The national, longitudinal NASCITA Cohort study: starting population profile

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Research Article

Keywords: Cohort Studies, Infant, Newborn, Child, Infant, Health, Public Health, Population Characteristics

Posted Date: February 21st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1323884/v1>

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Abstract

Background We set up a national level, population-based, prospective cohort study, the NASCITA Study, to better understand the early health status of Italian children and how it is affected by social and health determinants. Physical, cognitive, and psychological development of children during the first six years of life, and potentially associated factors, will be evaluated.

Methods Participating paediatricians enrolled, during their first well-child visit, all infants born April 2019 - July 2020. Multiple health outcomes will be studied, spanning child development and illness, as well as potentially related factors including parental characteristics and caregiving routines. We present the data on the entire enrolled population of 5054 newborns, at the time of their first out-of-hospital visit.

Results

Most mothers (86.6%) were born in Italy. Average age at delivery was 33.1 years. Folic acid supplementation was taken appropriately by 36.1% of mothers. One fourth (25.3%) of mothers was overweight or obese. In all, 31.7% were caesarean deliveries. Concerning the newborns, 6.2% were born prematurely and 7.9% were born with a neonatal disease. The exclusive breastfeeding rate at one month of age was 63.6%.

North-South differences were found in all areas, including parental education, behaviours in pregnancy (e.g., folic acid supplementation) and afterwards (e.g., breast feeding), and hospital practices (e.g., caesarean section).

When compared with national level data, the distribution of the cohort population, maternal socio-demographic characteristics, and newborn physical characteristics reflect those of the Italian population.

Conclusions

The large geographical differences in the attitudes of parents and healthcare professionals call for interventions to improve adherence to evidence based good practices associated with better neonatal growth and development.

Trial registration: Clinicaltrials.gov: NCT03894566

Background

Infancy and childhood are periods of rapid growth and development and contribute significantly to well-being, health status, and behaviour throughout life.[1] In fact, many common diseases and challenges in adult life can be traced back to early childhood,[2, 3] but how specific social factors, socioeconomic status, living conditions, parental and stakeholder care, and attitudes act on the well-being of children or in creating health inequalities among children is still poorly understood. Interactions between these health determinants also need to be investigated.[4, 5] The concept of the developmental origins of health and

disease (DOHAD), which includes the periconceptional period, is a key window during which poor maternal and paternal physiology and diet, among other things, can induce increased risk of chronic disease in offspring.[6]

Prospective birth cohort studies are studies that follow a group of newborns for an extended period of time and permit the collection of accurate information about exposures, outcomes, and several covariates.[7] Many birth cohorts have been set up worldwide,[8, 9] some as early as 1921 in Europe,[10] and have contributed to knowledge in numerous areas, from medical to social ones.[11–13]

Cohort characteristics vary greatly from one cohort to another, as do their objectives, with some cohorts focused on one specific area, such as environmental factors and their effect on health, and others on multiple areas. Some cohorts collect data retrospectively, others prospectively. Some collect only written data, others also biological samples.

Two reviews of cohorts in Europe have been carried out, one from 2013 that gave a general description of birth and pregnancy cohorts in Europe[8] and the second, from 2020, that gave a more detailed description of cohorts that recruited at birth and not during pregnancy.[14] These reviews showed that many cohorts have been set up in northern and western Europe and that the study areas, and their range, varied greatly. The more recent review[14] showed that many of the cohorts are relatively recent, with half of the 111 European cohorts beginning after 2000, and that their methodologies differed significantly. This review also showed that few, relatively recent cohorts focused on family context (nurturing care) and its impact. Nurturing care refers to the environment created by caregivers that is attentive to children's health and nutritional and social needs and has been shown to positively influence children's health, growth, and development.[2] It is a central issue,[15] it offers possibilities for interventions to promote maximum health, social and cognitive development, and should be a priority study area.

In Italy, the population is becoming more heterogeneous, and sociodemographic and geographic differences, such as education and migrant status, have been associated with health disparities.[16, 17] Italy, in fact, has a public, universal healthcare system that should pose no legal or financial barriers to subgroups of the population, but considerable health inequalities exist[16] and arise from differences in health behaviour, exposure, environment, genes, etc. Various cohorts have been carried out in Italy, most with general aims and with data collection limited in time or to specific geographical contexts.[18–26]

Nine prospective cohorts have been set up in Italy,[18, 21, 23, 24, 26–29] starting from 2000, some of which recruited in pregnancy and some at birth. All these cohorts began data collection at recruitment, through clinical visits, questionnaires, in-person or telephone interviews, and medical records. The largest of these cohorts, the NINFEA, is different from the others in that it recruited participants online. The population sizes of these cohorts ranged from 274–7500. The oldest cohort, the Genetic and Environment: Prospective Study on Infancy in Italy (GASPII), began in 2005, and the newest, the Neonatal Environmental and Health Outcomes (NEHO), in 2018. One cohort, MUBICOS, specifically enrolled twins, and did so by recruiting twins born in eight participating Italian hospitals. The MUBICOS cohort is the only

one currently recruiting. Only three of these cohorts aimed to be representative of the Italian geographical context, North, Centre, and South: the NINFEA, ICON, and MUBICOS cohorts.

