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# Dynamics of social inequalities in severe COVID-19 outcomes in metropolitan France from 2020 to 2022



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#### **Abstract**

**Background** Evidence on the dynamics of social inequalities throughout the COVID-19 healthcare pathway in France is sparse. This study examined the relationship between arealevel social deprivation and hospitalizations, intensive care unit (ICU) admissions, and deaths in metropolitan France during five pandemic waves (wave 2: 1 July-16 December 2020, wave 3: 23 December 2020-16 June 2021, wave 4: 23 June-20 October, wave 5: 27 October-2 March 2022, wave 6: 9 March-31 August 2022).

**Methods** Using comprehensive data from the French national surveillance hospitalization database, we built spatiotemporal Bayesian Poisson regression models to estimate, for each pandemic wave, Incidence Rate Ratios (IRR) and 95% credible interval (CrI) for the association between outcomes and quintiles of the European Deprivation Index, among the French general population and infected persons.

**Results** We show a growing social gradient for all outcomes among infected persons. For people living in the most deprived areas the IRR increases from 1.43 95%CrI (1.39-1.47) (wave 2) to 1.60(1.55-1.66) (wave 6) for hospitalizations, from 1.57(1.49-1.66) to 1.72(1.58-1.87) for ICU admissions, and from 1.35(1.28-1.42) to 1.70(1.55-1.87) for in-hospital deaths. Among the general population we also observe a social gradient in all outcomes which declines after wave 5.

**Conclusions** We find a social gradient related to severe forms of COVID-19 over the five pandemic waves studied, and this gradient increases among persons infected with the disease. Our study highlights the importance of considering social position when managing pandemics and underscores the need for targeted interventions for specific populations to minimize health inequalities.

The COVID-19 pandemic highlighted and exacerbated existing social inequalities in health in many countries. The first international studies examining the association between social inequalities and COVID-19 incidence found that exposure was strongly linked to occupational activity, income, and housing conditions<sup>1,2</sup>. Persons with low incomes, persons with low levels of education, and immigrant populations from non-European countries were more likely to be infected. They were also more likely to develop severe forms of COVID-19. Moreover, they had a greater risk of dying from COVID-19 during the first waves of the pandemic<sup>3-7</sup>. The

# Plain language summary

The COVID-19 pandemic has exacerbated social inequalities in health, yet how these inequalities changed across successive waves and stages of disease severity remains poorly understood. We analyzed the link between neighborhood social deprivation and the risk of hospitalization, ICU admission, and in-hospital death using national hospitalization data from metropolitan France across five pandemic waves (July 2020-August 2022). Our findings reveal that individuals living in disavantaged neighborhood faced significantly higher risks of severe outcomes, even after widespread vaccine rollout. These inequalities intensified among infected individuals over waves, while partially declining in the general population. Our findings suggest that structural factors—such as comorbidity burden, occupational exposure, and healthcare access - play a major role and highlight the need to integrate equity considerations into pandemic preparedness and routine health policies.

socially differentiated distribution of comorbidities and access to care that cause delays in diagnosis of COVID-19 were possible causes of inequalities in morbidity and mortality<sup>8</sup>. Social inequalities were present throughout the COVID-19 healthcare pathway, from the risk of infection to access to medical care<sup>4-6</sup>, testing<sup>9,10</sup>, prevention and especially vaccination. Despite recommendation of the World Health Organization to give equal access to vaccination for all populations, social inequalities in vaccination coverage remained<sup>10,11</sup>. In France, the government initiated multi-phase vaccination roll-out<sup>12</sup> starting 26 December 2020, with the aim of prioritizing groups

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most at risk including health workers, people with comorbidities, and elderly persons irrespective of their social position. However, the large French epidemiological study EpiCov<sup>11</sup> which was conducted between 24 June and 9 August 2021, found that people with lower incomes, lower levels of education, and non-European immigrants, were the least likely population groups to have been vaccinated. Taken together, all the above data show social inequalities in COVID-19 infection incidence, in the incidence of severe forms of the disease and death, and in vaccination during certain waves of the pandemic, both in France and elsewhere. France, like many other countries, experienced several waves of infection, each one impacting public health, healthcare systems, and societal measures differently. Although various studies focusing on specific waves have highlighted social inequalities throughout the COVID-19 healthcare pathway<sup>13–15</sup> few studies have used population-based data to investigate the dynamics of these social inequalities across different waves<sup>16</sup>.

In this study, we aimed to examine the relationship between social deprivation and severe forms of COVID-19 (hospitalization, intensive care unit (ICU) admission, and death in hospital) in metropolitan France. Our objective was to estimate the overall burden in the French general population and to assess disease severity among those infected with COVID-19. The study cover five pandemic waves from 1 July 2020 to 31 August 2022, in order to assess COVID-19-related temporal dynamics in social inequalities. We also aimed to evaluate the effect of the vaccination campaign on this relationship. Here, we present findings that show individuals living in deprived areas face significantly higher risks of severe outcomes, even after widespread vaccine rollout. These inequalities intensify among infected individuals over successive waves, while they partially decline in the general population.

