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CKJ REVIEW

Adherence to medication in patients with chronic kidney disease: a systematic review of qualitative research

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Abstract

Non-adherence to multipharmacological treatment increases the risk of morbidity, mortality and hospitalization. We know little about the perspective of patients with chronic kidney disease regarding factors influencing medicine taking. This study aimed to synthesize findings from qualitative studies of patients' experiences of factors that facilitate and hinder adherence to medication. A systematic review of qualitative studies adhering to the Enhancing transparency in reporting the synthesis of qualitative research (ENTREQ) framework. Systematic searches were conducted in several databases. We used thematic synthesis and the Confidence in the Evidence from Reviews of Qualitative Research (CERQual) approach to assess the confidence of the evidence. Nineteen studies involving 381 patients with chronic kidney disease were included. We identified three analytical themes; logistics, benchmarking the need for medication; and the quality of the patient-physician relationship, with seven descriptive sub-themes as factors influencing patients' adherence to medications. Helping patients to map their everyday activities and motivating them to associate medications with everyday activities may facilitate adherence to medications. Addressing patient beliefs about medications, supporting patients in coping with side effects of medications and eliciting patients' wishes for involvement in treatment decisions may also facilitate adherence. Barriers to adherence were the costs of buying medications, and lacking understanding of the indications and effects of medications. The findings in this synthesis resonate with previous research and extend the known literature by synthesizing and formally assessing confidence in the evidence.

Key words: chronic kidney disease, medication adherence, patient perspective, qualitative review, systematic review

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Introduction

Adherence to medication is defined as ‘the extent to which the patient’s behaviour matches agreed recommendations from the prescriber’ [1]. In chronic kidney disease (CKD), adherence to medication is a key component of effective disease management [2, 3]. The main goals of medication are to slow progression of the disease and monitor and correct disease-associated complications and comorbidities while treating the underlying aetiology [3]. Patients with CKD are prescribed a regime of multi-pharmacological treatment often starting with antihypertensives and antidiabetics and subsequently phosphate binders, vitamin D preparations, calcimimetics, erythropoiesis stimulating agents and iron supplements [4]. This infers a high burden of pill intake with sometimes >20 pills/day [2]. Managing multiple medications and health care appointments, including, for some, dialysis several times a week, is a challenging task. Not surprisingly, patients may miss medications, intentionally or un-intentionally (1). Estimates of non-adherence to medication vary from 17 to 74% among patients with CKD and from 3 to 80% among patients on haemodialysis, depending on the methods used to assess non-adherence [2, 3, 5]. This poses a major obstacle to achieving treatment goals and increases the risk of morbidity, mortality and hospitalization [3, 4]. Optimizing adherence to medicine is therefore a priority issue for health care providers.

There is a growing body of research into non-adherence to medication among patients with CKD. Quantitative studies have focused on the incidence of adherence and identification of potential risk factors for non-adherence [2]. These studies provide valuable insight into the prevalence of non-adherence and associated risk factors [2]. They do not, however, uncover life circumstances that may influence adherence from the patient perspective. Qualitative research may contribute to our knowledge by elaborating the patients’ perspectives on non-adherence. The aim of this qualitative systematic review was to synthesize the available qualitative research on factors that facilitate and hinder adherence to medication from the perspective of patients with CKD.

Materials and methods

A systematic review and thematic synthesis of qualitative studies was undertaken. The review was prospectively registered in PROSPERO (CRD42016033070) and conducted according to the Enhancing Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ) framework [6].

Inclusion criteria

We considered English-language studies that explored the experience of medicine taking in adults with CKD. We excluded studies involving kidney transplant recipients and alternative medicine. Due to the anticipated limited evidence base, no search restrictions with regard to year limits were imposed.

Data source and search

We searched MEDLINE, Embase and CINAHL using the systematic search method SPIDER (sample, phenomenon of interest, design, evaluation, research type) [7]. We combined search terms such as ‘chronic kidney failure’, ‘medication adherence’, ‘qualitative research’, ‘patient experience’ and ‘qualitative research’ among others (for a full overview of search terms see Table 1). The search strategy was refined in collaboration with an experienced librarian and adapted to each database, first

searching each set of search terms using the Boolean operator OR and subsequently combining these searches using the Boolean operator AND. Along with the electronic searches, we manually searched reference lists and grey literature.

We uploaded the search into the Covidence software, where two authors (T.M.N., T.T.) independently screened the search results for eligibility. The search was conducted in January 2016 and updated in June 2017. Figure 1 illustrates the literature search and selection.

Quality assessment

We used the Critical Appraisal Skills Programme (CASP) checklist for qualitative studies to assess individual study quality [8]. Two authors (T.M.N., M.F.J.) independently assessed the studies.

Data extraction and analysis

Included studies were imported into QSR NVivo 10 computer data analysis software (QRS International, Melbourne, VIC, Australia). Following the method for thematic synthesis described by Thomas and Harden [9], we extracted data about medicine taking from the included studies, for example, all relevant data presented in the ‘abstract, results and discussion’ section. To enhance transparency and reproducibility, two authors (T.M.N., M.F.J.) independently conducted the open line-by-line coding of extracted data. This resulted in a total of 31 initial codes that were condensed into 16 preliminary descriptive themes. The descriptive themes were subsequently discussed in the author group and a summary of the findings across studies was drafted. All authors commented on this draft and, through further discussion of the preliminary descriptive themes, three analytical themes with seven descriptive sub-themes emerged.

Assessment of confidence in the review findings

We used the Confidence in the Evidence from Reviews of Qualitative Research (CERQual) criteria to assess how much confidence could be placed in our findings [10, 11]. CERQual is based on four key components: methodological limitations, relevance to the review question, coherence and adequacy of the data contributing to a review finding [14]. Methodological limitations of the individual studies contributing to each review finding were assessed using the CASP tool. Relevance was assessed by evaluating the applicability of the review findings to the context (perspective, population, setting) of our review question. Coherence was assessed by the extent to which the pattern that constitutes a review finding was based on evidence that was consistent across multiple individual studies. Adequacy was assessed through an overall determination of the degree of richness and the quantity of data supporting a review finding [11]. After assessing each of the four components, we judged the confidence in the themes as high, moderate, low or very low. Our starting point was ‘high confidence’, reflecting the assumption that each review finding was a reasonable representation of the phenomenon of interest unless there were CERQual components that weakened this assumption [11]. See the summary of the qualitative findings and CERQual assessments in Table 2.

