



## ORIGINAL ARTICLE

# COVID-19 vaccination among Spanish nephrologists: Acceptance and side effects



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## KEYWORDS

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Healthcare workers;  
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Side effects

## Abstract

**Introduction:** Four vaccines against Covid-19 have been approved to date. Their acceptance and safety have not been addressed on healthcare workers. The aim of the present study is to evaluate vaccination rates and side effects among Spanish nephrologists.

**Methods:** All the Spanish nephrologists were invited to participate in this survey. Data on demographics, Covid-19 infection status, received vaccine doses and side effects were collected. Acceptance and side effects were analyzed for Covid-19 vaccination. Factors associated to vaccination were assessed and a multivariate adjusted model was constructed to determine independent predictors for Covid-19 vaccine side effects.

**Results:** A total of 708 nephrologists answered the survey (460 [65%] women, mean age  $44 \pm 11$  years). Six-hundred and eight (86%) had received the first dose and 513 (72%) were fully vaccinated. Most of the subjects (565, 93%) received BNT162b2 (Pfizer-BioNTech<sup>®</sup>) vaccine. Among vaccinated nephrologists, 453 (75%) presented any side effect; the most frequent was local reaction (68%), followed by myalgia (44%), tiredness (39%) and headache (34%). Age (OR 0.97, 95%CI [0.95–0.99],  $p < 0.0001$ ) and prior Covid-19 infection (OR 2.37, 95%CI [1.27–4.42],  $p = 0.007$ ) were independent predictors for developing side effects with Covid-19 vaccine. Overall side effects were similar with both vaccines, being myalgia ( $p = 0.006$ ) and tiredness ( $p = 0.032$ ) more frequent with the Pfizer-BioNTech<sup>®</sup> one.

**Conclusion:** Age and prior Covid-19 infection were predictors of vaccination side effects among Spanish nephrologists.

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## PALABRAS CLAVE

Vacunación Covid-19;  
Trabajador sanitario;  
Nefrólogos;  
Efectos secundarios

## Vacunación frente a la COVID-19 en nefrólogos: resultados de una encuesta nacional sobre aceptación y efectos adversos

### Resumen

**Introducción:** Hasta la fecha, 4 vacunas han sido aprobadas frente a la Covid-19. Su aceptación y la presencia de efectos secundarios en personal sanitario no ha sido evaluado. El objetivo del presente estudio fue evaluar la tasa de vacunación entre los nefrólogos que ejercen su profesión en España, así como los efectos secundarios.

**Métodos:** Se invitó a todos los nefrólogos españoles a completar una encuesta online sobre los objetivos del estudio. Se recogieron datos demográficos, sobre la situación infecciosa del Covid-19, la vacuna recibida y la aparición de efectos secundarios. Se analizaron los factores asociados a la vacunación, así como las variables predictoras de reacciones adversas.

**Resultados:** Un total de 708 nefrólogos respondieron a la encuesta (460 [65%] mujeres, edad  $44 \pm 11$  años). Seiscientos ocho (86%) de los nefrólogos encuestados recibieron al menos una dosis de la vacuna y 513 (72%) la vacunación completa. La mayor parte de ellos (565; 93%) recibieron la vacuna BNT162b2 (Pfizer-BioNTech®). Entre los nefrólogos vacunados, 453 (75%) presentaron algún efecto secundario; el más frecuente fue la reacción local (68%), seguido de mialgias (44%), astenia (39%) y cefalea (34%). La edad (OR: 0,97; IC95% [0,95-0,99];  $p < 0,0001$ ) y la infección previa por Covid-19 (OR: 2,37; IC95% [1,27-4,42];  $p = 0,007$ ) fueron predictores independientes del desarrollo de síntomas tras la vacuna. En conjunto, los efectos secundarios fueron similares con ambas vacunas, siendo las mialgias ( $p = 0,006$ ) y la astenia ( $p = 0,032$ ) más frecuentes con la vacuna Pfizer-BioNTech®.

**Conclusión:** La edad y el antecedente de infección por Covid-19 fueron predictores de efectos secundarios con la vacuna entre los nefrólogos que ejercen en España y que contestaron la encuesta.

