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Social inequalities in infant mortality related to congenital anomalies: a population-based study in Paris

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Abstract

Title: Social inequalities in infant mortality related to congenital anomalies: a population-based study in Paris

Background
Congenital anomalies (CAs) are a major cause of infant mortality. Despite universal prenatal care in France, social inequalities in CA outcomes may persist. This study aimed to: (1) assess socio-spatial disparities in CA prevalence and infant mortality; (2) examine associations between socioeconomic status (SES) and antenatal detection, termination of pregnancy for fetal anomaly (TOPFA), and live birth.

Methods
Data came from the Paris congenital anomaly registry (remaPAR) covering 2019–2022. Maternal addresses were geocoded to the IRIS level and linked to census data. A deprivation index (P-FDep) was constructed using principal component analysis. First, we estimated crude odds ratios (cOR) for risk of CA prevalence and infant mortality across deprivation quintiles using a census-based control population. We then estimated relative risks (RR) adjusted for individual SES variables (maternal occupation, insurance status, geographic origin) using Poisson regression models to assess the association between SES and key outcomes.

Results
Compared to the least deprived area (Q1), CA prevalence (cOR = 1.25, 95% CI: 1.11–1.40) and infant mortality (cOR = 3.70, 95% CI: 1.50–9.11) were higher in the most deprived areas (Q5). The antenatal detection rate was 71.2%, but it was significantly lower among women of sub-Saharan African origin (aRR = 0.85, 95% CI: 0.78–0.93). Among detected cases, women with no defined occupation (aRR = 0.73, 95% CI: 0.60–0.90) and those of North African (aRR = 0.85, 95% CI: 0.72–1.01) or sub-Saharan African origin (aRR = 0.81, 95% CI: 0.66–0.99) were less likely to terminate, contributing to higher proportions of live births in these groups. P-FDep was associated with all outcomes in unadjusted models, but these associations were attenuated after adjustment.

Conclusion
This study highlights social differences across the CA care pathway, which reflect both structural factors and variations in prenatal decision-making. Further research is needed to assess causal pathways and the contribution of each care stage to infant mortality.

Keywords: social inequalities, deprivation score, congenital anomalies, infant mortality

Résumé

Titre : *Inégalités sociales dans la mortalité infantile liée aux anomalies congénitales : une étude à partir du registre des anomalies congénitales de Paris.*

Contexte

Les anomalies congénitales (AC) sont une cause majeure de mortalité infantile. En France, malgré un accès universel aux soins prénatals, des inégalités sociales peuvent persister. Cette étude visait à : (1) évaluer les disparités socio-spatiales dans la prévalence des AC et la mortalité infantile ; (2) examiner les associations entre le statut socio-économique (SSE) et la détection prénatale, l'interruption médicale de grossesse pour anomalie fœtale et la naissance vivante.

Méthodes

Les données proviennent du registre des anomalies congénitales de Paris (remaPAR) en 2019-2022. Les adresses maternelles ont été géocodées au niveau de l'IRIS et appariées aux données de recensement. Un indice de déprivation (P-FDep) a été construit à l'aide d'une analyse en composantes principales. Nous avons d'abord estimé les odd ratios bruts (ORb) pour le risque de prévalence des AC et la mortalité infantile selon les quintiles de déprivation en utilisant une population de contrôle basée sur le recensement. Nous avons ensuite estimé les risques relatifs (RRa) ajustés sur les variables individuelles du SSE à l'aide de modèles de Poisson.

Résultats

Par rapport à la zone la moins défavorisée (Q1), la prévalence des AC (ORb = 1,25, IC 95 % : 1,11-1,40) et la mortalité infantile (ORb = 3,70, IC 95 % : 1,50-9,11) étaient plus élevées dans les zones les plus défavorisées (Q5). Le taux de détection prénatale était de 71,2%, mais il était plus faible chez les femmes originaires d'Afrique subsaharienne (RRa = 0,85, IC 95 % : 0,78-0,93). Parmi les cas détectés, les femmes sans profession définie (RRa = 0,73, IC 95 % : 0,60-0,90) et celles originaire d'Afrique du Nord (RRa = 0,85, IC 95 % : 0,72-1,01) ou subsaharienne (RRa = 0,81, IC 95 % : 0,66-0,99) étaient moins susceptibles d'interrompre leur grossesse, contribuant à des proportions plus élevées de naissances vivantes dans ces groupes. Le P-FDep était associé aux résultats de santé dans les modèles non ajustés, mais ces associations étaient atténuées après ajustement.

Conclusion

Cette étude met en évidence des différences sociales dans le parcours de soins de l'AC, qui peuvent refléter à la fois des facteurs structurels et des variations dans la prise de décision prénatale. Des recherches supplémentaires sont nécessaires pour évaluer la contribution de chaque étape de soins à la mortalité infantile.

Mots-clés : inégalités sociales, score de déprivation, anomalies congénitales, détection prénatale, mortalité infantile

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List of Abbreviations

AME	Aide Médicale de l'État
ART	Assisted Reproductive Technology
BMI	Body Mass Index
BPA	British Paediatric Association
CA	Congenital Anomalies
CER	Evaluation Committee of Registries
CHD	Congenital Heart Defects
CMU-C	Couverture Maladie Universelle Complémentaire
FNPS	French National Perinatal Survey
FDep	French Deprivation Index
GA	Gestational age
GEE	Generalised Estimating Equations
JRC-EUROCAT	Joint Research Centre - European Surveillance of Congenital Anomalies
ICD10	International Classification of Diseases 10th revision
IMG	Interruption Médicale de Grossesse
IMR	Infant Mortality Rate
INSEE	The National Institute of Statistics and Economic Studies
IRIS	Îlots Regroupés pour l'Information Statistique
MICE	Multiple Imputation by Chained Equations
NMR	Neonatal Mortality Rate
OMIM	Online Mendelian Inheritance in Man
OR	Odds Ratio
PCA	Principal Component Analysis
P-FDep	Perinatal – French Deprivation Index
remaPAR	Registre des malformations congénitales de Paris
RR	Relative Risk
SES	Socioeconomic Status
SS	Sécurité Sociale
SSA	Sub-Saharan Africa
TOPFA	Termination of pregnancy for fetal anomaly
WHO	World Health Organisation

1. Introduction

1.1. Infant mortality in France

The infant mortality rate (IMR) – defined as the number of deaths within the first year of life per 1000 live births – is a key indicator of perinatal health and healthcare system performance. Over the past three decades, significant global progress has been made in reducing the IMR by 58%, from 64 deaths per 1000 live births in 1990 to 27 in 2023 (1). While the global burden remains concentrated in low- and middle-income countries, recent trends in high-income settings have also raised concern. In some countries, including France, IMR has stopped declining and even begun to rise, going from 3.5 per 1,000 live births in 2011 to 4.0 in 2023 (2). This upward trend in infant mortality in France has been primarily driven by an increase in the neonatal mortality rate (NMR), i.e. deaths occurring within the first 28 days of life. Between 2001 and 2019, neonatal deaths accounted for nearly 80% of the observed rise in infant mortality, suggesting that the early neonatal period (death <7 days) is a key contributor to this concerning shift (3). France has been ranked 22nd out of 33 European countries for both NMR and stillbirth rates (4,5). One hypothesis for this stagnation is the growing impact of social and health inequalities.

A study in French metropolitan areas 2013 has demonstrated that both IMR and NMR are closely linked to socioeconomic conditions at individual and area levels (6). These findings suggest that socioeconomic disadvantage contributes to mortality not only through individual level socioeconomic characteristics—such as income or education—but also through broader structural barriers, like neighbourhood resources and healthcare access.

A recent study published in 2025 conducted a spatiotemporal analysis of neonatal mortality in France between 2001 and 2017, confirming persistent socioeconomic inequalities. Higher neonatal mortality rates were observed in more deprived areas, particularly in urban settings and in cities with a higher proportion of migrants (7). These findings reinforce earlier evidence from 2013 linking infant and neonatal mortality to socioeconomic conditions in French metropolitan areas, underscoring the enduring impact of both personal and contextual inequalities on perinatal survival (6).

1.2. Congenital anomalies

In high-income countries, congenital anomalies – also known as birth defects – are one of the leading causes of infant mortality, contributing to between 20 and 30% of deaths (8). Congenital anomalies (CA) are also responsible for long-term disabilities and morbidities (9,10). CA are defined by the World Health Organisation (WHO) as structural or functional

abnormalities that arise during intrauterine life and affect approximately 3-4% of all births (11). These abnormalities are typically associated with significant medical, social or cosmetic consequences (12).

They encompass a wide range of disorders, which can be classified into structural anomalies (physical anomalies of organs or body parts) and chromosomal or genetic anomalies (alterations in genetic material). Examples include structural anomalies like congenital heart defects (CHDs) or neural tube defects, and chromosomal anomalies such as Down syndrome. CHDs in particular are among the most frequent forms of CA and remain a leading cause of neonatal mortality (13). Studies have shown that CHDs might be associated with socioeconomic status (SES), whether measured at the individual level – through factors such as maternal smoking, obesity or diabetes, which are often regarded as socially patterned health behaviours – or at the area level (e.g. neighbourhood deprivation) (14–19).

1.3. CA: antenatal detection and termination policy in France

Socioeconomic inequalities in infant mortality due to CA can arise because of unequal access to screening programs or parental decisions about the management of severe anomalies during pregnancy. In France, there is a well-developed healthcare system that offers universal coverage through the national insurance scheme (Sécurité Sociale), with maternity care – including prenatal screening – fully covered. CA are mainly detected during pregnancy with ultrasounds. In France, three routine ultrasound examinations recommended at approximately 12, 22, and 32 weeks of gestation for all pregnant women with an objective of assessing fetal development and growth, and identifying structural anomalies. In addition to ultrasound, maternal serum screening are also recommended for all pregnant women at the end of the first trimester of pregnancy to detect chromosomal abnormalities, specifically the common trisomies: trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome). A study in France in 2001-2021 estimated that 70% of CA are detected antenatally (9).

When a severe CA is detected antenatally, couples can make a request for a termination of pregnancy for fetal anomaly (TOPFA), regardless of gestational age as permitted by French law (Interruption Médicale de Grossesse, or IMG), following approval by a multidisciplinary team (20). Unlike many other countries, France allows late TOPFA after 22 weeks of gestation.

Despite universal healthcare and active antenatal screening policies, access to and utilisation of these services still vary by socioeconomic status. Multiple studies have shown that structural inequalities, maternal characteristics (such as education, occupation, and health behaviours), neighbourhood deprivation, and cultural, religious, or ethical beliefs can all

influence access to prenatal diagnosis, decision-making around TOPFA, and ultimately, infant survival (14–19,21,22). Evidence from the UK indicates that women in more deprived areas were significantly less likely to terminate pregnancies for severe anomalies compared to women in least deprived areas, leading to higher rates of live births with anomalies and elevated neonatal mortality in these groups (19). In France, earlier national surveys have documented lower screening uptake and delayed initiation of prenatal care among immigrant and lower-income women, reflecting structural inequalities in access to care and information (20). These findings indicate that social disparities in perinatal outcomes persist even within universal healthcare systems. Such inequalities may also influence the prevalence of CA and related infant mortality. Addressing these disparities is essential for promoting health equity and informs the rationale for the present study.

1.3.1. Study gap and rationale

Given the high contribution of CA to infant mortality and the potential influence of SES, there is a clear need to investigate these issues in the French context. Despite this, research examining social inequalities in CA prevalence, detection, and management remains limited in France. One key challenge is that such investigations require data covering all fetuses and newborns affected by CA—not just those recorded as births or deaths from 22 weeks of gestation onwards, as is currently the case. These comprehensive data are available only in CA registries, which often contain limited socio-economic information and are not linked to other datasets describing live births with comparable SES indicators.

