Person-Centered Integrated Care for Chronic Kidney Disease
A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

Background and objectives The effectiveness of person-centered integrated care strategies for CKD is uncertain. We conducted a systematic review and meta-analysis of randomized, controlled trials to assess the effect of person-centered integrated care for CKD.

Design, setting, participants, & measurements We searched MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (from inception to April of 2016), and selected randomized, controlled trials of person-centered integrated care interventions with a minimum follow-up of 3 months. Random-effects meta-analysis was used to assess the effect of person-centered integrated care.

Results We included 14 eligible studies covering 4693 participants with a mean follow-up of 12 months. In moderate quality evidence, person-centered integrated care probably had no effect on all-cause mortality (relative risk [RR], 0.86; 95% confidence interval [95% CI], 0.68 to 1.08) or health-related quality of life (standardized mean difference, 0.02; 95% CI, −0.05 to 0.10). The effects on renal replacement therapy (RRT) (RR, 1.00; 95% CI, 0.65 to 1.55), serum creatinine levels (mean difference, 0.59 mg/dl; 95% CI, −0.38 to 0.36), and eGFR (mean difference, 1.51 ml/min per 1.73 m²; 95% CI, −3.25 to 6.27) were very uncertain. Quantitative analysis suggested that person-centered integrated care interventions may reduce all-cause hospitalization (RR, 0.38; 95% CI, 0.15 to 0.95) and improve BP control (RR, 1.20; 95% CI, 1.00 to 1.44), although the certainty of the evidence was very low.

Conclusions Person-centered integrated care may have little effect on mortality or quality of life. The effects on serum creatinine, eGFR, and RRT are uncertain, although person-centered integrated care may lead to fewer hospitalizations and improved BP control.


Introduction

Person-centered integrated care has been advocated as a way to improve the management and health outcomes of people with CKD (1–3). Several reviews have shown beneficial effects of person-centered integrated care for patients with other chronic diseases like diabetes (4,5), heart failure (6,7), depression (8,9), and chronic obstructive pulmonary disease (10). The World Health Organization describes person-centered integrated care as health services that are managed and delivered in a way so that patients receive a continuum of preventive and curative services according to their needs over time that is coordinated across different levels (e.g., clinical, professional, organizational) of the health system (11). Because person-centered integrated care interventions vary in terms of content, duration, and delivery, it is critical to understand the composition and specific types of interventions that might lead to improved clinical outcomes within a specific context (12). Following the Rainbow Model of Integrated Care (RMIC), person-centered integrated care has been defined as multifaceted health interventions aimed at coordinating care at the clinical (e.g., self-management, case management), professional (e.g., multidisciplinary care, continuity of care), or organizational (e.g., disease management, managed care programs) levels (13) (see Supplemental Table 1). Few studies so far have investigated whether effectiveness of person-centered integrated care approaches might differ between these types of interventions.

Although less attention has been paid to person-centered integrated care strategies for CKD, similar challenges are present regarding the effectiveness of interventions for the management of CKD (12,14–17). Wang et al. (18) provided the first systematic review of multidisciplinary care interventions for patients with CKD stages 3–5 on all-cause mortality, risk of hospitalization, and risk of starting RRT (hemodialysis, peritoneal dialysis, and kidney transplant). Multidisciplinary care was associated with lower all-cause mortality and dialysis in observational studies, but the effectiveness of person-centered integrated care was
not confirmed in randomized, controlled trials (RCTs). Limitations of the systematic review included a limited search strategy and paucity of outcome measures. In addition, existing evidence has not explored the extent to which differences in outcomes between studies could be explained by variences in type of interventions.

In this systematic review, we have summarized the current evidence of person-centered integrated care strategies for the management of CKD in published RCTs and assessed the extent to which differences in outcomes can be explained by different interventions, following the RMIC.