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## Introduction

Slightly more than one year after the first case of coronavirus disease 19 (Covid-19) was reported in Wuhan, China, four vaccines have already been approved by the U.S. Food and Drug Administration (FDA), the European Medicine Agency (EMA) and local regulatory agencies. Pivotal trials have shown that BNT162b2 (Pfizer-BioNTech®) and mRNA-1273 (Moderna®) vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), based on a novel nucleoside-modified RNA biotechnology, have high efficacy in preventing Covid-19.<sup>1,2</sup> Moreover, interim analyses of two phase 3 trials evaluating the adenovirus-based Sputnik V and AZD1222 vaccines also showed their efficacy.<sup>3-6</sup>

Worldwide, governments have started vaccination programs prioritizing healthcare workers (HCWs), especially those at first-line. Rates of SARS-CoV-2 infection are high among nephrologists as they have been required to assist Covid-19 patients in hemodialysis programs, in addition to regular hospitalized patients.<sup>7</sup> This group of patients has been one of the most affected by SARS-CoV-2 infection due to their requirement to receive in-hospital medical care several times per week. Nephrologists also have been integrated in Covid-19 patient care in non-Nephrology departments, thus increasing their exposure to SARS-CoV-2.<sup>8</sup> For all these reasons, nephrologists were considered as first-line HCWs, and were scheduled within the first group to receive the initial doses of Covid-19 vaccines that arrived in Spain.

Initial reluctance to Covid-19 vaccination in the general population and HCWs during the first phases of Covid-19 pandemic shifted to elevated rates of acceptance as the pandemic progresses.<sup>9</sup> However, data regarding vaccinations of HCWs, and specifically of nephrologists, remain to be assessed. The aim of the present study was to evaluate the rate of Covid-19 vaccination among Spanish nephrologists during the HCW vaccination campaign and to describe the safety and side effects of the different types of Covid-19 vaccines.

## Material and methods

Spanish nephrologists were invited by the Spanish Society of Nephrology to fulfill an online blinded survey to evaluate adherence and safety in the Covid-19 vaccination program.

## Survey

Nephrologists received a webpage link from the Secretary of the Spanish Society of Nephrology. The online survey (supplementary file 1) contained 13 questions encompassing demographic data (sex and age), place of work (hospital, dialysis center or both) and city. Questions about Covid-19 vaccination status and the vaccine type (BNT162b2 or mRNA-1273) were also included. For those who did not receive the vaccine, the survey allowed them to choose between three options to explain the reasons (medical reasons [pregnancy, Covid-19 infection within 3 months prior to vaccination],

lack of medical appointment or personal decision [free text for explanation]). Questions about prior Covid-19 infection and time between infection and vaccination were also included for vaccinated nephrologists. Prior Covid-19 infection was defined by a positive result in real-time reverse transcription-polymerase chain reaction (rRT-PCR) for SARS-CoV-2 in nasopharyngeal swabs, or by serum immunoglobulin (Ig) M and IgG antibodies in serology test. Side effects of the Covid-19 vaccine (temporally defined as immediate symptoms after the administration and during the next 7 days) were assessed using a multi-choice questionnaire (for both the first and the second dose).

The questionnaire was opened during a week between 12 and 19 February 2021, when only BNT162b2 or mRNA-1273 vaccines were authorized for use in Spain.

### Side effects

Side effects were defined as local reaction on the arm (pain or swelling), lymphadenopathy, tiredness, headache, diarrhea, nausea, chills, myalgia, low-grade fever (body temperature between 37 and 37.8 degrees Celsius), fever (body temperature 37.8 degrees Celsius or above), and others (free text). Finally, those nephrologists receiving Covid-19 vaccine were asked if they needed a sick leave due to side effects.

The study was approved by the Research Ethics Committee of Hospital Universitario de la Princesa (Madrid, Spain) with number 4419/21.

### Statistical analysis

Values are expressed as mean  $\pm$  standard deviation or median (interquartile range) depending on their distribution assessed by the Kolmogorov–Smirnov test. Participants were divided into two categories according to the presence of side effects after Covid-19 vaccination. All the variables were compared between both groups using Chi-square or *t*-test for parametric variables and Fisher test or Mann–Whitney test for non-parametric variables. Independent predictors for Covid-19 vaccine side effects were assessed using logistic regression including variables that showed  $p < 0.1$  in univariate analysis and confounders. All statistical analyses were performed with SPSS™ 24.0 (SPSS, Inc., Chicago, Illinois, USA). *p*-Values  $< 0.05$  were considered statistically significant.

