Chronic Kidney Disease and COVID-19 Mortality: A Systematic Review and Meta-Analysis

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Abstract

Introduction: The outbreak of the coronavirus disease 2019 (COVID-19) has caused a pandemic and continues to a play a role in the increasing mortality rates among high-risk populations such as individuals with comorbidities like cardiovascular disease, diabetes, and chronic kidney disease (CKD). In patients diagnosed with CKD, infections are a significant factor which contribute to mortality second only to cardiovascular complications. The aim of this review was to conduct a systematic review and meta-analyses to evaluate the mortality associated with CKD in patients diagnosed with COVID-19 and to stratify the effect estimates by sample size, progression of CKD (stages III-V only), or end-stage kidney disease (ESKD).

Methods: We searched the most updated and highest quality systematic reviews for primary articles and subsequently conducted a comprehensive systematic search of the Embase, PubMed, Epistemonikos, Cochrane, and Google Scholar databases from Sep 1st, 2020 to Jan 10th, 2021 for published articles. We also performed a search of the LiTCOVID, MEDRXIV, and SSRN databases for preprints of unpublished studies from Jan 1st, 2020 to Jan 5th, 2021.

Results: We identified 75 studies that reported effect estimates for mortality for patients diagnosed with COVID-19 and CKD. Mortality was significantly higher among patients with CKD and COVID-19 than their counterparts without CKD (HR 1.57, 95% CI [1.42, 1.73], P < 0.00001; OR 1.86, 95% CI [1.64, 2.11], P < 0.00001; RR 1.74, 95% CI [1.13, 2.69], P = 0.01). The subgroup analyses investigating the effect of CKD stage (III-V) revealed increased mortality (HR 2.02 (95% CI [1.39, 2.94], P = 0.0002) as well as those analyzing the effect of ESKD (HR 1.92, 95% CI [0.96, 3.81], P = 0.06; OR 1.44, 95% CI [1.15, 1.81], P = 0.002). Regardless of study sample size, the trend of increased mortality in patients with CKD and COVID-19 was apparent.

Conclusion: Our findings demonstrated that patients diagnosed with CKD or ESKD have an increased risk of mortality and that COVID-19 management strategies as well as policies should prioritize patients with CKD or ESKD.

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Chapter 1: Introduction

Systematic reviews typically seek to collate evidence that fits pre-specified eligibility criteria in order to answer a specific research question. Often, systematic reviews include a meta-analysis component which involves using statistical techniques to synthesize the data from several studies into a single pooled quantitative summary estimate [48]. Systematic reviews aim to minimize bias by using explicit and systematic methods documented in advance, and they can cover a wide range of questions including interventions, test accuracy, and prognostic reviews among others.

Globally, the prevalence of all-stages of chronic kidney disease (CKD) is estimated to be approximately between 9.1-13.4% [9, 49]. There are five stages within which CKD can be characterized according to estimated glomerular filtration rate (eGFR). The incidence of CKD escalates within a population as individuals age, and of note, almost 40% of the population diagnosed with CKD consists of individuals over 60 years old [20]. The risk of all-cause mortality as well as morbidity increases notably as CKD progresses in severity as denoted by an advanced stage of the disease [39]. Although infections contribute significantly to the source of non-cardiovascular morbidity as well as mortality associated with poorer CKD prognoses, cardiovascular complications account for about 50% of mortality in this population [23, 24, 34]. The highest likelihood of infection in patients diagnosed with advanced stages of CKD occurs in the pulmonary and genitourinary systems [12].

The novel coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially reported in a clinical setting in Wuhan, China located in the Hubei Province in December 2019 [51]. However, recent findings suggest that the viral disease was circulating at low levels within the province of Hubei in early November and potentially no earlier than October 2019 [81]. Due to the rapidity with which

COVID-19 continues to spread, clinicians and researchers are attempting to make strides to keep up with the disease and gain insight into its effects on various populations of interest. An increased interest in research on the impact of SARS-CoV-2 on the mortality of individuals diagnosed with varying comorbidities has accompanied the rise of the novel coronavirus pandemic.

Prognosis research provides information about the future health and well-being of individuals with specific diseases or conditions. Prognosis studies can provide information on the likelihood of a particular outcome; identify target groups for intervention; or identify factors associated with poor outcomes [2]. Prognosis systematic reviews can provide best evidence for healthcare decision-making relevant to clinical decisions and policies.

This paper aims to investigate the association between CKD and COVID-19 associated mortality. The primary outcome measure of interest was to assess mortality associated with CKD in patients diagnosed with COVID-19 and to stratify the effect estimates by sample size, progression of CKD (stages III-V only), or end-stage kidney disease (ESKD).

Chapter 2: Materials and Methods

We conducted a systematic review in accordance with a pre-specified registered protocol available from http://www.crd.york.ac.uk/PROSPERO (Registration number CRD42021227974). We reported the results according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [67].

2.1 Selection Criteria and Search Strategy

All systematic reviews and both eligible small as well as large primary studies from included systematic reviews were reviewed to appraise the robustness of reported mortality effect estimates among patients diagnosed with both CKD and COVID-19. Initially, the investigators assessed all systematic reviews reporting on COVID-19 outcomes in patients diagnosed with CKD and identified primary studies that met the inclusion criteria of this review. Then, the team updated the search and completed a systematic review of additional primary studies published after the last search in the reviews. The methods team conducted a search of the following electronic databases to identify systematic reviews: Cochrane. Embase, Epistemonikos, Google Scholar, and PubMed from January 1st, 2020 to January 5th, 2021. In addition, the team searched LiTCOVID, MEDRXIV, and SSRN for preprints of unpublished systematic reviews. Following this, we checked the references of all of systematic reviews meeting inclusion criteria. We then further extended the search from September 1st, 2020 to January 10th, 2021 to include additional primary studies that the systematic reviews did not include. We also included the results from two registries in the review and analysis of primary studies: Holman 2020 [50] and Williamson 2020 [102]. The detailed search strategies that were employed in the development of this review are both provided in Appendix A.

We included studies of different designs including cross-sectional, case-control, prospective, or retrospective cohorts that reported mortality in patients with CKD who have suspected or confirmed SARS-CoV-2 infection. The review included published as well as unpublished studies. We excluded studies focused primarily on kidney transplant, acute kidney injury, pregnancy, or pediatric patients. From the initially screened primary studies for inclusion, those reporting effect estimates in the form of odds ratios (ORs), hazard ratios (HRs), and risk ratios (RRs) for mortality in patients diagnosed with COVID-19 and CKD were included in the meta-analysis.

2.2 Data Extraction and Quality Assessment

We screened identified studies and performed data extraction using a pilot-tested and standardized form. Two investigators extracted all relevant data independently from each included trial characterized by a sample size of ≥1,000 patients. However, a single trained reviewer conducted screening and data collection for primary studies that investigated a patient population of <1,000. We included the publication with the most complete results when the same results were presented in more than one publication.

From included primary studies, we collected data on the author, study design, publication status (published vs. non-published), sample size, country and/or area, center status (single vs. multicenter), number of CKD patients, number of non-CKD patients, univariate or multivariate analysis, HR, OR, and RR of death with 95% confidence intervals (95% CIs). Additionally, we also reported hospitalization status (hospitalized vs. outpatients), CKD classification (CKD stages III, IV or V), dialysis-dependence (also known as end stage kidney disease (ESKD) or dialysis independence, and the baseline characteristics of the included patients, if the study included the information. Results of data extraction were compared, and any discrepancy was resolved by discussion or arbitration via collaborative discussion with the primary investigator and content expert (R. Mustafa).

To assess the confidence in the estimates of effect (i.e. quality of evidence) across studies we followed the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach by making judgments about the risk of bias, publication bias, indirectness, imprecision, and inconsistency among different trials [1]. Additionally, we assessed risk of bias (ROB) of each study using the Quality in Prognosis Studies (QUIPS) tool [46]. To assess publication bias we used the "funnel plot" and Egger's linear regression test [30].

2.3 Data Synthesis and Statistical Analysis

The effect estimates on mortality in patients with CKD and COVID-19 versus without CKD were combined quantitatively (pooled) from different studies. Estimations of overall ORs, HRs, and RRs along with their respective 95% CIs of mortality were calculated depending on what was reported in the primary studies. The Breslow-Day test was used to measure the percentage of total variation across studies due to heterogeneity (I^2). Data was considered worthy of exploration of heterogeneity when the I^2 statistic was more than 50%. Attempts were also made to explain heterogeneity based on patient clinical characteristics. Overall results were pooled using a random effects model, except when there were very few studies (< 5) a fixed effect model was used instead [18]. For all analyses, an alpha level of significance of 0.05 was used, and therefore, a p-value of <0.05 was of statistical significance.

In addition to the main overall pooled analyses of effect estimates of mortality, subgroup analyses to determine whether the summary effects vary in relation to clinical characteristics of the population in the included trials were pre-specified. The treatment effects were examined according to risk of bias. Two subgroup analyses were undertaken. The first compared the effect of small versus large study sample size ($N < 1,000$ versus $N \geq 1,000$). The second compared the effect of different CKD stages and classification (CKD or ESKD) and advancement of CKD (stage III, IV, V). The meta-analyses were performed using RevMan software version 5.4 provided by the Cochrane Collaboration [19]. Calculations of log-odds, log-hazards, and log-risk ratios along with respective log standard errors were verified using Microsoft Excel 2016, prior to utilizing the generic inverse variance analysis function in RevMan, where these values were inputted to achieve the final pooled effect estimates for all analyses conducted. All effect estimates for disease risks provided by the primary literature were transformed to logarithmic ratios and within-study standard errors for effect estimates were calculated according to a logarithmic scale, which is normally distributed, since adjusted multivariable and non-adjusted univariable effect estimates were pooled for analysis. From the logarithmic ratios, individual study effect estimates and overall effect estimates for disease risks were back-calculated. Forest plots of the data were constructed to provide a graphical representation of the data across the various categories of interest.

Chapter 3: Results

3.1 Literature Search and Selection Process

The search of the references of all the included systematic reviews that reported on any outcome for COVID-19 and CKD, resulted in the identification of 310 primary articles. The supplemental integrated search of the Embase, PubMed, Epistemonikos, and Cochrane databases for published primary literature and the search of the MedRXIV, SSRN, and LiTCovid databases for unpublished primary literature yielded 1,603 citations and 352 citations, respectively. After removing duplicates, we screened and identified a total of 1,791 records, of which 1,594 were excluded based on title and abstract. The remaining 507 primary articles were reviewed in full to assess eligibility, and 75 total primary articles met all inclusion criteria for the review and meta-analysis [4-8, 10, 11, 13-17, 22, 25, 28, 29, 31-33, 35-38, 40-45, 47, 50, 52-55, 58-66, 69-75, 77-80, 82-93, 97-104]. The selection process is included in Figure 1.

3.2 Study Characteristics

Table 1 presents the details about characteristics of included studies.

Studies*:* Of the studies selected for the final review, one was a case-control, four were cross-sectional studies, and seventy were cohort studies published in English. Fifty-four studies were characterized as multicenter, and the remaining twenty-one were conducted in a single center.

Participants*:* The included studies involved 34,243,324 participants. Twenty-eight of seventy-five studies were small with less than 1,000 participants and forty-seven were large with greater than or equal to 1,000 participants. The main inclusion criteria entailed adults (18 years or older) with variability in baseline diabetes, HTN, CVD, and CKD, and a suspected or confirmed diagnosis of COVID-19.

Intervention*:* Overall, the duration of each trial was short with follow up ranging from two weeks to five months. Of note, trials with prolonged follow-up had higher instances of participant dropout.

Outcomes*:* Thirty-one studies reported effect on mortality using HR, six using RR, and thirty-eight using OR.

Figure 1. Selection process for primary studies reporting on mortality.

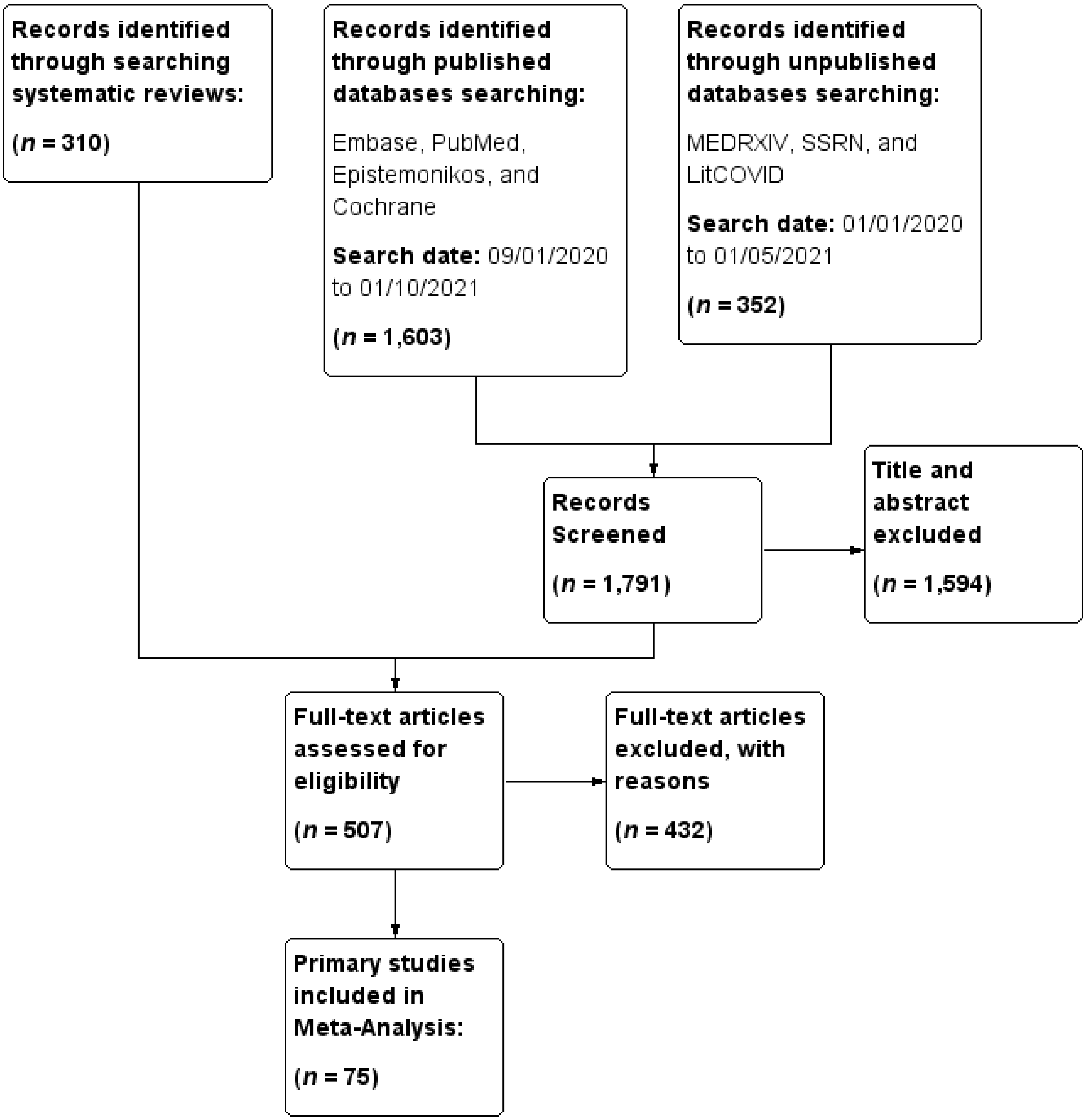


Table 1. Characteristics of included primary studies.

