Outcome and Effect of Vaccination in SARS-CoV-2 Omicron Infection in Hemodialysis Patients: a cohort study

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Abstract

Background

Hemodialysis patients are at high risk from Covid-19, though vaccination has significant efficacy in preventing and reducing the severity of infection. Little information is available on disease severity and vaccine efficacy since dissemination of the Omicron variant.

Methods

In a multi-center study, during a period of the epidemic driven by the Omicron variant, all hemodialysis patients positive for SARS-CoV-2 were identified. Outcomes were analysed according to predictor variables including vaccination status. Risk of infection was analysed using a Cox proportional hazards model.

Results

SARS-CoV-2 infection was identified in 1126 patients including 200 (18%) unvaccinated, 56 (5%) post first dose, 433 (38%) post second dose, and 437 (39%) at least 7 days beyond their third dose. The majority of patients had a mild course but 160 (14%) were hospitalised and 28 (2%) died. In regression models adjusted for age and comorbidity, two-dose vaccination was associated with a 39% (95%CI: 2-62%) reduction in admissions, but third doses provided additional protection, with a 51% (95%CI: 25-69%) further reduction in admissions. Amongst 1265 patients at risk at the start of the observation period, SARS-CoV-2 infection was observed in 211 (17%). Two-dose vaccination was associated with a 41% (95%CI: 3-64%) reduction in the incidence of infection, with no clear additional effect provided by third doses.

Conclusions

These data demonstrate lower incidence of SARS-CoV-2 infection after vaccination in dialysis patients during an Omicron dominant period of the epidemic. ~~epidemic dominated by the Omicron variant.~~ Amongst those developing infection, severe illness was less common with prior vaccination, particularly after third vaccine doses.

What is already known about this subject.

Patients receiving hemodialysis are both more likely to acquire SARS-CoV-2 infection, and more likely to experience severe Covid-19 outcomes, including death.

Although impaired immune responses have been reported, in clinical studies vaccination substantially reduces both the incidence and severity of infection in this group.

Severe Covid-19 can still occur in vaccinated hemodialysis patients, and vaccination may be less effective against the Omicron variant, which has become dominant in many regions.

What this study adds.

During an Omicron dominant period of the epidemic ~~epidemic dominated by the Omicron variant~~, vaccination remains associated with a lower incidence of infection in hemodialysis patients, and less severe outcomes in those developing infection.

Compared to two-dose vaccination, third doses did not further reduce the incidence of infection, but did provide significant additional protection from severe outcomes.

In this Omicron dominant period of the epidemic ~~Omicron dominated epidemic~~, severe Covid-19 was less common than in recent epidemics due to other variants, even in unvaccinated patients.

What impact this may have on practice or policy.

This study supports the continued promotion and prioritisation of vaccination in hemodialysis patients.

This study encourages vaccine uptake, and third doses in particular, amongst hemodialysis patients.

The study suggests that additional doses of current vaccines may be helpful in the future, in protecting hemodialysis patients from emerging SARS-CoV-2 variants.

Introduction

Patients receiving in-center hemodialysis face a dual hazard from SARS-CoV-2, since dialysis attendance creates a greater likelihood of exposure to infection, and infection is more severe once acquired (1,2). The development of vaccines has therefore been most welcome in this population, though as a group with comorbidity and impaired immune responses, there have been concerns that vaccination may be less efficacious.

Several studies have investigated either humoral (3-5) or cellular immune responses (6) to vaccination in dialysis patients, finding impaired but detectable responses in the majority, which weaken over time. Evidence of clinical effectiveness has also emerged, with two-dose vaccination associated with a much lower incidence of symptomatic infection (7,8). Although immunogenicity is impaired, vaccination therefore remains clinically efficacious, though patients remain vulnerable compared to those without kidney disease.

Waning immunity and emergence of new variants may alter these dynamics, and since Omicron became the dominant variant, many countries have seen further epidemic waves. Few studies have addressed infection severity or vaccine efficacy in this vulnerable population, but the clinical effectiveness of vaccination remains a pressing concern, and is vital for supporting vaccine uptake (9). This study aims to estimate the clinical efficacy of vaccination in preventing SARS-CoV-2 infection and severe disease in hemodialysis patients, during an epidemic wave driven by the Omicron variant.

