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

Nhung T.H. Trinh,[a] Sophie de Visme,[a,b] Jérémie F. Cohen,[a,c] Tim Bruckner,[d] Nathalie Lelong,[a] Pauline Adnot,[c] Jean-Christophe Rozé,[b,e] Béatrice Blondel,[a] François Goffinet,[a,f] Grégoire Rey,[g] Pierre-Yves Ancel,[a,h] Jennifer Zeitlin,[a] and Martin Chalumeau [a,c,*]

[a]Centre of Research in Epidemiology and Statistics (CRESS), Obstetrical, Perinatal and Pediatric Epidemiology Research Team, INSERM, Université de Paris, Maternité Port-Royal, 53 Avenue de l'Observatoire, 75014, Paris F-75004, France
[b]Clinical Investigation Centre, INSERM, Nantes University Hospital, CIC 1413, Nantes, France
[c]Department of General Pediatrics and Pediatric Infectious Diseases, Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Necker - Enfants malades, Université de Paris, Paris, France
[d]Program in Public Health and Center for Population, Inequality, and Policy, University of California, Irvine, CA, USA
[e]Department of Neonatology, Nantes University Hospital, Nantes, France
[f]Maternité Port-Royal, AP-HP, Hôpital Cochin, Université de Paris, Paris, France
[g]Center for Epidemiology on Medical Causes of Death (CépiDc), INSERM, Le Kremlin-Bicêtre, France
[h]Clinical Investigation Centre, AP-HP, P1419, Paris, France

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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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*Corresponding author at: Centre of Research in Epidemiology and Statistics (CRESS), Obstetrical, Perinatal and Pediatric Epidemiology Research Team, INSERM, Université de Paris, Maternité Port-Royal, 53 Avenue de l'Observatoire, 75014, Paris F-75004, France.
E-mail address: martin.chalumeau@inserm.fr (M. Chalumeau).

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.

Introduction

The reduction of preventable deaths in children is a cornerstone of United Nations reaffirmed goals for human development.[1] The vast majority of pediatric deaths occur in the first year of life,[2,3] and the infant mortality rate (IMR) has been defined as the number of deaths of children under one year of age [D0-D364] per 1000 live births in a given period.[4] Infant mortality is often classified into three age ranges, reflecting differences in the causes of death at these ages: the early neonatal period [D0-D6], the late neonatal period [D7-D27], and the post-neonatal period [D28-D364].[5–7] The IMR serves as a key indicator of population health, given its strong relationship with socio-economic development and quality of preventive and curative care.[8]

Over the last 30 years, the IMR has declined in all high-income countries (HICs), but the situation is heterogeneous. In some countries like Finland, Iceland, Japan, and Slovenia, IMR has been continuously decreasing since World War II, including in the most recent years, and has now reached very low levels of approximately 2 deaths per 1000 live births.[9] Conversely, in other HICs, the rate of decline in IMR seems to flatten in recent decades. For example, in France, the continual decrease observed since World War II appears to be slowing (**eFig. 1**), leading to a drop in the world rank for IMR, from the 7th in 1989 to 25th in 2017, with an IMR of 3·5 deaths per 1000 live births in 2017.[3,10–12] Differences in IMR across countries and within countries across time should be interpreted with caution because of variations of clinical practices in the perinatal period and birth and death registration policies (also called registration "artifacts").[13,14] However, the differences observed between HICs imply that around 1200 excess infant deaths occur each year in France. Despite this circumstance, the reduction of IMR in France has not been identified as a priority target by public health authorities.[15]

Although IMR data are regularly published, and concerns have been raised about stagnating mortality in comparison with European neighbors, there has been no in-depth analyses in France of its recent time trends and its different components.[11,16] This knowledge gap precludes its prioritization among public health issues, the identification of the main drivers of IMR trend, and the definition of corrective plans. In this exploratory study, we used a joinpoint time-series analysis to examine changes over time in IMR in France from 2001 to 2019. We also examined the age-specific components of IMR and the potential role of registration artifacts.

