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Does Conservative Kidney Management Offer A quantity or Quality of Life Benefit Compared to Dialysis? A Systematic Review

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Abstract

Background Patients with stage 5 chronic kidney disease (CKD5) collaborate with their clinicians when choosing their future treatment modality. Most elderly patients with CKD5 may only have two treatment options: dialysis or conservative kidney management (CKM). The objective of this systematic review is to investigate whether CKM offers a quantity or quality of life benefit compared to dialysis for some patients with CKD5.

Methods The databases MEDLINE, EMBASE, the Cochrane Library, and CINAHL were systematically searched for studies comparing patients with CKD5 treated with CKM or dialysis. The primary outcomes were survival and quality of life (QoL). Hospitalization, symptom burden, and place of death were secondary outcomes. For studies reporting hazard ratios, pooled values were calculated and forest plots conducted.

Results Twenty-four primary studies, all observational, were identified. All studies except one reported shorter survival in patients treated with CKM (pooled hazard ratio 0.53, 95% confidence interval 0.41-0.69). For patients aged ≥ 80 years and for elderly individuals with comorbidities, results were ambiguous. In most studies, CKM seemed advantageous for QoL and secondary outcomes. Findings were limited by the heterogeneity of studies and biased outcomes favouring dialysis.

Conclusions In general, patients with CKD5 live for a shorter time on CKM than on dialysis. In patients aged ≥ 80 years old, and in elderly individuals with comorbidities, the survival benefits of dialysis seem to be lost. Regarding QoL, symptom burden, hospitalization, and place of death, CKM may have advantages. Higher quality studies are needed to guide patients and clinicians in the decision-making process.

Introduction

Patients with CKD5 have high mortality rates (1). Most patients are older than 65 years old, and less than 20% are eligible for a kidney transplant (2).

Many of these older patients with CKD5 are not eligible for a kidney transplant because they are too frail. Therefore, when dialysis is needed, their treatment options are haemodialysis (HD) or peritoneal dialysis (PD), often in the form of assisted automated PD (AAPD). Dialysis can be burdensome for various reasons, including exhausting travel, complications related to the treatment, or the fact that it is so time-consuming. Thus, while dialysis may prolong patients' lives, it may adversely affect their QoL (3). For some patients, CKM could be a viable alternative to dialysis. CKM is a treatment strategy that gives patients all the same treatments as those on dialysis, omitting only the dialysis itself (4).

Patients and clinicians may find it challenging to discuss and decide on a future treatment modality based on both the best evidence and the individual patient's preferences. Various aspects have to be considered, which may lead to a complex decision-making process. What is important depends on

individual patients and may include survival, QoL, symptom burden, hospitalization, or place of death. Studies of this topic are sparse and heterogeneous, which presents challenges for clinical practice.

Usually, clinical guidelines inform clinical practice (5). The KDIGO guideline from 2012 (6) approaches the structure and process of CKM as an alternative treatment pathway for patients with CKD5 who choose not to pursue kidney replacement therapy. The guideline reports paucity in many of the areas reviewed. However, MEDLINE was the only database searched in establishing this guideline. The ERBP guideline from 2016 (7) addresses the question: *What is the benefit of dialysis in frail and older patients?* The guideline discusses many important factors related to treatment decision-making such as survival, QoL, symptom burden, and hospitalization. For some of the issues, however, only a few studies were identified. A more recent NICE guideline from 2018 (8) also addresses this question, but includes only mortality as an outcome. Given the lack of clinical guidelines, systematic reviews are beneficial in summarizing the evidence in studies around a specific topic. A number of systematic reviews of varying quality were published at around the same time as the ERBP guideline (9–12). To date, no randomized controlled trials (RCTs) have been published on this topic.

Recognizing the quality of the ERBP guideline from 2016, the objective of this systematic review is to investigate whether CKM involves quantity or quality of life compared to dialysis for some patients with CKD5 in terms of the outcomes of survival, QoL, hospitalization, symptom burden, and place of death.

Materials And Methods

The systematic review has been conducted as recommended by the Cochrane Collaboration (13). The process and results have been documented in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement for reporting systematic reviews (14, 15). The protocol for this review was prospectively registered with the Danish Health Authority, and no changes have been made. The review has been conducted by a working group involving doctors and nurses in nephrology as part of the preparation of a national clinical guideline. They have been supported with input from an interprofessional reference group consisting of representatives from the Danish Kidney Association and the Danish professional societies for nephrology, specialized palliative care, geriatrics, and general practitioners.

Eligibility Criteria

Participants

Based on the question *Does conservative kidney management offer a quantity or quality of life benefit compared to dialysis?* this review examined studies including adults aged 18 years old and above who had been diagnosed with CKD5. Studies that included adults with stage 1–4 chronic kidney disease (CKD1-4) or children were excluded.

Interventions

Studies investigating CKM interventions or any intervention defined as a treatment strategy without dialysis for patients with CKD5 were considered.

Comparators

The review included studies comparing interventions for patients treated with HD or PD.

Outcomes

The primary outcomes were survival and QoL. Secondary outcomes were hospitalization, symptom burden, and place of death, defined as whether the location of death was in accordance with a patient's preference.

Types of Studies Included

This review considered all study designs relevant for answering the PICO (Patient, Intervention, Comparison, Outcome) question, including secondary literature such as systematic reviews, clinical guidelines, and grey literature.

