# Vaccination and COVID-19 Dynamics in Dialysis Patients

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**Abstract:** Background and objectives: Dialysis patients have a high mortality risk after COVID-19 and an altered immunological response to vaccines, but vaccine clinical effectiveness remains unknown in this population.
Design, setting, participants, and measurement: Using Bayesian multivariable spatiotemporal models, we estimated the association between vaccine exposure and SARS-CoV-2 severe infections (with hospital admission) in dialysis patients from simultaneous incidence in the general population. For dialysis patients, cases were reported within the French end-stage kidney disease REIN registry from March 11, 2020 to April 29, 2021, and vaccine exposure (first dose) was reported in weekly national surveys since January 2021. Cases in the general population were obtained from the national exhaustive inpatient surveillance system (SI-VIC database), and vaccination coverage (first dose) was obtained from the National surveillance system (VAC-SI database).
Results: During the 1st wave, incidence in dialysis patients was approximately proportional to the general population. However, we showed a lower relative incidence for dialysis patients during the 2nd wave (compared to that observed in non-dialysis patients), suggesting an effect of prevention measures Moreover, from the beginning of the vaccination rollout, incidence in dialysis patients was reduced compared to predictions based on the 1st and 2nd waves. Adding vaccination coverages in dialysis and non-dialysis patients as predictors permitted to correctly fit the reported cases (3685 predicted cases, 95% CI: 3552, 3816 vs. 3620 reportedly) . Incidence rate ratios (IRR) were 0.37 (95% CI: 0.18, 0.71) for vaccine exposure in dialysis patients, and 0.50 (95% CI: 0.40, 0.61) per 10% increase in vaccination

coverage in the same-age general population, meaning that vaccine exposure in dialysis patients and general population was independently associated with lower hospitalization rate of dialysis patients. Conclusion: Our findings suggest that vaccination may yield a protective effect against severe forms of COVID-19 in dialysis patients, despite altered immunological vaccine responses.

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## Abstract

**Background and objectives**: Dialysis patients have a high mortality risk after COVID-19 and an altered immunological response to vaccines, but vaccine clinical effectiveness remains unknown in this population.

**Design, setting, participants, and measurement**: Using Bayesian multivariable spatiotemporal models, we estimated the association between vaccine exposure and SARS-CoV-2 severe infections (with hospital admission) in dialysis patients from simultaneous incidence in the general population. For dialysis patients, cases were reported within the French end-stage kidney disease REIN registry from March 11, 2020 to April 29, 2021, and vaccine exposure (first dose) was reported in weekly national surveys since January 2021. Cases in the general population were obtained from the national exhaustive inpatient surveillance system (SI-VIC database), and vaccination coverage (first dose) was obtained from the National surveillance system (VAC-SI database).

**Results:** During the 1st wave, incidence in dialysis patients was approximately proportional to the general population. However, we showed a lower relative incidence for dialysis patients during the 2nd wave (compared to that observed in non-dialysis patients), suggesting an effect of prevention measures Moreover, from the beginning of the vaccination rollout, incidence in dialysis patients was reduced compared to predictions based on the 1st and 2nd waves. Adding vaccination coverages in dialysis and non-dialysis patients as predictors permitted to correctly fit the reported cases (3685 predicted cases, 95% CI: 3552, 3816 vs. 3620 reportedly) . Incidence rate ratios (IRR) were 0.37 (95% CI: 0.18, 0.71) for vaccine exposure in dialysis patients, and 0.50 (95% CI: 0.40, 0.61) per 10% increase in vaccination coverage in the same-age general population, meaning that vaccine exposure in dialysis patients and general population was independently associated with lower hospitalization rate of dialysis patients.

**Conclusion:** Our findings suggest that vaccination may yield a protective effect against severe forms of COVID-19 in dialysis patients, despite altered immunological vaccine responses.

## Introduction

Patients with kidney failure requiring dialysis have a 20-25% risk of mortality after infection with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)[1–3]. Besides, in-center hemodialysis is associated with a higher risk of contact with health care professionals or other high-risk patients, which may explain the elevated incidence of COVID-19 observed in dialysis patients in early 2020[4,5]. To limit the transmission rate, infection prevention steps have been progressively taken in dialysis centers during the successive waves of the pandemics[4,6]. Although these measures certainly had a major role in limiting disease transmission, the precise quantification of their effect is lacking.

The rapid development of vaccination against SARS-CoV-2 had a major role in controlling COVID-19 spread, since vaccines have shown a dramatic efficacy in preventing symptomatic forms of COVID-19, both in clinical trials and nationwide studies[7]. However, dialysis patients have been largely excluded from vaccine trials for safety reasons. Moreover, altered vaccine responses have been previously described in dialysis population, which justified to urgently characterize SARS-CoV-2 vaccine responses in dialysis patients. To date, this characterization remains mainly based on humoral responses post-mRNA vaccines: most studies showed a 80-95% rate of positive serology in dialysis patients after complete vaccination[8], although this response appeared delayed and antibody levels slightly reduced when compared to the non-dialysis population[9]. These results led to prioritize vaccination in dialysis patients in France in early 2021, leading to a high vaccination coverage compared to the non-dialysis population. However, the evaluation of vaccine effectiveness against severe forms of COVID-19 in this population remains an unmet need.

In this work, we sought to characterize COVID-19 dynamics in dialysis patients at the population scale by using the general population incidence over time and space as a reflection of SARS-CoV-2 spread.

## Materials and Methods

The French kidney failure REIN registry[2,10] is intended to include all dialysis patients living in France. The national coordination center is based at the Agence de la Biomédecine, a public health agency that oversees the activity of organ and tissue procurement and transplantation. The REIN registry relies on a nationwide network of health professionals with exhaustive continuous registration of all dialysis patients. The participation rate of centers in all contributing regions is 100%. Thirty-two clinical research assistants regularly visit each dialysis center to check the completeness of patient and event registration and to ensure the quality of data. This study included all patients on dialysis on the French mainland and French overseas territories.

