnancies (*e.g.,* twins/triplets) (aRR 1.07, 95% CI 1.00, 1.11), children who were fed by nasogastric tube (aRR 1.07, 95% CI 1.01, 1.13) or those who benefitted from developmental care programs (aRR 1.10, 95% CI 1.02, 1.19). The NNSHs frequency was lower

if mothers were not born in France (aRR 0.70, 95% CI 0.64, 0.77), children had 2 or more older siblings (aRR 0.88, 95% CI 0.82, 0.96) or children were breast-fed at discharge (aRR 0.90, 95% CI 0.85, 0.95).

Conclusions: NNSHs at 2 years seemed associated with cultural background, development care programs and breast feeding. Whether NNSHs at 2 years among very preterm children are associated with future maxillofacial growth anomalies deserves further attention.

KEY WORDS

“Very preterm”; “non-nutritive sucking habits”; pacifier; “neonatal care”; “maxillofacial anomalies”; “cohort study”.

BACKGROUND

Non-nutritive sucking habits (NNSHs) refer to the practice of sucking (*e.g.,* by using fingers or pacifiers) for purposes other than nutrition, especially as an auto-tranquilizing mechanism.[1,2] NNSHs practiced with a finger is classified as a newborn action in which the finger, usually the thumb, is inserted into the mouth on the middle part of the tongue, exerting pressure on the palate. NNSHs can be practiced with a pacifier[3] or any other object imitating the shape of a nipple.

Several studies of full-term children have revealed that prolonged NNSHs (longer than 3 years) are associated with a higher risk of maxillofacial anomalies including altered palatal morphology and posterior crossbite (maxillofacial growth anomalies).[4–8] Prolonged NNSHs are often set at 3 years. However, in a study from the United Kingdom, NNSHs at age 2 years was already found associated with a higher risk of subsequent maxillofacial anomalies.[9] Factors associated with a higher frequency of NNSHs among the general population have been described in studies from the United Kingdom, Australia and Brazil[10–13] and included low maternal age, maternal country of birth, high maternal education, female sex, very low birthweight and short periods of breast feeding.

The sucking reflex is acquired *in utero* between 8 and 18 weeks' gestation (WG).[14] After 28 WG, the sucking function becomes more complex, especially with the development of the essential sucking–swallowing cycle, which continues to evolve until birth.[15,16] Among preterm neonates, the harmonious integration of this cycle (together with the breathing cycle) remains immature and uncoordinated[17]; thus, preterm infants may not be able to feed independently. An immature pattern of this physiological function is more marked in

extremely preterm children[18]; accordingly, the use of a pacifier in neonatal units is recommended to reinforce sucking reflexes and support the maturation of oral neuro-motor activities.[19,20] Pacifiers are also used for analgesic purposes because non-nutritive sucking (NNS) conditions infants for potentially painful medical procedures and reduces acute pain.[21,22] Whether this specific use of pacifiers in neonatal units has a role in further NNSHs is unknown.

Since their sucking function is still immature at birth and because NNSHs are widely encouraged in neonatal units, very preterm children are exposed to NNSHs in an uncharacteristic way. On the one hand, very preterm children are different with respect to NNSHs; on the other, prolonged NNSHs are a risk factor for later maxillofacial anomalies. Therefore, prior to studying the links between NNSHs and maxillofacial growth anomalies among very preterm children it was relevant to study the factors associated with prolonged NNSHs among this population.

The objectives of this exploratory study were first to describe the frequency of NNSHs at 2 years' corrected age (CA) and second to identify associated factors, including maternal, social and perinatal characteristics and infant health conditions and care practices, with data collected from a large cohort of very preterm children.

METHODS

Cohort selection

EPIPAGE-2 is a nationwide population-based cohort study in France designed to assess the health and development of preterm children born during 2011. In total, 21 of the 22 metropolitan regions and all 4 overseas regions participated; only one region, representing 2% of births in France in 2011, did not participate. The detailed protocol has been published elsewhere.[23] The recruitment period varied by gestational age: 8 months for children born at 22 to 26 WG and 6 months for those born at 27 to 31 WG. Survivors were enrolled for follow-up and were included in the study if their parents consented.

Data collection

Perinatal, maternal and neonatal data were collected from medical records by local obstetric and neonatal teams in both maternity and neonatology units. Maternal data included demographic and social information and delivery data. Neonatal data included the infant's condition at birth, neonatal complications and care received in neonatal intensive care units. Information related to family circumstances as well as child health and development at 2 years' CA was collected by using a self-administered questionnaire completed by the parents. The questionnaire was sent by post for completion manually or accessed online for completion through secure servers.

Exposure

In this exploratory study, we investigated various factors including maternal, social and perinatal characteristics as well as neonatal health conditions and care practices. The variables were selected *a priori*, first selecting factors associated with NNSHs among the general population in related literature and included maternal age; maternal country of birth; parity (0,1 and ≥2); parents' socioeconomic status defined as the highest occupational status (*e.g.*, professional, intermediate, administrative or public service or self-employed or students, shop assistants or service workers, manual workers and unknown occupation) of the parents or the mother alone if no father was present[23]; child sex; small-for-gestational-age defined as birthweight less than the 10th percentile according to gestational age and sex based on French EPOPé intrauterine growth curves[24]; and breast feeding at discharge. Second, we selected factors specific to preterm infants susceptible to be associated with NNSHs: gestational age defined as the best obstetric estimate, combining the last menstrual period and the first-trimester ultrasonography assessment; type of pregnancy (single or multiple: twins/triplets); severe neonatal morbidities; feeding by nasogastric tube at 36 weeks' CA; care practices in neonatal intensive care units (Newborn Individualized Developmental Care and Assessment Program [NIDCAP, Appendix, Note 1] or Sensory-motor Developmental Care Programs[25–28] and Oral Stimulation).