Materials and Methods

A systematic review was conducted according to a protocol registered at International Prospective Register of Systematic Reviews (registration number CRD42016038949; https://www.crd.york.ac.uk/prospero/) and to the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines (19).

Data Sources and Searches

We searched MEDLINE (1946 to April of 2016 through Ovid), Embase (1974 to April of 2016 through Ovid), and the Cochrane Library database (Cochrane CENTRAL), using disease-specific and integrated care–specific text words and medical subject headings (Supplemental Tables 2–4).

Study Selection

Study selection, assessment of eligibility criteria, risk of bias assessment, and data extraction were performed independently by two researchers (P.P.V. and F.A.P.), with disagreement resolved through iteration and discussion. In case this failed, a third arbitrary resolution was made by a third author (G.F.M.S. or H.J.M.V.). Studies were considered eligible if they were RCTs with follow-up of 3 months or longer; included patients with a diagnosis of CKD; and comprised evaluation of person-centered integrated care at the clinical, professional, or organizational levels according to the RMIC (13). Each intervention had to describe a structured, coordinated care planning activity, according to the descriptions in Supplemental Table 1. No language restrictions were applied in the retrieval of citations; potentially eligible studies warranting further review were translated into English as necessary.

Data Extraction and Risk of Bias Assessment

For each included study, two researchers (P.P.V. and F.A.P.) independently extracted data using a standardized data extraction form. Any inconsistency was resolved through iteration and discussion. The methodologic risks of bias for each selected study were assessed on sequence generation; allocation concealment; blinding of outcome assessors, care providers, and participants; completeness of outcome data; intention to treat analysis; and sponsor involvement in authorship (20).

Data Synthesis and Analysis

The primary outcomes included all-cause and cardiovascular mortality, all-cause hospitalization, and health-related quality of life (assessed by recognized and/or validated measures). Secondary outcomes of interest were kidney function (defined as eGFR, serum creatinine, or rate of RRT), BP (defined as rate of controlled BP [<130/80 mm Hg], or systolic and/or diastolic BP defined as mm Hg), cost, and process of care delivery (defined as care coordination, accessibility of care, patient satisfaction, or implementation of care assessed by recognized and/or validated measures).

We used DerSimonian and Laird random-effects model to summarize treatment effects and expressed results as relative risks (RR) for binary outcomes (mortality, hospitalization, RRT, and controlled BP), mean differences (MD) for continuous outcomes (eGFR, serum creatinine, and systolic and diastolic BP), and standardized mean differences (SMD) for continuous outcomes using different scales together with 95% confidence intervals (95% CIs). If there were multiple time points per reported outcome, we included only the last time point. We included all relevant studies in the systematic review, and for the meta and subgroup analyses we required a minimum of three independent studies to justify a meta-analysis (21).

Heterogeneity in treatment effects between studies was assessed using $I^2$ statistics, with $I^2$ values of 25%, 50%, and 75% corresponding to low, moderate, and high levels of heterogeneity (22). Potential sources of statistical heterogeneity were explored using a priori subgroup analysis to determine whether study design (RCT; cluster-RCT), follow-up time (3–12 months; >12 months), or stage of CKD (CKD stages 3–5; CKD stage 5D [on dialysis]; CKD and comorbidity). Evidence of small study effects was assessed by visual examination of funnel plots (23). We planned for sensitivity analysis on primary outcomes by excluding studies according to the following criteria: (1) high risk of bias, (2) long follow-up (>12 months), (3) non-English publications, and (4) severe stages of CKD (CKD stage 5D [on dialysis], or CKD and comorbidity), using a minimum of ten independent studies (20). All analyses were performed using Review Manager version 5.3 (Revman; The Cochrane Collaboration, Oxford, UK) (20).

