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### **Original Investigation**

# Incidence and Outcomes of COVID-19 in People With CKD: A Systematic Review and Meta-analysis

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Rationale & Objective: Coronavirus disease 2019 (COVID-19) disproportionately affects people with chronic diseases such as chronic kidney disease (CKD). We assessed the incidence and outcomes of COVID-19 in people with CKD.

**Study Design:** Systematic review and metaanalysis by searching MEDLINE, EMBASE, and PubMed through February 2021.

Setting & Study Populations: People with CKD with or without COVID-19.

Selection Criteria for Studies: Cohort and casecontrol studies.

Data Extraction: Incidences of COVID-19, death, respiratory failure, dyspnea, recovery, intensive care admission, hospital admission, need for supplemental oxygen, hospital discharge, sepsis, short-term dialysis, acute kidney injury, and fatigue.

Analytical Approach: Random-effects metaanalysis and evidence certainty adjudicated using an adapted version of GRADE (Grading of Recommendations Assessment, Development and Evaluation).

**Results:** 348 studies (382,407 participants with COVID-19 and CKD; 1,139,979 total participants with CKD) were included. Based on low-certainty evidence, the incidence of COVID-19 was higher in people with CKD treated with dialysis (105 per 10,000 personweeks; 95% Cl, 91-120; 95% prediction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in December 2019 as the cause of coronavirus disease 2019 (COVID-19) as defined by the World Health Organization (WHO). By May 2021, more

### Editorial, p. 777

than 151 million people were confirmed to have been infected with SARS-CoV-2, with more than 3.1 million deaths reported as a result of COVID-19 globally.<sup>1</sup> Initial evidence suggested a higher incidence of severe COVID-19 in people with chronic diseases, including chronic kidney disease (CKD),<sup>2</sup> and an association with acute kidney injury (AKI) due to SARS-CoV-2 infection of the tubular

interval [Prl], 25-235; 59 studies; 468,233 participants) than in those with CKD not requiring kidney replacement therapy (16 per 10,000 person-weeks; 95% Cl, 4-33; 95% Prl, 0-92; 5 studies; 70,683 participants) or in kidney or pancreas/kidney transplant recipients (23 per 10,000 person-weeks; 95% Cl, 18-30; 95% Prl, 2-67; 29 studies; 120,281 participants). Based on low-certainty evidence, the incidence of death in people with CKD and COVID-19 was 32 per 1,000 person-weeks (95% Cl, 30-35; 95% Prl, 4-81; 229 studies; 70,922 participants), which may be higher than in people with CKD without COVID-19 (incidence rate ratio, 10.26; 95% CI, 6.78-15.53; 95% Prl, 2.62-40.15; 4 studies; 18,347 participants).

Limitations: Analyses were generally based on low-certainty evidence. Few studies reported outcomes in people with CKD without COVID-19 to calculate the excess risk attributable to COVID-19, and potential confounders were not adjusted for in most studies.

**Conclusions:** The incidence of COVID-19 may be higher in people receiving maintenance dialysis than in those with CKD not requiring kidney replacement therapy or those who are kidney or pancreas/kidney transplant recipients. People with CKD and COVID-19 may have a higher incidence of death than people with CKD without COVID-19. Complete author and article information provided before references.

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epithelium and podocytes,<sup>3</sup> cytokine production, cardiac dysfunction, and hypoxemic tubular injury.<sup>4</sup> Initial evidence suggested a poor prognosis of COVID-19 in kidney transplant recipients,<sup>5</sup> with a 25% mortality rate, and further evidence highlighting CKD as a risk factor for severe COVID-19 has since been published.<sup>6</sup>

A systematic analysis of the incidence and prognosis of COVID-19 is necessary to understand the extent and severity of clinical outcomes associated with COVID-19 in people with CKD. This can inform patient and clinician knowledge, treatment and vaccination strategies, resource management, stratification according to risk of clinical outcomes in clinical guidelines, public health policymaking, and intervention trials. In this systematic review,





### PLAIN-LANGUAGE SUMMARY

Previous studies suggest that people with chronic kidney disease (CKD) may be severely affected by coronavirus disease 2019 (COVID-19). We searched for observational studies that investigated how many people with CKD were diagnosed with COVID-19 and experienced related health outcomes, including death, respiratory failure, and need for dialysis. Data were pooled from 348 studies that included a total of more than 1 million people with CKD. COVID-19 occurred more commonly in people who required long-term dialysis than in those with CKD not requiring dialysis (including kidney transplant recipients). People with CKD and COVID-19 may have a 10-fold higher risk of death than people with CKD without COVID-19.

we evaluated the incidence and outcomes of COVID-19 in adults and children with CKD, including those treated with kidney replacement therapy (KRT).

### **Methods**

### **Data Sources and Searches**

We searched MEDLINE, EMBASE, and PubMed (using LitCovid; https://www.ncbi.nlm.nih.gov/research/coronavirus/) between November 1, 2019, and February 22, 2021, using a highly sensitive search strategy designed by an information specialist (Item S1). We have reported this review in accordance with the PRISMA statement.<sup>7</sup>

### **Study Selection**

We included retrospective and prospective cohort studies or case-control studies investigating the incidence of COVID-19 or outcomes in adults and children with any level of CKD (including CKD treated by dialysis [CKD G5D] and kidney or pancreas/kidney transplant recipients [KTRs]) with or without COVID-19. We defined CKD using the KDIGO CKD guide-line<sup>8</sup> and defined COVID-19 using the WHO criteria<sup>9</sup> based on a positive reverse transcriptase–polymerase chain reaction assay for SARS-CoV-2.<sup>10</sup>

We included "gray literature," studies in any language, and studies including people with or without CKD, from which we extracted data on people with CKD. We excluded case series, case reports, randomized and quasirandomized trials, participants without preexisting CKD, and diagnoses of COVID-19 based on serologic evaluation. We excluded studies that included only deceased patients, patients admitted into the intensive care unit (ICU), or hospitalized patients in the analyses of the incidences of death, ICU admission, and hospital admission, respectively.

### **Data Extraction**

Using Cochrane COVID Rapid Review methods,<sup>11</sup> 11 review authors (EYMC, PN, AK, TEC, VMS, MR, EA, SJ, AL,

DJJD, and JCC) screened the citations retrieved in the literature search, and 1 reviewer (EYMC) checked the study selection. Any differences in study selection were resolved by consensus by author VMS (GFMS was also an adjudicator but was not needed). For companion publications, we focused on the analysis of the publication describing the longest follow-up from baseline and extracted outcomes from the publications with shorter follow-up intervals that were not reported in the publication with the longest follow-up.

