

## Implementation of the Greek national immunization program among nursery attendees in the urban area of Thessaloniki

Tasika E<sup>1</sup>, Farmaki E<sup>2</sup>, Roilides E<sup>1</sup>, Antachopoulos C<sup>1</sup>

<sup>1</sup>3<sup>rd</sup> Department of Pediatrics

<sup>2</sup>1<sup>st</sup> Department of Pediatrics

Aristotle University Faculty of Medicine, School of Health Sciences, Hippokration General Hospital, Thessaloniki, Greece

### Abstract

**Background:** The growing phenomenon of vaccine hesitancy and the severe economic crisis may have affected compliance with the National Immunization Program (NIP) in Greece over the last years. We investigated compliance with the NIP among children attending nurseries in the urban area of Thessaloniki.

**Methods:** A cross-sectional study was conducted, including nursery attendees born between 01/01/2014-01/10/2015 in each of the municipalities of Thessaloniki urban area. Public and private nurseries were randomly selected. Immunization data were anonymously collected from the child's health booklet. Both coverage and timeliness of immunization were recorded for all recommended vaccines according to the NIP.

**Results:** In total, 432 children with a mean age of 2.9 years were studied, of which 245 (57 %) were attending private nurseries. Full coverage was >90 % for most of the recommended vaccines except for pneumococcal (81 %), meningococcal serogroup C (68.3 % and 82 % for 2011 and 2015 schedule, respectively), hepatitis A (38.9 %) and rotavirus (25.9%) vaccine. Delay rates for one or more doses ranged between 21-90.3 % for all vaccines; time of median delay ranged between 3.8-6.7 months. Lower coverage and higher delay rates were observed for Roma children.

**Conclusions:** While high coverage appears to be sustained for most of the recommended vaccines, delay of scheduled shots may compromise age-appropriate protection. Suboptimal immunization against pneumococcal, meningococcal serogroup C, hepatitis A, and rotavirus infections may increase morbidity in this age group and needs to be addressed. HIPPOKRATIA 2019, 23(4): 147-153.

**Keywords:** Children, immunization, vaccines, coverage, nursery

**Corresponding author:** Charalampos Antachopoulos, MD, PhD, MRCPCH, 3<sup>rd</sup> Department of Pediatrics, Hippokration Hospital, 49 Konstantinoupoleos str., 54642 Thessaloniki, Greece, tel: +302310892446, fax: +302310992981, e-mail: antachop@auth.gr

### Introduction

Active immunization has been the most efficient way to prevent devastating human or animal infections worldwide, resulting in a marked decrease of associated deaths and disabilities in millions of susceptible hosts. Unfortunately, vaccines have been the "victim" of their efficacy: targeted infections are so rare nowadays that contemporary people, including healthcare providers, do not face the consequences of these infections and therefore do not understand the need for immunization. The rising and multifactorial phenomenon of "vaccine hesitancy", ranging from a complete refusal of immunizations to simple delay of scheduled shots, has been observed in several developed countries, including Greece, occasionally resulting in reduced vaccine coverage and loss of herd immunity<sup>1,2</sup>.

Besides vaccine hesitancy, the very severe economic crisis that temporarily caused the deprivation of health insurance and potentially limited access to health care providers for a large part of the population may have af-

ected compliance to National Immunization Program (NIP) in Greece over the last decade<sup>3-5</sup>. However, there is no organized system of registry and surveillance of vaccination coverage in Greece. Limited studies pertaining to this issue have been published over the last two decades<sup>6-9</sup>. The most recent one, a cross-sectional nationwide vaccination coverage study, included children born between January-December 2010<sup>9</sup>.

In the absence of more recent data capturing children born in the middle of the financial crisis of Greece starting around 2010, the primary objective of this study was to investigate compliance to the Greek NIP among nursery attendees born several years later (in 2014-2015) in the urban area of Thessaloniki, in terms of coverage and timeliness of immunization. Secondary objectives were differences in compliance (coverage/timeliness) among different municipalities, public and private nurseries, Greek and non-Greek families, as well as an assessment of compliance in Roma children.

