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The emergence of vaccine hesitancy among upper-class Brazilians: Results from four birth cohorts, 1982–2015

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ABSTRACT

Vaccine hesitancy has been increasingly reported in Brazil. We describe secular trends and socioeconomic disparities from 1982 to 2015, using data from four population-based birth cohorts carried out in the city of Pelotas. Full immunization coverage (FIC) was defined as having received four basic vaccines (one dose of BCG and measles, and three doses of polio and DTP) scheduled for the first year of life. Information on income was collected through standardized questionnaires, and the slope index of inequality (SII) was calculated to express the difference in percent points between the rich and poor extremes of the income distribution. Full immunization coverage was 80.9% (95% CI 79.8%; 82.0%) in 1982, 97.2% (96.1%; 98.0%) in 1993, 87.8% (86.7%; 88.8%) in 2004 and 77.2% (75.8%; 78.4%) in 2015. In 1982 there was a strong social gradient with higher coverage among children from wealthy families (SII = 25.0, P < 0.001); by 2015, the pattern was inverted with higher coverage among poor children (SII = −6.0; P = 0.01). Vertical immunization programs in the 1980s and creation of the National Health Services in 1980 eliminated the social gradient that had been present up to the 1980s, to reach near universal coverage. The recent decline in coverage is likely associated with the growing complexity of the vaccination schedule and underfunding of the health sector. In addition, the faster decline observed among children from wealthy families is probably due to vaccine hesitancy.

1. Introduction

Immunization is one of public health's most cost-effective interventions, having made an enormous contribution to global health [1]. Yet, approximately 6.3 million children still die each year and about a half of these deaths are caused by infections, including pneumonia and diarrhea, which could be prevented by vaccination [2].

In Brazil, the National Program of Immunizations has been held as a major success story with near universal vaccine coverage throughout the country [3]and having managed to eliminate four diseases: smallpox in 1971, poliomyelitis in 1989, measles in 2016 and maternal and neonatal tetanus in 2017 [4]. The program currently offers 27 types of vaccines, which are available at no cost to the population through the Unified Health System (SUS, Sistema Único de Saúde) [5]. Although federal legislation states that childhood vaccines are mandatory [6], this recommendation is not enforced, and there is no report of penalties being applied to families who refuse immunizations.

Up to 2014, coverage with specific vaccines (BCG, polio, DPT and meningitis C) was estimated as95% or higher for Brazil as a whole [5]. However, there is evidence that coverage with key vaccines fell by 10 to 20 percentage points in the recent past, and measles cases have been reported in Northeast Brazil since 2014, and more recently – with the influx of Venezuelan migrants – throughout the Amazon region [7]. The Venezuelan epidemic also spread to neighboring countries, and the region of the Americas lost its measles elimination status, just two years after it was secured in 2016 [8].

This decline in vaccine coverage was part of a global trend. DTP3 and first-dose measles vaccine coverage have plateaued globally at 85%, with declining levels in many countries [8]. Vaccine hesitancy, defined as a "delay in acceptance or refusal of

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vaccination despite availably of vaccination services" is a major driver of falling coverage in many countries, being influenced by complacency, convenience and lack of confidence in vaccines [9]. In many high-income countries, hesitancy is more frequent among parents who are more educated and wealthier than the population as a whole [10].

In a survey of 67 countries published in 2016, Brazil was ranked among the countries with high vaccine confidence indicators [11]. Yet, in a study carried out in 2012 in all state capitals in the country, full immunization by 18 months of age had reached 77% of children residing in wealthier census-tract quintile, compared to 81–86% in the other four quintiles [12].

In the city of Pelotas in Southern Brazil, four population-based cohort studies were carried out in 1982, 1993, 2004 and 2015. These children were followed up prospectively, making it possible to monitor changes in vaccine coverage by different socioeconomic strata over a 33-year period. We aimed to describe trends and socioeconomic disparities in full immunization coverage (FIC) from 1982 to 2015.

2. Methods

Each of the four birth cohorts recruited all hospital-delivered infants born during the calendar years of 1982, 1993, 2004 and 2015. Virtually all births in the city took place in one of its four hospitals, and refusal rates at recruitment were below 2% in all cohorts. The sample sizes were 5914; 5249; 4231 and 4275 live newborns whose families lived in the urban area of Pelotas, respectively. Participants of the four cohorts have been evaluated at several ages during childhood, when their mothers or caregivers answered pre-tested standardized questionnaires applied by trained interviewers. Further details on the methodology of the four cohorts have been published previously [13].