Quality of Evidence

The quality of evidence was rated for each pooled analysis using the Grades of Recommendation, Assessment, Development, and Evaluation approach (24). The quality of evidence was not downgraded for performance and/or detection bias because perfect blinding is considered problematic for a complex health intervention like person-centered integrated care (25). For each comparison, two researchers (P.P.V. and F.A.P.) independently rated the quality of evidence for each outcome as “high,” “moderate,” “low,” or “very low.” Any discrepancies were resolved through iteration and discussion.

Results

Search Results and Study Characteristics

The systematic search yielded 15 publications including four unique studies assessing 4693 patients (Figure 1). See Supplemental Table 5 for a detailed overview of the excluded publications, and Supplemental Table 6 for a detailed overview of the included studies. One study investigating the effect of person-centered integrated care on quality of life reported
inconsistent results; this resulted in 13 studies providing information on 4603 people with kidney disease to be included in the meta-analysis. Table 1 summarizes the characteristics of the included studies.

**Intervention Characteristics**

The characteristics of interventions in the included studies are summarized in Table 2. Most interventions were targeted at the clinical care coordination level (50%), including case management (four studies; 879 participants) or self-management support interventions (three studies; 580 participants). Care coordination interventions at the professional level (43%) included multidisciplinary care teams alone (four studies; 459 participants) or in combination with a case management intervention (two studies; 2636 participants). Only one study (7%) was targeted at the organizational care coordination level, including a multidisciplinary team and disease management intervention (one study; 139 participants). The duration of the interventions ranged from 3 to 24 months (median 12 months). Only two studies reported information on how the interventions were implemented (26,27) (see Table 2).

**Risks of Bias**

Risk of bias in the included studies is summarized in Supplemental Table 7. Studies were overall of moderate quality with high risk of bias for at least one of the quality domains in eight of 14 studies (57%), and unclear or high risks in all studies.

**Effect of Integrated Care Interventions**

**All-Cause and Cardiovascular Mortality.** Eleven studies (4127 participants) reported treatment effects on all-cause mortality. Person-centered integrated care of CKD had
Table 1. Description of studies included in the systematic review and meta-analysis

<table>
<thead>
<tr>
<th>Study, yr</th>
<th>Design</th>
<th>Country</th>
<th>Sample Size (I:C)</th>
<th>Setting</th>
<th>Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrett et al. (43)</td>
<td>Parallel</td>
<td>Canada</td>
<td>474 (238:236)</td>
<td>Outpatient care (general practice)</td>
<td>CKD 3–4</td>
</tr>
<tr>
<td>Blakeman et al. (26)</td>
<td>Parallel</td>
<td>United Kingdom</td>
<td>436 (215:221)</td>
<td>Outpatient care (general practice)</td>
<td>CKD 3</td>
</tr>
<tr>
<td>Chen et al. (44)</td>
<td>Parallel; open label</td>
<td>Taiwan</td>
<td>54 (27:27)</td>
<td>Outpatient care</td>
<td>CKD 3–5</td>
</tr>
<tr>
<td>Cooney et al. (32)</td>
<td>Parallel</td>
<td>USA</td>
<td>2199 (1070:1129)</td>
<td>Outpatient care (general practice)</td>
<td>CKD 3–5</td>
</tr>
<tr>
<td>Elios Russo et al. (45)</td>
<td>Parallel</td>
<td>Italy</td>
<td>40 (20:20)</td>
<td>Inpatient care (clinic/hospital)</td>
<td>CKD 5D (PD)</td>
</tr>
<tr>
<td>Harris et al. (29)</td>
<td>Parallel cluster</td>
<td>USA</td>
<td>437 (206:231)</td>
<td>Outpatient care</td>
<td>CKD 3–5</td>
</tr>
<tr>
<td>Hotu et al. (28)</td>
<td>Parallel</td>
<td>New Zealand</td>
<td>65 (33:32)</td>
<td>Outpatient care (general practice)</td>
<td>Diabetic nephropathic</td>
</tr>
<tr>
<td>Mokrzycki et al. (46)</td>
<td>Parallel cluster</td>
<td>USA</td>
<td>166 (111:55)</td>
<td>Inpatient care (clinic/hospital)</td>
<td>CKD 5D (HD)</td>
</tr>
<tr>
<td>Raiesifar et al. (47)</td>
<td>Parallel</td>
<td>Iran</td>
<td>90 (45:45)</td>
<td>NS</td>
<td>CKD 5T</td>
</tr>
<tr>
<td>Santschi et al. (48)</td>
<td>Parallel cluster</td>
<td>Canada</td>
<td>89 (48:41)</td>
<td>Outpatient care</td>
<td>CKD 3–5</td>
</tr>
<tr>
<td>Scherpbie-de Haan et al. (49)</td>
<td>Parallel cluster</td>
<td>The Netherlands</td>
<td>164 (90:74)</td>
<td>Outpatient care (general practice)</td>
<td>CKD 3–5</td>
</tr>
<tr>
<td>Weber et al. (30)</td>
<td>Parallel</td>
<td>Canada</td>
<td>139 (70:69)</td>
<td>Outpatient care</td>
<td>CKD-CVD-DM</td>
</tr>
<tr>
<td>Weisbord et al. (27)</td>
<td>Parallel cluster</td>
<td>USA</td>
<td>220 (100:120)</td>
<td>Outpatient care</td>
<td>CKD 5D (HD)</td>
</tr>
<tr>
<td>Wong et al. (31)</td>
<td>RCT</td>
<td>China</td>
<td>120 (60:60)</td>
<td>Combination (outpatient and inpatient care)</td>
<td>CKD 5D (PD)</td>
</tr>
</tbody>
</table>

