

BMJ Open Disparities of infant and neonatal mortality trends in Greece during the years of economic crisis by ethnicity, place of residence and human development index: a nationwide population study

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ABSTRACT

Objective To study trends of infant mortality rate (IMR) and neonatal mortality rate in Greece during the period 2004–2016 and explore the role of sociodemographic factors in the years of crisis.

Design Nationwide individual data for live births and infant (0–11 months) deaths provided by the Hellenic Statistical Authority were examined using Poisson, joinpoint regression and interrupted time series (ITS) analyses.

Setting Greece.

Participants All infant deaths (n=4862) over the 13-year period, of which 87.2% were born to Greek mothers, and respective live births.

Main outcome measures Evolution of IMR (0–364 days), early (<7 days) neonatal mortality rate (ENMR), late (7–27 days) neonatal mortality rate (LNMR) and post neonatal (28–364 days) mortality rate (PNMR) trends, by maternal nationality, place of residence and Human Development Index (HDI).

Results By Poisson regression, overall, during the study period, among infants of Greek mothers, IMR and PNMR declined significantly (−0.9%; 95% CI −1.7% to −0.1% and −1.6%; −3.0% to −0.2% annually, respectively), although differentially by place of residence (IMR_{urban}: −2.1%; −2.9% to −1.3%, IMR_{rural}: +10.6%; 7.6% to 13.6%). By contrast, among infants of non-Greek mothers, the low starting IMR/ENMR/LNMR/PNMR increased significantly (max ENMR: +12.5%; 8.6% to 16.5%) leading to a non-significant time–trend pattern overall in Greece. The inverse associations of HDI with IMR, ENMR and PNMR were restricted to Greek mothers' infants. Joinpoint regression analyses among Greek mothers' infants indicated non-significant increasing trends of IMR and ENMR following the crisis (+9.3%, 2012–2016, p=0.07 and +10.2%, 2011–2016, p=0.06, respectively). By contrast, the high (+17.1%; 8.1% to 26.9%, p=0.002) IMR increases among non-Greek infants were restricted to 2004–2011 and equalised to those of Greek mothers' infants thereafter. ITS analyses in preset years (2008, 2010, 2012) identified significantly increasing trends in

Strengths and limitations of this study

- Longest follow-up period of national data, as contrasted to previously Greek-based studies.
- Maternal ethnicity is for the first time considered in the analyses explaining part, if not most, of the heterogeneity of trends through the study period.
- Three complimentary statistical methodologies were used to describe the overall evolution of infant mortality and its components.
- Absence of a linkage system between birth and death data.
- Data on the role of biological factors or specific causes of infant death are missing.

IMR, LNMR and PNMR after 2012, and in ENMR after 2010, among Greek mothers' infants.

Conclusions HDI and rural residence were significantly associated with IMR. The strongly decreasing IMR trends among Greek-mothers' infants were stagnated after a lag time of ~4 years of crisis approximating the previously sharply increasing trends among non-Greeks.

INTRODUCTION

Socioeconomic factors have repeatedly been recognised as strong determinants of the health status of the population, including infants.^{1–3} Economic indicators, such as the per capita gross national product, were suggested to be at least as important contributors of infant mortality (IM) as narrowly defined factors relating to provision of medical care, for example, the relative number of doctors or hospital beds in a community.¹ Not surprisingly, the recent economic crisis of ~2008, has been linked with declines in population and child health reflected also by increased IM rates (IMR).^{4,5}

It is worth noting that in European Union countries, even a minor 1% cut in government healthcare spending was associated with significant increases in all mortality metrics, including neonatal and post neonatal IM.⁶

On the contrary, associations between the crisis and increased mortality have been questioned in other studies showing that most indicators of population health, apart from those relevant to suicides and mental health, continued improving after crisis initiation.^{7–10} Moreover, the economic crisis has been associated with some beneficial effects, that is, decline in rates of road traffic accidents, and smoking cessation.^{4,9} Reasonably, the impact of the crisis on health depends on several factors including the duration and intensity of the recession, the level of healthcare achieved prior to the recession and the type of austerity measures applied, but also on the type of the population studied with the most vulnerable groups being disproportionately affected.^{4,11,12} Due to the latter, it was proposed that studies should focus on analysing separately the subgroups most influenced by the crisis instead of presenting results as averages in a population.⁴

Greece has been markedly affected and still suffering the recent economic crisis. Between 2008 and 2016, the country's gross domestic product (GDP) per capita dropped by 26%, unemployment rate increased by more than 200% (from 7.6% to 23.3%) and the median disposable income decreased by 35%.^{13,14} The Gini index, which measures income inequality, increased by 22% and the proportion of individuals at risk of poverty or social exclusion climbed to almost 36% in 2016. Total health expenditures and government expenditure on healthcare were both decreased by 34% per capita over the period 2008–2016,^{13,14} whereas unmet healthcare needs increased.¹⁵ Besides, during the last years, Greece experienced large refugee flows^{16,17} with an anticipated negative impact on the country's economy and population health indicators. Adverse effects of financial crisis on perinatal factors, such as low birth weight, preterm birth and stillbirth rates, have been also observed^{18,19}; however, sparse data exist regarding the potential association of the crisis with IMR. It has been initially reported that during the period 2003–2012, IMR in Greece did not differ between the precrisis and crisis period whereas a later study showed that IMR increased between 2010 and 2015 as contrasted to the steady decrease observed during the preceding decade.^{20,21} Ecological correlations may be prone, however, to fallacies, whereas the different parts shaping the two main components of IM, namely neonatal (NM) and post neonatal mortality (PNM), should have been distinctly examined along with other factors possibly influencing the infants' health, especially socioeconomic status and access to healthcare delivery.