## Results

### Baseline characteristics

The survey was sent to 1909 active members of the Spanish Society of Nephrology and 708 (37%) completed it. Of them, 460 (65%) were women and mean age was  $44 \pm 11$  years. 603 nephrologists (85%) worked in hospitals, 80 (11%) in dialysis centers and 25 (4%) in both types of centers.

### Vaccination status

Among 708 nephrologists that responded to the survey, 607 (86%) had received the first dose of Covid-19 vaccine. Reasons for not receiving the vaccination included lack of medical appointment (in the moment of the survey) by their center in 71 subjects (71%), personal decision in 12 (12%) and medical reasons or contraindications in 18 (18%) (more details are shown in Fig. 1). Most of the nephrologists (565, 93%) received BNT162b2 (Pfizer-BioNTech®) vaccine, whereas only 42 (7%) received mRNA-1273 (Moderna®) vaccine. Among vaccinated nephrologists, 101 (17%) had a prior Covid-19 infection. Mean time between infection and vaccination was  $7.6 \pm 3.4$  months.

Ninety-Four (15%) of the nephrologists who had received the first dose of the Covid-19 vaccine, did not receive the second one. Reasons for not receiving the second dose were diverse. In 69 subjects (73%) the second dose was scheduled after the survey period, in 20 cases (21%) there was lack of vaccines due to delivery issues, 4 (4%) developed an inter-current Covid-19 infection and one (1%) refused to receive the second dose.

### Side effects

Among 607 vaccinated nephrologists, 453 (75%) presented any side effect. Four-hundred and eighteen (69%) subjects developed side effects after the first dose of the Covid-19 vaccine. Of the 513 subjects that were fully vaccinated, 291 (57%) presented side effects after the second dose. Two-hundred and fifty-six (42%) had side effects with both doses. We did not observe gender differences regarding adverse events in males and females ( $p = 0.237$  for the first dose and  $p = 0.458$  for the second dose). Presenting symptoms after the first dose was associated to any side effect after the second one (Odds ratio [OR] 9.6, 95%CI [6.1–14.9],  $p < 0.0001$ ). Local reaction (412, 68%), myalgia (267, 44%), tiredness (239, 39%) and headache (206, 34%) were reported by more than 30% of the vaccinated nephrologists. Fig. 2 shows side effect rates for each vaccine dose in detail.

Factors associated to development of side effects were lower age ( $p < 0.0001$ ) and prior Covid-19 infection ( $p = 0.002$ ). Fig. 3 shows the analysis of adverse events stratified by age. As shown in Table 1, those nephrologists who had prior Covid-19 infection presented more frequently side effects such as tiredness ( $p = 0.022$ ), chills ( $p < 0.001$ ), myalgia ( $p = 0.003$ ), low-grade fever ( $p < 0.001$ ) and fever ( $p < 0.001$ ). A multivariate model adjusted for sex, time between Covid-19 infection and vaccination and vaccine type, demonstrated that age (OR 0.97, 95%CI [0.95–0.99],  $p < 0.0001$ ) and prior Covid-19 infection (OR 2.37, 95%CI [1.27–4.42],  $p = 0.007$ ) were independent predictors of side effects.

Regarding the type of vaccine, as shown in Table 2, both Moderna® and Pfizer-BioNTech® presented similar overall adverse events. However, myalgia ( $p = 0.006$ ) and tiredness ( $p = 0.032$ ) were significantly more frequent with Pfizer-BioNTech®.

Side effects led to sick leave in 47 (8%) of the Nephrologists who received at least one dose of the Covid-19 vaccine.