Information Sources

According to the pre-specified protocol, a comprehensive literature search was conducted by the working group in collaboration with a literary search specialist from October 9, 2018 to May 13, 2019. This searched for guidelines in English, Danish, Norwegian, and Swedish published in electronic databases. The databases searched were Guidelines International Network (G-I-N), NICE (UK), Scottish Intercollegiate Guidelines Network (SIGN), HTA database, SBU (Sweden), Socialstyrelsen (Sweden), Helsedirektoratet (Norway), Kunnskapssenteret (Norway), MEDLINE, EMBASE, and CINAHL. The databases searched for secondary literature as well as primary literature were MEDLINE, EMBASE, the Cochrane Library, and CINAHL [see Additional file 1].

Search Strategy

A three-phase search strategy was used to locate eligible studies. First, a search for clinical guidelines was conducted, followed by a search for secondary literature (Cochrane reviews, systematic reviews, and meta-analyses). Finally, primary literature was searched with no time limit. The full search protocols are given in the supplementary material [see Additional file 1].

Study Selection

The process of selecting studies was administered through the systematic review management tool Covidence (16). Titles were checked for duplicates when entering the eligible literature into Covidence. Two authors independently screened the titles and abstracts of the remaining studies for full-text retrieval. Similarly, two authors independently assessed full-text eligibility for inclusion. Discrepancies in judgement were resolved by consensus.

Data Extraction

All relevant data and outcomes (survival, QoL, hospitalization, symptom burden, and place of death) for the PICO question were extracted from each study by two authors independently. Consensus was reached regarding any discrepancies.

Risk of Bias within Studies

To assess the quality of the studies selected, the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool was used because only observational studies were included. Assessment was carried out at outcome level and summarized.

Risk of Bias across Studies

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology was used to assess the quality of the body of evidence for each relevant outcome in the selected studies (17).

Data Synthesis

The data extracted from the selected studies was entered into the Review Manager (RevMan5) software (18), used for preparing and updating Cochrane Reviews. When applicable, outcomes were gathered and weighted in forest plots.

Means with standard deviations (SD), mean differences, and medians with confidence intervals at a 95% confidence level (95% CI) were gathered for continuous data where possible. Hazard ratios (HR), relative risks (RR), and odds ratios (OR) with 95% CI were collected from dichotomous data. A few outcomes are shown in forest plots but mostly relevant findings are presented narratively.

Results

After removal of duplicates, screening of titles and abstracts, and subsequent full-text assessment, a total of one guideline, four systematic reviews, and 24 primary studies were identified. The flow diagram in Fig. 1 gives details of the primary literature search process. Flow diagrams for the guideline search and review search are included in the supplementary material [see Additional file 2].

Guideline and Systematic Reviews

The ERBP guideline (7) covers the evidence relevant for our PICO question until the end of the guideline's literature search in May 2016. All four of the systematic reviews identified (9, 10, 12, 19) synthesized the evidence. Not all of the outcomes selected for the PICO question in this review were discussed in the earlier reviews. Two studies conducted meta-analyses, with one including hospitalization and mortality as outcomes (12), and the other looking at survival (9). The guideline and all the earlier reviews involved primary studies that were excluded from our review. In the supplementary material, we have provided an overview of the primary studies included in our review compared to studies included in the ERBP guideline and the four systematic reviews selected [see Additional file 3]. The supplementary material

also provides a list of studies present in the guideline or reviews that we did not include, with references and reasons for exclusion [see Additional file 4].

Primary Literature

Table 1 presents basic characteristics and data extraction for the 24 primary studies selected. All studies are observational: 9 prospective cohort studies (3, 20–27); 11 retrospective cohort studies (28–38); and 4 cross-sectional studies (39–42). In general, patients on CKM were older and, when reported, had more comorbidities and poorer functional status compared to other groups. The heterogeneity between studies in relation to interventions, comparators, statistical analyses, and treatment modalities affected the possibility of conducting forest plots for all outcomes except survival, mortality, and hospitalization. Even for these three outcomes, not all studies reported data suitable for forest plots. The quality assessments using ROBINS-I are presented in the supplementary material [see Additional file 5].

Table 1
Table with Details of the Primary Studies Selected for Inclusion

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Almutary, 2016 (40)	Non-dialysis group (CKD4 & CKM (CKD5)) Dialysis group (HD & PD)	Total group 48.29 (± 14.86) CKM (CKD5), 51.84 ± 15.11 HD, 47.71 ± 14.46 PD, 43.08 ± 15.09	CKM (CKD5), 38	HD, 287 PD, 42	*Symptom burden* (CKD-SBI) Dialysis vs. CKM (CKD5): HD: 23.36 ± 16.99; PD: 12.04 ± 6.58, vs. CKM (CKD5): 8.1 ± 8.04; $p < 0.001$
Carson, 2009 (23)	CKD5	Age ≥ 70 at inclusion CKM, mean 81.6; median 83 Dialysis, mean 76.4; median 75	CKM, 29	Dialysis, 173	*Hospitalization rate* Hospital days/patient days survived: CKM, 4.3 ± 0.26; RRT, 6.9 ± 0.71 *Place of death* Home/hospice: CKM, 40%; Dialysis 21%, Hospital: CKM, 36%; Dialysis 70%