Severe neonatal morbidities[23] included severe bronchopulmonary dysplasia, severe necrotising enterocolitis, severe retinopathy or severe cerebral abnormalities defined as cranial intraventricular haemorrhage grade III/IV or cystic periventricular leukomalacia (definitions in Note 2 of the Appendix).

Outcome

The primary outcome was NNSHs (No/Yes) at 2 years' CA. Three questions relating to NNSHs were included in the questionnaire completed by the parents: Does the child suck his or her thumb; Does the child suck his or her fingers; and, Does the child suck a pacifier? The possible answers to each question were "never", "sometimes", "often" and "all the time or almost". When the answer was "never" to all 3 questions, children were considered not to have NNSHs. When the answer was "sometimes", "often" or "all the time or almost" to one of the 3 questions, children were considered to have NNSHs.

Statistical analysis

Missing data

Multiple imputations by chained equations was used to correct for both loss to follow-up and missing data for the outcome (NNSHs) and others variables.[29–31] For the outcome variable, 20% of data were missing. For other co-variables, missing data were minimal (<1%) for perinatal factors (gestational age, small-for gestational-age and parity) and between 3 and 11% for neonatal care factors (NIDCAP, oral stimulation and feeding by nasogastric tube). In total, 50 independent imputed datasets were generated. Estimates were pooled according to Rubin's rule.[32] Imputation details are in eTable 1.

Perinatal and sociodemographic characteristics of the population studied, of those lost to follow-up and of those with missing data on the outcome were described. The distribution of NNSHs was described according to all studied factors. All percentages and crude risk ratios

(RRs) were weighted to account for differences in the sampling process between gestational age groups. We drew a directed acyclic graph (DAG) that shows the factors selected for study as potential risk factors and as well as their interdependencies (eFigure 1). The adjusted analysis was performed in 3 steps to identify the factors associated with NNSHs using multivariable log-linear regression models. First, model 1 aimed to identify antenatal factors (*i.e.,* maternal age, maternal country of birth, parity, type of pregnancy, parents' socioeconomic status and child sex) related to NNSHs. Secondly, model 2 analysed characteristics at birth (*i.e.,* gestational age and small-for-gestational-age) in relation with NNSHs, adjusting for the factors studied in model 1. Finally, the association of factors related to health status during hospitalization and developmental care practices (*i.e.,* feeding by nasogastric tube, NIDCAP or sensory-motor developmental care and oral stimulation), and the role of breast feeding at discharge with NNSHs were studied in model 3, adjusting for the factors studied in models 1 and 2. Because severe neonatal morbidities are too closely linked to feeding by nasogastric tube at 36 weeks' CA, they were not included in model 3. Also, because twins (or triplets) share family characteristics and environment and thus do not represent independent observations, generalized estimation equations were used to take into account intra-family correlations.[33] Results are reported as adjusted RRs (aRRs) with 95% confidence intervals (95% Cls).

Sensitivity analyses

A sensitivity analysis was performed on complete cases. Data were analysed with *R* v3.5.0.[34]

Ethics approval

Recruitment and data collection occurred only after families agreed to participate. The EPIPAGE-2 study was approved by the French Data Protection Authority (Commission Nationale de l'informatiques et des Libertés no. 911009) and the two relevant ethics committees [the Consultative Committee on the Treatment of Information on Personal Health Data for Research Purposes [CCTIRS], no. 10.626 and the Committee for the Protection of People Participating in Biomedical Research [CPP], no. SC-2873].

RESULTS

Study population

Of the 3253 children who survived to 2 years' CA, the parental questionnaire was completed for 2737, 2593 of whom had complete data regarding NNSHs questions. In total, 516 children were considered lost to follow-up, *i.e.,* the parents refused to participate or did not complete the parental questionnaire at 2 years' CA (Figure 1).

As compared with the children included, those lost to follow-up were more often 1) born to younger mothers or who had 2 or more older children (parity ≥2); 2) born in single births (not twins/triplets); and 3) born to parents with low socioeconomic status. Children with missing data on NNSHs were more often 1) boys; 2) born to mothers born outside of France or 3) to parents with low socioeconomic status. In both groups children were less frequently fed by nasogastric tube at 36 weeks' CA (eTable 2).

Outcome

Among the 2593 children with available information, 1800 (69%, 95% CI 68-71) had NNSHs at 2 years' CA. After multiple imputation, the frequency of NNSHs was 69% (95% CI 67-70). Among children with NNSHs: 86% used a pacifier, 13% a thumb or fingers and 1% a combination of pacifiers, thumb and fingers. Among children using a pacifier 78% of parents responded that their children sucked "often" and "all the time or almost". In cases involving those who use their thumbs and fingers, 38% of parents responded "often" and "all the time or almost". The frequency of NNSHs according to the studied factors is reported in Table 1.