Data extraction was performed by 11 review authors (EYMC, PN, AK, TC, VMS, MR, EA, SJ, AL, DJJD, and JCC) and checked by 1 reviewer (EYMC). Outcomes of interest were the incidence of COVID-19, COVID-19-attributable outcomes drawn from the global COVID-19 Core Outcomes Set (COS) initiative (death, respiratory failure defined as mechanical ventilation or acute respiratory distress syndrome), multiorgan failure, dyspnea, recovery from COVID-19 (as defined by study authors), ICU admission, hospital admission, hospital discharge, sepsis (defined as septicemia or bacteremia), financial impact, depression, lung function, physical function, and viral load/clearance,<sup>12</sup> and kidney-specific outcomes drawn from the Standardised Outcomes in Nephrology CKD (SONG-CKD) initiative (kidney failure, acute dialysis, AKI, vascular access thrombosis, myocardial infarction, stroke, limb amputation, fatigue, and life participation).<sup>13</sup>

#### **Risk of Bias Assessment**

Eleven review authors (EYMC, PN, AK, TEC, VMS, MR, EA, SJ, AL, DJJD, and JCC) assessed the risk of bias of the included studies, which was checked by 2 authors (EYMC, VMS). We resolved disagreements through discussion with another author (EMH, GFMS). We used the Quality In Prognosis Studies (QUIPS) tool for risk of bias assessment (Item S2).<sup>14,15</sup>

### **Data Synthesis**

We pooled the incidence of COVID-19 and outcomes in people with CKD using a random-effects model with the Freeman-Tukey double arcsine transformation for variance stabilization.<sup>16</sup> Meta-analysis of single proportions was performed using metaprop in the R meta package.<sup>17</sup> We used the Wilson approach for calculation of confidence intervals (CIs)<sup>18</sup> and reported the range of the effects using prediction intervals (PrIs) for analyses that included at least 3 studies to improve clinical interpretation of the range of COVID-19 incidence and related outcomes in people with CKD because individual included studies may have large sample sizes that result in narrow CIs.<sup>19-22</sup> When data were available in people with and without COVID-19, we pooled incidence rates as an incidence rate ratio using a random-effects model to evaluate the prognostic association between COVID-19 and outcomes in people with CKD. For meta-analysis of incidence rates, we used the metainc function in the R meta package.<sup>17</sup> We adjudicated evidence certainty using an adapted GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework for prognostic factor research, which involves evaluating 6 factors that can decrease evidence certainty (phase of investigation, study limitations, inconsistency, indirectness, imprecision, publication bias) and 2 factors that can increase it (moderate to large effect size, exposure-response gradient).<sup>23</sup>

### **Sensitivity Analysis**

We conducted sensitivity analyses based on study sample size ( $\geq 1,000$  vs  $\leq 1,000$  participants), studies with high risk of bias in any methodological domain, and studies reporting the incidences of both COVID-19 and death. When data were available, we performed subgroup analysis based on age, CKD stage, COVID-19 severity (defined by the study investigators), case definitions of COVID-19 (suspected, probable, and confirmed), WHO region (Africa, Americas, South-East Asia, European, Eastern Mediterranean, or Western Pacific), World Bank income group (low, low-middle, upper-middle, or high income), study location (hospital or community), diabetes, and obesity. Subgroup analysis was performed by testing the significance of the between-study variance with a  $\chi^2$  Q-test using the R packages meta and metainc.<sup>17</sup> Studies reporting the incidence of COVID-19 or outcomes across CKD categories (CKD without KRT, CKD G5D, and/or KTRs) but not in each subgroup were included in overall analyses but excluded from subgroup analyses.

### Results

### Study Selection and Population Characteristics

We identified 6,698 citations and included 348 studies (382,407 participants with CKD and COVID-19, 1,139,979 total participants with CKD; Fig 1), including 336 cohort studies (45 prospective, 245 retrospective, and 46 not reported as retrospective or prospective) and 12 case-control studies (references in Item S3). The casecontrol studies included all eligible participants with CKD without KRT, participants with CKD G5D, or KTRs during the study period, but CKD was not reported in the controls, and therefore only case participants with CKD were included. Gray literature included 29 conference abstracts, 2 government reports, and 4 preprints. The incidence of COVID-19 in people with CKD was reported in 110 studies (366,931 participants with CKD and COVID-19; 772,389 total participants with CKD),



Figure 1. Study identification and selection.

outcomes were reported in 330 studies (381,422 participants with COVID-19), and 309 studies (373,141 participants with CKD and COVID-19; 1,114,991 participants with CKD) reported on study duration for calculation of incidence rates. Outcomes were reported in 179 studies including hospitalized people (76,800 participants), 143 studies including people hospitalized or treated in the community (299,536 participants), and 22 studies including people treated in the community (6,009

Table 1. Characteristics of the Included Studies

Variable	Value
No. of studies	348
No. of participants	
With COVID-19	382,407
With CKD	1,139,979
Mean age	11-79 y in 162 studies (47%)
Male sex	0%-88% in 150 studies (43%)
Baseline eGFR	
CKD without KRT	44-74 mL/min/1.73 m <sup>2</sup> in 2 studies (0.6%)
KTR	24-60 mL/min/1.73 m <sup>2</sup> in 18 studies (5%)
Type of study	
Cohort study	336 (97%)
Case-control study	12 (3%)
Study duration	7-274 d in 308 studies (89%)
CKD category included in study	
CKD without KRT	153 (44%)
CKD G5D	163 (47%)
KTR	95 (27%)
Incidence of COVID-19 reported	110 (32%)
Outcomes of interest reported	330 (95%)
Inpatient	178 (51%)
Inpatient and outpatient	140 (40%)
Outpatient	26 (8%)
Unclear location of treatment	4 (1%)
WHO region	
Americas	115 (33%)
Europe	139 (40%)
Western Pacific	54 (16%)
South East Asia	8 (2%)
Eastern Mediterranean	22 (6%)
Africa	4 (1%)
Multiple regions	6 (2%)
World Bank income group	
High income	244 (70%)
Upper middle income	86 (25%)
Lower middle income	12 (3%)
Low income	1 (0.3%)
Multiple income groups	5 (1%)

Values for continuous variables given as ranges, with number (%) of studies reporting the variable. Abbreviations: CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; KRT, kidney replacement therapy; KTR, kidney transplant recipient; WHO, World Health Organization.

participants). Four studies reported the incidence of death in people with CKD without COVID-19. Otherwise, none of the included studies reported the incidences of outcomes in people with CKD without COVID-19.

Participant age ranged from 11 to 79 years, and 5 studies included children with CKD (165 participants; Table 1; Table S1). Baseline estimated glomerular filtration rate was reported in 18 studies of KTRs (24-60 mL/min/ $1.73 \text{ m}^2$ ) and 2 studies of participants with CKD without KRT (44-74 mL/min/ $1.73 \text{ m}^2$ ). Study duration ranged from 7 to 274 days in 308 studies. Most studies were performed in Europe, the Americas, and the Western Pacific region and in high- to upper-middle–income countries (Item S4).

### **Risk of Bias Assessment**

Study participation was adequate in 178 studies (51%), inadequate in 4 studies, and unclear in the remaining studies (Fig 2). Risk of bias from study attrition was low in 27 studies (30% of potential prospective studies), high in 5 studies, unclear in the remaining studies, and not applicable in 245 retrospective cohort studies and 12 casecontrol studies. COVID-19 diagnosis measurement was adequate in 218 studies (63%), inadequate in 15 studies, and unclear in the remaining studies. Outcome measurement was adequate in 310 studies (89%), inadequate in 6 studies, unclear in 13 studies, and not applicable in 19 studies that reported only the incidence of COVID-19. Risk of bias due to study confounding was low in 71 studies (20%), high in 201 studies (58%), and unclear in the remaining studies. Statistical analysis and reporting were adequate in 90 studies (26%), inadequate in 181 studies (52%), and unclear in the remaining studies.

