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An ecological analysis of socio-economic determinants associated with paediatric vaccination coverage in the Campania Region: A population-based study, years 2003–2017

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ABSTRACT

Introduction: Vaccines are the most cost-effective and straightforward intervention against severe infectious diseases. However, in Europe and in Italy, paediatric vaccination coverage for certain vaccines remains suboptimal, with considerable regional differences in Italy. Vaccine coverage varies significantly due to socio-economic and organisational factors. Aim of this study was to assess the influence of the Deprivation Index, the density of General Practitioners and General Paediatricians per inhabitants on the coverage of both mandatory and non-mandatory paediatric vaccinations across local health authorities and health districts in the Campania Region for birth cohorts from 2001 to 2015.

Materials and methods: Population-based, ecological time series analysis focusing on the Campania Region, most populous region in the south of Italy. Vaccination coverage data were extracted from the regional immunization database, whilst information on the Deprivation Index and number of primary care doctors and primary care paediatricians per local health district were extracted from public health records. Univariate descriptive statistics were employed to describe study characteristics, as appropriate, whilst and mixed-effect linear regression models were employed to assess the associations between variables of interest and vaccination coverage.

Results: Overall vaccination coverage has generally increased, except for the MMR vaccine, which showed coverage fluctuations. An increase in the Deprivation Index, indicative of less favourable socio-economic conditions, was associated with decreased vaccination coverage in the 24-month age group for some mandatory vaccines (DTaP: Coef −0.97, 95% CI −1.77 | −0.17; Poliomyelitis: Coef −0.98, 95% CI −1.78 | −0.17; Hepatitis B: Coef −0.90, 95% CI −1.71 | −0.10). Moreover, areas with a greater density of General Paediatricians per inhabitants saw increased coverage for Haemophilus influenzae type b in the 6-year age group (Coef 9.78, 95% CI 1.00 | 18.56).

Conclusions: It is necessary to target public health policies to address vaccination inequalities. These efforts should include expanding vaccination campaigns, enhancing catch-up programs, and increase resource allocation in primary care settings to facilitate the role of General Practitioners and Paediatricians in fostering awareness and adherence.

Introduction

Vaccines are the most cost-effective and straightforward intervention for protection against severe infectious diseases [1]. However, paediatric vaccination coverage in Europe and, particularly, in Italy, for some vaccines, remains suboptimal [2–4]. Nevertheless, current trends show an increase in vaccine coverage percentages, although in the Eurozone the optimal coverage of 95 % has not been achieved for some of the mandatory vaccinations, and there are still cases of vaccine-preventable diseases [3]. Furthermore, the WHO's target of a 95 % coverage rate for

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two doses of the measles vaccine, crucial to reach herd immunity and averting outbreaks, remains unachieved in various settings. This shortfall is often linked with the public perception of measles either a negligible or infrequent disease. Other factors to consider include the apprehensions about potential side effects of this vaccination, although very rare. Therefore, continuous surveillance of adverse events following immunization is paramount to affirm vaccine safety and reinforce public trust in immunization efforts [5]. In Italy, vaccination against Diphtheria, and Tetanus (typically administered as DTaP), as well as Poliomyelitis, and Hepatitis B have been mandatory before 1991 [6,7], while the Haemophilus influenzae type b, the Pertussis, the MMR vaccine and the Varicella vaccine became mandatory in 2017 [8,9]. Vaccination coverage increased over the years, although it has not achieved optimal coverage for booster doses of DTaP [10,11] and for the primary cycle of Measles, Rubella, and Mumps (MMR) vaccinations [8,9,12]. Moreover, notable inequalities in vaccine coverage across different regions continue to persist. The 2018 birth cohort shows that the coverage for the Tetanus vaccine at 24 months was markedly lower in PA Bolzano, recorded at 81 %, in contrast to the national average of 94 %. Similarly, the Measles vaccination coverage fell below the 80 % threshold in two Italian regions, diverging significantly from the national average of 94 %. These examples underscore the persistent issue of regional inequalities in vaccination coverage within Italy [2]. Differences in coverage levels across Europe and Italy can be explained by various factors, from perceived non-severity of the diseases, doubts about vaccine safety, problems regarding the flexibility of organisation and vaccination schedules, lack of information and knowledge, socioeconomic and cultural differences, difficulties in accessing health facilities, and lack of trust in authorities [13,14].