Study Characteristics	**Patient Selection (Inclusion/ Exclusion criteria)**	**Patients Characteristics**	**Analysis (Multivariate / Univariate):**
Primary studies N < 1,000 (n = 28)			
Alamdari NM **Retrospective cross-sectional** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Tehran, Iran **Hospital/Center name:** Shahid Modarres Hospital **Study inclusion period:** 1/30/2020-4/05/2020 **COVID-19 diagnosis method:** RT-PCR Positive	**N:** 459 **N CKD:** 99 **Age:** Mean 61.79 (49.9-73.68) **Gender:** F 130 (30.3%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 21.6%	Univariate
Chan L **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Dialysis Patients **Hospitalized or outpatient:** Hospitalized **City/Country:** New York, USA **Hospital/Center name:** Mount Sinai Health Care System **Study inclusion period:** 03/15/2020-06/07/2020 **COVID-19 diagnosis method:** RT-PCR Positive	**N:** 732 **N CKD:** 122 **Age Dialysis:** Median 65.6 (53.9-71.2) **Gender Dialysis:** F 36 (30%) **COVID-19 prevalence among CKD: NR** **CKD prevalence among COVID-19:** 16.6%	Multivariate
Cheng Y **Prospective**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:**	**N:** 701 **N CKD**: 101 **Age CKD:** Median:	Multivariate

Cohort **Single Center** **Published**	Dialysis unit **City/Country:** Wuhan, China **Hospital/Center name:** Tongji Hospital **Study inclusion period:** 01/28/2020-02/11/2020 **COVID-19 diagnosis method:** RT-PCR positive and/or clinical diagnosis	73 (62–79) **Gender CKD:** F 28 (27.7%) **COVID-19 prevalence among CKD: NR** **CKD prevalence among COVID-19:** 14.4%	
Chilimuri S **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Bronx, New York / USA **Hospital/Center name:** Bronxcare Health System **Study inclusion period:** 03/09/2020-04/09/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 375 **N CKD:** 51 **Age:** Median 63.0 (52.0-72.0) **Gender:** F 139 (37%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 13.6%	Multivariate
Ciceri F **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Milan, Italy **Hospital/Center name:** San Raffaele Hospital **Study inclusion period:** 02/25/2020-05/01/2020 **COVID-19 diagnosis method:** RT-PCR from nasal or throat	**N:** 410 **N CKD:** 47 **Age:** Median 65 (56-75) **Gender:** F 111 (27.1%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 11.5%	Univariate

	swab together with signs, symptoms, or radiological features suggesting COVID-19 pneumonia		
Coca A **Prospective Cohort** **Multicenter** **Published**	**Patients population:** Hospitalized patients with non-dialysis CKD **Hospitalized or outpatient:** Hospitalized **City/Country:** Spain **Hospital/Center name:** Three third-level Spanish academic hospitals **Study inclusion period:** 03/01/2020-04/15/2020 **COVID-19 diagnosis method:** RT-qPCR positive and/or serologic testing	**N:** 272 **N CKD:** 136 **Age:** Median 80 (74-86) **Gender:** F 56 (41.2%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** NR	Multivariate
Cummings MJ **Prospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** New York, USA **Hospital/Center name:** Milstein Hospital and Allen Hospital **Study inclusion period:** 03/02/2020-04/01/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 257 **N CKD:** 37 (14%) **Age:** Median 62 (51-72) **Gender:** F 86 (33%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 14%	Univariate
Filardo T	**Patients population:** Patients	**N:** 337 **N CKD:** 32	Multivariate

Retrospective cohort **Single Center** **Published**	with COVID-19 (≥ 18 y.o.) **Hospitalized or outpatient:** Hospitalized **City/Country:** New York, USA **Hospital/Center name:** Bellevue Hospital Center **Study inclusion period:** 03/09/2020-04/08/2020 **COVID-19 diagnosis method:** RT-PCR positive	**Age:** 58 (50-67) **Gender:** F 88 (32.6%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 11.9%	
Gasparini M **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 in ICU **Hospitalized or outpatient:** Hospitalized **City/Country:** London, UK **Hospital/Center name:** Hammersmith Hospital, Charing Cross Hospital, and St. Mary's Hospital **Study inclusion period:** 03/10/2020-07/23/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 372 **N CKD:** 41 **Age:** Median 60 (54-66) **Gender:** F 14 (34.14%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 11%	Univariate
Giannoglou D. **Retrospective Cohort** **Multicenter** **Pre-Print**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Attica region / Greece **Hospital/Center name:** 1st Regional Health Authority of	**N:** 512 **N CKD:** 25 **Age:** Mean 60.4 (STD 18.2) **Gender:** F 195 (38.1%) **COVID-19 prevalence among CKD:**	Multivariate

	Attica (14 General Hospitals) **Study inclusion period:** 02/21/2020-06/30/2020 **COVID-19 diagnosis method:** NR	**CKD prevalence among COVID-19:** 5.1%	
Gok M **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Istanbul, Turkey **Hospital/Center name:** Han Training Hospital **Study inclusion period:** NR-06/01/2020 **COVID-19 diagnosis method:** Turkish National Health Commission Guidelines	**N:** 609 **N CKD:** 126 **Age:** 73.57 +/- 10.61 **Gender:** F 61 (48.4%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 20.7%	Multivariate
Gu T **Nested Case-Control** **Multicenter** **Published**	**Patients population:** Publicly reported confirmed patients with COVID-19 **Hospitalized or outpatient:** NR **City/Country:** Mainland China – Outside of Hubei **Hospital/Center name:** National Health Committee of China **Study inclusion period:** 12/18/2019-03/08/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 275 **N CKD:** 12 **Age:** Median 68.0 (IQR 22) **Gender:** F 102 (37.1%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 4.36%	Multivariate
Harmouch F	**Patients population:** Patients	**N:** 563 **N CKD:** CKD ≥ 3 (110 [19.6%]) ;	Multivariate

Retrospective Cohort **Single Center** **Published**	with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Bethlehem, Pennsylvania / USA **Hospital/Center name:** St. Luke's University Hospital **Study inclusion period:** 03/01/2020-04/15/2020 **COVID-19 diagnosis method:** NR	ESRD (15 [2.7%]) **Age:** Median 63 (IQR 24) **Gender:** F 244 (43.3%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 19.6%	– CKD Univariate - ESKD
Javanian M **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Babol, Iran **Hospital/Center name:** Ayatollah Rohani Hospital, Shahid Beheshti Hospital, Yahyanejad Hospital) **Study inclusion period:** 02/25/2020-03/17/2020 **COVID-19 diagnosis method:** Physician and RT-PCR confirmed	**N:** 100 **N CKD:** 12 (12%) **Age:** Mean 60.12 (13.87 SD) **Gender:** F 49 (49%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 12%	Univariate
Khedr E **Retrospective Cohort** **Multicenter** **Pre-Print**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Egypt **Hospital/Center name:** Assiut and Aswan University Hospitals	**N:** 439 **N CKD:** 18 **Age:** Mean 51.2 +/- 17.2 (SD) **Gender:** F 215 (49%) **COVID-19 prevalence among CKD:** NR	Univariate

	Study inclusion period: 06/2020-07/2020 **COVID-19 diagnosis method:** RT-PCR positive and/or clinical systems and chest CT with 1 or 2 of the following positive: lymphopenia, high serum ferritin, or D-Dimer level	**CKD prevalence among COVID-19:** 4.1%	
Lanza E **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Lombardy, Italy **Hospital/Center name:** University Hospital in Milan **Study inclusion period:** 01/25/2020-04/28/2020 **COVID-19 diagnosis method:** RT-PCR positive on nasal or pharyngeal swab	**N:** 222 **N CKD:** 10 **Age:** Median 66.4 (IQR 53.8-75.8) **Gender:** F 59 (27%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 4.5%	Multivariate
Mendy A **Retrospective Cohort** **Multicenter** **Pre-Print**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized and outpatient **City/Country:** Cincinnati, Ohio; Kentucky; Indiana / USA **Hospital/Center name:** University of Cincinnati Health System **Study inclusion period:** 03/13/2020-05/31/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 689 **N CKD:** 81 (11.8%) **Age:** Median 49.5 (1.3 SE) **Gender:** F 324 (47%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 11.8%	Multivariate

	nasopharyngeal swab		
Nachega J **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Kinshasa, Democratic Republic of the Congo **Hospital/Center name:** 7 largest health facilities in Kinshasa (not named) **Study inclusion period:** 03/10/2020-07/31/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 766 **N CKD:** 7 (0.9%) **Age:** Median 46 (34-58 IQR) **Gender:** F 262 (34.4%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 0.9%	Multivariate
Okoh A **Retrospective Cohort** **Single Center** **Published**	**Patients population:** African American and Latino Hispanic Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Newark, New Jersey / USA **Hospital/Center name:** Newark Beth Israel Medical Center **Study inclusion period:** 03/10/2020-04/10/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 416 **N CKD:** 46 (18%) **Age:** Median 62 (49-74 IQR) **Gender:** F 122 (49%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 18%	Univariate
Rivera-Izquierdo M **Retrospective**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:**	**N:** 238 **N CKD:** Chronic Kidney Failure 23 (9.7%)	Multivariate

Cohort **Single Center** **Published**	Hospitalized **City/Country:** Granada, Spain **Hospital/Center name:** Hospital Universitario Clinico San Cecilio **Study inclusion period:** 03/16/2020-04/10/2020 **COVID-19 diagnosis method:** RT-PCR positive	**Age:** Median 67 **Gender:** F 101 (45%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 9.7%	
Russo E **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Genoa, Italy **Hospital/Center name:** Policlinico San Martino Hospital **Study inclusion period:** 02/25/2020-03/13/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 777 **N CKD:** 222 **Age CKD:** 80 +/-12 **Gender CKD:** 98 (44%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 28.6%	Multivariate
Salacup G **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Philadelphia, USA **Hospital/Center name:** Einstein Medical Center **Study inclusion period:** 03/01/2020-04/24/2020 **COVID-19 diagnosis method:** RT-PCR	**N:** 242 **N CKD:** 42 (17%) **Age:** Mean 66 (58-76 IQR) **Gender:** F 119 (49) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 17%	Multivariate

Shah P **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Georgia, USA **Hospital/Center name:** Phoebe Putney Health System **Study inclusion period:** 03/02/2020-05/06/2020 **COVID-19 diagnosis method:** RT-PCR positive by nasopharyngeal swab	**N:** 522 **N CKD:** CKD 78 (14.9%) ; ESRD 30 (5.8) **Age:** Median 63 (50-72 IQR) **Gender:** F 304 (58.2%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** CKD 14.9% ; ESRD 5.8%	Multivariate
Shang J **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Wuhan, China **Hospital/Center name:** Wuhan No.7 Hospital **Study inclusion period:** 12/25/2019-03/20/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 584 **N CKD:** 8 (1.4%) **Age:** Median 59 (25-75 IQR) **Gender:** F 307 (52.6%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 1.4%	Multivariate
Tehrani S **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Stockholm, Sweden **Hospital/Center name:**	**N:** 225 **N CKD:** 49 (19%) **Age:** Mean 66 +/- 17 **Gender:** F 105 (41%) **COVID-19 prevalence among CKD:** NR	Multivariate

	Danderyd University Hospital **Study inclusion period:** 03/05/2020-04/28/2020 **COVID-19 diagnosis method:** RT-PCR positive	**CKD prevalence among COVID-19:** 19%	
Thompson J **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Greater Manchester, UK **Hospital/Center name:** Royal Oldham Hospital **Study inclusion period:** 03/12/2020-05/19/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 470 **N CKD:** 76 (16.1%) **Age:** Mean 68.7 (17.4 SD) **Gender:** F 215 (45.7%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 16.1%	Univariate
Wang L **Retrospective Cohort** **Single Center** **Published**	**Patients population:** Patients with COVID-19 >60 years old **Hospitalized or outpatient:** Hospitalized **City/Country:** Wuhan, China **Hospital/Center name:** Renmin Hospital of Wuhan University **Study inclusion period:** 01/01/2020-02/06/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 339 **N CKD:** 13 (3.8%) **Age:** Median 69 (65-76 IQR) **Gender:** F 173 (51.0%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 3.8%	Univariate
Yang D **Retrospective**	**Patients population:** Patients with COVID-19	**N:** 836 **N CKD:** NDD-CKD: 24 ; DD-	Multivariate