Materials and Methods

This cohort study of SARS-CoV-2 infections in prevalent hemodialysis patients included all patients with positive PCR on surveillance or otherwise indicated testing, between 6th December 2021 and 16th January 2022. Dates were chosen to include the first wave of infection due to the Omicron variant. The study was sponsored by St George's Hospital and received approval from the National Research Ethics Service (IRAS Ref 283130). The data underlying this article may be shared by request to the corresponding author.

In-center hemodialysis is provided to approximately 5500 patients in London across seven nephrology centers, with enhanced infection surveillance and isolation of cases during the pandemic, described elsewhere (2). All London nephrology centers were included. The main study population included all prevalent in-center hemodialysis patients with SARS-CoV-2 infection, identified by positive PCR (Figure 1). During the study period all centers had a policy of temperature / symptom screening at every dialysis session, SARS-CoV-2 PCR testing of all patients on a weekly basis, and additional PCR testing of contacts of cases. Cases otherwise identified, with testing triggered by contact with a case or symptoms, for example presenting to emergency services, were also included. Patients receiving home dialysis were excluded, as were those receiving short-term dialysis for recoverable kidney disease. SARS-CoV-2 infection date was defined by the date of the first positive PCR during the observation period. Prior infection was defined if there was previous positive PCR before the observation period.

Clinical severity definitions included any hospital admission within 14 days (including a small number of infections acquired in patients already hospitalised), any period of sustained oxygen use within 28 days, any ventilatory support (including non-invasive methods) within 28 days, and death from any cause within 28 days (with or without hospital admission). These outcomes were defined hierarchically so that each category includes more severe Covid-19 outcomes. Hospital records were reviewed to determine supportive treatment required and outcome. Immune suppression was defined if at the onset of infection patients were receiving steroids (equivalent to prednisolone >10mg daily), tacrolimus, mycophenolate or azathioprine, or if they had received cytotoxic chemotherapy or immunomodulating biologic agents within the last six months. Ethnicity-associated differences in Covid-19 outcomes have been reported so patients were grouped as Asian/other, Black or White, using ethnicity data extracted from electronic records.

Time period of infection was included as a predictor variable to account for secular trends, making 3 time periods of two weeks each. Third dose vaccination was administered during this period using either BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna), with vaccination status considered to change after the 7th day post vaccine administration. Data were complete for comorbidity and clinical outcome, apart from two cases moving out of area, which were excluded from analysis. The observation period ended on 16th January

2022, with 28-day outcome complete on 13th February 2022. Data collection took place during and after the observation period, and was completed on 4th March 2022.

Covariates associated with clinical outcome were analysed using mixed logistic regression models, with fixed effects including age, gender, ethnicity, diabetes, immune suppression, prior SARS-CoV-2 and time period, with nephrology center as a random effect. Effect sizes were expressed as odds ratios with 95% confidence interval, and estimated vaccine efficacy, in preventing each outcome after SARS-CoV-2 infection, was defined as 1 - odds ratio. Vaccine effect was also analysed as a linear (per dose) trend, and by months since the last dose. Sub-group analyses were performed to estimate the effect of age and immune suppression on vaccine efficacy, as well as the effect of time since the second or third vaccine dose. Sensitivity analyses were performed in which patients with prior SARS-CoV-2 infection were excluded, and the analysis restricted to individual time periods.

In a secondary analysis, a subgroup for whom full vaccination data were available (comprising one nephrology center) was defined from those at risk from the start of the observation period (Figure 1), with the incidence of SARS-CoV-2 infection observed during the study period, defined by positive PCR. Variables associated with infection were analysed using a Cox proportional hazards model with third dose vaccination as a time-varying covariate, considered to change 7 days after administration. This analysis was repeated using a period-rate model using 2-week intervals with dialysis unit as a random effect. SPSS v27.0 (IBM, New York) was used for modelling.

Results

Between 6th December 2021 and 16th January 2022, SARS-CoV-2 infection was detected by PCR in 1126 hemodialysis patients (aged 19-94 years, 59% male, with ethnicity grouped as Asian/other 35%, Black 40% and White 25%) with a unimodal epidemic time course (Figure 2).