Additionally, it is now widely acknowledged that social inequalities in health and well-being are interrelated, becoming a priority for global public health policy [15]. Furthermore, ecological studies examining correlations in geographical areas indicate that vaccination uptake is lowest in the most deprived regions [16]. Nevertheless, following the MMR vaccine crisis, early 2000 s data showed the steepest decline in MMR uptake in the most affluent districts in the UK [17]. Furthermore, routinely collected healthcare data provide limited information on household data, including socio-economic conditions [18], rendering the analysis of vaccination coverage-related social inequalities exceedingly challenging. Nonetheless, differences in vaccination coverage [19] across the Local Health Authorities in the Italian regions may, in part, result from differences in how mandatory vaccination policies are implemented and translated into practice, including differences in the organisation of the Departments of Prevention and Health Districts at Local Health Authority level. These entities are granted autonomy in organising vaccination campaigns, contributing to differences in the implementation process. Furthermore, differences in vaccination coverage could also be partly attributed to community characteristics and socio-economic factors as well as quality of health data registries, socio-economic and educational inequalities [20]. Several studies have explored the relationship between adult influenza coverage and the Deprivation Index [21–26] in Italy, indicating a potential link with vaccination outcomes in the adult population. However, there is little available evidence regarding the impact of deprivation on paediatric vaccination coverage in European Health Systems [27].

Focusing on the Campania Region, located in South-Western Italy and one of the most populous and densely inhabited areas in Italy, with seven Local Health Authorities, vaccination services are provided by immunisation clinics [28], widely distributed across the region and various Health Districts. General Paediatricians can be available to administer vaccinations and assist parents in scheduling and adhering to the vaccination schedule. General Practitioners, as well as General Paediatricians, can also be consulted by parents for paediatric care and vaccination advice. Their collaboration, along with educational institutions and voluntary associations, can augment the efforts of the Local Health Authorities to improve vaccination coverage [29–31]. However, their role in paediatric vaccination coverage, as well as the impact of social deprivation in explaining local differences in paediatric vaccination coverage in a similar setting has not been explored.

The aim of the current study is to assess differences in paediatric vaccination coverage by Local Health Authorities and Districts of the Campania Region of Italy and assess the association between deprivation, density of General Practitioners and General Paediatricians per inhabitants, and paediatric vaccination coverage in the region between 2001 and 2015.

Methods

Study design

We employed an ecological, time series analysis to investigate the impact of the Deprivation Index, and the density of General Practitioners and General Paediatricians per inhabitants on paediatric vaccination coverage for both mandatory and non-mandatory vaccines in birth cohorts from 2001 to 2015 in the Campania region of Italy, the most populous region in Southern Italy. Ethical Committee approval was not required for this study as it utilised publicly available data. The research adhered to robust research practices and aligned with the principles of the Declaration of Helsinki.

Study variables

The study variables were obtained from different data sources, including Deprivation Index [32,33], Local Health Authorities database for assessing general healthcare availability, and the regional immunization registry to determine vaccination coverage.

The Deprivation Index measures the socioeconomic status and is calculated as the sum of standardised scores for five indicators, including percentage of the population with education at or below elementary school level, percentage of the active population unemployed or seeking first employment, percentage of occupied rental housing, percentage of single-parent families (comprising a single household), and housing density (occupants per 100 m^2) [32,33]. The Deprivation Index calculated is updated to the year 2011, the most suitable available data for the analysed time frame.

The primary care in Italy is delivered by Local Health Authorities and Health Districts. Health Districts comprise one or more cities, and multiple Health Districts are grouped under Local Health Authorities. Health District was selected as the primary unit for our study, considered as homogenous areas by national regulations in terms of population and geography [34]. The list of Health Districts and their corresponding Local Health Authorities is provided in Supplementary Material.

Considering the homogeneous distribution of vaccination clinicals within the region, we decided to investigate additional factors that might explain differences in the vaccination coverage, such as the density of General Practitioners and General Paediatricians per inhabitants, as a proxy of granularity and accessibility to primary care across LHAs. For some Health Districts, if available, data on the number of General Practitioners and General Paediatricians per 10,000 inhabitants were extracted from online Local Health Authorities database [35]. The density of General Practitioners per 10,000 inhabitants and the density General Paediatricians per 10,000 inhabitants were calculated to assess inequalities in general healthcare availability.

In Italy, DTaP and vaccination against Poliomyelitis, Hepatitis B, and Haemophilus influenzae type b can be co-administered at 3, 5, and 11–12 months of age in a single session. The first dose of the MMR vaccine, however, is administered at 13 months of age [36,37]. In the Campania Region, each Local Health Authority's Prevention Departments is responsible for promoting vaccination and catch-up campaigns. These departments have organisational autonomy, allowing them to tailor their strategies to the characteristics of their respective territories.

