Chapter 7: Blood pressure management in elderly persons with CKD ND

Kidney International Supplements (2012) **2,** 377–381; doi:10.1038/kisup.2012.57

INTRODUCTION

This chapter specifically addresses the BP management of older patients with CKD that is non-dialysis-dependent (i.e., CKD ND), many of whom have accumulated co-morbidities associated with aging, including vascular disease, osteoporosis, and general frailty. The term 'elderly' is used for persons $\geq$65 years of age,[354] whereas 'very elderly' is reserved for persons $>$80 years of age, consistent with the terminology used in the literature reviewed in this chapter.[43,149,355,356] In using these definitions, we recognize that chronological age is used as a surrogate for biological age, although this relationship is highly variable.

The elderly comprise the most rapidly growing proportion of the population in most parts of the world.[357] From 30 to 40 years of age, the GFR generally (but not invariably) declines, and in the older person, tubular and endocrine dysfunction in the kidney are common.[358,359] Combine this with the increased prevalence of type 2 diabetes mellitus and high BP among older persons, it is not surprising that the elderly constitute the most rapidly growing population of CKD patients.

In population health surveys, a large proportion of the elderly have a reduced GFR. In the United States, NHANES 1999–2004 data showed that 37.8% of subjects $>$70 years had a GFR of $<$60 ml/min/1.73 m^2 (measured using the MDRD equation); this prevalence had increased from 27.8% in the NHANES 1988–1994 data.[360,361] Nearly 50% of United States veterans aged $>$85 years fulfilled the definition for CKD.[362] Similarly in China,[363] Australia,[364] and Japan,[365] a high prevalence of CKD has been found in older populations. With greater access to health care among the elderly, this group is the fastest-growing population requiring dialysis, with 25% and 21.3% of dialysis patients in the United States and Australia, respectively, being $\geq$75 years of age[366,367] and between 31 and 36% of patients receiving renal replacement therapy in different regions of the United Kingdom being $>$65 years of age.[368]

7.1: Tailor BP treatment regimens in elderly patients with CKD ND by carefully considering age, co-morbidities and other therapies, with gradual escalation of treatment and close attention to adverse events related to BP treatment, including electrolyte disorders, acute deterioration in kidney function, orthostatic hypotension and drug side effects. *(Not Graded)*

RATIONALE

The relationships between CKD and BP in the elderly in the United States have recently been reviewed in detail.[369] Among NHANES III (1988–1994) subjects aged $\geq$60 years of age, either treated or not treated for a high BP, there was a J-shaped relationship between BP and CKD prevalence. Thus, persons with a systolic BP of 120 to 159 mm Hg or a diastolic BP of 80 to 99 mm Hg had the lowest CKD prevalence, with a higher prevalence associated with a systolic BP $<$120 mm Hg or diastolic BP $<$80 mm Hg and a systolic BP $\geq$160 mm Hg or a diastolic BP $\geq$100 mm Hg.[361] Analyses of data from the Kidney Early Evaluation Program (KEEP), as well as NHANES, indicate that with increasing age, there is an increase in the prevalence and severity of CKD, confirming the strong relationship between BP and CKD in the elderly.[370,371]

Despite these findings, there is little evidence on which to base recommendations for BP management in elderly patients with CKD. Systematic assessment of the evidence base underpinning this Guideline shows that many RCTs excluded patients $>$70 years of age. The mean age of participants rarely exceed 65 years with the upper limit of the 95% CI (i.e., the mean $\pm$ 2 SD) very uncommonly being $\geq$85 years, meaning no more than about 2.5% of the study population had an age above this cut-off point (Supplementary Table 65 online). We therefore cannot draw much direct evidence from these RCTs to indicate how to properly manage BP in elderly CKD patients, although some inferences might be drawn from BP studies in elderly populations not specifically chosen for the presence of CKD.

Measurement of BP in the elderly. Assessment of BP in the elderly is made more difficult by such common issues as the presence of atrial fibrillation (as seen in 25% of patients $\geq$ 70 years in the Chronic Renal Insufficiency Cohort (CRIC) study[372]), orthostatic hypotension[44,45] and the tendency for pulse pressure to widen with arterial stiffening, resulting in systolic hypertension.[32,42,373,374]

The literature on management of elderly patients has thus been focused more on systolic than diastolic BP. There is relevant observational evidence from the SHEP study.[374] In an analysis of 2181 persons $>$65 years of age in the placebo arm of this study, systolic BP was more predictive of decline in kidney function (i.e., rise in SCr by $\geq$0.4 mg/dl [35.4 μmol/l] over 5 years) than diastolic BP, pulse pressure, or MAP. The mean age was 72 years and patients with 'renal

failure' were excluded. Among those enrolled, the initial SCr level was 1.04 ± 0.23 mg/dl (92 ± 20 μmol/l). Hence, most subjects probably had normal kidney function or CKD stages 1–3.