### Incidence of COVID-19 in People With CKD

The incidence of COVID-19 in people with CKD was 66 per 10,000 person-weeks (95% CI, 58-75; 95% PrI, 10-169) in 88 studies of 14,972 participants with CKD and COVID-19 and 740,452 total participants with CKD (low-certainty evidence; Table 2). The incidence of COVID-19 in people with CKD without KRT was 16 per 10,000 person-weeks (95% CI, 4-33; 95% PrI, 0-92) in 5 studies of 701 participants with CKD and COVID-19 and 70,683 total participants with CKD (low-certainty evidence; Fig S1); the incidence in CKD G5D was 105 per 10,000 person-weeks (95% CI, 91-120; 95% PrI, 25-235) in 59



Figure 2. Risk of bias in the included studies.

### Table 2. Summary of Findings: The Incidence of COVID-19 and Outcomes in People With CKD

	Effect				
Incidence of Outcome	No. of Events	No. of Individuals	Incidenceª	No. of Studies	Evidence Certainty <sup>b</sup>
COVID-19 in people with CK	D (per 10,000	person-weeks)			
СКD	14,972	740,452	66 (58-75) [10-169]	88	Low <sup>c</sup>
CKD without KRT	701	70,683	16 (4-33) [0-92]	5	Low <sup>d</sup>
CKD G5D	12,208	468,233	105 (91-120) [25-235]	59	Low <sup>c</sup>
KTR	1,893	120,281	23 (18-30) [2-67]	29	Low <sup>c</sup>
COVID-19-attributable outco	omes in people	e with COVID-19 a	nd CKD (per 1,000 per	son-weeks)	
Death	19,938	70,922	32 (30-35) [4-81]	229	Low <sup>c</sup>
Respiratory failure	14,635	68,840	31 (27-35) [3-81]	101	Low <sup>c</sup>
Dyspnea	2,587	5,767	80 (66-95) [2-234]	75	Low <sup>c</sup>
COVID-19 recovery	1,473	3,463	83 (52-120) [0-304]	21	Very low <sup>e</sup>
Intensive care admission	17,590	76,532	27 (24-30) [4-63]	109	Low <sup>c</sup>
Hospital admission	120,953	286,176	93 (82-104) [15-223]	92	Low <sup>c</sup>
Hospital discharge	3,134	5,929	106 (90-123) [13-262]	63	Low <sup>c</sup>
Need for oxygen supplementation	3,014	8,996	96 (78-116) [4-272]	52	Low <sup>c</sup>
Sepsis	47	1,165	3 (0-8) [0-22]	10	Low <sup>f</sup>
Kidney disease-specific out	comes in peop	le with COVID-19	and CKD (per 1,000 pe	erson-weeks)	
Short-term dialysis	1,017	15,994	17 (11-24) [0-82]	48	Low <sup>c</sup>
Acute kidney injury	3,418	6,900	73 (60-87) [5-199]	59	Low <sup>c</sup>
Kidney allograft loss (death- censored)	47	1,101	3 (1-6) [0-18]	13	Low <sup>f</sup>
Myocardial infarction	21	308	9 (0-31) [0-101]	4	Very low <sup>g</sup>
Stroke	16	430	4 (0-9) [0-28]	5	Low <sup>f</sup>
Fatigue	731	2,017	57 (41-75) [0-180]	33	Low <sup>c</sup>

Abbreviations: CKD, chronic kidney disease; CKD G5D, CKD treated by dialysis; COVID-19, coronavirus disease 2019; KRT, kidney replacement therapy; Prl, prediction interval; KTR, kidney transplant recipient.

<sup>a</sup>Values in parentheses are 95% Cls; values in brackets are 95% prediction intervals.

<sup>b</sup>"High" indicates that further research is very unlikely to change our confidence in the estimate of effect. "Moderate" indicates that further research is likely to have an important effect on our confidence in the estimate of effect and may change the estimate. "Low" indicates that further research is very likely to have an important effect on our confidence in the estimate of effect and is likely to change the estimate.

<sup>c</sup>Evidence certainty downgraded for study methodological limitations and inconsistency with significant heterogeneity between studies.

<sup>d</sup>Evidence certainty downgraded for study methodological limitations and imprecision with excessively wide confidence intervals.

<sup>e</sup>Evidence downgraded for study methodological limitations, inconsistency with significant heterogeneity between studies, and imprecision with excessively wide confidence intervals.

<sup>f</sup>Evidence certainty downgraded for study methodological limitations and imprecision with inadequate study sample size.

<sup>g</sup>Evidence certainty downgraded for serious study methodological limitations and imprecision with inadequate study sample size.

studies of 12,208 participants with CKD and COVID-19 and 468,233 total participants with CKD (low-certainty evidence; Fig 3), and the incidence in KTRs was 23 per 10,000 person-weeks (95% CI, 18-30; 95% PrI, 2-67) in 29 studies of 1,893 participants with CKD and COVID-19 and 120,281 total participants with CKD (low-certainty evidence; P < 0.001 between CKD subgroups; Fig 4).

### COVID-19–Attributable Outcomes in People With COVID-19 and CKD

### Death

The incidence of death may be higher in people with CKD and COVID-19 than in people with CKD without COVID-19 (incidence rate ratio, 10.26; 95% CI, 6.78-15.53; 95% PrI, 2.62-40.15; 4 studies, 18,347 participants; low-certainty evidence; Fig S2). Compared with people without COVID-19, the incidence of death was higher in people with CKD G5D and COVID-19 (incidence rate ratio, 8.10; 95% CI, 6.29-10.42; 95% PrI, 3.38-19.37; 3 studies, 23,239 participants) and in KTRs with

COVID-19 (incidence rate ratio, 42.32; 95% CI, 15.38-116.44; 1 study, 3,293 participants; P = 0.002 between CKD subgroups). No studies reported death in people with non-KRT CKD without COVID-19.

The overall incidence of death in people with CKD and COVID-19 was 32 per 1,000 person-weeks (95% CI, 30-35; 95% PrI, 4-81; 229 studies, 70,922 participants; low-certainty evidence). The incidence of death in people with COVID-19 and CKD without KRT was 40 per 1,000 person-weeks (95% CI, 35-45; 95% PrI, 9-88; 75 studies, 28,459 participants; Fig S3), the incidence in CKD G5D was 30 per 1,000 person-weeks (95% CI, 26-35; 95% PrI, 2-85; 107 studies, 34,639 participants; Fig 5), and the incidence in KTRs was 31 per 1,000 person-weeks (95% CI, 24-38; 95% PrI, 0-100; 71 studies, 7,287 participants; P = 0.02 between CKD subgroups; Fig 6).