We analyzed aggregated weekly counts of severe SARS-CoV-2 infections (defined by infections followed by hospital admissions) in dialysis patients and in the French general population.

Cases in dialysis patients were reported within the REIN registry from March 11, 2020 to April 29, 2021[2,10]. Vaccine exposure in dialysis patients (first dose) was reported in weekly surveys sent to all French nephrology centers since January 2021. To account for the possible source of missing data regarding reporting of severe cases (some patients may be recently diagnosed with COVID-19, or reported as having a mild disease as information on their hospitalization or death is not yet available until a retrospective reclassification can be made), we set a 6-week delay between the end of the period considered for the analysis (April 29, 2021) and data extraction (June 10, 2021).

Weekly incidences of severe infections in the general population were obtained from the national exhaustive inpatient surveillance system (SI-VIC database), assuming a 11-day time lapse from illness onset to hospitalization. The chosen 11-day lag applied to hospitalization

dates relies on previous estimates[11] and was already used in several modeling studies[12–14]. Weekly vaccination coverage (first dose) in the general population was obtained from the National surveillance system (VAC-SI database)[15].

We estimated the expected weekly incidence of severe infections in dialysis patients from simultaneous cases reported for the same age class in the general population, using Bayesian hierarchical Poisson regressions accounting for spatial autocorrelation, with the log number of at-risk dialysis patients as an offset. Data was aggregated spatially at the department level (administrative division of France; there are 96 metropolitan departments) and temporally at the week level. Incidences and vaccination coverages were considered by 10-year age classes (25-35, 35-45, 45-55, 55-65, 65-75, 75-85 and > 85 years). Notably, in order to estimate the association of between vaccination in dialysis patients and their risk of severe infections at the population scale, we used data on time- and space-dependent incidence in the general population as a reflection of French incidence of SARS-CoV-2 infections (however, our study was not designed to provide a direct comparison of individual infections in dialysis and non-dialysis groups).

We built 3 statistical models. Model $M_1$ only used incident cases from the first epidemic wave (up to June 30, 2020). Model $M_2$ used similar data up to the end of the second wave and beginning of the vaccination campaign in dialysis patients (January 7, 2021), considering a possible risk change between the two waves. Model $M_3$ used similar data up to April 29, 2021 with vaccine coverages in the general population and in dialysis patients as additional predictors.

Among these models, $M_1$ (fitted from 1$^{st}$ wave data) was used to compare 2$^{nd}$ wave predictions to reported cases and identify changes in factors associated with incidence in dialysis patients from the beginning of the 2$^{nd}$ wave. $M_2$ (fitted from 1$^{st}$ and 2$^{nd}$ waves data) was used to compare 3$^{rd}$ wave predictions to reported cases and identify changes in factors associated with incidence

in dialysis patients from the beginning of the 3rd wave. $M_3$ (fitted from 1st to 3rd wave data) was used to identify factors associated with incidence in dialysis patients globally.

Weekly vaccination coverage data were lagged by 3 and 5 weeks in the general population and dialysis patients, respectively, to account for a possible effect of constituted immunity on infection risk[8,16–18]. We used a prolonged lag from vaccination in dialysis patients, given the delayed vaccine response consistently observed in this population[9] and conducted a sensitivity analysis using 3-week lags in both populations. Only patients aged at least 25 years were considered from all data sources. Statistical analyses are detailed in supplemental material. All analyses were performed using R Statistical Software (Foundation for Statistical Computing, Vienna, Austria) and the INLA package.

The institutional review board of the REIN registry gave ethical approval for this study protocol (04/28/2021), in adherence to the declaration of Helsinki.

**Results**

Vaccination coverages in dialysis patients and the general population are shown in Figure 1A. On April 8, 2021 (last date for which vaccinations were considered in this study), the cumulative numbers of vaccine shots in mainland France were 10,255,204 and 3,406,601 for doses 1 and 2, respectively. The global shares were 72.2% (9.8 M), 20.4% (2.7 M) and 7.4% (1.0 M) for Pfizer/BioNTech, Astrazeneca and Moderna vaccines, respectively.[15] A total of 53,635 at-risk dialysis patients were included in this analysis with an average follow-up time of 11.7 (SD 2.1) months (627,529 person-months). Among them, 3620 SARS-CoV-2 severe infections were reported (Figure 1B and Supplemental Table 2). Notably, throughout the period of the study, we observed no significant change in the size of the dialysis population, which varied from 45,035 to 46,750 (mean: 46,212). The size of the at-risk dialysis population continuously changed since some patients entered the registry after the beginning of the study

while others were removed as they presented the endpoint (severe SARS-CoV-2 infection), died or got a kidney transplant. In the meantime, 446,890 hospital admissions were reported in the general population (Figure 1B and Supplemental Table 2). Cumulative incidences of severe infections in dialysis patients were 2- to 28-fold higher in dialysis patients compared to non-dialysis patients, according to epidemic wave (1st, 2nd or 3rd) and age strata (Supplemental Table 2). Model $M_1$ (using incident cases from the first epidemic wave) showed that during the first wave, incidence in dialysis patients was approximately proportional to incidence in the general population (Figure 1C, Table 1). Incidence rate ratios (IRR) describe how a factor modulates the hospitalization risk of dialysis patients, assuming an otherwise proportionality with the same-age general population. IRR were higher in young dialysis patients: compared to patients aged 55-65 years, IRR were 4.04 (95% credible interval [CI]: 2.38, 6.51) and 0.87 (95% CI: 0.73, 1.04) in patients aged 25-35 and 75-85 years, respectively. This counterintuitive result suggests that dialysis patients show a higher hospitalization risk than the general population globally, and especially for younger dialysis patients, who have a relatively higher risk of hospitalization than older dialysis patients, when compared to the same-age general population (Table 2).

We next studied the observed cases during the second wave. Predictions from model $M_1$ overestimated incidence during the second wave, with 2092 predicted cases (95% CI: 1888, 2317) vs. 1447 reportedly (Figure 1C, Table 1). This suggests that prevention steps towards dialysis patients during the 2nd wave were associated with a reduction in observed cases compared to predicted cases based on first wave data.