CKD in the elderly. There are clear differences in the causes of CKD when comparing elderly and younger cohorts.[375] Autopsy studies indicate that arteriolar sclerosis, global glomerulosclerosis, and tubular atrophy are more common in the elderly, as are renal artery stenosis and cholesterol embolization.[376] Although selection bias is likely, a kidney biopsy series of 413 patients aged 66 to 79 years and 100 patients aged 80 to 89 years showed nephrosclerosis in 34% of patients >80 years and in 7% of those 66 to 79 yrs.[356] According to registries of kidney failure patients, 'arteriopathic disease' was the diagnosis in 17 to 38% of patients commencing dialysis on three continents.[375] Although a discussion as to whether or not nephrosclerosis is an aspect of kidney aging is beyond the scope of this Guideline, vascular disease within the kidney is often regarded as a major factor contributing to decline in kidney function. This predisposition to vascular disease may influence the response of the aging kidney to low BP and renin–angiotensin blockade, with the attendant risks of acute reduction in GFR and hyperkalemia. This has led to questions regarding the safety of renin–angiotensin-blocking agents such as ACE-Is and ARBs in the elderly.[377–379]

GFR estimation in the elderly. Most equations used to estimate GFR have been primarily developed in younger populations, although subgroup analyses show that these equations perform reasonably well in older people[380,381].

Co-morbidities. Co-morbidities are frequently present in the elderly and may influence BP management. Macrovascular disease is particularly common. This might influence BP targets or the preferred agents use to control BP, especially if heart failure, angina, cerebral vascular insufficiency, or peripheral vascular diseases are prominent. The presence of heart failure or cardiomyopathy may lead clinicians to initiate ACE-Is, ARBs,[382] beta-blockers,[383] or diuretics independently of BP treatment. Similarly, angina may be an indication for beta-blockers or calcium-channel blockers. Hypotension (orthostatic or persistent) due to BP-lowering treatment may exacerbate the risk of falls and fractures in the elderly, especially in patients with co-morbidities such as cerebrovascular disease, osteoporosis, or vitamin D deficiency.

Drugs and the elderly. The pharmacology and pharmacodynamics of BP drugs also change with age, mainly because of reduced GFR, but also due to changes in hepatic function, volume of distribution, and other issues that are less well characterized.[384] Side-effect profiles may also vary, either owing to altered end-organ sensitivity to the drugs, co-morbidities, or interactions with other medications, such as diuretics, NSAIDs and COX-2 inhibitors which may accentuate the adverse kidney effects of renin–angiotensin blockade.[384]

Goals of BP management in the elderly. It is particularly important to individualize care in the elderly, bearing co-morbidities in mind. A philosophy of patient-centered care (rather than disease-directed care) is particularly relevant as the elderly become very elderly.[385] The high likelihood of elderly patients developing cardiac and cerebrovascular complications in the context of a high BP, along with evidence that kidney function may decline more slowly in the elderly than in younger patients (particularly when the GFR is ≥ 45 ml/min/1.73 m^2),[386,387] should lead to a greater emphasis on vascular rather than kidney outcomes. Moreover, particularly in the very elderly, possible beneficial effects of therapy on morbidity and mortality should be balanced against any negative effects on quality of life.[388]

BP TARGETS IN THE ELDERLY

Although there have been many studies of treatment of high BP in the elderly, there is little evidence specific to the elderly with known CKD. Most relevant information comes from observational studies and RCTs involving entire populations of older hypertensive patients not specifically chosen on the basis of kidney function (Supplementary Table 66 online). 'Renal failure' or a designated upper limit for the SCr concentration have been an exclusion criterion in many studies, reducing the applicability of the data to CKD patients.