The aims of the current study were to explore time trends in early (<7 days of life) and late (7–27 days) NM, PNM (28–364 days) and total IM (0–364 days) in Greece during the period 2004–2016 after taking into account nationality and place of residence, as well as changes in the Human Development Index (HDI) during the study

period as a proxy of individual and collective measures of socioeconomic impact and healthcare access.

MATERIALS AND METHODS

Following personal contact and a signed agreement, individual data for all live births and infant (0–11 months) deaths were provided by the Hellenic Statistical Authority (ELSTAT) for a 13-year period (2004–2016) in two separate files: one including live births, and a second one, infant deaths; linkage of the two files was not possible as the personal identification number was not available in ELSTAT. Information on maternal demographic characteristics, such as nationality and place of residence, as well as on the infants' age at death, was also provided.

Mortality rates were calculated for infant (IM), early neonatal (0–6 days) (ENM), late neonatal (7–27 days) (LNM) and post neonatal (28–364 days) period (PNM) using respective numbers of deaths over the number of live births per year. Annual percent of change (APC) during the study period was initially estimated through univariate Poisson regression analysis using the underlying population of each set as an offset variable. Subsequently, data were stratified and analysed by maternal nationality (Greek vs non-Greek) and place of residence (urban/semiurban vs rural). Joinpoint regression analysis²² was thereafter applied to automatically derive, by a software programme, different segments in the mortality evolution curves overall as well as those by maternal nationality and place of residence. In details, the Joinpoint regression analysis is applied to study varying trends over time in order to identify the time point(s) in which the trend significantly changes. The location of the joinpoint is not known a priori and is to be estimated from the data. Therefore, the software takes trend data (eg, IMR) and fits the simplest joinpoint model based on the data. The user supplies the minimum and maximum number of joinpoints. The algorithm starts with the minimum number of joinpoint (eg, 0 joinpoints, which is a straight line) and tests whether more joinpoints are statistically significant and must be added to the model (up to that maximum number). Significance is tested using a Monte Carlo Permutation method. In all models examined in this study, a minimum number of 0 joinpoints and a maximum 1 of 2 joinpoints were tested. Interrupted time series (ITS) analyses were also undertaken as a sensitivity analysis to further explore the effect of crisis on IMR and its components in alternative prespecified years, notably 2008, considered to indicate the initiation of the crisis in Greece—as the value of the GDP of the country was maximum at that year but dropped afterwards¹³—and in two successive periods 2 years apart (2010 and 2012), to control for possible time lags in observing the impact of the crisis. All ITS models were verified and appropriately adjusted for possible autocorrelation; autoregressive integrated moving average models were used to control for autocorrelation and to estimate treatment effects over multiple periods. In our ITS analysis, a slope '<year

of interest' is fitted until the introduction of the crisis, '>year of interest' represents the change in the level of the mortality immediately following the initiation of the crisis and 'change of slope' represents the differences between precrisis and postcrisis intervention slopes.

HDI is a summary measure of average achievements of a country's population in three areas including life expectancy, education and per capita income indicators. Annual HDI values for the underlying populations in the year of death were extracted from the United Nations Development Programme website (<http://hdr.undp.org/en/composite/HDI>), whereas Poisson regression analysis was used to explore the association of 1 SD of HDI with total IM and its components. All statistical analyses were performed using the SAS software (V.9.4, SAS Institute), Stata software programme, V.13 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, Texas, USA: StataCorp LP) and Joinpoint Regression Program (Joinpoint Regression Program, V.4.5.0.1, June 2017; Statistical Methodology and Applications Branch, Surveillance Research Programme, National Cancer Institute).

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. No patients were asked to advise on interpretation or writing up of results. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

RESULTS

The annual average number of live births during the study period was 105 077, ranging from a high 118 302 (2008) to a low 91 847 live births in 2015. The annual average proportion of Greek mothers was 83.7%, whereas the remaining were mainly economic migrants. During the period 2004–2016, a total of 4862 infant deaths were recorded of whom 4238 (87.2%) were of infants born to Greek mothers, whereas among the remaining 615 deaths of infants born to non-Greek mothers, 298 (48.5%) were of infants born to Albanian mothers, 146 (23.7%) of infants born to mothers from Balkan countries and countries of the former Soviet Union, 77 (12.5%) from Asia, 47 (7.6%) from countries of the European Union or other developed countries and 47 (7.6%) from Africa. During the early and late neonatal period, 2107 (43.3%) and 1136 (23.4%) deaths occurred, respectively, whereas another 1617 (33.3%) of deaths were recorded in the post neonatal period. The annual average IMR was 3.5 over 1000 live births, whereas the corresponding figures for the early, late and post neonatal period were 1.5‰, 0.8‰ and 1.2‰, respectively. The number of live births and infant deaths, total IMR per 1000 live births in infants born to Greek and non-Greek mothers as well as HDI values in Greece during the study period are shown in [table 1](#). Moreover, infant deaths and total IMR by place of residence (urban/semiurban vs rural) are shown in online supplementary table 1.