Vaccine information was primarily collected from immunization cards which are kept at the family's homes and include all doses received by the child, regardless of which health facility provided the vaccine. Information on whether a vaccination card was shown to the interviewer was not collected in 1982. In 1993, 2004 and 2015, the proportions of children for whom cards were inspected were 71%, 91% and 89%, respectively. If the cards were available, the interviewer copied the vaccination dates (in 2015, the cards were photographed) and mothers were asked about the number of additional doses that had not been recorded, e.g. during a campaign. Recall was also relied upon when the card was not available, mothers were asked to report the number of doses of each vaccine.

The present analyses are restricted to doses of vaccines scheduled for the first year of life (Table 1). However, to improve comparability among the cohorts, we used the information on immunizations collected at the two-year visit for the full 1982, 2004 and 2015 cohorts; children from the 1993 cohort were not visited at two years, so that the information refers to the subsample of approximately one third of the cohort participants, who were seen at 48 months [14–17]. The option to study a subsample of children from the 1993 cohort was due to budgetary constraints.

Information was collected separately for each vaccine included in the National Childhood Immunization Schedule of the Brazilian Ministry of Health. Achild was classified as being covered with a particular vaccine if it had received the recommended number of doses for the first year of life, e.g. three doses for the diphtheria–tetanus–pertussis (DTP) vaccine. Table 1 shows how the recommended schedules evolved over time with the incorporation of new vaccines. Basic full immunization coverage (FIC) was defined as a child who has received the recommended routine vaccinations, including BCG vaccine at birth (information not available in 1982), three doses of DPT or other polyvalent vaccine including DPT, three doses of polio (either OPV or IPV – inactivated polio vaccine), and one dose of MCV (measles containing vaccines, including MMR - mumps-measles-rubella). Also, we report on expanded FIC for the 2004 and 2015 cohorts, defined as having received all recommended vaccines at the time of these cohorts.

Vaccine coverage indicators were stratified according to socioeconomic characteristics collected during the perinatal interview for each cohort. Maternal and paternal schooling were collected as continuous variables and recoded as 0–4, 5–8, 9–11 and $\geq$12 complete years of formal education. Family income during the month preceding the child's birth, reported by a parent, was collected as a continuous variable by summing the monthly wages of all household members and divided into quintiles. Income inequalities in the study site are wide, and reported income represents an excellent predictor of several child health and nutrition outcomes [18,19].

Study protocols were approved by the Medical Research Ethics Committee of the Federal University of Pelotas (School of Medicine for 1982, 1993 and 2004 cohorts and School of Physical Education for 2015 cohort). Parents provided written informed consent in 2004 and 2015, and oral consent in 1982 and 1993, as ethical guidelines at those times did not require written consent for observational studies without collection of biological samples.

Chi-squared tests for heterogeneity were used to test associations between FIC and explanatory variables (maternal and paternal schooling and family income) in each cohort. In addition, chi-squared tests for linear trends in proportions were used to assess changes in FIC over time, by subgroups of the population defined by the explanatory variables. Slope index of inequality and relative concentration index were used as measures of income-related inequality in health [20]. Analyses were performed using the software Stata version 14.1 (StataCorp, College Station, TX, USA).

3. Results

Follow-up rates for the birth cohorts at the two-year visits were 87.8% in 1982, 93.4% in 2004 and 95.2% in 2015. In the 1993 cohort, 87.2% of a systematic subsample were located at four years. The numbers of children available for analyses were 4934, 1273, 3860 and 4014, in the 1982, 1993, 2004 and 2015 cohorts, respectively. In 1982, the visit took place during the first half of 1984, so that the median age of the children was 19.4 months. Median ages were 54.3, 23.9 and 24.0 for the visits to the 1993, 2004, and 2015 cohorts, respectively. Children with missing information on vaccines were treated as not vaccinated (higher percentages of missing values: 0.2%, 0.5%, 9%, 8%, 1982, 1993, 2004 and 2015, respectively).