Cohort **Multicenter** **Published**	**Hospitalized or outpatient:** Hospitalized **City/Country:** Wuhan, China **Hospital/Center name:** Central Hospital of Wuhan and Wuhan Third Hospital **Study inclusion period:** 01/01/2020-03/23/2020 **COVID-19 diagnosis method:** Confirmed according to the Diagnosis and Treatment Plan for COVID-19 7th Edition	CKD: 15 **Age:** NDD-CKD: Median 73.5 (64.5-86.0 IQR) ; DD-CKD: Median 58.0 (47.0-68.0 IQR) **Gender:** NDD-CKD: F 6 (25.00%) ; DD-CKD: F 5 (33.33%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** NDD-CKD: 2.87% ; DD-CKD: 1.79%	
Primary studies N ≥ 1,000 (n = 47)			
Akchurin **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** New York/ USA **Hospital/Center name:** Weill Cornell Medical and New York Presbyterian Hospitals **Study inclusion period:** NR **COVID-19 diagnosis method:** RT-PCR positive	**N:** 4,378 **N CKD:** 280 **Age:** Median No CKD: 62 (IQR 48-75); Median CKD: 75 (IQR 65-84) **Gender:** No CKD: F 1,854 (45%); CKD: F 104 (37%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 280/4,378 (6%)	Multivariate
Almazeedi **Retrospective Cohort** **Single center** **Not Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Kuwait **Hospital/Center name:** Jaber Al-	**N:** 1,096 **N CKD:** 11 **Age:** Median 41, range 25-57 y. o. **Gender:** F 208 (19%) **COVID-19 prevalence among CKD:** NR	Multivariate

	Ahmad Al-Sabah hospital **Study inclusion period:** 02/24/2020 to 04/02/2020 **COVID-19 diagnosis method:** RT-PCR positive	**CKD prevalence among COVID-19:** 1%	
Atkins Retrospective Cohort Multicenter Published	**Patients population:** Patients from the UK biobank (>65 y. o.) **Hospitalized or outpatient:** Hospitalized and outpatient **City/Country:** England, Scotland, Wales **Hospital/Center name:** Multiple **Study inclusion period:** 03/16/2020 to 04/26/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 269,070 (COVID+: 507) **N CKD:** 3,875/268,563 (in COVID-19 neg) 23/507 (in COVID-19 pos patient) **Age:** Mean 74.3 in COVID-19 pos, 73.1 in COVID-19 neg **Gender:** F 196 (39%) in COVID-19 positive **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 23/507 (5%)	Multivariate
Baqui Cross-sectional Multicenter Published	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized, outpatient and ICU patients **City/Country:** Brazil **Hospital/Center name:** Multiple **Study inclusion period:** 02/27/2020 to 05/04/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 11,321 **N CKD:** 389/7,371 **Age:** NR **Gender:** NR **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 389/7,371 (5%)	Multivariate
Boulle Retrospective Cohort Multicenter	**Patients population:** All patients identified through the public sector (>20 y. o.) (positive and negative COVID-19)	**N:** 3,460,932 (COVID (+): 22,308) **N CKD:** (COVID (+): 1,661) **Age:** >20 y. o.	Multivariate

Published	**Hospitalized or outpatient:** Hospitalized, outpatient and ICU patients **City/Country:** Western Cape/ South Africa **Hospital/Center name:** Multiple **Study inclusion period:** 03/01/2020 to 06/09/2020 **COVID-19 diagnosis method:** RT-PCR positive	**Gender:** F 1,998,396 (58%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 3%	
Chishinga Retrospective Cohort Multicenter Not Published	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized, outpatient and ICU patients **City/Country:** Atlanta/ USA **Hospital/Center name:** NR St**udy inclusion period:** 03/02/2020 to 05/21/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 4,322 **N CKD:** 157 **Age:** Median age 54 (37-69) in hospitalized, 51(36-65) in ICU **Gender:** F 2,247 (52%) in total **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** NR	Multivariate
De Souza Cross-Sectional Multicenter Published	**Patients population:** Patients with COVID-19 (>60 y. o.) **Hospitalized or outpatient:** NR **City/Country:** Brazil **Hospital/Center name:** Multiple **Study inclusion period:** Study conducted on 08/02/2020 **COVID-19 diagnosis method:** NR	**N:** 9,807 **N CKD:** NR **Age:** Median 68 y. o., IQR: 12 **Gender:** F 5,198 (53%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** NR	Multivariate
Docherty Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 (all ages included) **Hospitalized or outpatient:** Hospitalized **City/Country:** England, Wales, and Scotland	**N:** 20,133 **N CKD:** 2,830 **Age:** Mean 73 y. o. (IQR 58-82, range 0-104) **Gender:** F 8,065 (40%) **COVID-19 prevalence**	Multivariate

	Hospital/Center name: Multiple **Study inclusion period:** 02/06/2020 to 04/19/2020 **COVID-19 diagnosis method:** RT-PCR positive and/or high clinical suspicion	**among CKD:** NR **CKD prevalence among COVID-19:** 2,830/17,506 (16%)	
Dominguez-Ramire **Retrospective Cohort** **Multicenter** **Not Published**	**Patients population:** Patients with COVID-19 (all ages included) **Hospitalized or outpatient:** Hospitalized, outpatient and ICU patients **City/Country:** Mexico **Hospital/Center name:** Multiple **Study inclusion period:** Up until 10/02/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 905,579 **N CKD:** 12,661 **Age:** Mean males= 45 +/- 16.9, females=43.7 +/- 16.5 **Gender:** F 440,500 (49%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 1%	Multivariate
Esme **Retrospective Cohort** **Registry** **Multicenter** **Published**	**Patients population:** Geriatric patients with COVID-19 identified using the national registry system of the ministry of health (>60 y. o.) **Hospitalized or outpatient:** Hospitalized and outpatient **City/Country:** Turkey/ Nationwide **Hospital/Center name:** Multiple/ Registry **Study inclusion period:** 03/11/2020 to 05/27/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 24,510 **N CKD:** 1,659 **Age:** Mean 71.2 y. o. **Gender:** F 8,635 (51%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** NR	Univariate

Flythe Retrospective Cohort Multicenter Published	**Patients population:** Critically ill COVID-19 patients **Hospitalized or outpatient:** ICU patients **City/Country:** USA **Hospital/Center name:** Multiple **Study inclusion period:** 03/04/2020 to 05/10/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 4,264 **N CKD:** 664 **Age:** Dialysis-dependent CKD: Median 65 y. o., non-dialysis dependent: Median 69 y. o., patients without CKD: Median 61 y. o. **Gender:** Dialysis-dependent CKD: F (46%) non-dialysis dependent: F (38%), patients without CKD: F (36%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 664/4,264	Multivariate
Fried Retrospective Cohort Multicenter Published	**Patients population:** Patients admitted across 245 hospitals with an ICD-10 code indicating COVID-19 infection (>18 y. o.) **Hospitalized or outpatient:** Hospitalized **City/Country:** USA **Hospital/Center name:** Multiple **Study inclusion period:** 02/15/2020 to 04/20/2020 **COVID-19 diagnosis method:** ICD-10 code	**N:** 11,721 **N CKD:** 1,427 **Age:** Mean reported by age groups: 18-40: 1,266/11,721, 41-60: 3,436/11,721, >60: 7,019/11,721 **Gender:** F 5,457 (46%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 1,427/11,721 (12%)	Multivariate
Grasselli Retrospective Cohort Multicenter Published	**Patients population:** All consecutive patients admitted **Hospitalized or outpatient:** ICU patients **City/Country:** Milan/ Italy **Hospital/Center name:**	**N:** 3,988 **N CKD:** 87 **Age:** Median 63 y. o. **Gender:** F 800 (19%) **COVID-19 prevalence among CKD:** NR **CKD prevalence**	Multivariate

	Fondazione IRCCS [Istituto di Ricovero e Cura a Carattere Scientifico] Ca' Granda spedale Maggiore Policlinico **Study inclusion period:** 02/20/2020 to 04/22/2020 **COVID-19 diagnosis method:** RT-PCR positive	**among COVID-19:** 2%	
Gude-Sampedro Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized and outpatient **City/Country:** Galicia/ Spain **Hospital/Center name:** NR S**tudy inclusion period:** 03/06/2020 to 05/07/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 10,454 **N CKD:** 101 **Age:** Mean 58 **Gender:** F 6,282 (60%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 0.9%	Multivariate
Harrison Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 identified through electronic medical records from participating healthcare organizations (>18 y. o.) **Hospitalized or outpatient:** Hospitalized and outpatient **City/Country:** USA **Hospital/Center name:** Multiple **Study inclusion period:** From 01/20/2020 to 05/26/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 33,488 **N CKD:** 2,735 **Age:** Median 50 y. o. **Gender:** F 17,155 (54%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 9%	Multivariate
Hewitt Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 (>18 y. o.) **Hospitalized or outpatient:** Hospitalized **City/Country:** UK and Italy	**N:** 1,564 **N CKD:** 570 **Age:** Median: 74 y. o. **Gender:** F 661 (42%) **COVID-19 prevalence among CKD:** NR	Multivariate

	Hospital/Center name: Multiple **Study inclusion period:** 02/27/2020 to 04/28/2020 **COVID-19 diagnosis method:** RT-PCR positive	**CKD prevalence among COVID-19:** 36%	
Holman Retrospective cohort Multicenter Published	**Patients population:** Patients with type 1 and type 2 diabetes identified through the national diabetes audit (UK) **Hospitalized or outpatient:** Hospital and community **City/Country:** UK **Hospital/Center name:** N/A. Population based **Study inclusion period:** 01/02/2,017 to 05/11/2020 **COVID-19 diagnosis method:** RT-PCR positive. (Through ICD-code U07.1)	**N:** 3,138,410 N CKD: NR **Age:** 1-110 y. o., 38% <40y. o. **Gender:** NR **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** NR	Multivariate
Imam Retrospective Cohort Multicenter Published	**Patients population:** Public data **Hospitalized or outpatient:** Hospitalized **City/Country:** Michigan/ USA **Hospital/Center name:** Multiple **Study inclusion period:** 03/01/2020 to 04/01/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 1,305 **N CKD:** 228 **Age:** Mean: 61 y. o. +/- 16.3 **Gender:** F 603 (46%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 18%	Univariate
Jimenez Retrospective Cohort Single Published	**Patients population:** Patients admitted to the hospital with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Spain **Hospital/Center name:** Infanta Leonor University Hospital **Study inclusion period:**	**N:** 1,549 **N CKD:** 104 **Age:** Median: 69 y. o. **Gender:** F 659 (43%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 7%	Multivariate

	03/01/2020 to 05/28/2020 **COVID-19 diagnosis method:** RT-PCR positive on nasopharyngeal swab		
Kalyanarama Retrospective Cohort Multicenter Published	**Patients population:** Patients tested for COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** New York/ USA **Hospital/Center name:** New York City Health + Hospitals (NYC H+H) **Study inclusion period:** 03/05/2020 to 04/09/2020 **COVID-19 diagnosis method:** RT-PCR positive on nasopharyngeal swabs	**N:** 22,254 (COVID (+): 13,442) **N CKD:** 1,129 (COVID (+): 809) **Age:** Median 52.7(39.5-64.5) **Gender:** F 5,961 (44%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 809/13,442 (8%)	Hospitalization Mortality
Kang Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 (>18 y. o.) **Hospitalized or outpatient:** Hospitalized **City/Country:** Korea **Hospital/Center name:** NR St**udy inclusion period:** 02/01/2020 to 05/15/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 7,341 **N CKD:** Dialysis dependent (DD): 14, non-dialysis dependent: 239 **Age:** Mean 47.1 y. o. **Gender:** F 2,970 (41%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** Dialysis dependent: 14/7,341 (0.2%), non-dialysis dependent: 239/7,341 (3%)	Multivariate
Kim DW Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 identified using the Korean National Health Insurance Service **Hospitalized or outpatient:** Hospitalized and outpatient	**N:** 9,148 **N CKD:** 62 **Age:** The most confirmed cases were 1,352 patients between the ages of 20 to 24, followed by 25 to 29.	Multivariate

	City/Country: South Korea **Hospital/Center name:** The Korean National Health Insurance Service **Study inclusion period:** Up until 03/26/2020 **COVID-19 diagnosis method:** RT-PCR positive	Gender: F 5,592 (61%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 0.7%	
Kim L **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 (>18 y. o.) **Hospitalized or outpatient:** Hospitalized **City/Country:** USA **Hospital/Center name:** Multiple **Study inclusion period:** 03/01/2020 to 05/02/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 2,491 **N CKD:** 386 **Age:** Median: 62 y. o. **Gender:** F 1,165 (47%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 16%	Multivariate
Klang **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Discharged or dead hospitalized patients with history of COVID-19 positive Rt-PCR **Exclusion Criteria:** Patients still hospitalized by the end of the Study inclusion period or patients without information on BMI. **Hospitalized or outpatient:** Hospitalized **City/Country:** New York/ USA **Hospital/Center name:** Mount Sinai Hospital, Mount Sinai Brooklyn, Mount Sinai Queens, Mount Sinai Morningside and Mount Sinai West **Study inclusion period:** 03/01/2020 to 05/17/2020 **COVID-19 diagnosis method:** RT-PCR positive on NP swab	**N:** 3,406 **N CKD:** 667 **Age:** median 43 in age group<50, median 72 in >50 y. o. group **Gender:** NR **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 667/3,406 (20%)	Multivariate

Lala **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** New York/ USA **Hospital/Center name:** Mount Sinai Health System hospitals **Study inclusion period:** 02/27/2020 to 04/12/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 2,736 **N CKD:** 273 **Age:** Mean 66.40 (+/- 15.80) **Gender:** F 1,106 (40%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 10%	Multivariate
Lee **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** COVID-19 patients (>18 y. o.) identified using the Korean Health Insurance Review and Assessment Service (HIRA) database **Hospitalized or outpatient:** Hospitalized and ICU **City/Country:** Korea **Hospital/Center name:** N/A, Korean Health Insurance Review and Assessment Service (HIRA) database **Study inclusion period:** up until 05/15/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 7,339 **N CKD:** 48 **Age:** Mean for non-CKD 61.75 +/- 17.67 **Gender:** F 4,403 (60%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 0.7%	Multivariate
Ioannou **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Veterans with COVID-19 identified using the COVID-19 Shared Data Resource **Hospitalized or outpatient:** Hospitalized and outpatient **City/Country:** USA **Hospital/Center name:** Multiple **Study inclusion period:** 02/28/2020 to 05/14/2020	**N:** 10,131 **N CKD:** 1,867 **Age:** Mean 61.6 y. o. **Gender:** F 910 (9%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 18%	Multivariate

