Recent historic increase of infant mortality in France: A time-series analysis, 2001 to 2019

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Summary

Background The infant mortality rate (IMR) serves as a key indicator of population health.

Methods We used data from the French National Institute of Statistics and Economic Studies on births and deaths during the first year of life from 2001 to 2019 to calculate IMR aggregated by month. We ran joinpoint regressions to identify inflection points and assess the linear trend of each segment. Exploratory analyses were performed for overall IMR, as well as by age at death subgroups (early neonatal [D0-D6], late neonatal [D7-27], and post-neonatal [D28-364]), and by sex. We performed sensitivity analyses by excluding deaths at D0 and using other time-series modeling strategies.

Results Over the 19-year study period, 53,077 infant deaths occurred, for an average IMR of 3.63/1000 (4.00 in male, 3.25 in female); 24.4% of these deaths occurred during the first day of life and 47.8% during the early neonatal period. Joinpoint analysis identified two inflection points in 2005 and 2012. The IMR decreased sharply from 2001 to 2005 (slope: -0.0167 deaths/1000 live births/month; 95%CI: -0.0219 to -0.0116) and then decreased slowly between 2005 and 2012 (slope: -0.0041; 95%CI: -0.0065 to -0.0016). From 2012 onwards, a significant increase in IMR was observed (slope: 0.0033; 95%CI: 0.0011 to 0.0056). Subgroup analyses indicated that these trends were driven notably by an increase in the early neonatal period. Sensitivity analyses provided consistent results.

Interpretation The recent historic increase in IMR since 2012 in France should prompt urgent in-depth investigation to understand the causes and prepare corrective actions.

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Research in context

Evidence before this study

Over the last 30 years, the infant mortality rate (IMR) has declined in all high-income countries, but the situation is heterogeneous. Besides some countries with continuously decreasing IMR since World War II, the rate of decline in IMR seems to flatten in recent decades in some other countries including France. Despite this circumstance, the reduction of IMR in France has not been identified as a priority target by public health authorities and no in-depth analysis of IMR in France was conducted.

Added value of this study

This study shows evidence of a recent increase in overall IMR, driven notably by an increase in the early neonatal period. Our findings were robust to various sensitivity analyses, including those accounting for variations of clinical practices in the perinatal period and registration artifacts.

Implications of all the available evidence

This historic increase of IMR in France should prompt in-depth investigations to prepare corrective actions. A first important action would involve routine provision, alongside age at death data during the first year of life and sex, of information regarding gestational age at birth, weight at birth, presence of a severe congenital malformation, and sociodemographic factors.

Methods

General design and data sources

We conducted a time-series analysis using registered data from the French National Institute of Statistics and Economic Studies (INSEE), a governmental agency that collects and publishes information about the French economy and population. INSEE receives from the Civil Registry all births and deaths certificates (INSEE, data producer − ADSIP, broadcaster of the official statistics data archives). We included monthly aggregated data on all live births and deaths during the first year of life from 2001 to 2019 that occurred in metropolitan France (i.e., excluding overseas territories). This period includes the longest series available to us, with the relevant variables (e.g., number of live births per month by sex), at the time of our analysis. The period of analysis did not go further than December 2019 because we anticipated that the COVID-19 pandemic might have impacted health indicators such as the IMR. Furthermore, as in most European countries, there is a lag before finalized birth and death data for a given year are available for research.

Live birth was defined based on a medical certificate stating that the infant was born alive and viable. In France, until 2001, viability was defined by law with a threshold of 180 days of gestation. Between 2002 and 2007, the viability was defined according to two of three
criteria of the World Health Organization definition: a gestational age of at least 22 weeks of amenorrhoea or a weight of at least 500 g. Since August 2008, there are no criteria for registering infants born without life as this decision is now made by the parents. Vital statistics data (e.g., born alive or without life) are therefore no longer used for monitoring the stillbirth rate. Data included singleton and multiple births.

Because we performed this study on anonymized and publicly available data, no ethical human subjects’ approval was needed. We followed the Strengthening The Reporting of Observational Studies in Epidemiology (STROBE) checklist for reporting.

Statistical analysis

Time-series analysis. We used a joinpoint regression model to explore potential patterns of IMR aggregated by month (i.e., number of deaths of infants under 1 year old /1000 live births registered in the same month), our main outcome measure. Joinpoint analysis identifies inflection points (i.e., joinpoints) where a significant change in linear trends occurs using a series of Monte Carlo permutation tests with Bonferroni adjustment for multiple comparisons. The number of joinpoints was selected based on permutation tests and the Bayesian Information Criterion which allowed segments with at least 22 time points (i.e., 10% of the total time points). Then we evaluated whether there was a statistically detectable linear trend in each time segment, using a p-value of less than 0.05 for detection. We added autoregressive (AR) error terms if autocorrelation remained in the residuals. Seasonality was assessed by visual inspection of the autocorrelation and partial autocorrelation functions and, if discovered, removed using AR terms. Then, we conducted subgroup analyses stratified by age at death and by sex, applying the same joinpoints as in the overall time series. We identified joinpoints using the Joinpoint trend analysis software from the Surveillance Research Program of the National Cancer Institute Version 4.8.0.1 (Statistical Research and Applications Branch, National Cancer Institute, US). Joinpoint linear regressions then involved the use of R software (R Foundation for Statistical Computing, Vienna, Austria).