### **Respiratory Failure**

The overall incidence of respiratory failure in people with CKD and COVID-19 was 31 per 1,000 person-weeks (95%



Church	<b>F</b> uente	Tatal	Walasht	Events per 10000 observations	Events per 10000 observations
Sludy Bigolow 2020		10121	weight	1004 90 [674 92: 1707 09]	IV, Random, 95% CI
Bigelow 2020	15	137	0.5%		
De La Flor Merino 2021	40	282	0.8%		
	40	354	1.0%		
Manes 2020	13	308	1.0%	353.26 [207.59; 594.94]	
Fontana 2020	15	437	1.0%	343.25 [209.10; 558.56]	
Albalate 2020	30	450	1.0%	800.00 [583.44; 1087.66]	
Rincon 2020	36	5/6	1.2%	625.00 [454.84; 853.13]	
Depetri 2020	16	645	1.2%	248.06 [153.26; 399.13]	
	12	/50	1.3%	158.73 [ 91.03; 275.38]	
Giaime 2020	24	810	1.3%	296.30 [199.91; 437.09]	
	38	9/1	1.4%	391.35 [286.43; 532.59]	
fau 2020	11	1010	1.4%	108.27 [ 60.56; 192.83]	
Wang 2020b	3/	1150	1.5%	321.74 [234.31; 440.32]	
	8	14/9	1.0%	54.09 [ 27.43; 106.37]	
	34	1023	1.0%	223.24 [160.19; 310.33]	
Dalli 2020	97	1040	1.0%		
Browiti 20200	20	1000	1.0%		
Ma 2020	0	1099	1.0%	42.13 [21.30, 02.91]	
Ina 2020	10	1939	1.0%	109 50 [ 70 47; 160 40]	
Mana 2020a	23	2110	1.7%		
Nooo 2020	10	2402	1.7%	20.20 [ 13.07, 30.10]	
Roper 2020	42	25/1	1.0 /0	214 62 [171 92: 267 90]	
Rosota 2020	26	4474	1.0 /0	214.03 [171.03, 207.00]	
Buiz 2020	115	4474	1.0 /0	00.40 [ 00.10, 111.19]	
	115	4001	1.0 /0	59 24 [ 40 12 · 94 75]	<b>—</b>
Apoto 2020	10	4020	1.0 /0	29 44 [ 24 22 . 60 69]	<b></b>
Apala 2020 Hendra 2021	164	4003	1.0%	3/1 05 [20/ 13: 307 23]	
McCafferty 2020	107	5101	1.0%	379 50 [330 85: 434 99]	
Galassi 2021	21	5351	1.0%	39 25 [ 25 68 59 92]	-
Zou 2020	66	5590	1.0%	118 07 [ 92 92 149 92]	
Petrulewicz 2020	23	7511	1.0%	30.62 [ 20.41 45.91]	+
Kumaresan 2020	24	7910	1.0%	30 34 [ 20 40 45 11]	+
Hamad 2020	8	7986	1.9%	10.02 [ 5.08 19.76]	
Corbett 2020	300	9180	1.9%	326.80 [292.34: 365.17]	<b>—</b>
Seidel 2020	56	9707	1.9%	57.69 [ 44.46; 74.83]	
Keller 2020	123	10576	1.9%	116.30 [ 97.57: 138.58]	
Clarke 2021	255	11618	1.9%	219.49 [194.38: 247.75]	-
Jiang 2021	8	13205	1.9%	6.06 [ 3.07: 11.95]	
Deshpande 2020	75	13674	1.9%	54.85 [ 43.78: 68.69]	-
Weiss 2020	306	13690	1.9%	223.52 [200.07; 249.66]	
Manganaro 2020	102	16400	1.9%	62.20 [ 51.27; 75.44]	
Silberzweig 2020	241	16481	1.9%	146.23 [129.00; 165.72]	
Tang 2020	52	18265	1.9%	28.47 [ 21.72; 37.31]	
Kular 2020	224	19107	1.9%	117.23 [102.92; 133.51]	+
Lano 2020	122	21691	1.9%	56.24 [ 47.13; 67.11]	
Bell 2020	86	28704	1.9%	29.96 24.27; 36.98	•
Sosa 2021	325	54874	2.0%	59.23 [ 53.14; 66.00]	
De Meester 2020	234	56173	2.0%	41.66 [ 36.66; 47.33]	•
Li 2020a	116	57697	2.0%	20.11 [ 16.77; 24.11]	
Xiong 2020	154	71540	2.0%	21.53 [ 18.39; 25.20]	
Hsu 2021	438	119220	2.0%	36.74 [ 33.46; 40.34]	
Sim 2021	133	131289	2.0%	10.13 [ 8.55; 12.00]	
Manley 2020	351	167164	2.0%	21.00 [ 18.91; 23.31]	
Sankarasubbaiyan 2020	39	176133	2.0%	2.21 [ 1.62; 3.03]	
Quintaliani 2020	1150	200000	2.0%	57.50 [ 54.28; 60.91]	
Taji 2021	187	289309	2.0%	6.46 [ 5.60; 7.46]	
Pio–Abreu 2020	1291	681336	2.0%	18.95 [ 17.94; 20.01]	
Izurieta 2021	4503	1600000	2.0%	28.14 [ 27.33; 28.98]	
Total (95% CI)	-	3899572	100.0%	104.81 [ 91.00; 119.56]	•
Heterogeneity: Tau <sup>2</sup> = 0.00	06; Chi <sup>2</sup> =	7762.98,	df = 58 (P	<sup>1</sup> = 0); l <sup>2</sup> = 99%	
					0 200 400 600 800 1200

Figure 3. Forest plot of the incidence of COVID-19 in people with chronic kidney disease treated by dialysis. Total and observations shown in person-weeks.

CI, 27-35; 95% PrI, 3-81; 101 studies, 68,840 participants; low-certainty evidence). The incidence of respiratory failure in people with COVID-19 and non-KRT CKD was 28 per 1,000 person-weeks (95% CI, 20-38; 95% PrI, 2-74; 17 studies, 57,077 participants), the incidence in CKD G5D was 30 per 1,000 person-weeks (95% CI, 22-38; 95% PrI, 0-100; 48 studies, 8,134 participants), and the incidence in KTRs was 40 per 1,000 person-weeks

(95% CI, 30-52; 95% PrI, 0-136; 48 studies, 3,210 participants; P = 0.1 between CKD subgroups).

