Kliiniline küsimus nr 1

Kas kroonilise neeruhaiguse suhtes tuleb sõeluda kõiki täiskasvanud patsiente (alates 18. eluaastast) *vs* sõeluda riskigrupi patsiente (vanus üle 50 eluaasta, neeruhaigus pereanamneesis, adipoossus, suitsetaja, suhkurtõbi, kõrgvererõhktõbi, südame- ja veresoonkonnahaigus)?

Kriitilised tulemusnäitajad: patsiendi elukvaliteet, patsiendi rahulolu, haigestumine kroonilisse neeruhaigusesse, neeruasendusravi, hospitaliseerimine, südame-veresoonkonna tüsistused, üldsuremuse vähenemine

Kliinilise küsimuse vastamiseks otsiti materjali eelnevalt sekretariaadi poolt Agree II meetodil hinnatud ravijuhenditest

- National Clinical Guideline Centre; National Institute for Health and Care Excellence. **Chronic kidney disease (partial update). Early identification and management of chronic kidney disease in adults in primary and secondary care**. Clinical Guideline 182. 2014 (http://www.nice.org.uk/guidance/cg182/evidence/cg182-chronic-kidney-disease-update-full-guideline3) **(NICE)**
- Academy of Medicine of Malaysia: **Management of Chronic Kidney Disease**, 2011 (http://www.acadmed.org.my/index.cfm?&menuid=67) **(Mal)**
- KHA-CARI Guideline: **Early chronic kidney disease: Detection, prevention and management**.2013 (http://www.cari.org.au/CKD/CKD%20early/ckd_early_ckd.html) **(CARI)**
- Scottish Intercollegiate Guidelines Network**: Diagnosis and management of chronic kidney disease**. A national clinical guideline 103. 2008. (http://www.sign.ac.uk/pdf/sign103.pdf) **(SIGN)**

Täiendava tõenduspõhise materjali otsimiseks teostati 06.04.15. PubMed andmebaasis otsingud:
(chronic kidney disease[MeSH Terms]) AND screening, kitsendused: *süstemaatiline ülevaade, metaanalüüs, viimase viie aasta jooksul avaldatud uuringud.* Leiti 180 artiklit, millest kliinilise küsimuse tõenduseks sobis 4artiklit.
(microalbuminuria OR albuminuria) OR proteinuria)) AND screening, kitsendused: *süstemaatiline ülevaade, metaanalüüs, viimase viie aasta jooksul avaldatud uuringud.* Leiti 110 artiklit, millest kliinilise küsimuse tõenduseks valiti 2 artiklit.

Ravijuhendid

Kroonilise neeruhaiguse suhtes sõelumist on käsitletud neljas hinnatud ravijuhendis (NICE 2014, CARI 2013, SIGN 2008, Mal 2011). Kuna KNH sõelumise kohta ei ole läbi viidud suure valimiga randomiseeritud kontrollitud uuringuid, põhinevad ravijuhendite soovitused peamiselt kohortuuringutel, pikemaajalistel vaatlusuuringutel, läbilõikeuuringutel, kulutõhususe analüüsidel ning ekspertarvamusel.

Mitte ühesgi vaadeldud ravijuhendis ei anta soovitust kogu täiskasvanud elanikkonna sõelumiseks kroonilise neeruhaiguse suhtes. Soovitatud on regulaarselt sõeluda riskigrupi patsiente. Kõigis vaadeldud ravijuhistes kuuluvad kindlalt sõelumist vajavate riskigruppide hulka patsiendid, kellel on diabeet või hüpertooniatõbi. Samuti on kõigis ravijuhistes kas kindel näidustus või tugev soovitus kaaluda KNH suhtes sõelumist

kardiovaskulaarhaigusega (südame isheemiatõbi, krooniline südamepuudulikkus, perifeersete arterite ateroskleroos, ateroskleroosist tingitud aju vereringe häired) patsientidel. Kolm ravijuhendit (NICE, CARI, Mal) annavad soovituse sõeluda patsiente, kellel on pereanamneesis neerupuudulikkus või pärilik neeruhaigus.

Rasvumise, soo, vanuse, rassi, halva sotsiaalmajandusliku olukorra ja suitsetamise olulisus KNH riskifaktorina ja seega eelnimetatute alusel KNH osas sõelumise vajadus on ravijuhistes vastukäiv. Rasvumist kui sõelumist vajavat riskifaktorit on nimetatud kahes ravijuhises (CARI, SIGN). Esimeses neist viidatakse lisaks rasvumisega kaasnevale üldisele suuremale KNH riskile ka viimasel aastakümnel sagenenud rasvumisega seotud glomeerulopaatia (s.h. fokaal-segmentaarse glomeeruloskleroosi) esinemisele. Ühes ravijuhedis seevastu (NICE) ei peeta rasvumust üksi KNH suhtes sõelumist vajavaks riskifaktoriks, küll aga on vajalik sõelumine metaboolse sündroomi esinemise korral. Metaboolset sündroomi KNH riskifaktorina on käsitletud ka Malaysia ravijuhendis, kuid eraldi soovitust selle kohta sõnastatud ei ole. Uuringud nais- või meessoo kui KNH riskifaktori kohta on vastukäivad, mistõttu soovitatakse vältida inimeste sõelumist KNH suhtes soost lähtuvalt (NICE). Vanust kui KNH riskitegurit on mainitud kõigis ravijuhendites, kuid soovituse sõelumiseks elanikkonda vanuses üle 65 eluaasta annab ainult 1 ravijuhend (Mal 2011). Seevastu NICE'i ravijuhend ütleb, et vanus üksi ei tohiks olla sõelumise näidustuseks. Rassierinevused sõelumise näidustusena on esitatud ühes ravijuhendis (CARI 2013) ja soovitus on selgelt vaid antud piirkonna rahvastiku etnilisele eripärale tuginev. Vastupidiselt soovitab NICE juhend vältida sõelumist soost lähtuvalt. Kehva sotsiaalmajanduslikku olukorda KNH riskifaktorina on esitatud kolmes ravijuhendis (NICE, CARI, SIGN), kuid konkreetse sõelumise näidustusena on see esitatud vaid ühes juhendis (CARI).