At the time of diagnosis, 200 patients (18%) were unvaccinated, 56 (5%) were at least 7 days beyond their first dose, 433 (38%) were at least 7 days beyond their second dose, and 437

188 (39%) were at least 7 days beyond their third dose. The majority of PCR samples were taken
189 in the dialysis unit as part of weekly surveillance, or in response to exposure or symptoms,
190 but 6% were taken on a Sunday. Immune suppressing treatments were taken by 185 patients
191 (16%), of which the majority were on tacrolimus monotherapy. Further patient
192 characteristics are given in Table 1.

193 A mild course was observed in 966 patients (86%) who did not require admission, but 83 (7%)
194 at least required oxygen and 28 (2%) died before 28 days. The association of clinical variables
195 with disease severity is shown in Table 2: older age, diabetes and immune suppressing
196 treatment were associated with greater illness severity. The Omicron variant accounted for
197 around half of infections in the first week, but rapidly became dominant thereafter,
198 accounting for 96% of infections in weeks 2-6 (Figure 2). Severe outcomes appeared to be
199 more frequent with the Delta variant, though the numbers were small, but there was no drift
200 in severity over time (Supplementary Table 1). Hospitalised cases and those occurring earlier
201 in the study period were more likely to be genotyped.

202 Compared to unvaccinated patients, severe Covid-19 outcomes were observed less often in
203 patients testing positive for SARS-CoV-2 after vaccination, reaching around half the frequency
204 after the third dose. In logistic regression models adjusted for demographics and
205 comorbidity, both two-dose and three-dose vaccination were associated with a lower risk of
206 admission, and three-dose vaccination was associated with a lower requirement for oxygen
207 treatment (Table 2). Compared to two doses, three-dose vaccination provided additional
208 protection, with a 51% (95%CI: 25-69%) further reduction in admissions, and 44% (95%CI: 1-
209 69%) further reduction in the requirement for oxygen. No clear protective effect of
210 vaccination was seen from more severe outcomes including death, but with mortality at 2%,
211 the numbers of severe outcomes were small compared with previous SARS-CoV-2 variants.

212 Similar protection from severe illness associated with vaccination was seen in patients over
213 65 years, and those receiving immune suppressive treatment (Supplementary Table 2). And
214 in sensitivity analyses, very similar vaccine effects were seen when those with prior SARS-
215 CoV-2 were excluded, or when the analysis was restricted to individual time periods
216 (Supplementary Table 3). In vaccinated patients more severe outcomes were associated with
217 greater time since the last vaccine dose, explained by quite a large effect in the two-dose

group (HR for admission 1.30 per month since the second dose, 95%CI 1.17-1.44) in whom infection was acquired at a median(IQR) of 252(220-270) days after the second vaccine dose (Supplementary Table 2).

In the secondary analysis of the subgroup of the patients at risk (Figure 1), the incidence of SARS-CoV-2 infection was observed in 1265 patients (aged 19-94, 61% male) who were on hemodialysis on 6th December 2021, with baseline characteristics given in Table 3. During the observation period SARS-CoV-2 infection developed in 211 (17%). In a Cox proportional hazards model censored for transplantation, death or transfer to another center, both two-dose (HR 0.59, 95%CI: 0.36-0.97) and three-dose (HR 0.48, 95%CI: 0.31-0.75) vaccination were associated with a lower incidence of infection, but there was no clear additional protection from the third dose (Table 4). Modest protection was observed in the 464 (37%) with prior infection identified by positive PCR before the observation period (HR 0.62, 95%CI 0.45-0.84). Similar effects were seen using a period-rate model, but neither analysis was able to demonstrate clearly any decay over time in vaccine efficacy against infection.

Discussion

In this multi-center study of hemodialysis patients with SARS-CoV-2 infection mostly due to Omicron variant, significant protection from severe disease was seen after vaccination, with hospitalisations 39% lower (95%CI: 2-62) after two doses, and 70% lower (95%CI: 50-83) after three doses. This suggests a substantial clinical benefit from vaccination in a population which is particularly vulnerable, and highlights the significant additional protection offered by the third dose. Amongst unvaccinated hemodialysis patients with infection in this study, 20% required admission and mortality was 3%: independent of vaccination therefore, Omicron appeared to cause less severe infection than Delta or other previous strains of SARS-CoV-2, though outcomes remain poor when compared to the general population.