Results

Study characteristics

Of 1044 potentially relevant articles identified in the search, we included 19 studies [12–30]. In total, 381 patients with CKD

Table 1. Search method (SPIDER) and search terms used

| Search | Query |
|------------------------|--|
| MEDLINE | |
| Sample | Search kidney diseases [Mesh] OR kidney failure, chronic [Mesh] OR renal insufficiency [Mesh] OR renal insufficiency, chronic [Mesh] OR acute kidney injury [Mesh] OR hypertension CKD OR CKD hypertension OR CKD treatment OR haemodialysis OR CKD OR peritoneal dialysis OR renal dialysis/pharmacology [Mesh] or kidney failure, chronic* OR renal dialysis* OR kidney failure, chronic/drug therapy [Mesh] OR kidney failure, chronic/nursing [Mesh] OR kidney disease* and |
| Phenomenon of interest | Search patient compliance/drug effects [Mesh] OR treatment refusal [Mesh] OR self-medication [Mesh] OR self-administration [Mesh] OR patient medication knowledge [Mesh] OR attitude to health/drug effects [Mesh] OR medication adherence [Mesh] OR concordance medication OR patient acceptance of health care/drug effects [Mesh] OR drug therapy OR polypharmacy OR treatment refusal* OR medication adherence* OR prescription drug* OR drug* and |
| Design | Search grounded theory OR hermeneutic method OR phenomenology OR ethnographic research OR narratives OR discourse analysis OR qualitative research [Mesh] OR nursing evaluation research [Mesh] OR interview [Publication Type] OR interviews as topic [Mesh] OR nursing methodology research [Mesh] OR observation [Mesh] OR grounded theory [Mesh] OR hermeneutics [Mesh] OR focus groups/methods [Mesh] OR interview* and |
| Evaluation | Search patient acceptance OR patient perception OR patient perspective OR patient satisfaction OR patient experience OR patient preference [Mesh] OR patient acceptance of health care [Mesh] OR life change events [Mesh] OR motivation [Mesh] OR patient motivation OR trust [Mesh] OR patient confidence OR health literacy* OR health knowledge, attitude, practice OR quality of life OR patient acceptance and |
| Research type | Search qualitative research [Mesh] |
| Embase | |
| Sample | Search kidney disease* OR kidney failure OR chronic kidney failure OR renal disease* OR renal insufficiency OR chronic renal insufficiency OR renal replacement therapy OR haemodialysis [Mesh] OR peritoneal dialysis [Mesh] OR dialysis patient* OR haemodialysis patient [Mesh] OR kidney disease/drug therapy [Mesh] OR chronic kidney failure/drug therapy [Mesh] OR kidney failure/drug therapy [Mesh] OR renal replacement therapy [Mesh] and |
| Phenomenon of interest | Search medication compliance [Mesh] OR patient compliance [Mesh] OR drug therapy [Mesh] OR treatment refusal [Mesh] OR drug refusal OR medication refusal OR health knowledge and behaviour OR self-medication [Mesh] OR drug self-administration [Mesh] OR medication adherence OR patient medication knowledge OR attitude to health [Mesh] OR polypharmacy OR chronic drug therapy OR drug, prescription OR prescription [Mesh] OR drug efficacy [Mesh] and |
| Design | Search qualitative research [Mesh] OR qualitative research OR qualitative method OR interview [Mesh] OR qualitative analysis [Mesh] OR research, nursing [Mesh] OR ethnographic research [Mesh] OR ethnography [Mesh] OR observational method [Mesh] OR observation [Mesh] OR focus group interview OR clinical nursing research [Mesh] OR grounded theory [Mesh] OR thematic analysis [Mesh] OR narrative [Mesh] OR phenomenology OR hermeneutics [Mesh] OR phenomenological research [Mesh] and |
| Evaluation | Search patient preference [Mesh] OR patient attitude [Mesh] OR patient satisfaction [Mesh] OR patient experience OR patient perception OR patient motivation OR motivation [Mesh] OR patient perspective OR Personal experience [Mesh] OR patient acceptance and |
| Research type | Search qualitative research [Mesh] |
| CINAHL | |
| Sample | Search kidney disease [Mesh] OR kidney failure, chronic [Mesh] OR renal insufficiency [Mesh] OR renal insufficiency, chronic [Mesh] OR renal replacement therapy [Mesh] OR haemodialysis [Mesh] OR peritoneal dialysis [Mesh] OR dialysis patient [Mesh] and |
| Phenomenon of interest | Search patient compliance/drug effects [Mesh] OR treatment refusal/drug effects [Mesh] OR treatment refusal OR pharmacological and biological treatments [Mesh] OR health behavior/drug effects [Mesh] OR self-medication [Mesh] OR self-administration [Mesh] OR patient medication knowledge [Mesh] OR knowledge medication [Mesh] OR medication history [Mesh] OR drug therapy [Mesh] OR drug therapy OR attitude to health/drug effects [Mesh] OR polypharmacy [Mesh] OR chronic drug therapy [Mesh] OR drug, prescription [Mesh] OR drugs [Mesh] OR medication adherence OR drug adherence and |
| Design | Search qualitative research [mesh] OR field study [mesh] or research, nursing [mesh] or ethnographic research [Mesh] or clinical nursing research [Mesh] OR interview [mesh] OR semi structured interview [Mesh] OR observational method [mesh] OR participant observation [Mesh] OR non participant observation [Mesh] OR focus group [mesh] or hermeneutics OR grounded theory [Mesh] OR discourse analysis or thematic analysis or narratives or phenomenological research [Mesh] and |

(continued)

Table 1. Continued

| Search | Query |
|---------------|--|
| Evaluation | Search patient preference OR patient experience OR patient perception or patient attitude [Mesh] OR patient motivation [Mesh] OR life experience [Mesh] OR patient acceptance or patient perspective OR patient satisfaction OR beliefs or health belief/drug effects [Mesh] or motivation/drug effects [Mesh] OR motivation or patient participation [Mesh] OR patient participation or health literacy |
| | and |
| Research type | Search qualitative research [Mesh] |