Lisaks on kahe ravijuhendi (NICE, Mal) alusel näidustatud sõelumine KNH suhtes ka järgmistel juhtudel: struktuursed urotrakti haigused, neerukivitõbi, beniigne prostata hüperplaasia, juhuslikult leitud hematuuria või proteinuuria, potentsiaalselt neeru kahjustav süsteemne haigus (nt. süsteemne erütematoosluupus) ning regulaarne nefrotoksiliste ravimite tarvitamine (s.h. NSAID-id). Lisaks eelnevale rõhutatakse NICE ravijuhendis vajalikkust jälgida haigeid võimaliku KNH tekke osas pärast ägeda neerukahjustuse episoodi 2-3 aasta jooksul.

KNH sõelumise kulutõhusust käsitleb 3 ravijuhendit (NICE, CARI, Mal), kusjuures NICE ravijuhise raames on lisaks varasemate uuringute järelduste refereerimisele koostatud ka täiendav kulutõhususe analüüs. Kõigis kolmes juhises jõutakse järeldusele, et kogu täiskasvanud elanikkonna sõelumine kroonilise neeruhaiguse suhtes ei ole kulutõhus, mistõttu soovitatakse sõeluda vaid riskigruppe. NICE toob välja, et sõelumine KNH suhtes kõrge riskiga populatsioonides (diabeetikud hüpertoonikud) on väga kulutõhus. Samas tuleneb antud ravijuhise süstemaatilisest ülevaatest, et inimestel, kes ei põe diabeeti või hüpertooniatõbe, on KNH suhtes sõelumine kulutõhus alles alates 80. eluaastast. CARI ravijuhise järeldus ütleb, et teatud riskigruppide (diabeet, hüpertoonia, kardiovaskulaarhaigus, KNH pereanamneesis) sõelumine KNH suhtes on kindlasti kulutõhusam kui üldpopulatsiooni sõelumine. Mal ravijuhendis on öeldud, et kulutõhususe seisukohast on kõige otstarbekam rakendada suunitletud sõelumist KNH kõrge riskiga gruppides.

NICE, 2014

lk.54 - 58

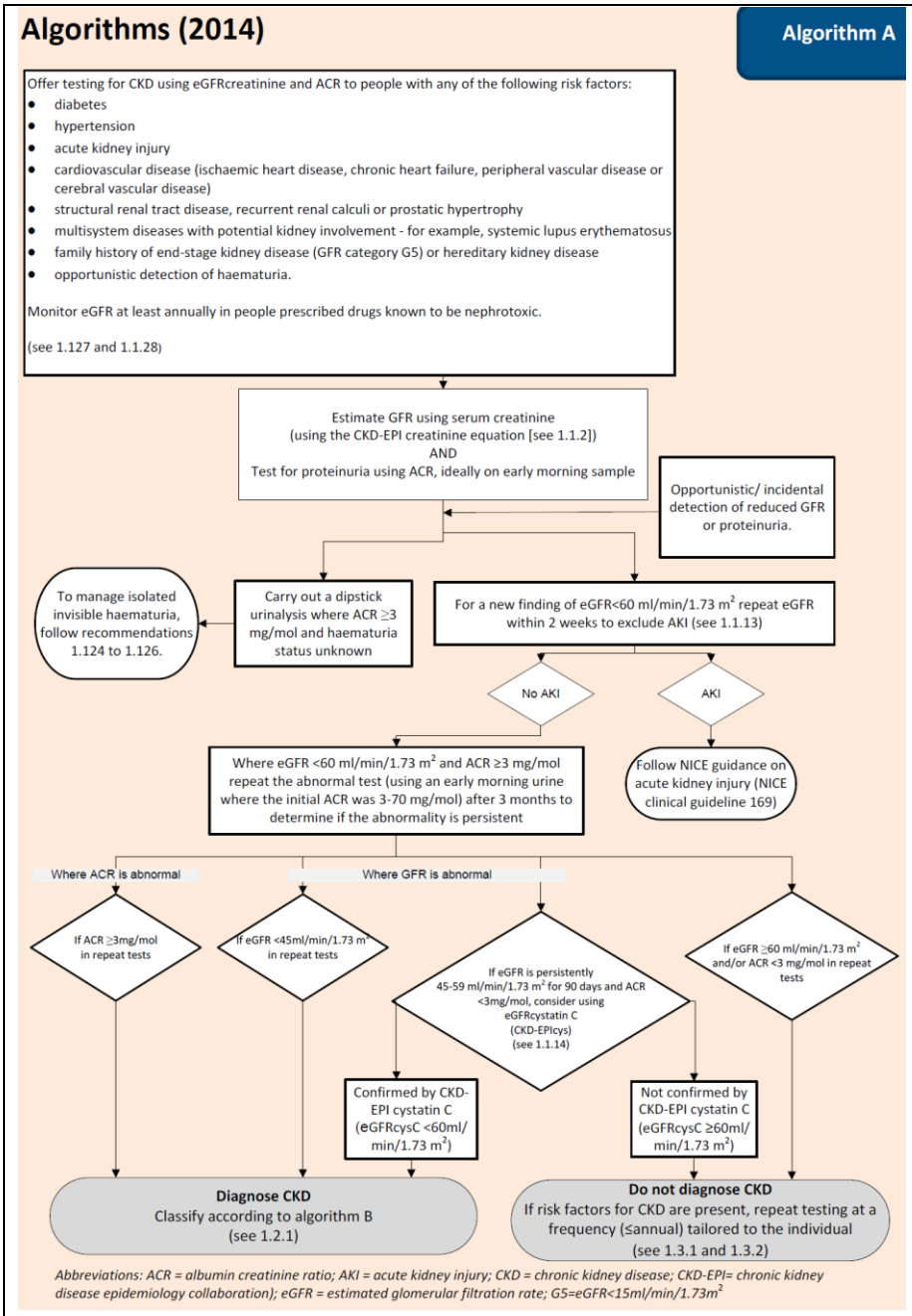
27. Monitor GFR at least annually in **people prescribed drugs known to be nephrotoxic**, such as calcineurin inhibitors (for example cyclosporin or tacrolimus), lithium and non-steroidal anti-inflammatory drugs (NSAIDs). [2008, amended 2014]