I:C, intervention:control; PD, peritoneal dialysis; AC, all cause; CV, cardiovascular; HD, hemodialysis; CVD, cardiovascular disease; DM, diabetes mellitus; RCT, randomized, controlled trial.

*Measured with the Health Utility Index 3.
*^1^Measured with the European Quality of Life–5 Dimensions.
*^2^Measured with the Kidney Disease Quality of Life Short Form instrument.
*^3^Measured with the Kidney Transplant Questionnaire (KTQ-25). Data are not included in meta-analysis.
*^4^Measured with the World Organization of National Colleges, Academies, and Academic Association of General Practitioners functional health status instrument.
*^5^Measured with the Kidney Disease Quality of Life instrument.
little effect on all-cause mortality (RR, 0.86; 95% CI, 0.68 to 1.08) compared with usual care (Figure 2, Table 3). Five studies (3054 participants) reported that professional integration interventions had an effect on all-cause mortality compared with usual care management (RR, 0.79; 95% CI, 0.63 to 0.98). There was no evidence of different effects on mortality on the basis of the level of care integration (professional, RR, 0.79; 95% CI, 0.63 to 0.98; clinical, RR, 1.33; 95% CI, 0.67 to 2.64; organizational level, RR, 1.36; 95% CI, 0.58 to 3.16; P value for subgroup difference=0.19). The quality of evidence for all-cause mortality was rated as moderate (Table 3).
<table>
<thead>
<tr>
<th>Study, yr</th>
<th>Type of Intervention(s)</th>
<th>Type of Targeted Behavior</th>
<th>Level of Care Coordination</th>
<th>Type of Provider(s) Involved</th>
<th>Multidisciplinary Team&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Implementation Fidelity Measured and Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrett et al. (43)</td>
<td>Case management Self-management support</td>
<td>Referrals Professional-patient communication</td>
<td>Clinical level 1;2;3;4;5</td>
<td>1;2,4</td>
<td>+</td>
<td>NS Intervention uptake reported</td>
</tr>
<tr>
<td>Blakeman et al. (26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chen et al. (44)</td>
<td>Self-management support</td>
<td>Patient education/advice; professional-patient education</td>
<td>Clinical level 2;4;5</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Cooney et al. (32)</td>
<td>Case management; and multidisciplinary care team</td>
<td>Professional education; professional-patient education</td>
<td>Clinical level 1;6</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Elios Russo et al. (45)</td>
<td>Multidisciplinary care team</td>
<td>NS</td>
<td>Professional level 2;3;4;7;8,9</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Harris et al. (29)</td>
<td>Case management; and multidisciplinary care team</td>
<td>Professional education; and patient-professional communication</td>
<td>Clinical level 1;2;3;4;5</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Hotu et al. (28)</td>
<td>Case management</td>
<td>Clinical prevention services</td>
<td>Clinical level 1;2;10</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Mokrzycki et al. (46)</td>
<td>Multidisciplinary care team</td>
<td>Professional education</td>
<td>Professional level 2;3;5</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Raiesifar et al. (47)</td>
<td>Self-management support</td>
<td>Patient education/advice; professional-patient education</td>
<td>Clinical level 1;2,3</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Santschi et al. (48)</td>
<td>Multidisciplinary care team</td>
<td>Professional education</td>
<td>Professional level 2;3;5</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Scherpbier-de Haan et al. (49)</td>
<td>Multidisciplinary care team</td>
<td>Professional education; professional-patient education</td>
<td>Professional level 1;2,3</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Weber et al. (30)</td>
<td>Multidisciplinary care team; and disease management</td>
<td>Financial-resource use</td>
<td>Professional; and organizational level 2;3;5;6;7;12</td>
<td>+</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Weisbord et al. (27)</td>
<td>Case management</td>
<td>General management of problem</td>
<td>Clinical level 2</td>
<td>–</td>
<td></td>
<td>Intervention uptake reported</td>
</tr>
<tr>
<td>Wong et al. (31)</td>
<td>Case management</td>
<td>Professional-patient education</td>
<td>Clinical level 2;3</td>
<td>–</td>
<td></td>
<td>NS</td>
</tr>
</tbody>
</table>