Of note, in the beginning of the study period in 2004, notably well before the initiation of the crisis, IMR and its components were twofold to fourfold higher among

Table 1 Live births, infant deaths, total infant mortality rates (IMR) per 1000 live births in infants born to Greek and non-Greek mothers, and Human Development Index (HDI), in Greece during the period 2004–2016

Year	Infants born to Greek mothers			Infants born to non-Greek mothers			HDI
	Live births (N)	Infant deaths (N)	Mortality rates/1000 live births	Live births (N)	Infant deaths (N)	Mortality rates/1000 live births	
2004	88 805	403	4.5	16 825	26	1.5	0.835
2005	89 819	383	4.3	17 678	26	1.5	0.845
2006	92 590	379	4.1	19 396	36	1.9	0.851
2007	91 462	359	3.9	20 412	38	1.9	0.849
2008	96 329	281	2.9	21 931	32	1.5	0.857
2009	95 640	307	3.2	22 244	58	2.6	0.858
2010	93 209	355	3.8	21 351	80	3.7	0.856
2011	87 445	282	3.2	18 680	74	4.0	0.852
2012	84 868	241	2.8	15 153	52	3.4	0.854
2013	80 938	292	3.6	13 063	53	4.1	0.856
2014	79 985	298	3.7	12 144	47	3.9	0.864
2015	79 919	320	4.0	11 919	44	3.7	0.866
2016	80 166	338	4.2	12 721	49	3.9	0.868

Excluding missing maternal nationality values.

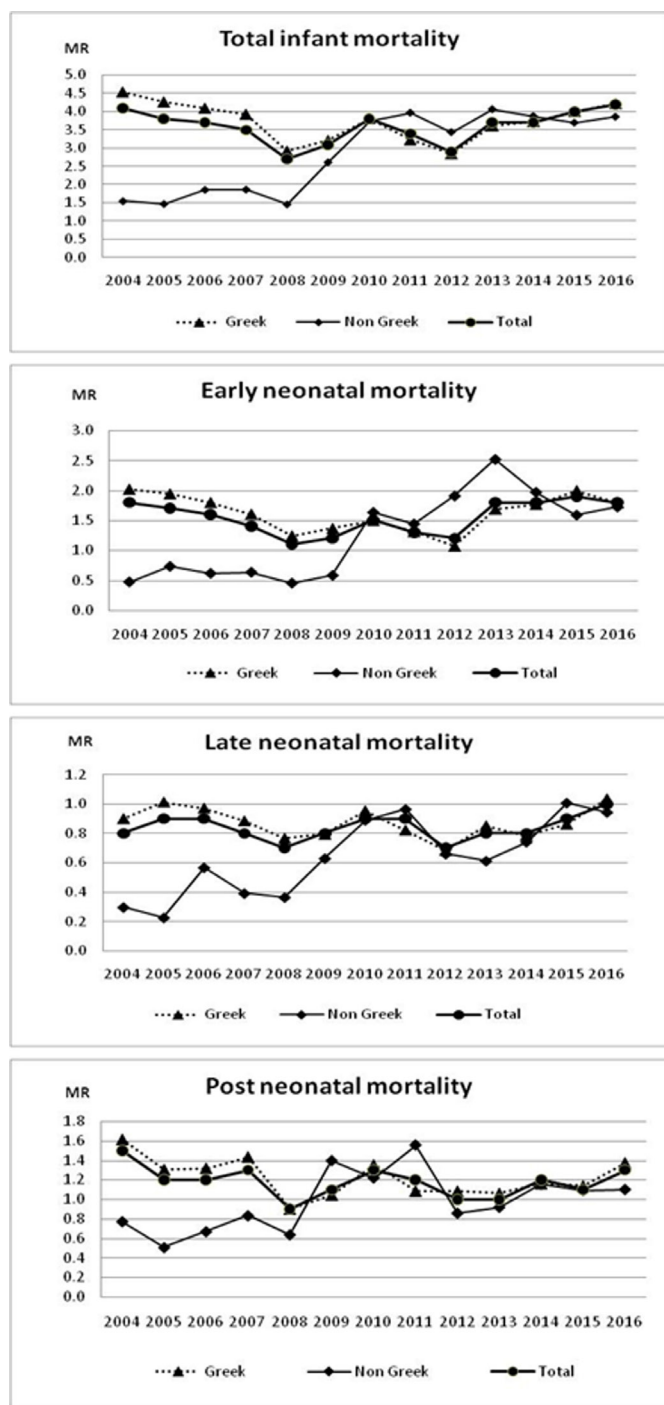


Figure 1 Evolution of infant early, late and post neonatal mortality rates in Greece (2004–2016) overall and by maternal nationality. MR, mortality rate/s.

infants born to Greek mothers in comparison with rates in infants born to non-Greek origin mothers. During the subsequent 4–5 years, however, rates among Greeks followed downward trends, whereas among non-Greeks inflated reaching almost similar values to those observed in infants born to Greek mothers (figure 1).

Overall, during the study period, among infants born to Greek mothers, Poisson regression analyses showed decreasing trends in IMR and PNM rate (PNMR) (−0.9%; 95% CI −1.7% to −0.1% and −1.6%; −3.0% to −0.2%