Table 2 shows how immunization with the four basic vaccines evolved over time. BCG coverage was virtually universal as this vaccine is administered in hospital soon after delivery, except for the 1982 cohort when BCG used to be administered at school entry. Coverage with the other three vaccines (polio, DPT and MCV) increased markedly from 1982 to 1993, when coverage was practically universal. There were slight declines in coverage from 1993 to 2004, and further declines as of 2015. These trends are reflected in the basic FIC indicator, for which 2015 levels were about the same as in 1982, with a peak in 1993.

The expanded FIC indicator for the 2004 cohort (87.5% CI95% 86.4; 88.5) was very similar to the basic FIC level, as the only new vaccine introduced up to that point was hepatitis B. With the introduction of four new vaccines after 2004, the expanded FIC in 2015 was reduced to 66.1% (CI95% 64.6; 67.5), particularly due to low coverage with rotavirus and hepatitis A vaccines (Table 3).

Table 1
Vaccination schedules during the first year of life in Brazil. 1982–2015.

Vaccines	Cohort			
	1982	1993	2004	2015
BCG	–	1 dose (birth)	1 dose (birth)	1 dose (birth)
Poliovirus	3 doses of OPV	3 doses of OPV (2, 4 and 6 months)	3 doses of OPV (2, 4 and 6 months)	2 doses of IPV (2 and 4 months) and 1 dose of OPV 6 months)
DTP or any polyvalent containing DTP	3 doses of DTP	3 doses of DTP (2, 4 and 6 months)	3 doses of tetravalent (2, 4 and 6 months)	3 doses of pentavalent (2, 4 and 6 months)
MCV	1 dose of measles (9 months)	1 dose of measles (9 months)	1 dose of MMR (12 months)	1 dose of MMR (12 months)
Hepatitis B	–	–	3 doses (birth. 1 and 6 months)	1 dose (birth)
10-valent pneumococcal conjugate	–	–	–	3 doses (2. 4 and 6 months)
C meningococcal	–	–	–	2 doses (3 and 5 months)
Rotavirus	–	–	–	2 doses (2 and 4 months)
Hepatitis A	–	–	–	1 dose (12 months)

BCG: bacilleCalmette-Guérin.
OPV: oral poliovaccine.
IPV: inactivatedpoliovaccine..
DTP: diphtheria–tetanus–pertussis
Tetravalent: DTP plus Haemophilusinfluenzaetype b.
Pentavalent: tetravalent plus hepatitis B.
MCV: measles containing vaccine (measles alone or in combination with other antigens).
MMR: measles-mumps-rubella.

Table 2
Coverage with vaccines scheduled for the first year of life in the four birth cohorts.

Immunization coverage	Cohort				
	1982 % (95% CI)	1993 % (95% CI)	2004 % (95% CI)	2015 % (95% CI)	p-value*
BCG (1 dose)	–	99.4	92.7	96.9	0.54
	–	(98.7; 99.7)	(91.8; 93.4)	(96.3; 97.4)	
POLIO (3 doses)	88.6	97.4	91.1	84.1	<0.001
	(87.6; 89.4)	(96.4; 98.2)	(90.1; 91.9)	(83.0; 85.2)	
DTP (3 doses)	83.4	99.1	89.5	92.9	<0.001
	(82.3; 84.4)	(98.3; 99.5)	(88.5; 90.5)	(92.1; 93.7)	
MVC (1 dose)	87.9	99.4	89.4	85.9	<0.001
	(87.0; 88.8)	(98.7; 99.7)	(88.4; 90.3)	(84.8; 86.9)	
FIC	80.9	97.2	87.8	77.2	<0.001
	(79.8; 82.0)	(96.1; 98.0)	(86.7; 88.8)	(75.8; 78.4)	

BCG: bacilleCalmette-Guérin; DTP: diphtheria-tetanus-pertussis; TETRA: DTP + Hib; PENTA: tetra + Hepatitis B; OPV: oral poliovaccine; IPV: inativatedpoliovaccine; MVC: measlescontainingvaccine; FIC: full immunizationcoverage.
Missing are treated as 0 (not vaccinated). BCG was not available in 1982.
Polio vaccine in 1982, 1993 and 2004 was OPV. In 2015 there was a combination of OPV and IPV.
DTP vaccine in 1982 and 1993. Tetravalent (DTP + Hib) in 2004. Pentavalent (tetravalent + Hepatitis B) in 2015.
MCV: measles alone in 1982 and 1993. Meales-mumps-rubella (MMR) in 2004 and 2015.