Factors associated with NNSHs

Table 2 presents multivariable models estimated by generalized estimation equations with multiple imputations. The frequency of NNSHs was higher for girls (aRR 1.12, 95% CI 1.05, 1.17-model 1), children born from multiple pregnancies (*e.g.,* twins/triplets) (aRR 1.07, 95% CI 1.00, 1.11-model 1), children who were fed by nasogastric tube at 36 weeks' CA (aRR 1.07, 95% CI 1.01, 1.13-model 3) and children who benefited from NIDCAP or Sensory-motor Development Care Programs (aRR 1.10, 95% CI 1.02, 1.19-model 3). NNSHs were less frequent if mothers were not born in France (aRR 0.70, 95% CI 0.64, 0.77-model 1), if the child had 2 or more older siblings (aRR 0.88, 95% CI 0.82, 0.96-model 1) and if the child was breast-fed at discharge (aRR 0.90, 95% CI 0.85, 0.95-model 3). Oral stimulation was not associated with NNSHs at 2 years' CA.

Sensitivity analyses

Results of the analysis with completed cases provided aRRs very similar to those of analyses based on imputed data (eTable 3).

COMMENT

Principal findings

This study revealed a 69% frequency of NNSHs at 2 years' CA among very preterm children. The frequency was higher among girls, if mothers were born in France and if children were not breast-fed at discharge but was lower if there were older siblings, all in agreement with related literature involving the general population. Our study also revealed that NNSHs were more common among children from multiple pregnancies (twins/triplets), children who were fed by nasogastric tube at 36 weeks' CA and those who benefitted from developmental care programs (NIDCAP or Sensory-motor Development Care).

Strengths of the study

The EPIPAGE-2 cohort allowed for simultaneous analysis of maternal, social and perinatal characteristics, infant health conditions and care practices specific to very preterm children. Neonatal data (including breast feeding at discharge) were collected prospectively, thus avoiding recall bias. The study's population-based design and large sample size provided reasonable precision in estimating frequencies and associations.

Limitations of the data

In total, 660 children were missing (lost to follow-up and with missing data on the outcome). Their characteristics differed from those of children included and were associated with a lower frequency of NNSHs; because children lost to follow-up were probably less prone to have NNSHs, the frequency may have been slightly overestimated. However, the estimated frequency of NNSHs by imputations and in complete cases was the same. The associations found between the studied factors and NNSHs were also similar in the two analyses.

We used a binary outcome variable, NNSHs (No/Yes), based on three questions referring to sucking a thumb, finger or pacifier. In our study, among children who were considered to have NNSHs, 86% used pacifiers and 13% thumbs and fingers. Among children who used a pacifier, 78% of parents responded to the modalities concerning frequency "often" or "all the time or almost", and in cases involving those who used the thumbs and fingers, 38% of parents responded "often" and "all the time or almost". While the difference between "often" and "all the time or almost" is probably very subjective since the concept "often" is vague, most children who practiced NNSHs were not occasionally suckers, therefore, we are confident in the binary nature of our outcome.

Interpretation

Frequency of NNSHs

The frequency of NNSHs observed in the limited existing literature was influenced by the age of the children involved and by cultural similarities and differences among the studied

populations. Comparing studies with wide age differences (7 months to 6 years) is problematic given the natural changes in habits during childhood. Moreover, all studies except one were performed in the general population. Our study observed a NNSHs frequency of 69% at 2 years' CA among children born preterm, whereas in Australia, the frequency was 79% among full-term children aged 7 months (N=670)[11] and in the United Kingdom, 51% among full-term children aged 24 months (N=867).[9] In a study in Senegal, the frequency of NNSHs was 33% based on 443 children at age 5 to 6 years,[35] whereas in China, it was 12% based on 734 children at age 3 years.[36] Apart from differences in age, these figures imply cultural differences in the frequency of NNSHs. Although comparing populations as different as those in Senegal, China and France regarding NNSHs is difficult, a recent, albeit limited, Brazilian study conducted in a single municipality (250 children age 3 to 5 years), compared full-term children and preterm children, finding a 54% frequency of NNSHs in full-term children but 80% in preterm children.[37] This result is consistent with ours even though the children in our study were somewhat younger (age 2). Although the Brazilian study was limited in sample size and geographical coverage, the findings suggests that the NNSHs frequency may be higher in preterm than full-term infants.

Family factors associated with NNSHs

In both France and Australia, countries geographically distant but in some ways more similar culturally than some other areas mentioned above, the NNSHs frequency was lower if the mother was born abroad.[11] Such results support the idea that sociocultural and family life customs affect NNSHs. Contrary to our initial hypothesis, we found no strong association between parental socioeconomic status and NNSHs. Maternal country of birth and

socioeconomic status are usually closely linked. Our results suggest that there is no association between socioeconomic status and NNSHs, after adjustment on maternal country of birth.

We sought to study the impact of family size by exploring parity (number of older siblings) and multiple pregnancies (single vs twins/triplets). NNSHs were less frequent among children with 2 or more older siblings but more frequent among children born as a twin/triplet. Among twins, a higher frequency of NNSHs might be explained by a greater need for self-reassurance because, having to simultaneously care for two children of the same age, parents may have reduced time available to concentrate on each child. Furthermore, many multiple pregnancies are due to infertility treatment. Parenting attitudes are likely to differ among mothers with infertility treatment (often older and with higher education) and among those who are multiparous (often with a different cultural environment). These differences may explain why associations between NNSHs and older siblings or multiple pregnancies were in opposite directions.

