SPECIAL ARTICLE

Nurse practitioners improve quality of care in chronic kidney disease: two-year results of a randomised study

A.D. van Zuilen[1]*, P.J. Blankestijn[1], M. van Buren[2], M.A.G.J. ten Dam[3], K.A.H. Kaasjager[4], G. Ligtenberg[5], Y.W.J Sijpkens[6], H.E. Sluiter[7], P.J.G. van de Ven[8], G. Vervoort[9], L. Vleming[2], M.L. Bots[10], J.F.M. Wetzels[9]

[1]Department of Nephrology, University Medical Center Utrecht, Utrecht, the Netherlands, [2]Department of Internal Medicine, Haga Hospital, the Hague, the Netherlands, [3]Department of Internal Medicine, Canisius Wilhelmina Hospital, Nijmegen, the Netherlands, [4]Department of Internal Medicine, Rijnstate Hospital, Arnhem, the Netherlands, [5]Dutch Health Care Insurance Board, Diemen, the Netherlands, [6]Department of Nephrology, Leiden University Medical Center, Leiden, the Netherlands, [7]Department of Internal Medicine, Deventer Hospital, Deventer, the Netherlands, [8]Department of Internal Medicine, Maasstad Hospital, Rotterdam, the Netherlands, [9]Department of Nephrology, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands, [10]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands, *corresponding author: tel.: +31-(0)887558683, fax:+31-(0)302543492, e-mail: a.vanzuilen@umcutrecht.nl

ABSTRACT

Background: Chronic kidney disease (CKD) is associated with increased cardiovascular risk. Here we evaluate whether strict implementation of guidelines aimed at multiple targets with the aid of nurse practitioners (NP) improves management in patients with CKD.

Methods: MASTERPLAN is a randomised controlled clinical trial, performed in nine Dutch hospitals. Patients with CKD (estimated glomerular filtration rate (eGFR) 20-70 ml/min) were randomised to receive NP support (intervention group (IG)) or physician care (control group (CG)). Patients were followed for a median of five years. Presented data are an interim analysis on risk factor control at two-year follow-up.

Results: We included 788 patients (532 M, 256 F), (393 CG, 395 IG), mean (±SD) age 59 (±13) years, eGFR 38 (±15) ml/min/1.73m2, blood pressure (BP) 138 (±21)/80 (±11) mmHg. At two years 698 patients (352 IG, 346 CG) could be analysed. IG as compared with CG had lower systolic (133 *vs* 135 mmHg; p= 0.04) and diastolic BP (77 *vs* 80 mmHg; p=0.007), LDL cholesterol (2.30 *vs* 2.45 mmol/l; p= 0.03), and increased use of ACE inhibitors, statins, aspirin and vitamin D. The intervention had no effect on smoking cessation, body weight, physical activity or sodium excretion.

Conclusion: In both groups, risk factor management improved. However, changes in BP control, lipid management and medication use were more pronounced in IG than in CG. Lifestyle interventions were not effective. Coaching by NPs thus benefits everyday care of CKD patients. Whether these changes translate into improvement in clinical endpoints remains to be established.

KEYWORDS

Blood pressure, cardiovascular disease, clinical epidemiology, chronic kidney disease, dyslipidaemia

INTRODUCTION

Chronic kidney disease (CKD) is consistently related to excess cardiovascular morbidity and mortality. The benefits of blood pressure (BP) management on cardiovascular risk in CKD have not been shown in dedicated trials although several post-hoc subgroup analyses among CKD patients have suggested benefit.[1,2] Only recently, statins were shown to be effective to reduce cardiovascular risk in CKD patients in the Study of Heart and Renal Protection.[3] Up till now intervention studies targeting other single risk factors to lower cardiovascular events (ADVANCE, CREATE, CHOIR) have not been very successful in CKD patients.[4-6]

Similarly, few strategies besides lowering of BP and proteinuria have proven effective to attenuate the deterioration of renal function in patients with CKD.[7]