A meta-analysis of observational studies conducted prior to 2002, including nearly 1 million subjects selected for having no previously known vascular disease, indicated that the rates of stroke, ischemic heart disease, and overall mortality increased with increasing BP, even among subjects 60 to 89 years of age, although the RR decreased with increasing age.[21]

RCTs involving elderly patients not selected for having CKD indicate that it is beneficial to treat high BP in patients >60 years of age. A 2009 Cochrane review of 15 RCTs in which persons >60 years of age with a systolic BP ≥ 140 mm Hg or a diastolic BP ≥ 90 mm Hg at baseline received either placebo or a BP-lowering agent indicated that active treatment reduced total mortality (RR 0.90; 95% CI 0.84–0.97) and total cardiovascular mortality and morbidity (RR 0.72; 95% CI 0.68–0.77), particularly due to a reduction in the incidence of stroke.[389] Withdrawals due to adverse events were poorly documented, but in three RCTs that did report these data, treatment was associated with 111 events/1000 patient-years, as compared with 65 events/1000 patient-years with placebo (RR 1.71; 95% CI 1.45–2.00). Although these findings support treatment of high BP in subjects >60 years of age, they do not inform us specifically about patients with CKD nor about the target BP and they suggest that some patients will have adverse reactions to drug therapy.

Of concern is that in this Cochrane review,[389] when patients aged ≥ 80 years were specifically considered, there was no overall reduction in the risk of total mortality with treatment of BP vs. no treatment (RR 1.01; 95% CI 0.90–1.13), although the reduction in risk of cardiovascular mortality (RR 0.75; 95% CI 0.65–0.87) was similar to that seen in patients 60 to 80 years of age. This is in accordance with a 1999 subgroup meta-analysis of seven RCTs representing 1670 patients aged ≥ 80 years (who had participated in trials of anti-hypertensive agents) indicating that treatment

vs. no treatment was associated with a decrease in the rates of strokes, major cardiovascular events and heart failure but, similar to the Cochrane findings, there was no benefit of treatment in terms of cardiovascular death or overall mortality.[355] Similarly, a 2010 meta-analysis of 8 RCTs involving treatment of BP in subjects 80 years and older found that treatment of high BP reduced the risk of stroke, cardiovascular events and heart failure, but had no effect on total mortality.[390] Meta-regression analysis suggested that mortality reduction was achieved in the trials with the least BP reductions and lowest intensity of therapy. These findings suggest that there might be deleterious effects resulting from BP treatment in the very elderly undermining the advantages brought about by the reduced risk of cardiovascular events.

An observational cohort study involving 4071 hypertensive individuals aged 80 years or older (mainly men, since they were recruited from the Veterans Affairs Administration) supports this notion.[43] All subjects were classified as 'hypertensive' according to the International Classification of Diseases (ICD-9) code, 9.9% as having 'chronic renal failure,' and 84.5% were taking anti-hypertensive medications. A J-shaped relationship between BP and survival was seen. Patients with BP $<$130–139 mm Hg systolic or $<$70–79 mm Hg diastolic were more likely to die during 5 years of follow-up than those with BP 130–139 mm Hg systolic or 70–79 mm Hg diastolic. With each further 10 mm Hg decrease in systolic or diastolic BP to $<$100 mm Hg systolic or $<$50 diastolic the risk increased, suggesting that overly aggressive BP control might be harmful in this age group.

A series of retrospective analyses of INVEST has further highlighted the issue of J-shaped relationships between systolic BP, diastolic BP and outcomes in elderly hypertensive patients with CAD.[40,42,231] The risk of all cause mortality and myocardial infarction, but not stroke, increased with reductions in diastolic BP in the patient group as a whole, all of whom had CAD and were being treated for high BP.[40] In elderly patients included in the study, nadirs of risk occurred at particular systolic and diastolic BP levels, with the nadirs generally increasing with age. In patients aged 70 to 80 years, risk increased once systolic BP was less than 135 mm Hg or diastolic BP $<$75 mm Hg, while the risk increasing when systolic BP was $<$140 mm Hg or diastolic BP $<$70 mm Hg in patients $\geq$80 yrs.[42] These relationships may be due to confounding and should not be used to set BP targets in this population.

In preparing the evidence review for this guideline, the ERT found four studies involving elderly patients in which treating to differing targets for BP was part of the study design (Supplementary Table 67 online).[149,389,391–393] The Shanghai Trial of Nifedipine in the Elderly (STONE) involved 1632 patients aged 60–79 years with a systolic BP $\geq$160 mm Hg, or a diastolic BP $\geq$96 mm Hg, who were randomized to nifedipine or placebo.[392] The mean achieved BP was 147/85 mm Hg in the nifedipine group and 156/92 mm Hg in the placebo group and although there was no significant difference in all-cause mortality, there were reductions in the rates of stroke and severe arrythmia in the lower-BP nifedipine treated group. Exclusion criteria included 'secondary hypertension' and a blood urea nitrogen level $\geq$40 mg/dl (14.3 mmol/l).