# **Methods**

#### Study population

This population-based study used the database from the French national surveillance system for hospitalizations (SI-VIC)<sup>17</sup>. All individuals included in this database tested positive for COVID-19. SI-VIC includes information on individuals' age, sex, date of hospitalization, and area of residence code i.e., the smallest geographical unit used in France for statistical information, called the IRIS (https://www.insee.fr/en/metadonnees/definition/c1523). IRIS codes comprise ~2000 inhabitants who are relatively homogenous in terms of their socioeconomic characteristics.

We included all patients hospitalized for COVID-19 from 1 July 2020 until 31 August 2022. Patients re-hospitalized more than 7 days after discharge were included as new patients. We excluded patients with missing data for area of residence, age and sex. We were not able to include patients hospitalized during the first wave of the pandemic (i.e., before July 2020) as the database was not fully operational at that time (because of a lack of coverage and missing values for IRIS). Accordingly, we investigated the temporal dynamics in social inequalities during the course of five pandemic waves, starting with the first day of the week as follows; Wave 2: 1 July-16 December 2020, Wave 3: 23 December-16 June 2021, Wave 4: 23 June-20 October 2021, Wave 5: 27 October-2 March 2022 and Wave 6: 9 March-31 August 2022. The cuts were determined based on the epidemic curve in France and the official periods during which there were sustained increases in the number of new hospitalization cases were observed, followed by a peak and then a decline.

#### **Outcomes**

We examined severe forms of COVID-19: hospitalization, ICU admission, and death during hospitalization.

#### Main explanatory variable

No individual social data is collected in the SI-VIC database. Accordingly, to obtain information on patients' social deprivation, we matched this database with the 2017 French version of the European Deprivation Index (EDI)—using patients' IRIS codes. The EDI calculation followed three steps:

First, calculation of an individual deprivation indicator from the French version of the European Union Statistics on Income and Living Conditions survey (EU-SILC) designed to study deprivation (https://ec.europa.eu/eurostat/statistics-explained/index.php?title=EU\_statistics\_on\_income\_and\_living\_conditions\_(EU-SILC)\_methodology). Second, selection of variables available both at individual level (EU-SILC survey) and in the French census population (aggregated variables at IRIS-level).

Third, a multivariate logistic regression was used to select among 11 individual explanatory variables that reflect different aspects of deprivation from EU-SILC survey, those associated with the individual deprivation indicator

Finally, ten variables were selected to build the EDI: proportion of individuals of non-French nationality, proportion of households without a car, proportion of individuals employed as managers or intermediate professionals, proportion of single-parent families, proportion of households with at least two members, proportion of non-owner occupied households, proportion of unemployed individuals, proportion of individuals without post-secondary school education, proportion of overcrowded dwellings, and proportion of non-married individuals.

The coefficients of the regression were used as weights for the corresponding aggregated variables, to calculate the EDI. The French EDI score at IRIS-level is obtained as a weighted sum of the ten variables<sup>18</sup>. Quintiles of the national distribution of EDI scores were computed for metropolitan France, with the first quintile (Q1) representing the least deprived areas and the fifth quintile (Q5) the most deprived areas.

#### Statistical analysis

In this study we used two reference populations at the IRIS level: (1) The 2020 French census population; (2) The population infected with COVID-19 (testing positive) during each week obtained from the national testing information system database SI-DEP<sup>13</sup>. This enabled us to investigate not only social inequalities relating to COVID-19 exposure but also whether these social inequalities persisted among infected individuals.

First, to describe the weekly dynamics of hospitalization, of ICU admission, and of death during hospitalization according to EDI quintiles, we calculated the corresponding age and sex standardized rates (i.e., direct standardization) using the two reference populations.

Second, to investigate the association between weekly counts of hospitalizations, ICU admissions and deaths with EDI quintiles for each pandemic wave, we employed spatiotemporal Bayesian Poisson regression models. These models were used to estimate incidence rate ratio (IRR) and 95% credible interval (CrI). The model specification included spatial random effect at the IRIS level following a scaled Besag-York-Mollié (BYM2) distribution with Penalized Complexity (PC) priors<sup>19</sup> to account for spatial dependencies between observation<sup>20–22</sup>. Additionally, we incorporated temporal random effect for the week, modeled using a second order random walk distribution to capture the weekly dynamics of the outcomes. The expected number of cases (i.e., age and sex indirect standardization) was included as an offset and calculated based to the two previously defined reference populations.