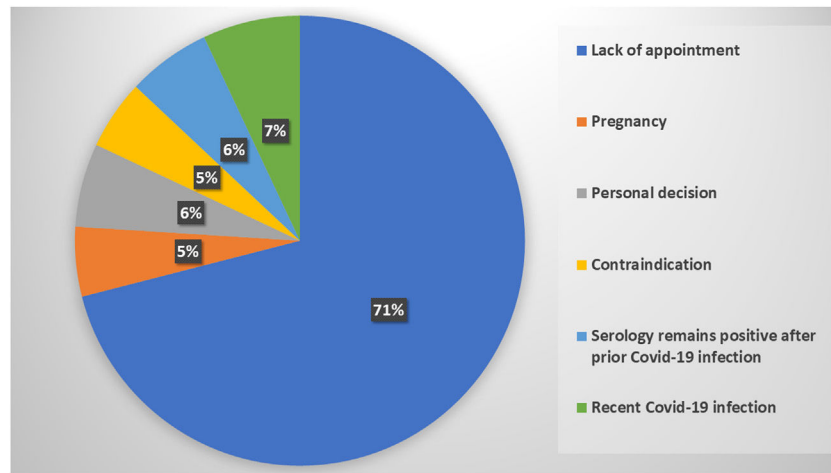


Figure 1 Reasons to refuse Covid-19 vaccination.

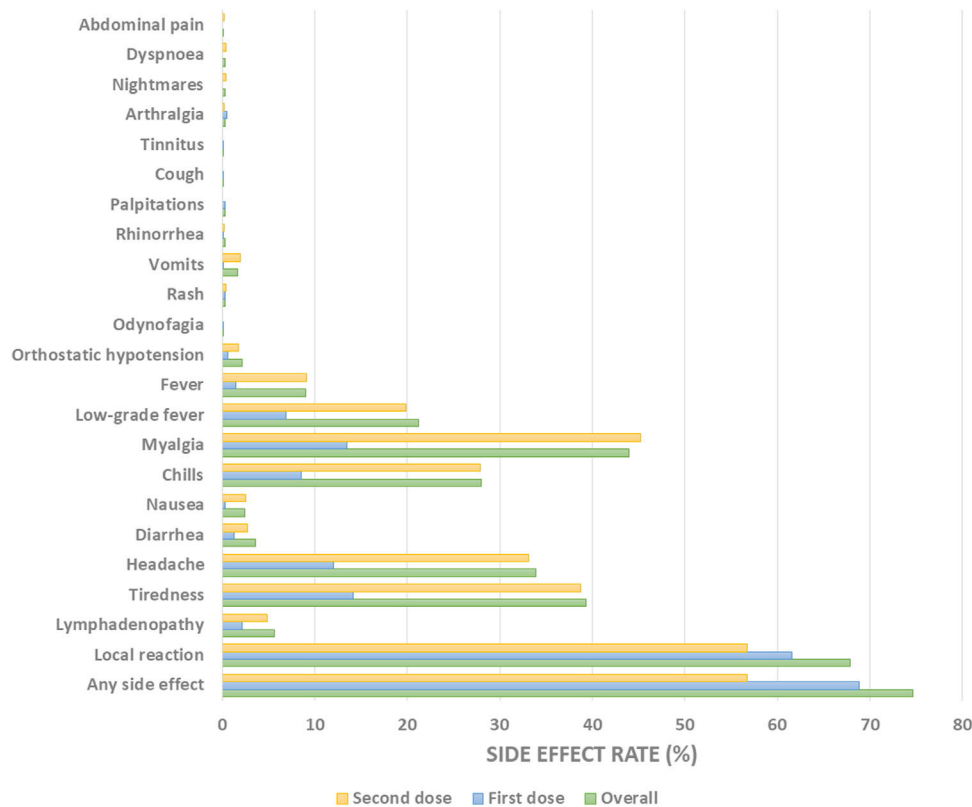
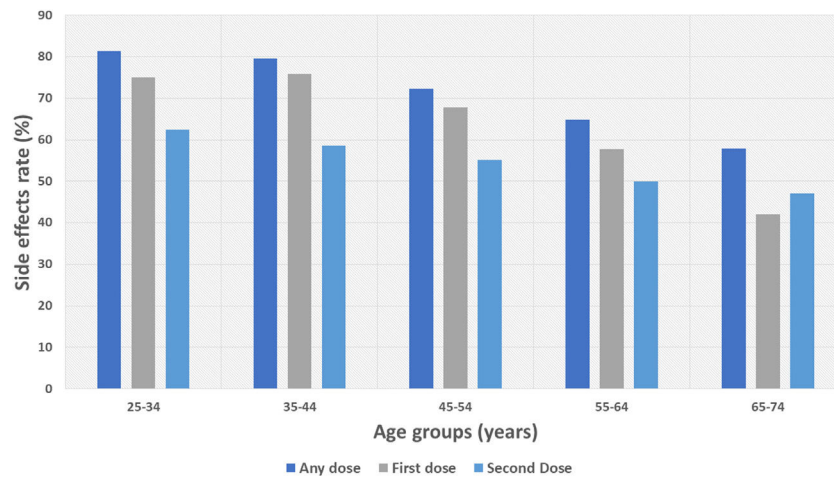


Figure 2 Side effects of the first and second dose of the Covid-19 vaccine.