1, general practitioner; 2, nurse; 3, nephrologist; 4, social worker; 5, dietician; +, care is provided by multidisciplinary team; NS, not stated; 6, pharmacist; –, care is not provided by multidisciplinary team; 7, cardiologist; 8, gastroenterologist; 9, psychologist; 10, home care assistant; 11, physiotherapist; 12, endocrinologist.

<sup>a</sup>Defined as more than two different disciplines.
All-Cause Hospitalization. Data on rates of hospitalization were reported in three studies (568 participants). In very-low-quality evidence, person-centered integrated care may reduce hospitalization (RR, 0.38; 95% CI, 0.15 to 0.95) (Figure 3, Table 3). However, there was evidence for high-level heterogeneity between studies ($I^2=74\%$).

Health-Related Quality of Life. Data for health-related quality of life were reported in four studies (2864 participants). Person-centered integrated care probably has little or no effect on health-related quality of life compared with standard care management (SMD, 0.02; 95% CI, −0.65 to 1.55; $I^2=0\%$) (Supplemental Figure 1). There was no evidence that different levels of person-centered care integration affected treatment effectiveness (clinical, SMD, 0.07; 95% CI, −0.11 to 0.26; professional, SMD, 0.01; 95% CI, −0.07 to 0.09; $P$ value for subgroup difference=0.57). There was no evidence of heterogeneity between studies ($I^2=0\%$). The quality of evidence for quality of life was graded as moderate (Table 3).

CKD Outcomes. Person-centered integrated care may lead to little or no difference in risks of needing RRT (dialysis or kidney transplant) (three studies; 403 participants; RR, 1.00; 95% CI, 0.65 to 1.55; $I^2=0\%$) (Supplemental Figure 1). eGFRs were reported in four studies involving 523 participants. Person-centered integrated care may lead to little or no difference in eGFR (MD, 1.51 ml/min per 1.73 m$^2$; 95% CI, −3.25 to 6.27) (Supplemental Figure 2), but results were markedly heterogeneous ($I^2=80\%$). In addition, person-centered integrated care may have little effect on serum creatinine levels (three studies; 589 participants; MD, −0.01 mg/dl; 95% CI, −0.38 to 0.36; $I^2=45\%$; Supplemental Figure 3). The quality of evidence for kidney function outcomes was very low (Table 3).