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Chandna, 2011 (38)	CKD5	CKM 77.5 ± 7.6 Dialysis 58.5 ± 15.0	CKM, 155	Dialysis, 689	*Survival* Survival in patients aged > 75: CKM vs. dialysis, HR: 1.18 (95% CI: 0.79–1.76); p = 0.428. In patients with comorbidity score > 4: Dialysis, 25.8 ± 4.4(SE); CKM, 20.4 ± 2.4(SE); p = 0.83.
Da Silva-Gane, 2012 (3)	CKD4-5	HD 60.6 ± 14.9 PD 48.0 ± 15.6 CKM 77.5 ± 6.5	CKM, 30	HD,80 PD, 44	*Survival* HD vs. CKM, HR 0.47 (95% CI: 0.20–1.10); p = 0.08 PD vs. CKM, HR: 0.39 (95% CI: 0.10–1.48); p = 0.17 *Quality of life* No difference over time in groups.
Hussain, 2013 (37)	CKD5	Age > 70 at inclusion	CKM, 172	Dialysis, 269	*Hospitalization* Dialysis vs. CKM, RR 1.6 (95% CI: 1.14–2.25), p < 0.05.

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Iyasere, 2019 (39)	CKD5	Median age (IQR) CKM, 83 (80–88) aAPD, 81 (79–88) HD, 82 (78–85)	CKM, 28	HD, 28 PD, 28	*Quality of life* SF-12, PCS: CKM, 28.9 ± 10.0; dialysis, 29.2 ± 8.3; p = 0.90 SF-12, MCS: CKM, 46.3 ± 12.1; dialysis, 49.9 ± 12.9; p = 0.28
Joly, 2003 (22)	CKD4-5	Age ≥ 80 at inclusion CKM 84.1 ± 2.9 Dialysis 83.2 ± 2.9	CKM, 43	Dialysis, 101	*Survival* CKM, 8.9 months (95% CI: 4–10); dialysis, 28.9 months (95% CI: 24–38); p < 0.0001
Kwok, 2016 (36)	CKD5	Age ≥ 65 at inclusion CKM 79.6 ± 6.8 Dialysis 74.2 ± 6.1	CKM, 432	Dialysis, 126	*Survival* CKM, 10.0 months (95% CI: 8.3–11.7); dialysis, 44.6 months (95% CI: 37.3–51.9); p < 0.001.

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

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Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Murtagh, 2007 (28)	CKD5	Age > 75 at inclusion CKM, 81.36 Dialyse, 78,17	CKM, 77	Dialysis, 52	*Survival* CKM vs. dialysis, HR: 2.90 (95% CI: 1.60–5.26); In patients with comorbidity score > 2: Dialysis vs CKM: log rank statistic < 0.001, df 1, p = 0.98, In patients with ischaemic heart disease: Dialysis vs CKM: log rank statistic 1.46, df 1, p < 0.27.
Raman, 2018 (21)	CKD5	Dialysis, 78.9 ± 2.8 CKM, 83.7 ± 4.2	CKM, 81	Dialysis, 123	*1-year survival* Dialysis vs. CKM, OR 0.38 (95% CI: 0.09–1.60); p = 0.19 *Hospitalization* Number of admission days (median (IQR)): CKM, 0.8 (0.0-8.7); dialysis, 2.2 (0.7–14.7); p = 0.005.
Reindl-Schwaighofer, 2017 (35)	CKD5	Age > 65 at inclusion HD, 74.06 ± 5.78 CKM, 81.22 ± 7.23	CKM, 174	HD, 8622	*Survival* HD vs. CKM, HR: 0.23 (95% CI: 0.18–0.29); p < 0.001.

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Shah, 2019 (41)	CKD5	Age ≥ 75 at inclusion *Median age (IQR)*: Dialysis, 81 (78–84) CKM, 83 (81–87) *Age ≤ 81, n (%)*: Dialysis 50 (6) CKM 19 (41) *Age > 81, n (%)*: Dialysis 33 (40) CKM 27 (59)	CKM, 46	Dialysis, 83	*Quality of life* Dialysis vs. CKM, adjusted differences in KDQOL-36 scores (95% CI): KDQOL-burden of disease: -28.59 (-41.77 to -15.42); p < .001 KDQOL-symptoms of disease: -5.93 (-14.61 to 2.73); p = 0.18 KDQOL-effects of disease: -16.49 (-25.98 to -6.99); p < 0.001
Shih, 2014 (34)	CKD5	Age ≥ 70 at inclusion CKM, 82.0 ± 6.4 Dialysis, 78.6 ± 7.1	CKM, 2049	Dialysis, 6292	*Mortality* Dialysis vs. CKM, HR: 1.39 (95% CI: 1.30–1.49), p < 0.001

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Shum, 2014 (33)	CKD5	Age 65–90 at inclusion Overall age, 73.8 ± 5.4 CKM, 75.3 ± 5.7 PD, 73.4 ± 5.3	CKM, 42	PD, 157	*Survival* PD vs. CKM, HR: 0.46 (95% CI 0.31–0.68), p < 0.001. *Hospitalization* Days per person year, median [IQR] PD, 16.17 [6.29–43.32] vs. CKM, 38.01 [6.75–76.56]; p = 0.03
Smith, 2003 (24)	CKD5	CKM (palliative care population), 71 ± 12; Dialysis, 59 ± 15	CKM, 63	Dialysis, 258	*Survival* Dialysis, median survival 8.3 months; CKM, median survival 6.3 months; N.S. *Place of death* Deaths at home or in a hospice: CKM, 22 of 34 deaths (65%) Dialysis, 11 of 41 deaths (27%); p = 0.001