28. Offer testing for CKD using eGFRcreatinine and ACR to people with any of the following risk factors:

- **diabetes**
- **hypertension**
- **acute kidney injury** (see recommendation 44)
- **cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)**
- **structural renal tract disease, recurrent renal calculi or prostatic hypertrophy**
- **multisystem diseases with potential kidney involvement - for example, systemic lupus erythematosus**
- **family history of end-stage kidney disease (GFR category G5) or hereditary kidney disease**
- **opportunistic detection of haematuria.** [new 2014]

29. **Do not use age, gender or ethnicity as risk markers to test people for CKD**. In the absence of metabolic syndrome, diabetes or hypertension, **do not use obesity alone as a risk marker to test people for CKD**. [2008, amended 2014]

44. Monitor people for the development or progression of CKD for at least 2–3 years after acute kidney injury, even if serum creatinine has returned to baseline. [new 2014]



<u>lk.120 – 132</u>

The early identification and treatment of CKD is essential to decrease the risk of cardiovascular disease, progression to ESRD, and mortality. Identification of high-risk groups can help clinicians monitor kidney function and identify people with CKD at an earlier disease stage. **Although general population screening may not be cost-effective, targeted screening directed at subgroups of the population who might derive the most benefit from CKD detection was shown to be an effective strategy**.[289] In those conditions where the prevalence of CKD is high and the risks of preventable complications are increased, testing for CKD is clearly warranted.

In adults, who should be tested for CKD?

Antud ravijuhendi raames on koostatud süstemaatiline ülevaade, milles uuriti seoseid erinevate riskifaktorite ja KNH kujunemise vahel. Süstemaatiline ülevaade põhineb kolmel

kohortuuringul ja kuueteistkümnel vaatlus- või läbilõikeuuringul. Vaatlusalusteks riskifaktoriteks olid: vanus, sugu, hüpertensioon, diabeet, kehamassiindeks ja metaboolne sündroom, kardiovaskulaarhaigus ja ateroskleroos, pärilikkus, etnilisus, suitsetamine, alkoholi tarvitamine, füüsiline aktiivsus, sotsiaalmajanduslik olukord.

Age as a risk factor for developing CKD

Four cross-sectional studies showed that **older people (over 65 years of age) had a greater risk of an eGFR <60 ml/min/1.73 m2 than younger people**.[56,70,93,132] Analysis of a Norwegian cross-sectional study showed that **screening people with diabetes or hypertension or people over 55 years of age identified 93% of cases with stage 3-5 CKD** (number needed to screen (NNS) 8.7, 95% CI 8.5–9.0).[133] (Level 3)

Gender as a risk factor for developing CKD

There was NS difference between men and women for prevalence of CKD.[70] (Level 3)
Two studies showed that women had a lower risk of CKD than men.[93,136] (Level 3)
However, an Australian study (AusDiab) and a Norwegian study (HUNT II) showed that women had a higher risk of CKD than men.[56,132] (Level 3)

Hypertension as a risk factor for developing CKD

Four studies showed that **people with hypertension had a significantly higher risk of developing CKD** than normotensive people.[56,70,132,136] (Level 3)

Diabetes as a risk factor for developing CKD

An Australian cross-sectional study showed that **people with diabetes had NS risk of kidney impairment compared with people without diabetes.**[56] (Level 3)
By contrast, NHANES III,[70] HUNT II,[132] a UK cross-sectional study[291] and a longitudinal study[136] all showed that diabetes was associated with a significantly increased risk for CKD. (Level 3)
In the paper by New et al, only 33% of people with diabetes with moderate CKD had serum creatinine values >120 μmol/l (upper limit of normal), indicating that measuring serum creatinine level alone failed to identify stage 3 CKD. Also, 63% of people with diabetes and eGFR <60 ml/min/1.73 m2 had normoalbuminuria, indicating that microalbuminuria testing was insensitive and used alone was not sufficient for screening for CKD.[291] (Level 3)

Body mass index or metabolic syndrome as risk factors for developing CKD

The risk of developing CKD (GFR <60 ml/min/1.73 m2) increased with increasing BMI (p=0.007). Compared to men who remained within 5% of their baseline BMI (n=5670), **men who had a >10% increase in BMI (n=1669) had a significantly increased risk of CKD** (OR 1.24, 95% CI 1.03–1.50).[121] (Level 2+)
By contrast, the NHANES II follow-up study showed **NS risk for a CKD-related death or ESRD at any level of BMI**.[384] (Level 3)
Metabolic syndrome was significantly associated with an increased risk of developing CKD. As the number of traits increased, there was a significant stepwise increase in risk of developing CKD. Those with 5 criteria had an OR of 2.45 (95% CI 1.32–4.54) for developing CKD compared to those with none.[205] (Level 2+)

Cardiovascular disease and atherosclerotic risk factors associated with CKD

People with baseline CVD (n=1787) had a significantly increased risk of either a rise in serum creatinine of ≥0.4 mg/dl or a eGFR decrease of ≥15 ml/min/1.73 m2 compared with people without baseline CVD (n=12,039).[100] (Level 3)

High triglycerides were associated with a significantly increased risk of a rise in creatinine ≥0.4 mg/dl from baseline. High HDL or HDL-2 cholesterol levels were associated with a significantly decreased risk of a rise in creatinine ≥0.4 mg/dl.[265] (Level 3)

Heredity as a risk factor for developing CKD

Diabetic siblings of people with diabetic nephropathy had a significantly increased risk of incipient or overt nephropathy compared to diabetic siblings of people without nephropathy (OR 4.9, 95% CI 1.3–19.1).[44] Seaquist et al. reported a **higher prevalence of nephropathy in the siblings of diabetics with nephropathy compared with siblings without nephropathy** (83% versus 17%, p<0.001). **ESRD was higher in the siblings of diabetics with nephropathy** (41%) compared to siblings of diabetics without nephropathy (0%).[369] (Level 3)