The Hypertension in the Very Elderly Trial (HYVET), involving patients 80 years of age or older, provided further assurance that BP lowering treatment of very elderly patients with a sustained BP of $\geq$160 mm Hg is beneficial.[149,391] Aiming to treat to a target BP of systolic $<$150 mm Hg and diastolic $<$80 mm Hg in the active-treatment group, the investigators achieved a BP of 145/79 mm Hg with indapamide plus perindopril (if needed), compared to 159/83 mm Hg with placebo. They demonstrated a reduction in the rates of all-cause mortality and stroke in the low-BP active-treatment group over a median 1.8 years of follow-up. Patients were withdrawn if systolic BP fell to $<$110 mm Hg. However, exclusion criteria included secondary hypertension (which might be of kidney origin) and a SCr level $>$1.7 mg/dl ($>$150 μmol/l) (which represents a GFR of 39 or 37 ml/min/1.73 m^2 for an 80-year-old white man, as estimated by either the MDRD or CKD Epidemiology Collaboration (CKD-EPI) equation, respectively and a GFR of 29 or 28 ml/min/1.73 m^2 for an 80-year-old white woman as estimated by the MDRD and CKD-EPI equations, respectively). The mean baseline creatinine levels were 88.6 μmol/l (1.0 mg/dl) and 89.2 μmol/L (1.0 mg/dl) in the active-treatment and placebo groups, respectively which were well below the exclusion level. Accordingly, direct extrapolation of these data to patients with known advanced CKD is not possible.

Although this evidence provides some reassurance regarding treatment of high BP in the very elderly, it only does so with respect to treatment to a BP target level of 150/80 mm Hg, and it does not specifically address CKD patients with a GFR $<$40 and $<$30 ml/min/1.73 m^2 for men and women, respectively. Very importantly, however, the evidence challenges any tendency toward 'therapeutic nihilism' in the very elderly with high BP and CKD 1–3.

Two Japanese studies failed to show any benefit or harm from reducing systolic BP to $<$140 mm Hg in otherwise healthy elderly patients.[393,394] The Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients (JATOS) aimed to assess optimal systolic BP in elderly hypertensive patients and randomized 4418 patients with 'essential hypertension' aged 65 to 85 years with a systolic BP $>$160 mm Hg to 'strict' BP control (target systolic BP $<$140 mm Hg) or 'mild' BP control (target systolic BP 140–160 mm Hg).[393] Patients with SCr of $\geq$1.5 mg/dl (133 μmol/l) were excluded, as were patients with multiple co-morbidities. Achieved mean $\pm$ SD systolic BP was 135.9 $\pm$ 11.7 mm Hg in the strict-control group and 145.6 $\pm$ 11.1 in the mild-control group ($P<0.001$), with significantly more drugs required in the strict-control group. There was no difference in cerebrovascular, cardiac, or kidney end points, nor in total mortality between the two groups at 2 years of follow-up. 'Renal failure' occurred in 8 and

9 patients, respectively. Rates of treatment withdrawal due to adverse events did not differ between the groups.

The Valsartan in Elderly Isolated Systolic Hypertension (VALISH) study involved 3260 Japanese participants aged 70 to 84 years, with systolic BP $\geq$160 mm Hg.[394] Like JATOS,[393] this study did not demonstrate any differences in outcomes or adverse events between the strict-control group (systolic BP goal $<$140 mm Hg, achieved mean systolic BP was 136.6 mm Hg) and the moderate-control group (systolic BP goal 140–150 mm Hg, achieved mean systolic BP was 142.0 mm Hg) after a median follow-up period of 3.07 years.[394] Although 43 of the 3260 patients had 'kidney insufficiency' (undefined) at study entry, none had a SCr level $\geq$2 mg/dl (177 μmol/l) since this was an exclusion criterion, as were many other co-morbidities. Doubling of the SCr, an increase in the SCr level to 2.0 mg/dl (177 μmol/l), or dialysis occurred in 5 and 2 patients, respectively (non-significant). The authors concluded that in relatively healthy elderly Japanese patients, a BP $<$140 mm Hg is safely achievable, but that the trial was underpowered to assess outcome benefits. No difference was seen between the two groups in terms of adverse event rates (18.2% with strict control and 17.9% with mild control, $P = 0.851$).