## Materials and methods

### Study design and sample selection

A cross-sectional study was conducted. The target population was preschool children born between 01/01/2014 and 01/10/2015, who were attending nurseries between 1/10/2017-30/11/2017 in each of the municipalities of Thessaloniki urban area: Ampelokipoi-Menemeni, Thessaloniki, Kalamaria, Kordelio-Evosmos, Neapoli-Sykies, Pavlou Mela, and Pylea-Chortiatis. Children of the Dendropotamos area (part of the municipality of Ampelokipoi-Menemeni) were studied separately, as they mostly belong to the Roma minority. Roma people tend to have limited access to healthcare structures, lower-income, and special beliefs regarding immunization resulting in suboptimal compliance in many parts of the world, including Greece<sup>10,11</sup>.

The size of the whole population under study was calculated based on the total number (209) of nurseries (both public and private) included in all municipalities of Thessaloniki urban area and an average of 20 children estimated based on preliminary information of Thessaloniki nursery demographics. Thus the estimated size of the whole population was 4,180 children. The sample size was subsequently calculated with OpenEpi tool (version 3.01) for descriptive studies, using the following settings: 1.2 for design effect, 50 % for anticipated frequency, and 95 % for confidence interval; these settings yielded the desired number of 423 children. We then randomly selected one public nursery for every ten public nurseries and one private for every ten private nurseries in each municipality. For practical purposes, the number of nurseries in every municipality was rounded to the proximal decade (i.e., if 24 nurseries were included, we randomly selected two, whereas if 26 nurseries were included, we selected three). One nursery (public/private) was at least included from every municipality, even if the total number of nurseries (public/private) in this municipality was less than five. Random selection was conducted using the RANDBETWEEN function in a Microsoft Excel sheet. We recorded data from all children of the toddler class of the nurseries selected that were born between 01/01/2014 and 01/10/2015.

### Data collection

Information was collected for every child, based on the copy of the immunizations' pages of the child's health booklet that parents are obliged to submit at the time of his/her registration at the nursery. The date of birth, as well as the type and dates of all immunizations administered, were recorded in a Microsoft Excel database; the child's name was not recorded. In addition, the type of nursery (public or private), the municipality where the nursery belonged, and the parents' nationalities were recorded. For analysis purposes, we defined Greek families as those with both parents of Greek nationality. Data were collected during October-November 2017.

### Data analysis

We assessed both coverage and timeliness of immu-

nization for all recommended vaccines according to the Greek NIP, namely: diphtheria-tetanus-acellular pertussis-inactivated polio vaccine (DTaP-IPV), *Haemophilus influenzae* type b (Hib), hepatitis B (Hep B), conjugated pneumococcal (PCV), conjugated meningococcal serogroup C (MCC), measles-mumps-rubella (MMR), varicella (VAR), hepatitis A (Hep A), as well as for rotavirus vaccine, which is partially reimbursed. To assess coverage, we calculated the percentage of children that were fully immunized at the time of recording (all recommended doses for age based on the NIP) or partially immunized (one, two, three, or more doses but not all recommended). In order to assess timeliness, we calculated delay rates for each of the NIP recommended vaccine doses. A dose was considered delayed if administered at least two months beyond the upper range of recommended age by the NIP. We also recorded the time of delay (expressed in months) for each delayed dose.

Coverage and delay rates for each of the NIP recommended vaccine doses were subsequently calculated and compared among different municipalities, among public and private nurseries, and among Greek and non-Greek families.

In order to assess coverage and delay rates for *Neisseria meningitidis* serogroup C vaccine, due to a relevant modification of the Greek NIP in January 2015, we divided our sample into two groups: children born until 30/6/2014, who should have been immunized according to the 2011 NIP, and those born at, or after, 1/7/2014, who should have been immunized according to 2015 NIP. For the first group, children were considered as fully vaccinated if they had received at least two doses, while for the second group, one dose at the age of 12 months sufficed.