#### Other

The incidences of dyspnea, recovery from COVID-19, ICU admission, hospital admission, hospital discharge, need for supplemental oxygen, and sepsis are reported in Table 2 and Item S5. None of the included studies reported on

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				Events per 10000 observatio	ns Ever	nts per	10000 0	bservat	ions
Study	Events	Total	Weight	IV, Random, 95% Cl		IV, Ra	ndom, 9	95% CI	
Gisondi 2020	1	670	1.6%	14.93 [ 2.64; 84.05]	-		_		
Binda 2020	1	776	1.8%	12.89 [ 2.28; 72.63]	-				
Yi 2020	14	1033	2.1%	135.53 [80.90; 226.20]				-	$\rightarrow$
Vistoli 2020	3	1641	2.5%	18.28 [ 6.22; 53.61]	-				
Clarke 2021	16	2302	2.8%	69.50 [42.83; 112.61]					
Jarrin Tejada 2020	25	3011	3.0%	83.03 [56.30; 122.29]					
Crespo 2020	20	3212	3.1%	62.27 [40.34; 95.98]					
Zhang 2020a	5	3397	3.1%	14.72 [ 6.29; 34.41]		_			
Akdur 2020	1	4436	3.3%	2.25 [ 0.40; 12.76]	-				
Silva 2020	5	5286	3.4%	9.46 [ 4.04; 22.13]					
Dhelr 2020	20	7329	3.6%	27.29 [17.67; 42.11]	-	-			
Ghaffari 2020	19	8547	3.6%	22.23 [14.24; 34.70]	-	-			
Elias 2020	66	10597	3.7%	62.28 [48.99; 79.15]		-	_		
Manganaro 2020	26	11129	3.7%	23.36 [15.95; 34.21]	-	-			
Jones 2021	45	11666	3.7%	38.57 [28.84; 51.57]		-			
Bannerjee 2020	7	12492	3.7%	5.60 [ 2.71; 11.56]					
Fava 2020	106	15197	3.8%	69.75 [57.71; 84.29]			-		
Santeusanio 2021	95	18830	3.8%	50.45 [41.29; 61.63]		-			
Sran 2020	66	22377	3.9%	29.49 [23.19; 37.50]		-			
Kumaresan 2020	16	25200	3.9%	6.35 [ 3.91; 10.31]					
Azzi 2020	201	29500	3.9%	68.14 [59.37; 78.19]		-	-		
De Meester 2020	46	39986	3.9%	11.50 [ 8.63; 15.34]	-				
Elec 2021	42	40447	3.9%	10.38 [ 7.68; 14.03]	-				
Bell 2020	24	43069	4.0%	5.57 [ 3.75; 8.29]	+				
Felldin 2021	31	45036	4.0%	6.88 [ 4.85; 9.77]	+				
Varnell 2021	24	58933	4.0%	4.07 [ 2.74; 6.06]	•				
Cravedi 2020	144	73134	4.0%	19.69 [16.73; 23.17]	+				
Quintaliani 2020	218	141966	4.0%	15.36 [13.45; 17.53]	+				
Thaunat 2020	606	568788	4.0%	10.65 [ 9.84; 11.54]	•				
Total (95% CI)		1209987	100.0%	23.50 [17.69; 30.07]	•	•			
Heterogeneity: Tau <sup>2</sup>	= 0.0003;	$Chi^{2} = 938$	3.97, df = 3	28 (P < 0.01); $\overline{l}^2 = 97\%$					
0, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,	-,				0	50	100	150	200

Figure 4. Forest plot of the incidence of COVID-19 in kidney and pancreas-kidney transplant recipients. Total and observations shown in person-weeks.

multiorgan failure, financial impact, depression, lung function, physical function, or viral load/clearance.

### Kidney Disease–Specific Outcomes in People With COVID-19 and CKD

The overall incidence of short-term dialysis in people with CKD and COVID-19 was 17 per 1,000 person-weeks (95% CI, 11-24; 95% PrI, 0-82; 48 studies, 15,994 participants; low-certainty evidence). The incidence of short-term dialysis in people with COVID-19 and non-KRT CKD was 19 per 1,000 person-weeks (95% CI, 5-42; 95% PrI, 0-145; 10 studies, 10,723 participants), and the incidence in KTRs was 15 per 1,000 person-weeks (95% CI, 10-21; 95% PrI, 0-57; 39 studies, 5,271 participants; P = 0.9 between CKD subgroups).

The incidences of AKI, death-censored kidney allograft loss, myocardial infarction, stroke, and fatigue are reported in Table 2 and Item S6. A single study reported on vascular access thrombosis, and none reported on kidney failure, life participation, or limb amputation.

### **Sensitivity and Subgroup Analyses**

Sensitivity analysis including only studies that reported incidence of COVID-19 and death revealed a higher incidence of death in patients with CKD G5D and KTRs than in those with CKD without KRT. The incidences of COVID-19, death, and respiratory failure in people with CKD were higher in studies with a low or unclear risk of bias, small sample size, or from the Americas or Europe compared with studies with a high risk of bias, large sample size, or from other WHO regions. Studies from high-income countries reported higher incidences of COVID-19 in people with CKD, respiratory failure, hospital admission, and short-term dialysis compared with upper- and lower-middle–income countries. Highand low-income countries reported a higher incidence of death than upper- and lower-middle–income countries. Children with CKD were reported to have a lower incidence of COVID-19 and associated outcomes than adults with CKD. The was no association between diabetes or obesity and death in people with CKD and COVID-19 (Items S7 and S8).

### Discussion

Three hundred forty-eight studies reported the incidence or prognosis of COVID-19 in people with CKD. The certainty of the evidence was generally low as a result of study limitations, inconsistency in the findings between studies, and/or imprecision in the calculated estimates. Study participants were mostly hospitalized adults; from Europe, the United States, or China; and from high- or uppermiddle income countries, which may limit the generalizability of our findings. With low-certainty evidence, we