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.[17]

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 amenorrhea or a weight of at least 500 g.[18] 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.[19,20] 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.[21]

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.[22,23] 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.[24] 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.[4] 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,[19,25,26] 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.[19,27] Although these changes in registering practices in 2002 and 2008 had their greater impacts on the stillbirths rate,[16] 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 joinpoint 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,

	Number (%)	Infant deaths per 1000 live births
Overall [D0-D364]	53,077 (100)	3·63
Subgroups		
Age at death		
Early neonatal [D0-D6]	25,160 (47·7)	1·72
Late neonatal [D7-D27]	11,065 (20·8)	0·76
Post neonatal [D28-D364]	16,852 (31·8)	1·15
Sex		
Male	29,902 (56·3)	4·00
Female	23,175 (43·7)	3·25

***Table 1*: Infant deaths registered in France (2001–2019).**

-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.

Age- and sex-specific trends in infant mortality rate

Analysis of IMR by age at death subgroups revealed heterogeneous patterns (Table 2). In the early neonatal period, there was a significant decrease in IMR in the first segment, then a stable period, followed by a significant rise from 2012 to 2019. In the late neonatal period, the IMR significantly decreased between 2001 and 2005 then significantly increased between 2005 and 2012 and remained stable between 2012 and 2019. In the post-neonatal period, the IMR significantly decreased between 2001 and 2005 and between 2005 and 2012 then remained stable between 2012 and 2019.

Analysis of IMR in males showed similar patterns compared to those for overall IMR, with a decrease in the first two segments and a significant increase in the last time segment (Table 2). In females, IMR decreased between 2001 and 2005 and remained stable afterwards.

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

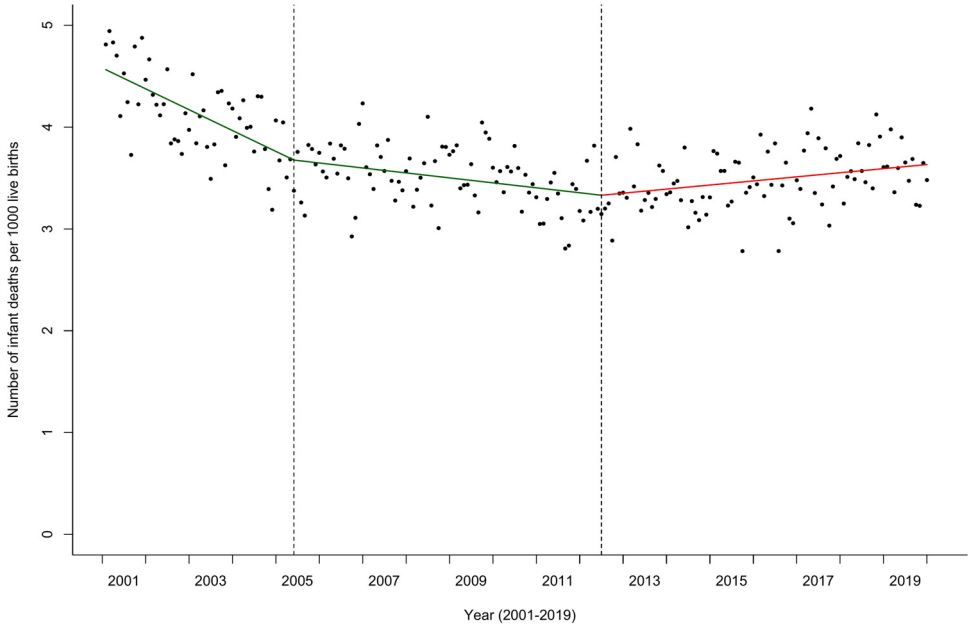

Figure 1. Infant mortality rate in France (2001–2019): temporal patterns of the monthly number of deaths of infants under one year of age per 1000 live births (continuous line) and breakpoints where the slope changed (dotted vertical line).