The outcome variable was vaccination coverage, considering vaccinations for Tetanus (as a proxy for DTaP – Diphtheria, Tetanus, and Pertussis), Poliomyelitis, Hepatitis B, Haemophilus influenzae type b, and Measles (as a proxy for MMR – Measles, Rubella, and Mumps vaccinations). The birth cohort ranged from 2001 to 2015, this refers to a phase prior to the extension of mandatory vaccination [9]. Age groupings were categorised as: from 0 to 24 months (24 months), from 0 to 36 months (36 months), from 0 to 6 years (6 years), and from 0 to 8 years (8 years). Vaccination coverage data were extracted from the regional immunization registry. The percentage coverage for each vaccination was calculated as the number of vaccinated individuals divided by the number of births [38] for each cohort, age group, and every Health District. If vaccination coverage in some Health Districts exceeded 100 %, likely because of errors or catch-up immunisation campaigns, it was adjusted down to 100 %. Two Health Districts were excluded due to incomplete digitalisation and unreliable data (Health Districts: 70, and 72).

The visual presentation of the data focuses on the vaccination year rather than the birth cohort, aligning with the information provided by the Italian Ministry of Health and, for easier access to the data, Tetanus vaccination is used as a proxy for DTaP and vaccination against Hepatitis B, and Poliomyelitis, considering collinearity and co-administration.

Statistical analyses

Variable characteristics were summarised using univariate descriptive statistics, as appropriate. The association between vaccination coverage and Deprivation Index was evaluated using mixed-effect linear regression models, controlling for cohort, age, and Local Health Authorities; to reduce the effect of territorial differences, Health Districts were included in the model as random intercept. The same analysis was applied to assess the association between vaccination coverage and the density of General Practitioners and General Paediatricians per inhabitants, substituting the ADI. Results were presented as regression coefficients (Coef.) and 95 % confidence intervals (95 % CI). Analyses were performed using Stata 15.0 MP.

Results

Vaccinations coverage

Considering the trend of vaccination coverage in the Campania region (Fig. 1), in the age groups of 24 months, 36 months, and 6 years, Tetanus vaccination coverage was consistently above 90 %, with a minor decrease in 2015. Coverage for Haemophilus influenzae type b increased since 2003, exceeding 85 % by 2008, paralleling the trend observed in Tetanus vaccination coverage. Measles vaccination coverage in the 24-month age group was approximately 10 percentage points lower than for Tetanus, with a fall in 2015, reducing to 5-points lower when considering the 36-months age group, with the lowest fall registered in 2016. In the 6-year group, the difference between Measles and Tetanus vaccine coverage is minimal, but drops in Measles coverage occurred in 2013, 2016, and 2017. The trend in the 8-year age group shows more uniformity across vaccines from 2011. All vaccines experienced a near 5-percentage point decrease in 2012, followed by a recovery and stabilisation above 90 %.

Stratifying analyses by age group and Local Health Authority (Fig. 2), we observed that for Tetanus vaccination coverage remained consistently high. In the 24-month group, it stayed above 80 %, with a peak around 96 %, though there was a decline in Naples and Caserta LHAs