One of the possible explanations is that CKD is a multifactorial disease process in which both traditional cardiovascular risk factors and non-traditional risk factors (inflammation, CKD-metabolic bone disease, anaemia, proteinuria) interact. No single factor may play the major causative role. Based on this hypothesis it can be expected that a multifactorial approach is the most appropriate way to reduce cardiovascular morbidity and preserve kidney function in patients with CKD. Such a strategy was proven effective in diabetic patients.[8]

Indeed, guidelines for the treatment of CKD involve management directed at multiple treatment targets. The guidelines published in 2003-2005, however, were based upon extrapolation from other populations because of the paucity of data in patients with CKD.[9] Implementation of these guidelines in routine clinical practice is difficult. We, and others, have shown that treatment targets are often not met.[10-12] In addition, differences between centres were present.[13,14] Positive results from single-centre studies may therefore not be generalisable.

To address the need for improvement in CKD care we evaluated the added value of specifically trained nurses in the care of CKD patients. In similar study protocols, specialised nurses, cooperating in teams with doctors, have improved care in outpatients with diabetes, myocardial infarction and heart failure.[8,15-17]

To evaluate this hypothesis the randomised controlled Multifactorial Approach and Superior Treatment Efficacy in Renal Patients with the Aid of Nurse practitioners (MASTERPLAN) study was designed. We present the interim results after two years of follow-up on improvement in care, attainment of treatment targets, and between-centre differences. The primary endpoints will be reported when available in another paper, expected 2012.

MATERIALS AND METHODS

The MASTERPLAN study [Trial registration ISRCTN registry: 73187232 (http://isrctn.org)] is a randomised controlled trial conducted in nine hospitals with a nephrology department in the Netherlands. The trial is reported in accordance with the CONSORT guidelines.[18] Rationale and design have been published elsewhere.[19,20] The effects of a multitargeted treatment regimen executed by a specialised nurse under the supervision of, and in collaboration with, a nephrologist are compared with the care delivered by the patients own nephrologists. In both arms of the study, the same treatment guidelines apply. The primary endpoint is a composite nonfatal myocardial infarction, stroke and cardiovascular mortality. Secondary endpoints are all-cause mortality, achievement of treatment goals for the various risk factors, decline of kidney function and quality of life.

Patients were eligible for inclusion when 18 years or older and diagnosed with CKD with a creatinine clearance estimated by the Cockcroft-Gault equation between 20 and 70 ml/min. The following conditions were considered exclusion criteria:

- A kidney transplant less than a year before inclusion.
- Acute kidney failure or rapidly progressive glomerulonephritis established by the treating physician.
- Any malignancy less than five years before inclusion other than basocellular or squamous cell carcinoma of the skin.
- Participation in other clinical trials requiring the use of study medication.

Recruitment began in April 2004 and continued until December 2005. From April 15th 2005 until the end of the inclusion period the Cockcroft-Gault equation was modified to take into account body surface area according to then prevailing insights into the applicability of formulas to estimate renal function.[21-24] This modification was approved by the medical ethics committee.

After the baseline evaluation, the patients were randomised to either nurse practitioner (NP) care or usual care in a 1:1 ratio. Randomisation to treatment was stratified by centre, gender and kidney transplant status using a web-based randomisation module and performed in predefined blocks. Patient, NP and physician were familiar with the treatment allocation. All investigators handling the data, however, were blinded until June 2010. Follow-up continued until June 2010. Endpoint evaluation and data analysis is scheduled for end 2011/beginning 2012. The study was approved by an institutional medical ethics committee and all subjects gave informed consent. All participating hospitals were teaching hospitals that offered a full range of nephrology treatment including kidney replacement therapy (both haemodialysis and peritoneal dialysis) and were involved in the care of kidney transplant recipients. Three hospitals were university clinics that offered tertiary care and had kidney transplant programs. The number of beds per hospital ranged from 414 to 953.