annually, respectively, $p=0.02$ for each), whereas no significant change in ENM rate (ENMR) and LNM rate (LNMR) was observed (table 2). Interestingly, mortality trends changed differentially by place of residence; significant decline of IMR trends (−2.1%; −2.9% to −1.3% annually, $p<0.0001$) and all its components was observed among infants born to Greek mothers living in urban areas, whereas among infants born to Greek mothers in rural areas, a significant increase of IMR (+10.6%; 7.6% to 13.6% annually, $p=0.002$), ENMR (+24.1%; 17.0% to 31.5% annually, $p<0.0001$) and LNMR trend (+12.7%; 6.5% to 19.2% annually, $p<0.0001$) was observed (table 2). By contrast, among infants of non-Greek mothers, the low starting IMR increased significantly (+9.4%; 6.9% to 11.9% annually, $p<0.0001$) due to significant increases of ENMR, LNMR and PNMR (max ENMR: +12.5%; 8.6% to 16.5% annually, $p<0.0001$) leading to a non-significant pattern of IMR evolution for Greece overall ($p=0.50$) (table 2). Further analysis by nationality of non-Greek mothers showed significant increases of IMR trends in all ethnic groups with average annual percent change 7.6% (95% CI 4.2% to 11.1%) in infants born to Albanian mothers, 8.6% (3.7% to 13.8%) in infants born to mothers from Balkan countries and countries of the former Soviet Union, 9.4% (2.8% to 16.3%) in infants born to mothers from Asia, 9.4% (1.1% to 18.3%) in infants born to mothers from countries of the European Union or other developed countries and 21.1% (11.0% to 32.3%) in infants born to mothers from Africa. HDI trends increased significantly, by 0.1% (95% CI 0.06% to 0.13%) annually, during the study period. Inverse associations of HDI with IMR, ENMR and PNMR, restricted to Greek mothers' infants, were observed (table 2).

In order to examine whether IMR, in our study population, might have been influenced by any variation in the registration of births in cases of uncertain viability, we analysed separately the infant deaths in the first day of life; trends of IMR in this age group, over the study period, were non-significant (average annual percent change: −1.22%; 95% CI −3.79% to 1.42%; $p=0.36$).

By Joinpoint regression analyses, a break was identified in the IMR curve among infants born to Greek mothers restricting the decreasing IMR trend to the period 2004–2012 (−4.5%; 95% CI −7.6% to −1.3% annually, $p=0.01$); a significant decline in ENMR trend until 2011 (−6.5%; 95% CI −11.4% to −1.4% annually, $p=0.02$) was also found (table 3). Of note, however, in the most recent study period following the crisis, non-significant increasing trends of IMR (2012–2016: +9.3% annually, $p=0.07$) and ENMR (2011–2016: +10.2% annually, $p=0.06$) were observed. By contrast, among infants born to non-Greek mothers, the high IMR increases (+17.1%; 95% CI 8.1% to 26.9% annually, $p=0.002$) were restricted to the period 2004–2011 with no statistically significant change thereafter (2011–2016); no break was identified for ENMR curve. Significant increases in IMR and ENMR trends after the year 2008 were observed in the total study population, whereas no break was found for LNMR and PNMR

Table 2 Poisson regression derived changes and 95% CI of infant (IMR), early (ENMR), late (LNMR) and post neonatal mortality rates (PNMR): annual percent of change (APC) for place of residence and maternal nationality (2004–2016); percent of change (PC) for 1 SD of Human Development Index (HDI) controlling for year of birth												
	IMR			ENMR			LNMR			PNMR		
	N	APC (95% CI)	P value	N	APC (95% CI)	P value	N	APC (95% CI)	P value	N	APC (95% CI)	P value
Maternal nationality												
Greek	4238	−0.9 (−1.7 to −0.1)	0.02	1849	−0.6 (−1.8 to 0.7)	0.35	995	−0.6 (−2.3 to 1.1)	0.46	1393	−1.6 (−3.0 to −0.2)	0.02
Non-Greek	615	9.4 (6.9 to 11.9)	<0.0001	258	12.5 (8.6 to 16.5)	<0.0001	138	8.0 (3.1 to 13.2)	0.001	218	4.4 (0.6 to 8.4)	0.02
All*	4862	0.3 (−0.5 to 1.0)	0.50	2107	0.9 (−0.3 to 2.1)	0.13	1136	0.4 (−1.2 to 2.0)	0.65	1617	−0.9 (−2.2 to 0.5)	0.20
Urbanisation												
Urban–semiurban												
Greek	3850	−2.1 (−2.9 to −1.3)	<0.0001	1738	−2.0 (−3.3 to −0.8)	0.002	906	−1.8 (−3.5 to 0.0)	0.05	1206	−2.4 (−3.9 to −0.9)	0.002
Non-Greek	563	8.8 (6.3 to 11.4)	<0.0001	243	13.2 (9.2 to 17.4)	<0.0001	123	6.7 (1.5 to 12.2)	0.01	197	4.9 (0.9 to 9.2)	0.02
Any*	4421	−0.8 (−1.6 to 0.0)	0.05	1981	−0.3 (−1.5 to 0.9)	0.61	1037	−0.8 (−2.4 to 0.9)	0.36	1408	−1.5 (−2.9 to 0.0)	0.04
Rural												
Greek	388	10.6 (7.6 to 13.6)	0.002	108	24.1 (17.0 to 31.5)	<0.0001	93	12.7 (6.5 to 19.2)	<0.0001	187	3.3 (−0.6 to 7.4)	0.09
Non-Greek	38	14.0 (4.0 to 24.9)	0.005	10	15.5 (−2.4 to 36.8)	0.09	11	18.1 (0.3 to 39.0)	0.05	17	4.9 (−7.6 to 19.1)	0.46
Any*	427	10.9 (8.1 to 13.9)	<0.0001	118	24.3 (17.6 to 31.4)	<0.0001	104	14.7 (8.6 to 21.1)	<0.0001	205	3.0 (−0.7 to 6.9)	0.11
HDI												
	PC			PC			PC			PC		
Greek	−8.6 (−14.8 to −1.9) 0.01			−11.3 (−20.8 to −1.4) 0.03			3.5 (−10.9 to 20.1) 0.66			−12.3 (−22.2 to −1.2) 0.03		
Non-Greek	−5.7 (−25.0 to 18.7) 0.62			−19.8 (−44.8 to 16.6) 0.25			20.0 (−28.6 to 101.7) 0.49			−1.3 (−30.7 to 40.5) 0.94		
All*	−9.5 (−15.3 to −3.2) 0.004			−14.0 (−22.3 to −4.7) 0.004			3.3 (−10.4 to 19.3) 0.65			−11.4 (−20.8 to −0.7) 0.04		

*Including missing maternal nationality values.