Using geocoding is one option for describing socioeconomic risk factors and assessing their impact on CA mortality, especially when this can be conducted at a fine-grained geographic scale. However, to date, no published research in France has utilised geocoded registry data at the IRIS level – the smallest administrative and statistical unit– to assess how CA are distributed and the socio-spatial differences in management or outcomes. Analysing data at this granular level enhances the ability to detect health inequalities that may be masked by larger-scale analyses (6,23,24).

France is uniquely positioned to investigate these issues due to its robust CA surveillance infrastructure. The country maintains several population-based registries, including the Paris Registry of Congenital Anomalies (remaPAR), which systematically records all CA within its geographic catchment area. Each case can be geocoded to the mother’s residence, enabling linkage with both individual-level (e.g., parental occupation, education) and area-level (e.g., neighbourhood deprivation index) socio-economic indicators. This dataset provides a unique opportunity to investigate the role of SES in CA prevalence and infant mortality, as well as in the likelihood of antenatal detection and pregnancy outcomes such as TOPFA and live birth.

The objectives of the study are twofold, aiming to:

1) Describe socio-spatial disparities in risk of CA prevalence and associated infant mortality
2) Assess the association between individual- and area-level SES and key outcomes along the congenital anomaly care pathway, specifically antenatal detection, TOPFA, and live birth.

2. Methodology

2.1. Data source

The primary source of data for the study is from remaPAR, a population-based registry established in 1981 to monitor CA in Paris, France. The registry includes all cases of CA, including chromosomal and genetic anomalies, detected during pregnancy and up to the infant's discharge from maternity ward or hospitalisation, from women residing and living in Paris. This includes live births and stillbirths ≥ 22 weeks of gestation and TOPFA at any gestational age. This geographical area amounts to approximately 22,000 births annually. Approximately 800 cases are recorded each year.

remaPAR adheres to the methodologies defined by the JRC-EUROCAT (Joint Research Centre - European Surveillance of Congenital Anomalies) network, a European population-based surveillance network for CA (25). As recommended by EUROCAT, CA are coded according to International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD10) and use a fifth character established by the British Paediatric Association (BPA) for more precise coding, along with OMIM codes for syndromes.

Case identification for CA in Paris is conducted through active surveillance using multiple data sources, including maternity, neonatology, intensive care, pediatric surgery, cytogenetics, fetopathology, and medical information departments, as well as health certificates (certificats de santé), which are mandatorily completed by a paediatrician within the first eight days of life for all newborns. All cases are identified and validated through comprehensive review of medical records, birth registries, diagnostic staff reports, and autopsy findings, up to the point of hospital discharge. Once validated, detailed data are extracted from medical records using a standardised form that includes parental sociodemographic characteristics (such as age, geographical origin, occupation, employment status, and insurance coverage), medical and family history, and pregnancy-related information (including medications taken during the first trimester, results of routine ultrasound scans, maternal serum screening for Down Syndrome, fetal samples, and pregnancy outcome). The registry also tracks the vital status of included infants up to one year of age.

Since 2019, the registry also collects residential addresses to allow geocoding to census blocks.

2.2. Ethical review

The remaPAR registry received type A approval from the Evaluation Committee of Registries (CER) in January 2022 for a five-year period (2022–2026), authorising its use for research purposes. CNIL authorisation (No. 913556) was updated in October 2016, and an impact analysis was conducted in accordance with the General Data Protection Regulation.

In addition, this study was approved by the University of Sheffield Research Ethics Committee – School of Medicine and Population Health in the United Kingdom, following a due consideration of ethical matters related to this study (Appendix 1).

2.3. Study population

The study population includes all fetuses and newborns with congenital anomalies from a pregnancy ending between 1st of January 2019 and 31st of December 2022 to women residing and delivering in Paris (N=3,028). This timeframe was selected because systematic collection of maternal residential addresses, necessary for geocoding, began in 2019 and the registry had validated data up to 2022 at the time of analysis. The analysis was conducted at the level of fetuses/newborns, not mothers; therefore, multiple gestations (e.g., twins with anomalies) and repeated pregnancies with congenital anomalies were treated as separate observations.

2.4. Outcomes, individual-level socioeconomic exposures and covariables

For our first objective, key outcome variables were CA prevalence and infant mortality. Infant mortality was defined as the death of a liveborn infant within the first year of life. In France, a live birth is defined as any birth showing signs of life from 22 weeks of gestation onwards or with a birthweight of at least 500 grams.

For our second objective, outcomes were antenatal detection, TOPFA and live birth. These were selected in order to investigate associations on the care pathway between CA occurrence and an infant death. Antenatal detection referred to the identification of at least one congenital anomaly during pregnancy. TOPFA included all medically indicated terminations following a prenatal diagnosis. Infant mortality was not an outcome in these analyses because of a low number of cases.

Individual-level SES variables collected in remaPAR include maternal occupational category, maternal geographic origin and insurance status.

Maternal occupational category was coded using the INSEE classification (no profession, farmer, craftsman/trader, executive, intermediate professional, civil service/administrative employee, commercial employee, private service personnel, qualified worker/driver, unskilled worker) and grouped into: *higher-level occupations* (executive, intermediate professional), *employees and service workers* (civil service/administrative employee, commercial employee, private service personnel), *manual workers* (farmer, craftsman/trader, qualified worker/driver, unskilled worker), and *no defined occupation* (no profession).

Insurance status included: none, Sécurité Sociale (SS), Couverture Maladie Universelle Complémentaire (CMU-C), Aide Médicale de l'État (AME), and other. These were grouped as: SS, other (CMU-C, AME, other) and none.

Maternal geographic origin included: France, Northern Europe, Portugal, Spain, Italy, Greece/Former Yugoslavia, North Africa (including Libya and Egypt), other African countries (including Mauritania), West Indies (DOM/TOM), Asia (including Lebanon, Turkey, Russia), Eastern Europe, and other. These were grouped into: *France* (mainland and overseas*), Other European countries* (Northern Europe, Portugal, Spain, Italy, Greece/Former Yugoslavia, Eastern Europe), *North Africa*, *Other African countries*, and *Other* (Asia, other).

Other covariables are variables that are related to the outcomes and the individual and socio-spatial SES exposures and include maternal age (<25, 25-34, 35-39, ≥40), use of assisted reproductive technology (ART), multiple pregnancy, consanguinity (yes/no), smoking status during first trimester (yes/no), maternal pre-pregnancy body-mass index (BMI) (<18.5, 18.5–24.9, 25.0–29.9, ≥30 kg/m²), and uptake of first trimester ultrasound screening (yes/no).

2.5. Measures of area-based deprivation

Measures of area-based deprivation were derived using census and administrative data describing the characteristics of the mother's place of residence at the beginning of pregnancy. This involved three steps: geocoding maternal addresses to the IRIS census unit, assigning administrative and census data for each unit and developing the deprivation scores.

2.5.1. Geocoding

Maternal residential addresses were geocoded to assign cases to their corresponding IRIS units (Îlots Regroupés pour l'Information Statistique), the smallest statistical areas defined by INSEE. There are three types of IRIS units: residential IRIS, business IRIS (containing more than 1000 employees) and miscellaneous IRIS (large areas with sparse population such as parks, forests etc.). Residential IRIS unit has on average 2000 inhabitants and is

homogeneous in terms of living environment and its boundaries are based on major dividing lines of the urban fabric. The city of Paris consists of 992 IRIS units (INSEE, 2024).

Automated geocoding was performed using the official French platform (adresse.data.gouv.fr), which returns geographic coordinates (longitude and latitude). For 40 cases with incomplete or irregular address formatting, manual geocoding was done using open-source mapping tools. Address inconsistencies between postal codes and administrative boundaries were reviewed and corrected. Final geographic coordinates were processed in RStudio to attribute each case to an IRIS code.

2.6. Linkage to socio-spatial data

Geocoding to the IRIS level enabled the integration of contextual sociodemographic and administrative from the 2019 national census. Although INSEE most recently validated and published census data for 2021, we used 2019 data to avoid potential distortions linked to the COVID-19 pandemic during 2020–2021 and due to the unavailability of 2022 data.

For each IRIS unit, INSEE provides data on population structure, median household income, unemployment rate, percentage of blue-collar workers, percentage of high school graduates, proportion of immigrants, proportion of non-homeowners, and proportion of single-parent families. These data provided the socio-spatial context for each case and served as the basis for constructing composite deprivation indices, described in the following section.

2.7. Deprivation indices

The French Deprivation Index (FDep), developed by Rey et al. (2009), is a composite index derived via principal component analysis (PCA) of four variables: median household income, unemployment rate, percentage of blue-collar workers, and percentage of high school graduates (26).

The FDep has demonstrated robust associations with a range of health outcomes, including all-cause and cause-specific mortality, and is routinely used in French public health research and policy (26,27). However, recent research has highlighted certain limitations of the FDep in the context of perinatal epidemiology. Specifically, the FDep may not fully capture aspects of deprivation that are particularly relevant to maternal and child health, such as family structure and housing stability (23,28).

To address these limitations, a Perinatal FDep (P-FDep) index was developed by the study team, incorporating five census indicators: median household income, unemployment rate, proportion of immigrants, proportion of non-homeowners, and proportion of single-parent families (unpublished paper). The inclusion of variables such as single-parent families and non-homeownership is supported by literature demonstrating their association with increased

risk of adverse perinatal outcomes, including preterm birth and low birthweight, as well as their role in mediating access to healthcare and social support (6,23,28).

We constructed both deprivation indices (P-FDep and FDep) using a PCA, consistent with the original FDep methodology. PCA is a statistical technique used to reduce the dimensionality of a dataset by transforming correlated variables into a smaller number of uncorrelated components that capture the most variance in the data. In this study, PCA was applied to area-level socioeconomic indicators to generate a unique composite deprivation index using the loadings of the first principal component from the PCA (Appendix 2). P-FDep scores were subsequently categorised into quintiles, in line with existing literature on deprivation and perinatal outcomes (22,29) . This categorisation allows for consistency and comparability across studies.

2.8. Reference population and population weighting

INSEE provides sociodemographic data for specific population groups, including children under the age of 2, but does not offer data disaggregated by births. We therefore used census counts of children under 2 years old in each IRIS as a proxy for the distribution of births, and as the reference population to weight the area-level deprivation scores. While not a perfect substitute, this approach was necessary given data limitations.

Data from the 2021 French National Perinatal Survey (ENP), which does include information by birth, were not suitable for deriving deprivation quintiles due to small sample sizes at the IRIS level. However, we used the ENP to validate our proxy: the distribution of births by IRIS in the ENP was consistent with the distribution of children under age 2, supporting the use of the under-two population as a reasonable approximation.

By applying these reference populations, we ensured that the division of areas into deprivation quintiles corresponded to equal fractions of the birth/infant population rather than equal numbers of IRISes. In other words, the most deprived quintile and the least deprived quintile each contain roughly 20% of the total births (or infants) in the reference population. This weighting approach gives a more meaningful comparison for perinatal outcomes, aligning the deprivation index with the population of births during the study period and makes it possible to use this population as a comparison group for deriving estimates of risk using odds ratios (OR).