### Statistical analysis

Data analysis was performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). The chi-square test was used for comparisons of coverage or delay rates, applying Bonferroni correction for multiple comparisons. A p value <0.05 indicated statistical significance.

### Study approval

For all public nurseries of each municipality, written approval for participation in the study was obtained centrally, from the Office of Pre-school Education (decision No 2168, date 6/7/2017). For each randomly selected private nursery, consent was requested from the director of the nursery. In case of denial, we were addressed to another, randomly selected, nursery. The study was conducted with respect to the Declaration of Helsinki's ethical principles for medical research involving human subjects.

## Results

Out of a total of 209 nurseries in greater Thessaloniki area, 140 (66.9 %) are private. Of 23 nurseries finally selected for the study, 14 (60.8 %) were private. The num-

ber (nine) of public nurseries selected slightly exceeded the 1/10 proportion since, following the study protocol, we included public nurseries from Ampelokipoi-Menemeni and Dendropotamos, both of which had less than five nurseries (Table 1). Three private nurseries did not consent for participation and were replaced by others, randomly selected. A total of 492 children were enrolled in the toddler classes of the nurseries included in the present study, with an average of 21.4 children/nursery class, which was close to what was expected from preliminary information. Demographic and immunization data from health booklets were available for 432 children, who were included in the analysis. The mean age of all children studied at the time of data collection was 2.9 years (range 2.5-3.3 years). Of those analyzed, 245 (57 %) were attending private nurseries, a number that parallels

the proportion of private nurseries selected, and 52 (12 %) had at least one non-Greek parent.

Full coverage in >90 % of children (all municipalities grouped together) was recorded for DTaP-IPV, Hib, HepB, MMR, and VAR vaccines. Coverage was lower for PCV (81 %) and MCC (68.3 % and 82 % for 2011 and 2015 schedule, respectively) and very low for HepA and rotavirus vaccines (38.9 % and 25.9 %, respectively, Table 2). Statistically significant differences in coverage among municipalities were recorded for Hib, PCV, and MCC (2011 schedule) immunization (Table 2). Coverage rates recorded in the Dendropotamos area for several of the recommended vaccines (DTaP-IPV, Hib, PCV, MCC-2011, and rotavirus) were substantially lower than those calculated for all municipalities grouped together. A notable exception was the HepA vaccine, for which cover-

**Table 1:** Distribution of public and private nurseries in municipalities of Thessaloniki urban area (total and selected according to the current study's design).

| Municipality                      | Public nurseries (all) | Public nurseries selected | Private nurseries (all) | Private nurseries selected | Total nurseries for each municipality | Total selected for each municipality |
|-----------------------------------|------------------------|---------------------------|-------------------------|----------------------------|---------------------------------------|--------------------------------------|
| Ampelokipoi-Menemeni              | 3                      | 1                         | 9                       | 1                          | 12                                    | 2                                    |
| Thessaloniki                      | 17                     | 2                         | 38                      | 4                          | 55                                    | 6                                    |
| Kalamaria                         | 10                     | 1                         | 13                      | 1                          | 23                                    | 2                                    |
| Kordelio-Evosmos                  | 10                     | 1                         | 30                      | 3                          | 40                                    | 4                                    |
| Neapoli-Sykies                    | 11                     | 1                         | 9                       | 1                          | 20                                    | 2                                    |
| Pylaia-Chortiatis                 | 6                      | 1                         | 29                      | 3                          | 35                                    | 4                                    |
| Pavlou Mela                       | 11                     | 1                         | 12                      | 1                          | 23                                    | 2                                    |
| Dendropotamos                     | 1                      | 1                         | 0                       | 0                          | 1                                     | 1                                    |
| <b>Total (all municipalities)</b> | <b>69</b>              | <b>9</b>                  | <b>140</b>              | <b>14</b>                  | <b>209</b>                            | <b>23</b>                            |