Thus BP targets in the elderly, with or without CKD, should be set only after consideration of co-morbidities and should be achieved gradually. Based on the evidence on BP in the elderly (not selected for CKD), recent guidelines and consensus documents generally agree that $<$140/90 mm Hg should be the target in uncomplicated hypertension.[117,395,396] The American College of Cardiology Foundation and American Heart Association (ACCF/AHA), in collaboration with a large group of other American and European bodies, acknowledge in their consensus document on hypertension in the elderly that although 'there is limited information for evidence-based guidelines to manage older hypertensive patients,' a target of $<$140/90 mm Hg is recommended in uncomplicated hypertension for the age range 65–79 years.[395] This document acknowledges that the target for $>$80 years is unclear, and refers to expert opinion and observational data (including KDOQI 2002 and JNC 7) suggesting $<$130/80 mm Hg as a target in CKD, irrespective of albuminuria.

From the UK, NICE has published a comprehensive guideline for management of hypertension in adults which also recommends BP $<$140/90 mm Hg for 'primary' hypertension up to 80 years of age, and for those over 80 years who are continuing therapy.[117] Caution is recommended when starting BP medications in those over 80 years of age, and no recommendation is given with respect to the elderly with CKD.

Although intuitively there must be a lower limit for safe BP control in the elderly and very elderly, there will probably never be an RCT designed specifically to address this limit in these populations. We can, however, gain insights from observations among elderly patients on treatment as outlined above.[42,43] While these date do not allow us to recommend a lower BP limit on treatment, they do suggest that in the elderly, it may be prudent not to reduce BP much below the target BP $<$140/90 mm Hg as recommended by ACCF/AHA and NICE.[117,395]

In addressing the risks associated with low BP in the elderly, it is relevant that orthostatic hypotension is more common than in younger populations, particularly among those treated for high BP or diabetes and those receiving sedatives.[44,45] As well as causing postural dizziness, low BP is associated with a higher risk of falls and fractures in elderly persons in studies that are likely to have included individuals with and without CKD.[9,10,358,397] An additional consideration when treating elderly CKD patients is that they may differ from those with well preserved kidney function in terms of their response to BP lowering agents.

The Work Group decided that it was not possible to recommend specific BP targets in the elderly with CKD. A reasonable approach might be to use BP targets as recommended in the younger CKD population ($\leq$140/90 mm Hg in non-albuminuric CKD and $\leq$130/80 mm Hg in albuminuric CKD as in Chapters 3 and 4), but to reach these targets gradually, bearing in mind that they may not be achievable without adverse effects particularly in a patient with multiple age-related co-morbidities. It is even more difficult to make recommendations in patients over 80 years of age with CKD due to the lack of evidence.

With consideration given to the adverse effects of treatment, the Work Group felt that it was good practice to ask elderly patients treated for high BP about postural dizziness and to measure BP immediately (within 1 minute) and a few minutes after standing as well as in the sitting position.[44]

METHODS FOR BP REDUCTION IN THE ELDERLY

Lifestyle modifications in the elderly, although often recommended, can compromise quality of life and may impair nutrition. The place of salt restriction, exercise and weight control is detailed in the aforementioned ACCF/AHA document.[395] Given that there is very little evidence to support lifestyle modifications in the treatment of BP in CKD patients in general, the Work Group decided not to make any such recommendations in the elderly with CKD. Although salt restriction might seem to be the most attractive intervention, it may impact the quality of life, particularly enjoyment of food. A recent observational study of elderly persons ($\geq$65 years of age) does not support alcohol restriction as an intervention to reduce decline in GFR.[398]

The Work Group felt that drug regimens should be tailored by carefully considering the elderly patient's co-morbidities and any changes in treatment should be very gradual. Close attention should be paid to potential adverse events related to BP treatment, including electrolyte disorders, acute deterioration in kidney function and orthostatic hypotension. Although many elderly patients with CKD will require several agents, studies comparing use of various agents in the elderly without CKD have produced somewhat conflicting results (see Supplementary Tables 66–68 online). The ability of the patient to adhere to complex poly-pharmacy should be taken into consideration. Some clinicians have expressed concerns about the use

of drugs that block the renin–angiotensin system in the elderly with CKD.[377–379] This concern is largely due to the perceived potential for these agents to cause more frequent adverse events in this population. A recent Cochrane review addressing pharmacotherapy of all types for treatment of hypertension in the elderly reported an increased risk of withdrawals due to adverse effects (RR 1.71; 95% CI 1.45–2.00).[389] Since quality of life is particularly important in the elderly, it may be worth avoiding drugs that may have negative quality of life implications, but no clear advice can be given.[388,399]

Thus given the many differences between the elderly (particularly the very elderly) with CKD and younger patients with CKD, it is not possible to recommend any particular drug class for the reduction of BP in older CKD patients. However, it is advisable to consider the severity of CKD, presence of albuminuria, and co-morbidities and their treatment when prescribing. Therapeutic changes should be made gradually, with close monitoring for adverse effects due to low BP or side effects from prescribed agents.