BP Control. Person-centered integrated care may slightly increase the frequency of BP control (four studies; 1626 participants; RR, 1.20; 95% CI, 1.00 to 1.44); however, there was considerable heterogeneity among studies ($I^2=63\%$) (Supplemental Figure 4). There was no evidence that specific levels of person-centered care integration had different effects on BP control (clinical, RR, 1.26; 95% CI, 1.11 to 1.43; professional, RR, 1.20; 95% CI, 0.70 to 2.61; $P$ value for subgroup difference=0.93). In four studies (692 participants), person-centered integrated care may decrease systolic BP (MD, −5.38 mm Hg; 95% CI, −8.45 to −2.3), but may have little or no effect on diastolic BP (MD, −1.67 mm Hg; −6.22 to 2.88) (Supplemental Figures 5 and 6) in low- to very-low-quality evidence (Table 3).

Qualitative Synthesis

The qualitative analysis showed that data for cardiovascular mortality were available in a single study comprising 65 participants and treatment effects were very uncertain (28) (Supplemental Table 8). In addition, three studies included in the qualitative analysis showed no effect of person-centered integrated care on hospitalization (29–31) (Supplemental Table 8). The costs of person-centered integrated care were reported in two studies (613 participants) (Supplemental Table 8) and effects of care on cost were very uncertain because the certainty of the evidence was low. One study reported satisfaction scores among patients allocated to person-centered integrated care (31) and two studies reported implementation rates during the intervention (27,32) (Supplemental Table 8).
Table 3. Summary of findings and assessment of quality of evidence for outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No of Patients (Studies)</th>
<th>Study Limitation</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Publication Bias</th>
<th>Summary of Findings</th>
<th>Anticipated Absolute Effects</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
<tr>
<td>All-cause mortality</td>
<td>4126 (11)</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>–1a</td>
<td>Undetected</td>
<td>0.86 (0.68 to 1.08)</td>
<td>9 per 100</td>
<td>⊕⊕⊕ Moderate</td>
</tr>
<tr>
<td>All-cause hospitalization</td>
<td>568 (3)</td>
<td>–2b</td>
<td>–2c</td>
<td>None</td>
<td>–1a</td>
<td>Not estimable</td>
<td>0.38 (0.15 to 0.95)</td>
<td>35 per 100</td>
<td>⊕ Very low</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td>2864 (4)</td>
<td>–1d</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Not estimable</td>
<td>—</td>
<td>The mean health-related quality of life ranged from 0.67 to 89.4e</td>
<td>⊕⊕⊗ Moderate</td>
</tr>
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<td></td>
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<td></td>
</tr>
<tr>
<td>eGFR, ml/min per 1.73 m²</td>
<td>523 (4)</td>
<td>–1d</td>
<td>–2c</td>
<td>None</td>
<td>–1a</td>
<td>Not estimable</td>
<td>—</td>
<td>The mean eGFR in the intervention group was 1.51 higher (3.25 lower to 6.27 higher)</td>
<td>⊕ skies Very low</td>
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<tr>
<td>RRT</td>
<td>403 (3)</td>
<td>–1d</td>
<td>–1f</td>
<td>None</td>
<td>–2e</td>
<td>Not estimable</td>
<td>1.00 (0.65 to 1.55)</td>
<td>14 per 100</td>
<td>⊕ skies Very low</td>
</tr>
<tr>
<td>Controlled BP, &lt;130/80 mm Hg</td>
<td>1626 (4)</td>
<td>–1d</td>
<td>–1f</td>
<td>None</td>
<td>–1a</td>
<td>Not estimable</td>
<td>1.20 (1.00 to 1.44)</td>
<td>45 per 100</td>
<td>⊕ skies Very low</td>
</tr>
</tbody>
</table>