We next developed a model $M_2$ based on data up to the end of the 2nd wave. $M_2$ estimated that the risk in dialysis patients decreased between waves 1 and 2, with IRR = 0.70 (95% CI: 0.64, 0.76) (Table 2). While $M_2$ correctly estimated the reported dialysis cases up to the end of the second wave (Figure 1C), predictions from this model overestimated the expected number of

cases from the beginning of the vaccination campaign (3rd wave): 1457 (95% CI: 1356, 1557) vs. 940 reported (Figure 1C and Table 1). This suggests that other epidemiologic factors which occurred during the 3rd wave have been associated with a reduction of observed cases, compared to prediction modeled from the dynamics of the 1st and 2nd waves. We thus hypothesized that vaccination policy might have been involved in this observation.

Using vaccination coverages as additional predictors in $M_3$ permitted to accurately estimate overall incidence during the 3rd wave (3685 predicted cases, 95% CI: 3552, 3816 vs. 3620 reported) and to correctly approximate the weekly reported number of cases (Figure 1C, Table 1). Interestingly, using $M_3$, IRR were 0.37 (95% CI: 0.18, 0.71) for vaccine exposure in dialysis patients, showing a ~3-fold reduction of hospitalization risk associated with vaccination. Moreover, for dialysis patients, IRR were 0.50 (95% CI: 0.40, 0.61) per 10% increase in vaccination coverage in the same-age general population, showing an inverse association between incidence of severe infections in dialysis patients and vaccination of the general population. This suggests that vaccine exposure in both dialysis patients and the general population was independently associated with reduction of hospitalization rates in dialysis patients, when compared to the same-age general population (Table 2). As for estimates from previous models, IRR calculated from model $M_3$ in dialysis patients were higher in younger patients: compared to dialysis patients aged 55-65 years, IRR were 2.92 (95% CI: 2.03, 4.09) and 0.78 (95% CI: 0.70, 0.88) in dialysis patients aged 25-35 and 75-85 years, respectively. This observation using model $M_3$ confirms that young dialysis patients had a higher risk than older ones throughout the follow-up, when compared to the same age general population. We then hypothesized that IRR associated with vaccine exposure may change according to age strata and therefore estimated the interaction between age and vaccine exposure in dialysis patients. We thus identified a lower IRR for vaccine exposure in younger patients.: compared to patients aged 55-65 years, IRR were 0.04 (95% CI: 0.00, 0.46) and 1.74 (95% CI: 0.80, 3.86)

in dialysis patients aged 25-35 and 75-85 years, respectively. These results suggest a higher impact of vaccination in reducing hospital admissions for younger dialysis patients, compared to the same-age general population (Supplemental Table 3). Coefficients from these models are reported in Table 2. Sensitivity analysis using 3-week lags in both populations disclosed similar results (Supplemental Table 4).

## Discussion

By modeling the dynamics of SARS-CoV-2 infections leading to hospital admissions among dialysis patients in France as a proportion of cases reported in the general population, we identified a relative reduction of cases in the 2nd wave, compared to a model based on the 1st wave only. This result suggests that, accounting for the epidemiologic trends in the general population, the hospitalization rate of dialysis patients in the 2nd wave was lower than expected from data of the first wave. This observation may be explained by the progressive implementation of prevention steps, earlier testing and better management of COVID-19 of dialysis patients during the 2nd wave. Indeed, since the beginning of the epidemic, protective strategies have been broadcasted by the French Society of Nephrology with weekly COVID-19 webinars. However, this effect could be also confounded by a trend to limit hospitalization of dialysis patients with milder cases. Notably, although a similar downward trend in COVID-19-related hospitalization and mortality since the first wave has been observed in the general population in the US[19], our results suggest an added reduction of adverse outcomes in dialysis patients.

Moreover, our models also suggest a reduction of hospitalized cases starting in early 2021, compared to a model based on the 1st and 2nd waves only. Therefore, we hypothesized that vaccination exposure could have had a role in limiting hospital admissions in dialysis patients,

who were prioritized by French vaccine policies (Figure 1A). Taking into account vaccine exposure in both the general population and dialysis patients using model $M_3$, we (i) could adequately predict the observed incidence during the 3rd wave, and (ii) found that the reduction of cases was independently associated with vaccine exposure in both dialysis patients and the same-age general population. These findings suggest that vaccination may have a protective effect from the first dose in dialysis patients. Moreover, these patients may indirectly benefit from vaccine policies at the population scale, probably thanks to a lessened exposure to the virus from their encounters.

Interestingly, we quantified an IRR of 0.37 (95% CI: 0.18, 0.71) for vaccine exposure in dialysis patients, meaning that vaccination was associated with a ~3-fold reduction in hospitalization rate of dialysis patients, when accounting for the epidemiologic trends in the same-age general population (Table 2). In a context of new variant spread with greater contagiousness, and waning of antibody levels in vaccinated patients, the statistical method presented in this study could allow quantifying the future persistence/decline of the protective effect of vaccination in dialysis patients at the population scale.

Importantly, in our study, vaccine exposure data were dependent on weekly reports from dialysis centers. Vaccine exposure could therefore be overestimated, since dialysis centers with high vaccination rates might tend to better report their data. However, despite this potential overestimation that would tend to undervalue the preventive effect of vaccination, we were able to show a reduction of hospitalization rates associated with vaccine exposure in dialysis patients. Consequently, vaccine exposure appears as a major factor associated with lower hospitalization in dialysis patients in early 2021.