The same set of guidelines and treatment goals applied to all patients. Both patients and physicians were provided with information about the beneficial effects of multifactorial risk factor management regardless of treatment allocation. In the intervention group NPs, supervised by a qualified nephrologist, actively pursued lifestyle intervention (physical activity, nutritional counselling, weight reduction and smoking cessation), the use of specified cardioprotective medication and the implementation of current guidelines. The NP regularly checked whether treatment goals were met

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and when deemed appropriate adjusted treatment to achieve target values. Modification of therapy was executed according to flowcharts that were derived from then current guidelines. For lifestyle-modifiable risk factors the NP applied motivational interviewing as a technique to improve lifestyle in the intervention group.[11] In the intervention group patients were also seen by their nephrologist regularly (although no minimum frequency was required in the study protocol). Acetylsalicylic acid was included in the intervention because of the then proposed status of CKD as a coronary heart disease risk equivalent and the possible (but untested) benefits of acetylsalicylic acid in this context.[25,26] This was in line with a then valid guideline firmly advocating the use of aspirin in primary prevention in patients with diabetes mellitus (which was, however, downgraded in a later version).[27,28] Use of aspirin as primary prevention was deemed contraindicated by protocol if patients had a history of a cerebral haemorrhagic event, autosomal dominant polycystic disease with a family history of cerebral haemorrhagic events, a known bleeding tendency or a history of pyrosis, reflux or gastrointestinal bleeding.

Physician care comprised 'usual care'. In contrast to the intervention group and in agreement with real-life practice no extra incentives to adhere to the guidelines were supplied.

Patients in the intervention group visited the NP at least every three months, whereas the frequency of visits of the control patients was left to the discretion of their nephrologist. Medication use was recorded every three months in an online case report form as were office BP, bodyweight and predefined laboratory measurements. In both patient groups twice yearly standardised oscillometric BP measurements after 15 minutes of supine rest were taken. Ankle brachial index and evaluation of endpoints were performed annually in both intervention and control groups. Additionally patients filled out questionnaires regarding quality of life and physical activity on a yearly basis. Under the assumption that patients were in a steady state, sodium excretion was applied as a measure of sodium intake. Blood was drawn and a 24-hour urine sample was collected. Blood and urine samples were analysed locally. Medical history was obtained from the medical records. History of CV disease was defined as a history of myocardial infarction, stroke or vascular intervention. Diabetes mellitus (DM) at baseline was defined as the use of glucose-lowering drugs or a fasting glucose over 7.0 mmol/l. Adherence to the Dutch Guidelines of Healthy Physical exercise was determined with the validated SQUASH questionnaire.[29] The underlying diagnosis of kidney disease was determined by the treating physician and categorised using the ERA-EDTA (European Renal Association) registration criteria. To allow for comparisons with other studies, we report eGFR using the abbreviated MDRD formula.[30]

STATISTICAL ANALYSIS

Baseline characteristics are expressed as means (SD) or proportions. For non-parametric data medians [range] have been supplied.

To address the effect of the intervention on risk factors after two years of follow-up we used generalised estimating equations (GEE) to assess time-dependent mean changes in risk factors within and between treatment arms.

The main assumption of the GEE approach is that measurements are assumed to be dependent within subjects and independent between subjects. The correlation matrix that represented the within-subject dependencies was estimated using an autoregressive relationship (i.e., correlation between variables within subjects are assumed to decline with time between the measurements). For the current analysis, the interest was in the mean difference over time in risk factor levels between treatment arms. GEE analyses were performed using the on-trial measurements with adjustments for baseline measurements. All p values were two-sided, and p values less than 0.05 were considered to indicate statistical significance. No adjustment for multiple statistical testing was made.[31]

We also evaluated if the specialised nursing care reduced the differences in care between centres. To this end we calculated the absolute difference between the group mean and centre mean for each risk factor. Relation of the absolute differences between group means and centre means with time was then calculated using a Spearman correlation coefficient, with a negative correlation illustrating a reduction of between-centre differences over time. All analyses were performed with SPSS 17.0 (SPSS inc., Chicago, USA).