In two case series, **a family history of ESRD was reported by 20% of people with incident ESRD**.[112,381] **Factors independently associated with a family history of ESRD were race, hypertension, diabetes, glomerulonephritis, BMI, and smoking**. Overweight people with ESRD (n=6584, BMI 25.0–29.9 kg/m2) had a 17% greater odds of reporting a family of ESRD compared with normal weight people with ESRD (n=9037, BMI 18.5–24.9 kg/m2, adjusted OR 1.17, 95% CI 1.08–1.26, p <0.001). Obese people with ESRD (n=3624, BMI 30–34.9 kg/m2) had a 25% greater odds of reporting a family of ESRD compared with normal weight people with ESRD (n=9037, BMI 18.5–24.9 kg/m2) (adjusted OR 1.25, 95% CI 1.14–1.37, p <0.001). Black people with ESRD (n=13,645) were significantly more likely to report a family history of ESRD than white people with ESRD (n=10,127) (adjusted OR 2.38, 95% CI 2.21–2.55, p <0.001). People with ESRD and a history of hypertension (n=19,987) were significantly more likely to report a family history of ESRD than people with ESRD and no history of hypertension (n=3835) (adjusted OR 1.12, 95% CI 1.02–1.23, p <0.001).[381] (Level 3)

Ethnicity as a risk factor for developing CKD

In the NHANES III study, **non-Hispanic black people (n=4163) were significantly less likely to have moderate CKD compared to non-Hispanic white people (n=6635). There was NS difference in prevalence of severe CKD in non-Hispanic black or white people.**[70] (Level 3)

In multivariate analysis of adults with newly diagnosed type 2 diabetes (n=2167) in the UKPDS, **African-Caribbeans had NS risk of developing microalbuminuria, macroalbuminuria or CrCl ≤60 ml/min/1.73 m2 compared with Caucasians. Indian Asians had a significantly increased risk of developing microalbuminuria, macroalbuminuria or a creatinine clearance ≤60 ml/min/1.73 m2 compared with Caucasians.**[340] (Level 3)

Smoking as a risk factor for developing CKD

Three studies showed that **smokers had a significantly higher risk for CKD than non-smokers.**[136,340,384] (Level 3)

Alcohol consumption as a risk factor for developing CKD

Alcohol consumption was **NS associated with a risk of ESRD or a CKD-related death.**[384] (Level 3)

Physical Inactivity as a risk factor for developing CKD

People with **low physical activity had a significantly higher risk of ESRD or a CKD-related death** than people who had high physical activity. People with moderate physical

activity have NS risk of CKD compared to people who had high physical activity (adjusted RR 1.2, 95% CI 0.7 to 2.0).[384] (Level 3)

Socioeconomic deprivation as a risk factor for developing CKD

People **who were least deprived (Townsend score =1) had a significantly lower risk of CKD compared to the overall population, whereas people who were most deprived (Townsend score =5) had a significantly higher risk of CKD compared to the overall population**.[93] (Level 3)

KNH suhtes sõelumise kulutõhusus

Leiti kolm kulutõhususe analüüsi, mis kõik põhinesid mudelarvutustel ja mõõtsid saadavat kasu tervisele kohandatud eluaastates (*quality-adjusted life-years,* QALYs). Esimene neist oli Kanada uuring, mis võrdles sõelumist mikroalbuminuuria suhtes sõelumisega hüpertoonia ja makroproteinuuria suhtes I tüüpi diabeedihaigetel ja leidis, et mikroalbuminuuria suhtes sõelumine oli iga saadud QALY kohta £14,000 kallim. Teine uuring hindas USA 50 – 75 aastaste populatsiooni iga-aastast sõelumist ja leidis, et varane proteinuuria diagnoosimine eesmärgiga KNH progressiooni aeglustada on kulutõhus vaid riskigruppides (hüpertoonikud, vanemaealised) või pikendades ajaintervalli ja skriinides antud populatsiooni iga 10 aasta tagant. Kolmas uuring hindas 50 – 69a. austraallaste sõelumist proteinuuria suhtes ja leidis, et iga saadud QALY maksumus oli £1600 kinnitades sellega sõelumise kulutõhusust.
Since none of these studies were from an NHS perspective, we made our own decision analysis to evaluate the cost-effectiveness of different case-finding strategies (see Appendix Q.3).

Original modelling: non-diabetic hypertensive

The base case analysis showed that one-off testing of hypertensive adults at various ages is highly cost-effective. **The initial use of ACR is more cost-effective than ACR after a positive reagent strip test. ACR is likely to be more cost-effective than PCR as long as it is sensitive enough to pick up 1% more cases than the PCR test.**

Original modelling: non-diabetic, non-hypertensive

The base case analysis showed that **testing of non-hypertensive, non-diabetic adults at ages 55–79 is not cost-effective. However, at age 80, testing appeared to be cost-effective.**

Comparisons between the guideline model and the published studies

Two previous studies have evaluated the cost-effectiveness of CKD testing in the general population. The first (US) study[45] found that, similar to our model, **testing for proteinuria in non-diabetic non-hypertensive people was not cost-effective around the ages 50–60 but did become cost-effective at older ages.** However, the second (Australian) study[157] found that, **testing for proteinuria in the general population age 50–69 was cost-effective.**

6.2.6 From evidence to recommendations

The GDG considered that multisystem diseases with the potential to involve the kidney, such as SLE, were clearly risk factors for CKD. The evidence principally assessed demographic and behavioural risk factors for CKD but in addition it was recognised that

diabetes and cardiovascular disease, particularly ischaemic heart disease, chronic heart failure, peripheral vascular disease and cerebrovascular disease are all risk factors for CKD.

The cost-effectiveness evidence suggests that testing for CKD in high-risk groups (such as those with hypertension or diabetes) is highly cost-effective. However, for over 55s without additional risk factors, the prevalence of CKD with proteinuria was too low for testing to be cost-effective.

The GDG did not consider the evidence about smoking, alcohol intake, abnormal lipids, obesity (in the absence of metabolic syndrome), lower socioeconomic status and ethnicity strong enough to recommend that people in these groups should be tested for CKD.

There was uncertainly regarding the significance of a family history of CKD but the GDG recommended that people with a family history of stage 5 CKD or hereditary kidney disease should be considered at risk of having CKD.

GDG consensus was that those with structural renal tract disease, multiple and recurrent renal calculi and urinary outflow tract obstruction should be considered at risk of having CKD. The GDG also recommended that people found incidentally to have haematuria or proteinuria on opportunistic medical testing should be considered at risk of having CKD.

