Models of care for chronic kidney disease: a systematic review

Ruairidh Nicoll[1], Lynn Robertson[1], Elliot Gemmell[1], Pawana Sharma[1], Corri Black[1,2], Angharad Marks[1]

[1]School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, United Kingdom

[2] The Farr Institute of Health Informatics Research

Corresponding author:

Dr Angharad Marks

Chronic Disease Research Group

Institute of Applied Health Sciences

School of Medicine, Medical Sciences and Nutrition

University of Aberdeen

United Kingdom

Email: a.marks@abdn.ac.uk

Tel: +44 (0)1224 437134

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ABSTRACT

Chronic kidney disease (CKD) is common and presents an increasing burden to patients and health services. However, the optimal model of care for patients with CKD is unclear. We systematically reviewed the clinical effectiveness of different models of care for the management of CKD. A comprehensive search of eight databases was undertaken for articles published from 1992 to 2016. We included randomised controlled trials which assessed any model of care in the management of adults with pre-dialysis CKD, reporting renal, cardiovascular, mortality and other outcomes. Data extraction and quality assessment was carried out independently by two authors. Results were summarized narratively. Nine articles (seven studies) were included. Four models of care were identified: nurse-led, multidisciplinary specialist team, pharmacist-led and self-management. Nurse and pharmacist-led care reported improved rates of prescribing of drugs relevant to CKD. Heterogeneity was high between studies and all studies were at high risk of bias. Nurse-led care and multidisciplinary specialist care were associated with small improvements in blood pressure control. Evidence of long term improvements in renal, cardiovascular or mortality endpoints was limited by short follow up. We found little published evidence about the effectiveness of different models of care to guide best practice for service design, although there was some evidence that models of care where health professionals deliver care according to a structured protocol or guideline may improve adherence to treatment targets.

Key Words. Chronic kidney disease, model of care, systematic review

INTRODUCTION

Chronic kidney disease (CKD) is common with an estimated global prevalence of 11-13%.[1] CKD prevalence is rising, driven by an ageing population and the increasing prevalence of obesity, diabetes and hypertension.[2] As a result, CKD presents an increasing burden to health services [3]. Most patients with mild to moderate CKD are asymptomatic, but have a higher risk of cardiovascular disease and are at risk of developing anemia, metabolic bone disease or progressing to end-stage renal disease (ESRD) requiring renal replacement therapy (RRT).[4, 5] Interventions recommended to reduce the risk of these endpoints include lifestyle modification, anti-hypertensive medication (specifically inhibitors of the renin-angiotensin-aldosterone system), lipid modification, and achieving glycemic control in patients with diabetes mellitus.[5]

Patients with mild to moderate CKD are usually managed within primary care and referred to specialist care as the condition progresses.[6] However, efforts to increase the awareness of CKD have led to the identification of large numbers of patients with mild to moderate CKD, creating challenges in the design and delivery of health services.[5] How health services should be organized to support patients with CKD most effectively, is unclear.[5, 7]

The existing literature on interventions to improve outcomes in CKD is of predominantly individual interventions, eg psychological support, pharmacist medication review, anti-hypertensive medication.[8-10] In clinical practice, many individual interventions are used together for an individual patient. This multidimensional approach, grouping packages of interventions forms a 'model of care'. Understanding the optimal model of care for CKD patients is important and would allow the design of health services to maximize health and well-being whilst making best use of limited resources.[11] In this systematic review, we assessed the relative effectiveness of different models of care for the management of CKD for a range of outcomes.

METHODS

Data sources and searches

Cochrane methodology was followed, with the exception that only one reviewer screened titles of publications identified from searches. Electronic searches were performed to identify articles published between 1992 and October 2014, and updated through to June 2016. A search strategy was developed for MEDLINE, and adapted for seven other databases (File S1), which was constructed to be highly sensitive to take account of the lack of consistent terminology to identify models of care studies. The reference list of included articles and any systematic reviews identified from the searches were also checked. All citations were downloaded to Refworks Reference Management Software (Version 2.0). Titles were screened by one author (LR, RN, EG or CB). Abstracts and full text were screened independently by two authors (LR, RN, EG, CB, AM or PS). Any disagreements were resolved by discussion and consensus.

Study selection

Studies were included which compared any two multidimensional models of care in adults with pre-dialysis CKD and reported any of a defined list of outcomes. We included randomized controlled trials (RCTs), published in English from 1992 onwards (10 years prior to the KDIGO CKD guidelines).[6] We excluded observational studies in order to limit the potential for bias. For this review, a model of care must have been capable of delivering more than one type of intervention targeted at more than one aspect of disease management.