**Table 2:** Vaccination coverage expressed as percentages with correspondent numbers of children in parentheses [% (n)] for all recommended vaccines presented for all municipalities of Thessaloniki in total and, separately, for the Dendropotamos area.

| Vaccine    | 0 doses    | 1 dose     | 2 doses    | 3 doses    | Full coverage (all municipalities) | p value among municipalities | Full coverage (Dendropotamos) |
|------------|------------|------------|------------|------------|------------------------------------|------------------------------|-------------------------------|
| DTaP-IPV   | 0.2 (1)    | 0 (0)      | 0.7 (3)    | 4.2 (18)   | 94.9 (410)                         | 0.48                         | 78.6 (11)                     |
| Hib        | 0.5 (2)    | 0 (0)      | 0.7 (3)    | 4.9 (21)   | 94 (406)                           | <b>0.009</b>                 | 71.4 (10)                     |
| HepB       | 0.5 (2)    | 0.2 (1)    | 1.4 (6)    | 98 (423)   | 98 (423)                           | 1.00                         | 92.9 (13)                     |
| PCV        | 0.5 (2)    | 0.9 (4)    | 3.2 (14)   | 14.4 (62)  | 81 (350)                           | <b>0.015</b>                 | 36 (5)                        |
| MCC (2011) | 1.1 (5)    | 8.6 (37)   | 21.9 (95)  | 68.3 (295) | 68.3 (295)                         | <b>&lt;0.001</b>             | 28.6 (4)                      |
| MCC (2015) | 18 (78)    | 82 (354)   | N/A        | N/A        | 82 (354)                           | 1.00                         | 86 (12)                       |
| MMR        | 4.4 (19)   | 95.6 (413) | N/A        | N/A        | 95.6 (413)                         | 1.00                         | 100 (14)                      |
| VAR        | 7.2 (31)   | 92.8 (401) | N/A        | N/A        | 92.8 (401)                         | 1.00                         | 92.9 (13)                     |
| HepA       | 23 (99)    | 38.3 (165) | 38.9 (168) | N/A        | 38.9 (168)                         | 0.09                         | 71.4 (10)                     |
| Rota       | 68.1 (294) | 3 (13)     | 16.2 (70)  | 12.7 (55)* | 25.9 (112)                         | 0.1                          | 0 (0)                         |

Reported p values are for comparison of coverage among municipalities. N/A: not applicable. DTaP-IPV: diphtheria-tetanus-acellular pertussis-inactivated polio, Hib: *Haemophilus influenzae* type b, HepB: hepatitis B, PCV: conjugated pneumococcal, MCC: conjugated meningococcal serogroup C, MMR: measles-mumps-rubella, VAR: varicella, HepA: hepatitis A, Rota: rotavirus, \*: applicable only for pentavalent rotavirus vaccine.

age in Dendropotamos (71.4 %) was higher than that of all municipalities together (38.9 %) (Table 2).

There were no differences in coverage rates between public and private nurseries for most NIP vaccines, except for PCV, MCC (2011 schedule), and rotavirus vaccines, for which coverage was higher in private nurseries compared to public ones (table 3). No differences in coverage rates were recorded between Greek and non-Greek families, except for the rotavirus vaccine, for which coverage was higher in Greek families (Table 3).

The main findings related to timeliness of immunization are presented in Table 4. Also, in this table, the numbers of children studied in each municipality are provided in the first column. A considerable proportion of

children from all municipalities received at least one dose of recommended vaccines at least two months beyond the recommended age range by the NIP. When all municipalities were grouped together, the highest delay rates were recorded for HepA (90.3 %) and PCV (76.4 %) vaccines and the lowest for MMR (21 %) and MCC (2015 schedule, 39.3 %). Differences in delay rates among municipalities were observed for HepB and PCV vaccines. The median delay time ranged from 3.8 months (for DTaP-IPV and HepB vaccines) to 6.7 months (for MCC-2011 schedule); it was also quite long for MCC (2015 schedule) and MMR (5.8 months) as well as for HepA vaccine (5.4 months) (Table 4).