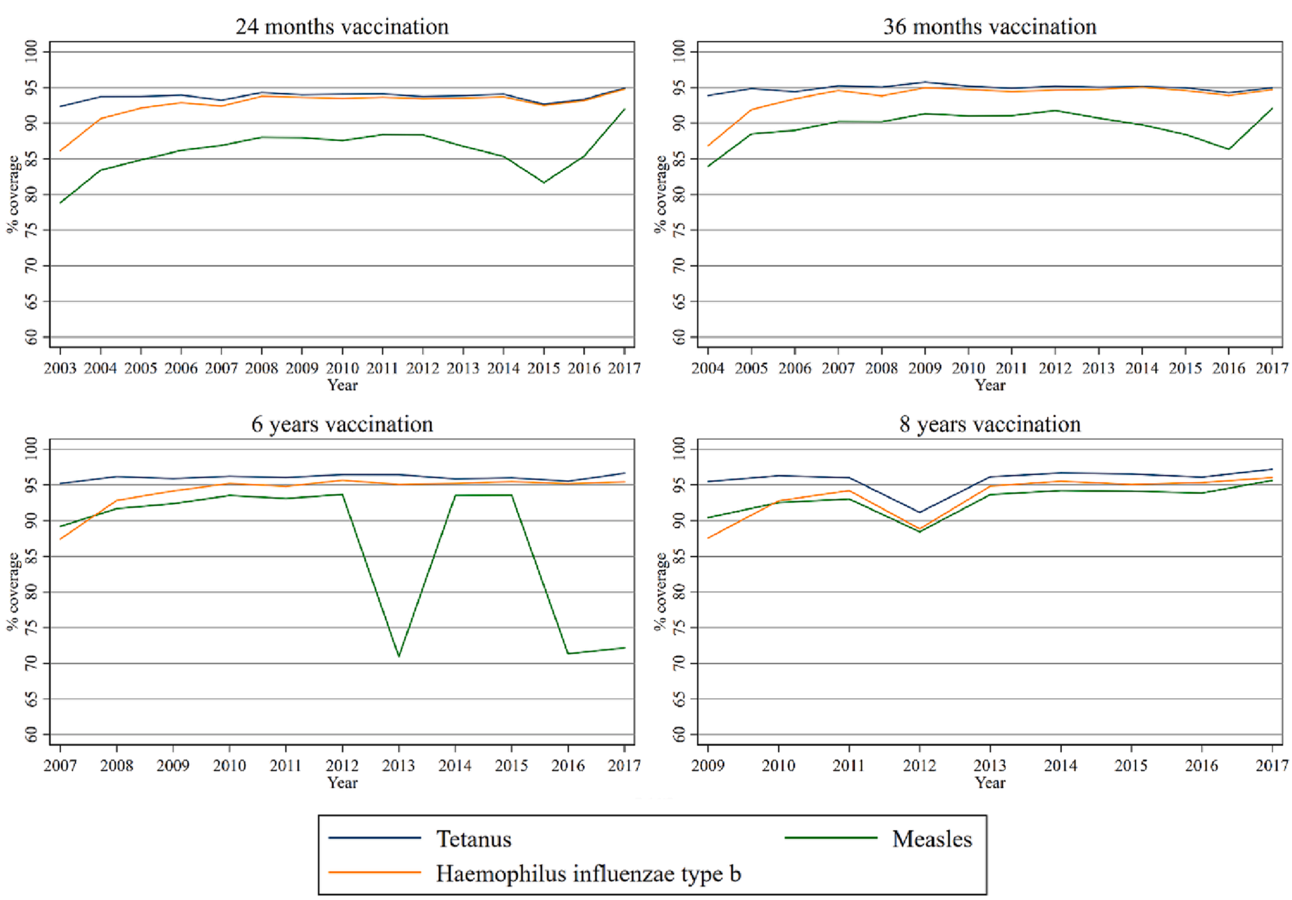

Fig. 1. Trends in Vaccination Coverage in the Campania Region. *Percentages of vaccination coverage (y-axis) achieved over the years (x-axis) for vaccines against Tetanus, Measles, and Haemophilus influenzae type b for age groups 24 months, 36 months, 6 years, and 8 years.*