RESULTS

About 60% of patients deemed eligible by their physician and asked to participate in the study actually participated and were included. The main reasons for non-participation were reluctance of the patient to changes in drug therapy and inability of the patient to attend the required visits.

A total of 793 patients were included in the study. Three patients did not meet inclusion criteria and two declined participation after randomisation. At two years of follow-up 346 patients in the control group and 352 patients in the intervention group were available for analysis (*figure 1*). Baseline demographics are shown in *table 1*. The mean age of patients was 59 (±13) years; 6.7% of patients are KDOQI CKD class 1 or 2, 60.8% class 3, 30.2% class 4 and 2.4% class 5. Of the patients, 17% had no albuminuria, 49% had microalbuminuria and 34% had overt proteinuria. All characteristics were well balanced between the groups

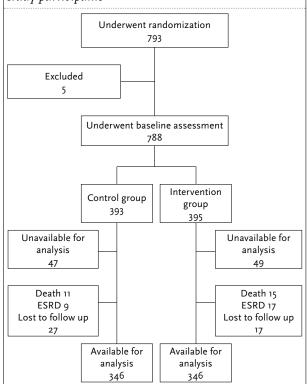Van Zuilen, et al. Nurse practitioners improve quality of care in patients with CKD.

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Figure 1. *Enrolment, randomization, and follow-up of study participants*

Table 1. *Baseline characteristics*

Parameter	Control group (n=393)	Intervention group (n=395)
Age (years)	59.3 (12.8)	58.9 (13.1)
Gender (male) (%)	68	67
Race (Caucasian)	93	91
Nephrological diagnosis (%)		
Diabetic nephropathy	9	11
Renovascular	28	26
Glomerulonephritis/ interstitial nephritis	34	28
Congenital disease	13	11
Unknown	16	24
Kidney transplantation (%)	14	14
Prior CV disease by questionnaire (%)	25	33
Creatinine (mcmol/l)	181 (67)	182 (64)
eGFR (ml/min/1.73m2)	37.7 (14.0)	38.4 (15.2)
Office systolic BP (mmHg)	139 (22)	138 (20)
Office diastolic BP (mmHg)	81 (11)	80 (11)
Proteinuria (g/24 h) Median [25th/75th percentile]	0.3 [0.1-0.8]	0.2 [0.1-0.8]
Albumin creatinine ratio (mg/mmol) Median [25th/75th percentile]	18.8 [6.8-51.9]	15.0 [5.6-47.5]
LDL cholesterol (mmol/l)	2.74 (0.90)	2.78 (0.95)
Haemoglobin (mmol/l)	8.2 (1.0)	8.2 (1.0)
History of DM (%)a	23	26
Phosphate (mmol/l)	1.10 (0.24)	1.10 (0.25)
PTH (pmol/l) [median 25th/75th percentile]	9 [5-14]	9 [5-15]
Sodium excretion (mmol/24 h) [median 25th/75th percentile]	150 [113-189]	148 [116-195]
BMI (kg/m2)	27.2 (4.9)	27.0 (4.6)
Physical exercise (adherence to Dutch physical activity guideline) (%)	60	57
Physical activity (activity score=intensity/min/week/1000)	6182 (4467)	5803 (3891)
Smoking (%)	24	19

Values are proportions, means with corresponding standard deviation, or median with inter-quartile ranges, whenever appropriate. a: History of diabetes mellitus defined as using blood glucose lowering medication or fasting glucose >7.0 mmol/l. CV = cardiovascular; eGFR = estimated glomerular filtration rate; LDL = low-density lipoprotein; DM = diabetes mellitus, PTH = parathyroid hormone; BMI = body mass index.

apart from a history of cardiovascular disease which was more prevalent in the intervention group and current smoking which was less prevalent in the intervention group.