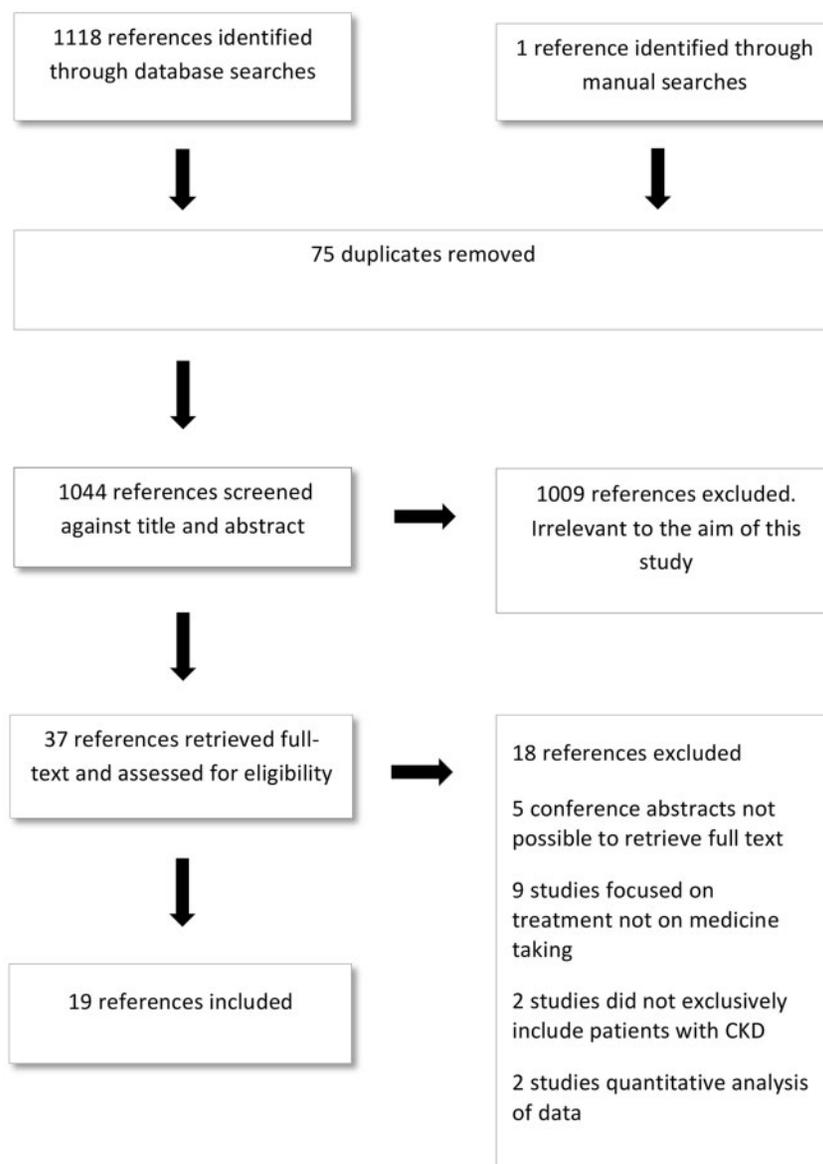


Fig. 1. Flow diagram illustrating literature search and selection.

participated in the included studies. Of these, 171 patients were on haemodialysis and/or peritoneal dialysis and 133 patients attended renal clinics; for 77 patients, treatments were not clearly described. For a full overview of study characteristics see Table 3. The studies originated from nine countries (Australia, Brazil, Canada, Chile, China, Singapore, Sweden, UK and USA). Data were collected using face-to-face interviews (13 studies),

motivational interviewing via telephone (2 studies), focus group interviews (2 studies) and face-to-face interviews and observation/focus group interviews in combination (2 studies). Sample sizes ranged from 7 to 39 patients and the overall age range was 19–90 years. The majority of studies were assessed to have minor to moderate methodological limitations (8 low, 6 medium, 5 high).

Table 2. Summary of qualitative findings and CERQual assessments

| Review finding | Relevant articles | CERQual assessment of confidence in the evidence | Explanation of CERQual assessment |
|---|--|--|--|
| Logistics | | | |
| Establishing and maintaining routines | [16, 17, 18, 19, 21, 23, 24, 25, 26, 27, 28, 29, 30] | High confidence | In all, 13 studies with minor to significant methodological limitations, where most studies had minor to moderate methodological limitations (6 low, 4 medium, 3 high). Thick data from six countries across five geographical continents, but predominantly high income countries. High coherence |
| The costs of buying medication | [16, 25, 27, 28, 29] | Moderate confidence | In all, five studies with minor to moderate methodological limitations (three low, two medium). Moderate data from two countries (Singapore and Australia) across two geographical continents and only high-income countries. High coherence |
| Benchmarking the need for medication | | | |
| Absence of effect from a lay perspective | [14, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 27, 28, 29, 30] | High confidence | In all, 15 studies with minor to significant methodological limitations, where most studies had minor to moderate methodological limitations (7 low, 5 medium, 3 high). Thick data from eight countries across seven geographical continents and predominantly high-income countries. High coherence |
| Lacking understanding of medication indications and effects | [12, 21, 22, 23, 24, 25, 27, 28, 29, 30] | Moderate confidence | In all, 10 studies with minor to significant methodological limitations, where most studies had minor to moderate methodological limitations (5 low, 3 medium, 2 high). Moderate data from five countries across four geographical continents and predominantly high-income. High coherence |
| Spurred by emergent symptoms | [13, 18, 25, 26, 27] | Moderate confidence | In all, five studies with minor to significant methodological limitations (one low, two medium, two high). Moderate data from three countries (UK, USA and Australia) across three geographical continents and only high-income countries. High coherence |
| The quality of the patient–physician relationship | | | |
| Eliciting patients' wishes for involvement in decisions concerning medication | [12, 13, 14, 15, 18, 22, 23, 24, 25, 26, 27, 28, 29] | High confidence | In all, 13 studies with minor to significant methodological limitations, where most studies had minor to moderate methodological limitations (5 low, 5 medium, 3 high). Thick data from five countries across five geographical continents and predominantly high-income. High coherence |

(continued)