Children characteristics associated with NNSHs

In our study, as in others, NNSHs were more frequent among girls than boys.[10,12] A Swedish study comparing NNS patterns in preterm children revealed a higher sucking rate and higher sucking amplitudes in girls than boys.[38] These observations agree with other studies suggesting that female children experience greater oral activity than boys, possibly because specific lingual structures and oral and lingual movements develop earlier in girls than boys.[39,40]

We also observed a higher frequency of NNSHs for children who were fed by nasogastric tube. Because the maturation of sucking abilities is not fully achieved in very preterm infants, neonatal units favour NNS for stimulating and developing the sucking reflex. This activity is essential to allow such children to feed normally and very important for the maturation of neuro-motor activity.[19,20,41,42] As expected, our study found higher NNSHs frequency at 2 years' CA among children who benefited from NIDCAP or Sensory-motor Developmental Care Programs; both include NNS to promote the development of oral function and alleviation of pain, although not always with pacifiers. Unexpectedly, we found no association between oral stimulation and NNSHs. Oral stimulation involves perioral and intraoral stimulation but not necessarily the use of a pacifier, which may explain the lack of association between oral stimulation and NNSHs.

Regarding breast feeding, NNSHs were less common among children who were breast-fed at the time of hospital discharge. This finding agrees with the literature: several authors observed an association between longer duration of breast feeding and less use of pacifiers.[11,13,37,43] In addition, we found no association between NNSHs and factors such as gestational age and small-for-gestational-age.

Perspectives pertaining to maxillofacial growth anomalies

Several studies of full-term children have shown regular NNSHs for more than 3 years associated with maxillofacial growth anomalies including altered palatal morphology and posterior crossbite. However, because development of the sucking reflex is different in preterm and full-term infants, especially very preterm children, the mechanisms that lead to anomalies of maxillofacial growth might differ.

According to the few available studies, preterm infants seem at higher risk of maxillofacial growth anomalies than full-term infants.[44] One study of very preterm children based on data from the EPIPAGE cohort study[45] observed that altered palatal morphology at 5 age years was more frequent in boys than girls, children with low gestational age or small-for-gestational-age.[46] Although NNSHs might be an intermediate or confounding factor in some of these associations, information about NNSHs was not available in the first EPIPAGE study. Thus, our study may provide a basis for future studies investigating the mechanisms that link NNSHs to related maxillofacial growth anomalies among preterm children.

CONCLUSIONS

This study has shown that in addition to factors associated with NNSHs among the general population (*i.e.,* child sex, family sociodemographic characteristics and breast feeding), NNSHs in very preterm children were more frequent when children were fed by nasogastric at 36 weeks' CA and when children benefited from NIDCAP or Sensory-motor Development Care Programs in neonatal units. Although the practice of NNSHs largely depends on the maternal environment and family attitudes, more in-depth studies are needed to better understand the role of neonatal development care with respect to NNSHs and its possible impact on maxillofacial growth anomalies in preterm children.

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APPENDIX

Note.1. **Newborn Individualized Developmental Care and Assessment Program (NIDCAP) and Sensory-motor Development Care Programs.** NIDCAP involves the observation of signs of stress during and after child caregiving procedures and proposes methods for adjusting care or the environment in an appropriate and supportive parental manner.[26]
The sensory-motor approach to development, which aims to stabilize the infant's sensoritonic balance by improving the environment and the quality of care, proposes sensorimotor experiences that assist in the maturation of the central nervous system, for example, by stimulating perioral and oral areas before meals with a cotton swab in a progressive manner based on a precise protocol so as to stimulate movement of the lips and the initiation of sucking activity.[47]

Note.2. **Severe neonatal morbidities.** The morbidities included any of the following conditions: 1) severe bronchopulmonary dysplasia (defined as administration of oxygen for at least 28 days plus the need for ≥ 30% oxygen and/or mechanical ventilatory support or continuous positive airway pressure at 36 weeks' postmenstrual age[48]; 2) necrotising enterocolitis stage 2-3 according to Bell *et. al.* [49]; 3) severe retinopathy of prematurity stage >3 according to the international classification[50] and/or laser treatment; 4) any of the following severe cerebral abnormalities at cranial ultrasonography: intraventricular haemorrhage grade III or IV and intraparenchymal haemorrhage (*i.e.*, large unilateral parenchymal hyperdensity or a large unilateral porencephalic cyst)[51] or cystic periventricular leukomalacia (*i.e.*, periventricular white matter echolucency).

