




# BMJ Open National, longitudinal NASCITA birth cohort study to investigate the health of Italian children and potential influencing factors

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## ABSTRACT

**Purpose** The NASCITA Study, a national-level, population-based, prospective cohort study, was set up to better understand the early health status of Italian children, comprising their physical, cognitive and psychological development, and how it is affected by social and health determinants, including nurturing care. NASCITA will also assess geographical differences and disparities in healthcare.

**Participants** Participating family paediatricians from throughout Italy enrolled infants born during the enrolment period (April 2019–July 2020). The 5054 newborns seen by the 139 paediatricians for at least two visits, including the first well-child visit, and for whom parental consent was given, make up the baseline population.

**Findings to date** Mothers had a mean age at delivery of 33.0 years and tended to have a high or medium level of education (42.5% university and 41.7% high school degrees) and to be employed (69.7%). One-third (36.1%) took folic acid supplementation appropriately, and 6.5% smoked or consumed alcohol (10.0%) during pregnancy. One-third (31.7%) of deliveries were caesarean deliveries. Concerning the newborns, 5.8% had a low birth weight and 6.2% were born prematurely. The majority (87.7%) slept in the supine position, and 63.6% were exclusively breast fed at 1 month, with a decreasing north to south prevalence ( $\chi^2$ , 52;  $p < 0.001$ ). Significant north–south differences were found in all areas, including parental education, behaviours in pregnancy and hospital practices. When compared with national level data, the cohort population's distribution, maternal sociodemographic characteristics and newborn physical characteristics reflect those of the Italian population.

**Future plans** Data will continue to be collected during the well-child visits until the children are 6 years old, and multiple health outcomes will be studied, spanning child development and illness, as well as potentially related factors including caregiving routines. The findings will be used to develop specific interventions to improve children's health.

**Trial registration number** NCT03894566.

## INTRODUCTION

Infancy and childhood are periods of rapid growth and development and contribute

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The Nascere e creScere in Italia (NASCITA) study is one of few involving paediatricians directly as protagonists in cohort design and data collection.
- ⇒ The newborn population involved is representative of the national newborn population in terms of geographical distribution and characteristics.
- ⇒ The population is restricted to the children assigned to the participating paediatricians, which might lead to a somewhat selected sample because many of the paediatricians are part of the national Paediatricians' Cultural Association (ACP) and may have joined because they are more inclined to participate in research than others; however, paediatricians do not choose which children will be placed in their care since children are assigned to them by the local health unit.
- ⇒ The newborn population reflects that of the newborn population normally followed by family paediatricians in Italy, but not those with serious health problems who are likely followed, at least in the first period of their lives, by hospital staff or specialists.
- ⇒ NASCITA does not collect biological samples due to the costs of data collection and storage and will therefore not be able to evaluate genetic or immunological factors for example.

significantly to well-being, health status and behaviour throughout life.<sup>1</sup> Research carried out worldwide has shown that many common diseases and challenges in adult life can be traced back to early childhood and that health and social determinants in early life play a strong role.<sup>2 3</sup> Specifically, certain social factors, socioeconomic status, living conditions, parental and stakeholder care, and attitudes influence the well-being of children and lead to health inequalities among children. In a developed region of the world such as Europe, most children are healthy, but inequalities between and within member states, lack of access to quality services and unhealthy lifestyles negatively affect health in

children and adolescents also in Europe.<sup>4</sup> In order to be able to set up the most effective interventions, tailored to those who would benefit the most, it is important to identify the existing inequalities and health determinants in specific countries. In Italy, research has been carried out on health determinants and on their interactions,<sup>5</sup> with similar findings compared with other European countries.<sup>6</sup> Low socioeconomic status, lower parental education and employment status were found to be associated with lower health and development outcomes. Despite complex interaction between exposure variables was found,<sup>7</sup> some determinants, such as promotion of autonomy in the home environment, were found to play a crucial role in child neurocognitive development. A 2019 review of inequalities in child health<sup>8</sup> found that behavioural determinants, however, are not as influential as socioeconomic status and living conditions. It would be useful to further investigate such influences in Italy. Interactions between health determinants are complex and also need to be investigated.<sup>6 8 9</sup>