Table 2. Continued

| Review finding | Relevant articles | CERQual assessment of confidence in the evidence | Explanation of CERQual assessment |
|---|------------------------------|--|---|
| behalf while others wished to collaborate as equal partners with physicians about treatment-related decisions, including medication. Lack of continuity, time, trust and involvement of patients wishing to partake in treatment led to patients taking matters into their own hands in relation to medicine taking. | | | |
| Lacking information | [14, 18, 22, 23, 24, 25, 28] | Moderate confidence | In all, seven studies with minor to significant methodological limitations, where most studies had minor to moderate methodological limitations (three low, three medium, one high). Moderate data from four countries across four geographical continents and only high-income countries. High coherence |
| Feeling insufficiently informed about the indications, effects and side effects and interactions between prescribed medications affected adherence negatively. Some patients suspected physicians of withholding information while others described getting conflicting information. For example, different information from different physicians or physician information that differed from the drug information sheet. This resulted in confusion and apprehension about the medication, which in some patients posed a barrier to adherence | | | |

Synthesis

We identified three analytical themes with seven descriptive subthemes.

(1) 'Logistics', with the subthemes establishing and maintaining routines, and the costs of buying medication.

(2) 'Benchmarking the need for medication', with the subthemes absence of effect from a lay perspective, lacking understanding of medication indications and effects and being spurred by emergent symptoms.

(3) 'Quality of the patient-physician relationship', with the subthemes eliciting patients' wishes for involvement in decisions concerning medication and lacking information.

A summary of the main analytical and descriptive themes are presented in Table 4. Table 5 presents a selection of patient quotations illustrating each descriptive theme.

Logistics

The logistics surrounding medicine taking were important for facilitating or hindering adherence. Logistics involved the practical challenges of managing complex medication regimes, numerous prescriptions and health care appointments, all of which were challenging in the patients' everyday lives. Furthermore, logistics included the costs of buying medication.

Establishing and maintaining routines (high CERQual confidence)

Establishing and maintaining daily routines in relation to medications facilitated adherence. Across studies, patients described the difficulty of remembering to take medications and coping with the complexity of a high pill burden, different dosage times throughout the day and specific instructions about how to take certain medications. They were also challenged by the task of remembering to renew prescriptions on time, as prescriptions expired at different times. Daily routines promoted the maintenance of prescriptions and medicine taking. Facilitating routines included memory aids (tally charts, calendars, mobile phone), assisting devices (dosette boxes), taking medicines in relation to daily activities (meal times or prayers) and reminders and/or practical support from family or pharmacists (preparing

medications, refilling dosette boxes, ordering and renewing prescriptions, reminders to take medications). Memory aids and dosette boxes appeared especially important for patients suffering from fatigue, nausea and poor memory. A downside of dosette boxes was that patients had to be able to see well enough to read the date and to be able to pick up or replace a lost pill with an identical one [16, 18, 25].

Participating in activities such as family and social gatherings, health care appointments and other meetings tended to disrupt daily routines. Potentially this resulted in patients forgetting to take their medication or deliberately leaving it at home and postponing the medication until later. Frequent changes in the number of medications, type, dosage and timing of medications also disrupted established routines and reduced adherence.

The costs of buying medication (moderate CERQual confidence)

In some studies, patients described the costs of buying prescribed medications as a barrier to adherence. Patients who were financially burdened tried to make their supply of medications last longer by skipping doses, taking lower doses of medicine than prescribed or, alternatively, asking their physician to prescribe double-strength medication to reduce the costs of buying medications.

Benchmarking the need for medication

Benchmarking the need for medication was both a facilitator and barrier to adherence. Patients used their lay beliefs and experiences of effects and side effects of medications to benchmark which medications were important to take and which medications could be omitted, completely or occasionally.

Absence of effect from a lay perspective (high CERQual confidence)

Patients prioritized the medications they felt produced noticeable effects such as symptom relief, pain relief or improved clinical parameters. Effective medications from the perspective of patients included antihypertensive medications, diabetes medications and analgesics. Medications with less noticeable effects were less important to patients and were more likely to be

Table 3. Characteristics of the included studies

| Study | Country | Treatment | Stage of disease | Total number of participants | Age (years) | Data collection | Methodology | Analysis | Topic |
|-----------------------------|-----------|---------------------------------------|--|------------------------------|-----------------|---|------------------------------|---------------------------------|--|
| Roso et al. [12] | Brazil | Attending renal clinic | CKD Stage 3-5 | 15 | 19-85 | Face-to-face interviews | Qualitative exploratory | Thematic | To explore how patients in conservative treatment of chronic renal insufficiency care for themselves |
| Clarkson and Robinson [13] | USA | Peritoneal dialysis and haemodialysis | CKD Stage 5 | 10 | 26-85 | Face-to-face interviews | Qualitative exploratory | Not stated | To explore the lived experience of patients with end-stage renal disease |
| Costantini [14] | Canada | Attending renal clinic | CKD Stage 1-3 | 14 | 19-69 | Face-to-face interviews | Qualitative exploratory | Content | To explore the self-management experiences of people with mild to moderate CKD |
| Curtin and Mapes [15] | USA | Haemodialysis | CKD Stage 5 | 18 | 38-63 | Face-to-face interviews | Qualitative exploratory | Content | To gain an insight into the factors that are associated with some dialysis patients' ability to live long lives on dialysis |
| Griva [16] | Singapore | Haemodialysis | CKD Stage 5 | 37 | 51.3 (mean age) | Face-to-face interviews and focus group interviews | Qualitative exploratory | Thematic | To explore cultural perspectives on facilitators and barriers to treatment adherence in HD patients |
| Guerra-Guerrero et al. [17] | Chile | Haemodialysis | CKD Stage 5 | 15 | 22-82 | Face-to-face interviews (indirect method observation) | Hermeneutic phenomenological | Thematic | To explore the lived experiences of patients on haemodialysis regarding adhering to treatment regimens and their perception of quality of life |
| McKillop and Joy [18] | UK | Attending renal clinic | CKD, stage not described (but not Stage 5) | 10 | 29-82 | Face-to-face interviews | Qualitative exploratory | Thematic | To explore attitudes towards medicines, polypharmacy and adherence in patients with CKD |
| Karamanidou et al. [19] | UK | Haemodialysis | CKD Stage 5 | 7 | 32-68 | Face-to-face interviews | Qualitative exploratory | Interpretative phenomenological | The experience of renal patients undergoing dialysis treatment, focusing on beliefs about their illness, prescribed treatment and the challenge of adherence |