Using our different models, we detected that IRR were higher in younger dialysis patients, compared to older dialysis patients. An explanation might be that dialysis is an additional risk factor for all patients, but this higher risk is not as important in older patients (in whom age is

already a major risk factor) as in younger ones in whom severe infections are very rare in the general population.[1] We thus hypothesized that vaccine impact on hospital admissions may also vary according to age strata. Indeed, we identified an interaction between age and vaccine exposure in dialysis patients leading to a lower IRR for vaccine exposure in younger dialysis patients (Table 2). This result suggests a higher impact of vaccination in lowering hospital admissions for younger dialysis patients, compared to older dialysis patients accounting for the epidemiologic trends in the same-age general population (Supplemental Table 3). These data could be related to a better vaccine response in young dialysis patients, as suggested in the general population.[20] However, vaccine policies in the general population may also explain this interaction. Indeed, in early 2021, vaccine policies for non-dialysis population targeted older individuals (nursing homes patients from December 27, patients over 75 years since January 18, patients over 65 years since early March and patients over 50 years since late March). Consequently, it is likely that a higher benefit of vaccine exposure in young dialysis patients could be linked to the low vaccination coverage in the same-age general population (Figure 1A).

The strength of our analysis is the large number of patients followed in the dialysis population since the beginning of the SARS-CoV-2 spread in France, thanks to the nationwide REIN registry[2,10]. However, in absence of individual data on vaccination, we were not able to evaluate the individual risk of severe form of COVID-19 post-vaccination[21]. Moreover, our models did not take into account the impact of previous SARS-CoV-2 asymptomatic or pauci-symptomatic infection, given the difficulty to reliably detect such infections in dialysis patients.[5,22] Besides, whether this analysis could be extended to other populations with different prevention measures (including types of vaccines and vaccination schemes) remains to be studied. Of note, our analyses end before the strategy of third vaccine injection starts in France (in late April 2021). Lastly, our data did not include important virological factors such as the spread of variant of

concern types in both populations.[23] However, no evidence to date suggests that SARS-CoV-2 variants may differently impact the relative susceptibility of dialysis patients compared to non-dialysis ones.

In conclusion, this study identifies vaccination coverage in both dialysis patients and the general population as independently associated with protection against severe infection in dialysis patients. Though causal relationships cannot be demonstrated from such an observational study, our findings suggest that both individual and herd vaccine-induced immunity may yield a protective effect against severe forms of COVID-19 in dialysis patients.

## Disclosures

C. Couchoud reports serving on the Editorial Boards of *BMC Nephrology*, *CJASN*, and *Nephrologie et Thérapeutique* and other interests or relationships as a member of a not-for-profit association that aims to promote collaborations and research in Renal Epidemiology "L'Association des Néphrologues pour la Recherche en Epidémiologie (EPINEPHRO)."

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The remaining authors have nothing to disclose.

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## Author Contributions

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Maryvonne Hourmant: Investigation, Supervision, Writing – original draft

Carole Ayav: Data curation

François Glowacki: Data curation, Investigation

Cécile Couchoud: Data curation, Formal analysis, Investigation, Methodology, Resources, Supervision, Validation, Visualization, Writing – review & editing

Nathanael Lapidus: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

## Data Sharing Statement

All data used in this study are available in this article.

## Supplemental Material

Supplemental Table 1 : Description of the study populations

Supplemental Table 2 : Crude number of hospitalizations, total at-risk population, cumulative incidence in dialysis and the general population and relative risk of hospitalization according to age classes and epidemic waves

Supplemental Table 3 : Relative risks (95% credible intervals) of severe infection in dialysis patients, predicted from model M3, between April 2 and April 8, 2021 in Paris

Supplemental Table 4 : Coefficients from the Poisson regression (exponentiated and reported as incidence rate ratios with their 95% credible intervals): model M3 (3- and 5-week lags between first dose and expected protection in the general population and in dialysis patients, respectively) and additional model with 3-week lags for all.

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# Figure Legends

**Figure 1: Nationwide vaccination coverage, and SARS-CoV-2 severe infections in patients needing maintenance dialysis and in the general population (adults aged at least 25 years).**

**Panel 1A:** vaccine policies started in mid-January and first targeted patients with compromising health conditions such as dialysis patients among whom vaccination quickly reached a high coverage. National vaccination policies in the healthy population first targeted older individuals (nursing homes patients from December 27, patients over 75 years since January 18, patients over 65 years since early March and patients over 50 years since late March).

**Panel 1B:** incidence of severe infections in dialysis patients was approximately proportional to the dynamics in the general population during the two first epidemic waves. The relative incidence in dialysis patients dropped in early 2021, following the beginning of the vaccine policies.

**Panel 1C:** Model $M_1$ fitted on 1$^{st}$ wave data failed to capture an incidence drop in dialysis patient incidence from the beginning of the second wave. Model $M_2$ fitted on 1$^{st}$ and 2$^{nd}$ wave data failed to capture the early 2021 dynamics of incidence in dialysis patients, contrary to Model $M_3$ using vaccine exposures as additional predictors.

# Tables

## Table 1: Observed and predicted number of hospital admissions for SARS-CoV-2 infections in dialysis patients

| | 1st wave | 2nd wave | 3rd wave | Total |
|---|---|---|---|---|
| Observed cases | 1233 | 1447 | 940 | 3620 |
| $M_1$ predictions | 1265 (1156, 1397) | 2092 (1888, 2317) | 2021 (1874, 2194) | 5378 (5031, 5868) |
| $M_2$ predictions | 1246 (1137, 1377) | 1475 (1371, 1577) | 1457 (1356, 1557) | 4179 (3957, 4382) |
| $M_3$ predictions | 1258 (1190, 1333) | 1461 (1386, 1544) | 957 (938, 998) | 3685 (3552, 3816) |

Predicted number of severe infections (infection leading to hospital admissions) in dialysis patients with 95% credible intervals from models $M_1$ (fitted on 1st wave data, March 11 to June 30, 2020), $M_2$ (fitted on 1st and 2nd wave data, up to January 7, 2021) and $M_3$ (fitted on all 3 waves, up to April 29, 2021).