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.<sup>10</sup> Many birth cohorts have been set up worldwide,<sup>11 12</sup> some as early as 1921 in Europe,<sup>13</sup> and have contributed to knowledge in numerous areas, from medical to social ones.<sup>14–16</sup>

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, while others collect data prospectively. Some collect only written data, while others also collect 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<sup>11</sup> and the second, from 2020, that gave a more detailed description of cohorts that recruited at birth and not during pregnancy.<sup>17</sup> 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<sup>17</sup> 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.<sup>2</sup> Nurturing care is a central issue<sup>18</sup>; 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.<sup>19 20</sup> 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 and arise from differences in health behaviour, exposure, environment, genes, etc.<sup>19</sup> Many of these inequalities are well known and relate to regional differences, with southern Italy often resulting at the greatest disadvantage due to cultural and economic factors.<sup>21</sup>

Various cohort studies have been carried out in Italy, most with general aims and with data collection limited in time or to specific geographical contexts.<sup>22–30</sup> Nine prospective cohorts have been set up in Italy,<sup>22 25 27–33</sup> 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 *Nascita e INFanzia: gli Effetti dell'Ambiente* (NINFEA), recruited participants online. The population sizes of these cohorts ranged from 274 to 7500. The oldest cohort, the Genetic and Environment: Prospective Study on Infancy in Italy, began in 2005, and the newest, the Neonatal Environmental and Health Outcomes, in 2018. One cohort, MUBICOS (Multiple births cohort study), specifically enrolled twins, and recruited them 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.

The *NAscere e creSCere in ITALIA* (NASCITA study), a longitudinal, prospective, national-level, population-based birth cohort, was set up in 2019 to improve the understanding of the early health status of Italian children and how it is affected by social and health determinants, including nurturing care. Like many other cohorts, it addresses multiple research questions.<sup>34 35</sup> 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, however, and is possible in Italy because primary care for children is guaranteed by the family paediatrician, unlike in many other countries.<sup>36</sup> 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 sociodemographic influences on data recall.<sup>37</sup> The synergy between the paediatrician's central role and this cohort study's focus on nurturing care make NASCITA different from most Italian and European cohort studies. NASCITA will also be able to collect data from throughout the national context and will therefore be able to better assess the regional differences and disparities in health behaviours and healthcare that exist in Italy.

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 6 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 that is being increasingly prioritised worldwide.<sup>38</sup>

This cohort profile paper describes the rationale behind the NASCITA cohort, the study design and characteristics of the population of enrolled newborns and those of their families. In particular, as region of residence is known to be strongly associated with both healthcare quality and behaviour, geographic differences were analysed.

## COHORT DESCRIPTION

In Italy, healthcare is provided free or at a minimal charge. Children are assigned to a family paediatrician by the local health unit and receive care from that paediatrician until they are at least 6 years old. Seven well-child visits are scheduled by the paediatrician in the first 6 years of a child's life to monitor growth and development and offer preventive care. Additional visits are organised 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: Associazione Culturale Pediatri) 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.

Paediatrician participation is voluntary, and no compensation is given. Recruitment details have been explained previously.<sup>39</sup> Briefly, locally representative paediatricians were identified, initially through the national ACP, after which paediatricians identified in each geographic area were asked to identify additional paediatricians from their area for invitation. Other paediatric and scientific societies were also contacted for collaboration. Paediatricians who chose to participate provided initial information, such as contact information and area of residence, through an online form. A total of 139 paediatricians from throughout Italy, representing all geographic areas of the country, agreed to participate.<sup>40</sup> Enrolment took place between April 2019 and July 2020 and, within this time frame, each paediatrician enrolled, for a 1-year period, all newborns presenting for their first visit (which routinely takes place in the first 45 days of life in Italy) and whose parents gave informed consent. No other inclusion or exclusion criteria were present for enrolment.