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Tam-Tham, 2018 (32)	CKD5	Age ≥ 65 at inclusion *Age 65 to < 75 (n, %)* Dialysis, 228 (45.6) CKM, 45 (13.3) *Age 75 to < 85 (n, %)* Dialysis, 220 (44.0) CKM, 143 (42.3) *Age ≥ 85 (n, %)* Dialysis, 52 (10.4) CKM, 150 (44.4)	CKM, 338	Dialysis, 500	*Mortality* Dialysis vs. CKM (0–3 years), HR: 0.56 (95% CI: 0.44–0.71); p < 0.001 Dialysis vs. CKM (after 3 years), HR: 1.98 (95% CI: 1.16–3.37); p = 0.12 *Hospitalization* Dialysis vs. CKM, HR: 1.40 (95% CI: 1.16–1.69), p = 0.001
Tan, 2017 (26)	CKD5	Age > 65 at inclusion CKM, 84 Dialysis, 73	CKM, 8	Dialysis, 12	*Symptom burden* Change (improvement) in mean symptom POS-score over 6 months: CKM, 1.5; dialysis, 7.58; p < 0.002.

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

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Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Teo, **2010 (25)**	CKD5	CKM, 67.4 ± 11.8 HD, 58.7 ± 12.9	CKM, 16	HD, 102	*Mortality* CKM, HR: 2.29 (95% CI: 1.16–4.45); HD, HR: 0.59 (95% CI: 0.33–1.05); p = 0.042
Teruel, **2015 (31)**	CKD5	Median age (IQR) Dialysis, 68 (54,76) CKM, 83 (78,86)	CKM, 90	Dialysis, 142	*Mortality* CKM, 8.2/100 patient months; Dialysis, 0.6/100 patient months; p < 0.001
van Loon, **2019 (20)**	CKD5	Age ≥ 65 at inclusion CKM, 82 ± 6 Dialysis, 75 ± 7	CKM, 89	Dialysis, 192	*12-month mortality* CKM vs. dialysis, HR: 2.12 (95% CI: 1.12–4.03); p = 0.02 *In patients < 80 years old*, HR: 5.05 (95% CI: 1.90–13.50); p < 0.01 *In patients ≥ 80 years old*, HR: 1.30 (95% CI: 0.58–2.91); p = 0.53 *Six-month quality of life* EQ-5D Index, mean (SE) change within group: CKM, 0.047 (0.022); p < 0.01

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
					Dialysis, 0.026 (0.014); p = 0.10 Between group difference, p < 0.01 *Hospitalization* Median number [IQR] of admissions: CKM, 1 [1–5]; Dialysis, [1–4]; p = 0.27 *Hospitalization* Median number [IQR] of admission days: Dialysis, 7 [3–15]; CKM, 4 [2–12]; p = 0.22

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Verberne, 2018 (30)	CKD5	CKM, 82.6 ± 4.5 Dialysis, 76.2 ± 4.4	CKM, 126	Dialysis, 240	*Survival* CKM vs. dialysis, HR: 1.67 (95% CI: 1.19–2.35), p = 0.003 Median [IQR] survival in years in patients ≥ 70 years old: CKM, 1.3 [0.5–2.5]; dialysis, 3.1 [1.7–6.4]; p < 0.001 Median [IQR] survival in years in patients ≥ 80 years old: CKM, 2.3 [1.3–3.7]; dialysis, 2.9 [1.9-6.0]; p = 0.13 *Quality of life* No difference between groups
Verberne, 2016 (29)	CKD5	CKM, 83 ± 4.5 Dialysis, 76 ± 4.4	CKM, 107	Dialysis, 204	*Survival* Dialysis vs. CKM, HR: 0.62 (95% CI: 0.42–0.92), p = 0.02. Median [IQR] survival in years in patients ≥ 80 years old: CKM, 1.4 [0.7-3.0]; dialysis, 2.1 [1.5–3.4]; p = 0.08.

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Author, year of publication	Population	Age (years)[1]	Intervention, n	Comparator, n	Main outcome measures and results[1]
Yong, 2009 (42)	CKD5	CKM, 73.1 ± 7.1 Dialysis, 58.2 ± 11.4	CKM, 45	Dialysis, 134	*Symptom burden* Number of symptoms CKM, 8.2 ± 3.9; dialysis 9.3 ± 4.7, p = 0.243
Yuen, 2016 (27)	CKD5	CKM, 76.8 ± 9.1 Dialysis, 58.6 ± 12.6	CKM, 335	Dialysis, 265	*One-year survival (%)* CKM, 57.3 ± 2.9; dialysis, 89.7 ± 2.1 *3-year survival (%)* CKM, 16 ± 2.7; dialysis, 74.6% ± 3.4

CKD4 and CKD5, stage 4 and 5 chronic kidney disease; CKM, conservative kidney management; HD, haemodialysis; PD, peritoneal dialysis; AAPD, assisted automated peritoneal dialysis; IQR, interquartile range; HR, hazard ratio; eGFR, estimated glomerular filtration rate; SE, standard error; RR, relative risk; CKD-SBI, The CKD Symptom Burden Index; SF-12, short form 12; MCS, mental component summary; PCS, physical component summary; KDQOL, Kidney Disease Quality of Life; POS, Palliative Outcome Scale; EQ-5D, European Quality of life-5 Dimensions.