The changes in risk factors after one and two years are shown in *table 2*. In both the intervention and control group changes in several risk factors were found. In both groups the systolic BP, diastolic BP, LDL cholesterol, haemoglobin and percentage of smokers decreased. In both groups statistically significant reductions in eGFR and an increase in use of ACE inhibitors or angiotensin receptor blockers, statins, vitamin D and aspirin were found (*table 2*).

Systolic BP, diastolic BP and LDL cholesterol were lower in the intervention group at two years and also declined significantly more than in the control group. At two years the difference between the two groups was 2 mmHg for systolic, 3 mmHg for diastolic BP and 0.15 mmol/l for LDL cholesterol. Use of cardioprotective medication increased more after two years in the intervention group than in the control group: ACE inhibitors or angiotensin receptor blockers (+8.6% *vs* +3.7%), statins (+21.2% *vs* 14.2%), acetylsalicylic acid (+23.4% *vs* +9.4%) and vitamin D supplements (+28.4% *vs* 16.1%). Of the patients in the intervention group, 20.4% used coumarin derivatives and an additional 4.3% had a contraindication and were therefore not prescribed acetylsalicylic acid.

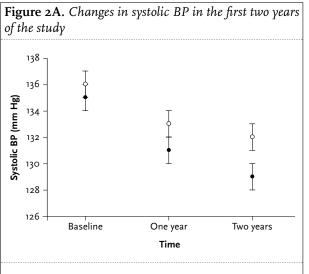In contrast, there were no significant changes in lifestyle variables between the groups.
At two years 46% of patients achieved the BP goal in the intervention group whereas this was only 35% in the control group (p=0.003). For the LDL goal this was 69% and 60% respectively (p=0.02).
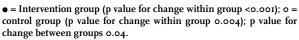*Table 2* and *figure 2* illustrate that the effect of most interventions was most prominent in the first year of the study. Changes were maintained during the second year. This applies both for the intervention and the control group.
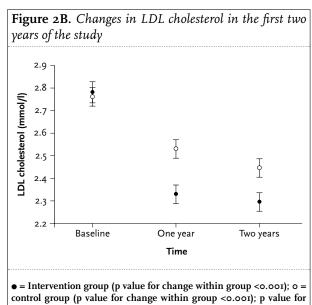
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Table 2. *Effects of the intervention after one and two years*