<u>A</u> ]	K	D

Study	Events	Total	Weight	Events per 1000 observations IV. Random. 95% CI	Events per 1000 observations IV. Random. 95% CI
Wagner 2020	1	17	0.2%	58.82 [ 10.46; 269.82]	
Fontana 2020 Abrishami 2020	6 0	21 23	0.3%	285.71 [138.14; 499.56] 0.00 [ 0.00: 143.12]	• • • • • • • • • • • • • • • • • • •
De La Flor Merino 2021	1	33	0.4%	30.30 [ 5.37; 153.19]	- <u>+</u>
Trujillo 2020 Boushab 2021	7	46 50	0.5%	152.17 [ 75.72; 282.24]	<b></b>
Petrulewicz 2020	5	53	0.5%	94.34 [ 40.97; 202.54]	
Filardo 2020 Bigolow 2020	4	58	0.5%	68.97 [ 27.14; 164.34]	
Giaime 2020	6	72	0.6%	83.33 [ 38.75; 170.12]	_ <b>_</b>
Previti 2020	2	72	0.6%	27.78 [ 7.65; 95.74]	<u>+</u>
Altonen 2020	3	89	0.6%	33.71 [ 11.53; 94.47]	
Quiroga 2021	4	103	0.7%	38.83 [ 15.20; 95.63]	<b>—</b>
Alberici 2020a Bincon 2020	27	107	0.7%	252.34 [179.60; 342.24] 64.81 [ 31.75; 127.78]	
Apata 2020	4	113	0.7%	35.40 [ 13.85; 87.50]	_ <del></del>
Maldonado 2020	2	115	0.7%	17.39 [ 4.78; 61.20] 15.50 [ 4.26; 54.77]	
Sipahi 2021	3	131	0.8%	22.90 [ 7.82; 65.17]	<b>-</b>
La Milia 2020	13	134	0.8%	97.01 [ 57.58; 158.92]	
Luo 2020	3	139	0.8%	21.58 [ 7.37; 61.53]	<b>₽</b>
Carlson 2021	9	146	0.8%	61.64 [ 32.77; 113.00]	
Trivedi 2020	14	153	0.8%	91.50 [ 55.29; 147.73]	- <b>-</b>
Sachdeva 2020	2	168	0.8%	11.90 [ 3.27; 42.36]	<b>•</b>
Yang 2020 Albalate 2020	10	179 180	0.8%	55.87 [ 30.62; 99.77] 33.33 [ 15.36: 70.80]	:= <mark></mark>
Jung 2020	2	180	0.8%	11.11 [ 3.05; 39.60]	• <u>•</u>
Wang 2020b Creput 2020	6	185 185	0.9%	32.43 [ 14.95; 68.94] 43.24 [ 22.07: 83.00]	<b>.</b>
Ibernon 2021	5	200	0.9%	25.00 [ 10.72; 57.18]	<b>₽</b>
Tortonese 2020	12	201	0.9%	59.70 [ 34.48; 101.44]	
Aydin Bahat 2020	5	223	0.9%	22.22 [ 9.53; 50.96]	
Mazzoleni 2020	11	229	0.9%	48.03 [ 27.03; 83.95]	
Zapata 2020 Corcillo 2020	13	240 244	0.9%	54.17 [ 31.93; 90.46] 40.98 [ 22.41: 73.79]	
Zeng 2021	15	247	0.9%	60.73 [ 37.14; 97.77]	-
Goupil 2020 Dirim 2021	9 14	253	0.9%	35.57 [ 18.83; 66.21] 50 54 [ 30 34: 83 04]	
Jackson 2020	6	315	1.0%	19.05 [ 8.76; 40.93]	<b>—</b>
Stefan 2021	7	317	1.0%	22.08 [ 10.74; 44.87]	
Tian 2021	2	343	1.0%	5.83 [ 1.60; 21.01]	
Torres Ortiz 2020	16	343	1.0%	46.65 [ 28.91; 74.42]	_ <b>=</b> -
Wu 2020 Muhammad 2021	4	350 351	1.0%	20.00 [ 9.72; 40.70] 11.40 [ 4.44; 28.93]	
Sankarasubbaiyan 2020	8	373	1.0%	21.45 [ 10.91; 41.74]	<b>.</b>
Broseta 2020 Gasparini 2020	13	375	1.0%	34.67 [ 20.37; 58.40]	
Roper 2020	7	402	1.0%	17.41 [ 8.46; 35.50]	i i i i i i i i i i i i i i i i i i i
Medjeral-Thomas 2020	16	424	1.0%	37.74 [ 23.36; 60.41]	_ <del></del>
Valeri 2020	18	425	1.0%	41.10 [ 26.15; 64.02]	<b>-</b>
Galassi 2021	5	488	1.0%	10.25 [ 4.38; 23.76]	
Navarrete 2020 Noce 2020	6	534 540	1.0%	11.24 [ 5.16; 24.29] 16.67 [ 8.79: 31.37]	
Jones 2021	6	567	1.0%	10.58 [ 4.86; 22.89]	<b>E</b>
Fisher 2020a	23	570	1.1%	40.35 [ 27.04; 59.82]	
Craig–Schapiro 2020	19	616	1.1%	30.84 [ 19.83; 47.67]	· · · · · · · · · · · · · · · · · · ·
Ossareh 2020	4	702	1.1%	5.70 [ 2.22; 14.56]	
Rastad 2021	28	707	1.1%	22.63 [ 13.98; 36.44] 39.55 [ 27.50; 56.56]	
Seidel 2020	15	720	1.1%	20.83 [ 12.67; 34.09]	
Zou 2020 McCafferty 2020	18 44	801	1.1%	22.47 [ 14.26; 35.24] 53 92 [ 40 41: 71 61]	
Daifi 2020	16	831	1.1%	19.25 [ 11.89; 31.05]	
Kumaresan 2020	2	840	1.1%	2.38 [ 0.65; 8.64]	•
Deshpande 2020	9	921	1.1%	9.77 [ 5.15; 18.47]	
Keller 2020	29	966	1.1%	30.02 [ 20.98; 42.78]	
Hu 2021 Li 2020a	50 57	1006	1.1%	49.70 [ 37.90; 64.93] 56.38 [ 43.77; 72.35]	
Hendra 2021	36	1054	1.1%	34.16 [ 24.77; 46.92]	• <b>•</b> _
Ozturk 2020 Lano 2020	63 38	1114	1.1%	56.55 [ 44.45; 71.70] 33.54 [ 24.53; 45.70]	
Xiong 2020	41	1310	1.1%	31.30 [ 23.15; 42.18]	
Chawki 2020 Chap 2020a	45	1417	1.1%	31.76 [ 23.82; 42.23]	
Gupta 2021	16	1500	1.1%	10.67 [ 6.58; 17.26]	•
Corbett 2020	61	1800	1.1%	33.89 [ 26.47; 43.29]	<u>e</u>
Sanchez-Alvarez 2020	145	1923	1.1%	72.68 [ 62.09; 84.91]	
Sim 2021	30	2318	1.1%	12.94 [ 9.08; 18.42]	<b>e</b> -
Kular 2020 Clarke 2021	51 81	2464 2477	1.1%	20.70 [ 15.78; 27.11] 32.70 [ 26.39: 40.46]	
Silberzweig 2020	55	2548	1.2%	21.59 [ 16.62; 27.99]	d i
De Meester 2020	66	2841	1.2%	23.23 [ 18.30; 29.45]	
Harrison 2021	110	3707	1.2%	29.67 [ 24.68; 35.64]	
Turgutalp 2021	93	3726	1.2%	24.96 [ 20.42; 30.48]	
Ng 2020	133	+328 5267	1.2%	25.25 [ 21.35; 29.85]	
Sosa 2021	90	5571	1.2%	16.16 [ 13.16; 19.81]	<b>2</b>
Hsu 2021 Lacson 2021	109 96	5631 6209	1.2%	19.36 [ 16.07; 23.30] 15.46 [ 12.68: 18.84]	
Quintaliani 2020	395	6407	1.2%	61.65 [ 56.02; 67.81]	
Pakhchanian 2021 Jager 2020	237 658	10350	1.2% 1.2%	22.90 [ 20.19; 25.96] 50.08 [ 46.48; 53.94]	
Pio-Abreu 2020	357	23238	1.2%	15.36 [ 13.86; 17.03]	<b>a</b>
Izurieta 2021	1777	24445	1.2%	72.69 [ 69.51; 76.02]	
Pena 2020	436 4829	348326	1.2%	5.74 [ 5.22; 6.30] 13.86 [ 13.48; 14.26]	
Total (05% CI)		502570	100 00	20 40 [ 26 14: 25 14]	
Heterogeneity: Tau <sup>2</sup> = 0.0035	5; Chi <sup>2</sup> = 5	308.10, c	If = 105 (F	$p = 0$ ; $l^2 = 98\%$	
					0 100 200 300 400

Figure 5. Forest plot of the incidence of death in people with dialysis-treated chronic kidney disease and COVID-19. Total and observations shown in person-weeks.