Data extraction and quality assessment

Standardized data extraction forms were developed. Data extraction was carried out independently by two authors and any disagreements were resolved through discussion and consensus. Data collected included setting, population details, quality assessment items, details of the intervention, model of care and comparison management details, and outcomes of interest. Quality assessment

was carried out using the Cochrane Collaboration's 'Risk of Bias' tool, without modification.[12] This uses pre-specified grading criteria to categorize the degree of risk as either low, unclear or high for multiple domains. The highest degree of risk for any of these domains is then used to determine the overall risk of bias. Risk of bias was assessed independently by two reviewers and any differences were resolved by consensus.

Outcomes

Outcomes of interest included clinical endpoints (progression of CKD, progression to ESRD without RRT, initiation of RRT, cardiovascular endpoints, mortality), management of risk factors (blood pressure, weight, anaemia, bone disease), prescribing of relevant medications, patient education, quality of life, health service satisfaction, health service use and health service costs.

Data synthesis and analysis

Study results were tabulated and reported qualitatively. Due to high levels of heterogeneity we were unable to perform a meta-analysis.

RESULTS

The searches identified 8672 citations (Figure 1). After removal of duplicates, title screening and abstract screening, 58 articles remained. Following full text review, 9 articles (7 studies) were deemed to meet the eligibility criteria and were included. Two trials were conducted in the Netherlands, two in the USA, one in Canada, one in China, and one in Taiwan. The characteristics of the included studies are shown in Table S2.

Description of studies and interventions

Studies were categorized according to the model of care assessed (Table 1). Three examined nurse-led care,[13-17] two examined multi-disciplinary specialist care,[18, 19] one examined pharmacist care[20]

and one examined a form of patient self-management care termed 'self-management support.[21] Studies ranged in size from 54 to 2199 participants. In the studies examining nurse-led care and multi-disciplinary specialist care, the intervention was compared against 'usual care' for the respective setting. However, in the studies examining pharmacist care and self-management support, these interventions were delivered in addition to usual care. The follow-up period for most studies was typically less than two years, with the exception of the MASTERPLAN study[13-15] examining nurse-led care, which had a mean follow-up of 5.7 years and Harris *et al*.[19] examining multi-disciplinary specialist care which had a five year follow-up period. A common feature to all of the models of care described in the studies was an increased emphasis on treatment that adhered to a standardized protocol or guideline.

Nurse-led care

In the MASTERPLAN study,[13-15] the intervention group received care delivered by specialist nurses working in secondary care under the supervision of nephrologists whilst the control group received nephrologist care. In Scherpbier de Haan *et al*.,[16] the intervention group received care delivered by nurse practitioners in a primary care setting under the supervision of General Practitioners (GPs) whilst the control group received usual care from GPs with the assistance of nurse practitioners. In Barrett *et al.*,[17] the intervention group received care led by nurses in primary care who could request assistance of GPs or nephrologists, as required, whilst the control group received usual care led by GPs.

Multidisciplinary specialist care

In Chan *et al.*,[18] the intervention group received structured multidisciplinary care from a diabetologist, endocrine trainees, diabetic nurses and a dietician in a secondary care setting whilst the control group received usual care as led by a diabetologist or general physician. In Harris *et al.*,[19]

the intervention group received structured multidisciplinary care from a nephrologist, renal nurse, dietician and social worker in a secondary care setting whilst those in the control group received usual care from GPs with other health professional input if requested.

Pharmacist care

In Cooney *et al.*,[20] the intervention group received pharmacy care input prior to previously arranged GP appointments whilst the control group received usual GP care only.

Self-management

In Chen *et al.*,[21] the intervention group participated in an intensive multidisciplinary programme to support self-management alongside usual nephrologist care whilst the control group received usual nephrologist care only.