Table 3
Coverage with vaccines added to the National Immunization Program after 1993. Results from the 2004 and 2015 Pelotas Birth Cohorts.

	2004		2015	
	%	95% CI	%	95% CI
Hepatitis B	90.4	89.4; 91.3	90.6	89.7; 91.5
10-valent pneumococcal	–	–	84.5	83.3; 85.5
C-meningococcal	–	–	88.0	87.0; 89.0
Rotavirus	–	–	83.0	81.8; 84.1
Hepatitis A	–	–	81.0	79.8; 82.2
Expanded FIC±	87.5	86.4; 88.5	66.1	64.6; 67.5

CI – Confidence interval.
±Expanded FIC defined as have reached the complete scheduled vaccine doses of national immunization program by 12 months of age according with year of birth.
Hepatitis B vaccine was introduced in the National Immunization Program in 1998. 10-valent pneumococcal, C-meningococcal, rotavirus and hepatitis A were introduced between 2006 and 2014, respectively.
Expanded FIC at 2004: 1 dose of BCG, three doses of polio, 3 doses of tetra, 1 dose of MMR and 3 doses of hepatitis B.
Expanded FIC at 2015: 1 dose of BCG, 3 doses of polio, 3 doses of tetra, 1 dose of MMR, 1 dose of hepatitis B, 1 dose of hepatitis A, 2 doses of rotavirus, 3 doses of C-meningococcal and 2 doses of 10-valent pneumococcal.

Table 4
Full immunization coverage with vaccines scheduled for the first year of life according to family income and parental education in the four cohorts.

	Cohort								
	1982		1993		2004		2015		
	%	95% IC	%	95% IC	%	95% IC	%	95% IC	p**
Family income (quintiles)	<0.001*		0.260*		0.007*		<0.001*		
Q1 (poorest)	68.5	65.4; 71.5	98.8	96.3; 99.6	84.6	81.9; 87.0	75.9	72.8; 78.8	<0.001
Q2	76.7	74.0; 79.2	97.0	94.4; 98.4	87.2	84.6; 98.4	79.4	76.5; 82.0	0.075
Q3	82.1	79.6; 84.3	97.0	93.9; 98.6	90.7	88.4; 92.6	80.9	78.1; 83.5	0.887
Q4	86.0	83.7; 88.0	95.5	92.0; 97.5	88.6	86.2; 90.7	80.4	77.5; 83.0	0.003
Q5 (richest)	89.8	87.8; 91.6	97.8	94.7; 99.1	87.7	85.2; 89.9	69.0	65.7; 72.1	<0.001
Maternal education (years)	<0.001*		0.345*		0.004*		<0.001*		
0 to 4	73.6	71.3; 75.7	96.6	94.2; 98.0	84.7	81.5; 87.4	73.0	68.2; 77.4	0.002
5 to 8	79.8	78.0; 81.4	96.9	95.1; 98.0	86.9	85.1; 88.5	78.0	75.4; 80.4	0.558
9 to 11	91.2	88.6; 93.3	98.6	95.8; 99.6	89.5	87.7; 91.1	81.0	78.8; 82.9	<0.001
12 or more	92.6	90.4; 94.3	98.9	92.5; 99.8	90.8	87.5; 93.4	73.3	70.8; 75.8	<0.001
Paternal education (years)	<0.001*		0.038*		0.227*		<0.001*		
0 to 4	73.5	71.0; 75.8	97.1	94.5; 98.5	85.8	82.5; 88.5	78.6	74.7; 82.0	<0.001
5 to 8	81.6	79.9; 83.2	97.6	96.0; 98.6	87.9	85.8; 89.7	77.3	74.7; 79.7	0.072
9 to 11	86.9	83.9; 89.5	94.4	90.4; 96.8	89.0	87.0; 90.8	82.4	80.1; 84.4	0.001
12 or more	91.4	89.1; 93.2	99.0	96.6; 99.9	89.6	85.8; 92.5	70.7	67.7; 73.5	<0.001

* p-value are displayed from intra-cohort chi-squared test.
** p-value are displayed from inter-cohorts chi squared trend test.
CI – Confidence interval.
#Black and brown were combined.
Full immunization coverage defined as having one dose of BCG, one dose of measles containing vaccine (MCV), three doses of either oral polio vaccine (OPV) or inactivated polio vaccine (IPV), and three doses of any DPT vaccine.