Parameter	Baseline		Year 1		Year 2		p-value for differences between treatment group
	Control	Intervention	Control	Intervention	Control	Intervention	
N	393	395	373	374	346	352	
eGFR (ml/min/1.73m²)	37.7 (14.0)	38.4 (15.2)	35.8 (15.2)	36.7 (15.6)	35.0 (16.2)*	36.2 (16.4)*	0.36
Office systolic BP (mmHg)	139 (22)	138 (20)	137 (20)	133 (20)	135 (19)*	133 (21)*	0.04
Office diastolic BP (mmHg)	81 (11)	80 (11)	80 (11)	78 (11)	80 (11)*	77 (10)*	0.007
Proteinuria (g/24 h)	0.3 [0.1-0.8]	0.2 [0.1-0.8]	0.3 [0.1-1.0]	0.2 [0.1-0.8]	0.3 [0.1-1.0]	0.2 [0.1-0.7]	0.33
Albumin-creatinine ratio (mg/mmol)	18.8 [6.8-51.9]	15.0 [5.6-47.5]	17.7 [6.6-53.1]	13.4 [4.7-41.1]	19.1 [7.0-62.4]	12.3 [5.0-46.3]	0.56
LDL cholesterol (mmol/l)	2.74 (0.90)	2.78 (0.95)	2.53 (0.89)	2.33 (0.74)	2.45 (0.81)*	2.30 (0.75)*	0.03
Haemoglobin (mmol/l)	8.2 (1.0)	8.2 (1.0)	8.1 (1.0)	8.1 (1.0)	8.0 (1.1)*	8.1 (1.1)	0.85
HbA1C (%)	6.1 (0.9)	6.1 (0.9)	6.1 (0.9)	6.1 (0.8)	6.1 (0.9)	6.1 (0.8)	0.95
Phosphate (mmol/l)	1.1 (0.2)	1.1 (0.2)	1.2 (0.3)	1.2 (0.3)	1.1 (0.3)	1.2 (0.3)	0.70
Calcium (mmol/l)	2.4 (0.1)	2.4 (0.1)	2.4 (0.1)	2.4 (0.1)	2.4 (0.1)	2.4 (0.1)	0.43
PTH (pmol/l)	9 [5-14]	9 [5-15]	8 [5-14]	8 [5-14]	9 [6-15]	9 [5-15]	0.64
Sodium excretion (mmol/24 h)	150 [113-189]	148 [116-195]	152 [120-191]	149 [116-198]	150 [117-190]	150 [120-193]	0.95
BMI (kg/m²)	27.2 (4.9)	27.0 (4.6)	27.1 (4.9)	26.8 (4.6)	27.0 (4.7)	26.8 (4.7)	0.53
Physical activity (intensity/min/week/1000)	5220 [3180-8520]	5175 [2885-7930]	4740 [2689-7380]	4800 [2100-7740]	5340 [2465-7793]	4920 [2330-7628]	0.31
Smoking (%)	24	19	22	16	17*	14	0.06
Use of ACE or ARB (%)	77.6	81.1	84.0	91.6	81.3*	89.7*	0.003
Use of statin (%)	63.4	66.9	74.8	87.7	77.6*	88.1*	<0.001
Use of acetyl salicylic acid (%)	34.6	39.4	46.2	63.4	44.0*	62.8*	<0.001
Use of vitamin D (%)	23.9	22.0	32.8	40.9	40.0*	50.4*	0.05
Use of phosphate binder (%)	13.2	9.6	15.2	11.0	18.4*	15.3	0.11

eGFR = estimated glomerular filtration rate; BP = blood pressure; LDL = low-density lipoprotein; PTH = parathyroid hormone; BMI = body mass index; ACE = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; * = p-value for change over time within treatment group <0.05, results are mean (± sd) or median [25th-75th percentile].
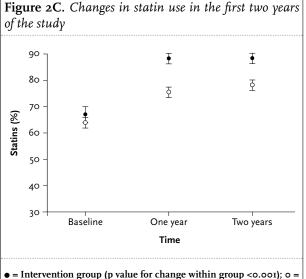
Figure 2A. *Changes in systolic BP in the first two years of the study*

● = Intervention group (p value for change within group <0.001); o = control group (p value for change within group 0.004); p value for change between groups 0.04.

Figure 2B. *Changes in LDL cholesterol in the first two years of the study*

● = Intervention group (p value for change within group <0.001); o = control group (p value for change within group <0.001); p value for change between groups 0.03.

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Figure 2C. *Changes in statin use in the first two years of the study*

● = Intervention group (p value for change within group <0.001); o = control group (p value for change within group <0.001); p value for change between groups <0.001.

Figure 2D. *Changes in aspirin use in the first two years of the study*

● = Intervention group (p value for change within group <0.001); o = control group (p value for change within group 0.008); p value for change between groups <0.001.

Table 3 shows the number of visits performed in the first two years of the study. There were more visits in the intervention arm but significantly less visits to the specialist.

We previously showed that differences in quality of care and BP between centres could be partially attributed to physician-related factors.[13] Therefore we hypothesised that the execution of patient care by uniformly trained NPs would attenuate between-centre differences. This was analysed by comparing the centre means for the variables influenced by the intervention (systolic BP and LDL cholesterol) to the cohort mean at baseline, one year and two years. For both risk factors the variation between the centres decreased with time in the intervention group as illustrated in *figure 3*.