Although many studies have examined immunogenicity of vaccines in hemodialysis patients, few have attempted to estimate clinical efficacy. Those which have, report vaccine efficacy against symptomatic infection around 69-78%, prior to the establishment of the Omicron variant as the dominant strain. For example, in a US study of over 12000 hemodialysis

patients receiving BNT162b2, the subsequent risk of symptomatic Covid-19 was substantially reduced compared to a matched unvaccinated cohort dialysing at the same facilities (HR 0.22, 95% CI 0.13-0.35) (7). Similarly, in a Canadian study of over 13000 hemodialysis patients, two-dose vaccination was associated with lower rates of SARS-CoV-2 infection (HR 0.31, 95%CI 0.22-0.42) and hospitalisation (HR 0.17, 95%CI 0.10-0.30) (8). An early report, on a subset of this study population, found a lower incidence of Omicron infection after three-dose vaccination compared to unvaccinated individuals (HR 0.50, 95%CI 0.29-0.92) (10). However, due to study size and possibly analytic limitations, no efficacy was demonstrated with fewer vaccine doses, and neither was any vaccine effect on disease severity observed. Without vaccination, outcomes are poor in hemodialysis patients (2), therefore, whilst substantially protected compared to their unvaccinated peers, vaccinated hemodialysis patients remain at high risk for severe Covid-19 outcomes when compared to individuals without kidney disease.

Alongside clinical efficacy, the likely effect of vaccination can also be inferred from immunogenicity: the ability of a vaccine to induce antibody and cellular immune responses in patients. Several studies have reported reduced antibody responses in dialysis patients, but impaired immunogenicity compared to healthy controls does not imply reduced clinical efficacy, which is defined by comparison with unvaccinated dialysis patients. In a meta-analysis of 32 studies comprising 4917 dialysis patients, mostly hemodialysis patients receiving two doses of BNT162b2, Chen reported detectable antibody responses in 86% of patients (95%CI 81-89%) (11). And after two-dose BNT162b2 vaccination, neutralising antibody titres (to variants other than Omicron) similar to healthy controls have been observed, with a weaker effect following AZD1222 (6). However, immunogenicity against Omicron is poorer after two-dose vaccination. Whereas neutralising antibodies to Delta were detected in most patients after BNT162b2, the median neutralising antibody titre against Omicron was below the limit of detection (<1:40), though after a third dose neutralising antibodies were detectable in most patients (12).

This study clearly demonstrates additional protection following the third dose of vaccine, with severe outcomes halved compared to those developing infection after two doses, though the effect of the third dose on the incidence of infection was unclear. Two-dose vaccination was still associated with useful protection however, both in terms of incidence and severity of infection. However, dose number is confounded by time since vaccination: the last

vaccination preceded infection by a median(IQR) of 64(51-80) days in the third dose group, versus 252(220-270) days in the two-dose group. It is therefore not clear whether third doses are restoring efficacy which has diminished over time, or otherwise enhancing efficacy against the Omicron variant.

These results are relevant to vaccine uptake, and third doses in particular, which have become standard for vaccination in many countries. Vaccine hesitancy remains a problem in dialysis patients (13), but by emphasising substantial clinical efficacy which persists despite the emergence of new variants, this study may be useful in reducing vaccine hesitancy in a group which remains vulnerable. In this regard it is noteworthy that similar vaccination efficacy was observed in older and younger patients, as well as in those taking immune suppressive treatment, though the smaller group sizes lead to wider confidence intervals.

An important limitation is that SARS-CoV-2 variant information was not available in the majority of cases. The proportion of infections known to be due to the Delta variant decreased rapidly during the study period, and though severe outcomes were more frequent with the Delta variant, the numbers were small, and not large enough to impact on severity or vaccine efficacy over time. Removing known Delta variant cases is not helpful, since Delta would also contribute to a small number of the non-genotyped cases. Conclusions therefore apply to a mixed epidemic, due mostly but not exclusively to the Omicron variant. This situation is similar to clinical risk in the real world: though one variant may be dominant, patients are still at risk of infection with other variants.