	COVID-19 diagnosis method: RT-PCR positive		
Macedo Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 (>18 y. o.) **Hospitalized or outpatient:** Hospitalized and ICU patients **City/Country:** State of Bahia/ Brazil **Hospital/Center name:** NR St**udy inclusion period:** 03/03/2020 to 07/29/2020 **COVID-19 diagnosis method:** WHO interim guidance	**N:** 3,896 **N CKD:** 155 **Age:** Mean 63 y. o. **Gender:** F 40% **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 4%	Multivariate
Martos-Benitez Retrospective Cohort Multicenter Published	**Patients population: Patients** with suspicion of viral respiratory disease including both COVID-19 positive and negative **Hospitalized or outpatient:** Hospitalized, outpatient, and ICU patients **City/Country:** Mexico/ National **Hospital/Center name:** Multiple **Study inclusion period:** 01/01/2020 to 05/12/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 65,535 (COVID (+): 38,324) **N CKD:** NR (COVID (+): 1,267) **Age:** COVID-19 (+): Mean 46.9 (+/- 15.7), COVID-19 (-): Mean 39.9 (+/- 17.6) **Gender:** COVID-19 (+): F (42%), COVID-19 (-): F (54%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 1,267 (2%)	Multivariate
Munblit Retrospective Cohort Multicenter Published	**Patients population:** Hospitalized patients with suspected or confirmed COVID-19 (>18 y. o.) **Hospitalized or outpatient:** Hospitalized and ICU patients **City/Country:** Moscow/ Russia **Hospital/Center name:**	**N:** 3,480 **N CKD:** 164 **Age:** Median- 56 (45-66) **Gender:** F 1,704 (49%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:**	Multivariate

	Sechenov University Hospital Network Hospitals **Study inclusion period:** 04/08/2020 to 05/28/2020 **COVID-19 diagnosis method:** RT-PCR positive and/or clinical diagnosis with CT findings suggestive of COVID-19	164/3,382 (5%)	
Murillo-Zamora Retrospective Cohort Multicenter Non-Published	**Patients population: Patients** hospitalized with COVID-19 (>18 y. o.) **Hospitalized or outpatient:** Hospitalized **City/Country:** Mexico/ Nationwide **Hospital/Center name:** Multiple **Study inclusion period:** 03/04/2020 to 05/05/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 5,393 **N CKD:** 299 **Age:** NR **Gender:** F 1,963 (36%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 299/5,393 (6%)	Multivariate
Ng Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 (>18 y. o.) **Hospitalized or outpatient:** Hospitalized **City/Country:** New York/ USA **Hospital/Center name:** H **Study inclusion period:** 03/01/2020 to 04/27/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 10,482 **N CKD:** 922 **Age:** Mean 66 (54-77) **Gender:** F 4,243 (41%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 9%	Multivariate
Ozturk Retrospective Cohort Multicenter Published	**Patients population: Patients** with confirmed or with high suspicion of COVID-19 (>18 y. o.) **Hospitalized or outpatient:** Hospitalized	**N:** 1,210 **N CKD:** Hemodialysis (390); CKD (289) **Age:** Total population:NR (Age CKD: Median age	Multivariate

	City/Country: Turkey **Hospital/Center name:** Multiple **Study inclusion period:** 04/17/2020 to 05/06/2020 **COVID-19 diagnosis method:** RT-PCR positive	hemodialysis: 64; IQR (55-71); Median age CKD: 71; IQR (63-79) **Gender CKD:** Gender hemodialysis: F 189 (48.5%); Gender CKD: F 125 (43.3.%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** NR	
Panagiotou Retrospective Cohort Multicenter Published	**Patients population: N**ursing home residents with patients with COVID-19 across 351 nursing homes **Hospitalized or outpatient:** Outpatient **City/Country:** USA **Hospital/Center name:** NA **Study inclusion period:** 03/16/2020 to 09/15/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 5,256 **N CKD:** 1,385 **Age:** Median Age: 79; IQR (69-88) **Gender:** F 3,185 (61%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 26%	Multivariate
Parra-Bracamonte Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 identified using the open datasource of Epidemiologic Surveillance Source of Respiratory Viral Dis-eases (Sistema de Vigilancia Epidemiológica de Enfermedades Respiratorias Virales **Hospitalized or outpatient:** Hospitalized and outpatient **City/Country:** Mexico **Hospital/Center name:** Multiple **Study inclusion period:** 05/2020 to 10/2020 **COVID-19 diagnosis method:**	**N:** 862,541 **N CKD:** 16,049 **Age:** NR **Gender:** NR **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 2%	Multivariate

	RT-PCR positive		
Petrilli **Prospective cohort** **Single center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized and outpatients **City/Country:** New York/ USA **Hospital/Center name:** NYU Langone Health **Study inclusion period:** 03/01/2020 to 04/08/2020 **COVID-19 diagnosis method:** RT-PCR positive on NP or OP swabs	**N:** 5,279 **N CKD:** 647 **Age:** Mean 54 (38-66) **Gender:** F 2,664 (52%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 12%	Multivariate
Portoles **Retrospective Cohort** **Single center** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Madrid/ Spain **Hospital/Center name:** Puerta de Hierro University Hospital **Study inclusion period:** 02/25/2020 to 04/24/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 1,603 **N CKD:** 146 **Age:** Mean 64.2 **Gender:** F 647 (40%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 9%	Multivariate
Rapp **Retrospective Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** New York/ USA **Hospital/Center name:** NR St**udy inclusion period:** 02/29/2020 to 05/19/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 4,062 **N CKD:** 481 **Age:** <40= 267, 40-69=1,947, >70=1,848 **Age CKD:** NR **Gender:** F 1,729 (43%) **Gender CKD:** NR **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 12%	Multivariate
Rossi **Prospective**	**Patients population:** Symptomatic patients with	**N:** 2,653 **N CKD:** 59 **Age:** NR	Multivariate

Cohort **Multicenter** **Not Published**	confirmed COVID-19 **Hospitalized or outpatient:** Hospitalized and non-hospitalized **City/Country:** Italy **Hospital/Center name:** Preventive services and hospital care in the province of Reggio Emilia, Northern Italy **Study inclusion period:** 02/27/2020 to 04/02/2020 **COVID-19 diagnosis method:** RT-PCR positive	**Gender:** F 1,325 (50%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 3%	
Salinas-Escudero **Retrospective** **Cohort** **Multicenter** **Published**	**Patients population:** All the confirmed cases of COVID-19 registered in Mexico **Hospitalized or outpatient:** **City/Country:** Mexico/ nationwide **Hospital/Center name:** Multiple **Study inclusion period:** 02/21/2020 to 04/28/2020 **COVID-19 diagnosis method:** Not specified	**N:** 16,752 **N CKD:** 388 **Age:** Mean 46.55 (+/- 15.55) **Gender:** F (42%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** (2%)	Multivariate
Santos **Retrospective** **Cohort** **Multicenter** **Published**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Brazil **Hospital/Center name:** NR St**udy inclusion period:** 02/20/2020 to 06/02/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 46,285 **N CKD:** NR **Age:** Populations based study, included all ages **Gender:** NR **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** NR	Multivariate
Soares **Retrospective** **Cohort** **Multicenter**	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized and non-hospitalized	**N:** 10,713 **N CKD:** 128 **Age:** age <60- 8,676 patients, >60- 2,037 **Gender:** F	Multivariate

Published	**City/Country:** Esp´ırito Santo state/ Brazil **Hospital/Center name:** NR St**udy inclusion period:** 02/29/2020 to 06/11/2020 **COVID-19 diagnosis method:** RT-PCR positive and/or history of close contact with a lab confirmed COVID-19 patitens.	5,909/10,713 (55%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 1%	
Surendra Retrospective Cohort Multicenter Not Published	**Patients population:** Patients with COVID-19 (all age groups included) **Hospitalized or outpatient:** Hospitalized **City/Country:** USA **Hospital/Center name:** Jakarta Health Office **Study inclusion period:** 03/02/2020 to 07/31/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 4,265 **N CKD:** 108 **Age:** Median 46 (32-57) **Gender:** F 2,220 (48%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 2%	Multivariate
Villar-Garcia Cross-sectional Multicenter Published	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized and outpatient **City/Country:** Spain **Hospital/Center name:** Catalan Health Surveillance System (CatSalut) **Study inclusion period:** 03/01/2020 to 06/01/2020 **COVID-19 diagnosis method:** RT-PCR positive and/or according to the stringent validated diagnostic criteria (current WHO/ECDC criteria)	**N:** 7,699,568 (COVID (+): 328,892) **N CKD:** 326,800 (COVID (+): 37,364) **Age:** NR **Gender:** F 3,919,648 (50.9%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 37,364/328,892 (11%)	Multivariate

Williamson Retrospective cohort Multicenter Registry/ Opensafely Published	**Patients population:** OpenSAFELY—a secure health analytics platform that covers 40% of all patients in England and holds patient data within the existing data center of a major vendor of primary care electronic health records (> **Hospitalized or outpatient:** NR **City/Country:** UK **Hospital/Center name:** NR **Study inclusion period:** 02/01/2020 to 05/06/2020 **COVID-19 diagnosis method:** RT-PCR positive and/or clinical suspect	**N:** 17,278,392 **N CKD:** 1,109,454 **Age:** NR **Gender:** F 8,639,196 (50%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 6%	Multivariate
Working group Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized, outpatient, and ICU patients **City/Country:** Spain **Hospital/Center name:** NR **Study inclusion period:** 01/31/2020 to 04/27/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 218,652 **N CKD:** 3,335 **Age:** Median 61 (46-78) **Gender:** F 122,870 (56.2 %) **Gender CKD:** F 1,682 (2.3%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 3%	Multivariate
Zandkarimi Retrospective Cohort Multicenter Published	**Patients population:** Patients with COVID-19 **Hospitalized or outpatient:** Hospitalized **City/Country:** Kurdistan/ Iran **Hospital/Center name:** NR **Study inclusion period:** 02/22/2020 to 05/18/2020 **COVID-19 diagnosis method:** RT-PCR positive	**N:** 1,831 **N CKD:** 48 **Age:** Mean: 52.74 y. o. **Gender:** F 812 (44.3%) **COVID-19 prevalence among CKD:** NR **CKD prevalence among COVID-19:** 2.6%	Multivariate

3.3 Pooled Analyses

For mortality in patients diagnosed with COVID-19 who also suffer from CKD, forest plots are depicted in Figures 2a, 2b, and 2c according to studies that presented mortality effect estimates in the form of HRs, ORs, and RRs, respectively. The random effects model (REM) analyses yielded statistically significant overall increased risk of mortality for patients diagnosed with both COVID-19 and CKD with pooled HR 1.57, 95% CI [1.42, 1.73], $P < 0.00001$, $I^2 = 93\%$ (moderate certainty of evidence) [Fig. 2a], pooled OR 1.86, 95% CI [1.64, 2.11], $P < 0.00001$, $I^2 = 61\%$ (moderate certainty of evidence) [Fig. 2b], and pooled RR 1.74, 95% CI [1.13, 2.69], $P = 0.01$, $I^2 = 98\%$ (moderate certainty of evidence) [Fig. 2c].

3.4 Subgroup Analyses

The subgroup analyses for the pooling of primary studies characterized by a sample size of N < 1,000 demonstrated a trend toward a more inflated risk of mortality when compared to pooled estimates from larger studies with N ≥ 1,000 (HR 2.07, 95% CI [1.58, 2.71], $P < 0.00001$, $I^2 = 46\%$ versus HR 1.48, 95% CI [1.33, 1.65], $P < 0.00001$, $I^2 = 95\%$); (OR 2.09, 95% CI [1.54, 2.84], $P < 0.00001$, $I^2 = 66\%$ versus OR 1.77, 95% CI [1.54, 2.02], $P < 0.00001$, $I^2 = 58\%$); (RR 1.87, 95% CI [1.13, 3.12], $P = 0.02$, $I^2 = 70\%$ versus RR 1.61, 95% CI [0.88, 2.92], $P = 0.12$, $I^2 = 99\%$). Studies that had larger sample sizes produced more conservative pooled effect estimates than their counterparts consisting of smaller sample sizes as shown in Figures 2a-c. However, there was no statistically significant subgroup effect.

Studies reporting on mortality in CKD stages III, IV, and V were also pooled in a subgroup analysis. Two large studies reported this information [50, 102]. Figure 3 displays the FEM model used for the pooled effect estimates for CKD stage III and stages IV-V mortalities which were HR 1.46 (95% CI [1.41, 1.51], $P < 0.00001$, $I^2 = 96\%$) and HR 2.84 (95% CI [2.69, 2.99], $P < 0.00001$, $I^2 = 94\%$), respectively, with an overall combined mortality effect estimate for CKD stages III-V as HR 1.79 (95% CI [1.74, 1.84], $P < 0.00001$, $I^2 = 99\%$).

As depicted in Figure 4a, additional subgroup analyses performed on studies reporting on ESKD in primary studies showed an increased hazard of dying in patients diagnosed with ESKD and COVID-19 (HR 1.92, 95% CI [0.96, 3.81], $P = 0.06$, $I^2 = 96\%$). In a fixed effects model (FEM), composite OR for both smalls and large studies reporting on mortality in patients with COVID-19 and ESKD also illustrated increase odds of death (OR 1.44, 95% CI [1.15, 1.81], $P = 0.002$, $I^2 = 75\%$) [Fig. 4b].

Chapter 4: Discussion

In this systematic review, we explore CKD as a prognostic factor and assess its association with death in patients with COVID-19. The results demonstrated that patients suffering from CKD while concurrently infected with the SARS-CoV-2 virus face a considerable increased risk of mortality (ranging from 57% to 86%) when compared to patients who do not have CKD. This increase in risk was consistent among different studies that included patients with variable characteristics and regardless of the size of the study. When the studies in the current meta-analyses were stratified by sample size of $N \geq 1,000$ and $N < 1,000$ patients, the overall observed trend was that studies characterized by small and large sample sizes produced more inflated and more conservative effect estimates for mortality, respectively, regardless of the type of effect estimate (HRs, ORs, or RRs). However, the difference between the effect estimates produced by large and small studies was not statistically significant.