2.9. Missing data

Missing data on individual variables

The proportion of missing data for individual level covariables ranged from 0% for maternal age to 6-7% for maternal occupation, insurance status and pre-pregnancy BMI, and 13.5% for maternal geographic origin. In all, 23.5% of the cases had at least one missing value for a variable used in the analysis. All analyses were conducted on imputed datasets to address missing data in individual-level covariates, including maternal BMI, occupation, geographic origin, and insurance status. We applied multiple imputation by chained equations (MICE), generating 20 datasets and 20 iterations per dataset, using all relevant variables in the imputation models. This method assumes that data are missing at random, conditional on observed values. Each of the 20 imputed datasets was analysed using the steps described above, and the results were pooled using Rubin's rules to obtain final estimates and standard errors that reflect imputation uncertainty (30). Logistic and polytomous regression models were used for binary and categorical variables. Diagnostic checks confirmed satisfactory convergence and consistency across imputations.

Missing data on census-derived variables

To address missing values in the census variables used to construct the deprivation indices, spatial imputation was applied at the IRIS level. Specifically, for any IRIS with missing data on one or more deprivation variables, the missing value was replaced by the mean of the corresponding variable across all spatially adjacent (contiguous) IRIS units. Adjacency was defined based on shared borders, and the list of neighbouring IRIS codes was derived from INSEE's official IRIS boundary shapefiles.

2.10. Analytic strategy

Objective 1: Assessing socio-spatial inequalities in CA prevalence and infant mortality

To address our first objective, we estimated the prevalence of all CAs and infant mortality across quintiles of area-level deprivation, using the P-FDep index. We calculated crude OR and 95% confidence intervals (95% CI) to measure the risk of having a CA and infant mortality associated with a CA by quintiles of P-FDep, using the reference population of children under 2 years. Adjusted analyses were not possible for this objective, as the CA registry and the reference population data do not share individual-level variables and only aggregated census counts are available.

Objective 2: Analysing the association of socioeconomic factors and management and outcomes of CA

For this objective, we began by describing the population of births with CA in the study sample. We then compared socioeconomic characteristics of the women by quintile of the deprivation index, to assess concordance and possible collinearity.

We then modelled three outcomes to describe the different mechanisms by which socioeconomic factors, at the area and individual levels, may affect CA mortality: antenatal detection of congenital anomalies, TOPFA, and live birth. The population for the analyses of detection and live birth comprised all fetuses and newborns with congenital anomalies, while the analysis of TOPFA was restricted to cases detected during pregnancy.

We used Poisson regression models with robust standard errors to estimate relative risks (RRs) and their 95% CI.

Poisson regression with a log link was chosen over logistic regression because the outcomes are common (e.g., antenatal detection occurred in over 70% of cases), and odds ratios from logistic regression overestimate relative risks in such contexts. Poisson regression with robust standard errors can be used to estimate relative risks directly, allowing for more accurate interpretation of results (31,32). Although the data were clustered at the IRIS level, the majority of IRISes contained very few cases (75% had four or fewer), resulting in limited between-cluster variance and reducing the need for multilevel or GEE models. Therefore, robust standard errors were used to account for any residual intra-cluster correlation.

We first produced estimates of the association between our outcomes and the socioeconomic exposures and other covariables using unadjusted models. In a second model, we included area-based and individual level SES variables (maternal occupation, insurance status, maternal geographic origin). This model sought to estimate the independent contribution of the area-based deprivation score to our outcomes, as individual SES are confounders for place of residence and the outcome. Our second adjusted model included the individual SES measures and measures of health behaviours that are patterned by social factors (maternal age, smoking, pre-pregnancy BMI, ART, first trimester ultrasound). This fully adjusted model is exploratory as these variables are on the pathway between area-based and individual socioeconomic factors and the outcomes.

2.11. Sensitivity analyses

To assess the robustness of the findings, two sensitivity analyses were conducted. First, a complete-case analysis (N=2300) was performed by excluding observations with missing covariate data. Additionally, for the live birth outcome, the unadjusted model was re-estimated on a subset of severe congenital anomalies to determine whether the associations persisted when focusing on the most serious cases. This was done to verify that observed patterns in

live-birth outcomes were not driven by the inclusion of less severe anomalies. In line with the EUROCAT classification used in previous studies, severe CAs were defined by the presence of at least one of the following eleven conditions: anencephaly, encephalocele, spina bifida, hydrocephalus, transposition of the great arteries, hypoplastic left heart syndrome, limb reduction defect, bilateral renal agenesis, diaphragmatic hernia, omphalocele, and gastroschisis (33,34).

Software and significance

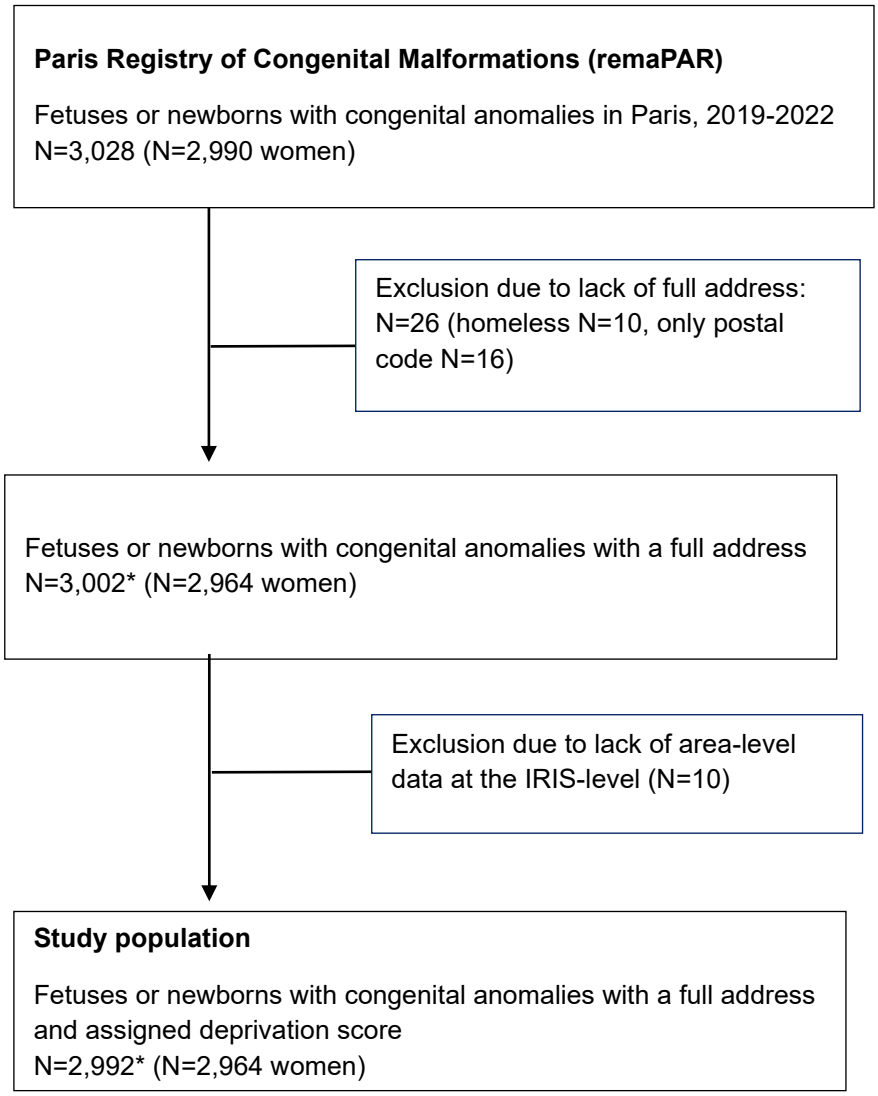
Analyses were conducted using R version 4.4.2 in RStudio. A two-sided p-value <0.05 was considered statistically significant.

3. Results

3.1. Study population

After excluding cases with incomplete address information (N = 26), including missing full addresses or reported maternal homelessness, and cases for which census data at the IRIS level could not be obtained (N = 10), the final analytical sample included 2,992 fetuses and newborns (Figure 1).

Figure 1. Flowchart



*out of which:

- N=38 cases with manual geocoding (N=38 women),
- N=64 cases (n=30 women who had several births affected with congenital anomalies during the study period)
- N=12 twins, both with anomaly (N=6 women)

Figure 2. Spatial distribution of P-FDep quintiles across IRIS units in Paris.

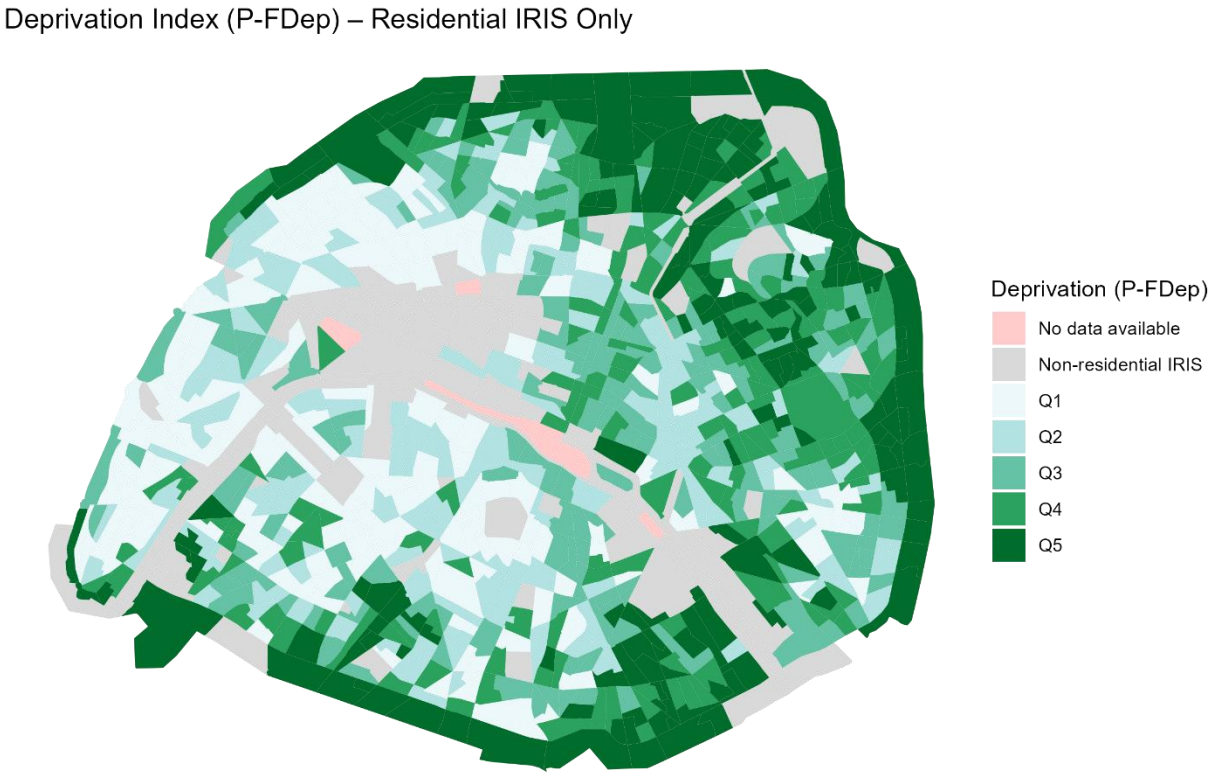


Figure 2 illustrates the spatial pattern of deprivation using P-FDep quintiles across Paris. This does not represent the distribution of the study population. The map shows the most deprived areas (dark green) concentrated in the north and eastern parts of the city, while the least deprived zones (light green) are located in the central and western areas. We also computed FDep quintiles for each IRIS, and observed a strong correlation with the P-FDep quintiles (Spearman's ρ = 0.86, $p < 0.001$), indicating high concordance between the two indices.