This study has several other important limitations, in particular the main study only addresses clinical severity once individuals are infected, with limited focus on the likelihood of acquiring infection, assessed in the secondary analysis only. Though weekly screening allows a consistent threshold for detection, the inclusion of mild cases may impair comparison with other studies. Only limited comorbidity data were available, and changes in clinical practice, for example as new treatments became available for non-hospitalised patients, may also have confounded the relationship between vaccination and severe Covid-19 outcomes.

This study, undertaken during an epidemic phase largely due to the Omicron variant, demonstrates that vaccination is associated with a lower incidence of SARS-CoV-2 infection,

and a substantially lower risk of severe Covid-19 outcomes in hemodialysis patients who develop infection, particularly after the third vaccine dose. Although significant vulnerability remains, this population have much to gain from vaccination, regardless of age. These results support a policy of promoting and prioritising vaccination, including third doses, in this vulnerable group.

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Conflicts of Interest

D. Banerjee reports receiving research funding from the British Heart Foundation; receiving grants from AstraZeneca and Kidney Research UK; and receiving honoraria from AstraZeneca, Pfizer, and Viforpharma. K. Bramham reports consultancy agreements with Alexion; receiving honoraria from Alexion and Otsuka; and serving as a scientific advisor or member of Alexion. B. Caplin reports consultancy agreements with LifeArc and receiving research funding from AstraZeneca and grants from Colt Foundation, Medical Research Council, and Royal Free Charity outside the submitted work. R. Hull reports consultancy agreements with AstraZeneca, Pharmocosmos UK Ltd., and Travere Pharmaceuticals; speakers bureau for Napp Phamaceuticals. K. McCafferty reports receiving research funding from AstraZeneca and receiving honoraria from Bayer, Napp, Pharmacosmos, and Vifor Fresenius. A. Salama reports receiving research funding from Chiesi and Natera; receiving honoraria from AnaptysBio, AstraZeneca, Hansa Medical, and Vifor Pharmaceuticals. C. Sharpe reports consultancy agreements with Novartis Pharmaceuticals; Travere Pharmaceuticals; and receives funding from AstraZenica. All remaining authors have nothing to disclose.

Author Contributions

DA, BC, DB and AS conceived the study;
All authors curated the data;
DA and RC analysed the data;

DA drafted the paper which was modified by other authors;
All authors approved the final version of the manuscript

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Supplementary materials

Contents

Supplementary Table 1. Severe Covid-19 outcomes by variant and time period.

Supplementary Table 2. Association of vaccination with severe Covid-19 outcomes in subgroups with SARS-CoV-2 infection.

Supplementary Table 3. Association of vaccination with severe Covid-19 outcomes in sensitivity analyses.

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401 **Table 1.** Characteristics and outcome of patients with SARS-CoV-2 infection stratified by vaccination status.
402

		Unvaccinated	First dose	Second dose	Third dose	Total
N		200	56	433	437	1126
Days post dose, median(IQR)			293 (158-344)	252 (220-270)	64 (51-80)	
Age, median(IQR)		55 (44-64)	62 (45-73)	60 (50-72)	64 (54-75)	61 (50-73)
Gender	Male	100 (50)	34 (61)	251 (58)	282 (65)	667 (59)
Ethnicity	Asian / other	44 (22)	20 (36)	141 (33)	186 (43)	391 (35)
	Black	119 (59)	27 (48)	180 (42)	128 (29)	454 (40)
	White	37 (19)	9 (16)	112 (26)	123 (28)	281 (25)
Diabetes		77 (39)	24 (43)	206 (48)	202 (46)	509 (45)
Immune suppression[a]		31 (16)	8 (14)	74 (17)	72 (16)	185 (16)
Prior SARS-CoV-2[b]		40 (20)	12 (21)	67 (15)	69 (16)	188 (17)
Outcome	Admission[c]	39 (20)	9 (16)	69 (16)	43 (10)	160 (14)
	Oxygen[d]	19 (10)	5 (9)	35 (8)	24 (5)	83 (7)
	Ventilation[d]	7 (4)	3 (5)	18 (4)	9 (2)	37 (3)
	Death[d]	5 (3)	2 (4)	14 (3)	7 (2)	28 (2)