Assessing methodological quality is critically important to ensure the validity of meta-analyses and systematic reviews. When constructing systematic reviews and meta-analyses, studies consisting of small and large sample sizes are both typically investigated for inclusion [68]. Thus, investigating the robustness of data derived from different sample sizes is important in the process of determining which studies should be selected for inclusion in the final review [21]. Among studies conducted which analyze reported treatment benefits from randomized clinical trials, many suggest that more substantial treatment benefits are reported in small trials than large trials [26, 27, 76, 94-96]. This phenomenon is recognized as the small-study effect and can contribute to the formulation of biased estimates of treatment effect [95], yet the impact of small studies on effect estimates is not evaluated in prognostic studies. From a statistical perspective, a larger effect estimate is expected to be produced when dealing with studies of a smaller sample size, and a conservative effect estimate is typically observed from studies consisting of large sample sizes [57]. Because of the increased potential for biased estimates of true disease effect on outcome, effect estimates curated from small studies are typically not as robust as those from large studies. Stratifying effect estimates for mortality based on sample size and identifying pooled estimates that are less likely to be skewed by greater random variation inherent in smaller studies is important for driving the development of best evidence for informing healthcare decision-making that is ultimately relevant to the formulation of clinical decisions and policies.

Furthermore, with regards to severity of CKD as defined by increasing stage of CKD, we observed a trend of increased mortality among patients with more advanced stages of CKD. This trend was not consistent among patients with ESKD. This difference is likely to be explained by the inclusion of different studies and patient populations. Additionally, it was at times not clear if the comparator was patients without CKD or those who do not have ESKD, which can lead to a meaningful difference in the effect estimates. From a clinical perspective, patients diagnosed with advanced stages of CKD tend to have subsequently poorer prognoses and are more susceptible to infection. Similarly, patients with ESKD also demonstrate a higher risk of infection and mortality which is overall consistent with our findings. Therefore, it is hypothesized that as kidney impairment increases with higher stages of CKD and ESKD, immunomodulatory mechanisms influenced by the kidneys become hampered, which could contribute to the increased risk of mortality in these patients when infected with COVID-19. Additionally, as rates of kidney clearance decrease in patients with advancing CKD and ESKD, the build-up of cytokines and uremic toxins increases, which places further strain on the body and has additional physiological consequences, contributing further to aberrant immunological regulation [3, 56]. Supplementing the physiological alterations that occur with CKD or ESKD, an infection with SARS-CoV-2 may impart additional damage to the immune system and increase the susceptibility of patients suffering from both diseases to increased infection by other pathogens and death.

Figure 2a. Forest plot depicting pooled hazard ratios for patients with and without CKD and Covid-19 diagnoses stratified by sample size. 95% CI, 95% confidence interval.

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
1.1.1 N = 1000+				
Baqui 2020	0.17395331	0.0643629	5.1%	1.19 [1.05, 1.35]
Boulle (All public sector) 2020	0.62057649	0.11494479	4.3%	1.86 [1.48, 2.33]
Docherty 2020	0.24686008	0.0420631	5.3%	1.28 [1.18, 1.39]
Flythe (Overall) 2020	0.25241368	0.06281204	5.1%	1.29 [1.14, 1.46]
Grasselli 2020	1.02245093	0.12186069	4.2%	2.78 [2.19, 3.53]
Hewitt 2020	0.35767444	0.10882913	4.4%	1.43 [1.16, 1.77]
Holman (Overall) 2020	0.67227005	0.02068709	5.5%	1.96 [1.88, 2.04]
Ioannou (Overall) 2020	0.13847099	0.06744225	5.0%	1.15 [1.01, 1.31]
Kang (Overall) 2020	-0.00002969	0.21588788	2.7%	1.00 [0.65, 1.53]
Lala A 2020	0.01980263	0.14677657	3.8%	1.02 [0.77, 1.36]
Murillo-Zamora 2020	0.3074847	0.02202662	5.5%	1.36 [1.30, 1.42]
Ozturk S (Overall) 2020	0.95351754	0.2325211	2.5%	2.59 [1.65, 4.09]
Petrilli CM 2020	-0.08338161	0.11826613	4.2%	0.92 [0.73, 1.16]
Portoles J 2020	0.66268797	0.15718926	3.6%	1.94 [1.43, 2.64]
Rossi 2020	0.40546511	0.28063589	2.0%	1.50 [0.87, 2.60]
Salinas-Escudero (Overall) 2020	0.60350429	0.10256635	4.5%	1.83 [1.50, 2.24]
Santos 2020	0.22314355	0.02780009	5.4%	1.25 [1.18, 1.32]
Surendra 2020	0.52472853	0.26303479	2.2%	1.69 [1.01, 2.83]
Williamson (Overall) 2020	0.53042233	0.02110031	5.5%	1.70 [1.63, 1.77]
Zandkarimi 2020	0.67803354	0.37146094	1.4%	1.97 [0.95, 4.08]
Subtotal (95% CI)			**82.3%**	**1.48 [1.33, 1.65]**
Heterogeneity: Tau² = 0.04; Chi² = 375.68, df = 19 (P < 0.00001); I² = 95%				
Test for overall effect: Z = 7.17 (P < 0.00001)				
1.1.2 N < 1000				
Cheng Y 2020	1.09527339	0.20516072	2.9%	2.99 [2.00, 4.47]
Ciceri F 2020	1.01160091	0.23979777	2.5%	2.75 [1.72, 4.40]
Coca A 2020	0.97455964	0.40576275	1.2%	2.65 [1.20, 5.87]
Cummings MJ 2020	0.40546511	0.25031781	2.3%	1.50 [0.92, 2.45]
Gu T 2020	0.70309751	0.46951189	1.0%	2.02 [0.80, 5.07]
Khedr EM 2020	0.53062825	0.39678804	1.2%	1.70 [0.78, 3.70]
Nachega JB 2020	1.67335124	0.53634095	0.8%	5.33 [1.86, 15.25]
Rivera-Izquierdo M 2020	-0.03045921	0.32386488	1.7%	0.97 [0.51, 1.83]
Russo E 2020	0.51879379	0.18197701	3.2%	1.68 [1.18, 2.40]
Shang J 2021	2.50968056	1.33328025	0.1%	12.30 [0.90, 167.81]
Wang L 2020	0.54812141	0.5169266	0.8%	1.73 [0.63, 4.76]
Subtotal (95% CI)			**17.7%**	**2.07 [1.58, 2.71]**
Heterogeneity: Tau² = 0.08; Chi² = 18.69, df = 10 (P = 0.04); I² = 46%				
Test for overall effect: Z = 5.30 (P < 0.00001)				
Total (95% CI)			**100.0%**	**1.57 [1.42, 1.73]**
Heterogeneity: Tau² = 0.05; Chi² = 404.16, df = 30 (P < 0.00001); I² = 93%				
Test for overall effect: Z = 8.97 (P < 0.00001)				
Test for subgroup differences: Chi² = 5.15, df = 1 (P = 0.02), I² = 80.6%				

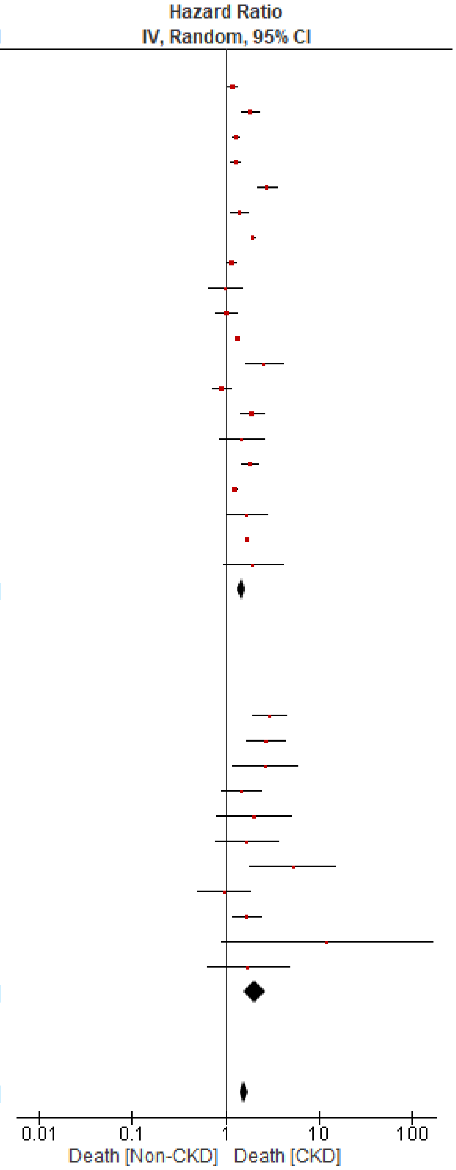


Figure 2b. Forest plot depicting pooled odds ratios for patients with and without CKD and Covid-19 diagnoses stratified by sample size. 95% CI, 95% confidence interval.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.2.1 N = 1000+				
Akchurin 2020	0.336	0.15580696	4.7%	1.40 [1.03, 1.90]
Almazeedi 2020	0.73476885	1.04212175	0.4%	2.08 [0.27, 16.08]
Atkins 2020	-0.12783337	0.47668839	1.4%	0.88 [0.35, 2.24]
Chishinga 2020	0.53062825	0.30651728	2.6%	1.70 [0.93, 3.10]
de Souza Cd 2020	0.70309751	0.23472107	3.5%	2.02 [1.28, 3.20]
Esme 2020	0.92028275	0.05578401	6.2%	2.51 [2.25, 2.80]
Fried 2020	0.5068176	0.07157431	6.0%	1.66 [1.44, 1.91]
Gude-Sampedro 2020	0.81977983	0.41825502	1.7%	2.27 [1.00, 5.15]
Harrison 2020	0.75612198	0.38577652	1.9%	2.13 [1.00, 4.54]
Imam 2020	0.62057649	0.31662066	2.5%	1.86 [1.00, 3.46]
Jimenez 2020	1.04027671	0.53075342	1.2%	2.83 [1.00, 8.01]
Kaeuffer 2020	0.83290912	0.42495363	1.7%	2.30 [1.00, 5.29]
Kim DW 2020	1.12167756	0.57228447	1.1%	3.07 [1.00, 9.42]
Klang (Overall) 2020	0.56946703	0.10460676	5.6%	1.77 [1.44, 2.17]
Lee SG 2020	1.13462273	0.57888915	1.0%	3.11 [1.00, 9.67]
Macedo 2020	0.87962675	0.44878916	1.6%	2.41 [1.00, 5.81]
Martos-Benitez 2020	0.77932488	0.39761473	1.9%	2.18 [1.00, 4.75]
Munblit 2020	1.09527339	0.55881295	1.1%	2.99 [1.00, 8.94]
Ng 2020	0.31481074	0.16061772	4.6%	1.37 [1.00, 1.88]
Panagiotou Oa 2020	0.28517894	0.14549946	4.9%	1.33 [1.00, 1.77]
Parra-Bracamonte GM 2020	0.69114518	0.35262509	2.2%	2.00 [1.00, 3.98]
Rapp 2020	0.3220835	0.16432832	4.6%	1.38 [1.00, 1.90]
Soares 2020	0.51879379	0.26469071	3.1%	1.68 [1.00, 2.82]
Working Group 2020	0.3852624	0.19656245	4.1%	1.47 [1.00, 2.16]
Subtotal (95% CI)			**69.7%**	**1.77 [1.54, 2.02]**
Heterogeneity: Tau² = 0.04; Chi² = 55.02, df = 23 (P = 0.0002); I² = 58%				
Test for overall effect: Z = 8.22 (P < 0.00001)				
1.2.2 N < 1000				
Alamdari 2020	0.88418068	0.29117677	2.8%	2.42 [1.37, 4.28]
Chan L 2020	-0.40047757	0.3686536	2.1%	0.67 [0.33, 1.38]
Chilimuri S 2020	0.28517894	0.3743206	2.0%	1.33 [0.64, 2.77]
Giannoglou D 2020	1.64287269	0.66164194	0.8%	5.17 [1.41, 18.91]
Gok M 2020	0.80647587	0.12108581	5.3%	2.24 [1.77, 2.84]
Harmouch F (Overall) 2020	1.00148937	0.32638199	2.4%	2.72 [1.44, 5.16]
Lanza E 2020	1.42069579	0.48446324	1.4%	4.14 [1.60, 10.70]
Mendy A 2020	1.49962305	0.4619993	1.5%	4.48 [1.81, 11.08]
Okoh AK 2020	1.23256026	0.34916446	2.2%	3.43 [1.73, 6.80]
Salacup G 2020	-0.21567154	0.47578329	1.4%	0.81 [0.32, 2.05]
Shah P 2020	0.07696104	0.38123184	2.0%	1.08 [0.51, 2.28]
Tehrani S 2020	-0.08338161	0.37536061	2.0%	0.92 [0.44, 1.92]
Thompson JV 2020	0.95551144	0.25430692	3.2%	2.60 [1.58, 4.28]
Yang D 2020	1.99470031	0.56946162	1.1%	7.35 [2.41, 22.44]
Subtotal (95% CI)			**30.3%**	**2.09 [1.54, 2.84]**
Heterogeneity: Tau² = 0.20; Chi² = 38.18, df = 13 (P = 0.0003); I² = 66%				
Test for overall effect: Z = 4.71 (P < 0.00001)				
Total (95% CI)			**100.0%**	**1.86 [1.64, 2.11]**
Heterogeneity: Tau² = 0.06; Chi² = 94.85, df = 37 (P < 0.00001); I² = 61%				
Test for overall effect: Z = 9.67 (P < 0.00001)				
Test for subgroup differences: Chi² = 0.98, df = 1 (P = 0.32), I² = 0%				

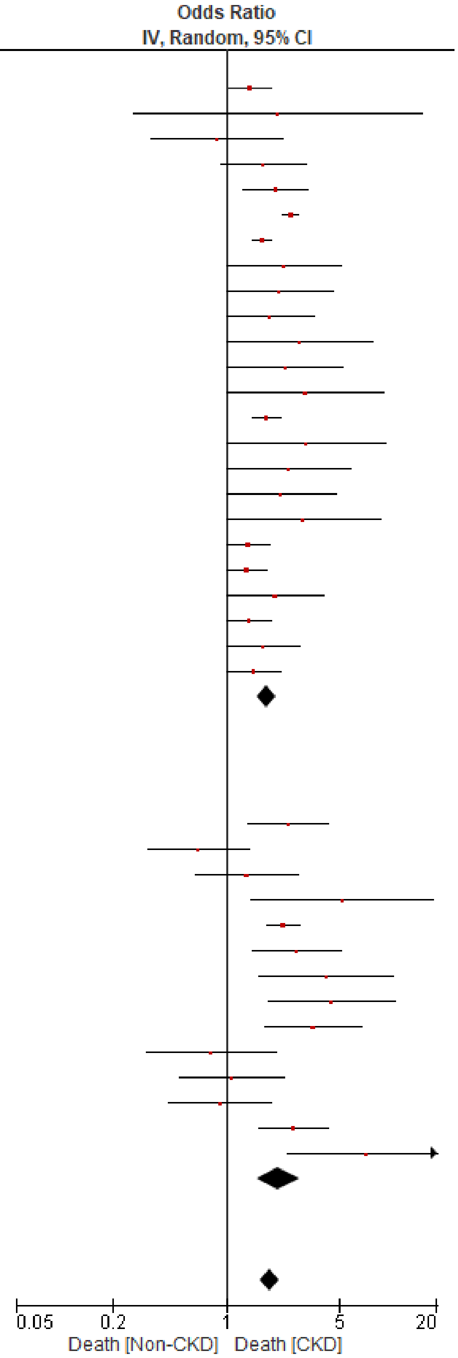


Figure 2c. Forest plot depicting pooled risk ratios for patients with and without CKD and Covid-19 diagnoses stratified by sample size. 95% CI, 95% confidence interval.