(continued)

Table 3. Continued

| Study | Country | Treatment | Stage of disease | Total number of participants | Age (years) | Data collection | Methodology | Analysis | Topic |
|----------------------------|-----------|---------------------------------------|-------------------------------------|------------------------------|-------------|-------------------------|-------------------------|---|--|
| Lam et al. [20] | China | Peritoneal dialysis | CKD Stage 5 | 36 | 35–76 | Face-to-face interviews | Qualitative exploratory | Content | To explore adherence from patients' perspectives and to describe changes in adherence to a therapeutic regimen among patients undergoing continuous ambulatory peritoneal dialysis |
| Lindberg and Lindberg [21] | Sweden | Peritoneal dialysis and haemodialysis | CKD Stage 5 | 10 | 39–83 | Face-to-face interviews | Qualitative exploratory | Content | To explore obstacles to adherence to phosphate-binding medication and to describe the measures taken by dialysis patients to overcome these obstacles |
| Mason et al. [22] | UK | Treatment not described | CKD, stage not described | 9 | 56–76 | Focus group interviews | Qualitative exploratory | Framework approach with tenets of grounded theory | To identify and explore knowledge and attitudes regarding the control of blood pressure, patient empowerment and educational needs |
| Rifkin et al. [23] | USA | Dialysis and attending renal clinic | CKD Stage 3–5 | 20 | 55–84 | Face-to-face interviews | Qualitative exploratory | Thematic and ethnographic | To explore the major themes surrounding medication use and adherence decisions in older kidney disease patients |
| Walker et al. [24] | UK | Attending renal clinic | CKD Stage 4 | 9 | 63–83 | Face-to-face interviews | Qualitative exploratory | Thematic | To explore the experiences of patients attempting to integrate lifestyle changes into their lives |
| Williams et al. [25] | Australia | Attending renal clinic | CKD Stage 1–5 (but not on dialysis) | 23 | 30–77 | Face-to-face interviews | Qualitative exploratory | Johnson's model of medication adherence | To explore factors affecting adherence to multiple prescribed medications for consumers with diabetic kidney disease from the time of prescription to the time they took their medications |

(continued)

Table 3. Continued

| Study | Country | Treatment | Stage of disease | Total number of participants | Age (years) | Data collection | Methodology | Analysis | Topic |
|-----------------------------|-----------|-------------------------|--|------------------------------|-----------------|--|-------------------------|--|--|
| Williams <i>et al.</i> [26] | Australia | Attending renal clinic | CKD, stage not described (but not on dialysis) | 23 | 59.3 (mean age) | Face-to-face interviews | Qualitative exploratory | Framework approach according to Ritchie and Spencer | To examine how irrational thinking affects people's adherence to multiple medicines prescribed to manage their diabetic kidney disease |
| Williams and Manias [27] | Australia | Attending renal clinic | CKD Stage 2-4 | 39 | 68 (mean age) | Motivational interviewing via telephone | Qualitative exploratory | Thematic approach incorporating the modified Health Belief Model | To explore the motivation and confidence of people with coexisting diabetes, CKD and hypertension to take their medicines as prescribed |
| Williams <i>et al.</i> [28] | Australia | Attending renal clinic | CKD, stage not described (but not on dialysis) | 26 | 73.5 (mean age) | Motivational interviewing via telephone with interpreter | Qualitative exploratory | Framework method according to Ritchie and Spencer | To examine the perceptions of a group of culturally and linguistically diverse participants with the comorbidities of diabetes, CKD and cardiovascular disease to determine factors that influence their medication self-efficacy through the use of motivational interviewing |
| Ghimire <i>et al.</i> [29] | Australia | Haemodialysis | CKD Stage 5 | 30 | 44-84 | Face-to-face interviews | Qualitative exploratory | Thematic approach incorporating WHO medication adherence model | To explore factors associated with medication adherence, and examine the differential perspectives on medication-taking behaviour shown by haemodialysis patients |
| Bowling <i>et al.</i> [30] | USA | Treatment not described | CKD Stage 3-5 | 30 | 75.1 (mean age) | Focus group interviews | Qualitative exploratory | Grounded theory | To identify and describe the relationship among factors that facilitate or impede CKD self-management for older veterans with moderate to severe CKD |

Table 4. Summary of the main analytical and descriptive themes

| Logistics | Benchmarking the need for medication | Quality of the patient–physician relationship |
|--|---|---|
| <ul style="list-style-type: none"> Establishing and maintaining routines (high CERQual confidence) Cost of buying medication (moderate CERQual confidence) | <ul style="list-style-type: none"> Absence of effect from a lay perspective (high CERQual confidence) Lacking understanding about medication indication and effects (moderate CERQual confidence) Spurred by emergent symptoms (moderate CERQual confidence) | <ul style="list-style-type: none"> Eliciting patients wishes for involvement in decisions concerning medication (high CERQual confidence) Lacking information (moderate CERQual confidence) |

skipped. Skipping ‘less important’ medications was most pronounced in patients with few or no symptoms and/or when patients experienced that ‘less important’ medications were hard to swallow or tasted bad [14, 16, 17, 19, 25, 33]. These medications included lipid-lowering agents, histamine H2-receptor antagonists, calcium, phosphate-binding agents, statins, aspirin, metoclopramide, pantoprazole and vitamins. Specifically, calcium and phosphate-binding agents were often missed because of their size, taste and texture [12, 13, 19, 25, 29].

Patients were also prone to non-adherence when they experienced that side effects outweighed intended therapeutic effects. Side effects could range from minor and tolerable to severe, affecting the patient’s quality of life. Side effects included loss of appetite, nausea, stomach pain, hair loss, body aches, muscle pain, weight loss, coated mouth, tremors, dizziness, skin discoloration, low blood sugar, headache, diarrhoea, constipation, loss of sexual function or ‘feeling terrible’. Concerns about side effects and long-term adverse effects of polypharmacy also affected adherence, with patients altering doses or the timing of medications or skipping medications to prevent side effects.