Risk of bias

Using the Cochrane assessment of bias tool, all included studies were classified as having high risk of bias, primarily because participants and personnel were not blinded in any of the studies although this would have been difficult due to the type of intervention being assessed (Table S3). When blinding was removed as a key domain, five out of seven studies remained at high risk of bias with the other two at unclear risk of bias. In three studies the randomization process was not described clearly. Sealed envelopes were used to conceal allocation status in one study[18] and in the remaining studies allocation concealment was either not described or not performed. Blinding of outcome assessment was clearly described in only three studies. Outcome reporting was incomplete in three studies. In two of these studies the reasons for losses to follow-up were not clear[19, 21] and in the

third the authors reported higher rates of use of drugs blocking the renin-angiotensin-aldosterone system but do not report the data to support this.[16] The potential for selective reporting was present or unclear in six studies as the original study protocol was unavailable (86%). Other sources of bias identified included the potential for recruitment bias in one study,[17] lack of assessment to protocol adherence,[17] and anomalies in the way patient flow was described.[21]

Outcomes

Renal

All seven studies reported renal outcomes (Table 2). Of the three studies investigating nurse-led care, one reported a small statistically significant reduction in mean rate of decline in eGFR in the intervention group (1.26 vs 1.71 ml/min/1.73m^2/year, p=0.01, mean follow-up 5.7 years).[13-15] However, in the same study there was no statistically significant difference in the number of reported ESRD events or the number of patients with greater than 50% rise in serum creatinine. The remaining two studies found no effect of nurse-led care on renal outcomes.[16, 17] Two studies investigated multidisciplinary specialist care and found no effect on renal outcomes.[18, 19] One study investigating pharmacist care found no effect on renal outcomes.[20] One small study investigating self-management support found that the absolute eGFR was higher in the intervention group after one year (29.1 vs 15.7 ml/min/1.73m^2, p=0.04) and that the number of patients with a greater than 50% decline in eGFR was lower (1 vs 9, p<0.05). However, there was a non-significant difference in mean eGFR at baseline and there was no difference in the number of patients who progressed to requiring RRT.[21]

Cardiovascular

Two studies reported cardiovascular outcomes. The MASTERPLAN study[13-15] which investigated nurse led care found no significant difference between groups for the composite cardiovascular (HR 0.90, 95% CI 0.58-1.39) or composite ischaemic heart disease endpoint (HR 1.15, 95% CI 0.71-1.86).

Chan *et al.*[18] which investigated multidisciplinary specialist care found no significant difference between groups for their composite cardiovascular endpoint.

Mortality

Five studies reported mortality rates (Table 3). None found any significant difference in mortality between intervention and comparator models of care.

Blood Pressure

Five studies reported blood pressure outcomes (Table S4). Three of these studies investigated nurse-led care. One found a statistically significant reduction in final mean systolic (134 vs 136mmHg) and diastolic (77 vs 79mmHg) blood pressure in the intervention group.[13-15] One found a statistically significant increase in the number of patients with systolic blood pressure <130mmHg (44.4% vs 21.6%) and diastolic blood pressure <80mmHg (71.1% vs 50.0%) at one year.[16] However, the third found no significant improvement in blood pressure control.[17] One study investigated multi-disciplinary specialist care and found a statistically significant increase in the proportion of patients achieving a blood pressure <130/80mmHg (49% vs 27%).[18] One study investigated pharmacist care and found no significant difference in blood pressure outcomes.[20]

Prescribing

Six studies reported drug prescribing rates (Table S5). Three investigated nurse-led care and all demonstrated statistically significant increases in the prescribing of relevant drugs. These included ACE inhibitors,[13-16] lipid-modifying agents,[13-17] Aspirin,[13-15] Vitamin D,[13-16] and iron supplements.[17] There was no significant difference in the rate of prescribing for phosphate binders.[13-15] Two studies investigated multidisciplinary specialist care. One demonstrated no significant difference in rates of prescribing.[19] The other demonstrated a significantly higher rate of prescribing for ACE inhibitors although this was also present at baseline.[18] One study investigated pharmacist care and

demonstrated a significantly higher rate of prescribing for Vitamin D and bicarbonate at the end of the study but this was not demonstrated for phosphate binders or ACE inhibitors.[20]

Body Mass Index and weight

Three studies reported body mass index (BMI) or weight (Table S6). None demonstrated any significant improvement in weight or BMI.

Health service use and costs

Three studies reported on health service use (Table S6). One study investigating nurse-led care found that whilst the mean number of total visits (including nurse visits) per year was higher in the intervention group (7.0 vs 4.7, $p<0.001$), the mean number of physician visits per year was lower (2.8 vs 3.7, $p<0.001$). Although the study was not designed to include a cost-benefit analysis, a crude estimate of costs and savings is reported as a supplement.[13-15] One study investigating multidisciplinary specialist care found that the mean total number of outpatient clinic visits at 3-5 years was higher in the intervention group (26.0 vs 18.0, $p<0.001$) but demonstrated no difference in the number of hospitalizations or emergency department visits. The annual direct costs of the intervention were reported as $484 per intervention patient.[19] One small study investigating self-management support found the total number of hospitalizations at 12 months was significantly lower in the intervention group (5 vs 12, $p<0.05$).[21]