CARI, 2013

Guideline grade. (1A, 1B, 1C, 1D, 2A, 2B, 2C, 2D)	Benefit vs. harms	Overall evidence grade (A, B, C, D)	Interpretation	Implications
1A – recommendation with a high quality of evidence.	Benefits clearly outweigh harms or vice versa	A. RCTs without important limitations or overwhelming evidence from high quality observational studies. Confident that the true effect lies close to that of the estimate of the effect.	Applicable to most patients in most circumstances.	Patients: Most would want the recommended course of action and only a small proportion would not. Clinicians: Most patients should receive the course of action. Policy: The recommendation can be adopted as a policy in most situations.
1B – recommendation with a moderate quality of evidence.		B. RCTs with some limitations (methodological, imprecision, indirectness, etc.) or strong evidence from high quality observational studies. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.		
1C – recommendation with a low quality of evidence		C. RCTs with serious limitations (methodological, imprecision, indirectness, etc.) or observational studies with some limitations. The true effect may be substantially different from the estimate of the effect.	Applicable to most patients in most circumstances, that: • may warrant review when higher quality evidence becomes available or • is an obvious course of action irrespective of the evidence (no further research warranted).	
1D – recommendation with a very low quality of evidence		D. Observational studies with limitations or case series. The estimate of the effect is very uncertain, and often will be far from the truth.		
2A – suggestion with a high quality of evidence	Benefits closely balanced harms	A. RCTs without important limitations or overwhelming evidence from high quality observational studies. Confident that the true effect lies close to that of the estimate of the effect.	The best action may differ depending on circumstances or patients' or societal values and other alternatives may be equally reasonable.	Patients: Most would want the recommended course of action, but some would not depending on individual circumstances and values. Clinicians: Different choices will be appropriate for different patients, and a management decision consistent with patients' values, preferences and circumstances should be reached. Policy: would require substantial debate and involvement of many stakeholders.
2B – suggestion with a moderate quality of evidence		B. RCTs with some limitations (methodological, imprecision, indirectness, etc.) or strong evidence from high quality observational studies. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.		
2C – suggestion with a low quality of evidence		C. RCTs with serious limitations (methodological, imprecision, indirectness, etc.) or observational studies with some limitations. The true effect may be substantially different from the estimate of the effect.	The best action may differ depending on circumstances or patients' or societal values and: • other alternatives may be equally reasonable. • suggestion may change when higher quality evidence is obtained.	
2D – suggestion with a very low quality of evidence		D. Observational studies with limitations or case series. The estimate of the effect is very uncertain, and often will be far from the truth.		

lk. 2 – 3

2. Risk factors for early chronic kidney disease

a. The following risk factors are associated with an appreciable (20–40%) risk of CKD: Obesity, hypertension, diabetes mellitus, cigarette smoking, established CVD, age > 60 years, Aboriginal and Torres Strait Islander peoples, Maori and Pacific peoples, family

history of stage 5 CKD or hereditary kidney disease in a first or second degree relative, severe socioeconomic disadvantage

b. Metabolic syndrome is associated with an increased risk for CKD but it is still not known whether this constellation improves risk prediction beyond that afforded by its individual components (hypertension, impaired glucose tolerance and dyslipidaemia).

c. The presence of kidney stones is associated with a modest increased risk of CKD (approximately 6% absolute risk).

d. There is conflicting evidence regarding the roles of alcohol consumption and benign prostatic hypertrophy as risk factors for CKD.

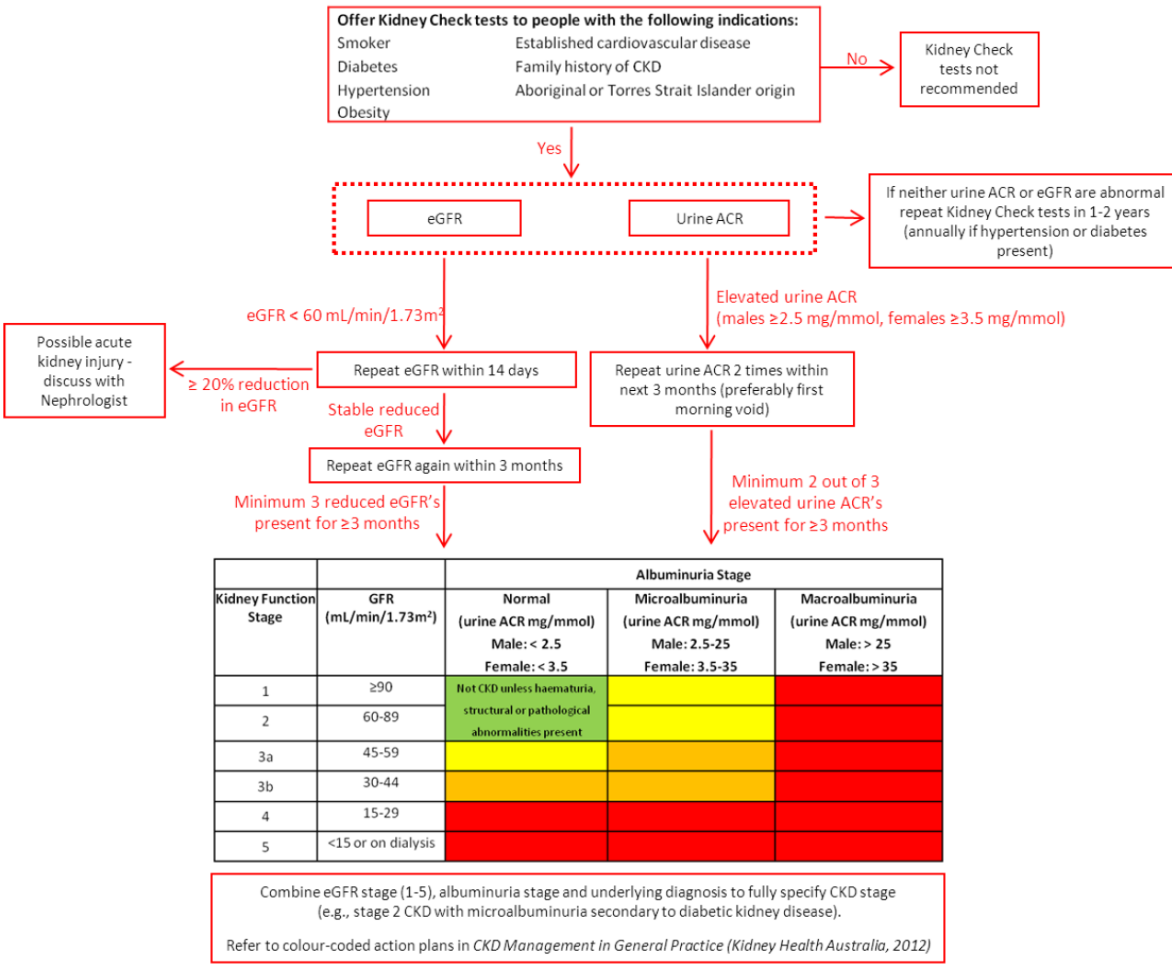
3. Screening for early chronic kidney disease

a. We recommend screening for CKD as it is an effective strategy to allow earlier detection and management to reduce the increasing CKD burden (1C).