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.3.1 N = 1000+				
Dominguez-Ramirez (Overall) 2020	0.97542498	0.04364489	19.0%	2.65 [2.43, 2.89]
Kim L 2020	0.28517894	0.09747716	18.5%	1.33 [1.10, 1.61]
Villar-Garcia 2020	0.15700375	0.02135057	19.1%	1.17 [1.12, 1.22]
Subtotal (95% CI)			**56.7%**	**1.61 [0.88, 2.92]**
Heterogeneity: Tau² = 0.28; Chi² = 283.82, df = 2 (P < 0.00001); I² = 99%				
Test for overall effect: Z = 1.55 (P = 0.12)				
1.3.2 N < 1000				
Filardo TD 2020	0.2390169	0.17224309	17.2%	1.27 [0.91, 1.78]
Gasparini M 2020	0.83290912	0.18419048	16.9%	2.30 [1.60, 3.30]
Javanian M 2020	1.11185752	0.52758866	9.2%	3.04 [1.08, 8.55]
Subtotal (95% CI)			**43.3%**	**1.87 [1.13, 3.12]**
Heterogeneity: Tau² = 0.13; Chi² = 6.75, df = 2 (P = 0.03); I² = 70%				
Test for overall effect: Z = 2.42 (P = 0.02)				
Total (95% CI)			**100.0%**	**1.74 [1.13, 2.69]**
Heterogeneity: Tau² = 0.26; Chi² = 294.15, df = 5 (P < 0.00001); I² = 98%				
Test for overall effect: Z = 2.49 (P = 0.01)				
Test for subgroup differences: Chi² = 0.15, df = 1 (P = 0.70), I² = 0%				

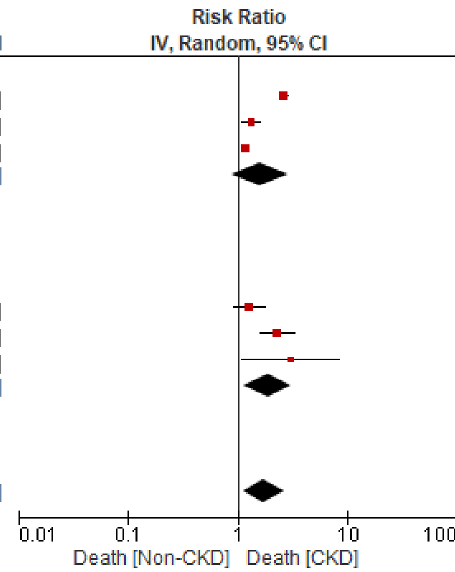


Figure 3. Forest plot depicting pooled hazard ratios by stage of advancement for patients with and without CKD and Covid-19 diagnoses. 95% CI, 95% confidence interval. GFR, glomerular filtration rate. Stage III CKD: GFR 30-60 mL/min/1.73 m². Stage IV CKD: GFR 15-30 mL/min/1.73 m^2. Stage V CKD: GFR <15 mL/min/1.73 m^2.

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
3.1.1 CKD Stage 3				
Holman (Overall - GFR 30-59) 2020	0.45878654	0.02486954	36.3%	1.58 [1.51, 1.66]
Williamson (GFR 30-60) 2020	0.28517894	0.02617005	32.8%	1.33 [1.26, 1.40]
Subtotal (95% CI)			**69.1%**	**1.46 [1.41, 1.51]**
Heterogeneity: Chi² = 23.12, df = 1 (P < 0.00001); I² = 96%				
Test for overall effect: Z = 20.88 (P < 0.00001)				
3.1.2 CKD Stages 4-5				
Holman (GFR below 29) 2020	1.15176163	0.03727143	16.2%	3.16 [2.94, 3.40]
Williamson (GFR below 30) 2020	0.9242589	0.03896581	14.8%	2.52 [2.33, 2.72]
Subtotal (95% CI)			**30.9%**	**2.84 [2.69, 2.99]**
Heterogeneity: Chi² = 17.80, df = 1 (P < 0.0001); I² = 94%				
Test for overall effect: Z = 38.73 (P < 0.00001)				
Total (95% CI)			**100.0%**	**1.79 [1.74, 1.84]**
Heterogeneity: Chi² = 464.02, df = 3 (P < 0.00001); I² = 99%				
Test for overall effect: Z = 38.89 (P < 0.00001)				
Test for subgroup differences: Chi² = 423.10, df = 1 (P < 0.00001), I² = 99.8%				

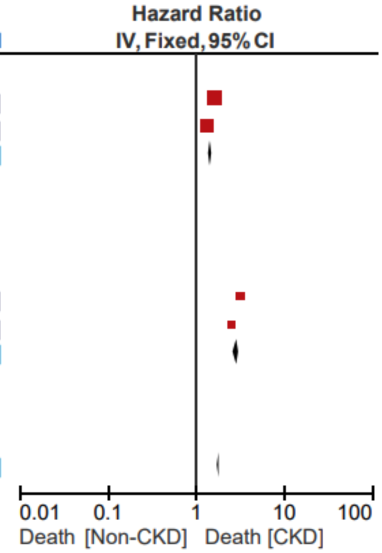


Figure 4a. Forest plot depicting pooled hazard ratios for patients with and without ESKD and Covid-19 diagnoses only. 95% CI, 95% confidence interval.

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
2.1.1 N = 1000+				
Flythe (DD) 2020	0.3435897	0.12741691	21.9%	1.41 [1.10, 1.81]
Ioannou (Dialysis) 2020	-0.18632958	0.14831102	21.7%	0.83 [0.62, 1.11]
Kang (NDD) 2020	1.08518927	0.51108382	15.3%	2.96 [1.09, 8.06]
Ozturk S (Hemodialysis) 2020	0.84372004	0.33316174	18.8%	2.32 [1.21, 4.47]
Williamson (ESKD) 2020	1.30562646	0.08862386	22.3%	3.69 [3.10, 4.39]
Subtotal (95% CI)			**100.0%**	**1.92 [0.96, 3.81]**
Heterogeneity: Tau² = 0.54; Chi² = 89.73, df = 4 (P < 0.00001); I² = 96%				
Test for overall effect: Z = 1.85 (P = 0.06)				
Total (95% CI)			**100.0%**	**1.92 [0.96, 3.81]**
Heterogeneity: Tau² = 0.54; Chi² = 89.73, df = 4 (P < 0.00001); I² = 96%				
Test for overall effect: Z = 1.85 (P = 0.06)				
Test for subgroup differences: Not applicable				

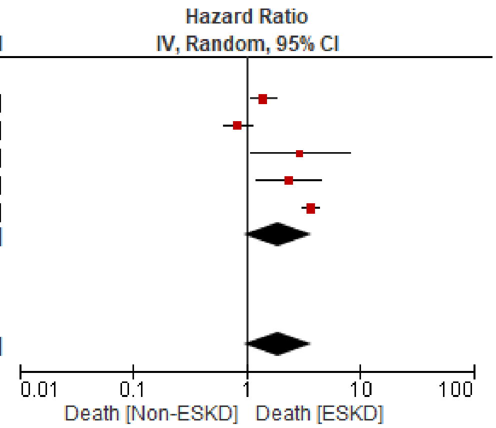
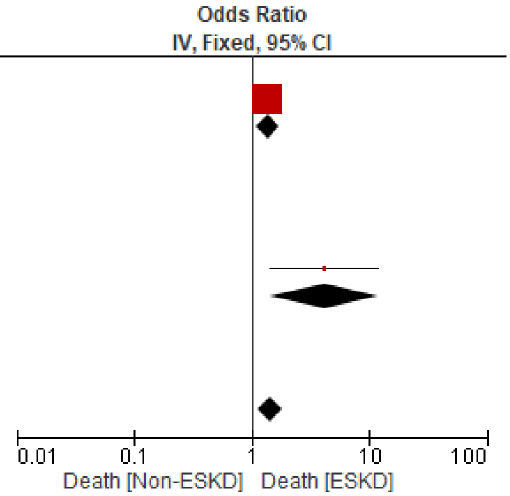


Figure 4b. Forest plot depicting pooled odds ratios for patients with and without ESKD and Covid-19 diagnoses stratified by sample size. 95% CI, 95% confidence interval.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
2.2.1 N = 1000+				
Ng 2020	0.31481074	0.11903606	95.4%	1.37 [1.08, 1.73]
Subtotal (95% CI)			**95.4%**	**1.37 [1.08, 1.73]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.64 (P = 0.008)				
2.2.2 N < 1000				
Harmouch F (ESKD) 2020	1.42983266	0.54148191	4.6%	4.18 [1.45, 12.07]
Subtotal (95% CI)			**4.6%**	**4.18 [1.45, 12.07]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.64 (P = 0.008)				
Total (95% CI)			**100.0%**	**1.44 [1.15, 1.81]**
Heterogeneity: Chi² = 4.04, df = 1 (P = 0.04); I² = 75%				
Test for overall effect: Z = 3.15 (P = 0.002)				
Test for subgroup differences: Chi² = 4.04, df = 1 (P = 0.04), I² = 75.3%				



4.1 Strengths and Limitations

This review has several strengths. It is very comprehensive and methodologically rigorous. We have identified and analyzed 75 more studies in this review. The comprehensive and up to date search makes it unlikely that relevant trials were missed. All steps including initial screening, selection of trials, and data abstraction were performed independently in duplicate for larger studies to minimize any potential biases arising from subjectivity. Additionally, we assessed ROB of each study using QUIPS. Finally, we analyzed sources of bias and explored reasons for diversity in the published literature.

This review has few limitations. Data pooled for the overall analyses were extracted from numerous studies which may have adjusted for different confounding variables than one another. Furthermore, across primary studies, reported methods of diagnosing CKD and measuring of confounders were not always explicitly detailed. Each population was not necessarily equivalent and patients with CKD and COVID-19 may have also been diagnosed with additional comorbidities. Therefore, it is difficult to precisely determine the true extent of the association between CKD and COVID-19 infection with increased risk of mortality. Additionally, due to the reliance on published systematic reviews to identify studies that were published prior to September 2020, it is possible that a few primary studies were missed. However, this occurrence is rather unlikely given the extensive effort that was exercised in the identification of high-quality and large studies. It is also unlikely that any major study which may have been missed during the search process would have a substantial influence on the conclusions presented. Of note, various systematic reviews and primary studies were unpublished pre-prints which were not subjected to a rigorous peer-review process

4.2 Implications for Practice and Policy

Overall, this study has implications with regards to alterations in practices and policies. Patients with CKD or ESKD should be identified as high-risk for COVID-19 and should be prioritized in testing and the utilization of preventative measures such as personal protective equipment (PPE). Additionally, patients that comprise this population should also be considered a high-risk group that should be prioritized for COVID-19 vaccinations. Dialysis centers should also seek to increase adherence to PPEs and implement appropriate guidelines that would help reduce their patient population's risk of COVID-19 infection. This study also highlights that if reviewers have limited capacity or if there are issues with feasibility, focusing on larger studies when a plethora of evidence exists may be acceptable.

4.3 Considerations for Future Research

Additional information highlighting the mortality risk in patients with varying stages of CKD and in patients with ESKD would help provide deeper insight into how severity of CKD diagnoses contributes to the increased risk of mortality in this population as there are limited primary studies that compare the different CKD stages or ESKD. Future research endeavors investigating the immunological impacts of the SARS-CoV-2 virus in relation to the immunomodulatory effects that the kidneys contribute to would be beneficial in shedding light on the degree to which CKD and ESKD influence the risk of mortality in patients with COVID-19.