The model specification used in this study is described below:

Let  $y_{o,we,i}$  be the number of cases for outcome o, during week we, in IRIS i.

$$y_{o,we,i} \sim Poisson(E_{o,we,i} \times \rho_{o,we,i})$$

Where  $E_{o,we,i}$  is the expected number of cases for outcome o, during week we, in IRIS i (see below), and  $\rho_{o,we,i}$  is the relative risk of outcome o, during week we, in IRIS i.

$$\log(\rho_{o,\text{we},i}) = \alpha_o + b_{o,i} + f_o(\text{we}) + \left(\beta_{2,o}Q2_i + \beta_{3,o}Q3_i + \beta_{4,o}Q4_i + \beta_{5,o}Q5_i\right)$$
(1)

#### Where

- $\alpha_o$  is the intercept for outcome o.
- $b_{o,i}$  is a spatial random effect at the IRIS level *i*. It follows a scaled Besag-York-Mollié (BYM2) distribution<sup>19</sup>.
- f<sub>o</sub>(we) is a temporal random effect for week we which follows a second order random walk distribution allowing a dependency in the two preceding weeks.
- $Qj_i$ , j = 2.5 is an index variable which equals 1 when the EDI value in IRIS code i falls within the jth quintile, and 0 otherwise;  $\beta_{j,o}$ , j = 2.5 is the coefficient associated with EDI quintile j for outcome o. Therefore, we derived the IRR associated with EDI quintile Qj relative to quintile Q1 for outcome o as:  $\exp\left(\beta_{j,o}\right)$ .

# Expected number of cases based on the 2020 population census

For each of the three outcomes, we first used the population distribution across IRIS codes provided by the 2020 census to calculate the expected number of cases for outcome o, using age and sex indirect standardization. Specifically, the expected number of cases for outcome o, for each week we, in IRIS i,  $E_{o,we,i}$ , was:

$$E_{o,we,i} = \sum_{a \in A, s \in \{F,M\}c} \left[ \frac{y_{o,a,s,w(we)} \times Pop_{a,s,i}}{n_{w(we)} \times Pop_{a,s}} \right]$$

Where w(we) is the wave that contains week we,  $y_{o,a,s,w(we)}$  is the cumulated number of cases of outcome o, 15-year age groups a and sex s, across wave w(we) in metropolitan France;  $Pop_{a,s,i}$  is the 2020 population in IRIS i of age group a and sex s;  $Pop_{a,s}$  is the 2020 population in metropolitan France belonging to age group a and sex s;  $n_{w(we)}$  is the number of weeks in wave w(we); A is the age group partitioning of the population; refers to female/male partitioning.

# Expected number of cases based on the number of positive cases

Second, we used the population tested positive to COVID-19 to compute the expected number of cases for outcome *o* in week *we* and IRIS *i*, using age and sex indirect standardization as follows:

$$E_{o,we,i} = \sum_{a \in A, s \in \{F,M\}} \left[ \frac{y_{o,a,s,w(we)} \times Pos_{a,s,w(we),i}}{n_{w(we)} \times Pos_{a,s,w(we),i}} \right]$$

Where  $Pos_{a,s,w(we),i}$  is the cumulated number of cases tested positive for COVID-19 over wave w(we), for age group a and sex s, in IRIS i;  $Pos_{a,s,w(we)}$  is the number of cases tested positive for COVID-19 for age group a, sex s, wave w(we), cumulated over all metropolitan France, and changed for each wave

Of note, with each standardization,  $E_{o,we,i}$  was constant over wave w(we).

### Adjustment for vaccination rates

We were interested in measuring the "direct" effect of the EDI on COVID-19 outcomes that was not accounted for by the lack of vaccination. To do this, we hypothesized that the vaccine rate might act as a mediating factor in the relationship between the EDI and the incidence of the three outcomes.

We calculated the age and sex standardized vaccine rates (i.e direct standardization) using the cumulative number of individuals fully vaccinated (with two or three doses) during a given week and municipality which contained IRIS, and the number of inhabitants living in this municipality according to the 2021 French population census data. To note, the number of individuals vaccinated at the IRIS level was not available.

We calculated these rates according to two periods to account for the booster dose introduced on 1 September 2021 as follows:

Period 1: 26 December 2020–20 October 2021 (i.e., covering waves 3 and 4): individuals fully vaccinated against COVID-19 with two doses.

Period 2: 1 September 2021 to 31 August 2022 (i.e., covering waves 5 and 6): individuals fully vaccinated against COVID-19 with three doses, or two doses if the second injection occurred in that period.

First, we tested to see whether the EDI was negatively associated with COVID-19 standardized vaccine rates, and whether COVID-19 standardized vaccine rates were negatively associated with the incidence of the three outcomes.

Second, we added the standardized vaccine rates assumed to follow a second order random walk distribution into the previous model (Eq. (1)).