3.2. Association between deprivation quintiles and risk of CA prevalence and infant mortality

Table 1 presents the distribution of CA and infant mortality associated with CAs across P-FDep quintiles, using the population of children under 2 years as the reference population. Quintile 1 (Q1), representing the least deprived areas, served as the reference group for all comparisons. The proportion of births with CAs increased with deprivation, from 17.8% in Q1 to 21.8% in Q5 (P-trend <0.001). Crude ORs were elevated in all higher quintiles, with the highest observed in Q5 (cOR: 1.25; 95% CI: 1.11–1.40). There were a total of 64 cases of

infant mortality among cases of CA and infant mortality also rose across deprivation levels, from 9.4% in Q1 to 34.4% in Q5 (cOR: 3.70; 95% CI: 1.50–9.11).

Table 1. The association of socio-spatial socioeconomic deprivation with risk of CA prevalence and infant mortality among births with congenital anomalies

	Reference <2 years old		All congenital anomalies			Infant mortality rate		
P-FDep	N	%	N=2992	%	cOR (95% CI)	N=64	%	cOR (95% CI)
Q1 (least deprived)	12 587	20.0	534	17.8	Ref	6	9.4	Ref
Q2	12 585	20.0	596	19.9	1.12 (1.00–1.26)	8	12.5	1.33 (0.46–3.83)
Q3	12 585	20.0	593	19.8	1.12 (0.99–1.26)	15	23.4	2.49 (0.97–6.42)
Q4	12 692	20.2	616	20.6	1.15 (1.02–1.30)	13	20.3	2.14 (0.81–5.64)
Q5 (most deprived)	12 472	19.8	653	21.8	1.25 (1.11–1.40)	22	34.4	3.70 (1.50–9.11)
Trend test				<0.001			0.001	

3.3. Description of the study population

Tables 2 and 3 present descriptive summaries of the study population. As illustrated in **Table 2**, among the 2992 births with CA, almost half of the mothers were aged 25–34 years (48.5%), with 14.7% aged 40 or above. Most were employed in higher-level occupations (59.3%), and 20.7% had no defined occupation. The predominant type of medical insurance was social security (86.6%). Nearly half of the mothers were of French origin (47.5%), 21.5% had a geographic origin of Sub-Saharan African countries and 14.1% from North Africa. In terms of maternal health and pregnancy characteristics, 11% of cases were associated with maternal obesity (BMI ≥30), 7.3% with maternal 1st trimester smoking and,4.0% were from were multiple pregnancies. First-trimester ultrasound screening was performed in 92.3% of pregnancies.

Table 3 shows that in the least deprived areas (Q1), 73.7% of individuals held higher-level occupations, 93.7% had standard social security, and 62.5% were of French origin. In the most deprived areas (Q5), these figures dropped to 34.5%, 79.6%, and 25.4%, respectively. The proportion with no defined occupation rose from 12.9% (Q1) to 32.9% (Q5), and alternative or no medical insurance increased from 6.3% to 20.4%. Individuals of SSA and North African origin were more represented in Q5 (40.0%) than Q1 (20.7%). Younger maternal age (<25 years) was more common in Q5 (7.0%) compared to Q1 (3.6%). Pre-pregnancy obesity rose from 6.3% to 18.9% across quintiles, as did consanguinity (0.8% to 4.2%). Smoking and multiple pregnancies varied little across quintiles.

Table 2. Description of individual level socioeconomic, demographic and pregnancy variables among births with congenital anomalies (N=2992)

Variables	n	%[i]
Maternal occupation§		
Higher-level	1672	59.3
Employees and service workers	424	15.2
Manual workers	136	4.8
No defined occupation	577	20.7
Missing	193	
Medical insurance		
SS	2462	86.6
Other (CMU, AME)	261	10.0
None	87	3.4
Missing	192	
Maternal geographic origin		
France	1197	47.5
Other European Countries	106	4.3
North Africa	375	14.1
Other African countries	590	21.5
Other	329	12.7
Missing	405	
Maternal age (years)		
<25	156	5.2
25-34	1457	48.5
35-39	949	31.6
≥40	440	14.7
Maternal pre-pregnancy BMI (kg/m²)		
<18.5	225	8.0
18.5-24.9	1769	62.6
25.0-29.9	518	18.5
≥30	303	11.0
Missing	187	
Smoking 1st trimester		
Yes	218	7.3
No	2784	92.7
ART		
Yes	206	6.9
No	2781	93.1
Missing	15	
Multiple pregnancy		
Yes	121	4.0
No	2881	96.0
First trimester scan performed		
Yes	2733	92.3
No	227	7.7
Missing	42	
Consanguinity		
Yes	70	2.4
No	2896	97.6
Missing	26	

[i] imputed percentages

BMI: body mass index; SS: Sécurité Sociale; CMU: Couverture Maladie Universelle Complémentaire (CMU-C); AME: Aide médicale de l'État, ART: Assisted Reproductive Technology

§ Higher-level: executive and intermediate occupations; Employees and service workers: civil service/ administrative employees, commercial employees, private service personnel; Manual workers: farmers, qualified worker/driver, unskilled workers, craftsman/trader; No defined occupation: no profession.

Table 3. Individual variables by P-FDep quintiles (N=2992)

	Q1 N=534	Q2 N=596	Q3 N=593	Q4 N=616	Q5 N=653
	%[i]	%[i]	%[i]	%[i]	%[i]
Occupation					
Higher-level	73.7	72.7	66.6	52.5	34.5
Employees and service workers	10.0	9.7	13.0	14.9	26.8
Manual workers	3.4	4.7	4.4	5.8	5.8
No defined occupation	12.9	12.9	16.1	26.8	32.9
Medical insurance					
SS	93.7	91.6	90.1	80.0	79.6
Other (CMU, AME)	4.5	6.0	7.9	5.4	15.5
None	1.8	2.4	2.0	14.6	4.9
Maternal geographic origin					
France	62.5	59.0	52.9	42.3	25.4
Other European Countries	6.4	3.2	5.7	4.2	2.2
North Africa	7.5	9.7	14.5	16.6	20.7
Other African countries	9.3	14.5	13.9	26.1	40.0
Other	14.3	13.6	13.0	10.8	11.7
Maternal age (years)					
<25	3.6	4.0	4.2	7.0	6.6
25-34	47.6	47.3	48.7	48.2	50.8
35-39	33.9	31.4	34.1	30.0	29.1
≥40	15.0	17.3	13.0	14.8	13.5
Maternal pre-pregnancy BMI (kg/m²)					
<18.5	8.2	12.4	8.4	6.7	4.5
18.5-24.9	72.3	67.1	64.5	60.1	51.1
25.0-29.9	13.2	13.3	18.8	20.4	25.5
≥30	6.3	7.2	8.3	12.9	18.9
Smoking 1st trimester					
Yes	7.9	7.2	7.9	7.2	6.3
No	92.1	92.8	92.1	92.8	93.7
ART					
Yes	8.0	7.7	8.3	6.9	3.9
No	92.0	92.3	91.7	93.1	96.1
Multiple pregnancy					
Yes	3.6	4.3	2.9	5.9	3.2
No	96.4	95.7	97.1	94.1	96.8
First trimester scan performed					
Yes	96.2	95.9	92.9	89.2	88.5
No	3.8	4.1	7.1	10.8	11.5
Consanguinity					
Yes	0.8	1.5	2.0	2.9	4.2
No	99.2	98.5	98.0	97.1	95.8

[i] imputed percentages

3.4. Regression results

Tables 4–6 present the associations of socio-spatial, socioeconomic, demographic, and pregnancy variables with 1) antenatal detection among all births with anomalies (Table 4), 2) TOPFA among detected cases (Table 5), and 3) live birth among all cases (Table 6).

Antenatal detection

Of the 2,992 births with congenital anomalies in the study population, 2,137 (71.2%) were detected antenatally (**Table 4**). Detection rates declined across deprivation quintiles, from 75.1% in the least deprived areas (Q1) to 67.7% in the most deprived (Q5). In unadjusted models, antenatal detection was slightly lower in Q4 (cRR: 0.91; 95% CI: 0.84–0.97) and Q5 (cRR: 0.90; 95% CI: 0.84–0.97) compared to the least deprived quintile (Q1). In adjusted models on other individual-level socioeconomic factors, this association weakened and was no longer statistically significant.

For individual-level socioeconomic factors, antenatal detection was lower among women with no defined occupation (cRR: 0.87; 95% CI: 0.81–0.93), no health insurance (cRR: 0.77; 95% CI: 0.64–0.93), or coverage through CMU/AME (cRR: 0.87; 95% CI: 0.79–0.95) in unadjusted models. However, after adjusting for individual-level SES (RR1), only maternal geographic origin remained significantly associated with detection. Specifically, women from sub-Saharan African countries had a significantly lower likelihood of antenatal detection compared to those of French origin (RR1: 0.83; 95% CI: 0.77–0.91), and this association persisted after full adjustment (RR2: 0.85; 95% CI: 0.78–0.93). Associations observed for occupation and insurance were attenuated and no longer statistically significant in adjusted models.

Among maternal demographic characteristics, women under 25 years had significantly lower detection in unadjusted models (cRR: 0.85; 95% CI: 0.74–0.98), though this was not maintained after adjustment. In contrast, detection was significantly higher among women aged 35–39 (RR2: 1.07; 95% CI: 1.02–1.13) and those aged 40 and older (RR2: 1.10; 95% CI: 1.04–1.18). No consistent associations were observed with BMI, smoking, ART, multiple pregnancy or consanguinity.

TOPFA

Among the 2,137 cases detected antenatally, 969 (45.4%) underwent TOPFA. The proportion decreased across deprivation quintiles, from 49.4% in Q1 to 36.0% in Q5. In unadjusted analyses, the most deprived group had significantly lower likelihood of TOPFA (cRR: 0.73;

95% CI: 0.62–0.85), but this association was not significant in adjusted models (aRR: 0.88; 95% CI: 0.75–1.04).

When examining individual-level socioeconomic characteristics, lower TOPFA rates were observed in unadjusted models among women with no defined occupation (cRR: 0.53; 95% CI: 0.44–0.63), those without health insurance (cRR: 0.65; 95% CI: 0.42–1.01), and those covered by CMU/AME (cRR: 0.58; 95% CI: 0.45–0.74), compared to women in higher-level occupations or with standard social security coverage. After adjusting for individual SES (RR1), the association with occupation remained significant only for women with no defined occupation (RR1: 0.65; 95% CI: 0.52–0.80), and persisted in the fully adjusted model (RR2: 0.73; 95% CI: 0.60–0.90). Associations for insurance status were attenuated and no longer statistically significant after adjustment. TOPFA was also significantly less likely among women from sub-Saharan Africa (cRR: 0.60; 95% CI: 0.51–0.72) and North Africa (cRR: 0.72; 95% CI: 0.61–0.84) compared to women of French origin; after full adjustment, the association remained significant for sub-Saharan African origin (RR2: 0.81; 95% CI: 0.66–0.99) and borderline significant for North African origin (RR2: 0.85; 95% CI: 0.72-1.01).

Regarding maternal characteristics, younger women (<25 years) were significantly less likely to terminate an affected pregnancy (cRR: 0.43; 95% CI: 0.27–0.69), and this association remained after adjustment (RR2: 0.52; 95% CI: 0.32–0.85). In contrast, termination was more likely among older women: RR2 was 1.34 (95% CI: 1.21–1.49) for women aged 35–39 and 1.63 (95% CI: 1.45–1.83) for those aged 40 and older, compared to the 25–34 reference group. Obesity (BMI ≥30) was associated with lower TOPFA rates in unadjusted models (cRR: 0.70; 95% CI: 0.57–0.87), but not after adjustment. The likelihood of TOPFA was lower when a first-trimester ultrasound had not been performed (cRR: 0.57; 95% CI: 0.43-0.76), though this was not statistically significant in adjusted models (RR2: 0.86; 95% CI: 0.64–1.15). Finally, consanguinity was associated with substantially lower TOPFA rates (cRR: 0.35; 95% CI: 0.18–0.66), and this association persisted after adjustment (RR2: 0.52; 95% CI: 0.28–0.96).