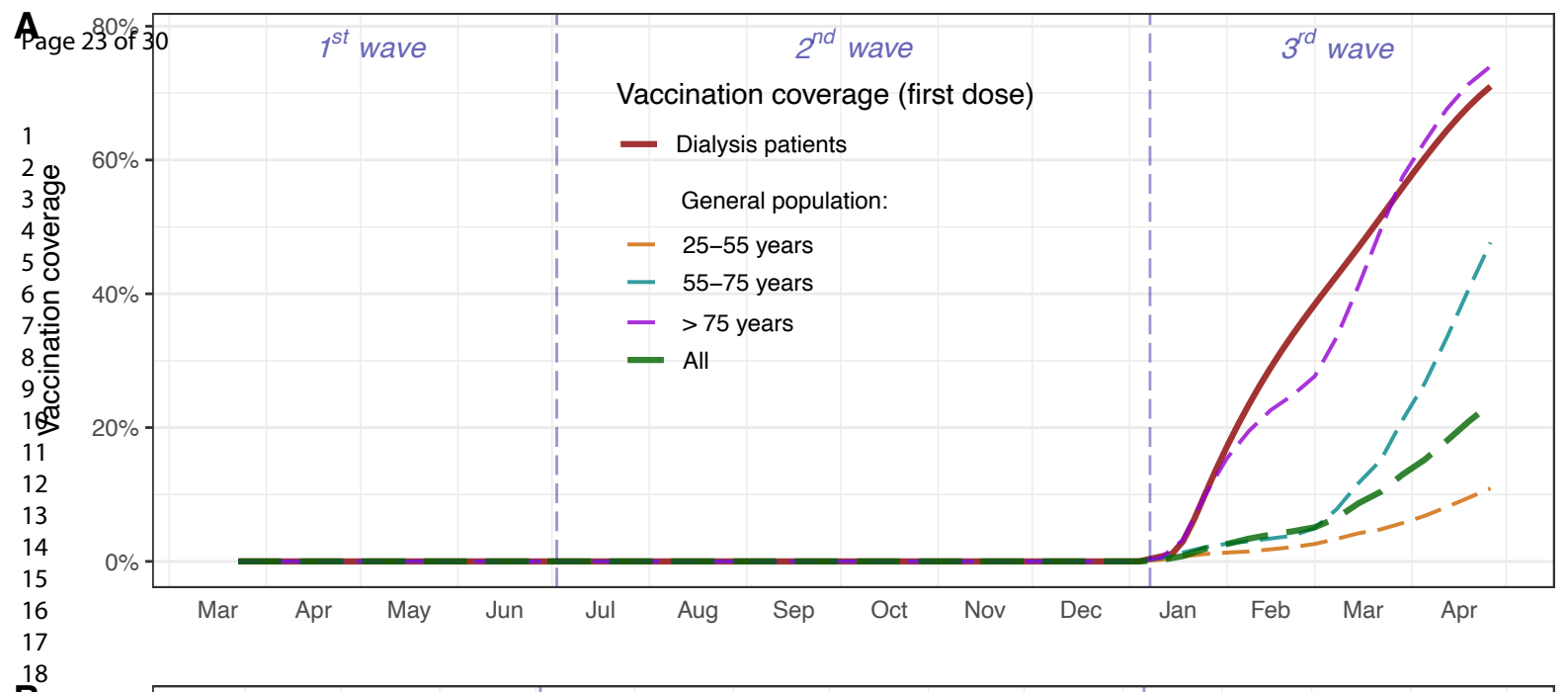
**Table 2 :** Coefficients from the Poisson regression models for incident hospitalizations for SARS-CoV-2 infection in dialysis patients

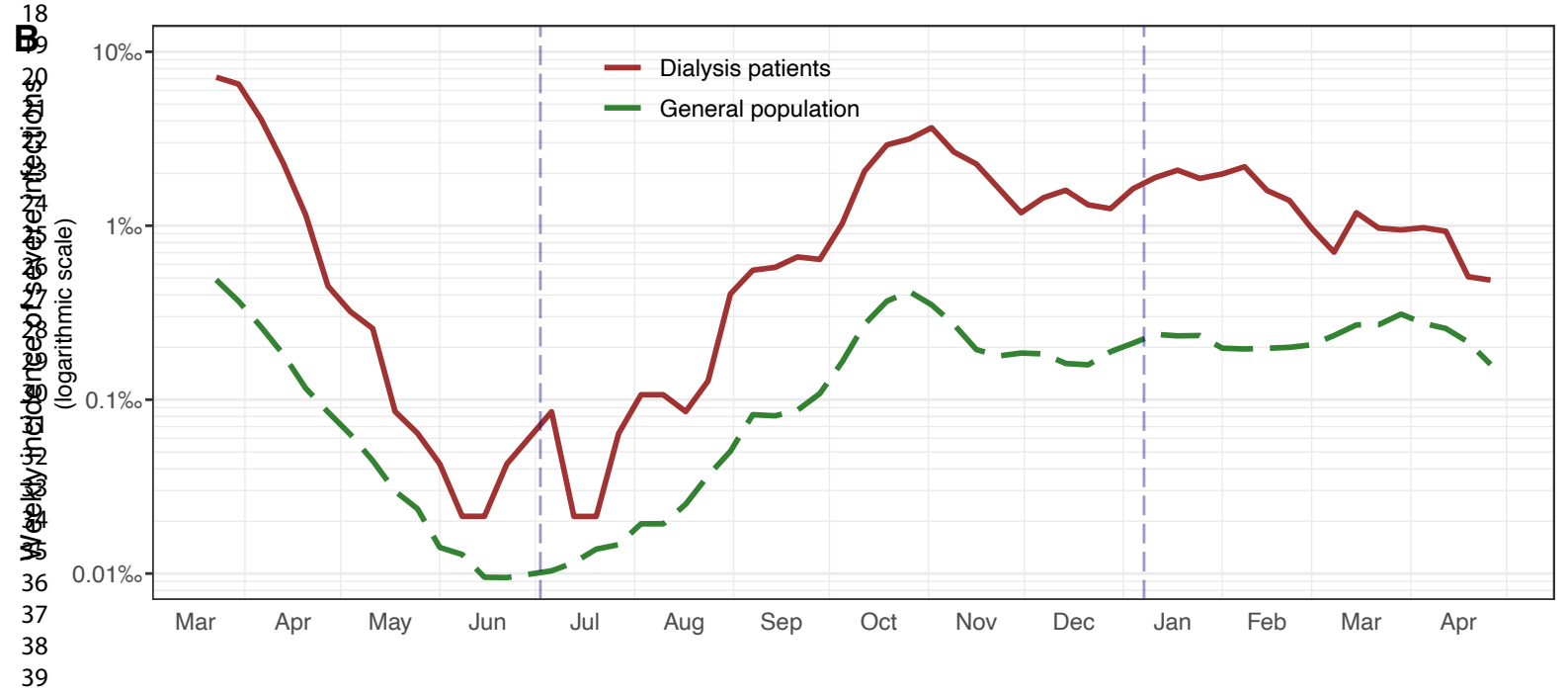
| Model $M_1$ | |
|---|---|
| **Variable** | **IRR (95% CI)** |
| • Age class (years) | |
| - 25-35 | 4.04 (2.38, 6.51) |
| - 35-45 | 2.57 (1.85, 3.52) |
| - 45-55 | 1.37 (1.06, 1.76) |
| - 55-65 | 1 (reference) |
| - 65-75 | 0.85 (0.71, 1.02) |
| - 75-85 | 0.87 (0.73, 1.04) |
| - > 85 | 0.90 (0.73, 1.10) |