b. We recommend that screening for CKD be targeted and performed in individuals at increased risk of developing CKD, including those with diabetes mellitus, hypertension, and established CVD (1B).

c. We recommend screening in those with additional CKD risk factors identified in Guideline 2a (obesity, cigarette smoking, Aboriginal and Torres Strait Islander peoples, family history of stage 5 CKD or hereditary kidney disease in a first or second degree relative and severe socioeconomic disadvantage) (1D).

Figure 1. Recommended screening algorithm for the detection of CKD.



CARI, 2013: Screening for early chronic kidney disease
http://www.cari.org.au/CKD/CKD%20early/Screening_CKD.pdf

lk.3 – 4; 9 - 11

Although population-wide screening is not cost-effective, targeting those at risk may be more appropriate to be able to institute early aspects of management, such as control of blood pressure, management of diabetes, and in patients with advanced CKD, preparation for dialysis or transplantation [22, 23].
Although the case for widespread population screening has been argued [24], the advantages of targeting CKD testing to high-risk groups have been demonstrated. **Screening programs targeted at known diabetics, hypertensives and those who are older have been described to be the most cost-effective to detect most CKD in the community.**

One large-scale general health survey of 65,604 people from a single community in Norway concluded that **screening people with hypertension, diabetes or age >55 years was the most effective strategy to detect people with CKD** [25]. After an 8-year follow-up, this cross-sectional study examined the occurrence of ESKD and cardiovascular death in this population and retrospectively assessed different screening strategies to compare their ability to detect CKD. **By targeting diabetes, hypertension and age >55 years, only 37% of the population would be screened and would have detected 93.2% (95% CI: 92.4 - 94.0%) of all CKD present in the community and only required 8.7 people to be screened per detected case of CKD stages 3-5 (eGFR <60mL/min/1.73m2).** Other strategies of targeting (eg. only people with diabetes and hypertension) detected a lower percentage of CKD (44.2%) and were less effective.

Another study reporting on the performance of similar screening strategies is the United States (US) Kidney Early Evaluation Program (KEEP), which targets individuals with diabetes, hypertension, or family history of diabetes or hypertension or CKD. Reported data from KEEP determined that **7 people with diabetes or hypertension or with first degree relatives with diabetes, hypertension or kidney disease need to be screened for one case of CKD to be found** [22, 23, 26].

A study in the United Kingdom (UK), the Kidney Evaluation and Awareness Program in Sheffield (KEAPS), reported that **the prevalence of microalbuminuria in the general population was 7.1% but only 1.3% in those without known risk factors for CKD** [27]. The main determinants for microalbuminuria in this study were age, diabetes, obesity and a family history of hypertension.

An Australian report by Howard et al. using cost-effectiveness modelling outlined the potential effectiveness of screening and intensive management of the "key" CKD risk factors - diabetes, hypertension and proteinuria [29]. The report determined that **a strategy based on screening of 50 to 69 year olds in general practice, plus intensive management of diabetes, hypertension and proteinuria, would be cost-effective.**

Another study with cost-effectiveness analysis by Boulware et al. and based on US NHANES (National Health and Nutrition Examination Survey) data used Markov decision modelling to specifically address the question **whether it is cost-effective to periodically**

screen adults aged 30-70 years (with no hypertension or diabetes) for proteinuria with a urine dipstick versus waiting for CKD to clinically emerge and be treated according to usual medical practice [30]. **In this study, annual screening, to take place in the general practitioners office, was not shown to be cost-effective unless targeted at such high-risk groups such as those >60 years and those with hypertension.** Cost-effectiveness was also shown if the frequency of screening in the general population was conducted at 10-year intervals.

One difficulty in targeted-screening to a population with known CKD risk factors such as hypertension and diabetes is that there are several epidemiologic studies showing **for every patient with known hypertension or diabetes there is one individual in the population for whom this diagnosis is not yet made but who already could have considerable associated end-organ damage [32-34]. Therefore targeted-screening programs for CKD may potentially miss many at-risk individuals.**

A cross-sectional survey by way of voluntary screening of relatives of patients with ESKD in the US found **there was a high prevalence of CKD and proteinuria among relatives of dialysis patients who participated in screening** [35]. 14% had a CrCl <60ml/min with proteinuria of 1+ or greater on dipstick found in 10% of participants. Another study, as part of the KEAPS program, also assessed relatives of patients with CKD [36]. Compared to the general population where the prevalence of microalbuminuria was 1.4%, prevalence of microalbuminuria in the 274 relatives of patients with CKD was 9.5%.

In summary, enrichment of the a priori probability of finding an individual with a progressive form of CKD will enhance the positive predictive value and minimise the negative predictive value of screening tests. Therefore, targeted-screening for CKD in people with diabetes, hypertension, cardiovascular disease or family history of renal disease would be more cost-effective than universal population-screening.

Riskigruppide sõelumine KNH suhtes on nii Austraalias kui USA-s läbiviidud uuringute kohaselt vähemalt sama kulutõhus kui teised rakendatavad sõeluuringud (nt. rinnavähi, emakakaelavähi, seedetrakti kasvajate suhtes) antud riigis.