Live birth

Overall, 1,966 (65.5%) of 2,992 pregnancies resulted in live births (**Table 6**). The proportion increased with deprivation, from 62.0% in Q1 to 72.6% in Q5. This association was statistically significant in unadjusted models (cRR: 1.17; 95% CI: 1.08–1.27), but was no longer significant after adjustment.

When examining associations between live birth and individual SES, live birth was significantly more likely among women with no defined occupation (cRR: 1.31; 95% CI: 1.24–1.39), and this association remained after adjustment for individual SES (RR1: 1.18; 95% CI: 1.09–1.28)

and all covariates (RR2: 1.13; 95% CI: 1.04–1.22). Similarly, women without health insurance (cRR: 1.20; 95% CI: 1.06–1.36) and those covered by CMU/AME (cRR: 1.25; 95% CI: 1.16–1.34) had higher live birth rates in unadjusted models, although these associations did not persist after adjustment. Live birth rates were also significantly higher among women from sub-Saharan Africa (cRR: 1.27; 95% CI: 1.20–1.36) and North African women (cRR: 1.16; 95% CI: 1.07-1.25), and this association remained statistically significant after full adjustment for SSA (RR2: 1.11; 95% CI: 1.02–1.21) and borderline significant for North African origin (RR2: 1.07; 95% CI: 0.98-1.16)

For maternal characteristics, younger women (<25 years) were significantly more likely to have a live birth (cRR: 1.20; 95% CI: 1.12–1.29), and this association persisted after adjustment (RR2: 1.11; 95% CI: 1.03–1.19). Conversely, live birth rates were significantly lower among older women: RR2 was 0.83 (95% CI: 0.78–0.88) for women aged 35–39, and 0.71 (95% CI: 0.64–0.78) for those aged 40 and older, compared to the 25–34 reference group. Obesity (BMI ≥30) was associated with increased likelihood of live birth (cRR: 1.18; 95% CI: 1.10–1.27), and this remained statistically significant after adjustment (RR2: 1.10; 95% CI: 1.02–1.19). Finally, women in consanguineous unions had higher live birth rates in unadjusted analyses (cRR: 1.25; 95% CI: 1.11–1.40).

Table 4. Association of SES and maternal characteristics with antenatal detection among all CA

Variables	n/N	%[i] detected	Unadjusted RR (95% CI)	Adjusted RR[1] (95% CI)	Adjusted RR[2] (95% CI)
All	2137/2992	71.2			
P-FDep					
Q1 (least deprived)	401/534	75.1	1	1	1
Q2	443/596	74.3	0.99 (0.93–1.06)	1.00 (0.93–1.07)	1.00 (0.93–1.07)
Q3	431/593	72.7	0.97 (0.90–1.04)	0.97 (0.91–1.04)	0.97 (0.91–1.04)
Q4	420/616	68.2	0.91 (0.84–0.97)	0.94 (0.87–1.01)	0.95 (0.88–1.02)
Q5 (most deprived)	442/653	67.7	0.90 (0.84–0.97)	0.95 (0.88–1.03)	0.96 (0.89–1.03)
Maternal occupation					
Higher-level	1221/1664	74.2	1	1	1
Employees and service workers	287/423	69.0	0.93 (0.87–1.00)	1.00 (0.93–1.07)	1.01 (0.94–1.09)
Manual workers	101/136	75.3	1.02 (0.92–1.12)	1.08 (0.97–1.20)	1.09 (0.98–1.21)
No defined occupation	367/576	64.3	0.87 (0.81–0.93)	0.96 (0.89–1.04)	1.00 (0.92–1.08)
Medical insurance					
SS	1774/2453	73.0	1	1	1
Other (CMU, AME)	159/260	63.4	0.87 (0.79–0.95)	0.97 (0.87–1.07)	0.98 (0.88–1.09)
None	46/87	54.9	0.77 (0.64–0.93)	0.90 (0.74–1.08)	0.93 (0.77–1.14)
Maternal geographic origin					
France	865/1194	74.3	1	1	1
Other European Countries	76/106	73.4	0.99 (0.88–1.11)	1.00 (0.89–1.11)	0.97 (0.87–1.09)
North Africa	283/374	76.5	1.03 (0.97–1.10)	1.07 (0.99–1.14)	1.07 (1.00–1.15)
Other African countries	335/588	59.0	0.79 (0.74–0.85)	0.83 (0.77–0.91)	0.85 (0.78–0.93)
Other	239/326	74.8	1.01 (0.94–1.08)	1.02 (0.95–1.10)	1.02 (0.95–1.10)
Maternal age (years)					
<25	91/154	59.0	0.85 (0.74–0.98)		0.92 (0.80–1.06)
25-34	1003/1454	69.0	1		1
35-39	106/945	74.7	1.08 (1.02–1.13)		1.07 (1.02–1.13)
≥40	337/439	76.8	1.11 (1.04–1.18)		1.10 (1.04–1.18)
Pre-pregnancy BMI (kg/m²)					
<18.5	173/224	77.3	1.06 (0.98–1.14)		1.05 (0.98–1.13)
18.5-24.9	1282/1762	73.1	1		1
25.0-29.9	343/517	66.9	0.92 (0.86–0.98)		0.96 (0.90–1.03)
≥30	197/302	65.5	0.90 (0.82–0.98)		0.95 (0.87–1.04)
Smoking 1st trimester					
Yes	151/216	71.1	0.99 (0.90–1.08)		0.97 (0.88–1.06)
No	1979/2776	71.4	1		1
ART					
Yes	153/205	73.8	1.03 (0.95–1.12)		0.97 (0.89–1.06)
No	1984/2772	71.3	1		1
Multiple pregnancy					
Yes	81/120	67.8	0.94 (0.83–1.07)		0.92 (0.81–1.05)
No	2056/2872	71.9	1		1
First trimester scan performed					
Yes	1981/2724	72.5	1		1
No	131/226	58.1	0.80 (0.72–0.90)		0.90 (0.80–1.01)
Consanguinity					
Yes	46/70	65.7	0.91 (0.77–1.08)		0.99 (0.84–1.17)
No	2079/2896	71.8	1		1

[i] *imputed percentages*
[1] *adjusted for maternal occupation, insurance status, geographic origin*
[2] *adjusted for maternal occupation, insurance status, geographic origin, maternal age, pre-pregnancy BMI, smoking, ART, multiplicity, 1st trimester ultrasound, consanguinity*

Table 5. Association of SES and maternal characteristics with TOPFA among all detected CA

Variables	n/N	%[i] TOPFA*	Unadjusted RR (95% CI)	Adjusted RR[1] (95% CI)	Adjusted RR[2] (95% CI)
All	969/2137	45.4			
P-FDep					
Q1 (least deprived)	198/401	49.4	1	1	1
Q2	215/443	48.5	0.98 (0.86–1.13)	0.99 (0.87–1.14)	0.98 (0.86-1.12)
Q3	216/431	50.1	1.01 (0.89–1.16)	1.05 (0.92–1.20)	1.05 (0.92-1.19)
Q4	181/420	43.1	0.87 (0.75–1.01)	0.97 (0.83–1.12)	0.97 (0.84-1.12)
Q5 (most deprived)	159/442	36.0	0.73 (0.62–0.85)	0.87 (0.74–1.03)	0.88 (0.75-1.04)
Maternal occupation					
Higher-level	609/1221	51.8	1	1	1
Employees and service workers	116/287	43.0	0.83 (0.72–0.96)	0.95 (0.81–1.11)	0.96 (0.83–1.12)
Manual workers	38/101	40.0	0.78 (0.60–1.00)	0.87 (0.67–1.12)	0.88 (0.68–1.13)
No defined occupation	89/367	27.3	0.53 (0.44–0.63)	0.65 (0.52–0.80)	0.73 (0.60–0.90)
Medical insurance					
SS	815/1774	47.6	1	1	1
Other (CMU, AME)	38/159	27.5	0.58 (0.45–0.74)	0.85 (0.64–1.13)	0.90 (0.68–1.19)
None	13/46	30.4	0.65 (0.42–1.01)	1.05 (0.65–1.70)	1.19 (0.73–1.93)
Maternal geographic origin					
France	416/865	51.4	1	1	1
Other European Countries	46/76	61.7	1.21 (1.00–1.45)	1.23 (1.01–1.48)	1.13 (0.94–1.36)
North Africa	93/283	37.0	0.72 (0.61–0.84)	0.84 (0.71–1.00)	0.85 (0.72–1.01)
Other African countries	90/335	31.0	0.60 (0.51–0.72)	0.78 (0.64–0.96)	0.81 (0.66–0.99)
Other	102/239	46.1	0.90 (0.77–1.04)	0.99 (0.86–1.15)	0.97 (0.84–1.12)
Maternal age (years)					
<25	15/91	17.4	0.43 (0.27–0.69)		0.52 (0.32–0.85)
25-34	382/1003	38.0	1		1
35-39	371/106	52.5	1.38 (1.24–1.53)		1.34 (1.21–1.49)
≥40	201/337	59.5	1.57 (1.39–1.76)		1.63 (1.45–1.83)
Pre-pregnancy BMI (kg/m²)					
<18.5	89/173	52.2	1.09 (0.93–1.27)		1.05 (0.91–1.22)
18.5-24.9	601/1282	47.9	1		1
25.0-29.9	129/343	39.2	0.82 (0.71–0.94)		0.93 (0.81–1.08)
≥30	62/197	34.0	0.70 (0.57–0.87)		0.86 (0.70–1.07)
Smoking 1st trimester					
Yes	67/151	43.9	0.95 (0.78–1.17)		0.89 (0.73–1.08)
No	902/1979	45.4	1		1
ART					
Yes	67/153	44.1	1.01 (0.83–1.24)		0.74 (0.60–0.92)
No	897/1984	45.4	1		1
Multiple pregnancy					
Yes	39/81	47.6	1.00 (0.77–1.31)		0.99 (0.76–1.29)
No	930/2056	45.0	1		1
First trimester scan performed					
Yes	928/1981	46.6	1		1
No	35/131	26.3	0.57 (0.43–0.76)		0.86 (0.64–1.15)
Consanguinity					
Yes	8/46	17.4	0.35 (0.18–0.66)		0.52 (0.28–0.96)
No	958/2079	46.1	1		1

[i] *imputed percentages*
[1] *adjusted for maternal occupation, insurance status, geographic origin*
[2] *adjusted for maternal occupation, insurance status, geographic origin, maternal age, pre-pregnancy BMI, smoking, ART, multiplicity, 1st trimester ultrasound, consanguinity*

Table 6. Association of SES and maternal characteristics with live birth among all CA