Table 3 Joinpoint regression derived annual percent of change (APC) and 95% CIs of infant (IMR), early neonatal (ENMR), late neonatal (LNMR) and post neonatal (PNMR) mortality rates by maternal nationality

IMR				ENMR			
Time period	N	APC (95% CI)	P value	Time period	N	APC (95% CI)	P value
Greek	2870	-4.5 (-7.6 to -1.3)	0.01	2004–2011	1118	-6.5 (-11.4, to -1.4)	0.02
2012–2016	1368	9.3 (-1.1 to 20.9)	0.07	2011–2016	731	10.2 (-0.4 to 21.9)	0.06
Non-Greek	333	17.1 (8.1 to 26.9)	0.002	2004–2016	258	13.8 (6.7 to 21.3)	0.001
2011–2016	282	0.2 (-11.5 to 13.5)	0.97				
All*	1807	-7.5 (-14.6 to 0.3)	0.06	2004–2008	780	-10.7 (-19.9 to -0.5)	0.04
2008–2016	3055	3.6 (0.7 to 6.6)	0.02	2008–2016	1327	6.1 (2.1 to 10.3)	0.01
LNMR				PNMR			
Time period	N	APC (95% CI)	P value	Time period	N	APC (95% CI)	P value
Greek	995	-0.6 (-2.5 to 1.4)	0.54	2004–16	1393	-1.7 (-4.0 to 0.8)	0.16
Non-Greek	138	9.1 (3.5 to 14.9)	0.003	2004–16	218	4.7 (-0.8 to 10.6)	0.09
All*	1136	0.6 (-1.3 to 2.5)	0.48	2004–16	1617	-0.8 (-3.0 to 1.4)	0.42

No break in the time period examined was identified for ENMR in non-Greeks, as well as for LNMR and PNMR measures in Greeks, non-Greeks or the total study population.

*Including missing maternal nationality values.

measures in Greeks, non-Greeks or the total study population (table 3).

The results of ITS analyses in the preset years 2008, 2010 and 2012 are shown in figures 2 and 3. Compared with the joinpoint regression showing non-significant increases in IMR from 2012 to 2016 for infants born to Greek mothers, ITS analysis showed a significant increase in IMR ($p=0.0001$) in this population during the same time period and further identified significant increases in LNMR ($p=0.0004$) and PNMR trends ($p=0.03$). Regarding the non-significant increases of ENMR trends after the year 2011 by Joinpoint regression in infants born to Greek mothers ($p=0.06$), ITS analysis showed a non-significant increase during the post 2012 time period ($p=0.07$); however, a significant increase during the post 2010 time period in these infants was observed ($p=0.01$) (figure 2). In infants born to non-Greek mothers, while a significant increase in IMR trends was found by Joinpoint regression analyses during the period 2004–2011, by ITS analyses—depending on when the year of interest was being defined (2010 or 2012)—the increase was either not significant (2004–2010, $p=0.11$) or significant (2004–2012, $p=0.001$); no change in IMR was identified by ITS analysis over the 2010–2016 or 2012–2016 time periods in non-Greek mothers' infants (figure 3).

DISCUSSION

Trends of neonatal and infant mortality in Greece, spanning from 2004—before the initiation of crisis in 2008—to 2016, are not homogeneous, given significant increases in the relatively small proportion of infants born to non-Greek nationality mothers as contrasted to declining IMR trends among Greek mothers' infants, differentials by place of residence and also increases in IM indices among Greek mothers' infants noted ~4 years after the crisis initiation. Specifically, the 'brake' of 2012 identified, by Jointpoint regression analysis, non-significant increases of ~10% annually, in IMR and ENMR trends, whereas by ITS analyses, significant increases in IMR, LNMR and PNMR trends were observed thereafter among infants born to Greek mothers, a fact indicating how sensitive the results are depending on the statistical method used. Changes in HDI during the study period were also reflected in the inverse associations of HDI with ENMR and IMR, but also PNMR, among infants born to Greek mothers.

Strengths of the present investigation, as contrasted to previously Greek-based published studies,^{9 18 20 21 23} include the longest follow-up period of national data, namely since 2004, before the crisis, when the first data on maternal ethnicity became electronically available, to the latest available year 2016. Of great importance is also the fact that, for the first time, the maternal ethnicity was considered in the analyses explaining part, if not most, of the heterogeneity of trends through the study period. To this end, three complimentary statistical methodologies were used to describe the overall evolution depicted