DISCUSSION

Our study showed that added support by highly qualified NPs improved the quality of treatment of patients with CKD. Specifically, we observed lower blood pressures,
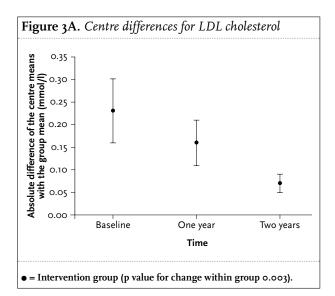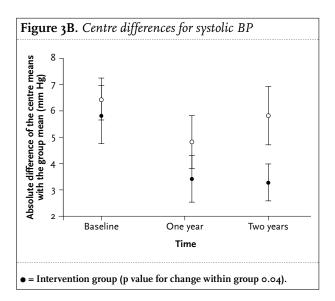
lower LDL cholesterol, and increased use of aspirin, vitamin D, and ACE inhibitors in the intervention group. However, in contrast with our expectations, the NP-guided intervention did not result in major changes in lifestyle factors.

Many studies have evaluated the effect of NP support in attaining treatment targets. Most studies were conducted in patients with diabetes[8,32-35] or patients with a high cardiovascular risk score.[36-40] They showed improvement in the management of some risk factors compared with usual care. In general, pharmacotherapy modifiable risk factors such as BP and cholesterol improved in the intervention groups, although in many studies beneficial effects were limited to only one of the evaluated interventions.[8,33,35,37,40,41] The size of the improvements of risk factors between baseline and two years in the intervention group particularly with regard to BP and LDL might well represent relevant improvements in cardiovascular risk.[42,43] However, whether the smaller difference between intervention and control group in this study translates to improved cardiovascular risk after longer follow-up still remains to be established. Some argue that multiple moderate improvements in several areas of risk factor

Table 3. *Number of visits per year in the first two years of the study in the control and intervention group*

| Year | Control | | | Intervention | | |
	Total visits	NP visits	Physician visits	Total visits	NP visits	Physician visits
1	4.6 (2.3)	1.0 (0.3)	3.6 (2.3)	7.4 (2.2)#	4.7 (1.4)	2.7 (1.9)*
2	4.7 (2.9)	1.0 (0.4)	3.7 (2.9)	7.0 (2.7)#	4.2 (1.4)	2.8 (2.2)*

p value for difference between intervention and control for total visits <0.001; *p value for difference between intervention and control for physician visits <0.001. NP = nurse practitioner.

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Figure 3A. *Centre differences for LDL cholesterol*

● = Intervention group (p value for change within group 0.003).

Figure 3B. *Centre differences for systolic BP*

● = Intervention group (p value for change within group 0.04).

management may translate into larger benefits on hard endpoints, as was also shown in the study by Gaede *et al.*[8,44,45]

It is unclear whether even lower BP goals would have resulted in lower BP in the intervention group. A recent study in 500 Canadian patients with stage 3-4 CKD followed for two years compared family physician care with care by a specialised nurse under supervision of a nephrologist. They failed to observe beneficial changes in BP and lipid profile and also did not note any difference on cardiovascular endpoints.[46] The patients in the CanPREVENT study were older, had better kidney function (higher eGFR and lower proteinuria) and had better controlled systolic BP (on average 8 mmHg lower) at baseline. These differences can certainly explain the different results between CanPREVENT and MASTERPLAN.