## Discussion

Our study demonstrates that most of the Spanish nephrologists have been vaccinated against Covid-19 with an acceptable safety profile. During the same dates, only the 5.7% of the Spanish population had been vaccinated in comparison to the 88% of the Nephrologists. Our national campaign, started 28 December 2020, included HCWs within the first group of people to be vaccinated. At 9 March 2021, vaccinated HCWs achieved rates of 86% and 46% for the first and second doses, respectively. As suggested

by previous published data, nephrologists are healthcare professionals working at first-line, hence their vaccination was considered as a priority. Although our data reveal high rates of acceptance, 12% of nephrologists have not been vaccinated yet due to personal decision, a low but surprising rate considering their knowledge of the devastating effects of the pandemic.<sup>10</sup> Indeed, according to a previous report of the Spanish Society of Nephrology, nearly 20% of nephrologists were infected by SARS-Cov-2, of whom 8% required hospitalization.<sup>7</sup> Reasons for this high rate of infection included lack of an appropriate personal



**Figure 3** Side effects of the Covid-19 vaccine stratified in different age groups.

**Table 1** Covid-19 vaccine side effects in nephrologists.

	Total vaccinated Nephrologists (n = 607)	Prior Covid-19 infection (n = 101)	No prior Covid-19 infection (n = 506)	p
Any side effect, n (%)	453 (75)	88 (87)	365 (72)	0.002
Local reaction, n (%)	412 (68)	71 (70)	341 (67)	0.568
Lymphadenopathy, n (%)	34 (6)	7 (7)	27 (5)	0.525
Tiredness, n (%)	239 (39)	50 (50)	189 (37)	0.022
Headache, n (%)	206 (34)	41 (41)	165 (33)	0.122
Diarrhea, n (%)	22 (4)	5 (5)	17 (3)	0.435
Nausea, n (%)	15 (2)	4 (4)	11 (2)	0.291
Chills, n (%)	170 (28)	49 (49)	121 (24)	<0.001
Myalgia, n (%)	267 (44)	58 (57)	209 (41)	0.003
Low-grade fever, n (%)	129 (21)	41 (41)	88 (17)	<0.001
Fever, n (%)	55 (9)	19 (19)	36 (7)	<0.001
Orthostatic hypotension, n (%)	13 (2)	4 (4)	9 (2)	0.167
Odynophagia, n (%)	1 (<1)	0 (0)	1 (<1)	0.655
Rash, n (%)	2 (<1)	0 (0)	2 (<1)	0.527
Vomits, n (%)	10 (2)	2 (2)	8 (2)	0.774
Rhinorrhea, n (%)	2 (<1)	0 (0)	2 (<1)	0.527
Palpitations, n (%)	2 (<1)	0 (0)	2 (<1)	0.527
Cough, n (%)	1 (<1)	0 (0)	1 (<1)	0.655
Tinnitus, n (%)	1 (<1)	0 (0)	1 (<1)	0.655
Arthralgia, n (%)	2 (<1)	1 (1)	1 (<1)	0.204
Nightmares, n (%)	2 (<1)	0 (0)	2 (<1)	0.527
Dyspnea, n (%)	2 (<1)	0 (0)	2 (<1)	0.527
Abdominal pain, n (%)	1 (<1)	1 (1)	0 (0)	0.166

protective equipment as well as their high exposure to Covid-19 patients.

Although side effect data from the randomized clinical trials (RCT) of the four approved Covid-19 vaccines have been reported,<sup>1-4</sup> there is a lack of information about vaccine side effects in real world. Indeed, a very recent nationwide-based study involving 596,618 persons in Israel confirmed the efficacy of the BNT162b2 mRNA vaccine, although its adverse effects were not analyzed.<sup>11</sup> Our survey shows that more than 75% of the vaccinated nephrologists suffered from any symptom, the most frequent being local

reaction, myalgia, tiredness or headache. In addition, they declared up to 22 different side effects of the vaccine. The appearance of such a wide variety of symptoms probably conditioned the refusal of some subjects to complete the vaccination.