The adjusted model has the following expression:

$$\log(\rho_{o,we,i}) = \alpha_o + b_{o,i} + f_o(we) + (\beta_{2,o}Q2_i + \beta_{3,o}Q3_i + \beta_{4,o}Q4_i + \beta_{5,o}Q5_i) + g_o(Vac_{we,m_i})$$
(2)

We used R software version 4.2. The spatiotemporal Bayesian Poisson regression models were implemented using the package R-INLA<sup>23</sup> package version 22.12.16 (www.r-inla.org).

#### **Ethics**

This study obtained ethical authorizations from the Comité éthique et scientifique pour les recherches les études et les évaluations dans le domaine de la santé (CESREES) 03/09/20 n°1880179bis and the Commission nationale de l'informatique et des libertés (CNIL) 18/08/21 (DSI-COVID décision DR-2021-238) demande d'autorisation n° 921160. As such, the requirement for informed consent was waived given the data used are extracted from administrative databases, and that enhanced data protection measures were implemented, including pseudonymization, to mitigate risks associated with the partially identifiable nature of the data. Access is strictly controlled and restricted to authorized researchers.

#### Results

During our study period (1 July 2020–31 August 2022) 594,130 hospitalizations for the disease were recorded in metropolitan France.

We excluded 10,828 (1.8%) hospitalizations due to missing data for age and sex. Additionally, we excluded 77,988 (13.1%) for missing IRIS data, 6168 (1%) due to IRIS mismatches between the EDI and SI-VIC databases, and 282 due IRIS mismatches between the SI-VIC and SI-DEP databases. Hospitalizations excluded due to the absence of IRIS codes (n = 84,438) corresponded more often to hospitalizations during the sixth wave. They showed significant differences in terms of age and gender, although these differences were very small and negligible (Supplementary Tables S1–S2).

Table 1 shows the distribution of hospitalizations included in the study population according to age, sex, pandemic wave, and EDI quintiles. Approximately two-thirds of the study population were 60 years old or more (Table 1). Men accounted for half of hospitalizations (52%), 64% of ICU admissions, and 58% of deaths during hospitalization. People living in the most deprived areas (Q5) accounted for 39% of hospitalizations, 42% of ICU admissions, and 37% of deaths.

Figure 1 shows the standardized hospitalization rate dynamics per week according to EDI quintiles using the French general population. It also indicates the five pandemic waves studied with the main government health measures implemented, notably the vaccination campaign starting on 26 December 2020, and the third lockdown during wave 3 (April 2021). Hospitalization rates were higher for patients living in the most deprived areas (Q5) (versus Q1), and during waves 2–5. The differential rates (Q5 versus Q1) decreased during wave 6 (Fig. 2a). We found a similar pattern for ICU admissions and deaths (Fig. 2b, c, Supplementary Table S3).

We also observed a social gradient during all five waves for hospitalization rates standardized among people infected with COVID-19 (Fig. 3a) and the same pattern was observed for other outcomes (Fig. 3b, c, Supplementary Table S4).

Models using the general population showed a social gradient for the three outcomes (Fig. 4, see not adjusted IRR, Supplementary Table S5): the

higher the level of deprivation, the greater the risk of being hospitalized, of being admitted to ICU, and of dying, irrespective of the pandemic wave. The strength of this gradient changed over the five waves: compared to Q1, the IRR for hospitalization among people living in Q5 increased from IRR = 1.64 95%CrI (1.59–1.69) in wave 2–2.17 (2.06–2.29) in wave 4, then

Table 1 | Characteristics of the study population, from 1 July 2020–31 August 2022

	Hospitalizations (n = 498,864)	ICU admissions (n = 89,338)	Deaths (n = 74,872)
Sex			
Women	48% (239,493)	36% (31,973)	42% (31,483)
Men	52% (259,371)	64% (57,365)	58% (43,389)
Age category (years)			
00–14	3% (15,096)	2% (1515)	<1% (43)
15–29	4% (19,795)	3% (2258)	<1% (103)
30–44	8% (39,250)	8% (7119)	1% (529)
45–59	15% (74,765)	22% (20,031)	4% (3355)
60–74	26% (130,068)	42% (38,124)	23% (17,027)
≥75	44% (219,890)	23% (20,291)	72% (53,815)
EDI quintiles			
Q1 — Least deprived areas	12% (57,443)	11% (10,046)	11% (8513)
Q2	13% (65,702)	12% (11,112)	13% (9910)
Q3	16% (79,766)	15% (13,286)	16% (12,108)
Q4	21% (102,723)	19% (17,191)	22% (16,354)
Q5 – Most deprived areas	38% (193,230)	43% (37,703)	38% (27,987)
Epidemic waves			
Wave 2	24% (117,890)	22% (19,530)	29% (21,778)
Wave 3	31% (160,006)	39% (35,072)	37% (27,998)
Wave 4	6% (29,340)	8% (7517)	5% (3543)
Wave 5	23% (112,637)	22% (19,289)	20% (15,101)
Wave 6	16% (78,991)	9% (7930)	9% (6452)

ICU Intensive Care Unit; n number of hospitalizations, ICU admissions, or in-hospital deaths; EDI quintiles European Deprivation Index quintiles from the least deprived areas (Quintile 1, i.e., Q1) to the most deprived areas (Quintile 5, i.e., Q5).

decreased until wave 6-1.33 (1.29-1.37). A similar pattern was observed for ICU admissions with an increase from 1.84 (1.74-1.95) in wave 2-2.58 (2.36-2.84) in wave 4, and then a decrease until wave 6-1.36(1.26-1.48). The same was also observed for deaths during hospitalization with an increase from 1.66 (1.57-1.76) in wave 2-2.22 (1.95-2.52) in wave 4, followed by a decrease until wave 6-1.43 (1.30-1.56).