For most of the recommended vaccines, there were

**Table 3:** Vaccination coverage for public and private nurseries, and for Greek and non-Greek families, for all recommended vaccines. Data represent full coverage and are expressed as percentages with correspondent numbers of children in parentheses [% (n)].

| Vaccine    | Public nurseries (n=187) | Private nurseries (n=245) | p (public vs private) | Greek families (n=380) | Non-Greek families (n=52) | p (Greek vs non-Greek) |
|------------|--------------------------|---------------------------|-----------------------|------------------------|---------------------------|------------------------|
| DTaP-IPV   | 93.6 (175)               | 95.9 (235)                | 0.27                  | 95 (361)               | 94.2 (49)                 | 0.73                   |
| Hib        | 92.5 (173)               | 95.1 (233)                | 0.26                  | 93.9 (357)             | 94.2 (49)                 | 1.0                    |
| HepB       | 96.8 (181)               | 98.8 (242)                | 0.15                  | 97.8 (372)             | 97.9 (51)                 | 1.0                    |
| PCV        | 74.3 (139)               | 85.7 (210)                | <b>0.003</b>          | 81 (308)               | 71 (37)                   | 0.06                   |
| MCC (2011) | 47.6 (89)                | 82.4 (202)                | <b>&lt;0.001</b>      | 68.1 (259)             | 69.2 (36)                 | 1.00                   |
| MCC (2015) | 82.3 (154)               | 82 (201)                  | 0.98                  | 82.1 (312)             | 82.6 (43)                 | 0.96                   |
| MMR        | 95.2 (178)               | 95.9 (235)                | 0.71                  | 95.5 (363)             | 96 (50)                   | 1.0                    |
| VAR        | 91.4 (171)               | 93.9 (230)                | 0.33                  | 92.9 (353)             | 92.3 (48)                 | 0.77                   |
| HepA       | 33.7 (63)                | 42.4 (104)                | 0.06                  | 38.9 (148)             | 36.5 (19)                 | 0.68                   |
| Rota       | 19.8 (37)                | 30.6 (75)                 | <b>0.01</b>           | 27.9 (106)             | 13.4 (7)                  | <b>0.03</b>            |

Reported p values are for comparisons between public versus private nurseries and Greek versus non-Greek families. DTaP-IPV: diphtheria-tetanus-acellular pertussis-inactivated polio, Hib: *Haemophilus influenzae* type b, HepB: hepatitis B, PCV: conjugated pneumococcal, MCC: conjugated meningococcal serogroup C, MMR: measles-mumps-rubella, VAR: varicella, HepA: hepatitis A, Rota: rotavirus.

**Table 4:** Delay rates for at least one dose of recommended vaccines among municipalities of Thessaloniki expressed as percentages with correspondent numbers of children in parentheses [% (n)], and median delay time for all municipalities together.