A recent analysis of the PREVEND data reported a potentially favourable cost-effectiveness of population-based screening for albuminuria in the Dutch population [98]. This study also reported that **limiting the screening to those over 50 increased the cost-effectiveness of screening**. Another cost-effectiveness study by Atthobari et al. showed that **screening of an adult population for elevated UAC (in this case albuminuria >15mg/d) and subsequent treatment of individuals with positive screening results with an ACE inhibitor was cost-effective when calculated to prevent cardiovascular end-points** [99]. (*Differences between this analysis and that done by Boulware et al. in the US population [30] were that cardiovascular benefits were incorporated and screening was undertaken by spot morning urine samples that were delivered by mail in the former study, as opposed to only assessing the reduction of ESKD and performing screening in the general practitioner"s office in the latter analysis*.) A more recent Japanese study also reported potential cost-effectiveness of population screening with urine dipstick with or without the addition of serum creatinine, but argued that the high prevalence of CKD in Asian countries provided justification [100].

General population screening is impractical and does not appear to be cost-effective, and much of the evidence suggests that targeted-screening with urine testing followed by eGFR measurements is most beneficial. Screening for CKD should be performed in individuals at increased risk of developing CKD, including those with diabetes mellitus, hypertension and cardiovascular disease.

Mal, 2011

LEVELS OF EVIDENCE

Level	Study design
I	Evidence from at least one properly randomised controlled trial
II -1	Evidence obtained from well-designed controlled trials without randomisation
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	Evidence from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

GRADES OF RECOMMENDATION

A	At least one meta analysis, systematic review, or RCT, or evidence rated as good and directly applicable to the target population
B	Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic review, or RCT
C	Evidence from expert committee reports, or opinions and /or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality

lk.2 – 3; 6 - 7

• **Patients with diabetes mellitus and/or hypertension should be screened at least yearly for chronic kidney disease (CKD). (Grade C)**
• **Screening can be considered for patients with:**
o Age >65 years old
o Family history of stage 5 CKD or hereditary kidney disease
o Structural renal tract disease, renal calculi or prostatic hypertrophy
o Opportunistic (incidental) detection of haematuria or proteinuria
o Chronic use of non-steroidal anti-inflammatory drugs (NSAIDs) or other nephrotoxic drugs
o Cardiovascular disease (CVD)
o Multisystem diseases with potential kidney involvement such as systemic lupus erythematosus. (Grade C)

Suurt osa antud ravijuhendi koostamisel aluseks olnud uuringutest põhjalikumalt tutvustatud juba eespool (NICE 2014 ja KHA-CARI 2013 ravijuhendite tõenduspõhisuse osas). Käesolevalt lühike kokkuvõte:

Diabetes Mellitus (DM) - DM is significantly associated with increased risk for CKD.[8 - 10, level III;11, level II-2]

Hypertension - Large studies showed that patients with hypertension had a significantly higher risk of developing CKD compared with normotensive patients.[10, level III; 12 - 13, level III]

Metabolic Syndrome - Metabolic syndrome has been shown to be an independent risk factor for CKD. Large studies suggested that metabolic syndrome was significantly associated with CKD.[14 - 15, level II-2; 16, level III] The number of metabolic syndrome components was proportional to the prevalence of CKD[16, level III] and negatively correlated to estimated glomerular filtration rate (eGFR).[16 - 17, level III] There was also a significant association of metabolic syndrome and the risk of CKD in subjects without diabetes and hypertension.[14 - 15, level II-2]

Age - People aged >65 years old have an increased risk of renal impairment and decline in renal function.[9 - 10, level III; 12 - 13, level III; 25, level III]

Family History - A longitudinal study with 25 years follow-up showed that a family history of kidney disease in a first degree relative had a 40% increased risk of CKD.[18, level II-2]

Cardiovascular Disease (CVD) - Patients with atherosclerotic vascular disease had 1.4 times greater
risk of developing CKD compared with those without the disease in a 2 year follow-up study.[12, level II-2]

Chronic Use of NSAIDs and Analgesics - There was conflicting evidence in the association between chronic NSAIDs, aspirin and paracetamol usage and the development of CKD. In a case-control study, an average intake >500 g/year of aspirin was associated with over 3-fold increase of developing CKD.[19, level II-2] In contrast, one prospective cohort study of physicians showed that occasional to moderate analgesic intake
of aspirin, paracetamol, or NSAIDs did not appear to increase the risk of decline in kidney function during a period of 14 years followup.[20, level II-2] An 11-year follow-up of Nurses' Health study had shown higher lifetime use of aspirin and NSAIDs was not associated with renal function decline, but high paracetamol (>3,000 g) use may increase the risk of loss of renal function.[21, level II-2]

Other Risk Factors - Other possible risk factors include autoimmune disease, nephrolithiasis,[2, level III] low birth weight of <2,500g,[22, level II-2] central obesity,[2, level III] smoking,[11, level III; 23 - 24, level III] low socioeconomic status,[25, level III] anaemia, hyperuricaemia, nocturia,[18, level II-2] and physical inactivity,[24, level III] Certain herbal products including those containing aristolochic acid had also been associated with CKD.[26, level III]

COST-EFFECTIVENESS OF SCREENING

Screening should be directed towards the high risk groups as it is not cost-effective to screen the general population.[35, level III]

A study among US population aged 50 - 75 years found that early detection of urine protein to slow progression of CKD was not cost effective unless selectively directed towards high-risk groups (older people and patients with hypertension) or conducted at an infrequent interval of 10 years.[36, level III]

In an Australian study, primary care screening of 50 - 69 years old for diabetes, hypertension, and proteinuria, with subsequent intensive management including ACE inhibitors for all patients with proteinuria was cost-effective.[37, level II-2]

Another study had shown that screening for microalbuminuria was cost-effective in patients with diabetes or hypertension, but was not cost-effective for patients with neither diabetes nor hypertension unless screening is conducted at longer intervals or as part of existing physician visits.[39, level II-2]

SIGN, 2008

LEVELS OF EVIDENCE

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

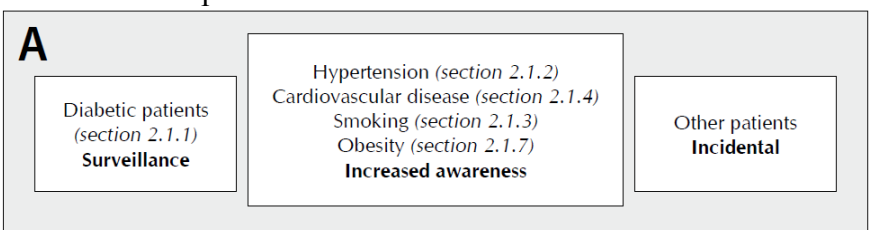
A	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