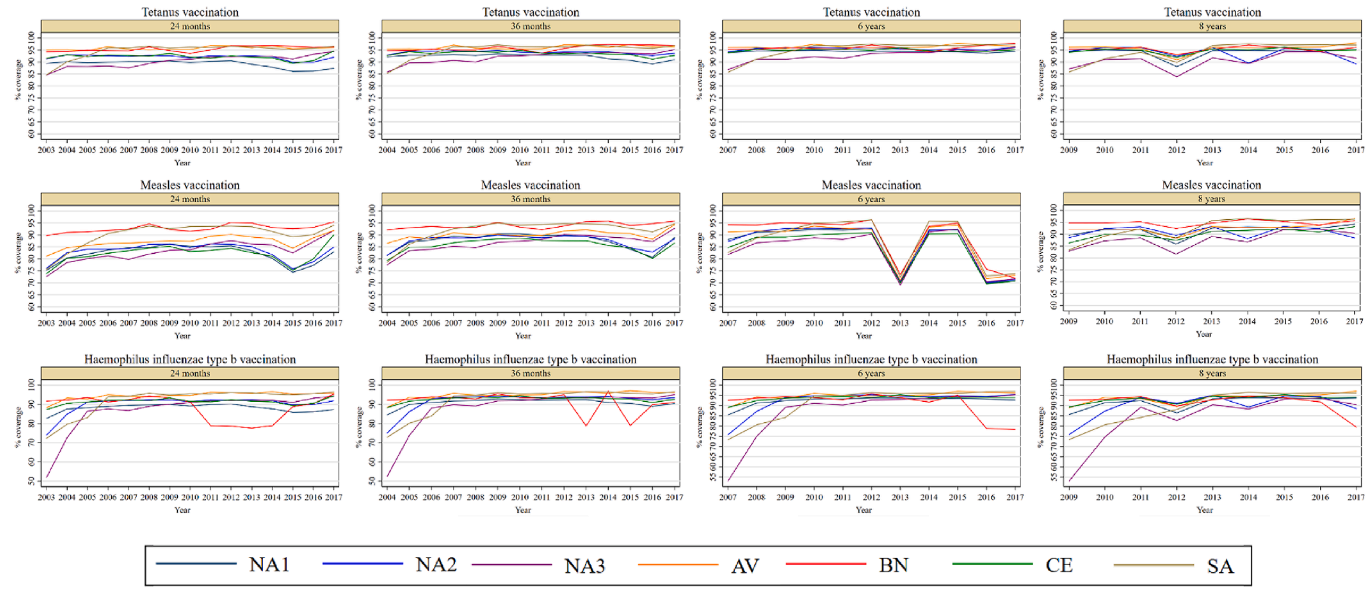

Fig. 2. Vaccination coverage trends among Local Health Authorities in the Campania Region. *Graphic shows the percentage of vaccination coverage (y-axis) across years (x-axis). The vaccinations displayed include Tetanus (top row), Measles (middle row), and Haemophilus influenzae type b (bottom row), categorized by age groups: 24 months (first column), 36 months (second column), 6 years (third column), and 8 years (fourth column). NA1: Naples 1 Centre LHA; NA2: Naples 2 North LHA; NA3: Naples 3 South LHA; AV: Avellino LHA; BN: Benevento LHA; CE: Caserta LHA; SA: Salerno LHA.*

around 2015–2016. The 36-month group showed modest variations in coverage among different LHAs. In the 6-year and 8-year groups, Tetanus vaccination coverage was generally stable, with minor decreases in 2012, 2014 and 2017. Haemophilus influenzae type b vaccination coverage in the 24-month group moved from 50 % to 95 % to 85 %-95 % but experienced a dip around 2015–2016. In the 36-month group, there was a slight decline in 2016, with Benevento LHA showing substantial drops in 2013 and 2015. The coverage in the 6-year age group exceeded 90 %, with the exception of the Local Health Authority (LHA) in Benevento during 2016–2017. The 8-year group increased with occasional decreases, particularly in specific LHAs. Measles vaccination coverage exhibited a heterogeneous trend across LHAs. In the 24-month group, coverage remained above 90 % only in Benevento LHA. In the 36-month group, the highest coverage was observed in Benevento and Avellino LHAs, while the lowest was in Naples 1 Centre, Naples 2 North, and Caserta LHAs. For the 6-year group, coverage generally stayed above 85 %, except in certain specific years. In the 8-year group, there was a notable variation in coverage between LHAs, with the highest in Benevento LHA and the lowest in Naples 3 SouthLHA. Deprivation levels vary across LHAs, with a higher deprivation index for the LHAs of the metropolitan city of Naples as compared with other Campania provinces (Supplementary Material).

Deprivation index, general practitioners and general paediatricians

We found a significant reduction in vaccination coverage for the 24 months age group for the Tetanus vaccine (Coef −0.97, 95 % CI −1.77 | −0.17), Poliomyelitis vaccine (Coef −0.98, 95 % CI −1.78 | −0.17), and Hepatitis B vaccine (Coef −0.90, 95 % CI −1.71 | −0.10) with increasing in the Deprivation Index. Furthermore, a positive association was observed between increasing vaccine coverage for Haemophilus influenzae type b and the density of General Paediatricians per inhabitants (Coef 9.78, 95 % CI 1.00 | 18.56). However, no additional association was found (Fig. 3).

Discussions

In our population-based study between 2003 and 2017 we observed an increase in vaccination coverage for DTaP, Poliomyelitis, and Hepatitis B and Haemophilus influenzae type b across various age groups. DTaP, Poliomyelitis, Hepatitis B and Haemophilus influenzae type b vaccination coverage exhibited a consistent increase, with minor differences between different Local Health Authorities. Discrepancies in vaccination coverage were kept within a 15 percentage difference across the LHAs for the DTaP, Poliomyelitis, and Hepatitis B vaccines, as well as for the Haemophilus influenzae type b vaccine after 2009, with the only exception of the Benevento LHA. In contrast, MMR coverage has been lower and more variable over the years, with notable variations among different LHAs, particularly in the 6-year age group.