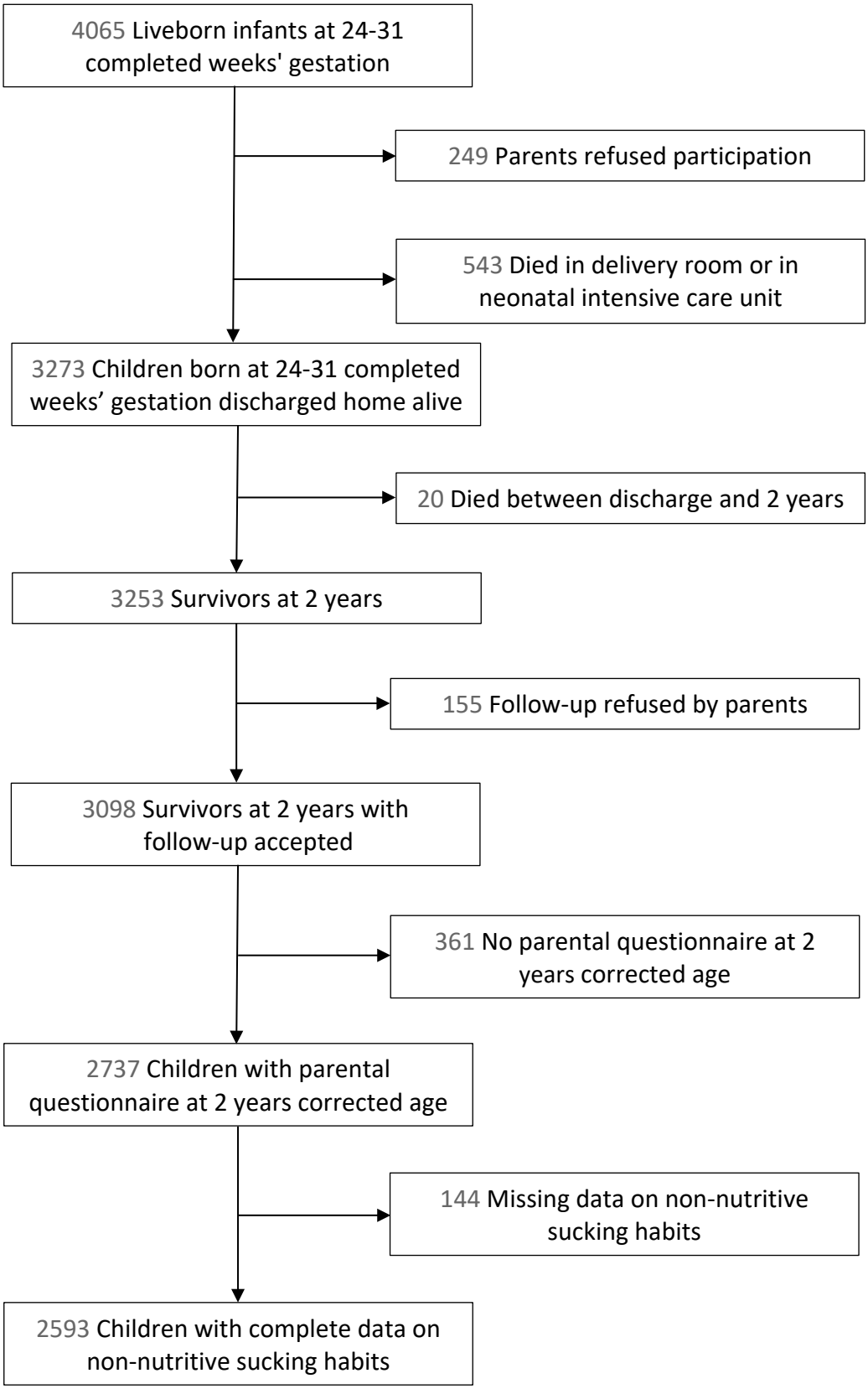

4065 Liveborn infants at 24-31 completed weeks' gestation
249 Parents refused participation
543 Died in delivery room or in neonatal intensive care unit
3273 Children born at 24-31 completed weeks' gestation discharged home alive
20 Died between discharge and 2 years
3253 Survivors at 2 years
155 Follow-up refused by parents
3098 Survivors at 2 years with follow-up accepted
361 No parental questionnaire at 2 years corrected age
2737 Children with parental questionnaire at 2 years corrected age
144 Missing data on non-nutritive sucking habits
2593 Children with complete data on non-nutritive sucking habits

FIGURE 1 Flow chart of study population: EPIPAGE-2 cohort at 2 years' corrected age.

TABLE 1 Sample description and non-nutritive sucking habits (NNSHs) at 2 years corrected age according to maternal and neonatal characteristics and care practices

			NNSHs	
	N	%[a]	n	%[a]
Total	2593	100	1800	69.4
Maternal characteristics				
Maternal age (years)				
< 25	401	15.5	266	66.4
25-34	1603	61.7	1137	70.9
≥ 35	589	22.8	397	67.4
Country of birth				
France	2021	78.4	1502	74.4
Other	562	21.6	292	51.5
Parity				
0	1447	56.1	1038	71.8
1	600	23.5	433	72.1
≥ 2	524	20.4	314	59.7
Type of pregnancy				
Single	1731	66.7	1166	67.3
Multiple	862	33.3	634	73.6
Parents' socioeconomic status[b]				
Professional	585	23.4	410	70.3
Intermediate	559	22.7	425	75.9
Administrative, public service, self-employed, students	665	27.0	464	69.8
Shop assistants, service workers	343	13.6	227	66.3
Manual workers	271	11.0	173	62.8
Unknown	60	2.3	31	52.2
Neonatal characteristics				
Sex				
Boys	1345	52.0	887	65.9
Girls	1248	48.0	913	73.2
Gestational age (weeks)				
24-26	422	12.6	294	69.7
27-31	2171	87.4	1506	69.4
Small-for-gestational-age[c]				
No	1684	64.3	1147	68.1
Yes	909	35.7	653	71.7
Health status during hospitalization				
Severe neonatal morbidities[d]				
No	2070	84.8	1412	68.2
Yes	400	15.2	295	74.2
Feeding by nasogastric tube at 36 weeks' corrected age				
No	787	34.9	513	65.1
Yes	1529	65.1	1090	71.4