[1]Unless otherwise noted, values are expressed as mean ± SD.

Survival/mortality

In total, 18 of both prospective and retrospective primary observational studies comparing CKM and dialysis, patients on CKM had shorter survival or higher mortality rates (3, 20–25, 27–33, 35–38). Forest plots are presented in Figs. 2–4. One retrospective study, however, reported a 1.4-fold increase in risk of mortality for patients ≥ 70 years old who were treated with dialysis (34). In a study of patients ≥ 75 years old, the difference between the poorer survival rate for those on CKM compared to dialysis was significantly further reduced in patients with high comorbidities, especially ischemic heart disease (28). For patients ≥ 80 years, the results seem to be conflicting. One study investigating octogenarians reported shorter survival for patients on CKM (22). In contrast, three other studies found overall that survival was equal for patients ≥ 80 years old (20, 29, 30).

Quality of life

One prospective cohort study found that patients with CKD5 on CKM had poorer self-reported QoL at baseline compared to patients on dialysis, but only with a borderline significance (p = 0.05) (20). At a six-month follow-up, self-reported QoL was higher among patients on CKM compared to those on dialysis (p < 0.01). Another prospective cohort study found no difference in the mental health summary scores at baseline but significant difference in the physical health summary scores (p = 0.001). There were, however, no difference in QoL over time (3). In a retrospective cohort study, there were no difference

between patients managed conservatively and dialysis patients on physical and mental health summary scores (30). The results of two cross-sectional studies are heterogeneous (39, 41). One study found no difference in self-reported QoL (SF-36) between patients on CKM, HD, or PD (39). Results from the other cross-sectional study varied depending on the tool used to measure QoL.

Symptom burden

In a small prospective study, commencement of dialysis in a younger cohort of elderly patients was associated with decrease in overall symptom burden (26). Two cross-sectional primary comparative studies found that patients on CKM had a lower symptom burden compared to patients on dialysis (40, 41). A third cross-sectional study comparing a group of patients with CKD5 receiving palliative care and patients on dialysis found overlapping symptom prevalence and intensity between the groups (42).

Hospitalization

We identified three prospective (20, 21, 23) and three retrospective (32, 33, 37) primary cohort studies comparing the hospitalization of patients. Results were heterogeneous. Most studies found that patients on CKM had fewer hospital admissions or a significantly lower risk of hospitalization than patients on dialysis (21, 23, 32, 37). Figure 5 shows a meta-analysis of the number of admission days. One study observed no difference in number of hospital admissions and number of days spent in hospital between groups (20). Finally, one study comparing patients treated with CKM to patients on PD observed fewer days spent in hospital per person year for the patients treated with PD (33).

Place of death

Results from two primary studies indicate that patients on CKM more often die at home or in a hospice compared to patients on dialysis, who more often die in hospital (23, 24).

Discussion

Summary of Evidence

This review identified 24 studies comparing patients with CKD5 receiving CKM with those on dialysis to investigate the outcomes of survival, QoL, symptom burden, hospitalization, and place of death. The studies were of variable quality, and there was substantial heterogeneity in presentation of the data, making it difficult to conduct an adequate forest plot for most outcomes.

Based on the available evidence, according to our review, CKM does not provide the same or extended survival in patients with CKD5 compared to dialysis. This is in line with previous systematic reviews (9, 12). Overall, in contrast to CKM, dialysis is life prolonging. However, some studies indicate that the two treatment strategies may provide equal rates of survival for patients who are 80 years old and above, or elderly patients with high comorbidities (20, 28, 29, 34). Thus, information on CKM may be considered in clinical practice in relation to this patient group. Some studies indicate that CKM may result in higher QoL compared to dialysis, and patients who receive CKM seem to have less hospitalization than patients on

dialysis (20, 39–41). Regarding symptom burden, results are conflicting. A recently published systematic review (Epub ahead of print) concludes that in selected older patients, CKM has the potential to achieve similar QoL compared to a dialysis pathway (43).

Most of the studies identified compared patients on HD with those treated with PD or did not report details of dialysis modality. There is very little data comparing patients on CKM with patients on PD. Our findings suggest that there may be differences between these two patient groups for the outcomes of symptom burden and hospitalization. Thus, these aspects should be considered in the decision-making process involved in choosing a patient's preferred treatment strategy.

Only one study investigated whether preferred place of death for patients with CKD5 on either CKM or dialysis was congruent with their actual place of death (23). The study indicated that patients on the CKM pathway more often die at home or in a hospice compared to patients on dialysis, who more often die in hospital. Studies of the general public and of patients with cancer have shown that most people would prefer to die at home (44, 45). Based on our review, dying at home or in a hospice seems more likely to be the outcome for patients managed conservatively compared to patients on dialysis (23, 24). Whether this result fulfils patients' preferences is, however, unclear.

Strengths and Limitations

This review was conducted rigorously, using robust processes and relevant software tools. However, the study does have some limitations. All previous studies analysed were of observational design with variable sample size and quality, and investigated patient groups that were heterogeneously defined. Furthermore, outcomes were assessed over different time periods. The quality of studies was reduced due to lead time bias when estimating survival, and by confounders mostly favouring dialysis. Data heterogeneity restricted the use of forest plots.