In order to improve the understanding of the early health status of Italian children and how it is affected by social and health determinants, we decided to set up a longitudinal, prospective, national level, population-based birth cohort, the NASCITA study (*NAscere e creSCere in ITAlia*) (Clinicaltrials.gov registration number NCT03894566, 28/03/2019). Like many other cohorts, it addresses multiple research questions.[30, 31] Unlike in many other cohorts, however, the data will be based on the paediatrician's assessment and diagnosis of health status and outcomes instead of on parental recounting or medical records, leading to more accurate data and avoiding possible cultural and socio-demographic influences on data recall.[32] The central role of the paediatrician in data collection on overall health and growth and in interaction with patients is a unique quality of NASCITA and is possible in Italy because primary care for children is guaranteed by the family paediatrician, unlike in many other countries.[33]

The main aim of the NASCITA cohort is to build a national observatory, starting from the paediatricians' office, to evaluate physical, cognitive, and psychological development, and health status and health resource use during the first six years of life in a group of newborns, and to evaluate potentially associated factors. The findings will be used to develop specific prevention measures and interventions to improve the health status of children, contributing to the life-course approach being increasingly prioritized world-wide.[34]

The current article describes the FINAL newborn population's characteristics, and those of their parents, after the end of the enrolment period and up to the first paediatrician visit, and provides data on parental behaviours such as breastfeeding and smoking.

Methods

The methods of the NASCITA cohort have been described elsewhere.[35, 36] Briefly, Italian health care is provided free or at a minimal charge. Children receive care from a family paediatrician until they are at least six years old. Seven well-child visits are scheduled by the paediatrician in the first six years of a child's life to monitor growth and development and offer preventive care. Additional visits are organized when needed. The NASCITA cohort was set up by the Laboratory for Mother and Child Health of the Istituto di Ricerche Farmacologiche Mario Negri IRCCS in Milan in collaboration with the national Paediatric Cultural Association (ACP) and was designed to be embedded in Italian paediatric primary care practice. Data are, in fact, collected directly by the paediatrician and mostly during the well-child visits. The study was approved by the Fondazione IRCCS Istituto Neurologico "Carlo Besta" ethics committee.

Paediatrician participation is voluntary and no compensation is given. Paediatricians who chose to participate provided initial information, such as contact information and area of residence, through an online form. Newborns were enrolled during their first visit with the paediatrician and will be followed-up until they are at least six years old.

Cohort selection

The newborn population consists of all infants born during the enrolment period (April 2019 – July 2020) and seen by the paediatricians for at least two visits, including the first well-child visit. Newborns were enrolled only if informed consent to participate was obtained by parents and/or their legal guardians. Children who had not had a second visit were excluded in order to exclude those seen by the paediatrician only in a transitory manner.

Outcomes

Multiple health outcomes will be studied, including the relationship between child development and nurturing care. Specific factors that will be evaluated are disease prevention and treatment actions, nutrition (breastfeeding and diet), caregiving routine, home opportunities to explore and learn, parental adherence to the recommendations for better child care and development, and how all these things relate to child growth and development. Some maternal and paternal periconceptional characteristics will also be evaluated, considering their role in offspring health. The possible influence of geographical settings in educational and socialization opportunities available for young children and in the care provided by the family paediatricians and by the national health service will also be evaluated.

Data collection

During the year of enrolment, the paediatricians collected data on the newborns mostly during the well-child visits through online forms accessible on the NASCITA portal. The children's records could be accessed at any time to complete any missing data. Efforts, such as emailing or calling paediatricians and implementing a system of red, yellow, and green “traffic lights” on the portal notifying the paediatricians if specific participant records were incomplete, were made to reduce the amount of missing information. The more technological aspects of the NASCITA study, such as the web portal and online platform for data input and modification, have been described elsewhere.[36] The NASCITA study's website is available at <https://coortenascita.marionegri.it>.

Statistical analysis

Categorical variables were summarized using proportions and associations were tested using the chi-square test. Continuous variables were summarized using means, standard deviations, medians, and quartiles. To test difference of means for normally distributed continuous variables and The Mann Whitney U test or the Kruskal-Wallis test were used to test differences. Statistical significance was evaluated using a two-tailed *P value* < 0.05. All data management and analyses were performed using SAS software.

Missing data

Missing data were excluded from the percentages because they were limited to < 2,5% for all the main variables, except maternal pregnancy body mass index (BMI) (and were limited, in this case, to < 5%).