Developmental care practices					
NIDCAP[e] or Sensory-motor Developmental Care Programs					
	No	2270	90.1	1559	68.7
	Yes	253	9.9	194	76.6
Oral stimulation					
	No	718	29.4	498	69.5
	Yes	1736	70.6	1203	69.2
Breast feeding at discharge					
	No	1503	60.6	1093	72.9
	Yes	965	39.4	622	64.2

[a]Percentages weighted to account for differences in the sampling process between gestational age groups.
[b]Defined as the highest occupational status of the mother and father or occupation of mother only if living alone.
[c]Defined as birth weight less than the 10th centile for gestational age and sex based on the French EPOPé intrauterine growth curves (Ego 2016).
[d]Severe neonatal morbidity was defined as severe bronchopulmonary dysplasia or necrotising enterocolitis stage 2-3 or severe retinopathy of prematurity stage >3 or any of the following severe cerebral abnormalities on cranial ultrasonography: intraventricular haemorrhage grade III/IV or cystic periventricular leukomalacia.
[e]NIDCAP, Newborn Individualized Developmental Care Program.

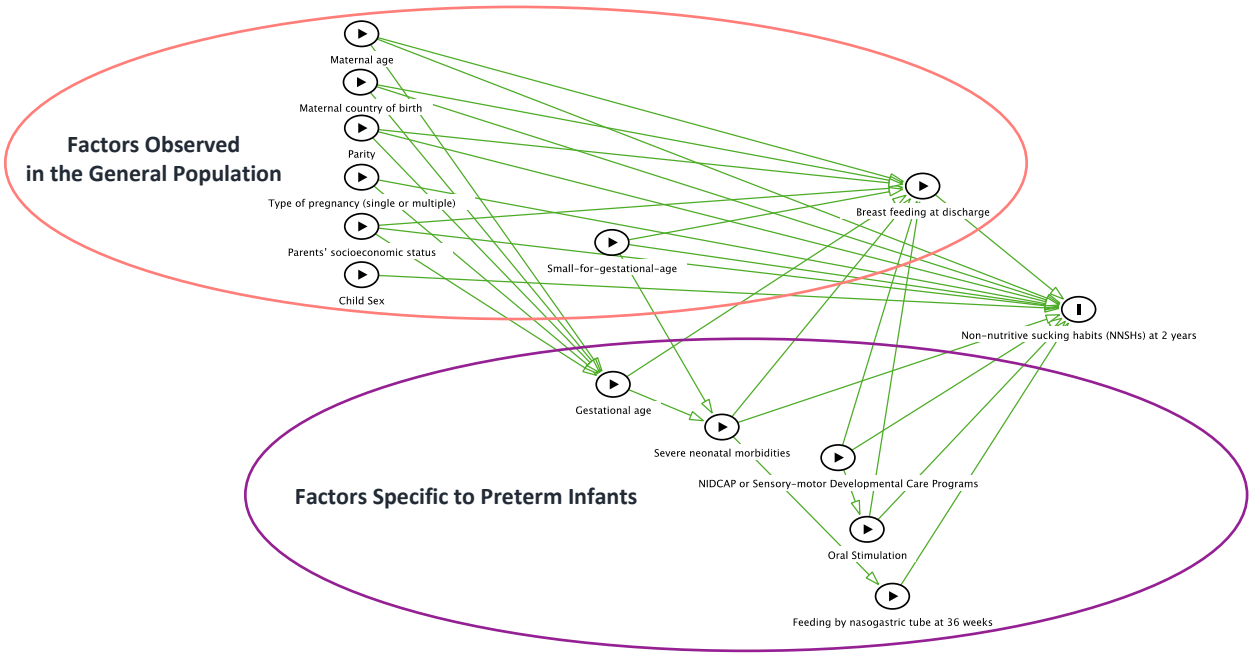
TABLE 2 Non-nutritive sucking habits (NNSHs) at 2 years corrected age according to maternal and neonatal characteristics and care practices: unadjusted and adjusted Risk Ratios (RRs), multivariable log-linear regression models with generalized estimating equations (GEE) with multiple imputation (N=3253)

	Unadjusted RR (95% CI)[a]	Model 1 aRR (95% CI)[b]	Model 2 aRR (95% CI)[c]	Model 3 aRR (95% CI)[d]
Maternal age (years)				
< 25	0.93 (0.87, 0.99)	0.96 (0.88, 1.03)		
25-34	1.00 (Reference)	1.00 (Reference)		
≥ 35	0.96 (0.91, 1.02)	1.01 (0.94, 1.07)		
Maternal country of birth				
France	1.00 (Reference)	1.00 (Reference)		
Other	0.67 (0.62, 0.72)	0.70 (0.64, 0.77)		
Parity				
0	1.00 (Reference)	1.00 (Reference)		
1	1.00 (0.96, 1.06)	1.02 (0.96, 1.08)		
≥ 2	0.89 (0.83, 0.94)	0.88 (0.82, 0.96)		
Type of pregnancy				
Single	1.00 (Reference)	1.00 (Reference)		
Multiple	1.07 (1.01, 1.11)	1.07 (1.00, 1.11)		
Parents' socioeconomic status[e]				
Professional	0.93 (0.87, 1.00)	0.93 (0.86, 1.00)		
Intermediate	1.00 (Reference)	1.00 (Reference)		
Administrative, public service, self-employed, students	0.91 (0.86, 0.97)	0.96 (0.90, 1.03)		
Shop assistants, service workers	0.89 (0.82, 0.96)	0.94 (0.86, 1.02)		
Manual workers	0.87 (0.80, 0.95)	0.95 (0.86, 1.05)		
Unknown	0.66 (0.55, 0.79)	0.78 (0.63, 0.98)		
Sex				
Boys	1.00 (Reference)	1.00 (Reference)		
Girls	1.10 (1.05, 1.16)	1.12 (1.05, 1.17)		
Gestational age (weeks)				
24-26	1.02 (0.95, 1.08)		1.02 (0.96, 1.09)	
27-31	1.00 (Reference)		1.00 (Reference)	
Small-for-gestational age[f]				
No	1.00 (Reference)		1.00 (Reference)	
Yes	1.05 (0.92, 1.06)		1.06 (0.99, 1.12)	
Feeding by nasogastric tube at 36 weeks' corrected age				
No	1.00 (Reference)			1.00 (Reference)
Yes	1.10 (1.04, 1.15)			1.07 (1.01, 1.13)
NIDCAP[g] or Sensory-motor Developmental Care Programs				
No	1.00 (Reference)			1.00 (Reference)
Yes	1.17 (1.09, 1.23)			1.10 (1.02, 1.19)
Oral stimulation				
No	1.00 (Reference)			1.00 (Reference)
Yes	0.98 (0.96, 1.06)			0.98 (0.93, 1.04)
Breast feeding at discharge				
No	1.00 (Reference)			1.00 (Reference)
Yes	0.90 (0.86, 0.95)			0.90 (0.85, 0.95)