Patient education

One study investigating self-management support found a statistically significant increase in patient education status using a standardized CKD knowledge score in the intervention group at one year (10.13 vs 5.51, $p<0.01$).[21]

Quality of Life

One study investigating pharmacist care found no significant difference between intervention and comparator model of care with regards to quality of life outcomes.[20]

Patient satisfaction

Two studies reported satisfaction on with care, but only in the intervention group. Both reported high satisfaction with care received.[17, 20]

DISCUSSION

To our knowledge, this is the first systematic review of RCTs of the effectiveness of different models of care for CKD against a range of outcomes. The seven studies included in this review evaluated four different categories of models of care. Those examining nurse-led care and multi-disciplinary specialist care compared these models of care against usual care, whereas in those examining pharmacist-care and self-management support, the interventions were delivered in addition to usual care.

Although the majority of studies did not find a significant effect on outcomes, there was some evidence of improved short term clinical outcomes (e.g. blood pressure) and care utilization outcomes (e.g. prescribing). This was particularly true where models of care were protocol-driven through nurse and pharmacist led approaches. There was little evidence that these improvements translated into improvements in the rates of key clinical outcomes, including renal, cardiovascular or mortality endpoints. However, these were not reported in all studies with only two studies reporting cardiovascular outcomes and five reporting mortality. Furthermore, only two studies followed patients for more than two years and had statistical power calculations performed to ensure they were of sufficient size to detect a difference.

With regards to non-clinical outcomes, there was some evidence that nurse-led care led to a reduced number of physician visits, although this was necessarily associated with an increased number of nurse visits. The only study to investigate the addition of self-management support to usual care found a clinically and statistically significant reduction in the rate of hospital admissions in the intervention group. However, as this was a small study, the results should be treated with caution until replicated in a larger population.

Although there was significant heterogeneity between studies, there were common elements between studies and between different categories of model of care. In the majority of studies there was an increased use of either nursing or allied health professionals to deliver care. In addition, in the majority of studies, health professionals used a structured protocol or guideline focused on specific treatment targets to help them deliver care. This may explain why improvements in some outcomes were noted across different categories of models of care. There may also be variation with regard to country, setting, clinical practice, resources and practitioners' roles, eg qualified to prescribe or otherwise.

Other reviews of CKD models of care have included observational studies alongside RCTs. One review investigated multidisciplinary care in the management of CKD and found some evidence of improved renal and metabolic outcomes.[22] However, this systematic review included four studies, two of which were observational, and the majority of the positive findings were derived from the non-randomized observational studies. Of the two RCTs within this review, one was included within our review[19] and the other was excluded as it did not meet our definition of a multidimensional model of care.[23] Another review investigated pharmacist interventions in the management of CKD.[24] Most of the studies included were observational but it found some evidence that pharmacist

interventions led to improved prescribing and metabolic outcomes. None of these studies met the inclusion criteria for our review.

Our study has many strengths. With the exception of the initial title-screening, all parts of the selection process, quality assessment and data extraction were performed independently by two reviewers to limit the potential for bias. Eight databases were searched using a highly sensitive search strategy to take account of the lack of consistent terminology to identify models of care studies. The search was restricted to RCTs to limit the potential for bias.[25] However, there are study limitations. Although the search strategy was chosen to maximize sensitivity there may be relevant published studies not identified by our searches. Unpublished studies were not included, which may leave the review at risk of reporting bias. In addition, restricting the review to only include RCTs meant that any good quality observational studies were not included. The RCTs identified, however, were all classified as having a high risk of bias.

Despite the increasing recognition of the importance of identifying effective models of care for patients with long-term conditions such as CKD, there was little published evidence to guide best practice for service design.[26] This review identified only seven studies assessing four different multidimensional models of care between them. One potential reason may be perceived difficulty in designing studies to assess complex interventions. However, there are solutions including use of cluster RCTs and stepped wedge designs.[25] When a model of care is identified as improving outcomes, it is important to carefully define the intervention and identify which elements of care are responsible as this allows designers to improve services with minimal change. Models of care should be evaluated as complex interventions including the emerging approaches to shared care.[25]