Variables	n/N	%[i] live birth	Unadjusted RR (95% CI)	Adjusted RR[1] (95% CI)	Adjusted RR[2] (95% CI)
All	1966/2992	65.5			
P-FDep					
Q1 (least deprived)	331/534	62.0	1	1	1
Q2	369/596	61.9	1.00 (0.91-1.09)	0.99 (0.90–1.08)	0.99 (0.90–1.08)
Q3	366/593	61.7	1.00 (0.91-1.09)	0.98 (0.89–1.07)	0.97 (0.88–1.06)
Q4	426/616	69.2	1.11 (1.02-1.21)	1.05 (0.96–1.14)	1.04 (0.96–1.14)
Q5 (most deprived)	474/653	72.6	1.17 (1.08-1.27)	1.06 (0.97–1.16)	1.05 (0.97–1.15)
Maternal occupation					
Higher-level	1040/1664	60.6	1	1	1
Employees and service workers	293/423	67.3	1.11 (1.03–1.20)	1.03 (0.94–1.12)	1.02 (0.94–1.11)
Manual workers	92/136	65.8	1.08 (0.95–1.24)	1.02 (0.89–1.16)	1.02 (0.89–1.16)
No defined occupation	469/576	79.2	1.31 (1.24–1.39)	1.18 (1.09–1.28)	1.13 (1.04–1.22)
Medical insurance					
SS	1601/2453	63.7	1	1	1
Other (CMU, AME)	214/260	79.2	1.25 (1.16–1.34)	1.04 (0.96–1.14)	1.03 (0.94–1.12)
None	69/87	76.5	1.20 (1.06–1.36)	0.97 (0.85–1.11)	0.93 (0.80–1.07)
Maternal geographic origin					
France	765/1194	60.7	1	1	1
Other European Countries	60/106	53.9	0.89 (0.74–1.07)	0.88 (0.74–1.06)	0.94 (0.79–1.12)
North Africa	275/374	70.3	1.16 (1.07–1.25)	1.07 (0.98–1.16)	1.07 (0.98–1.16)
Other African countries	472/588	77.4	1.27 (1.20–1.36)	1.14 (1.05–1.23)	1.11 (1.02–1.21)
Other	218/326	63.7	1.05 (0.95–1.15)	1.00 (0.91–1.10)	1.01 (0.92–1.12)
Maternal age (years)					
<25	133/154	85.3	1.20 (1.12–1.29)		1.11 (1.03-1.19)
25-34	1043/1454	71.6	1		1
35-39	560/945	59.0	0.83 (0.78–0.88)		0.83 (0.78–0.88)
≥40	230/439	52.3	0.73 (0.66–0.80)		0.71 (0.64-0.78)
Pre-pregnancy BMI (kg/m²)					
<18.5	133/224	58.4	0.92 (0.82–1.04)		0.94 (0.84–1.05)
18.5-24.9	1133/1762	63.4	1		1
25.0-29.9	376/517	71.4	1.13 (1.06–1.20)		1.07 (1.00–1.14)
≥30	231/302	75.0	1.18 (1.10–1.27)		1.10 (1.02–1.19)
Smoking 1st trimester					
Yes	142/216	65.1	1.00 (0.91–1.11)		1.03 (0.93–1.14)
No	1824/2776	65.5	1		1
ART					
Yes	135/205	65.5	1.00 (0.90–1.11)		1.18 (1.06–1.32)
No	1821/2772	65.7	1		1
Multiple pregnancy					
Yes	77/120	63.6	0.98 (0.85–1.12)		0.97 (0.84–1.11)
No	1889/2872	65.6	1		1
First trimester scan performed					
Yes	1755/2724	64.6	1		1
No	177/226	78.6	1.21 (1.13–1.31)		1.02 (0.94–1.11)
Consanguinity					
Yes	57/70	81.4	1.25 (1.11–1.40)		1.09 (0.97–1.22)
No	1887/2896	65.2	1		1

[i] *imputed percentages*
[1] *adjusted for maternal occupation, insurance status, geographic origin*
[2] *adjusted for maternal occupation, insurance status, geographic origin, maternal age, pre-pregnancy BMI, smoking, ART, multiplicity, 1st trimester ultrasound, consanguinity*

3.5. Sensitivity analyses

Sensitivity analyses confirmed the robustness of the main findings. First, a complete-case analysis excluding observations with missing covariate data (N=2300) yielded results consistent with those obtained from the imputed datasets, suggesting that the handling of missing data did not substantially affect the estimates (Appendix 5). Second, to assess whether associations observed for live birth were influenced by the inclusion of less severe CA, we re-estimated the unadjusted model on a restricted sample of severe cases only. Although the sample size was smaller (N=343), the direction and magnitude of associations remained similar, indicating that the observed patterns in live birth outcomes were not driven by the presence of milder anomalies (Appendix 6).

4. Discussion

4.1. Summary of main findings

This study investigated socioeconomic and spatial inequalities in the prevalence and outcomes of congenital anomalies in Paris between 2019 and 2022 using population-based registry data linked to area-level deprivation indicators. We first showed a slight gradient across deprivation quintiles in the proportion of births with congenital anomalies (17.8% in the least deprived to 21.8% in the most deprived) alongside a much more pronounced gradient for infant mortality (9.4% to 34.4%), translating into an over 3.5 higher risk of infant mortality in Q5 compared to Q1. This latter result confirms hypotheses of marked socio-spatial disparities in infant mortality, as well as the contribution of CA to overall infant mortality disparities. By investigating all CA in the remaPAR registry, we found that deprivation quintiles were associated with all steps in the pathway leading to infant mortality: antenatal detection of CA, TOPFA after detection and live birth. In all models, however, socio-spatial associations were no longer significant after accounting for individual-level socioeconomic characteristics. For detection, associations remained after adjustment only among women of sub-Saharan African origin (aRR: 0.85; 95 CI%: 0.78-0.93). For TOPFA after detection, no defined occupation (aRR: 0.73; 95 CI%: 0.60-0.90) and sub-Saharan or North Africa origin (aRR: 0.81; 95% CI: 0.66-0.99) and aRR: 0.85; 95% CI: 0.72-1.01), respectively) were associated with TOPFA. Live birth patterns were broadly inverse to those observed for TOPFA, with higher proportions among subgroups with lower likelihood of termination. These results provide insight into infant mortality differences by revealing different patterns in the detection and management of CA across quintiles which are largely explained by individual characteristics and notably geographic origin.

4.2. Interpretation of findings

4.2.1. IMR and CA

These socio-spatial patterns echo findings from other high-income countries, where both the prevalence of CA and associated adverse outcomes—such as perinatal mortality, preterm birth, and small for gestational age—are consistently higher in deprived areas (8,15,18,35). In England, a population-based study found substantial socioeconomic inequalities in outcomes linked to congenital anomalies: the most deprived areas had a 61% higher rate of live births (1.61, 1.21 to 2.15) and a 98% higher rate of neonatal mortality associated with CA (1.98, 1.20 to 3.27), compared with the least deprived areas (22).

In the French context, a recent spatiotemporal study of neonatal mortality from 2001 to 2017 confirmed persistent socioeconomic disparities, with higher neonatal mortality rates observed in more deprived urban areas and cities with a higher proportion of migrants (7). These findings align with earlier spatial analyses showing clustering of infant mortality in disadvantaged zones in metropolitan France (6). Given that CA are among the leading causes of infant mortality in high-income countries (10), these socio-spatial patterns raise serious concerns, particularly in light of recent trends in France's rising neonatal deaths (3,7). As neonatal mortality is strongly influenced by the presence of severe CA, our findings contribute to this picture, indicating that even within a universal healthcare system, structural inequalities may continue to shape early-life health outcomes.

4.2.2. CA prevalence

We found a gradient in CA prevalence across quintiles that may contribute to infant mortality disparities. Our findings are concordant with a recent report from the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) in the UK confirms this pattern, identifying significantly higher prevalence of several anomaly types, including congenital heart defects and neural tube defects, in the most deprived areas of England, where an overall birth prevalence of CA was 15% higher in the most deprived areas compared to the least deprived (255.3 vs 221.5 per 10,000 births; risk ratio: 1.15, 95% CI: 1.1–1.2), and 30% higher for non-genetic anomalies (190.3 vs 145.8 per 10,000; risk ratio: 1.30, 95% CI: 1.2–1.4) (36). In our study, the odds of CA were 25% higher in the most deprived quintile (Q5) compared to the least deprived (Q1) (cOR: 1.25; 95% CI: 1.11–1.40; p for trend < 0.001), showing a comparable socio-spatial gradient.

4.2.3. Antenatal detection, TOPFA, and live birth

Although we did not find a statistically significant association between area-level deprivation and antenatal detection after adjustment, there was a trend of lower detection rates in the most deprived quintiles, and some associations were observed with individual-level SES. Specifically, mothers of sub-Saharan African origin were significantly less likely to have anomalies detected during pregnancy. While earlier studies in France and the UK reported no socioeconomic differences in prenatal detection (21,40), our findings suggest possible disparities linked to maternal geographic origin. This may reflect evolving population dynamics or persistent barriers in accessing and navigating prenatal care. Despite the widespread availability of prenatal screening in France, differences in health literacy, language proficiency, and familiarity with the healthcare system may contribute to unequal uptake. Additionally, detection was significantly higher among older mothers, likely due to closer medical monitoring and the higher prevalence of trisomy 21 in this group (37). A systematic review found that migrant women in high-income countries were significantly more likely to receive inadequate prenatal care, particularly those who were younger, less educated, had limited language proficiency, or lacked health insurance—factors that may also affect screening uptake (38). In France, demographic changes over the past decade (39)—including increased diversity in the maternity population— may have introduced new challenges related to communication, cultural expectations, and navigating the healthcare system. However, lower detection rates among certain groups may also reflect a conscious decision to decline prenatal screening. In some communities, screening is not sought because, regardless of the diagnosis, there is no intention to terminate the pregnancy. These culturally grounded preferences highlight that disparities in detection may arise not only from barriers to access, but also from differences in values and decision-making. These findings underscore the importance of ensuring that universal coverage is accompanied by equity in service uptake and outcomes—while recognising that decisions around prenatal screening are closely intertwined with those around pregnancy termination.

Our findings on TOPFA and live births suggest that, unlike antenatal detection, social disparities remain more pronounced in decisions following diagnosis. There was a trend in a decrease of probability of TOPFA in most deprived quintile although the association was not statistically significant after adjustment. This pattern aligns with earlier findings from the UK, which reported significantly lower termination rates following antenatal diagnosis in more deprived areas compared with the least deprived areas (63% v 79%; rate ratio 0.80, 0.65 to 0.97) (22). In our study, individual-level characteristics were more strongly associated with the

likelihood of TOPFA: women with no defined occupation, younger women, and those of sub-Saharan African or North African origin were less likely to terminate an affected pregnancy. These differences in decision-making likely reflect a complex interplay of socioeconomic, cultural, and structural factors. While cultural and religious beliefs may influence choices around TOPFA—factors that must be respected— they can also shape the willingness to accept prenatal screening in the first place. These beliefs may intersect with differences in access to information or the quality of counselling, contributing to unequal engagement with the prenatal care pathway. Given that many CAs are associated with substantial long-term health needs (10), the decision to continue a pregnancy may place additional burdens on families already experiencing social disadvantage. We observed a corresponding gradient in live births, with socially disadvantaged women more likely to carry affected pregnancies to term. This pattern aligns with the lower antenatal detection and TOPFA rates observed in these groups, suggesting that disparities in detection and decisions around termination contribute to the social gradient in live births. These outcomes may further compound existing inequalities, as families with fewer resources are more likely to face the long-term burdens of care. Our findings underscore the need for comprehensive and culturally sensitive prenatal counselling that supports informed decision-making and respects reproductive autonomy across diverse social and cultural backgrounds.

4.3. Public health implications and further research

Our findings point to possible socio-economic disparities in CA outcomes, even within a healthcare system that offers near-universal prenatal care. This suggests that equal service provision does not necessarily translate to equal utilisation or benefit. In practical terms, certain areas of Paris—particularly those identified as more deprived—may require targeted public health interventions. This could include improving access to prenatal information through translated materials, community outreach, or support from local clinics and maternity services. It also underscores the need to ensure that postnatal care and support services are available and accessible to families in these areas, especially given the higher number of live births with anomalies. Reducing these disparities will require focused efforts not only within the healthcare system but also through broader social support that addresses the everyday constraints faced by disadvantaged families.