Implications for Clinical Practice and Further Research

Discussion of treatment options with clinicians is crucial for patients with CKD5 regardless of their preferred modality of treatment. In a recent qualitative study from the UK, 20 patients receiving CKM were interviewed (46). The patients' experience was that clinicians avoided talking about diagnosis and prognosis related to their disease. The patients expressed a desire to receive information related to their disease and possible treatment choices. At the same time, however, they were ambivalent about receiving detailed knowledge on the progression of their disease. Although the evidence in our review relies on observational data, the results suggest a CKM pathway can be an acceptable alternative to dialysis for patients aged 80 years and above or elderly patients with comorbidities. Consequently, discussion of CKM as a future treatment modality with this group of patients is important. A Canadian survey from 2010 showed that 60% of the patients receiving dialysis regretted having started the treatment (47). The findings of one qualitative review indicated that patients with CKD are capable of prioritizing QoL and freedom over survival (48). Based on the findings of this review, aspects of QoL, symptom burden, and

hospitalization should be considered in the decision-making process when choosing the preferred treatment strategy.

To date, the evidence of outcomes for patients with CKD5 receiving dialysis compared to patients on a CKM pathway has been drawn from observational studies of varying quality, many of which were retrospective. No randomized controlled studies have yet been published in this area. For ethical reasons, conducting such studies may be very problematic or even impossible. Thus, future research may also have to rely mainly on observational studies. Such studies should be carefully planned, with a prospective design and a strict methodology to minimize bias and the influence of confounders. Comparative studies of patients on CKM or PD may provide a more nuanced basis for discussions of future treatment choices for patients with CKD5.

Conclusions

In this systematic review, we explored studies evaluating CKM as an alternative to dialysis for adult patients with CKD5 in relation to survival, QoL, hospitalization, symptom burden, and place of death. Overall, patients with CKD5 on CKM have poorer survival compared to patients on dialysis. However, we observed that for patients aged 80 years and above, or elderly patients with severe comorbidities, the improved survival on dialysis over CKM appears to vanish. Despite some inconsistencies, the results suggest CKM has advantages compared to dialysis for the outcomes of QoL, hospitalization, symptom burden, and place of death. These findings should be addressed when discussing future treatment options with patients. More rigorously conducted studies are needed to establish a better base for such a decision-making process.

List Of Abbreviations

CKD5 Stage 5 chronic kidney disease

CKM Conservative kidney management

QoL Quality of life

HD Haemodialysis

PD Peritoneal dialysis

AAPD Assisted automated peritoneal dialysis

RCTs Randomized controlled trials

PRISMA Preferred reporting items for systematic reviews and meta-analyses

CKD 1-4 Stage 1-4 chronic kidney disease

PICO Patient, Intervention, Comparison, Outcome

ROBINS-I Risk Of Bias In Non-randomized Studies of Interventions tool

GRADE The Grading of Recommendations Assessment, Development and Evaluation methodology

RevMan5 Review Manager software

SD Standard deviations

95% CI 95% confidence Interval

HR Hazard ratios

RR Relative risks

OR Odds ratios (OR)

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Data sharing is not applicable to this article as no dataset were generated or analysed during the current study

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

All authors collected the data and conducted the analyses. Buur LE drafted the manuscript in collaboration with Finderup J. All authors critically reviewed and provided intellectual input to the manuscript. All authors read and approved the final manuscript.