| Municipality (number of children studied)         | DTaP-IPV*  | Hib        | HepB             | PCV          | MCC (2011) | MCC (2015) | MMR       | VAR        | HepA       |
|---|------------|------------|------------------|--------------|------------|------------|-----------|------------|------------|
| Ampelokipoi-Menemeni (28)                         | 71.4 (20)  | 67.9 (19)  | 78.6 (22)        | 96.4 (27)    | 60.7 (17)  | 32.1 (9)   | 25.0 (7)  | 60.7 (17)  | 92.8 (26)  |
| Thessaloniki (147)                                | 43.5 (64)  | 47.6 (70)  | 34.0 (50)        | 67.3 (99)    | 55.7 (82)  | 43.5 (64)  | 25.2 (37) | 47.6 (70)  | 87.8 (129) |
| Kalamaria (49)                                    | 55.1 (27)  | 55.1 (27)  | 40.8 (20)        | 77.5 (38)    | 57.1 (28)  | 46.9 (23)  | 30.6 (15) | 69.4 (34)  | 100.0 (49) |
| Kordelio-Evosmos (59)                             | 50.8 (30)  | 52.5 (31)  | 49.2 (29)        | 93.2 (55)    | 69.5 (41)  | 45.7 (27)  | 16.9 (10) | 57.6 (34)  | 93.2 (55)  |
| Neapoli-Sykies (36)                               | 52.8 (19)  | 52.8 (19)  | 33.3 (12)        | 72.2 (26)    | 61.1 (22)  | 44.4 (16)  | 13.9 (5)  | 44.4 (16)  | 97.2 (35)  |
| Pylaia-Chortiatis (57)                            | 42.1 (24)  | 42.1 (24)  | 42.1 (24)        | 64.9 (37)    | 56.1 (32)  | 33.3 (19)  | 26.3 (15) | 43.8 (25)  | 84.2 (48)  |
| Pavlou Mela (42)                                  | 40.5 (17)  | 47.6 (20)  | 35.7 (15)        | 85.7 (36)    | 73.8 (31)  | 19.0 (8)   | 26.2 (11) | 35.7 (15)  | 80.9 (34)  |
| Dendropotamos (14)                                | 85.7 (12)  | 85.7 (12)  | 85.7 (12)        | 85.7 (12)    | 85.7 (12)  | 28.6 (4)   | 42.9 (6)  | 78.6 (11)  | 100 (14)   |
| All municipalities (432)                          | 49.3 (213) | 51.4 (222) | 42.5 (184)       | 76.4 (330)   | 61.3 (265) | 39.3 (170) | 21.0 (91) | 47.9 (207) | 90.3 (390) |
| p among municipalities                            | 0.09       | 0.49       | <b>&lt;0.001</b> | <b>0.002</b> | 1.00       | 0.56       | 1.00      | 0.06       | 0.11       |
| Median delay time for all municipalities (months) | 3.8        | 4.6        | 3.8              | 4.8          | 6.7        | 5.8        | 5.8       | 4.3        | 5.4        |

Reported p values are for comparison of delay rates among municipalities. DTaP-IPV: diphtheria-tetanus-acellular pertussis-inactivated polio, Hib: *Haemophilus influenzae* type b, HepB: hepatitis B, PCV: conjugated pneumococcal, MCC: conjugated meningococcal serogroup C, MMR: measles-mumps-rubella, VAR: varicella, HepA: hepatitis A.

no differences in delay rates between public and private nurseries, except HepB and MCC (2011 schedule) vaccines, for which delay rates were lower in private nurseries than public ones (Table 5). No differences in delay rates were also recorded between Greek and non-Greek families for most vaccines, with the exception of DTαP-IPV and Hib, for which rates were higher in non-Greek families (Table 5).

In the latest national study<sup>9</sup>, compliance to NIP for the MCC vaccine was assessed based on the 2011 schedule; full compliance was 77.6 %. In the present study, full coverage according to the MCC-2011 schedule was even lower (68.3 %); coverage according to the MCC-2015 schedule was 82 %. Delay rates were lower for MCC-2015 compared to the MCC-2011 schedule, but even for the MCC-2015 schedule, the median delay was 5.8 months. These findings suggest suboptimal and not

**Table 5:** Delay rates for at least one dose of recommended vaccines for public and private nurseries, and for Greek and non-Greek families. Data are expressed as percentages with correspondent numbers of children in parentheses [% (n)].