RESEARCH RECOMMENDATIONS

An important NIH funded trial- SPRINT- is currently ongoing in the United States randomizing patients without diabetes or significant proteinuria to a systolic BP of <140 mm Hg or <120 mm Hg. Since it contains both elderly patients and those with CKD, it is likely to provide important evidence to guide BP management in this subpopulation.[171,172]

A workshop on kidney disease including the American Society of Nephrology, the National Institute on Aging, the American Geriatrics Society, and the National Institute of Diabetes and Digestive and Kidney Diseases resulted in the 2009 publication of a list of priority areas for research in kidney disease in the elderly (Table 3).[400] Although BP was not specifically addressed, it highlighted the many areas of ignorance regarding CKD in the elderly.

Important areas for future research suggested by this KDIGO Work Group include:

- The effects of different BP targets (e.g., 150/90 mm Hg vs. 140/90 mm Hg) in elderly and very elderly patients with advanced CKD (CKD 3–4) should be assessed by prospective RCTs using a fixed-sequential BP-agent protocol (e.g., diuretic, ACE-I or ARB, beta-blocker, and calcium-channel blocker) excluding only patients with angina or cardiomyopathy.
- The effect of various combinations of agents in the elderly and very elderly populations should be examined.

Table 3 | Questions for future research

Mechanisms and biology
Is CKD in elderly people the same condition as CKD in young adults?
How do age-related mechanisms such as fibrosis and cellular senescence interact with mechanisms underlying CKD progression?
How much risk for CKD progression is determined by age versus factors such as AKI?
How does fibrosis versus vessel dropout change with age?
Do age- and CKD-associated changes in vascular biology differ from other parenchymal kidney disease changes associated with age?
Measurement and prognosis
Are there better ways to estimate GFR in older adults to identify CKD?
What are the morphologic correlates of CKD in elderly people?
Are there other markers that can contribute to assessment of CKD prognosis in elderly people, beyond GFR and cystatin?
CVD
How do age-related changes in vascular biology contribute to CKD-associated increases in cardiovascular risk?
What are the age-related changes in non-traditional cardiovascular risk factors in patients with CKD?
Other comorbidities
How do comorbidities differ during the transition from CKD to kidney failure and need for dialysis?
Can the deterioration in physical functioning and subsequent frailty in patients with CKD be prevented by physical activity interventions?
How does age interact with exercise in prevention or reduction of comorbidities associated with CKD progression?
What is the natural history of cognitive impairment associated with CKD progression, and what happens to cognitive function with the start of dialysis?
What mechanisms link CKD with cognitive impairment in elderly people?
Are there any interventions to attenuate the development of cognitive impairment in patients with CKD?
How does preclinical kidney disease relate to other prefrailty risk factors?
Management and care
How can geriatricians, internists, general family practitioners, and nephrologists work together to optimize the care of elderly patients with CKD and kidney failure?
Can age-related declines in kidney function and progression to CKD be modulated?

AKI, acute kidney injury; CKD chronic kidney disease; GFR, glomerular filtration rate. Adapted from Anderson S, Halter JB, Hazzard WR *et al.* Prediction, progression, and outcomes of chronic kidney disease in older adults. *J Am Soc Nephrol* 2009; 20: 1199–209 with permission from American Society of Nephrology[400] conveyed through Copyright Clearance Center, Inc.; accessed http://jasn.asnjournals.org/content/20/6/1199.long.

DISCLAIMER

SUPPLEMENTARY MATERIAL

Supplementary Table 65. Age restriction in all RCTs for DM CKD, non-DM CKD, Transplant and CKD subgroups.
Supplementary Table 66. PICO criteria for blood pressure targets in elderly studies.
Supplementary Table 67. Ages and BP targets in elderly studies.
Supplementary Table 68. PICO criteria for blood pressure agents in elderly studies.
Supplementary material is linked to the online version of the paper at http://www.kdigo.org/clinical_practice_guidelines/bp.php