Sensitivity analyses. The number of deaths registered during the first day of life may have changed over time due to changes in legislation (see above), particularly from 2008. Variability on the definition of viability, depending on local clinical practices (in particular the initiation of neonatal care) or the wishes of the parents, could have affected registering practices. In addition, a growing number of fetuses or stillbirths could have been declared as live born during the study period, to allow parents to organize funerals and ease mourning. Although these changes in registering practices in 2002 and 2008 had their greater impacts on the stillbirths rate, we checked if they were also associated with an immediate change in IMR. Thus, we performed segmented linear regression with interruption points in January 2002 and August 2008, without lag time, on the data from January 2001 to December 2011 (i.e., 40 months after the adoption of the new registering practice in August 2008). Because the implementation of the new registering legislation may have taken time, we also ran models with six-then twelve-month lag times (i.e., the six and twelve months following the interruption points were excluded from the model, respectively). Finally, we ran a regression mixing the inflection points previously identified by the joinpoint regression and the interruption points that were associated with a significant immediate change in segmented linear regressions.

To test the robustness of our exploration, we repeated the main analyses excluding deaths during the first day of life. We also performed sensitivity analyses on the overall IMR using autoregressive-integrated-moving average (ARIMA) time series models and segmented linear regression adjusting for seasonality and autocorrelation (if needed), with the inflection points identified previously in the joinpoint regression (see Appendix for more details). ARIMA modeling was performed in SCA (Scientific Computing Associate Corp., Chicago, Illinois, USA) software and segmented linear regression in STATA (Stata Corp, College Station, Texas, USA).

Results

Descriptive analysis

Over the 19-year study period, there were 53,077 infant deaths among 14,622,096 live births. The overall IMR over the study period was 3.63 per 1000 live births. Males accounted for 56.3% of infant deaths (IMR 4.00) and females for 43.7% (IMR 3.25). A total of 25,160/53,077 (47.4%) and 11,065/53,077 (20.8%) deaths occurred in the early and late neonatal periods, respectively (Table 1).

Overall trends in infant mortality rate

The evolution of IMR over the study period was not monotonic (Figure 1). Autocorrelation plots showed no clear seasonality. The best-fitting model for overall IMR using jointpoint regression included two break points at the 53rd (May 2005) and 138th (June 2012) months of the series, further defining three time segments (Figure 1).

From January 2001 to May 2005 (Table 2), the overall IMR significantly decreased over time (slope,
-0.0167 deaths/1000 live births/month; 95% confidence interval [CI], -0.0219 to -0.0116). Between May 2005 and June 2012, the overall IMR significantly decreased but at a much slower pace (slope, -0.0041; 95%CI, -0.0065 to -0.0016). From June 2012 to December 2019, however, a significant increase was observed in overall IMR (slope, 0.0033; 95%CI, 0.0011 to 0.0056). This monthly increase corresponds to an annual increase in IMR of +0.04 per 1000 live births.

**Sensitivity analyses**

Deaths that occurred during the first day of life represented 24.4% (12,932/53,077) of total infant deaths. This share increased from 24.2% in 2001 to 26.3% in 2019 (eFig. 2) in both males and females. When excluding deaths that occurred during the first day of life, patterns of overall IMR were not affected (Table S1). Sensitivity analyses using ARIMA and segmented linear regression modeling strategies also yielded consistent results, including for the significant increase in IMR in the 2012–2019 period (Table S1).

Segmented linear regressions did not detect any impact of the 2002 changes in birth registering practices on IMR level and trend (Table S2 and eFig. 3). The adoption of new registering legislation in 2008, however, preceded a significant immediate increase in IMR.
of 0·3203 deaths/1000 live births (95%CI: 0·1027 to 0·5380) while the trend was not significantly affected and remained in downward trend until December 2011 (Table S2 and eFig. 3). Similar findings were found when 6-month and 12-month lags were introduced into the models (Table S2 and eFig. 3). A final regression model mixing the two inflection points detected by the joinpoint regression (May 2005 and June 2012) and the single interruption point associated with a significant immediate change in segmented regression (August 2008) summarizes our findings and confirms an increase in IMR after 2012 (slope, 0·0037; 95%CI, 0·0020 to 0·0054 - eFig. 4).