In conclusion despite the growing burden from CKD, there was little published evidence about the effectiveness of different models of care to guide best practice for service design. There was limited

evidence, from studies classified as having a high risk of bias, that models of care where nurses or allied health professionals deliver care according to a structured protocol or guidelines may improve adherence to treatment targets; and also that self-management may reduce hospitalizations. In order to drive future policy recommendations, a multi-centre RCT of a highly protocolized model of care vs usual care that randomized on centre (considering a step-wedge methodology if necessary), with long follow-up of at least five years to allow assessment of hard outcomes such as mortality, readmission and health service use in addition to short term process related outcomes such as BP, and of sufficient size is required. To aid intervention design for future RCTs, a review of observational studies is recommended.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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SUPPORTING INFORMATION

File S1: Search strategy

Table S2: Characteristics of includes studies

Table S3: Risk of bias in included studies

Table S4: Blood pressure outcomes

Table S5: Prescribing outcomes

Table S6: Other outcomes

FIGURE LEGEND

Figure 1. Flow diagram of search and study selection process

Table 1. Description and components of models of care

Study	Number of participants	Follow-up (years)	Intervention Model of Care	Frequency of contact	Team Members (intervention)	Use of protocol	Patient Education	Lifestyle advice	Prescribing	Psychosocial support	Comparator Model of Care	Details of Comparator Model of Care
Peeters, Van Zuilen et al Masterplan Study	788	5.7 (mean)	Nurse-led care	3 monthly	Nurses, Nephrologist	✓	✓	✓	✓	×	Nephrologist-led care	Not stated
Scherpbier de Haan et al	164	1 (limited)	Nurse-led care	3 monthly	Nurse, Nephrologist, General practitioner	✓	×	✓	✓	×	GP-led care	Not stated
Barrett et al	474	2.0 (median)	Nurse-led care	4 monthly	Nurse, Nephrologist, GP	✓	×	✓	✓	×	GP-led care	Not stated
Chan et al	205	2	Multi-disciplinary specialist care	3 monthly	Diabetologist, Diabetic nurse and dietician.	✓	×	✓	✓	×	Physician-led care	Not stated
Harris et al	437	5	Multi-disciplinary specialist care	3-6 monthly	Nephrologist, Renal nurse, Dietician, Social worker	✓	×	×	✓	×	GP-led care	Not stated
Cooney et al	2199	1 (limited)	Pharmacist care†	Prior to GP review	Pharmacist, GP	✓	✓	✓	✓	×	GP-led care	Not stated
Chen et al	54	1 (limited)	Self-management support†	Weekly	Nephrologist, Dietician, Peers, CKD nurse specialist	✓	✓	✓	×	✓	Nephrologist-led care	Not stated

GP, general practitioner; CKD, chronic kidney disease

✓ included, × not included

† Intervention provided in addition to usual care (equivalent to the comparator group)

Table 2. Renal outcomes

Study	Study Category	Outcomes Reported	Intervention	Control	Significance
Peeters, Van Zuilen (2011, 2012, 2014)	Nurse-led care	Mean Rate of eGFR decline(ml/min/1.73m^2/year) (mean, Standard Deviation)	1.26 (0.12)	1.71 (0.12)	HR 0.45 (95%CI 0.12-0.78), p=0.01
		Renal replacement therapy events (n)	77	89	HR 0.75 (95%CI 0.51-1.08), p=0.12
		≥50% rise in serum creatinine at end of study (n)	130	153	HR 0.81 (95% CI 0.64-1.03), p=0.09
Scherpbier de Haan (2013)	Nurse-led care	eGFR (ml/min/1.73m^2) at 1 year (mean, Standard Deviation)	48.6 (8.7)	49.4 (8.0)	p=0.83
Barrett (2011)	Nurse-led care	Decline in eGFR >4ml/min/1.73m^2 after 20 months (%)	17.0	13.9	p=0.43
Chan (2009)	Multidisciplinary specialist care	ESRD (Creatinine >500µmol/L) at follow-up (%) Renal replacement therapy events (%)	11.0 6.6	14.6 8.3	p=0.14 p=0.28
Harris (1998)	Multidisciplinary specialist care	CrCl (ml/min) at follow-up (mean, Standard Deviation)	30 (16)	34 (24)	p=0.10
Cooney (2015)	Pharmacist-led care	ESRD at 1 year (number, %)	26 (2.4)	20 (1.8)	p=0.28
Chen (2011)	Self-management support	eGFR (ml/min/1.73m^2) at baseline (mean, Standard Deviation)	27.1 (14.8)	23.6 (13.1)	p=0.36
		eGFR (ml/min/1.73m^2)at 1 year (mean, Standard Deviation)	29.1 (20.6)	15.7 (10.7)	p=0.04
		Renal replacement therapy events (number, %)	4 (14.5)	5 (18.5)	p>0.05
		Greater than 50% decline in eGFR from baseline (number, %)	1 (3.7)	9 (33.3)	p<0.05

eGFR, estimated Glomerular Filtration Rate; CrCl, creatinine clearance; ESRD, end stage renal disease; HR, hazard ratio; CI, confidence interval