While cultural and religious factors may influence women's decisions around prenatal screening and TOPFA, these preferences were not directly measured in our study. As this latter information is available in remaPAR, future work should examine this information in

relation to the specific causes of infant death to shed more light on the role of care access, severity, and timing.

This study was exploratory and descriptive in nature. Our objective was to map the full CA care pathway—ranging from antenatal detection to TOPFA, live birth, and infant mortality—in relation to socioeconomic and spatial factors. While we identified clear social gradients across outcomes, the study was not powered to quantify the specific contribution of each outcome (e.g. detection vs. TOPFA) to excess infant mortality. Subgroup analyses by anomaly type (e.g. CHDs) were also limited by sample size. Future studies with larger datasets could help disentangle the causal chain and assess relative contributions more precisely. Such subgroup-specific analyses could better inform public health interventions tailored to specific conditions and populations.

While this study adjusted for individual-level characteristics, these variables may lie on the causal pathway; formal mediation analysis could help disentangle their respective contributions.

This study also illustrates the value of using socio-spatial indicators for surveillance of perinatal outcomes. Using quintiles of the P-FDep index, we were able to identify zones with high infant mortality and lower detection rates. This information can allow for monitoring over time and targeting of public health actions to neighbourhoods most in need. They also complement analyses using individual level data. We found that individual level characteristics – not neighbourhood characteristics – were those of most importance in this study, which can also inform interventions. However, this may not be the case for all perinatal outcomes in cases where area-level characteristics have an independent impact (35). For this analysis, we used the perinatal-specific deprivation index (P-FDep), a composite measure tailored to capture aspects of disadvantage most relevant to maternal and infant health (23,27,28). Compared to the more general French Deprivation Index (FDep), P-FDep includes additional variables such as non-homeownership, immigration, and single-parent households. However, the correlation between the two indices was very high (Spearman's $\rho = 0.86$), indicating consistency in the measurement of deprivation, which was confirmed in sensitivity analyses, while also justifying the choice of the more context-sensitive index. Nonetheless, although P-FDep was selected for its relevance to maternal and child health, further work is needed to explore its impact in a French context and in relation to other deprivation indices exist (e.g. EDI) to allow robust recommendations about area-based monitoring of socioeconomic inequalities in France.

4.4. Strengths and Limitations

This study has multiple strengths linked to its use of comprehensive data from a population-based CA registry. Importantly, remaPAR is the only registry in France that collects systematic data on infant mortality linked to CA, allowing for robust analysis of outcomes beyond birth. A second major strength is the granularity of the geographic resolution: maternal addresses were geocoded to the IRIS level—the smallest statistical unit in France—enabling fine-grained analysis of spatial inequalities. This allowed for more precise assessment of socio-spatial disparities in CA prevalence, infant mortality, antenatal detection, and pregnancy outcomes (TOPFA and live birth). The study combined individual-level sociodemographic variables with area-level deprivation index, enabling assessment of socioeconomic effects at multiple levels.

As part of its analytic strategy, the study also included several sensitivity analyses—complete-case analyses and restriction to severe anomalies—which produced consistent results, further validating the analytical approach. Additionally, the reference population was validated against the 2021 National Perinatal Survey (ENP), supporting the choice of children under age two as a reasonable proxy population.

Despite these strengths, several limitations should be acknowledged. A primary constraint was the lack of individual-level denominator data for the general maternity population, which limited the ability to calculate precise population-based rates. To address this, we used INSEE census counts of children under age two at the IRIS level as a proxy denominator and for deprivation classification. Although validated against external data, this approach may still lead to misclassification or imprecise estimates. Furthermore, the remaPAR registry, while comprehensive, is based on retrospective data collection. This may introduce information bias, particularly for variables such as maternal health behaviours and some socio-demographic indicators. Missing data were also a concern, notably for maternal occupation (6.5%) and geographic origin (13.5%), which may have been reported heterogeneously (e.g. by country of birth or self-identified origin). We addressed missingness through multiple imputation, and sensitivity analyses confirmed the robustness of the results.

While the overall sample size was relatively large (N = 2,992), the subgroup stratified analyses were limited by small numbers, reducing statistical power to detect differences and leading us to focus on the full population for our study.

5. Conclusion

This study mapped the congenital anomaly care pathway in Paris, highlighting important socio-spatial disparities across prevalence, antenatal detection, termination, live birth, and infant

mortality. While antenatal detection was overall high, it was lower among some groups, particularly women of sub-Saharan African origin. The likelihood of TOPFA was also significantly lower among women with no defined occupation and those of North or sub-Saharan African origin, contributing to a higher proportion of live births among these groups

These findings underscore how social inequalities shape both clinical outcomes and reproductive decisions following prenatal diagnosis. Addressing such disparities requires targeted efforts to improve access to screening, culturally sensitive counselling, and equitable follow-up care. At the same time, it is essential to respect individual and culturally informed decisions around pregnancy continuation.

The study also highlights the value of routine monitoring using indices like P-FDep to identify area-level disparities and inform targeted interventions. Integrating area-level deprivation measures into perinatal surveillance systems could support the development of responsive public health strategies and reduce the long-term burden on already disadvantaged populations.

Finally, this research contributes to clarifying the dual pathways through which socio-spatial disparities in infant mortality from CA may arise—through differential access to care and through personal choices. Further work is needed to assess the causal contributions of each stage in the care pathway to infant mortality. Complementary qualitative studies among specific subgroups would also offer valuable insights into the social, cultural, and structural contexts that shape reproductive decision-making.

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Appendix 1. UoS Ethics Approval

The University Of Sheffield.

Downloaded: 15/04/2025
Approved: 15/04/2025

Bermet Amirova
Registration number: 230137453
School of Medicine and Population Health
Programme: Europubhealth

Dear Bermet

PROJECT TITLE: Social inequalities in infant mortality due to congenital anomalies: a register-based study in Paris (remaPAR)
APPLICATION: Reference Number 067443

This letter confirms that you have signed a University Research Ethics Committee-approved self-declaration to confirm that your research will involve only existing research, clinical or other data that has been robustly anonymised. You have judged it to be unlikely that this project would cause offence to those who originally provided the data, should they become aware of it.

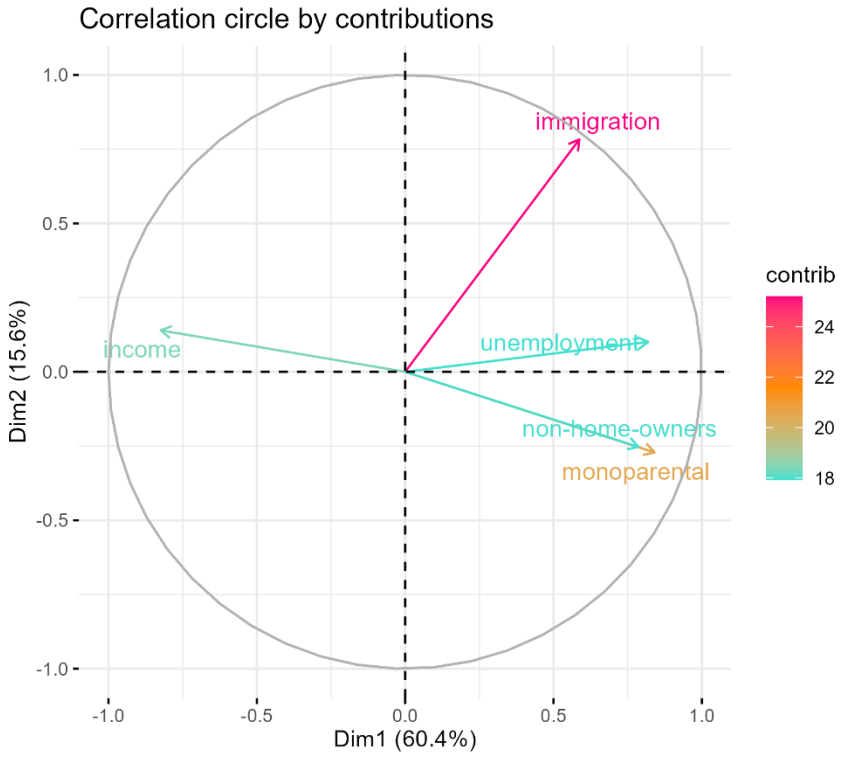
As such, on behalf of the University Research Ethics Committee, I can confirm that your project can go ahead on the basis of this self-declaration.

If during the course of the project you need to deviate significantly from the above-approved documentation please inform me since full ethical review may be required.

Yours sincerely

Charlotte Cole
Departmental Ethics Administrator

Appendix 2. Correlation circle plot and factor loadings for the PCA to compute P-FDep



Appendix 3. Individual variables by FDep quintiles (N=2991)

	Q1 N=507	Q2 N=628	Q3 N=583	Q4 N=625	Q5 N=648
	%	%	%	%	%
Occupation					
Higher-level	75.8	71.1	64.7	54.9	34.5
Employees and service workers	7.2	11.8	14.2	14.5	26.3
Manual workers	3.1	4.8	5.0	5.3	5.9
No defined occupation	13.8	12.3	16.2	25.3	33.3
Medical insurance					
SS	93.5	93.2	89.8	83.0	79.5
Other (CMU, AME)	4.7	4.9	8.2	11.9	16.2
None	1.8	1.9	2.0	5.2	4.3
Maternal geographic origin					
France	60.2	56.5	53.4	42.3	25.1
Other European Countries	6.0	5.0	3.9	3.8	2.5
North Africa	7.3	10.9	13.9	17.4	20.1
Other African countries	12.0	11.7	18.9	25.0	40.6
Other	14.5	15.9	10.0	11.5	11.7
Maternal age (years)					
<25	3.4	4.8	3.9	5.8	7.6
25-34	48.1	45.2	50.8	47.8	51.1
35-39	32.7	33.1	32.2	30.2	29.6
≥40	15.8	16.9	13.0	16.2	11.7
Maternal pre-pregnancy BMI (kg/m²)					
<18.5	10.8	10.8	7.4	6.7	4.7
18.5-24.9	71.5	66.8	65.0	61.4	51.3
25.0-29.9	11.9	15.5	18.5	20.0	25.0
≥30	5.8	6.9	9.1	12.0	19.1
Smoking 1st trimester					
Yes	7.9	7.2	7.9	7.2	6.3
No	92.1	92.8	92.1	92.8	93.7
ART					
Yes	8.0	7.7	8.3	6.9	3.9
No	92.0	92.3	91.7	93.1	96.1
Multiple pregnancy					
Yes	3.6	4.3	2.9	5.9	3.2
No	96.4	95.7	97.1	94.1	96.8
First trimester scan performed					
Yes	96.2	95.9	92.9	89.2	88.5
No	3.8	4.1	7.1	10.8	11.5
Consanguinity					
Yes	0.8	1.5	2.0	2.9	4.2
No	99.2	98.5	98.0	97.1	95.8

Appendix 4. The association of socio-spatial socioeconomic deprivation (FDep) with prevalence and infant mortality among births with congenital anomalies

	Reference <2 years old		All congenital anomalies			Infant mortality rate		
FDep	N	%	N=2991§	%	cOR (95% CI)	N=64	%	cOR (95% CI)
Q1 (least deprived)	12616	20.1	507	17.0	Ref	5	7.8	Ref
Q2	12629	20.1	628	21.0	1.25 (1.11–1.41)	13	20.3	2.60 (0.93–7.29)
Q3	12594	20.0	583	19.5	1.16 (1.03–1.31)	10	15.6	2.00 (0.68–5.87)
Q4	12600	20.0	625	20.9	1.25 (1.11–1.41)	16	25.0	3.21 (1.17–8.76)
Q5 (most deprived)	12482	19.8	648	21.7	1.31 (1.16–1.47)	20	31.3	4.05 (1.52–10.79)
Trend test				<0.001			0.003	
§census data for FDep available only for N=2991								