Table 5
Family income and parental education categories according to children evaluated at 24-month* follow-ups in the four cohorts.

	Cohort							
	1982		1993		2004		2015	
	N	%	N	%	N	%	N	%
Family income (quintiles)								
Q1 (poorest)	906	18.4	249	19.9	773	20.0	798	19.9
Q2	987	20.0	302	24.1	771	19.9	806	20.1
Q3	1022	20.7	236	18.8	764	19.8	802	19.9
Q4	1034	20.9	244	19.5	801	20.7	812	20.2
Q5 (richest)	985	20.0	223	17.8	759	19.6	794	19.8
Maternal education (years)								
0 to 4	1563	31.7	356	28.1	588	15.4	356	8.9
5 to 8	2095	42.5	604	47.6	1578	41.2	1036	25.8
9 to 11	559	11.3	219	17.3	1281	33.5	1386	34.5
12 or more	712	14.4	90	7.1	382	9.9	1235	30.8
Paternal education (years)								
0 to 4	1277	27.7	313	26.2	528	17.5	481	12.8
5 to 8	2048	44.4	588	49.2	1076	35.7	1107	29.5
9 to 11	574	12.4	214	17.9	1086	36.0	1197	31.9
12 or more	717	15.5	79	6.6	327	10.8	962	25.7

*Except for the 1993 which has been followed up at 48-month.

Table 4 shows how the FIC indicator evolved over time according to family income and parental education, and Table 5 shows the numbers of children in each category. Coverage results by income quintile are striking (Fig. 1). Whereas in 1982 coverage in the wealthiest quintile was over 20 percent points higher than in the poorest quintile, by 2015 the lowest coverage levels were found in the richest quintile, with an inverse U-shaped pattern with the highest coverage in children born to middle-class families. Results for 1993 show that all income groups had coverage around 95%, and thus income-related inequalities were eliminated. In 2004, the inverse-U-shaped pattern starts to appear, which as mentioned became more evident by 2015.

Table 6 shows the values of the slope and concentration indices in the four cohorts, which represent numerical, summary measures of the equity patterns shown in Fig. 1. In 1982, there was substantial inequality with significant positive values of both summary indices, indicating that coverage increased with family income. By 1993, both indices were close to zero and non-significant, thus indicating lack of inequality, and in 2004 the indices were slightly positive with borderline significance, consistent with marginally higher coverage among the rich. In contrast, by 2015 the opposite pattern was observed, with significantly lower coverage among children from wealthy families.

Results by maternal and paternal education (Table4) are mostly consistent with the patterns observed for family income: strong inequality in 1982 with increasing coverage with higher education, lack of inequality in 1993, and slight inverse U-shaped patterns in 2015. Differently from the income results, in 2004 FIC increased with maternal education, albeit slightly, but the association with paternal education was not significant.

4. Discussion

Our study shows that coverage (individual vaccines and FIC) increased markedly from 1982 to 1993. Then, there were slight declines in coverage from 1993 to 2004, and further declines as of 2015. In 1982 there was a strong social gradient with higher coverage among children from the highest socioeconomic level; by

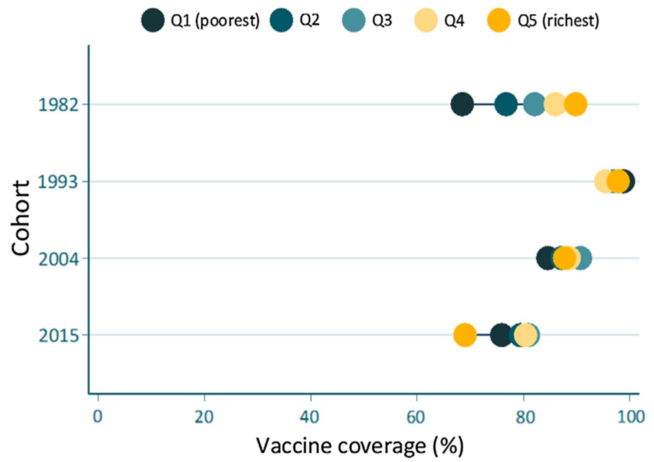

Fig. 1. Full immunization coverage with the basic vaccines recommended for the first year of life, by family income quintiles (in 1982, BCG was not considered as this vaccine was administered at school entrance).