| Vaccine    | Public nurseries (n =187) | Private nurseries (n =245) | p (public vs private) | Greek families (n =380) | Non-Greek families (n =52) | p (Greek vs non-Greek) |
|------------|---------------------------|----------------------------|-----------------------|-------------------------|----------------------------|------------------------|
| DTαP-IPV   | 52.4 (98)                 | 46.5 (114)                 | 0.24                  | 45.7 (174)              | 65.3 (34)                  | <b>0.03</b>            |
| Hib        | 54.5 (102)                | 48.6 (119)                 | 0.21                  | 49.2 (187)              | 65.4 (35)                  | <b>0.03</b>            |
| HepB       | 48.1 (90)                 | 38.5 (88)                  | <b>0.01</b>           | 41.6 (158)              | 52.0 (27)                  | 0.16                   |
| PCV        | 80.7 (151)                | 72.6 (178)                 | 0.05                  | 76.8 (292)              | 71.1 (37)                  | 0.45                   |
| MCC (2011) | 73.8 (138)                | 54.2 (133)                 | <b>&lt;0.001</b>      | 63.2 (240)              | 53.8 (28)                  | 0.6                    |
| MCC (2015) | 35.8 (67)                 | 41.2 (101)                 | 0.31                  | 38.4 (146)              | 44.2 (23)                  | 0.56                   |
| MMR        | 27.3 (51)                 | 20.8 (51)                  | 0.12                  | 24.7 (94)               | 17.3 (9)                   | 0.18                   |
| VAR        | 47.1 (88)                 | 47.7 (117)                 | 0.89                  | 46.6 (177)              | 53.8 (28)                  | 0.34                   |
| HepA       | 92.5 (173)                | 89.4 (219)                 | 0.34                  | 89.7 (341)              | 98 (51)                    | 0.15                   |
| Rota       | 59.8 (112)                | 53.8 (132)                 | 0.47                  | 56.8 (216)              | 53.8 (28)                  | 0.89                   |

Reported p values are for comparisons between public versus private nurseries and Greek versus non-Greek families. DTαP-IPV: diphtheria-tetanus-acellular pertussis-inactivated polio, Hib: *Haemophilus influenzae* type b, HepB: hepatitis B, PCV: conjugated pneumococcal, MCC: conjugated meningococcal serogroup C, MMR: measles-mumps-rubella, VAR: varicella, HepA: hepatitis A, Rota: rotavirus.

## Discussion

This cross-sectional study assessed the implementation of the NIP for children born between 01/01/2014-01/10/2015 in the urban area of Thessaloniki in terms of coverage and timeliness of immunization.

It is reassuring that full coverage for many of the recommended vaccines (DTαP-IPV, Hib, HepB, MMR, VAR) remains above 90 %, in levels similar with previous national studies including children of the first grade of Primary School (born in 2000 and 2006) and preschool children born in 2010<sup>6,7,9</sup>.

Lower coverage rates (81 %) for PCV in our population are similar to those reported by previous studies in Greece<sup>9,12,13</sup>, and Cyprus<sup>14</sup> but lower than the mean calculated coverage among European Union countries, which is approximately 90 %<sup>15</sup>. The observed delay rates (76.4 % for at least one dose) and median delay time (4.8 months, Table 4) are consistent with previous Greek studies<sup>8,9</sup> and suggest suboptimal immunization against pneumococcus. This is alarming, as pneumococcal infections are particularly common among infants and toddlers and may lead to serious sequelae. When further analyzing the subset (62, or 14.4 %) of children who received only three doses of PCV (Table 2), we found that 20 (32 %) of them were immunized following a 2+1 schedule (two doses during infancy and the third after the first year of life) as it is recommended in many European countries and the latest (2019) version of the Greek NIP.

timely protection against MCC, possibly due to lack of alertness of health professionals and parents following the markedly reduced incidence of invasive infections due to *N. meningitidis* serogroup C in our country over the last 15 years.