We hypothesised that specialised nursing care could also be of particular benefit by helping patients to improve their lifestyle. In our current analysis no such effect was observed. This was also reported by Gaede *et al.* They studied patients with diabetes mellitus type 2 and observed improvement in BP, cholesterol, glycaemic control and aspirin use. In contrast, lifestyle factors were not affected.[8,47] Earlier NP-led single intervention studies did show benefit in modifying the lifestyle factors studied in our study (smoking cessation, weight loss , dietary sodium restriction and physical activity).[48-53] In contrast, many recent reports in preventive medicine have pointed out the difficulties in reaching any relevant benefits in studies investigating a multiple health behavioural change. Effects were, if any, mostly limited in size.[39,54,55] A recent review by Blokstra *et al.* in patients with established cardiovascular disease concluded that a multifactorial lifestyle intervention can affect diet, activity, smoking behaviour and reduce the occurrence of cardiovascular disease and/or mortality particularly in high-risk groups.[56] The original studies described had a far more rigorous lifestyle intervention than was applied in our study.[57] In other high-risk categories the results were far less outspoken, possibly suggesting that patients who had experienced a cardiovascular event were more motivated to execute lifestyle changes.[56]

Why then were no lifestyle benefits found in our cohort? Firstly CKD is a silent disease, and all efforts are taken as preventive measures. It is likely that CKD patients have lower motivation to ameliorate lifestyle than patients who have experienced a cardiovascular event. Secondly Jacobs *et al.* suggested that in a multifactorial intervention the number of possible choices may overwhelm the participants and thus result in lower effects.[58] This might also be relevant in our study, since we have formulated 11 treatment targets for our patients, four of which are to be considered lifestyle interventions.

Finally another effect might be relevant not only with regard to lifestyle but also with regard to other risk factors. Because of the study design, patients were randomised within a centre; therefore the same physician coaching the NP would see patients of the control group during their outpatient visits. Patients in the control group might thus also experience better care than they would have received had they been treated in a centre not associated with the study. A possible indication of this is the clear reduction in the percentage of smokers in both cohorts. This effect is further illustrated in the control group by the reduction of LDL cholesterol and the rapid increase in the prescription of statins and aspirin during the first year of the study (*figure 2*). The increase in treatment of cardiovascular risk factors in the control group could also be explained in another fashion, namely as a consequence

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of an increased nationwide awareness of cardiovascular risk in this decennium. Several key publications and guidelines were published prior to or during the early years of our study and may have prompted physicians to alter their therapeutic strategy (e.g. KDOQi and Dutch federation of Nephrology guidelines).[59,60]

Patients were seen more frequently in the intervention group (*table 3*). This was part of the study design and could be a factor in the observed difference in BP and LDL cholesterol; however, apparently this did not affect changes in lifestyle.

Earlier we reported clear between-centre differences for several risk factors and explored this phenomenon more thoroughly for blood pressure.[13,14] We suggested that physician-related factors might explain some of the differences. Our current data support this view, since between-centre differences were less for those risk factors that were improved in the nursing intervention group.

We conclude that specialised nursing care can help to improve specialist nephrological care to patients with stage 3 and 4 CKD. This is readily apparent with pharmacotherapy modifiable risk factors, but less so with lifestyle interventions. Whether this translates into improved cardiovascular risk remains to be established during the remainder of the follow-up of the study.

LIMITATIONS OF THE ANALYSIS

Not all interventions applied in our study can be considered evidence based or part of the then current guidelines. Patients with an eGFR below 50 ml/min/1.73 m2 were supposed to receive active vitamin D and certainly more current guidelines suggest measurement of vitamin D before supplementation.[61] Also aspirin was advocated in our study based upon the conviction of the study group that this might be beneficial in CKD, just like other groups had suggested.[25,26,62]

Another limitation is the earlier mentioned evident improvement of risk factor management in the control group. The effect of improved care in the control group could be an explanation for the modest differences between intervention and control and might also influence the effect on cardiovascular events.

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- The Dutch Nephrology Congress, Veldhoven: Effect of a multifactorial intervention with the aid of nurse practitioners in patients with chronic kidney disease: two years results from a randomised controlled trial. March 2011.
- EDTA, Prague: Effect of a multifactorial intervention with the aid of nurse practitioners in patients with chronic kidney disease: two years results from a randomised controlled trial. Juni 2011.

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