[a]Unadjusted RRs weighted to account for differences in the sampling process between gestational age groups.
[b]aRR, adjusted RRs; 95% CI, 95% confidence interval; adjusted for maternal age, maternal country of birth, parity, type of pregnancy, parents' socioeconomic status and child sex, GEE multivariable log-linear regression model.
[c]aRRs; 95% CI; adjusted for maternal age, maternal country of birth, parity, type of pregnancy, parents' socioeconomic status, child sex, gestational age and small-for-gestational-age, GEE multivariable log-linear regression model.
[d]aRRs; 95% CI; adjusted for all variables in the table, GEE multivariable log-linear regression model.
[e]Defined as the highest occupational status of the mother and father or occupation of mother only if living alone.

[f]Defined as birth weight less than the 10th centile for gestational age and sex based on French EPOPé intrauterine growth curves (Ego 2016).
[g]NIDCAP, Newborn Individualized Developmental Care Program.

eFigure 1 Directed Acyclic Graph (DAG) of factors associated with non-nutritive sucking habits at 2 years of age



DAG created with the web-based application: www.dagitty.net

eFigure 1 Directed Acyclic Graph (DAG) of factors associated with non-nutritive sucking habits at 2 years of age among very preterm children.

eTable 1 Type of variable, model used to predict missing data, and percentages of values missing for each variable included in the imputation model (N=3253 survivors at 2 years' corrected age)

Variable	Type of variable	Model used to predict missing data	Percentages of values missing
Non-nutritive sucking habits (NNSHs)	Binary	Logistic regression	20%
Maternal age (years)	Categorical (3 categories)	Multinomial regression	<1%
Maternal country of birth	Binary	Logistic regression	17%
Parity	Categorical (3 categories)	Multinomial regression	1%
Type of pregnancy	Binary	No missing data	0%
Parents' socioeconomic status[a]	Categorical (6 categories)	Multinomial regression	5%
Sex	Binary	No missing data	0%
Gestational age (weeks)	Binary	No missing data	0%
Small-for-gestational-age[b]	Binary	No missing data	0%
Feeding by nasogastric tube at 36 weeks' corrected age	Binary	Logistic regression	11%
NIDCAP[c] or Sensory-motor Developmental Care Programs	Binary	Logistic regression	3%
Oral stimulation	Binary	Logistic regression	6%
Breast feeding at discharge	Binary	Logistic regression	5%

[a]Defined as the highest occupational status of the mother and father or occupation of mother only if living alone.
[b]Defined as birth weight less than the 10th centile for gestational age and sex based on the French EPOPé intrauterine growth curves (Ego 2016).
[c]NIDCAP, Newborn Individualized Developmental Care Program.

eTable 2 Maternal, social and neonatal characteristics of the study population, children lost to follow-up and those with missing data on the outcome

	Study Population		Lost to follow-up		Missing data	
	N	%[a]	n	%[a]	n	%[a]
Total	2593	100	516	100	144	100
Maternal characteristics						
Maternal age (years)						
< 25	401	15.5	177	34.1	34	23.5
25-34	1603	61.7	248	48.2	70	49.5
≥ 35	589	22.8	91	17.7	39	27.0
Maternal country of birth						
France	2021	78.4	364	73.6	70	49.2
Other	562	21.6	129	26.4	71	50.8
Parity						
0	1447	56.1	224	44.6	75	53.1
1	600	23.5	121	23.8	39	26.8
≥ 2	524	20.4	158	31.6	29	20.1
Type of pregnancy						
Single	1731	66.7	376	73.2	92	63.2
Multiple	862	33.3	140	26.8	52	36.8
Parents' socioeconomic status[b]						
Professional	585	23.4	41	9.1	30	21.5
Intermediate	559	22.7	58	13.0	14	10.3
Administrative, public service, self-employed, students	665	27.0	134	29.8	40	28.7
Shop assistants, service workers	343	13.6	83	18.5	23	16.8
Manual workers	271	11.0	91	19.5	28	20.5
Unknown	60	2.3	46	10.1	3	2.2
Neonatal characteristics						
Sex						
Boys	1345	52.0	270	52.3	83	57.4
Girls	1248	48.0	246	47.7	61	42.6
Gestational age (weeks)						
24-26	422	12.6	98	14.8	24	12.9
27-31	2171	87.4	418	85.2	120	87.1
Small-for-gestational-age[c]						
No	1684	64.3	342	65.4	93	63.7
Yes	909	35.7	174	34.6	51	36.3
Health status during hospitalization						
Severe neonatal morbidities[d]						
No	2070	84.8	393	82.9	117	85.3
Yes	400	15.2	88	17.1	21	14.7
Feeding by nasogastric tube at 36 weeks' corrected age						
No	787	34.9	178	42.7	54	41.5
Yes	1529	65.1	251	57.3	79	58.5