Discussion

Main findings and strengths
This study used advanced time-series modeling to explore time trends and components of IMR in France using the most up-to-date nationwide data, covering nearly two decades. This study shows evidence of a recent increase in overall IMR, driven notably by an increase in the early neonatal period. Our findings were robust to various sensitivity analyses, including those accounting for variations of clinical practices in the perinatal period and registration artifacts. Indeed, sensitivity analyses showed that 2008 changes in registering legislation preceded a slight immediate increase in IMR level but not in IMR trend. IMR showed a downward trend in the three years following the 2008 changes, suggesting that the recent worrisome increase in IMR is not driven by registration artifacts.

Previous studies in England also found a sustained IMR rate increase since 2014.28,29 Our study and the study by Nath et al. make the same observation that the recent increases in both countries were driven by deaths in the early neonatal period. Nath et al. suggested that registration practices may play a role in the increasing deaths registered as live births <23 weeks, but we demonstrated that it was not the case in France.29 The consistent timing and structure of the change in IMR in France and England, as well as other data showing heterogeneous patterns in IMR rates in other HICs (eFigure 5), warrant more studies investigating whether the same phenomenon occurred in other HICs.29,30

Limitations
We acknowledge some limitations of this study. The publicly available data we used do not contain information regarding major IMR risk factors such as gestational age at birth, weight at birth, or presence of a severe congenital malformation.16 Thus, we were not able to explore the exact role of these factors in the recent increase of IMR, notably for the neonates who die in the early neonatal period.16,31,32 Second, previous studies conducted in Western Europe and the USA demonstrated the association between inequalities in numerous aspects of health and infant mortality.11 Notably, in England, IMR rose sharply in the most disadvantaged areas.28 Because information on sociodemographic factors known as risk factors for IMR (mother’s age, nationality, education level, and social and geographic contexts)16 were not available in our dataset, we could not explore these associations. More generally, unlike other HICs, in France, clinical birth characteristics, such as gestational age, are not recorded on the birth certificates and there is no medical birth registry collecting data on mortality and morbidity of every newborn, their medical care, and those of their mother. Yet, the rate of child poverty in France has recently shown an alarming upward trend.16,34
**Interpretation**

Our study was not designed to decipher the precise causes of the recent increase in IMR, but some can be discussed post hoc. Our findings suggest that the increase in IMR was mainly driven by an increase in early neonatal deaths. The key risk factors of early neonatal deaths reported in the literature include indicators of health at birth (e.g., prematurity, presence of congenital anomalies), and these factors are in turn affected by maternal health before and during pregnancy, and upstream socioeconomic factors affecting family wellbeing during pregnancy. Regarding maternal health before and during pregnancy, the French National Perinatal Surveys revealed that maternal age, body mass index, and smoking during pregnancy had increased steadily during the study period. Of note, the proportion of mothers ≥ 35 years old increased from 12.5% to 21.3% between 1995 and 2016 and the proportion of obese women rose from 7.5% to 11.8% between 2003 and 2016. Furthermore, nearly one-fourth of women who gave birth in 2018 were born abroad, and this proportion is growing. Migrants have a higher risk of inadequate prenatal care utilization, potentially related to social inequality. Thus they have a higher risk of adverse maternal and fetal outcomes than women born in France. Regarding severe congenital malformations, there is an active national screening and pregnancy termination policy in France and declining trends and stagnation of their prevalence are observed as in other European countries. Regarding prematurity, the rate of preterm birth in France increased steadily from 4.5% in 1995 to 6.5% in 2016 while the survival rate of very and extremely premature babies remained low compared to other countries. However, recent studies showed improvement in the survival rate of very preterm children in France. Improved care for mothers at high risk of pregnancy complications may lead to the prevention of stillbirths but this may also defer some deaths to the neonatal period. These findings indicate that France is not closing the gap with the HICs showing the lowest IMR rate and continued decreases. This increase in IMR in France should prompt in-depth investigations to identify its causes, prepare corrective actions and monitor future trends. A first important action would involve routine provision, alongside age at death data during the first year of life and sex, of information regarding gestational age at birth, weight at birth, presence of a severe congenital malformation, and sociodemographic factors.

**Conclusion**

Our study highlights a recent significant and historically unprecedented rise in IMR in France since 2012. The study results were robust to sensitivity analyses considering changes in clinical practices and potential artifacts, including registering issues of deaths during the first day of life. This rise occurred more specifically during the early neonatal period. These findings indicate that France is not closing the gap with the HICs showing the lowest IMR rate and continued decreases. This increase in IMR in France should prompt in-depth investigations to identify its causes, prepare corrective actions and monitor future trends. A first important action would involve routine provision, alongside age at death data during the first year of life and sex, of information regarding gestational age at birth, weight at birth, presence of a severe congenital malformation, and sociodemographic factors.

**Contributors**

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**Declaration of interests**

The authors have no conflict of interest to declare. We affirm that this manuscript is an honest, accurate, and
transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of any organization or company.

Supplementary materials
Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lanepre.2022.100339.

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