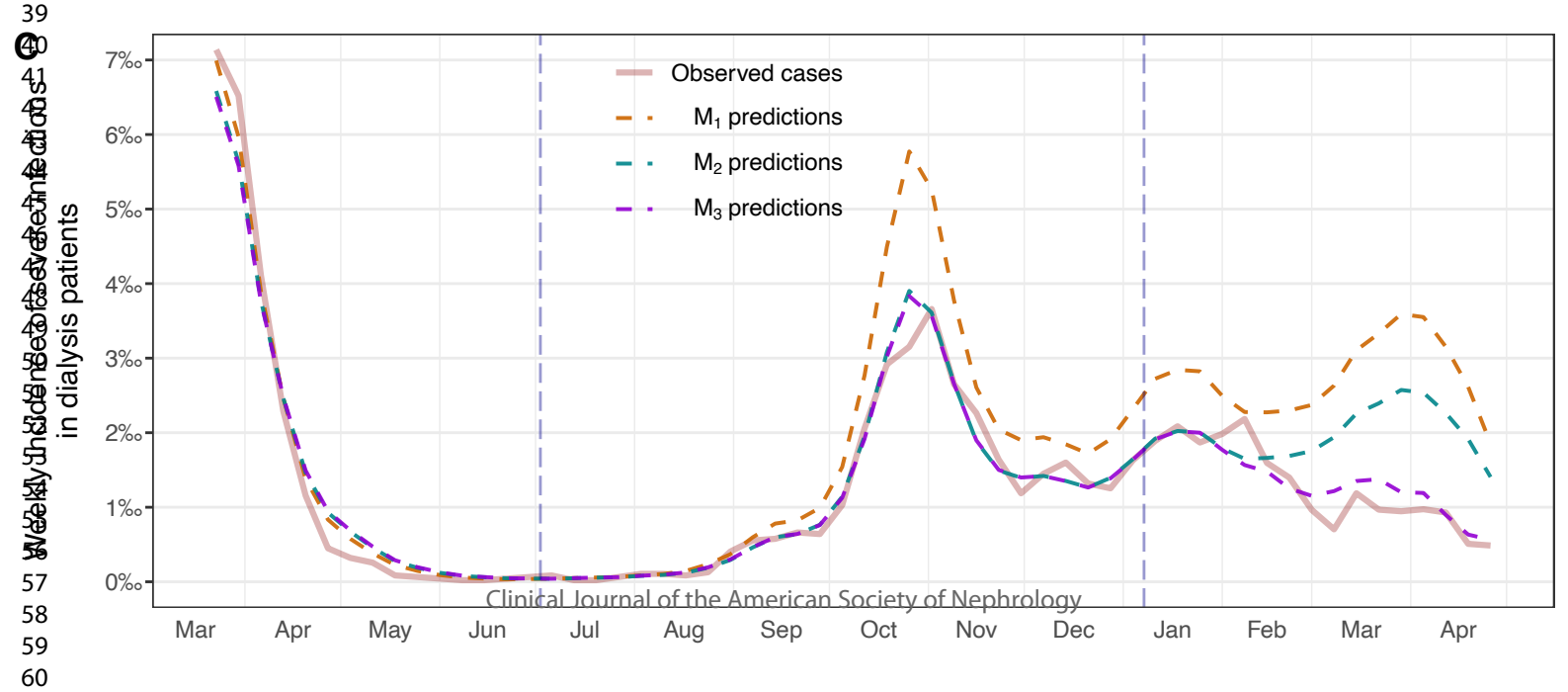
| Model $M_2$ | |
|---|---|
| **Variable** | **IRR (95% CI)** |
| • Age class (years) | |
| - 25-35 | 2.82 (1.90, 4.06) |
| - 35-45 | 2.17 (1.70, 2.75) |
| - 45-55 | 1.26 (1.04, 1.52) |
| - 55-65 | 1 (reference) |
| - 65-75 | 0.83 (0.74, 0.94) |
| - 75-85 | 0.74 (0.66, 0.85) |
| - > 85 | 0.82 (0.72, 0.95) |
| • Epidemic wave ≥ 2 | 0.70 (0.64, 0.76) |

| Model $M_3$ | |
|---|---|
| **Variable** | **IRR (95% CI)** |
| • Age class (years) | |
| - 25-35 | 2.92 (2.03, 4.09) |
| - 35-45 | 2.19 (1.74, 2.73) |
| - 45-55 | 1.32 (1.11, 1.56) |
| - 55-65 | 1 (reference) |
| - 65-75 | 0.88 (0.78, 0.98) |
| - 75-85 | 0.78 (0.70, 0.88) |
| - > 85 | 0.86 (0.76, 0.97) |
| • Epidemic wave ≥ 2 | 0.70 (0.64, 0.76) |
| • Vaccination coverage in the general population (per 10% increase) | 0.50 (0.40, 0.61) |
| • Vaccine exposure in dialysis patients | 0.37 (0.18, 0.71) |
| • Age–vaccine interaction in dialysis patients (years) | |
| - 25-35 | 0.00 (0.00, 4.66) |
| - 35-45 | 0.04 (0.00, 0.46) |
| - 45-55 | 0.55 (0.16, 1.72) |
| - 55-65 | reference |
| - 65-75 | 0.94 (0.43, 2.11) |
| - 75-85 | 1.74 (0.80, 3.86) |
| - > 85 | 2.30 (0.95, 5.56) |

Coefficients from the Poisson regression models are exponentiated and reported as incidence rate ratios (IRR) with their 95% credible intervals (CI).