Models using the population infected with COVID-19 highlighted the same gradient between deprivation and the study outcomes (Fig. 5, see not adjusted IRR, Supplementary Table S6): people living in Q5 had a higher risk of hospitalization, ICU admission and death. Although we observed a slight decrease in this gradient between waves 2 and 3, overall (i.e., over the five waves) the risk increased for all three outcomes (hospitalizations from IRR = 1.43 (1.39–1.47) in wave 2–1.60 (1.55–1.66) in wave 6, ICU admissions from 1.57 (1.49–1.66) to 1.72(1.58-1.87), and deaths during hospitalization from 1.35 (1.28–1.42) to 1.70 (1.55–1.87).

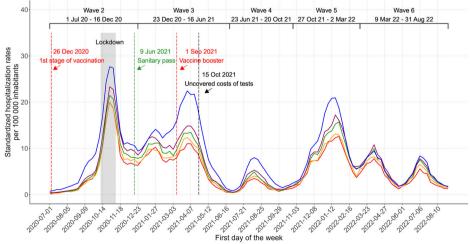
Finally, the association between deprivation and our three outcomes remain unchanged after adjustment for standardized vaccination rates; an excess risk of hospitalization, ICU admission and death remained in all quintiles compared to the least deprived quintile (Q1) over the four pandemic waves (i.e., waves 3–6), whatever the reference population used for standardization (Figs. 4 and 5, see adjusted IRR, Supplementary Tables S7–S8).

#### **Discussion**

In this French population-based study, we found social inequalities related to severe forms of COVID-19. Specifically, a marked social gradient in the incidence of COVID-19-related severe outcomes across pandemic waves was apparent. People living in more socially disadvantaged areas had a greater risk of being hospitalized, admitted to ICU and of death, compared to their counterparts living in socially advantaged areas. In the general population and for all three outcomes, social inequalities increased from wave 2 (July–December 2020) until wave 4 (June–October 2021), a period corresponding to the French government's recommendation for two vaccination doses for all individuals aged 12 years and older) then decreased from wave 5 (November 2021–February 2022). Among individuals infected with COVID-19, social inequalities increased for all three outcomes, from waves 2–3 to waves 4–6. The observed social gradient persisted for the three outcomes for both populations after adjustment for vaccination rates over all four waves (wave 3 to wave 6).

The social gradient we observed for the three outcomes in our study aligns with findings from studies conducted in Switzerland<sup>4</sup>, Sweden<sup>6</sup> and Spain<sup>24</sup> during the first year of the pandemic. However, those studies did not cover the entire period of our study. Another Swedish study, which covered the same period as ours found an income-based gradient for the risk of

Fig. 1 | Temporal dynamics of hospitalization rates standardized with the 2020 French general population by week, according to EDI quintiles, from 1 July 2020 to 31 August 2022. EDI quintiles European deprivation index quintiles from the least deprived areas (Quintile 1, i.e., Q1) to the most deprived areas (Quintile 5, i.e., Q5).



EDI Quintiles - Q1 - Least deprived - Q2 - Q3 - Q4 - Q5 - Most deprived

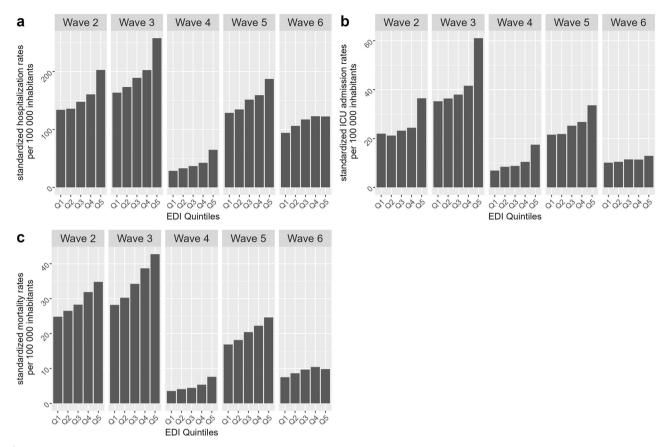


Fig. 2 | Temporal dynamics of hospitalization rates, ICU rates and mortality rates standardized with the French general population by pandemic wave, according to EDI quintiles, from 1 July 2020 to 31 August 2022. EDI quintiles European Deprivation Index quintiles from the least deprived areas (Quintile 1 i.e., Q1) to the

most deprived areas (Quintile 5 i.e., Q5). **a** Standardized hospitalization rates, **b** Standardized ICU admission rates, **c** Standardized mortality rates. These rates were calculated using the direct standardization and the French general population (Supplementary Table S3).

admission to ICU that increased over waves<sup>16</sup>. For the record, in Sweden, "collective immunity" strategy was chosen at the opposite of France with coercive measures (lockdown, travel restrictions).