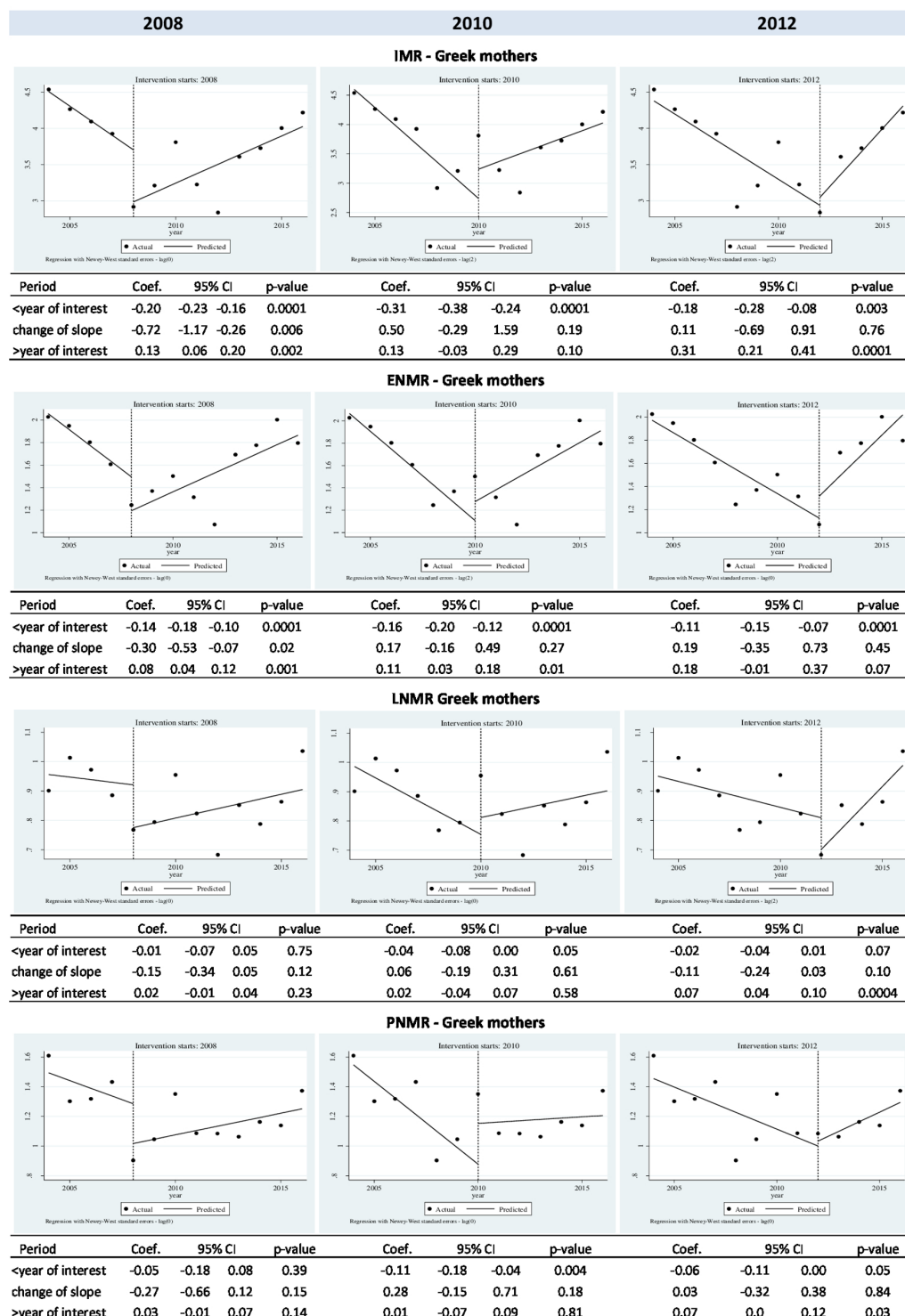


Figure 2 Interrupted time series analyses for evolution of infant (IMR), early (ENMR), late (LNMR) and post neonatal mortality rates (PNMR) in alternative prespecified years of interest (2008, 2010 and 2012) in infants born to Greek mothers.

in figure 1. Thus, we were able to enhance the validity of the results pertaining to the study of the evolution of individual IMR components, namely ENMR, LNMR and PNMR, in association with socioeconomic factors (ie, maternal nationality, place of residence and HDI) for which individual data have been available on a nationwide level among both deaths and live births during the study period. Calculation of IMR and its components was

based on the number of live births; yet, the absence of a linkage system between birth and death data consists a limitation of the study. The absence of a linkage system, as well as that of other official registries in Greece, has not allowed use of known determinants of socioeconomic deprivation or social coherence, such as parental education, employment/occupation, marital status, family income and household size, neither were data on the role