Folic acid supplementation was classified as “appropriate” if folic acid was taken from at least one month before, and throughout, at least the first trimester of pregnancy. It was classified as “inappropriate” if folic acid was taken only once the pregnancy began, even if throughout the pregnancy, or if it was taken, but data were missing as to how and when. The BMI categories used were underweight (BMI $\leq$ 18.5), normal (18.6–24.9), overweight (25.0–29.9), and obese ($\geq$ 30.0). To evaluate gestational weight gain (GWG), the weight variations recommended by the Institute of Medicine criteria were applied after grouping the mothers according to the pre-pregnancy BMI.[37, 38] The distribution of weight for gestational age was estimated using the Italian Neonatal Study (INeS) charts.[39]

Twenty-one geographic clusters were identified for the NASCITA study as representative of Italy based on geographic and administrative divisions, using the National Statistics Institute (ISTAT) definitions for each town/city,[40] in order to be able to assess whether the paediatrician population is distributed throughout the territory.

Results

Data from the total cohort population of 5054 newborns, and their families, are described in this article.

In all, 139 paediatricians are involved and recruited an average of 76.2% of the newborns assigned to them by the local health unit. A total of 17 of the 21 geographical clusters are represented by the paediatricians, and the presence of paediatricians in each cluster reflects the national distribution.

Parents

The demographic characteristics of the parents are described in Table 1. The mean age of the mothers at delivery was 33.1 years (median 33). If only primiparas are considered, average maternal age was 32.3 years (range 16–54 years). The majority of mothers and fathers was born in Italy (86.6% and 88.7%, respectively), with only 8.6% of cases in which both parents were born abroad. A higher rate of parents born abroad was found for families in the North compared to the South of Italy. Mothers tended to have a high or medium level of education (42.5% had a university degree and 41.7 a high school degree), and to be employed (69.7%). Fewer fathers had a high level of education (26.7% university degree), but the majority was employed (96.1%). In general, there were higher levels of maternal and paternal education in the Centre, and lower levels of maternal and paternal employment in the South. Most children lived with both parents (98.2%).

Table 1
Maternal and paternal characteristics

	North <i>n</i> (%)	Centre <i>n</i> (%)	South <i>n</i> (%)	Total <i>n</i> (%)	<i>P</i> value
Average maternal age at delivery, yrs; SD	32.9; 5.2	33.7; 5.3	32.9; 5.6	33.1; 5.4	0.0005*
Median maternal age at delivery, yrs; min-max	33.0; 18– 51	34; 17– 54	33; 16– 51	33; 16– 54	
Maternal age class at delivery, yrs					0.0034*
< 25	142 (6.1)	46 (4.8)	118 (7.1)	306 (6.2)	
25–29	436 (18.9)	136 (14.3)	328 (19.7)	900 (18.2)	
30–34	836 (36.2)	353 (37.0)	582 (34.9)	1771 (35.9)	
35–39	667 (28.9)	309 (32.4)	462 (27.7)	1438 (29.2)	
40+	229 (9.9)	110 (11.5)	179 (10.7)	518 (10.5)	
Mother born in Italy	1894 (81.1)	837 (86.5)	1626 (93.9)	4357 (86.6)	< 0.0001*
Father born in Italy	1950 (83.9)	841 (87.5)	1646 (95.8)	4437 (88.7)	< 0.0001 *
Both parents born abroad	305 (13.1)	87 (9.1)	38 (2.2)	430 (8.6)	< 0.0001 *
Maternal education					< 0.0001 *
Elementary/Middle school	365 (15.8)	95 (9.8)	331 (19.4)	971 (15.8)	
Highschool	1020 (44.0)	337 (34.9)	725 (42.4)	2082 (41.7)	
University	933 (40.3)	535 (55.3)	655 (38.3)	2123 (42.5)	
Maternal employment	1740 (74.8)	747 (76.5)	1009 (58.8)	3496 (69.7)	< 0.0001 *

	North <i>n</i> (%)	Centre <i>n</i> (%)	South <i>n</i> (%)	Total <i>n</i> (%)	<i>P</i> value
Paternal education					< 0.0001 *
Elementary/Middle school	547 (23.7)	137 (14.3)	471 (27.8)	1155 (23.3)	
Highschool	1191 (51.8)	454 (47.5)	826 (48.8)	2471 (50.0)	
University	561 (24.4)	364 (38.1)	394 (23.3)	1319 (26.7)	
Paternal employment	2281 (98.4)	929 (96.2)	1586 (93.1)	4796 (96.1)	< 0.0001 *
Maternal civil status					< 0.0001 *
Married/living together	2222 (96.0)	897 (93.0)	1653 (96.9)	4772 (95.7)	
Single/separated/divorced/widow	92 (4.0)	68 (7.0)	53 (3.1)	213 (4.3)	
Child living with both parents	2305 (98.6)	957 (98.0)	1687 (97.6)	4949 (98.2)	0.0550

Many mothers (19.2%) had a chronic disease, such as hyper- or hypothyroidism, or asthma (40.1% and 10.2% of mothers with a chronic disease, respectively) (Table 2). The presence of chronic diseases in the mothers, and in the families in general, was more frequent in southern Italy.