The main factors which might explain these social inequalities have been well-established in the literature. First, during the pandemic, people who are socially disadvantaged had a greater risk of being infected. Essential workers, who mainly come from disadvantaged socioeconomic groups, had a higher risk of exposure to COVID-19 because they traveled more and had more contact with people (e.g., frontline healthcare workers, persons working in transportation, food services, and other sectors) compared to manager who worked from home. This increased exposure contributed to higher rates of infection<sup>4,13</sup> and hospitalization<sup>25</sup> in these groups. Furthermore, overcrowded high population density neighborhoods and substandard living conditions, which are more frequent among disadvantaged socioeconomic groups, made physical distancing and self-isolation by infected individuals difficult to implement, leading to higher transmission rates in different generations living in households<sup>13</sup>.

Second, people who are socially disadvantaged have a higher risk of underlying health conditions (e.g., diabetes, hypertension, obesity). This higher risk of underlying health conditions may be due to a variety of factors ranging from structural determinants such as living conditions - which influence, for example, access to food and opportunities for physical activity - to more individual determinants such as cultural aspects and literacy levels, which influence a person's relationship with health prevention. The association between lower socioeconomic status and health behaviors is well-established in the literature, with some studies suggesting that these factors may account for up to 30% of social inequalities in mortality.

Third, socially disadvantaged populations in France face barriers which limit their access to healthcare services including (i) a lack of supplementary

health insurance to complement reimbursement for care provided by the French social security system, (ii) structural problems (transportation, inadequate services and too few healthcare facilities in their neighborhoods), (iii) financial barriers for certain types of care, (iv) limited health literacy and insufficient understanding of the health system organization, (v) the need to prioritize other needs (e.g., children's clothes), (vi) different perceptions of healthcare needs and (vii) discrimination and cultural barriers. During the COVID-19 pandemic, these barriers resulted in a delay in seeking medical care and prevention, leading to more severe outcomes. As of 17 October 2021, 76% of the population had received at least one dose of the vaccine<sup>27</sup> which indicates insufficient coverage to curb the spread of the disease especially among the most disadvantaged people. This reflects findings from a meta-analysis of national cohort studies in England, Northern Ireland, Scotland, and Wales which highlighted that socially deprived people were less likely to be fully vaccinated<sup>28</sup>.

In terms of temporal dynamics, our results showed that the social gradient decreased from wave 5 onward in the general population. We can assume that this is due, at least in part, to natural immunity or vaccination at this point in the pandemic. However, adjusting for vaccination rates did not change our results which may be due to structural barriers to healthcare, or to the scale at which vaccination rates were calculated, or to the reliability of this indicator. We also found that the social gradient among individuals infected with COVID-19 continued to increase over all five waves. Once again, the fact that adjusting for vaccination rates did not change the results raises questions about the quality of the indicator. This difference in temporal dynamics between the two reference populations may also be due to a change in the characteristics of the population carrying out tests in terms of behavior and health status as a function of pandemic wave and the EDI. This change is probably linked to the management of the pandemic (e.g.,

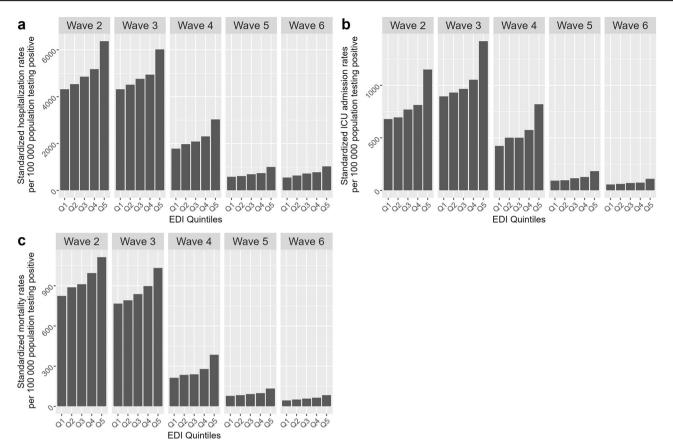
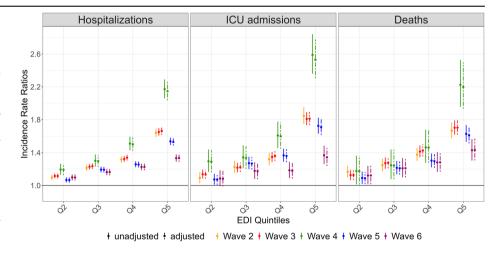