References

1. *What is GRADE? | BMJ Best Practice*.
2. *What is Prognostic Research?* ; Available from: https://methods.cochrane.org/prognosis/about-us.
3. *Overall immune profile and effect of chronic kidney disease on vaccination schedule.* Indian Journal of Nephrology, 2016. **26**(Suppl 1): p. S2-S4.
4. Akchurin, O., et al., *COVID-19 in Patients with CKD in New York City.* Kidney360, 2021. **2**(1): p. 63-70.
5. Alamdari, N.M., et al., *Mortality Risk Factors among Hospitalized COVID-19 Patients in a Major Referral Center in Iran.* The Tohoku Journal of Experimental Medicine, 2020. **252**(1): p. 73-84.
6. Almazeedi, S., et al., *Characteristics, risk factors and outcomes among the first consecutive 1096 patients diagnosed with COVID-19 in Kuwait.* EClinicalMedicine, 2020. **24**.
7. Atkins, J.L., et al., *Preexisting Comorbidities Predicting COVID-19 and Mortality in the UK Biobank Community Cohort.* The Journals of Gerontology: Series A, 2020. **75**(11): p. 2224-2230.
8. Baqui, P., et al., *Ethnic and regional variations in hospital mortality from COVID-19 in Brazil: a cross-sectional observational study.* The Lancet Global Health, 2020. **8**(8): p. e1018-e1026.
9. Bikbov, B., et al., *Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017.* The Lancet, 2020. **395**(10225): p. 709-733.
10. Boulle, A., et al., *Risk factors for COVID-19 death in a population cohort study from the Western Cape Province, South Africa.* Clinical Infectious Diseases, 2020.
11. Chan, L., et al., *Outcomes of Patients on Maintenance Dialysis Hospitalized with COVID-19.* Clinical Journal of the American Society of Nephrology, 2020: p. CJN.12360720.
12. Chang, C.-H., et al., *Infection in Advanced Chronic Kidney Disease and Subsequent Adverse Outcomes after Dialysis Initiation: A Nationwide Cohort Study.* Scientific Reports, 2020. **10**(1).
13. Cheng, Y., et al., *Kidney disease is associated with in-hospital death of patients with COVID-19.* Kidney International, 2020. **97**(5): p. 829-838.
14. Chilimuri, S., et al., *Predictors of Mortality in Adults Admitted with COVID-19: Retrospective Cohort Study from New York City.* Western Journal of Emergency Medicine, 2020. **21**(4).
15. Chishinga, N., et al., *Characteristics and Risk Factors for Hospitalization and Mortality among Persons with COVID-19 in Atlanta Metropolitan Area*. 2020, Cold Spring Harbor Laboratory.
16. Ciceri, F., et al., *Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy.* Clinical Immunology, 2020. **217**: p. 108509.
17. Coca, A., et al., *Outcomes of COVID-19 Among Hospitalized Patients With Non-dialysis CKD.* Frontiers in Medicine, 2020. **7**.
18. Collaboration, T.C. *Comparing fixed and random-effects estimates*. Available from: https://handbook-5-

1.cochrane.org/chapter_10/10_4_4_1_comparing_fixed_and_random_effects_estimates.htm.
19. Collaboration, T.C., *Review Manager (RevMan) [Computer Program]*. (Version 5.4).
20. Control, C.f.D. *Chronic Kidney Disease in the United States, 2021*. 2021 2021/03/09/T04:15:14Z [cited 2021 March 20, 2021]; Available from: https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html.
21. Cook, D.A. and R. Hatala, *Got power? A systematic review of sample size adequacy in health professions education research.* Adv Health Sci Educ Theory Pract, 2015. **20**(1): p. 73-83.
22. Cummings, M.J., et al., *Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study.* The Lancet, 2020. **395**(10239): p. 1763-1770.
23. Dalrymple, L.S. and A.S. Go, *Epidemiology of Acute Infections among Patients with Chronic Kidney Disease: Figure 1.* Clinical Journal of the American Society of Nephrology, 2008. **3**(5): p. 1487-1493.
24. De Jager, D.J., *Cardiovascular and Noncardiovascular Mortality Among Patients Starting Dialysis.* JAMA, 2009. **302**(16): p. 1782.
25. De Souza, C.D., et al., *Clinical manifestations and factors associated with mortality from COVID -19 in older adults: Retrospective population-based study with 9807 older Brazilian COVID-19 patients.* Geriatrics & Gerontology International, 2020. **20**(12): p. 1177-1181.
26. Dechartres, A., et al., *Association Between Analytic Strategy and Estimates of Treatment Outcomes in Meta-analyses.* JAMA, 2014. **312**(6): p. 623-630.
27. Dechartres, A., et al., *Influence of trial sample size on treatment effect estimates: meta-epidemiological study.* Bmj, 2013. **346**: p. f2304.
28. Docherty, A.B., et al., *Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study.* BMJ, 2020: p. m1985.
29. Dominguez-Ramirez, L., et al., *The role of metabolic comorbidity in COVID-19 mortality of middle-aged adults. The case of Mexico.* medRxiv, 2020: p. 2020.12.15.20244160.
30. Egger, M., et al., *Bias in meta-analysis detected by a simple, graphical test.* BMJ, 1997. **315**(7109): p. 629-34.
31. Esme, M., et al., *Older Adults With Coronavirus Disease 2019: A Nationwide Study in Turkey.* The Journals of Gerontology: Series A, 2021. **76**(3): p. e68-e75.
32. Filardo, T.D., et al., *Comorbidity and clinical factors associated with COVID-19 critical illness and mortality at a large public hospital in New York City in the early phase of the pandemic (March-April 2020).* PLOS ONE, 2020. **15**(11): p. e0242760.
33. Flythe, J.E., et al., *Characteristics and Outcomes of Individuals With Pre-existing Kidney Disease and COVID-19 Admitted to Intensive Care Units in the United States.* American Journal of Kidney Diseases, 2021. **77**(2): p. 190-203.e1.
34. Fried, L.F., et al., *Kidney Function as a Predictor of Noncardiovascular Mortality.* Journal of the American Society of Nephrology, 2005. **16**(12): p. 3728-3735.
35. Fried, M.W., et al., *Patient Characteristics and Outcomes of 11 721 Patients With Coronavirus Disease 2019 (COVID-19) Hospitalized Across the United States.* Clinical Infectious Diseases, 2020.

36. Gasparini, M., et al., *Renal impairment and its impact on clinical outcomes in patients who are critically ill with COVID-19: a multicentre observational study.* Anaesthesia, 2021. **76**(3): p. 320-326.
37. Giannoglou, D., et al., *Predictors of mortality in hospitalized COVID-19 patients in Athens, Greece*. 2020, Cold Spring Harbor Laboratory.
38. Giorgi Rossi, P., et al., *Characteristics and outcomes of a cohort of COVID-19 patients in the Province of Reggio Emilia, Italy.* PLOS ONE, 2020. **15**(8): p. e0238281.
39. Go, A.S., et al., *Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization.* New England Journal of Medicine, 2004. **351**(13): p. 1296-1305.
40. Gok, M., et al., *Chronic kidney disease predicts poor outcomes of COVID-19 patients.* International Urology and Nephrology, 2021.
41. Grasselli, G., et al., *Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy.* JAMA Internal Medicine, 2020. **180**(10): p. 1345.
42. Gu, T., et al., *History of coronary heart disease increased the mortality rate of patients with COVID-19: a nested case–control study.* BMJ Open, 2020. **10**(9): p. e038976.
43. Gude-Sampedro, F., et al., *Development and validation of a prognostic model based on comorbidities to predict Covid-19 severity. A population-based study.* International Journal of Epidemiology, 2020.
44. Harmouch, F., et al., *Is it all in the heart? Myocardial injury as major predictor of mortality among hospitalized COVID-19 patients.* Journal of Medical Virology, 2021. **93**(2): p. 973-982.
45. Harrison, S.L., et al., *Comorbidities associated with mortality in 31,461 adults with COVID-19 in the United States: A federated electronic medical record analysis.* PLOS Medicine, 2020. **17**(9): p. e1003321.
46. Hayden, J.A., et al., *Assessing Bias in Studies of Prognostic Factors.* Annals of Internal Medicine, 2013. **158**(4): p. 280-286.
47. Hewitt, J., et al., *The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study.* The Lancet Public Health, 2020. **5**(8): p. e444-e451.
48. Higgins, J.P., et al., *The Cochrane Collaboration's tool for assessing risk of bias in randomised trials.* Bmj, 2011. **343**: p. d5928.
49. Hill, N.R., et al., *Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis.* PLOS ONE, 2016. **11**(7): p. e0158765.
50. Holman, N., et al., *Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study.* The Lancet Diabetes & Endocrinology, 2020. **8**(10): p. 823-833.
51. Huang, C., et al., *Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.* The Lancet, 2020. **395**(10223): p. 497-506.
52. Imam, Z., et al., *Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States.* Journal of Internal Medicine, 2020. **288**(4): p. 469-476.
53. Ioannou, G.N., et al., *Risk Factors for Hospitalization, Mechanical Ventilation, or Death Among 10 131 US Veterans With SARS-CoV-2 Infection.* JAMA Network Open, 2020. **3**(9): p. e2022310.

54. Javanian, M., et al., *Clinical and laboratory findings from patients with COVID-19 pneumonia in Babol North of Iran: a retrospective cohort study.* Romanian Journal of Internal Medicine, 2020. **58**(3): p. 161-167.
55. Jiménez, E., et al., *Characteristics, complications and outcomes among 1549 patients hospitalised with COVID-19 in a secondary hospital in Madrid, Spain: a retrospective case series study.* BMJ Open, 2020. **10**(11): p. e042398.
56. Johnson, D.W. and S.J. Fleming, *The use of vaccines in renal failure.* Clin Pharmacokinet, 1992. **22**(6): p. 434-46.
57. Kadam, P. and S. Bhalerao, *Sample size calculation.* Int J Ayurveda Res, 2010. **1**(1): p. 55-7.
58. Kaeuffer, C., et al., *Clinical characteristics and risk factors associated with severe COVID-19: prospective analysis of 1,045 hospitalised cases in North-Eastern France, March 2020.* Eurosurveillance, 2020. **25**(48): p. 2000895.
59. Kang, S.H., et al., *Association between Chronic Kidney Disease or Acute Kidney Injury and Clinical Outcomes in COVID-19 Patients.* Journal of Korean Medical Science, 2020. **35**(50).
60. Khedr, E.M., et al., *Impact of comorbidities on COVID-19 outcome*. 2020, Cold Spring Harbor Laboratory.
61. Kim, D.W., et al., *The Correlation of Comorbidities on the Mortality in Patients with COVID-19: an Observational Study Based on the Korean National Health Insurance Big Data*. Journal of Korean Medical Science, 2020. **35**(26).
62. Kim, L., et al., *Risk Factors for Intensive Care Unit Admission and In-hospital Mortality Among Hospitalized Adults Identified through the US Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET).* Clinical Infectious Diseases, 2020.
63. Klang, E., et al., *Severe Obesity as an Independent Risk Factor for COVID-19 Mortality in Hospitalized Patients Younger than 50.* Obesity, 2020. **28**(9): p. 1595-1599.
64. Lala, A., et al., *Prevalence and Impact of Myocardial Injury in Patients Hospitalized With COVID-19 Infection.* Journal of the American College of Cardiology, 2020. **76**(5): p. 533-546.
65. Lanza, E., et al., *Quantitative chest CT analysis in COVID-19 to predict the need for oxygenation support and intubation.* European Radiology, 2020. **30**(12): p. 6770-6778.
66. Lee, S.-G., et al., *Clinical Characteristics and Risk Factors for Fatality and Severity in Patients with Coronavirus Disease in Korea: A Nationwide Population-Based Retrospective Study Using the Korean Health Insurance Review and Assessment Service (HIRA) Database.* International Journal of Environmental Research and Public Health, 2020. **17**(22): p. 8559.
67. Liberati, A., et al., *The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration.* BMJ, 2009. **339**: p. b2700.
68. Lin, L., *Bias caused by sampling error in meta-analysis with small sample sizes.* PloS one, 2018. **13**(9): p. e0204056-e0204056.
69. Macedo, M.C.F., et al., *Correlation between hospitalized patients' demographics, symptoms, comorbidities, and COVID-19 pandemic in Bahia, Brazil.* PLOS ONE, 2020. **15**(12): p. e0243966.

70. Martos-Benítez, F.D., C.D. Soler-Morejón, and D. García-Del Barco, *Chronic comorbidities and clinical outcomes in patients with and without COVID-19: a large population-based study using national administrative healthcare open data of Mexico.* Internal and Emergency Medicine, 2021.
71. Mendy, A., et al., *Factors Associated with Hospitalization and Disease Severity in a Racially and Ethnically Diverse Population of COVID-19 Patients*. 2020, Cold Spring Harbor Laboratory.
72. Munblit, D., et al., *StopCOVID cohort: An observational study of 3,480 patients admitted to the Sechenov University hospital network in Moscow city for suspected COVID-19 infection.* Clinical Infectious Diseases, 2020.
73. Murillo-Zamora, E. and C.M. Hernandez-Suarez, *Survival in adult inpatients with COVID-19.* Public Health, 2021. **190**: p. 1-3.
74. Nachega, J.B., et al., *Clinical Characteristics and Outcomes of Patients Hospitalized for COVID-19 in Africa: Early Insights from the Democratic Republic of the Congo.* The American Journal of Tropical Medicine and Hygiene, 2020. **103**(6): p. 2419-2428.
75. Ng, J.H., et al., *Outcomes of patients with end-stage kidney disease hospitalized with COVID-19.* Kidney International, 2020. **98**(6): p. 1530-1539.
76. Nüesch, E., et al., *Small study effects in meta-analyses of osteoarthritis trials: meta-epidemiological study.* Bmj, 2010. **341**: p. c3515.
77. Okoh, A.K., et al., *Coronavirus disease 19 in minority populations of Newark, New Jersey.* International Journal for Equity in Health, 2020. **19**(1).
78. Ozturk, S., et al., *Mortality analysis of COVID-19 infection in chronic kidney disease, haemodialysis and renal transplant patients compared with patients without kidney disease: a nationwide analysis from Turkey.* Nephrology Dialysis Transplantation, 2020. **35**(12): p. 2083-2095.
79. Panagiotou, O.A., et al., *Risk Factors Associated With All-Cause 30-Day Mortality in Nursing Home Residents With COVID-19.* JAMA Internal Medicine, 2021.
80. Parra-Bracamonte, G.M., et al., *Chronic kidney disease is a very significant comorbidity for high risk of death in patients with COVID -19 in Mexico.* Nephrology, 2021. **26**(3): p. 248-251.
81. Pekar, J., et al., *Timing the SARS-CoV-2 index case in Hubei province.* Science, 2021: p. eabf8003.
82. Petrilli, C.M., et al., *Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study.* BMJ, 2020: p. m1966.
83. Portolés, J., et al., *Chronic kidney disease and acute kidney injury in the COVID-19 Spanish outbreak.* Nephrology Dialysis Transplantation, 2020. **35**(8): p. 1353-1361.
84. Rapp, J.L., et al., *Male Sex, Severe Obesity, Older Age, and Chronic Kidney Disease Are Associated With COVID-19 Severity and Mortality in New York City.* Chest, 2021. **159**(1): p. 112-115.
85. Rivera-Izquierdo, M., et al., *Sociodemographic, clinical and laboratory factors on admission associated with COVID-19 mortality in hospitalized patients: A retrospective observational study.* PLOS ONE, 2020. **15**(6): p. e0235107.
86. Russo, E., et al., *Kidney disease and all-cause mortality in patients with COVID-19 hospitalized in Genoa, Northern Italy.* Journal of Nephrology, 2020.