Table 2
Pregnancy characteristics

	North n (%)	Centre n (%)	South n (%)	Total n (%)	P value
Natural conception	2204 (94.4)	912 (93.2)	1594 (94.7)	4710 (94.2)	0.229
Parity: Primiparous	1235 (53.0)	594 (60.9)	962 (55.6)	2791 (55.4)	0.0002 *
No previous pregnancies (<i>primigravida</i>)	1033 (44.3)	477 (49.0)	824 (47.8)	2334 (46.4)	0.0180 *
<i>n</i> previous pregnancies (2697 women)					0.0986
1	708 (54.8)	285 (58.0)	467 (52.6)	1460 (54.7)	
2	389 (30.1)	151 (30.8)	274 (30.9)	814 (30.5)	
> 2	195 (15.1)	55 (11.2)	146 (16.5)	396 (14.8)	
Pre-pregnancy BMI					< 0.0001 *
Underweight	208 (9.3)	80 (8.6)	94 (5.6)	382 (7.9)	
Normal weight	1.489 (66.5)	653 (70.2)	1.098 (65.4)	3.240 (66.8)	
Overweight	362 (16.2)	145 (15.6)	339 (20.2)	846 (17.5)	
Obese	179 (8.0)	52 (5.6)	149 (8.9)	380 (7.8)	
Gestational weight gain					0.3498
Inadequate	804 (36.2)	344 (37.1)	609 (36.7)	1.757 (36.6)	
Optimal	876 (39.5)	378 (40.8)	628 (37.9)	1.882 (39.2)	
Excessive	538 (24.3)	204 (22.0)	422 (25.4)	1.164 (24.2)	
Healthy pregnancy	1992 (85.2)	839 (85.9)	1497 (86.5)	4328 (85.8)	0.4839
Chronic disease in mother	397 (17.0)	188 (19.2)	387 (22.3)	972 (19.2)	0.0001 *

	North n (%)	Centre n (%)	South n (%)	Total n (%)	P value
Folic acid taken appropriately	910 (39.5)	400 (41.0)	496 (28.6)	1806 (36.1)	< 0.0001 *
Vaccination in pregnancy	1121 (49.1)	278 (28.9)	229 (13.4)	1628 (32.8)	< 0.0001 *
Most common vaccines					
DTaP	1076 (21.3)	267 (5.3)	199 (3.9)	1542 (30.5)	< 0.0001 *
Influenza	239 (4.7)	89 (1.8)	73 (1.4)	401 (7.9)	< 0.0001 *
If current smoker					
Any smoke during pregnancy	163 (7.0)	64 (6.7)	97 (5.7)	324 (6.5)	0.2238
Occasionally	58 (36.0)	22 (34.4)	36 (37.5)	116 (36.1)	
Daily	103 (64.0)	42 (65.6)	60 (62.5)	205 (63.9)	
<i>If DAILY, how much</i>					
Little (≤ 10 /day)	91 (88.3)	38 (90.5)	49 (81.7)	178 (86.8)	0.4055
Moderate (11–19/day)	10 (9.7)	2 (4.8)	9 (15.0)	21 (10.2)	
A lot (1 pack/day)	2 (1.9)	2 (4.8)	2 (3.3)	6 (2.9)	
If alcohol use in pregnancy					< 0.0001 *
Any alcohol during pregnancy	335 (14.8)	63 (6.6)	96 (5.6)	494 (10.0)	
Occasionally	325 (97.0)	61 (96.8)	94 (97.9)	480 (97.2)	0.9208
Daily	10 (3.0)	2 (3.2)	2 (2.1)	14 (2.8)	

Pregnancy

The pregnancy characteristics, reported in Table 2, revealed a 94.2% rate of natural conception. In all, 14.2% of mothers had a gestational disorder, in 35.0% of whom it was gestational diabetes. Concerning maternal behaviours in pregnancy, folic acid supplementation was often inappropriate (3043 mothers, 60.8%), or not present at all (160, 3.2%), and vaccination rates in pregnancy were low (1628, 32.8%), involving mostly DTaP (94.8%). In terms of geographical differences, there were lower rates of proper folic acid supplementation and vaccination in the South. A total of 324 (6.5%) mothers smoked during

pregnancy, 63.9% of whom smoked daily. Alcohol was consumed by 494 (10.0%) mothers, 14 of whom drank it on a daily basis. The rate of alcohol consumption during pregnancy was higher in the North. Maternal pre-pregnancy BMI showed that one fourth (25.3%) of mothers was overweight or obese, with a higher in southern Italy compared to the North and Centre. In general, one fourth of mothers (24.2%) gained an amount of weight greater than that recommended by the US Institute of Medicine (IOM).