Fig. 3 | Temporal dynamics of hospitalization rates, ICU rates and mortality rates standardized with the population infected with COVID-19 by pandemic wave, according to EDI quintiles, from 1 July 2020 to 31 August 2022. EDI quintiles European Deprivation Index quintiles from the least deprived areas (Quintile 1, i.e.,

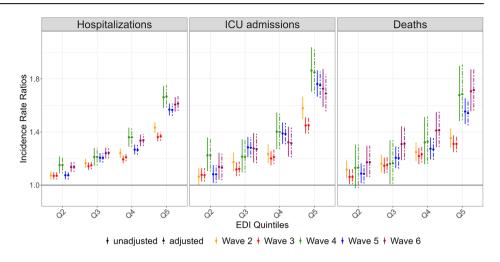
Q1) to the most deprived areas (Quintile 5, i.e., Q5). a Standardized hospitalization rates, **b** Standardized ICU admission rates, **c** Standardized mortality rates. These rates were calculated using the direct standardization and the population infected with COVID-19 (Supplementary Table S4).

Fig. 4 | Incidence Rate Ratios of COVID-19-related hospitalizations, ICU admissions and deaths in hospital for different deprivation levels (i.e., EDI quintiles) in the French general population, according to pandemic wave, from 1 July 2020 to 31 August 2022. Notes: ICU Intensive Care Unit; EDI quintiles European Deprivation Index quintiles from the least deprived areas (Quintile 1, i.e., Q1) to the most deprived areas (Quintile 5, i.e., Q5), Q1 being the reference quintile for comparison. The French general population was the denominator used to compute the expected number of cases. Points represent the Incidence Rate Ratio (IRR), with error bars showing 95% credible intervals. IRR unadjusted refer to the model Eq. (1) (unadjusted for standardized vaccination rates, Supplementary Table S5). Adjusted IRR refer to the model Eq. (2) (adjusted for standardized vaccination rates, Supplementary Table S7).



government lockdowns, health pass, company rules regarding testing and/ or vaccination, the ending of reimbursement for COVID-19 tests, vaccination campaigns). Vaccination may have discouraged testing because people no longer thought it was useful. The governmental measure to no longer reimburse unprescribed tests from October 2021 (i.e., beginning of wave 5) for unvaccinated people may have been a barrier to testing for people living in socioeconomically deprived areas. Our results among people infected with COVID-19 showed an increase in social inequalities from the beginning of wave 4 onwards, which coincides with the end of national two-dose vaccination campaign and the end of reimbursement for tests. Our findings align with research carried out in urban areas of Italy during the COVID-19 vaccine rollout from January to November 2021 that revealed that as vaccination coverage increased, there was a corresponding rise in relative socioeconomic inequalities related to infection, hospitalization, and death<sup>29</sup>. Another study<sup>30</sup> found that early and widespread vaccination led to reduction in inequality, especially in high-income countries.

Fig. 5 | Incidence Rate Ratios of COVID-19related hospitalizations, ICU admissions and deaths in hospital for different deprivation levels (i.e., EDI quintiles), in the population infected with COVID-19, according to pandemic wave, from 1 July 2020 to 31 August 2022. ICU Intensive Care Unit; EDI quintiles European Deprivation Index quintiles from the least deprived areas (Quintile 1, i.e., Q1) to the most deprived areas (Quintile 5, i.e., Q5), Q1 being the reference quintile for comparison. The population infected with COVID-19 was the denominator used to compute the expected number of cases. Points represent the Incidence Rate Ratio (IRR), with error bars showing 95% credible intervals. IRR unadjusted refer to the model Eq. (1) (unadjusted for standardized vaccination rates, Supplementary Table S6). Adjusted IRR refer to the model Eq. (2) (adjusted for standardized vaccination rates, Supplementary Table S8).