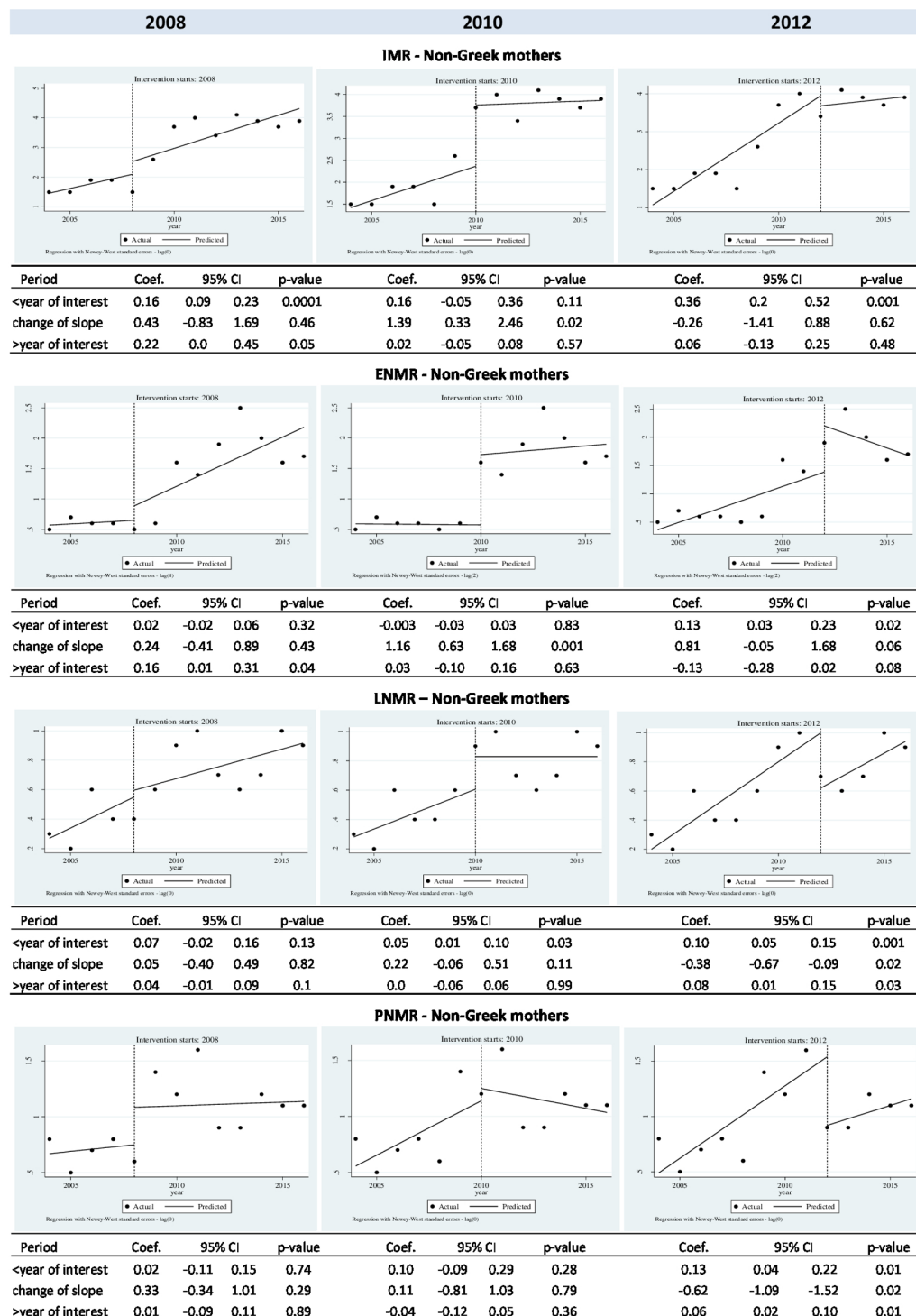


Figure 3 Interrupted time series analyses for evolution of infant (IMR), early (ENMR), late (LNMR) and post neonatal mortality rates (PNMR) in alternative prespecified years of interest (2008, 2010 and 2012) in infants born to non-Greek mothers.

of biological factors, such as parental age, gestational age and birth weight, or multiplicity of pregnancy available for both the live births and deaths series.^{5 19 24} Besides, the study period, with available information on maternal nationality and place of residence, was rather short leading to ITS analyses with few data points; however, ITS analysis can be used even for few observations; no log transformation is needed but the results should be interpreted with caution as the power depends on various

factors.²⁵ Lastly, analyses by specific cause of infant death were not set among the outcome measures of this study.

Assessing migration as a determinant of perinatal health outcome and infant death in the developed countries is a complex undertaking resulting in conflicting results of published studies. Specifically, some studies have shown that ethnic minority is a significant risk factor for unfavourable perinatal outcomes and increased neonatal and infant mortality,^{18 26–33} especially if it coincides with a

financial crisis, as was the case in Greece. Factors possibly contributing to the increased risk for poorer outcomes among children born to migrants include socioeconomic disadvantage, poor communication, discrimination, reduced utilisation of health facilities, low quality of care, and also stress and consanguinity or differing attitudes to screening and termination of pregnancy associated with preterm birth, low birth weight or congenital anomalies and lethal inherited diseases.^{26 30 34–36} By contrast, other studies present similar or even better perinatal health outcomes among some migrant groups than among natives ('healthy migrant effect/paradox').^{26–28 37 38} Refugees have been recognised as the most vulnerable group suffering increased severe neonatal morbidity and infant mortality risk,^{26 28} although no absolutely clear pattern regarding refugee or non-refugee status among migrants has been identified.³⁴

In our study, starting rates of IMR and its components among infants born to non-Greek mothers were lower compared with those of Greek mothers. Of note, the ratio of non-Greek infants among live births during 2009–2016 versus 2004–2008 was only 1.32, whereas the respective figure among infant deaths was almost threefold (data not shown). Actually, in the precrisis era, non-Greek mothers of newborns comprised mainly economic migrants, most of them of Albanian nationality living for many years, or even born, in Greece. After 2008, Greece experienced an influx of refugees with the majority of them fleeing from war and terror in Syria, Occupied Palestinian Territory, but also from Afghanistan, Iraq and other countries.^{16 17} It could be suggested that changes in the homogeneity of foreign mothers during the study period, in association with the country's economic difficulties, might have led from the 'healthy migrant effect', observed before 2008, to the deterioration of IM indicators and IMR trends, afterwards, in infants born to non-Greek mothers. We did observe significant increases in IMR trends in all ethnic groups of non-Greek mothers during the study period, especially in infants born to mothers from Africa; however, as the numbers by individual maternal nationality were rather small, this issue needs to be further studied.