Delivery

Concerning the birth characteristics (Table 3), almost all births were in-hospital (4980, 98.8%), 4895 (97.1%) were singleton births, and 1600 (31.7%) were caesarean births. Hospitals provided skin to skin contact in three fourths of cases (3676, 73.8%), provided intramuscular vitamin K prophylaxis at birth (4644, 92.9%), and gave newborns artificial milk (1987, 40.1%), sugared water (215, 4.3%), or water (17, 0.3%). The rate of exclusive breastfeeding at discharge was 69.6% (3509 mothers). In terms of national-level differences, in the South of Italy caesarean births were more common, and rates of use of formula milk and sugared water during hospital stay were higher. Concerning exclusive breastfeeding at discharge, the rate was lower in the south (62.1% compared to 73.7% and 72.8% in the North and Centre, respectively).

Newborns

Concerning the newborns' characteristics, reported in Table 3, 2471 (48.9%) were female and birthweight ranged from 635 to 5885 grams (median 3270 grams), with 294 (5.8%) low birthweight (< 2500 grams) newborns and 234 (4.6%) weighing > 4000 grams. A total of 315 (6.2%) newborns were born prematurely (22–36 weeks gestational age), five (1.6%) of whom were extremely preterm (< 28 weeks gestational age). Concerning weight and gestational age, 525 (10.5%) infants were small for gestational age (SGA) and 452 (9.0%) were large for gestational age (LGA). In all, 161 (3.2%) newborns needed resuscitation at birth, 161 (3.2%) were born with birth defects, and 398 (7.9%) were born with a neonatal disease. The most common diseases were jaundice (106 newborns), respiratory distress (59), and neonatal hypoglycaemia (47). Furthermore, 16.5% of newborns had to be admitted to a neonatal care ward and 4.3% to a neonatal

Table 3
Birth, in-hospital, breast feeding, and newborn characteristics

	North n (%)	Centre n (%)	South n (%)	Total n (%)	P value
Mean gestational age at birth, wks; SD	39.0; 1.7	39.0; 1.6	38.9; 1.8	39.0; 1.7	0.0006
Gestational age category (weeks)					0.0009*
22–36	124 (5.3)	50 (5.1)	141 (8.1)	315 (6.2)	
37–41	2197 (93.9)	923 (94.3)	1571 (90.8)	4691 (92.9)	
42–44	18 (0.8)	6 (0.6)	19 (1.1)	43 (0.9)	
Birth in hospital	2323 (99.4)	966 (98.9)	1691 (98.0)	4980 (98.8)	0.0003*
Single vs twin births					< 0.0001*
Single birth	2294 (98.2)	954 (97.5)	1647 (95.3)	4895 (97.1)	
Twins	42 (1.8)	23 (2.4)	82 (4.7)	147 (2.9)	
Birth type					< 0.0001*
Spontaneous	1639 (70.0)	608 (62.1)	993 (57.3)	3240 (64.1)	
Caesarean	575 (24.6)	328 (33.5)	697 (40.2)	1600 (31.7)	
Instrumental birth	126 (5.4)	43 (4.4)	44 (2.5)	213 (4.2)	
Skin to skin contact immediately after birth	1880 (82.1)	778 (80.1)	1018 (59.2)	3676 (73.8)	< 0.0001*
Intramuscular Vitamin K at birth	2204 (95.2)	940 (96.7)	1500 (87.7)	4644 (92.9)	< 0.0001*
Breast feeding in hospital	2098 (91.4)	906 (93.0)	1476 (87.7)	4480 (90.5)	< 0.0001*
Exclusively breastfed upon hospital discharge	1720 (73.7)	713 (72.8)	1076 (62.1)	3509 (69.6)	< 0.0001*

	North n (%)	Centre n (%)	South n (%)	Total n (%)	P value
NEWBORNS					
Female	1116 (47.7)	515 (52.6)	843 (48.6)	2474 (49.0)	0.0361 *
Mean birthweight, gr; SD	3278.0; 483.8	3250.3; 487.5	3225.8; 501.4	3254.7; 491.1	0.0055 *
Median birthweight, gr; min-max	3290.0; 635–4850	3250.0; 1.155–4750	3250.0; 1160–5885	3270.0; 635.0–5885.0	
Birthweight class, gr					0.0589
< 2.500	124 (5.3)	53 (5.4)	117 (6.8)	294 (5.8)	
2.500-4.000	2098 (89.7)	874 (89.3)	1552 (89.6)	4524 (89.5)	
> 4.000	118 (5.0)	52 (5.3)	64 (3.7)	234 (4.6)	
Weight for gestational age					0.8335
Small for gestational age (SGA)	236 (10.1)	97 (10.0)	192 (11.2)	525 (10.5)	
Appropriate for gestational age (AGA)	1884 (80.9)	785 (80.8)	1373 (79.9)	4042 (80.5)	
Large for gestational age (LGA)	210 (9.0)	89 (9.2)	153 (8.9)	452 (9.0)	
Mean length, cm; SD	49.7; 2.5	49.8; 2.3	49.5; 2.4	49.6; 2.4	0.0018 *
Malformation at birth	80 (3.4)	28 (2.9)	53 (3.1)	161 (3.2)	0.6565
Disease at birth	172 (7.4)	77 (7.9)	149 (8.6)	398 (7.9)	0.3466
Admitted to Neonatal Unit	398 (17.4)	181 (18.7)	241 (14.0)	820 (16.5)	0.0019 *
Admitted to Neonatal Intensive Care Unit	84 (3.6)	34 (3.5)	97 (5.6)	215 (4.3)	0.0030 *

First visit with the family paediatrician

The average age of the newborns at their first out-of-hospital visit was 25.7 days, with a median of 24.0 days (Table 4). A total of 3187 (63.6%) newborns were being exclusively breastfed at the time of their first visit, while, of the remaining newborns, over one third (35.9%) were receiving formula milk and two thirds (64.1%) were receiving a mixed feeding regimen.