Appendix 5. Association of socio-spatial, socioeconomic, demographic and pregnancy variables with detection, TOPFA, and live birth (complete-case analysis)

Variables	Detection			TOPFA			Live birth		
PFDEP	Unadjusted RR (95% CI)	Adjusted RR[1] (95% CI)	Adjusted RR[2](95% CI)	Unadjusted RR (95% CI)	Adjusted RR[1](95% CI)	Adjusted RR[2](95% CI)	Unadjusted RR (95% CI)	Adjusted RR[1](95% CI)	Adjusted RR[2](95% CI)
Q1	1	1	1	1	1	1	1	1	
Q2	0.99 (0.93–1.06)	1.00 (0.92–1.08)	0.99 (0.91–1.08)	0.98 (0.86–1.13)	1.01 (0.86–1.20)	1.02 (0.86–1.21)	1.00 (0.91-1.09)	0.98 (0.89-1.08)	0.98 (0.89–1.08)
Q3	0.97 (0.90–1.04)	0.96 (0.89–1.04)	0.96 (0.88–1.04)	1.01 (0.89–1.16)	1.05 (0.89-1.24)	1.04 (0.88–1.23)	1.00 (0.91-1.09)	0.99 (0.90-1.09)	0.99 (0.90–1.09)
Q4	0.91 (0.84–0.97)	0.93 (0.85–1.01)	0.93 (0.86–1.02)	0.87 (0.75–1.01)	0.94 (0.79–1.13)	0.94 (0.78–1.13)	1.11 (1.02-1.21)	1.06 (0.97–1.16)	1.06 (0.97–1.16)
Q5	0.90 (0.84–0.97)	0.94 (0.86–1.03)	0.94 (0.86–1.03)	0.73 (0.62–0.85)	0.89 (0.73-1.08)	0.89 (0.73–1.09)	1.17 (1.08-1.27)	1.06 (0.97–1.15)	1.05 (0.96–1.15)
Occupation									
Higher-level	1	1	1	1	1	1	1	1	
Employees and service workers	0.92 (0.86–0.99)	1.02 (0.94–1.11)	1.04 (0.96–1.13)	0.81 (0.70–0.95)	0.96 (0.81–1.15)	0.96 (0.80–1.14)	1.11 (1.03–1.19)	1.01 (0.93–1.10)	1.02 (0.94–1.10)
Manual workers	1.02 (0.92–1.13)	1.13 (1.01–1.26)	1.14 (1.02–1.28)	0.76 (0.59–0.98)	0.96 (0.74–1.25)	0.89 (0.67–1.20)	1.08 (0.96–1.22)	0.96 (0.84–1.10)	0.99 (0.87–1.13)
No defined occupation	0.87 (0.81–0.93)	0.94 (0.86–1.04)	0.97 (0.88–1.07)	0.49 (0.41–0.59)	0.61 (0.48–0.78)	0.69 (0.54–0.89)	1.30 (1.23–1.37)	1.17 (1.09–1.26)	1.13 (1.05–1.22)
Medical insurance									
SS	1	1	1	1	1	1	1	1	1
Other (CMU, AME)	0.85 (0.77–0.94)	0.98 (0.87–1.10)	0.98 (0.87–1.11)	0.53 (0.40–0.70)	0.86 (0.63–1.17)	0.96 (0.71–1.30)	1.26 (1.18–1.34)	1.03 (0.95–1.11)	1.00 (0.93–1.09)
None	0.75 (0.61–0.91)	0.95 (0.77–1.16)	1.00 (0.80–1.25)	0.62 (0.39–0.98)	1.19 (0.74–1.94)	1.09 (0.60–1.96)	1.22 (1.09–1.36)	0.96 (0.85–1.09)	0.95 (0.84–1.08)
Geographic origin									
France	1	1	1	1	1	1	1	1	1
Other European Countries	0.99 (0.87–1.12)	1.00 (0.88–1.13)	0.96 (0.84–1.09)	1.26 (1.04–1.53)	1.29 (1.05–1.57)	1.22 (1.00–1.48)	0.88 (0.74–1.05)	0.87 (0.74–1.04)	0.92 (0.78–1.09)
North Africa	1.05 (0.98–1.12)	1.09 (1.01–1.17)	1.10 (1.01–1.19)	0.68 (0.57–0.82)	0.83 (0.69–1.01)	0.88 (0.72–1.06)	1.15 (1.07–1.24)	1.05 (0.97–1.15)	1.04 (0.96–1.13)
Other African countries	0.79 (0.73–0.85)	0.81 (0.74–0.90)	0.83 (0.75–0.92)	0.56 (0.46–0.67)	0.69 (0.55–0.87)	0.70 (0.55–0.90)	1.25 (1.18–1.33)	1.14 (1.06–1.23)	1.12 (1.03–1.21)
Other	1.01 (0.94–1.09)	1.02 (0.94–1.10)	1.02 (0.93–1.11)	0.89 (0.76–1.05)	0.98 (0.82–1.16)	0.97 (0.82–1.16)	1.04 (0.96–1.14)	1.02 (0.93–1.11)	1.01 (0.92–1.11)
Age (years)									
<25	0.85 (0.74–0.98)		0.95 (0.80–1.11)	0.46 (0.29–0.72)		0.50 (0.27–0.94)	1.20 (1.12–1.29)		1.07 (0.99–1.16)
25-34	1		1	1		1	1		1
35-39	1.08 (1.02–1.13)		1.08 (1.01–1.14)	1.38 (1.24–1.53)		1.33 (1.16–1.51)	0.83 (0.78–0.88)		0.86 (0.81–0.92)
≥40	1.11 (1.04–1.18)		1.12 (1.04–1.20)	1.56 (1.39–1.76)		1.71 (1.48–1.98)	0.73 (0.66–0.80)		0.72 (0.65–0.80)

Variables	Detection		TOPFA		Live birth	
Pre-pregnancy BMI (kg/m²)						
<18.5	1.06 (0.98–1.14)	1.05 (0.96–1.15)	1.09 (0.93–1.28)	1.01 (0.83–1.21)	0.92 (0.82–1.03)	0.97 (0.87–1.10)
18.5-24.9	1	1	1	1	1	1
25.0-29.9	0.92 (0.86–0.98)	0.95 (0.88–1.03)	0.80 (0.69–0.93)	0.86 (0.71–1.03)	1.13 (1.06–1.20)	1.09 (1.02–1.16)
≥30	0.90 (0.82–0.98)	0.96 (0.86–1.06)	0.67 (0.54–0.83)	0.85 (0.66–1.09)	1.19 (1.11–1.28)	1.08 (1.00–1.17)
Smoking 1st trimester						
Yes	0.99 (0.90–1.08)	0.96 (0.87–1.07)	0.96 (0.80–1.16)	0.95 (0.76–1.18)	1.00 (0.91–1.11)	1.02 (0.92–1.13)
No	1	1	1	1	1	1
ART						
Yes	1.03 (0.95–1.12)	1.01 (0.91–1.11)	0.98 (0.81–1.18)	0.73 (0.58–0.94)	1.00 (0.91–1.11)	1.16 (1.03–1.30)
No	1	1	1	1	1	1
Multiple						
Yes	0.94 (0.83–1.07)	0.92 (0.79–1.07)	1.06 (0.84–1.34)	1.12 (0.84–1.49)	0.98 (0.85–1.12)	0.93 (0.80–1.09)
No	1	1	1	1	1	1
First trimester scan performed						
Yes	1	1	1	1	1	1
No	0.80 (0.67–0.95)	0.90 (0.71–1.11)	0.57 (0.43–0.76)	0.95 (0.68–1.33)	1.21 (1.03–1.41)	1.02 (0.84–1.24)
Consanguinity						
Yes	0.91 (0.77–1.08)	1.02 (0.85–1.24)	0.38 (0.20–0.71)	0.65 (0.35–1.22)	1.25 (1.11–1.40)	1.04 (0.91–1.18)
No	1	1	1	1	1	1

[1] *adjusted for maternal occupation, insurance status, geographic origin*
[2] *adjusted for maternal occupation, insurance status, geographic origin, maternal age, pre-pregnancy BMI, smoking, ART, multiplicity, 1st trimester ultrasound, consanguinity*

Appendix 6. Association of SES and maternal characteristics with live birth among severe CA (N=343)

Variables	Live birth among severe CA n/N	% live birth	Unadjusted RR (95% CI)	Live birth among all CA Unadjusted RR (95% CI)
All	113/343	32.9		
P-FDep				
Q1	24/74	32.4	1	1
Q2	22/68	32.4	1.00 (0.62–1.61)	1.00 (0.91-1.09)
Q3	20/76	26.3	0.81 (0.49–1.34)	1.00 (0.91-1.09)
Q4	21/58	36.2	1.12 (0.69–1.79)	1.11 (1.02-1.21)
Q5	26/66	39.4	1.21 (0.78–1.89)	1.17 (1.08-1.27)
Occupation				
Higher-level	54/211	25.6	1	1
Employees and service workers	20/45	44.4	1.60 (1.05–2.44)	1.11 (1.03–1.20)
Manual workers	6/16	37.5	1.68 (0.88–3.20)	1.08 (0.95–1.24)
No defined occupation	33/71	46.5	1.93 (1.38–2.68)	1.31 (1.24–1.39)
Medical insurance				
SS	90/294	30.6	1	1
Other (CMU, AME)	17/34	50.0	1.60 (1.09–2.36)	1.25 (1.16–1.34)
None	5/14	35.7	1.07 (0.51–2.23)	1.20 (1.06–1.36)
Geographic origin				
France	56/184	30.4	1	1
Other European Countries	3/13	23.1	0.83 (0.34–1.99)	0.89 (0.74–1.07)
North Africa	15/45	33.3	1.13 (0.71–1.80)	1.16 (1.07–1.25)
Other African countries	24/59	40.7	1.39 (0.94–2.03)	1.27 (1.20–1.36)
Other	15/43	34.9	1.17 (0.75–1.83)	1.05 (0.95–1.15)
Age (years)				
<25	21/32	65.6	2.20 (1.59–3.04)	1.20 (1.12–1.29)
25-34	58/188	30.9	1	1
35-39	22/81	27.2	0.88 (0.58–1.33)	0.83 (0.78–0.88)
≥40	12/42	28.6	0.93 (0.55–1.56)	0.73 (0.66–0.80)
Pre-pregnancy BMI (kg/m²)				
<18.5	9/35	25.7	0.97 (0.55–1.71)	0.92 (0.82–1.04)
18.5-24.9	64/213	30.0	1	1
25.0-29.9	26/54	48.1	1.57 (1.10–2.25)	1.13 (1.06–1.20)
≥30	14/41	34.1	1.38 (0.89–2.15)	1.18 (1.10–1.27)
Smoking 1st trimester				
Yes	9/27	33.3	1.05 (0.61–1.83)	1.00 (0.91–1.11)
No	104/316	32.9	1	1
ART				
Yes	6/27	22.2	0.65 (0.32–1.35	1.00 (0.90–1.11)
No	111/316	35.1	1	1
Multiple pregnancy				
Yes	2/13	15.4	0.46 (0.13–1.65)	0.98 (0.85–1.12)
No	111/330	33.6	1	1
First trimester scan performed				
Yes	99/308	32.1	1	1
No	14/35	40.0	1.27 (0.82–1.96)	1.21 (1.03–1.41)
Consanguinity				
Yes	4/6	66.7	2.05 (1.14–3.68)	1.25 (1.11–1.40)
No	109/335	32.5	1	1