87. Salacup, G., et al., *Characteristics and clinical outcomes of COVID-19 patients in an underserved-inner city population: A single tertiary center cohort.* Journal of Medical Virology, 2021. **93**(1): p. 416-423.
88. Salinas-Escudero, G., et al., *A survival analysis of COVID-19 in the Mexican population.* BMC Public Health, 2020. **20**(1).
89. Santos, M.M., et al., *Survival and predictors of deaths of patients hospitalised due to COVID-19 from a retrospective and multicentre cohort study in Brazil.* Epidemiology and Infection, 2020. **148**.
90. Shah, P., et al., *Demographics, comorbidities and outcomes in hospitalized Covid-19 patients in rural southwest Georgia.* Annals of Medicine, 2020. **52**(7): p. 354-360.
91. Shang, J., et al., *The Relationship Between Diabetes Mellitus and COVID-19 Prognosis: A Retrospective Cohort Study in Wuhan, China.* The American Journal of Medicine, 2021. **134**(1): p. e6-e14.
92. Soares, R.D.C.M., L.R. Mattos, and L.M. Raposo, *Risk Factors for Hospitalization and Mortality due to COVID-19 in Espírito Santo State, Brazil.* The American Journal of Tropical Medicine and Hygiene, 2020. **103**(3): p. 1184-1190.
93. Spain, W.g.f.t.s.a.c.o.C.-i., *The first wave of the COVID-19 pandemic in Spain: characterisation of cases and risk factors for severe outcomes, as at 27 April 2020.* Eurosurveillance, 2020. **25**(50).
94. Sterne, J.A., M. Egger, and G.D. Smith, *Systematic reviews in health care: Investigating and dealing with publication and other biases in meta-analysis.* BMJ (Clinical research ed.), 2001. **323**(7304): p. 101-105.
95. Sterne, J.A., D. Gavaghan, and M. Egger, *Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature.* J Clin Epidemiol, 2000. **53**(11): p. 1119-29.
96. Sterne, J.A., et al., *Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials.* Bmj, 2011. **343**: p. d4002.
97. Surendra, H., et al., *Clinical characteristics and mortality associated with COVID-19 in Jakarta, Indonesia: a hospital-based retrospective cohort study*. 2020, Cold Spring Harbor Laboratory.
98. Tehrani, S., et al., *Risk factors for death in adult COVID-19 patients: Frailty predicts fatal outcome in older patients.* International Journal of Infectious Diseases, 2021. **102**: p. 415-421.
99. Thompson, J.V., et al., *Patient characteristics and predictors of mortality in 470 adults admitted to a district general hospital in England with Covid-19.* Epidemiology and Infection, 2020. **148**: p. 1-28.
100. Villar-García, J., et al., *Risk factors for SARS-CoV-2 infection, hospitalisation, and death in Catalonia, Spain: a population-based cross-sectional study*. 2020, Cold Spring Harbor Laboratory.
101. Wang, L., et al., *Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up.* Journal of Infection, 2020. **80**(6): p. 639-645.
102. Williamson, E.J., et al., *Factors associated with COVID-19-related death using OpenSAFELY.* Nature, 2020. **584**(7821): p. 430-436.
103. Yang, D., et al., *COVID-19 and chronic renal disease: clinical characteristics and prognosis.* QJM: An International Journal of Medicine, 2020. **113**(11): p. 799-805.

104. Zandkarimi, E., G. Moradi, and B. Mohsenpour, *The Prognostic Factors Affecting the Survival of Kurdistan Province COVID-19 Patients: A Cross-sectional Study From February to May 2020.* International Journal of Health Policy and Management, 2020.

Appendix A: Search Strategy

1. Systematic Reviews search strategy

Search date: 01/01/2020-01/05/2021

a. Embase 1974 to 01/05/2021

and

b. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to 01/05/2021

COVID-19 terms

Medline:

1. exp coronavirus/ or ((corona* or corono*) adj1 (virus* or viral* or virinae*)).ti,ab,kw. or (coronavirus* or coronovirus* or coronavirinae* or Coronavirus* or Coronovirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCoV or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARSCoV-2" or "SARSCoV2" or "SARS-CoV2" or SARSCov19 or "SARS-Cov19" or "SARSCov-19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ti,ab,kw. or (((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or "seafood market*" or "food market*") adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*)).ti,ab,kw. or ((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*)).ti,ab,kw. or "severe acute respiratory syndrome*".ti,ab,kw. or exp Coronavirus Infections/

Embase:

1. exp coronavirus/ or ((corona* or corono*) adj1 (virus* or viral* or virinae*)).ti,ab,kw. or (coronavirus* or coronovirus* or coronavirinae* or Coronavirus* or Coronovirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCoV or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARSCoV-2" or "SARSCoV2" or "SARS-CoV2" or SARSCov19 or "SARS-Cov19" or "SARSCov-19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ti,ab,kw. or (((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or "seafood market*" or "food market*") adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*)).ti,ab,kw. or ((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*)).ti,ab,kw. or "severe acute respiratory syndrome*".ti,ab,kw. or exp Coronavirus Infections/

Chronic Kidney disease terms

Medline:

1. exp Renal Dialysis/
2. (hemodialysis or haemodialysis).tw.
3. (hemofiltration or haemofiltration).tw.
4. (hemodiafiltration or haemodiafiltration).tw.
5. dialysis.tw.

6. (PD or CAPD or CCPD or APD).tw.
7. Renal Insufficiency/
8. Kidney Failure/
9. exp Renal Insufficiency, Chronic/
10. Kidney Diseases/
11. Uremia/
12. (end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw.
13. (ESRF or ESKF or ESRD or ESKD).tw.
14. (chronic kidney or chronic renal).tw.
15. (CKF or CKD or CRF or CRD).tw.
16. (predialysis or pre-dialysis).tw.
17. ur?emi$.tw.
18. or/1-17

Embase:

1. exp Renal Replacement Therapy/
2. (hemodialysis or haemodialysis).tw
3. (hemofiltration or haemofiltration).tw.
4. (hemodiafiltration or haemodiafiltration).tw.
5. dialysis.tw.
6. (PD or CAPD or CCPD or APD).tw.
7. Kidney Disease/
8. Chronic Kidney Disease/
9. Kidney Failure/
10. Chronic Kidney Failure/
11. Uremia/
12. (chronic kidney or chronic renal).tw.
13. (CKF or CKD or CRF or CRD).tw.
14. (end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw.
15. (ESRF or ESKF or ESRD or ESKD).tw.
16. ur?emi$.tw.
17. exp Kidney Transplantation/
18. or/1-17

Systematic Review filter:

Medline, Embase:

1. meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/
2. Meta Analysis.pt.
3. (meta analy* or metaanaly* or health technolog* assess*).ti,ab,kw.
4. (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
5. (((systematic* or methodologic*) adj3 (review* or overview*)) or pooled analysis or

published studies or published literature or hand search* or handsearch* or medline or pub med or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab,kw

6. (cochrane or (health adj2 technology assessment) or evidence report).jw.

Medrxiv

Terms used in medrxiv: “renal covid review”, “kidney covid review”, “End stage COVID review”, “kidney 2019 review”, “kidney corona review”, “renal corona review”, “dialysis corona review”, “dialysis COVID review”, “hemo covid review”, “hemodialysis corona review”, “hemodialysis covid-19 review”, “CKD corona review”, “CKD COVID review”, “Chronic kidney disease COVID-19 review”, “renal corona analysis”, “renal covid analysis”, “kidney covid analysis”, “kidney corona analysis”, “kidney sars-cov-2 analysis”, “renal sars-cov-2 analysis”, “kidney hcov-19 review”, “kidney hcov2 review”, “renal hcov2 review”, “renal hcov-19 review “ , “renal hcov-19 analysis”, “renal hcov2 analysis”, “kidney hcov-19 analysis”, “kidney hcov2 analysis”

Epistemonikos:

(title:(renal) OR abstract:(renal)) OR (title:(kidney) OR abstract:(kidney)) OR (title:(end stage) OR abstract:(end stage)) OR (title:(dialysis) OR abstract:(dialysis)) OR (title:(hemodialysis) OR abstract:(hemodialysis)) OR (title:(CKD) OR abstract:(CKD)) OR (title:(Chronic disease) OR abstract:(Chronic disease)) AND (title:(COVID-19) OR abstract:(COVID-19))

AND

(title:(COVID-19) OR abstract:(COVID-19)) OR (title:(Coronavirus) OR abstract:(Coronavirus)) OR (title:(SARS-COV-2) OR abstract:(SARS-COV-2)) OR (title:(SARS) OR abstract:(SARS)) OR (title:(hcov2) OR abstract:(hcov2)) OR (title:(hcov-19) OR abstract:(hcov-19))

AND

Systematic Reviews filter

AND

01012020 till 01052021

Cochrane Database:

"kidney disease" in Title Abstract Keyword OR CKD in Title Abstract Keyword OR kidney in Title Abstract Keyword OR dialysis in Title Abstract Keyword OR hemodialysis in Title Abstract Keyword - (Word variations have been searched)

AND

Last year filter

LitCOVID and SSRN:

Searched manually using keywords related to the topic (e.g. “CKD COVID-19 review”).

2. Primary studies search strategy
Search Date: 09/01/2020- 01/10/2021:

a. Embase 1974 to 01/10/2021

1. exp coronavirus/ or ((corona* or corono*) adj1 (virus* or viral* or virinae*)).ti,ab,kw. or (coronavirus* or coronovirus* or coronavirinae* or Coronavirus* or Coronovirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCoV or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARSCoV-2" or "SARSCoV2" or "SARS-CoV2" or SARSCov19 or "SARS-Cov19" or "SARSCov-19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ti,ab,kw. or (((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or "seafood market*" or "food market*") adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*)).ti,ab,kw. or ((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*)).ti,ab,kw. or "severe acute respiratory syndrome*".ti,ab,kw. or exp Coronavirus Infections/
2. exp Renal Replacement Therapy/
3. (hemodialysis or haemodialysis).tw.
4. (hemofiltration or haemofiltration).tw.
5. (hemodiafiltration or haemodiafiltration).tw.
6. dialysis.tw.
7. (PD or CAPD or CCPD or APD).tw.
8. Kidney Disease/
9. Chronic Kidney Disease/
10. Kidney Failure/
11. Chronic Kidney Failure/
12. Uremia/
13. (chronic kidney or chronic renal).tw.
14. (CKF or CKD or CRF or CRD).tw.
15. (end stage renal or end stage kidney or endstage renal or endstage kidney).tw.
16. ur?emi$.tw.
17. exp Kidney Transplantation/
18. (ESRF or ESKF or ESRD or ESKD).tw.

19. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18

20. 1 and 19

21. limit 20 to human

22. limit 21 to yr="2020 -Current"

b. OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to 01/10/2021

1. exp coronavirus/ or ((corona* or corono*) adj1 (virus* or viral* or virinae*)).ti,ab,kw. or (coronavirus* or coronovirus* or coronavirinae* or Coronavirus* or Coronovirus* or Wuhan* or Hubei* or Huanan or "2019-nCoV" or 2019nCoV or nCoV2019 or "nCoV-2019" or "COVID-19" or COVID19 or "CORVID-19" or CORVID19 or "WN-CoV" or WNCoV or "HCoV-19" or HCoV19 or CoV or "2019 novel*" or Ncov or "n-cov" or "SARS-CoV-2" or "SARSCoV-2" or "SARSCoV2" or "SARS-CoV2" or SARSCov19 or "SARS-Cov19" or "SARSCov-19" or "SARS-Cov-19" or Ncovor or Ncorona* or Ncorono* or NcovWuhan* or NcovHubei* or NcovChina* or NcovChinese*).ti,ab,kw. or (((respiratory* adj2 (symptom* or disease* or illness* or condition*)) or "seafood market*" or "food market*") adj10 (Wuhan* or Hubei* or China* or Chinese* or Huanan*)).ti,ab,kw. or ((outbreak* or wildlife* or pandemic* or epidemic*) adj1 (China* or Chinese* or Huanan*)).ti,ab,kw. or "severe acute respiratory syndrome*".ti,ab,kw. or exp Coronavirus Infections/

2. exp Renal Dialysis/

3. (hemodialysis or haemodialysis).tw.

4. (hemofiltration or haemofiltration).tw.

5. (hemodiafiltration or haemodiafiltration).tw.

6. dialysis.tw.

7. (PD or CAPD or CCPD or APD).tw.

8. Renal Insufficiency/

9. Kidney Failure/

10. exp Renal Insufficiency, Chronic/

11. Kidney Diseases/

12. Uremia/

13. (end stage renal or end stage kidney or endstage renal or endstage kidney).tw.

14. (ESRF or ESKF or ESRD or ESKD).tw.

15. (chronic kidney or chronic renal).tw.

16. (CKF or CKD or CRF or CRD).tw.

17. (predialysis or pre dialysis).tw.

18. ur?emi$.tw.

19. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18

20. 1 and 19

21. limit 20 to (humans and yr="2020 -Current")

c. Medrxiv

Terms used in medrxiv: “renal covid”, “kidney covid”, “End stage COVID”, “kidney 2019 ”, “kidney corona ”, “renal corona ”, “dialysis corona ”, “dialysis COVID ”, “hemo covid ”, “hemodialysis corona ”, “hemodialysis covid-19 ”, “CKD corona ”, “CKD COVID ”, “Chronic kidney disease COVID-19 ”, “renal corona ”, “renal covid ”, “kidney covid ”, “kidney corona ”, “kidney sars-cov-2 ”, “renal sars-cov-2 ”, “kidney hcov-19 ”, “kidney hcov2 ”, “renal hcov2 ”, “renal hcov-19 “ , “renal hcov-19 ”, “renal hcov2 ”, “kidney hcov-19 ”, “kidney hcov2 ”

c. Epistemonikos:

NA

d. Cochrane Database:

"kidney disease" in Title Abstract Keyword OR CKD in Title Abstract Keyword OR kidney in Title Abstract Keyword OR dialysis in Title Abstract Keyword OR hemodialysis in Title Abstract Keyword - (Word variations have been searched)

AND

Last year filter

e. LitCOVID and SSRN:

Searched manually using keywords related to the topic (e.g. “CKD COVID-19 review”).