403 Except where stated data are N (%)
404 Clinical outcomes are 'all cause', not specifically due to Covid-19
405 Vaccination status considered to change after the 7th post dose day
406 [a]Any immune suppression treatment including steroids, tacrolimus, mycophenolate, azathioprine, cytotoxic and biologic agents

407 [b]PCR positive at least 90 days prior to the current infection
408 [c]Within 14 days of positive PCR
409 [d]Within 28 days of positive PCR
410

411

412 **Table 2.** Factors associated with severe Covid-19 outcomes in patients with SARS-CoV-2 infection.
413

		Odds ratio (95%CI) for severe Covid-19 outcomes							
		Admission[h]		Oxygen[i]		Ventilation[i]		Death[i]	
Age	/ year	**1.03**	**(1.01-1.04)**	**1.03**	**(1.01-1.05)**	1.02	(1.00-1.03)	1.02	(1.00-1.04)
Gender	Male	0.98	(0.68-1.40)	0.76	(0.47-1.23)	0.88	(0.51-1.53)	0.87	(0.48-1.55)
Ethnicity[a]	Asian / other	0.77	(0.49-1.21)	0.71	(0.40-1.26)	0.68	(0.34-1.34)	0.76	(0.37-1.57)
	Black	**0.59**	**(0.38-0.92)**	**0.41**	**(0.22-0.75)**	0.59	(0.30-1.15)	0.66	(0.32-1.35)
Diabetes		**1.73**	**(1.20-2.48)**	**2.17**	**(1.32-3.56)**	1.31	(0.75-2.29)	1.16	(0.64-2.09)
Immune suppression[b]		**2.42**	**(1.55-3.77)**	**2.74**	**(1.52-4.93)**	1.49	(0.74-3.01)	1.17	(0.53-2.58)
Prior SARS-CoV-2[c]		0.64	(0.38-1.09)	0.81	(0.41-1.62)	1.24	(0.62-2.50)	1.07	(0.50-2.31)
Time period[d]	Weeks 3-4	1.08	(0.64-1.81)	1.00	(0.51-1.95)	1.17	(0.50-2.73)	1.12	(0.46-2.72)
	Weeks 5-6	0.80	(0.44-1.44)	0.60	(0.27-1.30)	1.03	(0.41-2.61)	1.03	(0.39-2.74)
Vaccination[e]	One	0.64	(0.28-1.48)	0.76	(0.26-2.24)	1.20	(0.34-4.20)	1.09	(0.27-4.34)
	Two	**0.61**	**(0.38-0.98)**	0.62	(0.33-1.16)	0.96	(0.44-2.08)	0.99	(0.43-2.25)
	Three	**0.30**	**(0.17-0.50)**	**0.34**	**(0.17-0.69)**	0.66	(0.29-1.51)	0.72	(0.30-1.73)
	Three (ref Two)	**0.49**	**(0.31-0.75)**	**0.56**	**(0.31-0.99)**	0.69	(0.36-1.30)	0.73	(0.37-1.42)
Vaccination (per dose)[f]		**0.69**	**(0.58-0.81)**	**0.71**	**(0.57-0.89)**	0.86	(0.67-1.12)	0.89	(0.68-1.17)
Vaccination (months since)[g]		**1.06**	**(1.00-1.13)**	1.08	(1.00-1.18)	1.04	(0.95-1.14)	1.04	(0.94-1.14)

414 Odds ratio (95% CI) by multivariable logistic regression model, adjusted for all variables shown

Clinical outcomes are 'all cause', not specifically due to Covid-19
Vaccination status considered to change after the 7th post dose day
[a]Reference ethnicity White
[b]Any immune suppression treatment including steroids, tacrolimus, mycophenolate, azathioprine, cytotoxic and biologic agents
[c]PCR positive at least 90 days prior to the current infection
[d]Reference time period weeks 1-2
~~[e]Reference none (unvaccinated) except where stated~~
[e]Vaccination reference group: none (unvaccinated) except where stated
[f]Vaccination as number of doses (linear effect, 0=unvaccinated)
[g]Vaccination as time since last vaccine dose (unvaccinated excluded)
[h]Within 14 days of positive PCR
[i]Within 28 days of positive PCR

Table 3. Characteristics of subgroup patients (N=1265) stratified by SARS-CoV-2 PCR status.