The very low coverage rates reported herein for HepA and rotavirus vaccines are also in accordance with the findings of the latest national study<sup>9</sup> with no trend for improvement over the years. Until 2008 the HepA vaccine was recommended only for high-risk groups while the prevalence of the disease in Greece is low (1.17/100,000), with 26 % of cases reported among the Roma minority<sup>16</sup>. Consequently, it seems that physicians and parents consider the HepA vaccine as of lower priority during the second year of life and postpone it for later in childhood, resulting in low vaccination coverage. A similar perception of low priority, together with partial reimbursement, may explain low coverage with a rotavirus vaccine.

Among municipalities, compliance and timeliness were lower for several vaccines in the area of Dendropotamos, reflecting the socioeconomic level, cultural beliefs, lack of information, and misconceptions about vaccine efficacy of the Roma population residing in this area<sup>17</sup>. This result points out the need for intervention and social alertness to prevent outbreaks among high-risk populations. However, the final vaccination coverage and



timely vaccination in our sample are higher than a cross-sectional study of Greek Roma children conducted in 2012-13<sup>11</sup>. This could be at least partially due to a selection bias in our study, as families whose children attend nurseries may have better access to health care and compliance to NIP. A study from 12 countries in central and south-east Europe found that Roma children had a lower probability of being vaccinated compared to non-Roma (odds ratio=0.325) with DTP, polio, and MMR vaccines. The probability of being vaccinated increased with access to health care<sup>10</sup>.

Apart from coverage, timeliness of immunization is equally important to ensure age-appropriate population protection. There are different ways to quantify timeliness, and therefore comparison with previous studies is challenging<sup>8,9</sup>. Despite high final coverage, delayed vaccination was observed for all vaccines in the present study. This may be due to a number of reasons, such as overcrowding of the NIP in the first year of life and easiness to postpone administration of vaccine doses due to minor infections (which do not justify postponement of immunization) by physicians and parents. However, delaying shots may also be a manifestation of vaccine hesitancy<sup>18</sup>. Smith et al reported that 26 % of parents had deliberately delayed their children's immunization, and 78 % of them expressed fears for possible side effects of the vaccines, resulting in an average loss of six vaccine doses. Vaccine coverage was lower among families who delayed shots compared to those adhering to the immunization schedule<sup>19</sup>.

Our comparisons of coverage and timeliness of immunization between public and private nurseries and between Greek and non-Greek families did not reveal significant or sustained differences. Compliance was better for private nurseries or Greek families for a limited number of vaccines (Table 3 and Table 5). This is reassuring, as in other studies, compliance to immunization schedule was lower among children covered by public services or those with immigrant status<sup>8,20,21</sup>.

Efforts to improve coverage and timeliness of immunization should focus on improving access to health care and vaccine availability, and promoting vaccine acceptance by parents and the community. The latter could be achieved by a number of initiatives, such as i) understanding and addressing hesitant people's concerns regarding vaccines, ii) monitoring of the media conversation regarding vaccination, iii) using social media and other contemporary ways of communication to convey information regarding the benefits and safety of immunization broadly, and iv) educate health care providers regarding optimal approaches of parental hesitancy issues<sup>22,23</sup>. In some countries, changes in legislation have been considered, including the elimination of the possibility of non-medical exemptions from immunization<sup>24</sup>, characterizing vaccine refusal as medical neglect<sup>25</sup>, or enforcing mandatory vaccination, as it has happened in Italy and France<sup>15</sup>.

In summary, we found sustained high coverage for

most vaccines included in the NIP for preschool children in Thessaloniki born in 2014-15, with the exception of PCV, MCC, HepA, and rotavirus vaccines. Considerable delay rates for at least one dose were recorded for all vaccines, with a median delay time of several months. No sustained differences were observed between children of public and private nurseries or Greek and non-Greek families. Lower coverage and higher delays were observed for nursery attendees of the Roma minority, with a possible improvement compared to previous years. This study's findings suggest the need for targeted efforts to improve coverage of certain vaccines as well as timeliness of immunization in the general population and in Roma children. Physicians need to dedicate sufficient time for discussion with parents to convince them regarding the need and safety of timely immunization.

### Conflict of interest

Authors declare no conflict of interest.

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