We found that an increase in the Deprivation Index, indicating worsening socio-economic conditions, was associated with a decrease in vaccination coverage against DTaP, Poliomyelitis, and Hepatitis B in the 24-months age group. Conversely, a higher density of General Paediatricians per inhabitants was associated with increased coverage for Haemophilus influenzae type b in the 6-years age group.

Differences in vaccination coverage within the Campania region, especially for the MMR vaccine, mirror national trends in Italy [2]. This similarity prompted the introduction of the 2017 National Vaccination Prevention Plan (PNPV), extending mandatory vaccination to MMR + V vaccine (Measles, Rubella, Mumps and Varicella) [9], this decision followed an increase in Measles cases [39]. The declining in MMR vaccine coverage, as along with other vaccines, has been observed not only in Italy but also across Europe and globally. Italy exhibits lower vaccination rates, similar to those observed in the UK and Greece. Remarkably, differences in the vaccination coverage are not explained by differences in the healthcare system model adopted by different European nations. Throughout Europe, the extent of measles vaccination coverage shows variation that is independent of both geographical location and the structure of the healthcare system [12,40]. This trend is partly attributed to the spread of misinformation online, which has eroded public trust in vaccines and contributed to increased vaccine hesitancy [41–44]. The impact of the 2017 PNPV's introduction presents a valuable subject for future analysis, as well as the impact of the COVID-19 pandemic on reduction in vaccination coverage [45–47].

Existing literature shows that disadvantaged groups tend to have lower vaccination coverage across various nations, each with its distinct health system organisation [48–50]. However, in Europe, inequalities in vaccination coverage across nations are more often linked to differences