Table 4
Characteristics at first visit with paediatrician (7–45 days old)

	North n (%)	Centre n (%)	South n (%)	Total n (%)	P value
Mean age, days; SD				25.7; 24.9	
Breast feeding					< 0.0001 *
Exclusive	1577 (67.9)	639 (65.5)	971 (56.7)	3187 (63.6)	
Mixed breast feeding	476 (20.4)	252 (25.8)	440 (25.6)	1168 (64.1)	
Artificial formula	270 (11.7)	84 (8.7)	300 (17.7)	654 (35.9)	
Usual sleep position					< 0.0001 *
Supine	2069 (90.3)	849 (87.3)	1444 (84.5)	4362 (87.7)	
Side	92 (4.0)	65 (6.7)	215 (12.6)	372 (7.5)	
Prone	130 (5.7)	59 (6.0)	50 (2.9)	239 (4.8)	
Vitamin D prophylaxis ongoing/initiated at visit	2.297 (98.7)	942 (96.3)	1.642 (95.6)	4881 (97.4)	< 0.0001
Drug prescribed at visit (excluding vitamin D)	108 (4.6)	27 (2.8)	41 (2.4)	176 (3.5)	< 0.0001

The prevalence of exclusive breastfeeding at the first well-child visit decreased from North to South ($\chi^2_{\text{t}} 52$; $p < 0.001$). In the South of Italy, 17.5% of newborns received only formula, versus 11.6% in the North and 8.6% in the Centre.

Concerning sleeping position, the majority of newborns slept in the supine position (87.7%), while 4.8% slept in the prone position. There were geographical differences in sleeping position as well: the percentage of supine position was higher in the North (90%) and lower in the South (84%) ($\chi^2_{\text{t}} 31.2$; $p < 0.001$).

Concerning prophylaxis, 97.4% were receiving vitamin D prophylaxis at their first visit. A total of 176 (3.5%) newborns received a drug prescription during their visit and the drugs most commonly prescribed were simethicone (17%), nystatin (14%), and ophthalmic tobramycin (10%).

The results of the screening procedures for normal development (Table 4) show that most of the newborns had positive developmental assessment results. Very few were found to have problems with motor (nine newborns) or sensory and social (seven) skills.

Discussion

The distribution of the cohort population reflects that of the Italian population, based on the ISTAT data from 2019,[41] which report that 46% of the national population resides in the North, 20% in the Centre, and 34% in the South/islands. The socio-demographic characteristics of the mothers also reflect national level data, where the mothers' average age at birth of the first child is 32.1 years, as reported in the 2019 Eurostat data for Italy,[42] compared to 32.3 in the NASCITA cohort. The main characteristics at birth of mothers and newborns in the NASCITA cohort and in the national reference data, the Ministry of Health's Certificato di assistenza al parto (CeDAP) 2019 data,[43] are listed in Additional File 1. The maternal level of education is higher in NASCITA compared to national level data (42.5% compared to 31.2% of mothers have a university degree),[43] while the percentage of foreign-born mothers on the other hand, is lower in NASCITA (13.4% vs 21%), with both results likely to be due to language barriers that preclude recruitment and to the more frequent transfers to other areas/paediatricians on the part of families with parents who were born abroad. These differences are also true when NASCITA cohort data are compared with those of the Italian NINFEA[23] and PiccoliPiù[44] cohorts, i.e., the general population characteristics are similar, while the maternal level of education is higher in NASCITA and the percentage of foreign-born parents is lower. The distribution of the newborns' anthropometric measures is also comparable with that of the national data.[39]

Italy is one of the European countries with the highest maternal age at birth, with a median of 32.8 years (33.0 in the NASCITA cohort), compared to 31.4 years in Europe (2019 data). The NASCITA data show a rate of 39.7% of mothers giving birth at ≥ 35 years compared to an average of 25.9% in Europe.[45] The older age of mothers in NASCITA may, in part, be explained by the fact that older mothers are more inclined to participate in research, although age-related data are conflicting, or may be due to the higher socio-economic status or higher educational level, which tends to be higher in older mothers.[46] Childbearing later in life has, in any case, increased in Europe over the last ten years,[47] also as a result of factors such as socio-economic circumstances and artificial reproduction technologies.[48] Given the increased risks related to having children in advanced maternal age,[48] more effective policies and initiatives aimed at decreasing this growing trend, informing women of the increased risks of late childbearing, and addressing their needs in pregnancy, need to be implemented.