found a COVID-19 incidence in people with CKD of 66 per 10,000 person-weeks, which is higher than the global COVID-19 incidence of 5 per 100,000 person-weeks.<sup>24</sup> This may be in part due to ascertainment bias because people with CKD are more likely to receive close health care monitoring than the general population. Also with low-certainty evidence, we found a higher incidence of COVID-19 in people with CKD G5D than in people with CKD without KRT or in KTRs, which may be attributable to greater exposure to SARS-CoV-2 from greater use of health facilities in people undergoing maintenance hemodialysis.<sup>25</sup> This hypothesis is supported by the single included study that reported a COVID-19 incidence in people receiving home-based dialysis of 6 per 10,000 personweeks,<sup>26</sup> which is similar to the reported incidence in the general populations in Italy and the United States of 2-6 per 10,000 person-weeks.<sup>27,28</sup> Based on low-certainty evidence, people with CKD and COVID-19 may have a tenfold higher incidence of death than those without COVID-19. The incidence of death from COVID-19 of 16 per 1,000 person-weeks in the general population is lower than our findings in people with CKD,<sup>1</sup> which may be attributed to a dysfunctional immune system in CKD.<sup>29-31</sup> We found a higher incidence of COVID-19 and associated death in people with CKD from the Americas and Europe compared with other regions, and in adults compared with children, which is similar to the general population.<sup>1,32,33</sup> Therefore, the heterogeneity observed in most of our analyses could be partially explained by similar variations in the general population based on geographic location and age. However, such significant heterogeneity lowers our confidence in the summary estimates, which need to be interpreted in the context of the 95% PrIs. Data were absent on outcomes other than death in people with CKD without COVID-19 and on COVID-19 severity stratified by CKD subgroup, preventing comprehensive evaluation of COVID-19 as a prognostic factor in people with CKD.

Although multiple systematic reviews have evaluated the prognostic impact of preexisting CKD in people with COVID-19,34-36 the incidence rates of COVID-19 and associated outcomes in people with CKD have not been comprehensively assessed. A systematic review of people receiving maintenance hemodialysis that included 29 studies reported an incidence of COVID-19 of 7.7%, death in 22.4%, acute respiratory distress syndrome in 18.5%, and ICU admission in 6.6%.<sup>37</sup> Another systematic review of KTRs with COVID-19 that included 15 studies reported a mortality rate of 24% and AKI in 50%.<sup>38</sup> Two systematic reviews also found CKD to be associated with severe COVID-19.<sup>39,40</sup> However, time periods were not reported in these reviews, preventing calculation of an incidence rate and comparison with our results. These systematic reviews also included substantially fewer studies than our review, and none adjudicated evidence certainty using GRADE or reported other COVID-19 COS outcomes. A

# AJKD

0		<b>T</b>		Events per 1000 observations	Events per 1000 observations
Study Marathi 2020	Events	Iotai	weight	IV, Random, 95% CI	IV, Random, 95% CI
Akdur 2020	0	0 0	0.3%	0.00 [ 0.00 299 15]	• ´
Silva 2020	1	14	0.0%	71 43 [ 12 72: 314 69]	
Alberici 2020	5	20	0.5%	250.00 [111.86: 468.70]	
Fernandez-Ruiz 2020	2	21	0.5%	95.24 [ 26.52; 289.14]	
Bannerjee 2020	1	42	0.8%	23.81 [ 4.22; 123.21]	
Trujillo 2020	6	48	0.9%	125.00 [ 58.57; 247.00]	
Zhu 2020	1	51	0.9%	19.61 [ 3.47; 103.05]	-
Chen 2020d	6	56	1.0%	107.14 [ 50.04; 214.68]	
Devresse 2020	2	57	1.0%	35.09 [ 9.68; 119.21]	
Khalid 2021	4	58	1.0%	68.97 [ 27.14; 164.34]	
Crespo 2020	8	64	1.0%	125.00 [ 64.72; 227.75]	
Meziyerh 2020	6	64	1.0%	93.75 [ 43.68; 189.83]	<b>_</b>
Ghaffari 2020	9	65	1.0%	138.46 [ 74.59; 242.68]	
Molael 2020	2	71	1.1%	28.17 [ 7.76; 97.02]	
Candolfini 2020	3	72	1.1%	41.67 [ 14.27; 115.49]	
Gandollini 2020	3	/3	1.1%	41.10 [ 14.07; 114.00]	
Corcillo 2020	0	01	1.1%	74.07 [ 34.39, 152.33] 41.67 [ 16.20: 102.09]	
Δkalin 2020	10	108	1.2%	92 59 [ 51 07· 162 10]	
Gasparini 2020	6	123	1.3%	48 78 [ 22 55: 102 35]	
Hartzell 2020	7	123	1.3%	56 91 [ 27 84: 112 82]	
Hardesty 2021	1	124	1.3%	8 06 [ 1 43: 44 27]	
Mehta 2020	6	140	1.0%	42 86 [ 19 79 90 34]	
Clarke 2021	6	155	1.4%	38.71 [ 17.86: 81.87]	
Mahmoud 2020	5	158	1.4%	31.65 [ 13.59; 71.93]	<b>—</b>
Merhi 2020	1	181	1.4%	5.52 [ 0.98; 30.63]	-
Demir 2020	5	183	1.5%	27.32 [ 11.73; 62.36]	<b>—</b> —
Chavarot 2020	26	186	1.5%	139.78 [ 97.21; 196.94]	— <mark>—</mark> ——
Hussain 2020	10	186	1.5%	53.76 [ 29.46; 96.12]	
Monfared 2020	6	189	1.5%	31.75 [ 14.63; 67.52]	<b>-</b>
Chaudhry 2020	7	190	1.5%	36.84 [ 17.96; 74.08]	<b>#</b>
Bossini 2020	15	197	1.5%	76.14 [ 46.68; 121.82]	
Mohamed 2021	9	204	1.5%	44.12 [ 23.38; 81.71]	
Pascual 2020	11	206	1.5%	53.40 [ 30.07; 93.07]	
Abolghasemi 2020	10	213	1.5%	46.95 [ 25.70; 84.25]	
Jarrin Tejada 2020	1	221	1.5%	4.52 [ 0.80; 25.18]	<b>•</b>
Fava 2020	28	227	1.5%	123.35 [ 86.74; 172.50]	
Shrivastava 2021	9	228	1.5%	39.47 [ 20.90; 73.30]	
Nair 2020	10	201	1.0 %	38 31 [ 20 04: 60 08]	<b>.</b>
1 ubetzky 2020	7	285	1.0%	24 56 [ 11 95: 49 82]	<b>.</b>
Ortiz 2020	10	288	1.6%	34 72 [ 18 97: 62 73]	<b>—</b> —
Santeusanio 2021	11	337	1.6%	32 64 [ 18 32: 57 49]	
Vistoli 2020	11	377	1.6%	29.18 [ 16.37: 51.48]	-
Dhelr 2020	2	386	1.6%	5.18 [ 1.42: 18.69]	<b>•</b>
Benotmane 2020	9	406	1.7%	22.17 [ 11.71; 41.59]	
Cucchiari 2020	5	437	1.7%	11.44 [ 4.90; 26.50]	
Varnell 2021	0	518	1.7%	0.00 [ 0.00; 7.36]	•
Sran 2020	12	519	1.7%	23.12 [ 13.27; 39.98]	<b>-</b>
Lum 2020	4	527	1.7%	7.59 [ 2.96; 19.35]	<b>—</b>
Felldin 2021	3	545	1.7%	5.50 [ 1.87; 16.06]	<b>F</b>
De Meester 2020	6	559	1.7%	10.73 [ 4.93; 23.22]	<u></u>
Kumaresan 2020	3	560	1.7%	5.36 [ 1.82; 15.63]	
Elias 2020	16	575	1.7%	27.83 [ 17.20; 44.72]	_ <mark>_</mark>
Jones 2021	9	823	1.8%	10.94 [ 5.76; 20.65]	
Craig–Schapiro 2020	13	891	1.8%	14.59 [ 8.55; 24.80]	- <u></u>
Perez–Saez 2020	26	914	1.8%	28.45 [ 19.49; 41.35]	
Sanchez-Alvarez 2020	53	981	1.8%	54.03 [ 41.54; 69.99]	
Mamode 2021	36	1003	1.8%	35.89 [ 26.04; 49.29]	
Cravedi 2020	40	1150	1.8%	42.99 [ 32.38; 56.87]	
	/ 4=	1170	1.0%	0.04 [ 2.33; 12.42]	
Ouintaliani 2020	45 E 4	1015	1.0% 1.0%	30.40 [ 20.87; 51.08]	
Hillbrande 2020	54 65	1210	1.0 <sup>-</sup> /0	44.44 [ 04.22, 07.04] 53.28 [ 12.09, 67.21]	
Azzi 2020	28	1580	1.0 %	17 72 [ 12 29 25 49]	
Crespo 2020a	100	2602	1.0%	41 89 [ 34 84 50 29]	
Jager 2020	191	4052	1.8%	47.14 [ 41.03 54 10]	+
Kute 2020	29	6321	1.9%	4.59 [ 3.20 6.58]	<b>•</b>
Thaunat 2020	122	8051	1.9%	15.15 [ 12.71 18.06]	
Lapalu 2021	137	23918	1.9%	5.73 [ 4.85: 6.77]	
•					—
Total (95% CI)		68292	100.0%	30.81 [ 24.25; 38.01]	<b>•</b>
Heterogeneity: Tau <sup>2</sup> = 0.0	047; Chi <sup>2</sup>	= 1162.	65, df = 7	0 (P < 0.01); l <sup>2</sup> = 94%	
					0 100 200 300 400