Contrary to previous published data,<sup>2</sup> prior Covid-19 infection increased the rate of post-vaccination reactions in nephrologists. Among the published studies, the only one addressing prior Covid-19 infection of the included subjects demonstrated that less than 1% of the participants presented a previous infection.<sup>2</sup> Our study shows that

**Table 2** Side effects in nephrologists with the different vaccines (Pfizer-BioNTech® and Moderna®).

	Pfizer-BioNTech (n = 565)	Moderna (n = 42)	p
Any side effect, n (%)	422 (75)	31 (74)	0.899
Local reaction, n (%)	384 (68)	28 (67)	0.862
Lymphadenopathy, n (%)	34 (6)	0 (0)	0.102
Tiredness, n (%)	229 (41)	10 (24)	0.032
Headache, n (%)	194 (34)	12 (29)	0.447
Diarrhea, n (%)	19 (3)	3 (7)	0.206
Nausea, n (%)	14 (3)	1 (2)	0.969
Chills, n (%)	163 (29)	7 (17)	0.090
Myalgia, n (%)	257 (46)	10 (24)	0.006
Low-grade fever, n (%)	122 (22)	7 (17)	0.451
Fever, n (%)	53 (9)	2 (5)	0.314
Orthostatic hypotension, n (%)	13 (2)	0 (0)	0.320
Odynophagia, n (%)	1 (<1)	0 (0)	0.785
Rash, n (%)	2 (<1)	0 (0)	0.699
Vomits, n (%)	10 (2)	0 (0)	0.385
Rhinorrhea, n (%)	2 (<1)	0 (0)	0.699
Palpitations, n (%)	2 (<1)	0 (0)	0.699
Cough, n (%)	1 (<1)	0 (0)	0.785
Tinnitus, n (%)	1 (<1)	0 (0)	0.785
Arthralgia, n (%)	2 (<1)	0 (0)	0.699
Nightmares, n (%)	2 (<1)	0 (0)	0.699
Dyspnea, n (%)	2 (<1)	0 (0)	0.699
Abdominal pain, n (%)	1 (<1)	0 (0)	0.785

previous Covid-19 infection was specifically associated to higher rates of tiredness, chills, myalgia and fever. This flu-like syndrome has been constant in the extrapulmonary symptoms of Covid-19 infections, in infections by other endemic human coronaviruses as well as in side effects of vaccines against other viruses.<sup>12,13</sup> In this regard, some experts and preliminary studies have suggested that one dose could confer enough efficacy to allow for a delayed administration of the second dose, especially in those patients with prior Covid-19 infection.<sup>14,15</sup>

BNT162b2 (Pfizer-BioNTech®) and mRNA-1273 (Moderna®) vaccines (both based on nucleoside-modified RNA) presented a similar safety profile in their phase 2/3 studies, with local reactogenicity in more than the 70% of the participants. Those studies showed that local and systemic events were more frequent in younger vaccine recipients and also after the second dose.<sup>1,2</sup> Our survey also shows higher reaction in younger recipients; however, unlike those pivotal studies, our results showed lower reactogenicity after the second dose. The comparison between both vaccines revealed similar overall adverse events, being myalgia and tiredness more frequent with Pfizer-BioNTech®.

Our study have some limitations. First, it is a survey-based analysis relying on data provided voluntarily that lack information such as comorbidities or laboratory values. However, as previously stated, nephrologists can be considered as healthy population with higher rates of previous Covid-19. In addition, we obtained a large sample size that provides sufficient statistic power to support the results of the study. Second, the study subjects provide subjective information

based on how they feel their symptoms, which could lead to some heterogeneity. Nevertheless, the results are in accordance with previous published data in other populations.<sup>16</sup> Finally, this survey included the situation of the members of the Spanish Society of Nephrology and not all the Spanish Nephrologists. However, we understand the sample is representative in terms of size and also in place of work of the total Nephrologists in Spain.

## Conclusions

In conclusion, Spanish nephrologists who answered survey, as first-line HCWs, have received Covid-19 vaccines with acceptable self-limited side effects. Lower age and prior Covid-19 infection were predictors of higher side effect rates, especially tiredness, chills, myalgia, low-grade fever and fever.

## Conflict of interest

None.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jhqr.2021.05.002.

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