A high maternal pre-pregnancy BMI is associated with adverse maternal and neonatal outcomes, as well as with long-term health outcomes.[38, 49] It has also been found that women with higher pre-pregnancy BMI gain more weight than recommended in pregnancy,[50] and inadequate weight variations in pregnancy can also affect birth outcomes.[37] The fact that one fourth of the NASCITA cohort mothers were overweight or obese is therefore worrying, although this rate seems to be lower than the European rate of 30%-50%.[47] In our sample, for 61% of the mothers the weight gained during pregnancy was not

consistent with the recommendations made by IOM. In comparison with recent Italian studies,[38] the NASCITA data shows a slightly higher percentage of mothers with a GWG above that recommended by the IOM (24 versus 16%).[38]

The rate of caesarean births in the NASCITA cohort, involving almost one in three births, confirms Italy's standing as one of the countries with the highest rate in Europe, and has been a matter of concern for years. Large regional differences exist, with much higher rates in the South.[51] A dedicated, national strategy set up in 2010[52] to improve safety and quality of birthing procedures and to reduce caesarean births, and this may have helped Italy become one of the European countries with the largest decrease in rate between 2010 and 2015,[47] although the rate in Italy remains disproportionately high, especially among Italian mothers and in private medical centres.[43] Unfortunately, a complex situation in which policy, practice, legal and social issues, and individual preferences all apparently contribute.[51]

A series of maternal behaviours that are important for later offspring health and that can be implemented from before pregnancy to the first few months of life and beyond, such as folic acid intake, smoke and alcohol avoidance, and breastfeeding, have been acknowledged worldwide. In Italy, projects such as GenitoriPiù[53] and Progetto Sorveglianza 0–2[54] were set up to endorse these good health promotion and prevention practices. The NASCITA project is collecting data on these behaviours and has so far shown that, despite information initiatives promoting these good practices, more must be done. Concerning exclusive breastfeeding, for example, the rates in Italy at hospital discharge were already low, represented by just over two thirds of mothers (69.6%), and the rate decreased to 63.6% at the first visit with the paediatrician. Similar data were found in the PiccoliPiù study (2011–2015 data), with a rate of 86% that decreased to 66% at one month of age.[55] Concerning folic acid supplementation, a majority of mothers took folic acid, but only about one third took it in an appropriate manner, with an even worse situation in the South. This low rate reflects that from an Italian surveillance system on almost 30 000 mothers from 11/20 Italian regions, which found that 21% of mothers took folic acid appropriately.[54] Concerning smoking and alcohol use, the NASCITA data, showing that 6.5% of mothers continued to smoke during pregnancy and that one in ten drank alcohol during pregnancy, also reflected data from the surveillance study, which reported that 6.2% of mothers smoked during pregnancy and 19.7% drank alcohol at least once a month, and from the PiccoliPiù study (9.1% of mothers smoked in pregnancy[44]). Despite national initiatives to inform parents about the effects of smoke, recent data show that the phenomenon continues to exist.[50]

Geographical differences in the health status and in the care of mother and newborns are striking, in particular when looking at the South of Italy. Pregnant women living in southern Italy were less compliant with folic acid prophylaxis and with recommended vaccinations. They were also at greater risk of being overweight or obese at the beginning of the pregnancy. A greater rate of caesarean delivery was reported, neonates were less frequently exposed to skin-to-skin contact with their mothers at birth, and were less likely to be breastfed at discharge from the hospital, and consequently, also at the first well-child visit. Differences in the exclusive breastfeeding rate at hospital discharge after delivery between the South and other geographic areas of Italy persist also when excluding preterm or low birthweight newborns, or

newborns with congenital malformations (data not shown), from the analyses. Lastly, slight differences were observed concerning sleeping position. The above differences have already been observed in previous studies.[51, 55, 56]

Despite the fact that these inequalities in the health of mothers and their neonates are well-known, there has been negligible change over the years. This reality is frustrating and has to do with the health system organization, the attitudes of physicians, and with sociodemographic and cultural differences within Italy. [57]

COVID-19 was officially declared a pandemic in March 2020. Cohorts were immediately set up to study the effects of the pandemic, including the direct effects on the hospital care of pregnant women with SARS-CoV-2 infection.[58] The SARS-COV-2 virus created large difficulties for paediatricians, and disrupted care-seeking and preventive interventions on the part of parents in Italy and throughout Europe. [59, 60] Enrolment in NASCITA was consequently hindered, leading to a drop in number of newborns enrolled between April and July 2020 because of the increased workload for paediatricians and the limitations in daily life. The NASCITA cohort data will, however, permit us to study short and long-term health-related consequences with respect to COVID-19, since data related to the infection are being collected.

One of the aims of the present report is to describe the starting characteristics of the population enrolled that will be followed for at least six years, as a stimulus for sharing suggestions and cooperation within the interested scientific community.