		PCR positive	PCR negative
N		211	1054
Age, median(IQR)		62 (49-73)	66 (55-45)
Gender	Male	123 (58)	649 (62)
Ethnicity	Asian / other	95 (45)	492 (47)
	Black	73 (35)	253 (24)
	White	43 (20)	309 (29)
Diabetes		94 (45)	397 (38)
Prior SARS-CoV-2		58 (27)	406 (39)
Vaccine [a]	Unvaccinated	26 (12)	52 (5)
	First dose	8 (4)	30 (3)
	Second dose	44 (21)	166 (16)
	Third dose	133 (63)	806 (76)

Except where stated data are N (%)

Vaccination status considered to change after the 7th post dose day

[a]Status at positive PCR, or end of observation in those with negative PCR

Table 4. Predictors of SARS-CoV-2 infection in a subgroup of the population at risk (N=1265).

		Hazard ratio (95% CI) for SARS-CoV-2 infection			
		Proportional hazard model[a]		Period-rate model[b]	
Age	/ year	**0.98**	**(0.98-0.99)**	**0.98**	**(0.97-0.99)**
Gender	Male	0.93	(0.71-1.23)	0.91	(0.68-1.22)
Ethnicity[c]	Asian / other	1.33	(0.92-1.91)	1.36	(0.93-1.98)
	Black	**1.70**	**(1.15-2.50)**	**1.78**	**(1.18-2.66)**
Diabetes		**1.48**	**(1.12-1.97)**	**1.53**	**(1.14-2.07)**
Prior SARS-CoV-2[d]		**0.62**	**(0.45-0.84)**	**0.60**	**(0.44-0.82)**
Vaccination[e]	One	0.79	(0.38-1.64)	0.81	(0.37-1.80)
	Two	**0.59**	**(0.36-0.97)**	**0.52**	**(0.31-0.89)**
	Three	**0.48**	**(0.31-0.75)**	**0.46**	**(0.28-0.75)**
	Three (ref Two)	0.80	(0.57-1.14)	0.88	(0.61-1.28)
Vaccination (per dose)[f]		**0.78**	**(0.68-0.90)**	**0.78**	**(0.67-0.91)**
Vaccination (months since)[g]		1.04	(1.00-1.09)	1.04	(0.98-1.09)

[a]Cox proportional hazards model censored for transplantation, death or transfer to another center
[b]Period-rate model using 2-week intervals with dialysis unit as random effect
[c]Reference ethnicity White
[d]PCR positive at least 90 days prior to the current infection
[e]~~Reference none (unvaccinated) except where stated~~
[e]Vaccination reference group: none (unvaccinated) except where stated

[f]Vaccination as number of doses (linear effect, 0=unvaccinated)
[g]Vaccination as time since last vaccine dose (unvaccinated excluded)
Vaccination status considered to change after the 7th post dose day

454 **Figure legends**

455 **Figure 1. Study populations.** The whole population at risk contains all those receiving
456 hemodialysis (in-center) during the observation period at one of the seven London
457 nephrology centers. Weekly PCR screening was carried out in this population, with additional
458 PCR testing as indicated by symptoms or contact with a case. The main study population (grey
459 shading) contains all SARS-CoV-2 infections, defined by positive PCR (in any setting) during
460 the observation period, and is used to assess the risk of severe disease in those with infection.
461 The supplementary study population (striped shading) contains a subset of the whole
462 population at risk, comprising one nephrology center, for whom full vaccination data were
463 available, and is only used to assess the risk of developing infection. [a] Within 14 days of
464 positive PCR. [b] Within 28 days of positive PCR.

465 **Figure 2. Epidemic time course.** Number of new SARS-CoV-2 infections by date and
466 vaccination status. The proportions of Delta and Omicron variants are provided as
467 percentages (of those known) along with the percentage genotyped.

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