Our study has limitations. First, the number of individuals infected with COVID-19 in the general population may have been underestimated because testing was not systematic for all infected people due to absence of symptoms or mild non-specific symptoms, hesitancy (about testing), and for later waves; testing fatigue, and already being vaccinated. However, the number of positive cases was extracted from the national testing database, which is exhaustive. Second, we used a social deprivation index rather than the level of deprivation at individual level; this index was used as we did not have access to individual socioeconomic data. We used the smallest geographical scale (IRIS) to assign a deprivation score calculated at the area level for each individual; this may have led to misclassification for some individuals, which in turn would have decreased the inequalities that would be observed at individual level<sup>31</sup>. Third, our study used Baron and Kenny's<sup>32</sup> to explore the effect of vaccination rates in our model. Various methods could have been used to conduct a more in-depth mediation analysis, but this was not the purpose of our analysis. Additionally, vaccination rates were analyzed at the municipality level rather than at the IRIS level or individual level due to data availability constraints. This geographical scale might not provide the necessary precision to fully capture the mediating effects between deprivation and the three individual-level outcomes. Fourth, it was not possible to distinguish patients hospitalized for COVID-19 before January 2021 from those hospitalized for another reason but positively diagnosed with COVID-19 during their hospital stay. While it is likely that all people hospitalized in 2020 who were infected with COVID-19 were hospitalized for this reason, we cannot be sure; this may have led to misclassifications. Fifth, this study included COVID-19 related deaths in hospitals only; deaths at home were not counted so the overall number is certainly underestimated. Sixth, it is crucial to consider potential sources of selection bias, such as the exclusion of subjects due to missing IRIS data or incomplete hospitalization information. Our analysis did not include data from the first wave (15 March-30 June 2020) due to insufficient coverage and missing data. Additionally, we excluded patients with missing information on age, sex, and IRIS, who were significantly different from those included in the study. We cannot rule out the possibility that this excluded population may have had a distinct profile concerning COVID-19 risk and its progression. We did not include data from French overseas territories as the context in terms of the spread of the pandemic and management measures was different to that of metropolitan France.

Our study also has strengths. The main one is the use of national exhaustive database to cover five pandemic waves. Each wave was characterized by a specific viral variant and by specific governmental measures like lockdowns and vaccine campaigns. Moreover, we used two reference populations, the French general population and the population infected with COVID-19, to investigate dynamics in social inequalities in terms of

the risk of having a severe form of COVID-19. By conducting our study over a long period, we were able to investigate if any temporal change occurred in the dynamics of social inequalities.

Finally, our findings could help design new computational models of disease spread that take into account the effect of socioeconomic inequities as fundamental causes of hospitalization and death risk of infectious diseases like COVID-19. Recognizing multiple intervening mechanisms that drive infection risks and adverse outcomes, that are not evenly distributed across populations, researchers should improve integrating structural social determinants and behavioral factors into their models. This shift aims to capture the complex interplay between socioeconomic status and disease transmission and severity, thereby providing a more accurate and comprehensive understanding of epidemic spread. Key contributions in this emerging field include the work of Bedson et al.<sup>33</sup>, Zelner et al.<sup>34</sup>, Tizzoni et al.<sup>35</sup>. By rethinking how we model infection risks, and promote a more holistic approach these studies advocate for more equitable and targeted strategies to mitigate disease spread and more accurate modeling-based decision-making during pandemics.

In conclusion, this nationwide French study found a social gradient: people living in deprived areas were more likely to be hospitalized for COVID-19, to be admitted to an ICU, and to die during hospitalization compared to those living in less deprived areas. These social inequalities increased over time among individuals infected by COVID-19, whereas among the general population, the gradient decreased from wave 5 onwards (Omicron variant). Under-vaccination and the higher prevalence of comorbidities among the disadvantaged population most likely contributed to the higher risk of the three study outcomes. The social gradient continued until wave 6 (March-August 2022) suggesting that vaccination campaigns did not reduce it. Social structural factors play a critical role in driving social inequalities in health. Addressing these factors requires comprehensive, tailor-made strategies which tackle underlying social determinants of health in the most disadvantaged populations such as health mediation implemented in different deprived areas<sup>36</sup>. These strategies guarantee equitable distribution of care and prevention resources, and combat vaccine hesitancy and encourage vaccine acceptance, especially among individuals with serious comorbidities. Above all, more comprehensive societal efforts are required to address the social determinants of health that contribute to these social inequalities.

### Data availability

Due to the small number of cases in certain geographical units, some data supporting the findings of this study may be potentially identifying and are therefore subject to access restrictions. While the raw data are not publicly available, aggregated data can be accessed via the French Public Health

Agency's website using the link below. https://geodes.santepubliquefrance. fr/#c=indicator&f=0&i=covid\_hosp\_ad\_age.newadmhospit&s=2020-S35&t=a01&view=map1. The source data for Fig. 1 is accessible under the above link. The source data for Figs. 2–5 is in the Supplementary.

# Code availability

We used R software version 4.2. The spatiotemporal Bayesian Poisson regression models were implemented using the package R-INLA<sup>23</sup> package version 22.12.16 (www.r-inla.org). The R codes for the analyses are available from the corresponding author on reasonable request.

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#### Author contributions

All authors (S.S., C.P., E.C., A.S., M.K.I., J.G., C.D., S.V.) contributed to the study conception and design. Material preparation, data collection and analysis were performed by S.S. and A.S. The first draft of the manuscript was written by S.S. All authors (S.S., C.P., E.C., A.S., M.K.I., J.G., C.D., S.V.) read, contributed to the drafting and approved the final manuscript for submission.

# **Competing interests**

The authors declare no competing interests.

### Additional information

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