A
1st wave
2nd wave
3rd wave
Vaccination coverage (first dose)
Dialysis patients
General population:
25–55 years
55–75 years
> 75 years
All
Vaccination coverage
80%
60%
40%
20%
0%
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr


B
Dialysis patients
General population
Weekly incidence of severe infections
(logarithmic scale)
10‰
1‰
0.1‰
0.01‰
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr


C
Observed cases
M1 predictions
M2 predictions
M3 predictions
Weekly incidence of severe infections
in dialysis patients
7‰
6‰
5‰
4‰
3‰
2‰
1‰
0‰
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr

# Vaccination and COVID-19 Dynamics in Dialysis Patients

# Supplemental Material

## Statistical model

### *Infection dates*

Infection dates in hemodialysis patients were actually those of diagnoses (either suspicious clinical symptom or chest scan / positive RT-PCR), which can be approximately considered as the dates of symptoms onset (1). Dates for severe infections in the general population were those of hospital admissions. In order to relate severe infections in dialysis patients (with known dates of symptoms onset) to those occurring simultaneously in the general population (with known dates of hospital admission), we subtracted the expected delay between symptoms onset and hospital admission. The chosen 11-day lag applied to hospitalization dates relies on previous estimates (2) and was already used in several modeling studies (3,4).

### *Modeling*

We modeled weekly incidences SARS-CoV-2 severe infections (COVID-19 cases leading to hospital admissions) in dialysis patients from same-age incidences in the general population, with the use of hierarchical Bayesian Poisson regressions accounting for spatial autocorrelation.

All multivariable models were built from the following pattern:

$$log\left(\frac{E\left(n_{a,d,w}\right)}{e_{a,d,w}}\right) = \alpha + \beta\ log\left(N_{a,d,w}\right) + \gamma_a\ a + \cdots + \omega_d$$

With:

- $E\left(n_{a,d,w}\right)$: expected number of cases in dialysis patients for age class $a$ in department $d$ on week $w$ ($n_{a,d,w}$ following a Poisson distribution);
- $e_{a,d,w}$: exposed (at-risk) MHD patients for the same age / department / week;
- $N_{a,d,w}$: estimated incidence of severe infections in the general population for age class $a$ in department $d$ on week $w$;
- $\beta, \gamma_a$: fixed effects to be estimated;
- $\omega_d$: random effect accounting for spatial autocorrelation in department $d$;
- ... : optional predictors with their associated fixed effects.

Spatial random effects were estimated with a covariance structure depending on neighborhood departments from a BYM model (5). Bayesian inference was performed using integrated nested Laplace approximation (6) and weakly informative priors.

Optional predictors were considered to fit the models:

- estimated incidence of severe infections in the general population for age class $a$ in department $d$ on week $w-1$;
- epidemic wave on week $w$ (dummy variables to identify epidemic waves 1 to 3);
- vaccination coverage (1st dose) in the general population in department $d$ on week $w-3$ (either in the age class $a$ or globally);
- vaccination coverage (1st dose) in MHD patients in department $d$ on week $w-3$ (data stratified by age class was not available).

Other regression models (zero-inflated Poisson and negative binomial) were also considered to improve goodness-of-fit.

Predictors were selected to improve goodness-of-fit according to the Watanabe–Akaike information criterion (WAIC).
The following models were selected:

$$\text{M}_1: \quad log\left(\frac{E\left(n_{a,d,w}\right)}{e_{a,d,w}}\right) = \alpha + \beta\ log\left(N_{a,d,w}\right) + \beta' log\left(N_{a,d,w-1}\right) + \gamma_a\ a + \omega_d$$

$$\text{M}_2: \quad log\left(\frac{E\left(n_{a,d,w}\right)}{e_{a,d,w}}\right) = \alpha + \beta\ log\left(N_{a,d,w}\right) + \beta' log\left(N_{a,d,w-1}\right) + \gamma_a\ a + \delta\ k_w + \omega_d$$

With $k_w$ taking values according to the epidemic wave ($k_w$ = 0 if week $w$ falls into the 1st wave and 1 otherwise) and $\delta$ the associated fixed effect to be estimated.

$$\text{M}_3: \quad log\left(\frac{E\left(n_{a,d,w}\right)}{e_{a,d,w}}\right) = \alpha + \beta\ log\left(N_{a,d,w}\right) + \beta' log\left(N_{a,d,w-1}\right) + \gamma_a\ a + \delta\ k_w + \xi_0\ u_{a,d,w-5} + \xi_a\ a \times\ u_{a,d,w-5} + \zeta\ v_{a,d,w-3} + \omega_d$$

With $u_{a,d,w}$ and $v_{a,d,w}$ the vaccination coverages in MHD patients and in the general population, respectively, for age class $a$ on week $w$ in department $d$, $\xi_0$ and $\zeta$ the associated fixed effects and $\xi_a$ the fixed effect for interaction between $a$ and $u_{a,d,w}$ to be estimated. The 3- and 5-week time lapses were set to account for a humoral response likely to impact incidence in the general population (7–10) and dialysis patients (11,12), respectively .
All analyses were conducted with R statistical software version 4.0. Models were fitted with the INLA package (13).