95% CI, 95% confidence interval; ⊕, level of evidence; ⊖, no level of evidence; —, not applicable; SMD, standardized mean difference.
95% confidence interval includes possible benefits from both usual care and integrated care.
Wide variance of point estimates across studies and significant heterogeneity between studies.
Most of the studies had an unclear risk of bias on allocation concealment and/or selective reporting, and high or unclear risk of bias for blinding of participants or outcome assessors.
Measured with different health-related quality-of-life scales (e.g., Health Utility Index 3, European Quality of Life-5 Dimensions, Kidney Disease Quality of Life Short Form, World Organization of National Colleges, Academies and Academic Association of General Practitioners, and Kidney Disease Quality of Life).
Wide variance of point estimates across studies or large heterogeneity between studies (I² ≥ 50%).
Adverse event in only small proportion of studies and 95% confidence interval includes possible benefits from both usual care and integrated care.
Publication Bias, Subgroup, and Sensitivity Analyses

There was no evidence of funnel plot asymmetry in treatment effects for all-cause mortality (Supplemental Figure 7). In addition, there was no evidence that person-centered integrated care had different effects on all-cause mortality on the basis of study design (P=0.30), follow-up duration (P=0.42), or stage of CKD (P=0.40). Sensitivity analysis showed that restricting analyses to studies with lower risks of bias, follow up <12 months, English language publications, or CKD stages 3–5 provided no different treatment effects for all-cause mortality (Supplemental Table 9).

Discussion

Principal Findings

This systematic review of randomized trials found that person-centered integrated care for management of CKD has little evidence of effect on all-cause mortality or health-related quality of life and may have no effect on kidney outcomes including requiring dialysis or kidney transplantation. Person-centered integrated management of CKD may reduce hospitalization and improve the likelihood of BP control compared with usual care. Studies were generally not designed to evaluate cardiovascular mortality. There was no evidence that different levels of care integration had different effects on clinical outcomes, although these analyses were constrained by the lack of data available for organization-level care integration. The lack of high-quality evidence for all-cause mortality, hospitalization, and BP reinforces the need for further primary research into person-centered integrated care for CKD.

Comparisons with Other Studies

Wang et al. (18) reported limited evidence of the effects of person-centered care integration on the risk of all-cause mortality in randomized trials, whereas multidisciplinary care was associated with lower mortality in cohort studies. In addition, we found also beneficial effects of professional integration interventions in preventing mortality. The difference in the overall effect for mortality might simply reflect a shorter duration of follow-up in randomized trials (median of 12 months) compared with available cohort studies (median of 38 months) as well as a paucity of RCTs. Consequently, information linking person-centered integrated care to improved mortality in CKD is hypothesis-generating and requires confirmation in further studies.

In this analysis, there was low certainty that person-centered integrated CKD management decreased rates of hospitalization. Our finding that person-centered integrated care may reduce hospital admission is consistent with other studies showing a decrease in hospitalization rates with integrated care. The evidence is supported by previous studies showing that integrated care can improve clinical outcomes and reduce hospitalization rates. However, further research is needed to confirm these findings.

Figure 3. | Effect of person-centered integrated care on all-cause hospitalization. 95% CI, 95% confidence interval; RR, relative risk.

Figure 4. | Effect of person-centered integrated care on health-related quality of life. 95% CI, 95% confidence interval; MD, mean difference; SMD, standardized mean difference.
with earlier studies in patients with diabetes, heart failure, or chronic obstructive pulmonary disease (5,6,10,33,34).

This review observes that person-centered integrated care has little effect on health-related quality of life among people with CKD. Notably, we could only include four studies evaluating health-related quality of life using a range of measures. Because other short-term (<3 months) randomized trials have reported statistically significant effects of person-centered integrated care on quality of life (35–37), this effect of care integration requires further exploration.