Lacking an understanding of medication indications and effects (moderate CERQual confidence)

Lacking an understanding of the indication for medications, primarily the importance of preventive medications, was a barrier to adherence. Some patients did not know why medications were prescribed or how they worked, resulting in a lack of understanding of the importance of taking the medication. Conversely, knowing why medications were prescribed and how they worked facilitated adherence.

Spurred by emergent symptoms (moderate CERQual confidence)

Patients suffering from disease-related complications expressed regret about having been non-adherent. Facing dialysis and disease-associated complications, these patients acknowledged the importance of medical adherence. Emergent symptoms changed how they benchmarked the importance of medications, leading to a higher degree of adherence.

The quality of the patient–physician relationship

The quality of the patient–physician relationship was both a facilitator and barrier to adherence. Some patients highlighted that they were more likely to adhere to medications when they felt well-informed and involved in decisions concerning medication. Others happily delegated medication decisions. Patients who lacked information or felt their side effects were not considered tended to be less adherent to prescribed medications.

Eliciting patients’ wishes for involvement in decisions concerning medication (high CERQual confidence)

Patients expressed different wishes for being involved in decisions concerning medications. Some placed all their trust in physicians and readily let the physician take control and make decisions on their behalf. Others wished to collaborate as equal partners with physicians about treatment-related decisions, including medication. They wanted physicians to acknowledge their concerns and opinions about medication and wished to discuss the pros and cons of changes in medications, doses and effects versus side effects. They also wished to discuss how to manage the disease, the prescribed medication and side effects to suit their lifestyle preferences, including what to expect if they chose not to follow the prescribed treatment. Some wished to negotiate medicine doses in order to minimize side effects. In several studies, patients experienced insufficient time for discussing medications with physicians in the outpatient clinic [16, 18, 19, 33], a large turnover in physicians [16, 17], mistrust of the reasons for prescriptions (some suspected that medications were prescribed for research or financial gain) [15, 19, 25, 27] and non-empathetic communication [14, 15, 17, 19]. Lack of continuity, time, trust and involvement of patients wishing to partake in treatment decisions led to patients taking matters into their own hands in relation to medicine taking.

Lacking information (moderate CERQual confidence)

Feeling insufficiently informed about the indications, effects, side effects and interactions of prescribed medications affected adherence negatively. Some patients suspected physicians of withholding information, while others described getting conflicting information. For example, different information from different physicians or physician information differed from the drug information sheet. This resulted in apprehension, which in some patients posed a barrier to adherence.

Discussion

The aim of this review was to synthesize the available qualitative evidence on patient experiences of factors that facilitate and hinder adherence to medication in patients with CKD. We identified three main themes: logistics, benchmarking the need for medication and the quality of the patient–physician relationship.

Logistics referred to the complexity of managing and adhering to polypharmacy. Patients’ efforts to cope with this complexity included daily medication routines, aids and practical help from family and others. We assessed the confidence of the evidence for this theme to be high. Similar to our findings, a cross-sectional study of medication adherence among kidney transplant recipients’ showed that practical barriers, including

Table 5. Selection of quotes from patients to illustrate each descriptive theme

| Themes | Quotations | Contributing studies |
|--|--|--|
| Logistics | | |
| Establishing and maintaining routines | <p>'When you get into a habit, you're less likely to forget taking one.' [26]</p> <p>'...once or twice you might forget or if I am somewhere and the medication is at home or you are with friends at a particular time you were supposed to have taken the medication when you don't have the medication with you so at that time...I try not to do that but... ' [19]</p> <p>'I have, as I said, a table system when my tablets are running out to re-order because there are so many of them it's not just as easy as saying once a month, but they all run out different times and take different levels and what have you. So, I have to keep track of what we've got and when we have got it.' [24]</p> <p>'They've [the pharmacy] run out of the drug, go to get the prescription and find the prescription has run out, got to go back to the doctor to get another prescription before I get another tablet and that might take a couple of days and then you find you're back to square one [disease is uncontrolled].' [25]</p> <p>'...I have two pill organizers that I prepare at the same time...put five in the first compartment in the box and the rest in the others. I take the first ones straight away in the morning when I wake up...drink coffee and eat in the morning...and then I take my other morning medications.' [21]</p> <p>'...my medicine is part of my prayers, okay? So that's a good way to remember it. Like, I gotta say my prayers; I have to take my [medication].' [23]</p> <p>'I'm okay if I'm in the house. It's when I go out...half the time I'm sitting thinking I forgot my tablets.' [18]</p> <p>'Has so many pills I get daughter to refill [medicine prescriptions].' [28]</p> <p>'My wife makes sure I take them...she helps. She gets all medicines ready.' [29]</p> <p>'Been given new tabs (hypoglycaemic agents) to replace other ones. Does not know what they are-chemist fills Domette box.' [28]</p> | [16, 17, 18, 19, 21, 23, 24, 25, 26, 27, 28, 29, 30] |
| The cost of buying medication | <p>'...and they cost money more every month...I take but I take half...sometimes...I make test take half and if I feel OK then OK...Lasts longer and save money...If I feel bad then I go polyclinic and take all.' [16]</p> <p>'I'm living on my savings...and a bit of pension and a bit of superannuation...so now you only get one month's supply, so that makes it much more expensive...which is a lot of money when you're just living on the pension. It's just money I saved when I was working.' [25]</p> | [16, 25, 27, 28, 29] |
| Benchmarking the need for medication | | |
| Absence of effect from a lay perspective | <p>'It's to control the blood pressure for your kidneys. Even if I was to miss the other seven, I will take that one because I know to keep my blood pressure at a good level.' [18]</p> <p>'And I said, yeah, well, no problem I'm gonna take [niacin]. It's a benefit for my heart...I'm gonna go for it. And I took it for a while...but I didn't notice any benefit. I mean, nothing direct. I didn't feel it. If I take niacin, or I don't take it, no difference. I don't take metoprolol, I know there's a difference. I feel different, I feel some fatigue, I feel something missing.' [23]</p> <p>'If my Levomepromazine wasn't as good and effective for me I wouldn't take it because of the side effects.' [18]</p> <p>'I spent a good I'd say at least 6 months dancing around with my treatment, just not taking it serious. I wouldn't say really serious, just it seemed a bit excessive the amount of medication... There's no way it could be that bad, you feel good, that's the worst thing about it in the beginning you don't realize...' [14]</p> <p>'Take all the medicines that I need—just not statin and aspirin—and only take half coversyl [perindopril Prefer ramipril... ' [28]</p> <p>'I think it's just calcium tablets; it's not important. I skip it. I dare not do this with other medicines.' [20]</p> <p>'I had to take [antihypertensive medication], whether it was totally necessary or not, never really occurred to me, it was more like "well this is a preventative measure," so if I ran out of prescriptions sometimes I wouldn't go and get it filled straight away and I'd go for days, sometimes weeks without taking those medications.' [25]</p> <p>'...the tablets are so disgusting, their consistency is so disgusting, so disgusting you don't want to take...it's a big enough job taking the pills I'm supposed to take...they (the phosphate binding agent) didn't taste that great. They're orange flavoured so that chewing on them is no great joy...the chewable tablet was much too big. You couldn't take it with you anywhere.' [21]</p> <p>'Sometimes I wonder if it's the tablets so I miss them to see and it definitely does affect how I feel, if I'm feeling a bit yucky for a while, feeling a bit nauseous and just want to lie down basically. So I do get side effects that put me off taking them.' [24]</p> <p>'...but then I have other pills against nausea that I add to it...my stomach is so weak...nourishment first...for me it (the phosphate-binding agent) is absorbed just as well after a meal...nowadays I go and lie down for a while (after taking the phosphate-binding agent). Ten to fifteen minutes...' [21]</p> | [14, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 27, 28, 29, 30] |