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Figures

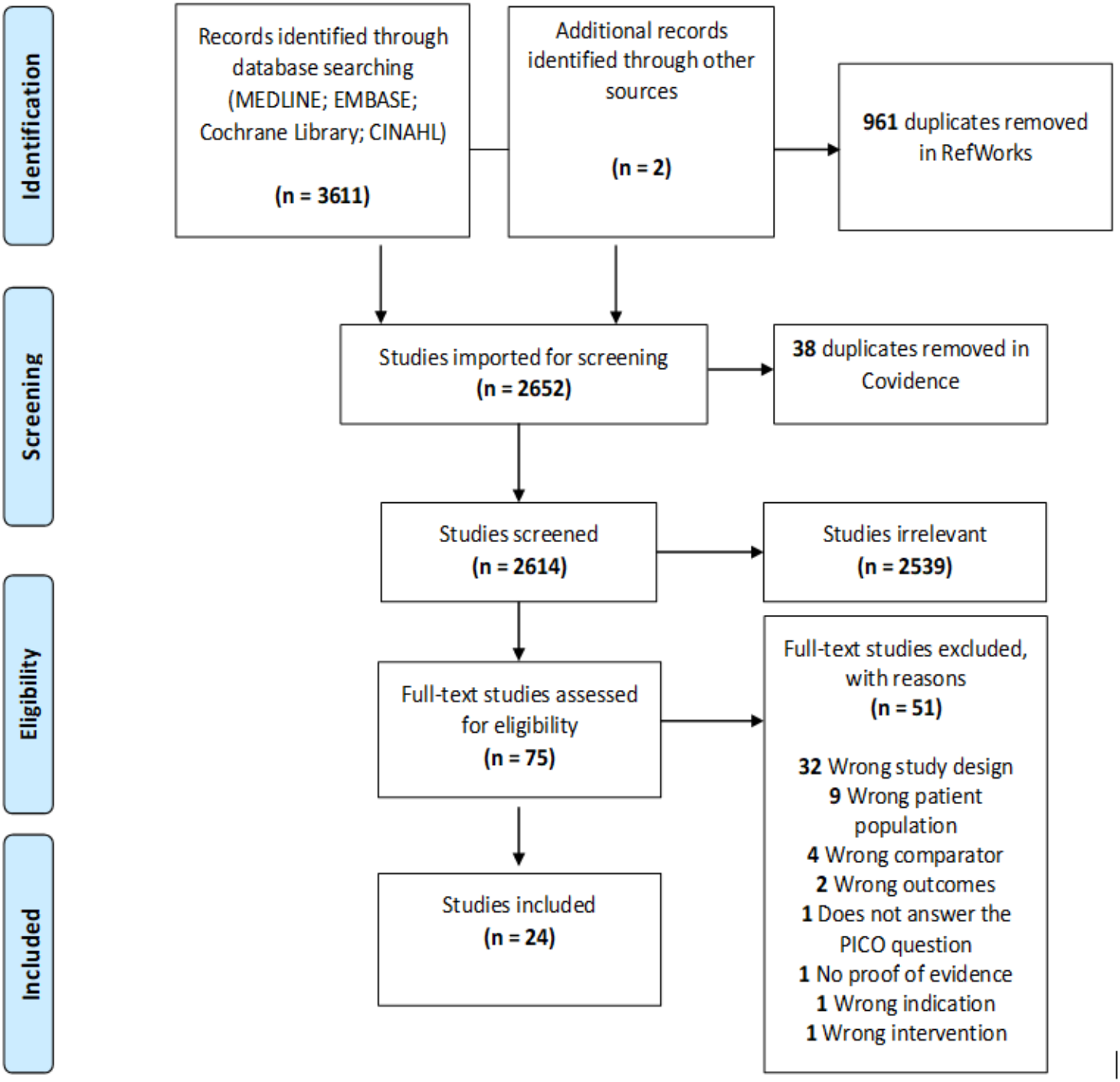

Figure 1

Flow chart for primary literature search

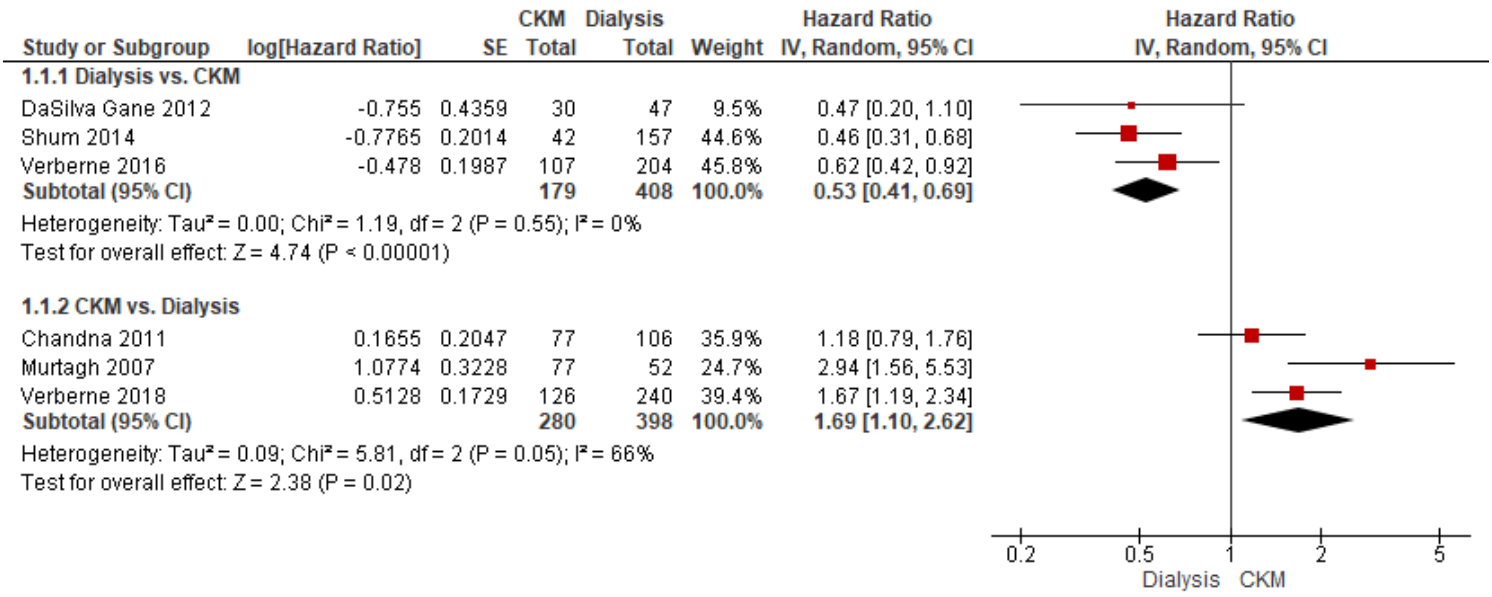

Figure 2

Forest plots of comparison: CKM versus dialysis for outcome: survival

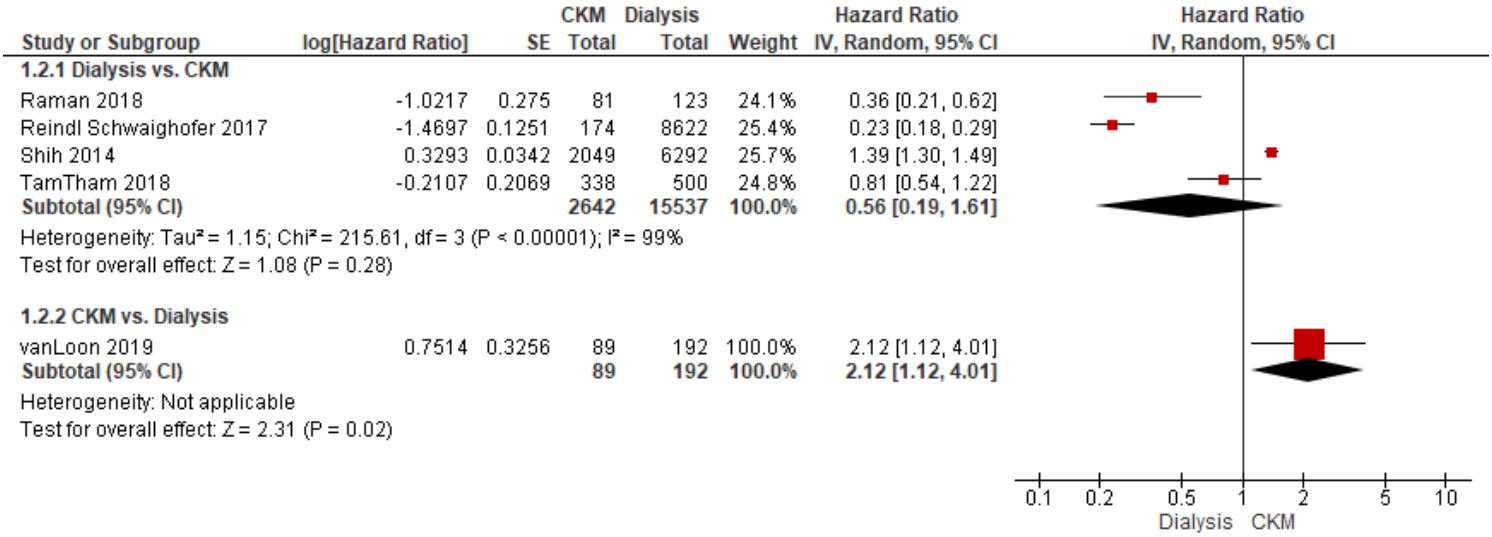

Figure 3

Forest plots of comparison: CKM versus dialysis for outcome: mortality