2015, the pattern was inverted with the lowest coverage among the richest. Routine statistics on vaccine coverage, based on the number of doses reported by health facilities divided by the estimated child population, are affected by the quality of health services and information systems in Brazil [21]. Even so, our findings from the cohorts are consistent with the routine coverage data for the state of Rio Grande do Sul – where Pelotas is located– that show DPT coverage levels of around 80% in the 1980s, rising to between 90% and 100% from the 1990s to about 2014, and falling thereafter [22]. The results are also consistent with coverage levels reported by the National Immunization System for the whole country for the period 1994–2018, showing an increase to near universal coverage levels with DPT, polio and measles vaccines up to 2015, followed by a clear reduction from 2015 onwards [7].

The increase in vaccination coverage levels during the 1980s may be attributed to the expansion of the National Immunization Program, with periodic vaccination campaigns, and to the creation of the Unified Health System in 1990 which made health services freely accessible to the whole population [3,23].

Our findings on socioeconomic inequalities must be interpreted in terms of spatial and temporal trends. Earlier studies throughout the country [24], and recent analyses from the poorest Brazilian states show lower coverage levels among children from poor families. This was observed in a 2010 study in Rio Branco in the Amazon region [25], and two studies from 2006 and 2010 in São Luis, in the Northeast region [26,27]. In contrast, a 2002 study from the more developed city of Curitiba, in the South of the country, did not reveal any socioeconomic gradients in coverage [28].

The most informative study on socioeconomic inequalities is a large population-based survey of children born in 2007–2008 in 27 state capitals and in Brasilia. It showed that socioeconomic inequalities in coverage were not observed in most cities, but in eight cities there was evidence of lower coverage among the better off families, thus suggesting that vaccine hesitancy was starting to appear in the country [12]. Brazilian studies [29]suggest that several factors may have contributed to the decline in vaccine coverage levels, as well as to appearance of vaccine hesitancy in the country. The eradication of smallpox, polio, measles and newborn tetanus, and the near eradication of diphtheria led to a perception that these vaccines were no longer necessary [30], and health workers seem to have been unable to counter this perception [31]. A qualitative study on the opinions of high-income parents in Sao Paulo state showed a clear division among three groups: those who strongly believed in the protection afforded by all vaccines, those who partly complied with recommendations and were selective regarding which vaccines to administer to their children, and those who refused all vaccines due to concerns with their safety. The last two groups were critical about the role of the government in – in the words of several parents – "imposing" vaccines upon the population. Seven types of concerns were raised by these parents: that the diseases were eradicated or under control; existence of side effects; concerns about the chemical components included in the vaccine; impression that immunity provided by the disease is superior to that provided by a vaccine; criticisms about the multiple contacts needed for immunization, and with the fact that several vaccines were given at the same time; notion that their children are unlikely to be affected by infectious diseases due to poor nutrition and sanitation; and concerns with big pharma and commercial interests behind vaccines [32]. Parental justifications for hesitancy among Brazilian parents are similar to those described in the international literature [33–35]. Paradoxically, unfounded negative statements about vaccine safety tend to receive much more publicity throughout society than the well-established benefits of immunization [32,36].

Nevertheless, parents bear only part of the responsibility as health services also played a role. Vaccination schedules became much more complex over time. Whereas in 1982 five contacts were required during the first year of life to deliver eight doses of four vaccines, by 2015 seven contacts were required to deliver 17 doses of nine different vaccines up to the age of 12 months (Table 1). Hypothetically, a more complex scheme may lead to lower compliance due to the demands on time and transportation costs for parents, as is suggested by lower uptake of recently introduced vaccines as shown in the present study and elsewhere in the country [27,37]. In recent years, the Unified Health System has suffered from gross under funding [38], which has affected the quality of basic health services, a factor which must have contributed to the decline in coverage.