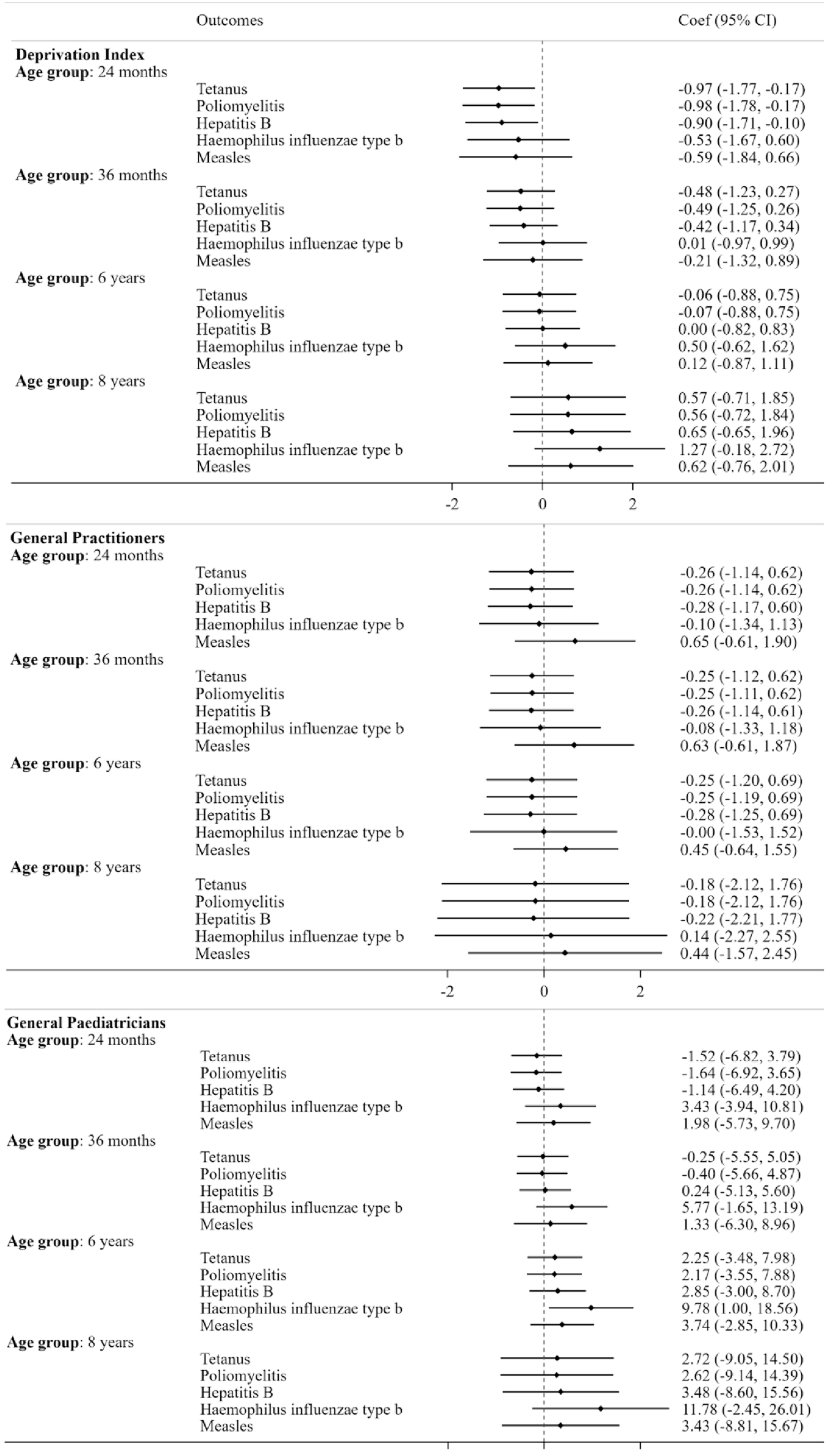

Fig. 3. Association between Deprivation Index, density of General Practitioners and General Paediatricians per inhabitants, and vaccine coverage. *Association between vaccination coverages and Deprivation Index or density of General Practitioners per inhabitants or density of General Paediatricians per inhabitants was evaluated using mixed-effect linear regression models, controlling for cohort, age, and Local Health Authority; to reduce the effect of territorial differences, Health District was included in the model as a random intercept. Those models were performed for each age group.*

in health system organisation than to socioeconomic conditions [40]. In our study, an increase in the Deprivation Index was associated with lower vaccination coverage for the 24-months age group in the longer-established mandatory vaccines (Tetanus, serving as a proxy for DTaP, Poliomyelitis, and Hepatitis B). However, this association was not observed for Haemophilus influenzae type b and Measles vaccines. These vaccines, typically administered within the first year of life, often provoke parental concerns about potential side-effects according to the vaccination schedule, should be completed within the first year of the child's life, a phase when parents often fear potential side effects [51–53]. Beyond the age of 24 months, the inequalities in vaccination coverage among different vaccines tend to diminish in relation to the Deprivation Index. This trend may be due to effective catch-up campaigns by Local Health Authorities, which optimise vaccination schedules to facilitate catch-up vaccination [54]. Additionally, the start of primary school and the promotion of vaccination within educational settings might contribute to this recovery in coverage [29–31]. Although there is evidence that catch up strategies are effective, it is important to improve the 0–24 months coverage, considering that exposure to pathogens during the first two years of life can impact children's health considerably [55,56]. Compared with DTaP vaccines, other vaccines, especially the Measles vaccine, generally show lower vaccination coverage across all age groups, regardless of the Deprivation Index. These findings somewhat contradict previous literature that identified lower vaccination coverage in disadvantaged areas [17] including studies on influenza vaccines [21–26] and paediatric vaccinations [27]. However, the target population in these studies mainly comprised adults, focusing on voluntary vaccinations or paediatric populations in different settings [27]. Although, the absence of an association between vaccination coverage percentages and the deprivation index, except for more exposed age groups, confirms what has been previously found regarding the reduction of social and health inequalities where national Health Systems characterised by optimal structuring and organisation have been implemented and, in the context of paediatric vaccination, various studies suggest that socioeconomic status plays a limited role in explaining vaccination coverage [12,40]. Further investigation is warranted, especially regarding the Measles vaccine, which was not mandatory during the study period. Our results might reflect the effective organisation and promotion and vaccination campaigns by the Regional Health Service and a generally positive attitude towards vaccination in the geographic areas studied. In this context, a systematic review analysing the organisational and structural drivers of childhood Immunization in the European Region [57] identifies strategies to enhance childhood immunization, including Mandatory Immunisation Policy (MIP), reminder systems (cards, electronic reminders), parental education, and optimising vaccine schedules. Nevertheless, hesitancy may arise when multiple vaccines are administered in a single session.

It is worth noting the association between the density of General Paediatricians per inhabitants and vaccination coverage. Specifically, areas with a higher density of General Paediatricians per inhabitants showed an increase in vaccination coverage against Haemophilus influenzae type b exhibited in the 6-year-old cohort. This finding might suggest the proactive role of General Paediatricians in facilitating catch-up vaccination programmes [58,59]. The lack of association between vaccination coverage and the density of General Practitioners and General Paediatricians per inhabitants could be explained either by the effectiveness of healthcare organisation in mitigating inequalities or by the higher public knowledge and associated perception of increased health risks for specific disease, such as Tetanus, and Hepatitis B, subject to mandatory vaccination for a longer time period [60–62]. Furthermore, the role of Healthcare Workers in influencing vaccination perceptions and uptake cannot be overstated. Their central role in healthcare delivery means they are often the primary source of information and reassurance about vaccinations for both the paediatric and adult population. Enhancing HCWs' awareness and understanding of vaccination benefits could significantly improve vaccination coverage rates, through more effective communication and public engagement from the first point of contact in healthcare settings [60–63].