Only children who were seen by the paediatricians for at least two visits, including the first well-child visit, were considered for the baseline population. Children who had not had a second visit (n. 112) were excluded in order to avoid including those seen by the paediatrician

only in a transitory manner. Newborns will be followed up until they are at least 6 years old.

Multiple health outcomes will be studied in the NASCITA cohort, including the relationship between child development and nurturing care.<sup>39</sup> Nurturing care which, as mentioned above, refers to those behaviours put in place by parents and caregivers that create an optimal environment for children to thrive, and involves factors to be implemented from before pregnancy to the first few months of life and beyond, such as folic acid intake, smoke and alcohol avoidance, and breast feeding. Specific factors that will be evaluated in this cohort are disease prevention and treatment actions, nutrition (breast feeding 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 influence of geographical setting on educational and socialisation opportunities available for young children and in the care provided by the family paediatricians and by the national health service will also be evaluated.

Paediatricians collected data on the newborns and on parental sociodemographic and lifestyle characteristics such as employment status, educational level and smoking habits, during the well-child visits held so far through online forms. These forms were created for each of the planned well-child visits, based on the foreseen age range,<sup>39</sup> and were revised by a group of paediatricians and other participants (pharmacists, educators and parents), who make up the technical-scientific committee. The data collected vary as the children grow, with age-appropriate measures (eg, breast feeding, neurodevelopmental parameters) and include questions to ask parents during the visits on their habits and parenting behaviours. Most data are already collected by paediatricians using routine data collection forms and checklists. Additional data collected were integrated with validated tools for recording data of particular interest (eg, the CDC - Centers for Disease Control and Prevention - checklist for developmental milestones).<sup>41</sup> An additional form is available online to paediatricians to also collect data during any caregiver-paediatrician telephone contact or extra visits. The children's records can be accessed at any time to complete any missing data. Efforts are being made to reduce the amount of missing information, such as emailing or calling paediatricians and implementing a system that notifies the paediatricians about incomplete data. The more technological aspects of the NASCITA study, such as the web portal and online platform for data input and modification, have been described in detail in a separate article.<sup>40</sup>

Data are continuously being monitored and cleaned and are analysed periodically. The Kruskal-Wallis test was used to analyse continuous variables, and the  $\chi^2$  test was used for the categorical variables. All p values <0.05 were

**Table 1** Maternal and paternal characteristics

	Total n (%)	North n (%)	Centre n (%)	South n (%)	P value
Average maternal age at delivery, years; SD	33.0; 5.3	32.9; 5.2	33.7; 5.3	32.9; 5.6	0.0006*
Median maternal age at delivery, years; min–max	33; 16–54	33.0; 18–51	34; 17–54	33; 16–51	
Maternal age class at delivery, years					0.0052*
<25	307 (6.2)	143 (6.2)	46 (4.8)	118 (7.1)	
25–29	908 (18.4)	439 (19.0)	139 (14.6)	330 (19.8)	
30–34	1768 (35.8)	834 (36.1)	352 (36.9)	582 (34.9)	
35–39	1432 (29.0)	665 (28.8)	307 (32.2)	460 (27.6)	
40+	518 (10.5)	229 (9.9)	110 (11.5)	179 (10.7)	
Mother born in Italy	4357 (86.6)	1894 (81.1)	837 (86.5)	1626 (93.9)	<0.0001*
Father born in Italy	4437 (88.7)	1950 (83.9)	841 (87.5)	1646 (95.8)	<0.0001*
Both parents born abroad	430 (8.6)	305 (13.1)	87 (9.1)	38 (2.2)	<0.0001*
Maternal education					<0.0001*
Elementary/middle school	791 (15.7)	365 (15.8)	95 (9.8)	331 (19.4)	
High school	2082 (41.7)	1020 (44.0)	337 (34.9)	725 (42.4)	
University	2123 (42.5)	933 (40.3)	535 (55.3)	655 (38.3)	
Maternal employment	3496 (69.7)	1740 (74.8)	747 (76.5)	1009 (58.8)	<0.0001*
Paternal education					<0.0001*
Elementary/middle school	1155 (23.3)	547 (23.7)	137 (14.3)	471 (27.8)	
High school	2471 (50.0)	1191 (51.8)	454 (47.5)	826 (48.8)	
University	1319 (26.7)	561 (24.4)	364 (38.1)	394 (23.3)	
Paternal employment	4796 (96.1)	2281 (98.4)	929 (96.2)	1586 (93.1)	<0.0001*
Maternal civil status					<0.0001*
Married/living together	4772 (95.7)	2222 (96.0)	897 (93.0)	1653 (96.9)	
Single/separated/divorced/widow	213 (4.3)	92 (4.0)	68 (7.0)	53 (3.1)	
Child living with both parents	4950 (98.2)	2306 (98.6)	957 (98.0)	1687 (97.6)	0.0548