Table 3. Mortality

Study	Study Category	Outcomes Reported	Intervention	Control	Intervention Minus Control (%)	Significance
Peeters, Van Zuilen (2011, 2012, 2014)	Nurse-led care	Deaths after mean follow-up 5.7 years (n, %)	68/395 (17.2)	74/393 (18.8)	-1.6	HR 0.85 (95% CI 0.62-1.18), p=0.34
Harris (1998)	Multidisciplinary specialist care	Deaths after 3-5 years (n, %)	59/206 (28.6)	77/231 (33.3)	-4.7	p=0.29
Chan (2009)	Multidisciplinary specialist care	Deaths after 2 years (n, %)	8/104 (7.6)	11/101 (10.9)	-8.8	Not significant
Chen (2011)	Self-management support	Deaths at 1 year (n, %)	0/ 27 (0)	1/27 (3.7)	-3.7	Not reported
Cooney (2015)	Pharmacist-led care	Deaths at 1 year (n, %)	50/1070 (4.7)	74/1129 (6.6)	-1.9	p=0.06

n, number; HR, hazard ratio; CI, confidence interval

File S1. Search strategy

Databases searched

MEDLINE, EMBASE, Health Management and Information Consortium, Central Nursing and Allied Health Literature, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects and the Health Technology Assessment.

MEDLINE search terms

1 Renal Insufficiency, Chronic/di, dh, dt, ec, mo, nu, pc, rh, su, th [Diagnosis, Diet Therapy, Drug Therapy, Economics, Mortality, Nursing, Prevention & Control, Rehabilitation, Surgery, Therapy]
2 exp Diabetic Nephropathies/di, dh, dt, ec, mo, nu, pc, rh, su, th [Diagnosis, Diet Therapy, Drug Therapy, Economics, Mortality, Nursing, Prevention & Control, Rehabilitation, Surgery, Therapy]
3 exp Uremia/di, dh, dt, mo, nu, pc, rh, su, th [Diagnosis, Diet Therapy, Drug Therapy, Mortality, Nursing, Prevention & Control, Rehabilitation, Surgery, Therapy]
4 (CKD or CKF or CRD).tw.
5 chronic kidney disease.tw.
6 chronic renal insufficiency.tw.
7 diabetic kidney disease.tw.
8 diabetic nephropath$.tw.
9 diabetic kidney failure.tw.
10 pre-dialysis.tw.
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12 models, nursing/
13 models, organizational/
14 exp Patient Care/ae, ec, is, mt, mo, st, sn, ut [Adverse Effects, Economics, Instrumentation, Methods, Mortality, Standards, Statistics & Numerical Data, Utilization]
15 exp Patient Care Management/ec, mt, og, st, sn, td, ut [Economics, Methods, Organization & Administration, Standards, Statistics & Numerical Data, Trends, Utilization]
16 "referral and consultation"/ or gatekeeping/ or remote consultation/ or secondary care/ or tertiary healthcare/
17 Patient Education as Topic/ec, ed, ma, mt, og, st, sn, td, ut [Economics, Education, Manpower, Methods, Organization & Administration, Standards, Statistics & Numerical Data, Trends, Utilization]
18 Nurse Clinicians/og [Organization & Administration]
19 preventive health services/ or diagnostic services/ or "early intervention (education)"/ or early medical intervention/ or health education/
20 model? of care.tw.
21 care system.tw.
22 care program$.tw.
23 care pathway.tw.
24 nursing model.tw.
25 organi?ational model.tw.
26 (nephrol$ adj4 refer).tw.
27 (patient adj4 refer).tw.
28 preventive health services.tw.
29 (multidisciplinary adj3 care).tw.
30 (interdisciplinary adj3 care).tw.
31 low clearance clinic.tw.
32 shared care.tw.