Simultaneously with immigration to/through Greece, the country experienced the third wave of mass emigration in the 20th and 21st centuries; over 400 000 Greek citizens left Greece since the onset of the economic crisis, in 2008, seeking new opportunities and employment in other countries, mainly Germany, the UK and the Netherlands.^{39 40} The current emigration wave of Greeks involved mostly highly educated people (the so called 'brain-drain') of young age, leading to a decrease in the number of Greek women of childbearing age.⁴¹ This fact, along with the decrease in the fertility rate by almost 10% between 2008 and 2016, contributes significantly to the reduction in the annual number of live births in Greece by almost 23% during the period of the economic crisis.^{41 42} Furthermore, the flow of mostly affluent and well-educated people going outside Greece could also

contribute to increases in IMR among Greek children following the crisis.

Indeed, the strongly decreasing IMR trends among Greek infants were stagnated after a lag time of ~4 years of crisis and equalised with the previously sharply increasing trends among non-Greek maternal nationality infants; this time lag is reasonable⁴³ and in line with previous findings showing that following reductions in the government healthcare spending in Europe, the greatest negative effect on neonatal and post neonatal mortality was 4 and 5 years later, respectively.⁶ The irony is that the period 2012–2016, during which the crisis was deepening^{13 14} and stricter economic austerity measures were applied,⁴⁴ disparities gap in IMR trends diminished against the Greek population; IMR trends deteriorated only in infants born to Greek mothers, whereas in infants born to non-Greek mothers, IMR trends approached an anelastic highest value up to 2011 with no statistically significant change thereafter.

Disparities in IMR exist across geographic areas even in well-developed countries; that is, IMR in the USA vary by urbanisation level of maternal residency being lowest in large urban counties but highest in rural areas.⁴⁵ Rural women may face health challenges related to geographic barriers to care (less timely and/or appropriate care) and physician shortages, but they may also present differences in a number of socioeconomic and demographic risk factors, such as less education, lower income, younger age at pregnancy or greater number of children, in comparison with their urban counterparts.^{46 47} The increasing IMR trends during the study period in infants born to Greek mothers living in rural areas, as opposed to the declining IMR trends in those born to Greek mothers living in urban/semiurban areas, is worrisome. Specific causes should be further studied and addressed. Regarding infants born to non-Greek mothers, the increasing IMR trends despite living in urban areas can be explained by previous reports showing that other risk factors, that is, young maternal age (<20 years) or maternal ethnic minority, may be more powerful than place of residence.⁴⁷

Among the three IMR components, ENMR seemed to be the most 'sensitive' in reflecting adverse impacts on child health. Specifically, ENMR was overall positively associated with rural place of residence of Greek mothers' children and also presented the most sizeable increase among IM indices in non-Greeks (table 2). Moreover, among the three IM components, ENMR was the first or the only one, depending on the statistical method used, that increased after the crisis initiation in infants born to Greek mothers. ENMR, in developed countries, including Greece, represents more than 70% of neonatal deaths on account mainly of prematurity/low birth weight and congenital anomalies.^{14 48–51} Actually, it reflects perinatal health and care during pregnancy and labour, and also postnatal care in the first week of life.⁵⁰ Increased incidence of impaired perinatal parameters including low birth weight, prematurity and increased maternal age

and rate of caesarian section has been reported during the years of the economic decline in Greece.^{18 19} Cuts in public health expenditures between 2008 and 2016, reduction in healthcare workforce and paediatric nurses as well as reduction in the number of obstetrics beds, obstetricians and midwives (−45.5%, −60.2% and −27.5%, respectively)¹⁴ could possibly explain, at least in part, the observed positive ENMR trends during the postcrisis period in Greece.

The exact mechanisms leading to the disparities in trends of neonatal and infant mortality observed in this study remain to be further explored. Specific maternal, family and infant features, including detailed and punctual information on the causes of infant deaths, would have shed more light on the links between IMR trends and socioeconomic factors but were beyond the scope of this article and left for future research. Meanwhile, policies and programmes should be implemented to mitigate the negative impact of the crisis on population and infant health in Greece. Vulnerable groups, such as mothers of non-Greek nationality, of low income or of rural place of residence, should be specifically addressed and their rights to health protected. Barriers in the access of refugees to the Greek healthcare system have been identified; they are mostly related to language, culture and inadequate information about the healthcare system, but also include difficulties in the coordination of Health Services, transportation problems, issues in obtaining expertise medical assessment in the camps, lack of continuity of care, financial difficulties in making out-of-pocket payments for health and social care services and administrative barriers, among others.⁵² In response, the Greek government and several non-governmental organisations initiated commendable actions, that is, National Health System services free of charge for uninsured and vulnerable social groups including asylum seekers, translation services in public hospitals, access to specialist care/treatment with gynecologists (mostly women), midwives, dentists, psychologists and psychiatrists being lately included in the camp clinics.⁵² These actions may have prevented deterioration of IMR which are being kept at steady levels after 2011–2012 in infants of non-Greek mothers. Efforts should be continued and intensified, however, to ensure equity with local populations. Strong governmental integration policy for minorities paired with initiatives to improve social coherence, a deeply rooted mechanism for protection of health among those in need in the Greek society, along with further improvements in primary healthcare delivery could help to alleviate the cost in infant lives and ensure healthy adulthood.^{32 51} Irrespective of the crisis, improvements in the quality of perinatal and neonatal care, including centralisation of very preterm deliveries, establishment of regional perinatal centres, monitoring of the implementation of evidence-based practices in maternity and neonatal units, as well as increase in health expenditures, healthcare workforce, number of doctors and midwives/nurses, could decrease ENMR, eventually leading to overall decrease in IMR in Greece.⁵⁰

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