Developmental care practices							
NIDCAP[e] or Sensory-motor Developmental Care Programs							
	No	2270	90.1	426	87.5	132	93.0
	Yes	253	9.9	62	12.5	10	7.0
Oral stimulation							
	No	718	29.4	143	31.7	47	33.5
	Yes	1736	70.6	317	68.3	93	66.5
Breast feeding at discharge							
	No	1503	60.6	349	73.1	89	65.0
	Yes	965	39.4	126	26.9	47	35.0

[a]Percentages weighted to account for differences in the sampling process between gestational age groups.

[b]Defined as the highest occupational status of the mother and father or occupation of mother only if living alone.

[c]Defined as birth weight less than the 10th centile for gestational age and sex based on French EPOPé intrauterine growth curves (Ego 2016).

[d]Severe neonatal morbidity was defined as severe bronchopulmonary dysplasia or necrotising enterocolitis stage 2-3, severe retinopathy of prematurity stage >3 or any of the following severe cerebral abnormalities on cranial ultrasonography: intraventricular haemorrhage grade III/IV or cystic periventricular leukomalacia.

[e]NIDCAP, Newborn Individualized Developmental Care Program.

eTable 3 Non-nutritive sucking habits (NNSHs) at 2 years corrected age according to maternal and neonatal characteristics and care practices: multivariable log-linear regression models with generalized estimating equations (GEE)

	Multiple Imputation N=3253	Complete Cases N=1863
	aRR (95% CI)[a]	aRR (95% CI)[a]
Maternal age (years)		
< 25	0.95 (0.89, 1.02)	0.98 (0.89, 1.08)
25-34	1.00 (Reference)	1.00 (Reference)
≥ 35	1.00 (0.94, 1.07)	1.01 (0.93, 1.09)
Maternal country of birth		
France	1.00 (Reference)	1.00 (Reference)
Other	0.72 (0.65, 0.78)	0.75 (0.68, 0.82)
Parity		
0	1.00 (Reference)	1.00 (Reference)
1	1.03 (0.97, 1.09)	1.08 (1.01, 1.16)
≥ 2	0.88 (0.82, 0.96)	0.90 (0.81, 0.99)
Type of pregnancy		
Single	1.00 (Reference)	1.00 (Reference)
Multiple	1.06 (1.00, 1.11)	1.09 (1.02, 1.17)
Parents' socioeconomic status[b]		
Professional	0.94 (0.88, 1.01)	0.94 (0.87, 1.03)
Intermediate	1.00 (Reference)	1.00 (Reference)
Administrative, public service, self-employed, students	0.95 (0.89, 1.02)	0.93 (0.85, 1.01)
Shop assistants, service workers	0.92 (0.85, 1.01)	0.94 (0.85, 1.05)
Manual workers	0.94 (0.85, 1.03)	0.89 (0.79, 1.01)
Unknown	0.78 (0.62, 0.97)	0.74 (0.53, 1.03)
Sex		
Boys	1.00 (Reference)	1.00 (Reference)
Girls	1.11 (1.06, 1.17)	1.08 (1.02, 1.15)
Gestational age (weeks)		
24-26	0.99 (0.93, 1.06)	1.00 (0.92, 1.09)
27-31	1.00 (Reference)	1.00 (Reference)
Small-for-gestational-age[c]		
No	1.00 (Reference)	1.00 (Reference)
Yes	1.04 (0.99, 1.10)	1.04 (0.97, 1.10)
Feeding by nasogastric tube at 36 weeks' corrected age		
No	1.00 (Reference)	1.00 (Reference)
Yes	1.07 (1.01, 1.13)	1.06 (0.99, 1.13)
NIDCAP[d] or Sensory-motor Developmental Care Programs		
No	1.00 (Reference)	1.00 (Reference)
Yes	1.10 (1.02, 1.19)	1.10 (1.02, 1.20)
Oral stimulation		
No	1.00 (Reference)	1.00 (Reference)

	Yes	0.98 (0.93, 1.04)	1.01 (0.94, 1.09)
Breast feeding at discharge			
	No	1.00 (Reference)	1.00 (Reference)
	Yes	0.90 (0.85, 0.95)	0.90 (0.85, 0.97)

[a]aRR, adjusted Risk Ratio; 95% CI, 95% confidence interval; adjusted for all variables in the table, GEE multivariable log-linear regression models.

[b]Defined as the highest occupational status of the mother and father or occupation of mother only if living alone.

[c]Defined as birth weight less than the 10th centile for gestational age and sex based on the French EPOPé intrauterine growth curves (Ego 2016).

[d]NIDCAP, Newborn Individualized Developmental Care Program.