Our analyses have limitations. Firstly, we have likely overestimated vaccine coverage in the first year of life because the information was collected at the age of two years in 1982, 2004 and 2015, and at the age of four years in 1993; this may also result in higher vaccination rates in the 1993 cohort, as children were older. A Brazilian study confirmed that overestimation can occur when information does not take into account the exact age at

Table 6
Slope index of inequality and concentration index for FIC according to family income quintiles in the four cohorts.

Cohort	Slope index (absolute inequality)			Concentration index (relative inequality)		
	β	SE	p-value	B	SE	p-value
1982	25.0	2.0	<0.001	5.0	0.0	<0.001
1993	−2.0	1.0	0.16	−0.3	0.2	0.2
2004	4.0	2.0	0.05	0.8	0.4	0.03
2015	−6.0	2.0	0.01	−1.0	1.0	0.02

β: regression coefficient; SE: standard error; p level reflects the probability that the index is different from zero (no inequality).
β and SE were multiplied by 100.

which doses were delivered [39]. Nevertheless, this is unlikely to have affected the study of inequalities within each cohort. Secondly, about 30% of the information in 1993 was based on maternal recall, and about 10% in 2004 and 2015; this information is not available for the 1982 cohort. Recall may have been more precise up to 2004, when the number of vaccines was small, than for 2015 when the schedule was complex. The literature suggests that recall may either underestimate or overestimate vaccine coverage compared to cards, but that the differences tend to be small [40–42]. We did not attempt to validate the information on maternal recall in any of the cohorts. Lastly, missing values for immunizations were higher in the most recent cohorts, which may be related to the larger number of vaccines administered to children. Nevertheless, missingness was not associated with income or parental education, which reduces the likelihood of bias.

The strengths of the present study include reliance on prospective, population-based birth cohorts carried out by the same group of investigators using similar instruments. Information on the vaccination status of individual children provides a more accurate picture than routine coverage estimates based on number of doses delivered in health facilities divided by a target population. Attrition was low in the four cohorts, thus minimizing bias due to losses to follow-up. Unlike routine data on coverage, we were able to ascertain family income and parental education and produce detailed analyses of inequalities over time. Lastly, the long period of time covered by the four cohorts provides a unique opportunity for examining time trends.

5. Conclusions

Summing up, our analyses of levels and inequalities in vaccine coverage over four decades in a Brazilian city show that the initial pattern of pro-rich inequalities in the 1980s evolved to near-universal coverage in the 1990s and 2000s, when socioeconomic inequalities were eliminated. By 2015, however, there was an important reversal, with declining trends in overall coverage and a shift to lower coverage among children from better-off families than for the rest of the population, and it is reasonable to wonder whether vaccine hesitancy may trickle down to other groups in society. Initially postulated in Brazil, the inverse equity hypothesis [43] proposes that upper socioeconomic families tend to be early adopters of new health interventions, and that eventually these will be disseminated throughout the whole society and reduce inequalities in the long run. A study from the United Kingdom applied the hypothesis to explain why richer, more educated families were early adopters of what they perceived as a positive behavior – namely, refusing vaccination – and that such a behavior will eventually become adopted by other groups in society [44].

The antivax movement in Brazil, which has initially been adopted by well-off families in large cities – such as São Paulo – in the most developed part of the country, may possibly expand throughout society. Growing reliance on social media throughout the country with the dissemination of fake news [45], allied to the present crisis in funding health services, presents a real challenge that has already contributed to thousands of measles cases and nine deaths in São Paulo as of mid-October 2019 [46]. Hesitancy must be tackled by the dissemination of scientific information about immunization and by in adequate funding services throughout the country [31,47].

6. Contributorship

MFS, RB and CV designed the study and wrote the manuscript. RB performed the analysis. MFS, RB, CV and RBB contributed to the interpretation of the results. MFS, ADB, AJB, AM, ISS, AMM, HG, FCB and CV participated in the design and conduct of the original cohort studies as well as in interpreting results and critical reviewing of the manuscript. All authors approved the final version.

7. Disclosure of interest

None declared.

8. Availability of data and materials

Due to confidentiality restrictions related to the ethics approval for this study, no identifying information about participants may be released. Dataset without identification used during the current study are available from the corresponding author on reasonable request.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2019.10.070.

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