33 clinical pathway.tw.
34 renal service.tw.
35 nephrol$ service.tw.
36 integrated care.tw.
37 (nurse-led adj3 care).tw.
38 (nurse-based adj3 care).tw.
39 (nurse-led adj3 clinic).tw.
40 (nurse-led adj3 program$).tw.
41 (nurse-coordinated adj3 care).tw.
42 (nurse-coordinated adj3 clinic).tw.
43 patient led.tw.
44 self-led.tw.
45 nephrol$ care.tw.
46 ((patient or people) adj3 education program$).tw.
47 nurse clinicians.tw.
48 self management.tw.
49 case manag$.tw.
50 disease management program$.tw.
51 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50
52 11 and 51
53 animals/
54 52 not 53
55 limit 54 to (english language and yr="1992 -Current")

Table S2. Characteristics of included studies

Study ID	Population	Setting	Intervention	Comparator	Outcomes Measured	Length of Study (years)
Peeters, Van Zuilen et al (12,14) Masterplan Study Netherlands	Age >18 years, CKD (CrCl 20-70)	Secondary care	Nurse-led care	Nephrologist-led care	Renal, Death, Cardiovascular, BP, BMI, Prescribing, Health service use	5.7 (mean follow-up)
Scherpbier de Haan et al (15) Netherlands	Age >18 years, CKD (eGFR <60)	Primary and secondary care	Nurse-led care	GP-led care	Renal, Death, BP, BMI, Prescribing, Quality of Life	1
Barrett et al (16) Canada	Age 40-75 years, CKD (eGFR 25-60)	Primary care	Nurse-led care	GP-led care	Renal, BP, Prescribing	2.0 (median follow-up)
Chan et al (17) China	Age 35-75 years, Type 2 Diabetes, CKD (serum creatinine 150-350µmol/L)	Secondary care	Multi-disciplinary specialist care	Physician-led care	Renal, Death, Cardiovascular, BP, Prescribing	2
Harris et al (18) USA	CKD (CrCl <50)	Secondary care	Multi-disciplinary specialist care	GP-led care	Renal, Death, Prescribing, BMI, Health service use	5
Cooney et al (19) USA	Age 18-85 years, CKD (eGFR< 45)	Primary care	Pharmacist care[a]	GP-led care	Renal, Death, BP, Prescribing Quality of life, PTH measurements	1
Chen et al (20) Taiwan	Age 18-80 years, CKD (eGFR 30-60)	Secondary care	Self-management support[a]	Nephrologist-led care	Renal, Death, Health service use, Patient education	1

CKD, chronic kidney disease; CrCl, creatinine clearance ml/min; eGFR, estimated glomerular filtration rate MDRD formula, ml/min/1.73m^2; BP, blood pressure; BMI, body mass index; GP, general practitioner

[a] in addition to usual care (equivalent to the comparator group)

Table S3. Risk of bias in included studies

Study Author	Intervention	Random Sequence Generation	Allocation Concealment	Blinding of participants and Personel	Blinding of outcome assessment	Incomplete outcome data addressed	Selective reporting	Other sources of Bias	Overall risk of bias
Peeters, Van Zuilen et al	Nurse-led care	+	?	-	+	+	?	+	-
Scherpbier de Haan et al	Nurse-led care	?	-	-	?	-	-	+	-
Barrett et al	Nurse-led care	?	?	-	-	+	?	-	-
Chan et al	Multidisciplinary specialist care	+	+	-	-	+	+	-	-
Harris et al	Multidisciplinary specialist care	?	?	-	?	-	?	+	-
Cooney et al	Pharmacist care	+	?	-	+	+	?	+	-
Chen et al	Self-management	+	?	-	+	-	?	-	-

+	Low Risk
?	Unclear Risk
-	High Risk

Table S4. Blood pressure outcomes

Study	Study Category	Outcomes Reported	Intervention	Control	Significance
Peeters, Van Zuilen (2011,2012,2014)	Nurse-led care	Final systolic blood Pressure (mmHg)(mean, 95%CI)	134 (132-135)	136 (135-138)	p=0.03
		Final diastolic blood Pressure (mmHg)(mean, 95%CI)	77 (77-78)	79 (78-80)	p=0.01
Scherpbier de Haan (2013)	Nurse-led care	Change in systolic blood pressure at 1 year (mmHg) (mean, 95% CI)	-8.1 (-11.3, -4.8)	0.2 (-3.6-3.8)	Not reported
		Patients with systolic blood pressure <130mmHg at 1 year (n, %)	40 (44.4)	16 (21.6)	p=0.003
		Change in diastolic blood pressure at 1 year (mmHg) (mean, 95% CI)	-1.1 (-3.2, 1.0)	0.5 (-1.8, 2.9)	Not reported
		Patients with diastolic blood pressure <80mmHg (n, %)	64 (71.1)	37(50)	p=0.007
Barrett (2011)	Nurse-led care	Patients with blood pressure <130/80mmHg (2 years) (%)	63	47	p=0.76
Chan (2009)	Multidisciplinary specialist care	Last available systolic blood pressure (mmHg) (mean, SD)	135 (25)	137 (21)	p=0.15
		Last available diastolic blood pressure (mmHg) (mean, SD)	68 (12)	71 (12)	p=0.02
		Patients with blood pressure <130/80 mmHg (%)	49	27	p<0.01
Cooney (2015)	Pharmacist-led care	Final systolic blood pressure in patients with baseline blood pressure >130/80 (mmHg) (mean, SD)	135.1 (17.4)	134.4 (17.6)	p=0.57