\* Statistically significant

considered statistically significant and were labelled with an asterisk in the tables. Additional details on the NASCITA cohort are described in the protocol.<sup>39</sup> The NASCITA study's website is available at <https://coortena-scita.marionegri.it>.

## FINDINGS TO DATE

### Characteristics of study participants

The cohort population consists of 5054 newborns, recruited by 139 paediatricians. The paediatricians enrolled an average of 76.2% of the newborns assigned to them by the local health unit.

The demographic characteristics of the parents are reported in [table 1](#). Missing data were excluded from the percentages in all tables because they were limited to <2.5% for all the main variables, except maternal pregnancy body mass index (BMI) (limited to <5%). 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 were born in Italy

(86.6% and 88.7%, respectively). A higher rate of both parents born abroad was found for families in the north compared with 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 were 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.

Many mothers (20.5%) had a chronic disease, such as hyperthyroidism 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.

### 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



**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)	0.2529
Parity: primiparous	1235 (53.0)	594 (60.9)	962 (55.6)	2791 (55.4)	0.0002*
No previous pregnancies (primigravida)	1033 (44.3)	477 (49.0)	824 (47.8)	2334 (46.4)	0.0180*
n 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)	
Prepregnancy BMI					<0.0001*
Underweight	208 (9.3)	80 (8.6)	94 (5.6)	382 (7.9)	
Normal weight	1489 (66.5)	653 (70.2)	1098 (65.4)	3240 (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)	1757 (36.6)	
Optimal	876 (39.5)	378 (40.8)	628 (37.9)	1882 (39.2)	
Excessive	538 (24.3)	204 (22.0)	422 (25.4)	1164 (24.2)	
Healthy pregnancy	1992 (85.2)	839 (85.9)	1497 (86.5)	4328 (85.8)	0.4839
Chronic disease in mother	416 (17.8)	193 (19.7)	425 (24.5)	1034 (20.5)	0.0001*
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*
Recommended vaccines					
DTaP	1076 (46.0)	267 (27.2)	199 (11.5)	1542 (30.5)	<0.0001*
Influenza	239 (10.2)	89 (9.1)	73 (4.2)	401 (7.9)	<0.0001*
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)	
If daily, how much					
Little ( $\leq 10$ /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 (one pack/day)	2 (1.9)	2 (4.8)	2 (3.3)	6 (2.9)	
Any alcohol during pregnancy	335 (14.8)	63 (6.6)	96 (5.6)	494 (10.0)	<0.0001*
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)	

\*Statistically significant

†Folic acid supplementation was considered appropriate if folic acid was taken from at least 1 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.

BMI, body mass index; DTaP, Diphtheria, Tetanus and Pertussis Vaccine.

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 prepregnancy BMI showed that one-fourth (25.3%) of mothers was overweight or obese, with a higher rate in southern Italy compared with 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.