Strengths And Limitations

The NASCITA study is one of the few involving the paediatricians directly as protagonists in cohort design and data collection. A pilot project was carried out by a group of paediatricians in three regions in Italy between 2007–2010 to test a surveillance system on diet and physical activity, although this was part of a larger project and limited to a specific topic.[61] The paediatricians' primary role in the NASCITA cohort permits them to contribute first-hand to improving the cohort's functioning and to implement the recommended changes in practice resulting from the findings. The paediatrician's direct role in data collection is a major strength in that it permits a "holistic" evaluation. It includes information on growth, health status, drug prescriptions, diagnostic exams and specialist visits, data from clinical examinations, and screenings integrated with information obtained from the parents. Another strength of this study is that the newborn population is representative of the national newborn population in terms of geographical distribution and characteristics. Furthermore, strategies were implemented to maintain paediatrician participation and to minimize loss to follow-up.[62] These involved, for example, maintaining contact with the paediatricians through periodic emails providing updates on the progress of the cohort, providing paediatricians with timely email assistance with data input, and sending periodic newsletters listing recent publications relevant to cohort studies from around the world. These initiatives are already underway. Strategies used to maintain parental participation and minimize loss to follow-up

of the newborns involved providing information dedicated to parents on the NASCITA study's web portal with information on, for example, common childhood diseases. Another strength of the NASCITA study is that efforts were made to retrospectively collect data on the mothers and fathers from before, and during, the pregnancy, given the increasing awareness of the importance of such periods on health at birth and in later life, i.e. the concept of DOHAD.

The limitations of this study are that the population is restricted to the children assigned to the participating paediatricians. The paediatricians may be a somewhat selected sample because many are part of the ACP network and may have joined the network because they are more inclined to participate in research than others. The geographic distribution of the paediatricians, however, is representative of Italy's North-Centre-South division, and the paediatricians do not choose which children to follow, but receive those assigned to them by the local health unit.

The newborn population reflects that of the newborn population normally followed by family paediatricians in Italy. This population includes all newborns that do not have serious health problems that would prevent them from being regularly followed, at least in the first period of their lives, by a family paediatrician. Newborns with serious health problems are usually followed by hospital staff or specialists, and would therefore not likely have been taken to the first well-child visit within the first 45 days of life (when paediatricians enrolled newborns in the study).

Another limit of the NASCITA cohort is that it does not collect biological samples due to the costs of data collection and storage. It will therefore not be able to evaluate genetic or immunological factors, for example. Resources and efforts were utilized, however, to achieve the largest population size possible in order to have enough power to study common child exposures and outcomes.

Conclusions

Newborns participating in the NASCITA cohort, and their families, are representative of the Italian population in terms of geographical distribution and sociodemographic characteristics. The analysis of the characteristics during pregnancy and at birth confirms the existence of large geographical differences in attitudes, in particular concerning folic acid intake, immunization, caesarean birth, and exclusive breastfeeding prevalence. This underlines the need for an organizational and educational intervention aimed at improving the adherence by parents and healthcare professionals to evidence based good practices associated with better growth, health status, and development in neonates.

Abbreviations

ACP: Paediatric Cultural Association

BMI : body mass index

CeDAP: Certificato di assistenza al parto

DOHAD: Developmental origins of health and disease

GWG: gestational weight gain

INeS: Italian neonatal study charts

IOM: US Institute of Medicine

ISTAT: Italian National Statistics Institute

Declarations

Ethics approval and consent to participate

Newborns were enrolled only if informed consent to participate was obtained by parents and/or their legal guardians. The study was approved by the Fondazione IRCCS Istituto Neurologico "Carlo Besta" ethics committee on 6 February 2019 (Verbale n 59). All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to the fact that requests to access the data must be approved by NASCITA's scientific committee and must be for non-commercial purposes, as stated in the NASCITA Cohort's protocol, but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by resources from the Laboratory for Mother and Child Health and by an economic contribution by the *Associazione Amici del Mario Negri*.

Authors' contributions

MB designed the Study. MB and AC directed the study's implementation. AC and MC designed the analytical strategy. MC carried out the statistical analyses. AC and MC helped to interpret the findings. CP conducted the literature review and was a major contributor in writing the manuscript. All authors contributed to, and revised, the article. All authors read and approved the final manuscript.

Acknowledgements

The authors would like to thank Claudia Pansieri for her collaboration in setting up and running the NASCITA Cohort, Michele Zanetti for the informatics aspects of the setting up and running of the cohort and its website, and Maria Grazia Calati, Rita Campi, and Daniela Miglio for assistance in management of the cohort and in communication with the paediatricians.

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Mariangela Valera, Edda Vernile, Valeria Vicario, Lucia Vignutelli, Paolo Vinci, Lucia Vizziello, Rosette Zand, Marco Zanette, Federica Zanetto, Graziano Zucchi, Maria Luisa Zuccolo. Roberto Cionini and Giuseppa Scornavacca unfortunately passed away.

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