CI, confidence interval; SD, standard deviation

Table S5. Prescribing outcomes

Study	Study Category	Outcomes Reported	Intervention	Comparator	Significance
Peeters, Van Zuilen (2011, 2012, 2014)	Nurse-led care	Use of ACE inhibitors at end of follow-up (%)	90.0	83.0	p<0.001
		Use of Statin at end of follow-up (%)	84.0	75.0	p<0.001
		Use of Aspirin at end of follow-up(%)	69.0	49.0	p<0.001
		Use of Vitamin D at end of follow-up(%)	47.0	37.0	p=0.002
		Use of Phosphate binder at end of follow-up(%)	15.0	18.0	p=0.14
Scherpbier de Haan (2013)	Nurse-led care	Use of lipid-modifying agent (%) (1 year)	73	59	p=0.004
		Use of Vitamin D (%)(1 year)	16	1	p=0.002
		Use of ACE inhibitor or ARB (%) (1 year)	81	73	p=0.01
Barrett (2011)	Nurse-led care	Use of statin in patients with LDL >2.5mmol/L (%) (2 years)	84	51	p=0.0003
		Use of iron supplement in patients with iron saturation <0.2 (%) (1 year)	35	14	p=0.005
Chan (2009)	Multidisciplinary specialist care	Use of ACE inhibitors or ARB (%) (2 years)	69	49	p<0.01
Harris (1998)	Multidisciplinary specialist care	Use of ACE inhibitors at 3-5 years (%)	36	33	p=0.40
Cooney (2015)	Pharmacist led care	Use of ACE inhibitor or ARB at end of study (%)	64.2	61.7	p=0.41
		Use of Phosphate binder at end of study (%)	22.4	23.5	p=0.87
		Use of Vitamin D at end of study (%)	61.9	52.4	p=0.004
		Use of Bicarbonate at end of study (%)	24.0	13.0	p=0.03

ACE, angiotensin converting enzyme; LDL, low density lipoprotein

Table S6. Other outcomes

Study	Study Category	Outcomes Reported	Intervention	Control	Satistical Significance
Weight and BMI					
Peeters, Van Zuilen (2011, 2012, 2014)	Nurse-led care	BMI at end of study (kg/m^2) (mean, 95%CI)	27.0 (26.6, 27.5)	27.1 (26.6, 27.6)	p=0.83
Scherpbier de Haan (2013)	Nurse-led care	BMI at 1 year (kg/m^2) (mean, SD)	28.9 (4.7)	28.4 (4.6)	p=0.68
Harris (1998)	Multidisciplinary specialist care	Weight at 3-5 years (kg) mean (SD)	76 (20)	75 (18)	p=0.65
Health service use					
Peeters, Van Zuilen (2011, 2012, 2014)	Nurse-led care	Visits per year at 2 years (mean, SD)	7.0 (2.9)	4.7 (2.9)	p<0.001
		Nurse practitioner visits per year at 2 years (mean, SD)	4.2 (1.4)	1.0 (0.4)	Not Reported
		Physician visits per year at 2 years (mean, SD)	2.8 (2.2)	3.7 (2.9)	p<0.001
Harris (1998)	Multidisciplinary specialist care	Hospitalisations at 3-5 years (mean, SD)	1.3 (1.8)	1.3 (2.1)	p=0.94
		Emergency department visits at 3-5 years (mean, SD)	2.6 (3.5)	2.8 (5.0)	p=0.52
		Outpatient clinic visits at 3-5 years (mean, SD)	26.0 (28.0)	18.0 (19.0)	p<0.001
Chen (2011)	Self-management support	Hospitalisations at 12 months (number, %)	5 (18.5)	12 (44.5)	p<0.05

BMI, body mass index; SD, standard deviation; CI, confidence interval