**Table 3** Delivery, in-hospital, breastfeeding and newborn characteristics

	North n (%)	Centre n (%)	South n (%)	Total n (%)	P value
Mean gestational age at birth, weeks; SD	39.0; 1.7	39.0; 1.6	38.9; 1.8	39.0; 1.7	0.0158*
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 versus twin births					<0.0001*
Single birth	2294 (98.2)	954 (97.5)	1647 (95.3)	4895 (97.1)	
Twins	42 (1.8)	24 (2.5)	82 (4.7)	148 (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 breast fed on hospital discharge	1720 (73.7)	713 (72.8)	1076 (62.1)	3509 (69.6)	<0.0001*
Newborns					
Female	1116 (47.7)	515 (52.6)	843 (48.6)	2474 (49.0)	0.0361*
Mean birth weight, g; SD	3278.0; 483.8	3250.3; 487.5	3225.8; 501.4	3254.7; 491.1	0.0055*
Median birth weight, g; min-max	3290.0; 635–4850	3250.0; 1155–4750	3250.0; 1160–5885	3270.0; 635.0–5885.0	
Birth weight class, g					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*

\* Statistically significant

## 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 breast feeding at discharge was 69.6% (3509 mothers). In terms of national-level differences, in the south, caesarean births were more common, and rates of use of formula milk and sugared water during hospital stay were higher. The rate of exclusive breast feeding at discharge was lower in the

south (62.1% compared with 73.7% and 72.8% in the north and centre, respectively).

## Newborns

Table 3 reports the newborns' characteristics. In all, 2474 (48.9%) were female. Birth weight ranged from 635 to 5885 g (median 3270 grams), with 294 (5.8%) low birth weight (<2500g) newborns and 234 (4.6%) weighing >4000g. A total of 315 (6.2%) newborns were born prematurely (22–36 weeks' gestational age (GA)), five (1.6%) of whom were extremely preterm (<28 weeks' GA). Concerning weight and GA, 525 (10.5%) infants were small for gestational age and 452 (9.0%) were large for gestational age, based on the Italian Neonatal Study charts.<sup>42</sup>

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

	North n (%)	Centre n (%)	South n (%)	Total n (%)	P value
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 (23.3)	
Artificial formula only	270 (11.6)	84 (8.6)	300 (17.5)	654 (13.1)	
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 (6.1)	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*

\* Statistically significant

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 intensive care unit.

#### 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 24.9 days (table 4). A total of 3187 (63.6%) newborns were being exclusively breast fed 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.

The prevalence of exclusive breast feeding at the first well-child visit decreased from north to south ( $\chi^2$ , 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 (90.3%) and lower in the south (84.5%) ( $\chi^2$  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 show that most of the newborns had positive developmental assessment results. Very few were found to have problems with motor (9 newborns) or sensory and social (7) skills.

The distribution of the cohort population reflects that of the Italian population, based on the Istituto nazionale di statistica (ISTAT) data from 2019,<sup>43</sup> which report that 46% of the national population resides in the north, 20% in the centre and 34% in the south/islands. The sociodemographic 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,<sup>44</sup> compared with 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 2019 data,<sup>45</sup> are listed in table 5. The maternal level of education is higher in NASCITA compared with national level data (42.5% compared with 31.2% of mothers have a university degree),<sup>45</sup> while the percentage of foreign-born mothers, however, 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<sup>27</sup> and PiccoliPiù<sup>46</sup> cohorts, that is, 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.<sup>47</sup>

Newborns participating in the NASCITA cohort, and their families, are generally representative of the Italian population in terms of geographical distribution<sup>40</sup> and sociodemographic characteristics, with the exception of the lower prevalence of foreign-born mothers, as reported previously. The analysis of the characteristics during pregnancy and at birth confirms the existence of large geographical differences in attitudes, in particular concerning folic acid

**Table 5** Main characteristics at birth of mothers and newborns in the NASCITA cohort and in the national reference data (CeDAP)