Our findings underscore the importance of continuing to investigate variables that could shed light on the inequality in vaccination coverage across different vaccines, years, and geographical regions. Future research should consider factors such as the organisation of Local Health Authorities, the role of educational institutions, the involvement of volunteer groups, and the Paediatricians' perceptions of vaccine efficacy, and potential side effects. Equally important is understanding the reasons behind parents' decisions to delay or refuse vaccinations for their children, thereby potentially exposing them to risk during their most vulnerable stages of development.

Strengths and limitations

The strengths of this research lie in its use of routinely collected healthcare data at population level, a large sample size, and its extensive coverage in terms of time frame, geographical area, and population involved. However, several caveats merit discussions. Firstly, the database encompassing General Practitioners and Paediatricians was not uniformly available across all Local Health Authorities, leading to potential inconsistencies. Secondly, the risk of transcription errors or incomplete information is inherent in any large database, which could impact the quality of the data. Despite this risk, the extensive volume of data collected somewhat offsets these concerns. Thirdly, the Deprivation Index used in this study does not directly measure economic status but instead relies on proxies like rental housing; it is important to note, however, that vaccines are freely provided to the population. Fourthly, the study does not account for potential geographical distances from vaccination clinics, despite these clinics being widely distributed across the territory. Fifthly, while the ecological design of our study is beneficial for broad assessments and essential for analysing geographical trends and comparing different Local Health Authorities, it inherently limits the ability to establish direct causal relationships at the individual level. Sixthly, we did not directly assess the causes of vaccine hesitancy. However, we employed vaccination coverage as a proxy of vaccination hesitancy, considering that it encompasses hesitancy related to fears for vaccine-associated side effects, organisational challenges, or any factors that might adversely affect vaccination coverage. Seventh, we did not investigate the Varicella vaccine coverage as complete and reliable databases were not available, considering the shift to mandatory vaccination only in recent years and the possibility to co-administer with the MMR vaccination. Finally, the impact of institutions or volunteer organisations on vaccination rates was not factored into our analysis.

Policy implications and conclusions

In our population-based, ecological study, we analysed vaccination data against Diphtheria, Tetanus, Pertussis, Poliomyelitis, Hepatitis B, Haemophilus influenzae type b, Measles, Rubella, and Mumps for different age groups (24 months, 36 months, 6 years, and 8 years) within birth cohorts ranging from 2001 to 2015. Our analysis indicated that a higher Deprivation Index, indicative of less favourable socio-economic conditions, negatively impacts vaccination uptake, especially in the most susceptible and exposed age groups. The study also highlighted the pivotal role of General Paediatricians in promoting adherence to vaccination schedules and addressing instances of missed vaccinations. Despite the implementation of mandatory vaccination policies, our study observed persistent geographical inequalities in vaccine coverage. Addressing these inequalities is imperative, necessitating the revision and enhancement of policies aimed at boosting vaccination rates in areas with lower coverage. Effective strategies may include the expansion of vaccination campaigns in disadvantaged areas and strengthening of catch-up programmes for mitigating these inequalities. Enhancing awareness among General Paediatricians and parents, particularly for engaging with vaccine-hesitant groups, is crucial. The increased involvement of General Paediatricians is vital for the effective dissemination of health programs. Furthermore, our findings indicate the need for additional research to explore the diverse factors affecting vaccination coverage. This encompasses the analysis of healthcare system organisation, the impact of educational institutions, the contributions of voluntary organisations, and the complexities of parental decision-making in relation to vaccinations. These insights are essential for informing future public health strategies and interventions.

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Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki.

CRediT authorship contribution statement

Michelangelo Mercogliano: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Ronan Lemwel Valdecantos:** Writing – original draft, Investigation. **Gianluca Fevola:** Writing – original draft, Investigation. **Michele Sorrentino:** Writing – original draft, Investigation. **Gaetano Buonocore:** Writing – original draft. **Maria Triassi:** Writing – review & editing, Writing – original draft. **Raffaele Palladino:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation.

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.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvacx.2024.100482.

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