	Slope of trend**		
Period	**Jan 2001 - May 2005***	**May 2005 - June 2012***	**June 2012 – Dec 2019**
Overall	-0·0167 (-0·0219; -0·0116)**	-0·0041 (-0·0065; -0·0016)	0·0033 (0·0011; 0·0056)
Subgroup			
Age at death			
Early neonatal [D0-D6]	-0·0096 (-0·0129; -0·0064)	-0·0009 (-0·0025; 0·0007)	0·0031 (0·0018; 0·0044)
Late neonatal [D7-D27]	-0·0007 (-0·0011; -0·0004)	0·0023 (0·0005; 0·0041)	-0·0111 (-0·0254; 0·0033)
Post-neonatal [D28-D364]	-0·0182 (-0·0312; -0·0051)	-0·0027 (-0·0032; -0·0021)	0·0009 (-0·0019; 0·0038)
Sex			
Male	-0·0469 (-0·0768; -0·0170)	-0·0079 (-0·0102; -0·0056)	0·0041 (0·0013; 0·0069)
Female	-0·0144 (-0·0198; -0·0092)	-0·0017 (-0·0039; 0·0006)	0·0032 (-0·0003; 0·0068)

***Table 2*: Trends in infant mortality rate in France (2001−2019): joinpoint linear regression analysis.**
Abbreviation: CI, confidence interval; D, day.
*inflection points identified using joinpoint analysis.
**coefficient (95%CI), unit: number of deaths/1000 live births/month
Color code: statistically significant decreases ($p < 0·05$) are in green; statistically significant increases ($p < 0·05$) are in red; non statistically significant changes ($p \geq 0·05$) are in yellow (decrease) or orange (increase).

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.[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.[33] 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*.[2] 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.[35,36] 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.[37,38] 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.[38] Furthermore, nearly one-fourth of women who gave birth in 2018 were born abroad, and this proportion is growing.[39] 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.[40] 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.[41] Regarding prematurity, the rate of preterm birth in France increased steadily from 4·5% in 1995 to 6·0% in 2016 while the survival rate of very and extremely premature babies remained low compared to other countries.[38,42] However, recent studies showed improvement in the survival rate of very preterm children in France.[38,42,43] 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 and increase neonatal mortality. However, data from the Euro-Peristat network suggests an increase in the stillbirth rate in France from 4·3% in 2010 to 4·8% in 2015, supporting the concerns raised in this analysis of IMR. Up-to-date data on the potential factors associated with IMR should be routinely collected and analyzed. In the meantime, strategies to improve further the quality of French perinatal care, especially among infants born extremely premature are thus urgently needed.[44]

The increase in IMR was also partially driven by an increase in infant male deaths.[45] We found that the IMR in males was higher than in females, consistently with previous assessments.[16] Males are generally disadvantaged regarding infant mortality because of their greater vulnerability to mortality from conditions associated with prematurity and development.[33,46] Males also appear more sensitive to ambient stressors in ways that increase the risk of being delivered preterm.[47] Furthermore, the IMR of male infants born extremely preterm was found about 30% higher than that of females.[48,49] However, we can not exclude that the lack of significant IMR trend among females was only related to a lower statistical power given a lower IMR rate.

The components of IMR after the early neonatal period have also stopped declining in France. One of the explanations could be the high level of sudden infant death syndrome rate in France compared to other European countries.[36]

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 of 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

Nhung TH Trinh: formal analysis, methodology, visualisation, software, writing-original draft, writing-review&editing.

Sophie de Visme: data curation, methodology, visualisation, writing-review&editing.

Jérémie F Cohen: conceptualisation, methodology, supervision, writing-review&editing.

Tim Bruckner: methodology, writing-review&editing

Nathalie Lelong: data curation, writing-review&editing.

Pauline Adnot: writing-review&editing.

Jean-Christophe Rozé: methodology, writing-review&editing.

Béatrice Blondel: methodology, writing-review&editing

François Goffinet: methodology, writing-review&editing

Grégoire Rey: methodology, writing-review&editing

Pierre-Yves Ancel: methodology, writing-review&editing

Jennifer Zeitlin: methodology, writing-review&editing.

Martin Chalumeau: conceptualisation, methodology, supervision, writing-review&editing.

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.lanepe.2022.100339.

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