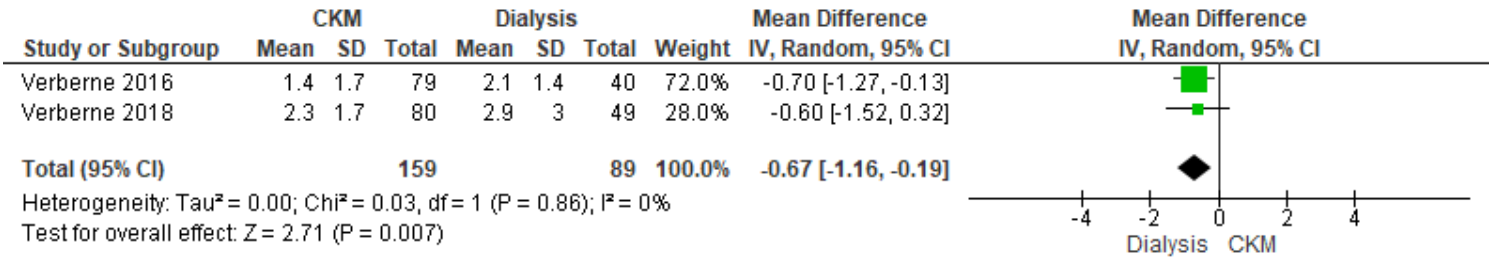

Figure 4

Forest plot of comparison: CKM versus dialysis for outcome: survival aged ≥ 80 years

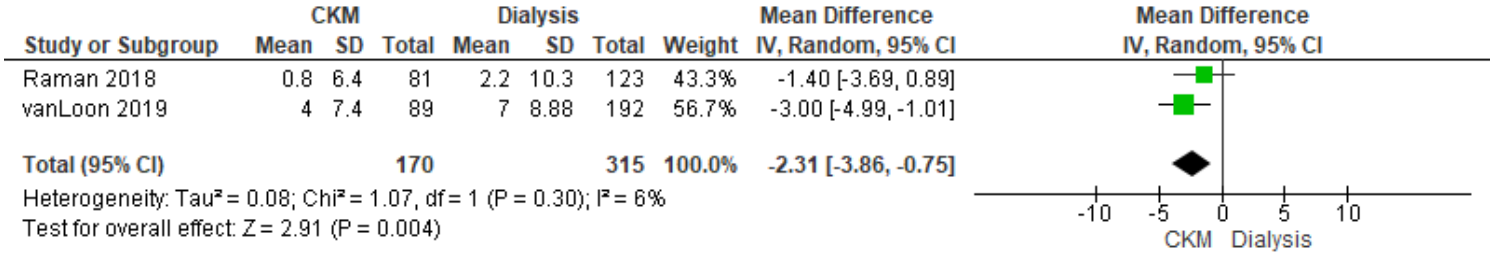

Figure 5

Forest plot of comparison: CKM versus dialysis for outcome: hospitalization – number of days spent in hospital

Supplementary Files

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