(continued)

Table 5. Continued

| Themes | Quotations | Contributing studies |
|---|--|--|
| Lacking understanding of medication indications and effects | <p>'I don't take medicine for my kidneys; there is no medicine for kidneys, only for high blood pressure. There is one for the heart, which is metoprolol, and there are two for high blood pressure, which are losartan and amlodipine. I only take these three medicines. And at night I take simvastatin, but only sometimes; I don't take it often, because I do the diet and so I sleep well.' [12]</p> <p>'Well I know what some of them are for but I don't know what they're all for. Like when you were asking me before, merely because I can't read what's on the packet, I just pick which ones I like but I couldn't tell you which one's doing what job.' [25]</p> <p>'I've managed to get away with it. It's only the transplant people [who have to take their medicines strictly].' [27]</p> | [12, 21, 22, 23, 24, 25, 27, 28, 29, 30] |
| Spurred by emergent symptoms | <p>'...if I had known that not taking my binders would cause my bones to get brittle from the beginning, I would not care how sick they were making me, and...keep having side effects and nobody explained why I have this or what caused it.' [13]</p> <p>'I was a lot more spasmodic [taking medications] until my kidney function got to a point where it is now and I'm looking down the barrel of dialysis and that. I'm probably far more regimented than, and more fearful of not taking it, whereas in the past you know I've probably gone six months without...sort of (taking my tablets).' [25]</p> <p>'I wasn't aware of [the dangers of] blood pressure earlier and if I was, it would have been different.' [27]</p> | [13, 18, 25, 26, 27] |
| Quality of the patient-physician relationship | | |
| Eliciting patients' wishes for involvement in decisions concerning medication | <p>'Explaining the disease to the fullest, the meds, what's involved, what can happen, changes that are going to be happening in your life so that when it happens you're not wondering what's going on now.' [14]</p> <p>'But I...I adjust by myself, cause you can't listen to the doctor all the time, because I don't know whether they're writing a thesis or what, the way they prescribe the medication, every time you know more and more medications. But it doesn't work with me. I refuse to listen, I said no, I don't want to take. Too much of medication you know... ah. Even the renal tablets...I never touch.' [15]</p> <p>'These [two medicines] are for cholesterol, and I was only taking one pill for cholesterol, and my cholesterol was fine. Sometimes I think these salesmen come around and talk to the doctors and sell them a bill of goods, and the next thing you know, you're on it.' [23]</p> <p>'If you read what's on the prescription [insert] you'd be dead...but they should've said, "If you have any side effects such as," and then only two or three of the major ones...Those are not discussed. So, I had to assume that there's nothing adverse except in rare cases. Well, it turns out that's not true because everyone I've mentioned the [edema] to, they didn't blink an eye. They sort of smiled, "Oh, we know." That irritated me a lot...They acted as if they were getting paid to [prescribe it].' [23]</p> <p>'The problem I see is that it's making me lose my hair...They say it aren't the medicine. But naturally they're going to say it can't be the medicine. But what else can it be...I've tried stopping them all! I go every other night! Then I notice I don't lose so much hair...He tells me it aren't got nothing to do with the medication. But I still believe it does.' [23]</p> <p>'I think I'm the boss in this...you've got to be the one to do it. So basically I think I've played a major role. The doctor can only guide you; you've got to be the one to basically do it.' [14]</p> <p>'Does what doctor tells me to do. I really don't want to take medicines but doctor tells me I have to.' [28]</p> <p>'They usually tell me what they're giving me and why. And what the result should be and that's really all I need to know.' [23]</p> | [12, 13, 14, 15, 18, 22, 23, 24, 25, 26, 27, 28, 29] |
| Lacking information | <p>'I think information should be offered in the beginning, it shouldn't be withheld, and it's much harsher to find it out in the end. Hey okay, you're looking at being on these blood pressure meds the rest of your life, it's not going to go away. You need to have that realistic expectation from the beginning.' [14]</p> <p>'So see these are things doctors never tell you...Everything I get I go home and check it. Every single one of my other medicines says the same thing. And you know, you say: "Well, which one is it?"' [23]</p> <p>'Now I go to somebody senior to him (previous doctor) and when I go to see him...he says...well you shouldn't have been on this and you shouldn't have been on that...and you do tend to get confused!' [22]</p> | [14, 18, 22, 23, 24, 25, 28] |

changes in daily routines, were associated with non-adherence [31]. In another qualitative study, kidney transplant recipients' reported the importance of developing and maintaining routines to facilitate medication adherence [22].

Like other studies, we found that memory aids, assisting devices, associated activities, reminders and practical help from family and pharmacists facilitated adherence [23, 24, 35]. Living with a partner or spouse has likewise been shown to increase adherence [23, 35].