Figure 6. Forest plot of the incidence of death in kidney and pancreas-kidney transplant recipients with COVID-19. Total and observations shown in person-weeks.

large systematic review found increased risks of death in people with CKD G5D and organ transplant recipients with

COVID-19 compared with people with CKD without KRT,  $^{41}$  which is not consistent with our findings. These

discrepant findings could be due to a falsely high incidence of death in people with non-KRT CKD in our study because of an inaccurate denominator of all people with non-KRT CKD or reporting of mostly hospitalized people.<sup>41,42</sup>

There are several strengths and limitations to this review. We performed a systematic search designed by an information specialist for studies evaluating COVID-19 in people with any level of CKD. We evaluated COVID-19 incidence and prognosis using the COVID-19 COS and SONG core outcomes.

Limitations of our review included the limited measurement of known confounding factors impacting the incidence and outcomes of COVID-19 in people with CKD, such as old age, male sex, Black or South Asian ethnicity, lower socioeconomic status, obesity, diabetes, malignancy, or respiratory, cardiovascular, liver, neurologic, or autoimmune diseases.<sup>41</sup> Second, the lack of reporting of prognostic outcomes in people with CKD but without COVID-19 limited the evaluation of COVID-19 as a prognostic factor in people with CKD. Third, for those not receiving KRT, different stages of CKD were not reported in most studies, preventing investigation of the differing risk of COVID-19 and prognostic outcomes with worsening kidney function. Fourth, more than half of the included studies reported outcomes in only hospitalized people with COVID-19, which may not reflect the risk of prognostic outcomes in the community. Obtaining an accurate denominator for the calculation of the incidence of COVID-19 and prognostic outcomes is especially difficult with people with CKD without KRT, which is often underreported,<sup>43</sup> lowering the generalizability of our results for people with CKD without KRT. Furthermore, detection of CKD in our review is limited by the lack of reporting of albuminuria and a high proportion of studies (49%) in which there was a high or unclear risk of inadequate participation by all eligible participants with CKD. Fifth, only a subset of the prespecified outcomes were reported in each study. Although this may be understandable for kidney-specific outcomes, selective reporting of the COVID-19 COS represents a significant risk of selective reporting.44 This was highlighted by our finding of a higher incidence of COVID-19 in people with CKD G5D but no difference in the incidence of death as a result of different studies reporting each outcome. Indeed, sensitivity analysis including only studies that reported the incidences of COVID-19 and death found that CKD G5D was also associated with a higher incidence of death. Sixth, the median study duration varied from 7 to 274 days, which was inadequate in a significant proportion of studies for the detection of patient-level outcomes. Seventh, variability in study definitions of COVID-19 and prognostic outcomes may have affected the accuracy of our results. The method of COVID-19 diagnosis was inadequate or unclear in 37% of included studies, the definition of recovery was not defined in most studies, and there was heterogeneity in the definition of AKI. Most studies were

retrospective in nature, which may lead to higher risks of selection bias, misclassification bias, and confounding compared with prospective studies. Last, we reported the incidence rate of COVID-19 in people with CKD, which assumes a constant risk of COVID-19 regardless of the time interval, even though this assumption is unlikely to be true because the incidence of COVID-19 in the general population varies from month to month.<sup>1</sup> In particular, our search of results up to February 2021 does not account for the impact of COVID-19 vaccination implementation strategies in many countries or the impact of recent surges of COVID-19 in countries such as India.

Our systematic review found that people with CKD may be at a higher risk of COVID-19 than the general population and may be at a higher risk of death than people with CKD without COVID-19. Decision-making by clinicians and policy makers should focus on preventive measures for people with CKD, particularly people receiving maintenance dialysis. Future studies that measure and adjust for confounders, and that are adequately powered to report the COVID-19 COS and SONG CKD core outcomes in people with CKD with and without COVID-19, are needed to better evaluate the prognostic effect of COVID-19 in people with CKD.

### **Supplementary Material**

### Supplementary File (PDF)

**Figure S1:** Forest plot of the incidence of COVID-19 in people with CKD without KRT.

**Figure S2:** Forest plot of the incidence rate ratio of death in people with CKD and COVID-19 compared with people with CKD without COVID-19.

Figure S3: Forest plot of the incidence of death in people with CKD without KRT and COVID-19.

Item S1: Electronic database search strategies.

**Item S2:** QUIPS tool for assessing the risk of bias in studies of the prognostic factor.

Item S3: References for the included studies.

Item S4: Studies classified by WHO regions and World Bank income Group.

Item S5: Other COVID-19–attributable outcomes in people with COVID-19 and CKD.

Item S6: Other kidney disease-specific outcomes in people with COVID-19 and CKD.

**Item S7:** Sensitivity analysis by study sample size, risk of bias, and studies reporting the incidences of COVID-19 and death.

**Item S8:** Subgroup analysis by WHO region, World Bank income Group, age, study location, diabetes. and obesity.

Table S1: Characteristics of each included study

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