	NASCITA % population	CeDAP % population
Mothers		
Mother born in Italy	86.6	79
Mother's age, years		
≤29	24.4	25.3
30–39	65.1	63.5
40+	10.5	11.2
Maternal education		
Elementary/middle school	23.3	25.9
Highschool	50.0	42.9
University	42.5	31.2
Maternal employment	69.7	55.0
Healthy pregnancy	85.8	85.2
Natural conception	94.2	96.9
Caesarean section	31.7	31.8
Newborns		
Twins	2.9	1.6
Birth weight		
<1500 g	0.5	0.9
1500–2499 g	5.3	6.2
2500–3999 g	89.5	87.6
>4000 g	4.6	5.2
Gestational age at birth/preterm birth		
22–36 weeks	6.2	6.8
37–41	92.9	92.7
>41	0.9	0.5
Malformation at birth	3.2	1.3
CeDAP, Certificato di assistenza al parto.		

intake, immunisation, caesarean birth and exclusive breastfeeding prevalence.

One-fourth of the NASCITA cohort mothers (25.3%) were overweight or obese, although this rate seems to be lower than the European rate of 30%–50%.<sup>48</sup> 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. Large regional differences exist, with much higher rates in the South.<sup>49</sup>

Concerning aspects related to nurturing care and good practices, the data collected on these behaviours show that more must be done. When considering exclusive breast feeding, 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. Concerning folic acid supplementation, only

about one-third of mothers took it in an appropriate manner, with an even worse situation in the south. Concerning smoking and alcohol use, the NASCITA data showed that 6.5% of mothers continued to smoke during pregnancy and that 1 in 10 drank alcohol during pregnancy.

North to South differences in the health status and in the care of mother and newborns are striking, in particular when looking at southern 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 breast fed 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 birth weight newborns or newborns with congenital malformations (data not shown). Geographical differences have been already documented by previous studies,<sup>19 35</sup> and according to our findings, little has changed in the meantime. Several factors can be associated with these differences (organisation of the healthcare system at the local level, physicians' attitudes and cultural and socioeconomic factors), and multifaceted interventions are needed. Even after adjusting for sociodemographic variables (eg, maternal age at delivery, educational level, employment status, Italian nationality, parity, etc), compliance with good practices remained low in southern Italy (data not shown). Differences in socioeconomic status may have a role, but other variables are likely involved. Moreover, the fact that the exclusive breastfeeding rate at hospital discharge was 62.1% in the south may suggest that there is a need for educational interventions for health professionals involved in assistance at delivery and for organisational changes with the aim to support mothers who desire to breast feed.

### Strengths and limitations

The NASCITA study confirms what is known about national level and regional level differences in healthcare practices and behaviours from other studies, such as smoking and alcohol data, but it is also the first study capable of assessing, at the national and regional levels, other variables such as pertussis vaccination in pregnancy. Furthermore, the NASCITA cohort is one of the few studies involving the paediatricians directly as protagonists in cohort design and data collection. The paediatricians' direct role in data collection is a major strength in that it permits a 'holistic' evaluation, including 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 minimise loss to follow-up,<sup>40</sup> involving, 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 on other cohort studies. Similarly, strategies were implemented to maintain parental participation and minimise loss to follow-up of the newborns, such as providing information dedicated to parents on the NASCITA study's web portal on common childhood diseases. A further 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.

The limitations of this study are, first, that the population is restricted to the children assigned to the participating paediatricians, and this may lead to a somewhat selected sample because many of the paediatricians are part of the national ACP and may have joined NASCITA 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.

A second limitation is that the newborn population reflects that of the newborn population normally followed by family paediatricians in Italy, which includes all newborns who 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).

A third 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 used, however, to achieve the largest population size possible in order to have enough power to study common child exposures and outcomes.

### Patient and public involvement

Patients were indirectly involved in the development of the research questions and questionnaires in that

the technical-scientific committee that was set up to supervise the study, and that collaborates in creating and revising the questionnaires, involves professionals (eg, paediatricians, pharmacists, educators) who are also parents. The public is involved through the dissemination of cohort results and information on childhood diseases or conditions to parents and the general public on the study's website.

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