Overall, this review found that person-centered integrated CKD management may improve BP control, consistent with other studies of integrated care reviews (38,39). Data reporting for the delivery of care integration (implementation fidelity) were notably under-reported as has been observed in other integrated care research (34).

Implications for Clinicians, Policymakers, and Research

The marked lack of high-quality evidence for person-centered integrated CKD care management reinforces the need for primary research investigating whether any specific elements of a person-centered integrated care approach can improve outcomes for patients with CKD. Because most existing studies focus on short-term interventions aimed at coordinating care at the clinical level, additional longitudinal research could help to evaluate the effectiveness of interventions targeted at a wider range of clinical (e.g., self-management, case management), professional (e.g., multidisciplinary care, continuity of care), and organizational (e.g., disease management, managed care programs) levels of care. Embedding of research trials within usual care might assist to improve the “real-world” assessment of clinical practice models using an efficient research design.

The underlying assumption is that a significant effect on clinical, quality-of-care, and economic outcomes requires various multiple interacting interventions targeted at multiple clinical, professional, organizational, and system levels (12). Unfortunately, traditional randomized trials, such as reported in this review, offer limited insight into the “black box” of an intervention by exploring the underlying processes of implementation and mechanisms of action, and how these vary by contextual characteristics (25,40,41). Future studies might, therefore, focus more on the implementation and likely effects of person-centered integrated care within different settings and populations by uniting realist with reductionist evaluation methods (e.g., realist RCTs) (42). In future studies, it would be helpful to knowledge generation and implementation to embed specific person-centered integrated care and outcome measures within a theoretical framework such as the RMIC (12,13).

Strengths and Limitations

The strength of this systematic review is that it was systematic, included a comprehensive literature search, documented key aspects of the interventions reported in the literature, and quantified the effectiveness of those interventions and confidence in the treatment effects across a broad range of outcome measures. However, several limitations of this review might be taken into account when interpreting the findings. First, our review included a relatively small number of RCTs (n=14) and participants (n=4693) that may have lacked sufficient power to detect intervention effects. Quasi-experimental study designs, which are common across person-centered integrated care research, were not included. It is possible that unpublished studies or those not retrieved by the literature search were missed and their inclusion may have altered the magnitude and/or certainty of the results. In addition, studies were generally short-term and few had a duration of intervention or follow-up beyond 12 months. The effect of person-centered integrated care may require a longer period of time to be embedded within organizational and clinical practices to be detectable. Second, most of the included studies had important methodologic limitations that reduced the confidence in the treatment estimates. For example, intraclass coefficients were not reported in the trials, so sample sizes could not be adjusted for cluster randomized trials. Future research studies might observe different treatment estimates. Third, cardiovascular mortality, healthcare costs, and process-of-care outcomes were under-reported, which are critical for clinical and managerial responses to the evidence as well as for policy decision-making. Fourth, most studies reported few details on how the care integration was implemented. Although we abstracted and summarized the key aspects of the interventions, there were few data on implementation fidelity. Moreover, studies did not provide sufficient data about the intensity and dose of the interventions, or sufficient details regarding the process of care delivery. Finally, applicability of this evidence is challenged by health system complexity (e.g., type of intervention, team composition) that might affect the effect of specific integration methods. The review had low statistical power to generate explanatory analyses (e.g., subgroup and sensitivity analysis) to explore these contextual characteristics.

Person-centered integrated care of CKD has little evidence of effect on all-cause mortality or health-related quality of life, and may have little or no effect on CKD outcomes. Person-centered integrated care may reduce hospitalization and improve BP control. Evaluation of the effects of person-centered integrated CKD care is limited. These findings highlight the need for further primary research into the relationship between person-centered integrated care and outcomes of people with CKD.

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Disclosures

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