## Supplemental Tables

**Supplemental Table 1 :** Description of the study populations

| | Dialysis patients (%) | General population (%) |
|---|---|---|
| Female sex | 38.5 | 52.8 |
| Age class (years) | | |
| • 25-35 | 2.2 | 16.3 |
| • 35-45 | 4.7 | 17.6 |
| • 45-55 | 8.7 | 18.6 |
| • 55-65 | 16.3 | 17.9 |
| • 65-75 | 28.5 | 16.0 |
| • 75-85 | 26.1 | 8.7 |
| • > 85 | 13.6 | 4.9 |
| Medical history | | |
| • Diabetes | 44.1 | |
| • Cancer | 10.2 | |
| • Respiratory disease | 15.8 | |
| • Coronary heart disease | 24.8 | |
| • Peripheral artery disease | 22.8 | |
| • Stroke | 12.1 | |
| • Obesity | 25.0 | |

**Supplemental Table 2 :** Crude number of hospitalizations, total at-risk population, cumulative incidence in dialysis and the general population and relative risk of hospitalization according to age classes and epidemic waves

| | | Dialysis patients | | | General population | | | |
|---|---|---|---|---|---|---|---|---|
| Age class | wave | At-risk subjects | COVID-19 hospitalizations | Cumulative incidence (%) | At-risk subjects | COVID-19 hospitalizations | Cumulative incidence (%) | Relative risk (95% CI) |
| 25-55 | 1st | 7050 | 159 | 2.3% | 24,184,787 | 18,981 | 0.1% | 28.7 (24.6, 33.6) |
| | 2nd | 7204 | 116 | 1.6% | 24,122,679 | 26,903 | 0.1% | 14.4 (12, 17.3) |
| | 3rd | 6986 | 75 | 1.1% | 24,060,571 | 34,460 | 0.1% | 7.5 (6, 9.4) |
| 55-75 | 1st | 19,304 | 512 | 2.7% | 15,328,488 | 32,833 | 0.2% | 12.4 (11.3, 13.5) |
| | 2nd | 20,522 | 612 | 3% | 15,433,881 | 56,158 | 0.4% | 8.2 (7.6, 8.9) |
| | 3rd | 20,144 | 395 | 2% | 15,539,273 | 60,795 | 0.4% | 5 (4.5, 5.5) |
| > 75 | 1st | 16,974 | 562 | 3.3% | 6,194,203 | 47,424 | 0.8% | 4.3 (4, 4.7) |
| | 2nd | 18,086 | 719 | 4% | 6,217,063 | 94,375 | 1.5% | 2.6 (2.4, 2.8) |
| | 3rd | 18,036 | 470 | 2.6% | 6,239,923 | 74,961 | 1.2% | 2.2 (2, 2.4) |

**Supplemental Table 3 :** Relative risks (95% credible intervals) of severe infection in dialysis patients, predicted from model $M_3$, between April 2 and April 8, 2021 in Paris.

| | Vaccine exposure | |
|---|---|---|
| **Age class (years)** | **No** | **Yes** |
| 25-35 | 0.74 (0.50, 1.09) | 0.00 (0.00, 12.4) |
| 35-45 | 1.01 (0.76, 1.35) | 0.02 (0.00, 0.21) |
| 45-55 | 0.98 (0.77, 1.26) | 0.20 (0.07, 0.54) |
| 55-65 | 1 (reference) | 0.37 (0.20, 0.69) |
| 65-75 | 0.89 (0.72, 1.11) | 0.31 (0.19, 0.52) |
| 75-85 | 0.70 (0.56, 0.87) | 0.45 (0.27, 0.73) |
| > 85 | 0.67 (0.53, 0.84) | 0.57 (0.30, 1.06) |

*These relative risks of severe infection depend on the considered week and department, as their estimations use data on local vaccination coverage in dialysis patients and the general population. For this example, we chose the week and department with the highest number of cases during the third wave.*

**Supplemental Table 4 :** Coefficients from the Poisson regression (exponentiated and reported as incidence rate ratios with their 95% credible intervals): model M3 (3- and 5-week lags between first dose and expected protection in the general population and in dialysis patients, respectively) and additional model with 3-week lags for all.

| Variable | Model $M_3$ (3- and 5-week lags) | Sensitivity analysis (3-week-lags) |
|---|---|---|
| Age class (years) | | |
| - 25-35 | 2.92 (2.03, 4.09) | 2.85 (1.97, 4.02) |
| - 35-45 | 2.19 (1.74, 2.73) | 2.20 (1.75, 2.74) |
| - 45-55 | 1.32 (1.11, 1.56) | 1.35 (1.14, 1.60) |
| - 55-65 | 1 (reference) | 1 (reference) |
| - 65-75 | 0.88 (0.78, 0.98) | 0.87 (0.78, 0.98) |
| - 75-85 | 0.78 (0.70, 0.88) | 0.77 (0.69, 0.87) |
| - > 85 | 0.86 (0.76, 0.97) | 0.84 (0.74, 0.96) |
| Epidemic wave ≥ 2 | 0.70 (0.64, 0.76) | 0.69 (0.64, 0.75) |
| Vaccination coverage in the general population (per 10% increase) | 0.50 (0.40, 0.61) | 0.47 (0.38, 0.58) |
| Vaccine exposure in dialysis patients | 0.37 (0.18, 0.71) | 0.46 (0.26, 0.78) |
| Age class–vaccine interaction (years) | | |
| - 25-35 | 0.00 (0.00, 4.66) | 0.12 (0.00, 1.59) |
| - 35-45 | 0.04 (0.00, 0.46) | 0.13 (0.02, 1.56) |
| - 45-55 | 0.55 (0.16, 1.72) | 0.38 (0.13, 1.04) |
| - 55-65 | 1 (reference) | 1 (reference) |
| - 65-75 | 0.94 (0.43, 2.11) | 0.99 (0.53, 1.87) |
| - 75-85 | 1.74 (0.80, 3.86) | 1.80 (0.98, 3.37) |
| - > 85 | 2.30 (0.95, 5.56) | 2.48 (1.25, 4.92) |

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