Using tools such as dosette boxes and memory tools may affect adherence both positively and negatively [1, 23, 36]. These tools may constitute a potential barrier to adherence for patients with impaired vision, sensory disturbances or reading difficulties. Clinicians should also be aware that medicine packaging, memory tools and multicompartiment devices such as dosette boxes do not necessarily increase medication adherence [1, 36]. They may, however, be helpful for patients who are forgetful or have practical problems with managing complex medication regimes [1, 36]. The potential benefits of memory tools for adherence in patients with physical and/or cognitive impairments warrant further examination.

Adherence improved when patients associated medications with daily routines. An approach to supporting medication adherence could be that clinicians systematically help patients map their everyday activities and encourage them to associate medication routines with these activities [1, 35–38].

Patients used their lay beliefs and experiences of effects versus side effects of medications to benchmark which medications to take and which to potentially omit. The confidence of the evidence for this theme was high. The Necessity–Concerns Framework (NCF) suggests that medication adherence is influenced by individual beliefs about the necessity of medications and their potential adverse effects [39]. For patients in the early stages of kidney disease who did not experience a high symptom burden, it appeared harder to acknowledge the need for medications, particularly if unpleasant side effects overshadowed therapeutic effects. Studies have previously found that side effects and the way in which they are addressed by health professionals influence adherence to medication [23, 24]. Those patients experiencing side effects that were acknowledged and well-managed became more adherent [23]. A recent systematic review found that behavioural interventions for coping with side effects increased adherence in patients with type 2 diabetes [40]. Acknowledging patient experiences of side effects and exploring patient preferences for managing side effects, reducing doses and switching medications are alternative approaches [1].

The quality of the patient–physician relationship was important for adherence. The confidence of the evidence for this theme was also high. Importantly, while some patients were happy to delegate medication and other treatment decisions to physicians, others desired more information, continuity and involvement in decisions concerning treatment and medications. These findings are confirmed in a systematic review of patient preferences for shared decisions in which the majority of patients preferred shared decisions [41]. Similarly, all studies identified a subset of patients who wanted to delegate decisions [41]. Consequently, the challenge for health professionals is to solicit patient preferences for involvement and tailor consultations accordingly [41]. Furthermore, health professionals need to be aware that patient preferences may evolve over time [41]. In line with this, current guidelines urge health professionals to support patients in making informed decisions about

treatment, including decisions to not take medications if this is what they wish [1, 36].

Several instruments have been created to elicit patients' preferences for involvement in decision making, but none of them have been found feasible in routine clinical settings [1, 36]. Chewning et al. [41] stress that we need neutral modes of assessing patient preferences for involvement in decision making in clinical practice so patients do not feel coerced into involvement or non-involvement. Measures for assessing patient wishes should therefore include explicit response options for both shared decision making and decision delegation [41]. Furthermore, we need insight into how patients perceive decisional processes regarding medications and which decisions they prefer to share with health professionals [41].

A recent Cochrane review assessing decision aids in people facing screening and treatment decisions concluded that decision aids improved people's knowledge of risks and benefits and their feeling of being informed and clear about their values [42]. The authors further concluded that more research is needed regarding the effect of decision aids on adherence to decisions taken [42]. There is evidence that educational and behavioural interventions increase adherence to phosphate control in adults receiving haemodialysis [43]. Elwyn et al. [44] expand the field by advocating the potential of integrating shared decision making and motivational interviewing, an integration that would be relevant to examine in the context of medication adherence in patients with CKD.

The strengths of our study include a comprehensive systematic review method adhering to the ENTREQ framework, the use of investigator triangulation to enhance transparency and reproducibility and the use of the CERQual approach to assess the confidence in our findings. In our review, we report on patient-experienced factors influencing adherence to medication. They correspond to those identified in a World Health Organization (WHO) report on adherence to medication across a range of chronic conditions [45]. The focus of our synthesis was patient-experienced factors. Therefore, we cannot comment on, for example, political or organizational influences mentioned in the WHO report [45]. The sample sizes in the included studies could be characterized as relatively small (median 20). Nevertheless, all studies reported that data saturation was achieved. We cannot rule out dissemination bias [46]. In all, 4 of 19 studies included were from the same group of authors. We cannot rule out that this may have introduced a risk of systematic distortion of the phenomenon of interest [11]. We defined data as all text labelled 'results' or 'findings', including patient quotations, as described by Thomas and Harden [9]. This involved the use of patient quotations gathered in one context to answer the review question specified in the current article. To assess the extent to which quotations and other data from the primary studies supporting our findings were applicable to the context (perspective or population, phenomenon of interest, setting) specified in our review question, we used the CERQual component relevance [11]. We attempted to distinguish variations in factors influencing adherence across treatments and stages of disease throughout the analysis. However, it was difficult to conclude decisively about the influence of, for example, stages of disease on this basis. Finally, the CERQual approach is a developing method for assessing how much confidence to place in findings from a qualitative evidence synthesis [11]. As it is still under development, experience with the approach is increasing and will contribute to further development. A limitation of CERQual is that it does not currently address the potential risk of dissemination bias.

Implications for research and clinical practice

We need more evidence on the effect of memory tools, including digital solutions, in patients with CKD, including those with cognitive and/or physical impairments. Studies examining the effect of behavioural interventions for coping with side effects are also relevant. Furthermore, research into the effect of models for shared decision making on adherence in patients with CKD is needed. Finally, additional qualitative studies involving subgroups of patients with CKD and different treatment regimens and stages of disease are needed to further contextualize adherence.

Our review suggests that health professionals play an important role in influencing patients' medication adherence. Helping patients to map daily routines and associate medicine taking with daily routines may facilitate adherence. Likewise, our findings indicate that health professionals should acknowledge patients' wishes for being involved in decisions concerning medications.

Conclusion

Helping patients to map their everyday activities and associate medications with everyday activities may facilitate adherence to medications. Memory aids supported medicine taking in patients with memory problems. Eliciting patient beliefs and values about medications and supporting patients to cope with side effects influenced adherence positively. Finally, a patient-centred approach addressing patients' wishes for involvement in medication decisions facilitated adherence. The findings in this synthesis resonate with previous research. It extends the known literature by synthesizing and formally assessing the confidence in our review findings.

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Conflict of interest statement

None declared.

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