GOOD PRACTICE POINTS

☑	Recommended best practice based on the clinical experience of the guideline development group.

lk. 3 – 5; 13

KNH riskifaktoritena on ravijuhendis nimetatud järgmised: diabeet, hüpertensioon ja muud kardiovaskulaarhaigused, suitsetamine, vanus, krooniline NSAID-de kasutamine, rasvumus ja kehv sotsiaalmajanduslik olukord. Samas ei ütle ravijuhend otseselt, et kõigi eelpool loetletud riskigruppide sõelumine oleks tingimata kohustuslik. KNH sõelumise ja diagnoosimise algoritmis on toodud esile riskigrupid, kelle puhul tuleks olla KNH tekke osas eriti tähelepanelik:



All patients with diabetes should have regular surveillance of renal function. (D)
Patients who are on antihypertensive or lipid lowering therapy should have renal function assessed at least annually. (Good practice point)
Smoking should be considered as a risk factor for the development of chronic kidney disease. (C)
Low socioeconomic status should be considered as a risk factor for the development of chronic kidney disease. (C)

Süstemaatilised ülevaated

Leiti 3 süstemaatilist ülevaadet, kus on käsitletud sõelumist kroonilise neeruhaiguse suhtes. Esimeses nimetatud uuringutest (Fink et al 2012) seadsid autorid eesmärgiks uurida seoseid KNH sõelumise ja ravitulemuste vahel, kuid kuna vastavasisulisi randomiseeritud kontrollitud uuringuid ei leitud, ei olnud võimalik ka järeldusi sõnastada.
Teises süstemaatilises ülevaates (Wu et al 2013) uuriti KNH sõelumise meetodeid ja kulutõhusust üldpopulatsioonis. Leitud uuringute alusel jõuti järeldusele, et mikroalbuminuuria määramine riskigruppides (diabeet, hüpertooniatõbi, eakad) KNH suhtes sõelumise eesmärgil on kulutõhus. Samas ei saanud leitud materjalile tuginedes anda üldiseid soovitusi üldpopulatsiooni sõelumise osas.
Ka kolmandas süstemaatilises ülevaates (Komenda et al 2014) leiti, et riskigruppide (diabeet, hüpertooniatõbi) sõelumine on kulutõhus. Lisaks võib olla kultõhus ka teatud populatsioonide sõelumine, kellel esmashaigestumine KNH-sse on sagedasem, KNH progresseerumine on kiirem ja on võimalik rakendada efektiivset ravi.

Lisaks on käesolevas tõenduspõhisuse kokkuvõttes toodud ära ka kolm süstemaatilist ülevaadet (Li et al 2014; Huang et al 2014; Thomas et al 2011), mis viitavad teatud haigustele või seisunditele (hüperurikeemia, prehüpertensioon, metaboolne sündroom) kui KNH riskifaktoritele. Nimetatud uuringutes ei anta otseselt soovitusi KNH sõelumise osas, kuid rõhutatakse nimetatud haiguste ravi olulisust KNH tekke ja progresseerumise vältimise seisukohalt.

Viited

Kokkuvõte	**Viide kirjandusallikale**
BACKGROUND: Screening and monitoring for chronic kidney disease (CKD) could lead to earlier interventions that improve clinical outcomes. **PURPOSE:** To summarize evidence about the benefits and harms of screening for and monitoring and treatment of CKD stages 1 to 3 in adults. **DATA SOURCES:** MEDLINE (1985 through November 2011), reference lists, and expert suggestions. **STUDY SELECTION:** English-language, randomized, controlled trials that evaluated screening for or monitoring or treatment of CKD and that reported clinical outcomes. **DATA EXTRACTION:** Two reviewers assessed study characteristics and rated quality and strength of evidence. **DATA SYNTHESIS:** No trials evaluated screening or monitoring, and 110 evaluated treatments. Angiotensin-converting enzyme inhibitors (relative risk, 0.65 [95% CI, 0.49 to 0.88]) and angiotensin II-receptor blockers (relative risk, 0.77 [CI, 0.66	Ann Intern Med. 2012 Apr 17;156(8):570-81. **Screening for, monitoring, and treatment of chronic kidney disease stages 1 to 3: a systematic review for the U.S. Preventive Services Task Force and for an American College of Physicians Clinical Practice Guideline.** Fink HA, Ishani A, Taylor BC, Greer NL, MacDonald R, Rossini D, Sadiq S, Lankireddy S, Kane RL, Wilt TJ.

to 0.90]) reduced end-stage renal disease versus placebo, primarily in patients with diabetes who have macroalbuminuria. Angiotensin-converting enzyme inhibitors reduced mortality versus placebo (relative risk, 0.79 [CI, 0.66 to 0.96]) in patients with microalbuminuria and cardiovascular disease or high-risk diabetes. Statins and β-blockers reduced mortality and cardiovascular events versus placebo or control in patients with impaired estimated glomerular filtration rate and either hyperlipidemia or congestive heart failure, respectively. Risks for mortality, end-stage renal disease, or other clinical outcomes did not significantly differ between strict and usual blood pressure control. The strength of evidence was rated high for angiotensin II-receptor blockers and statins, moderate for angiotensin-converting enzyme inhibitors and β-blockers, and low for strict blood pressure control. **CONCLUSION:** **The role of CKD screening or monitoring in improving clinical outcomes is uncertain**. Evidence for CKD treatment benefit is strongest for angiotensin-converting enzyme inhibitors and angiotensin II-receptor blockers, and in patients with albuminuria combined with diabetes or cardiovascular disease.	
BACKGROUND: Microalbuminuria screening is widely used in high-risk populations but seldom used in the general population for detecting chronic kidney disease (CKD). Systematic reviews focused on screening for CKD are rare, and the issues about microalbuminuria screening in the general population have never been reviewed. We systematically reviewed studies regarding microalbuminuria screening and evaluated the benefits and harms of this screening method in the general population. **METHODS:** We systematically searched MEDLINE, PubMed, and the Cochrane Library for English articles published from January 1970 to 13 December 2011. Quality assessments were performed using the QUADAS tool or the Drummond's 10-point checklist. Due to the high heterogeneity of the study designs, meta-analysis for the study results was not possible. Therefore, we performed a narrative synthesis. **RESULTS:** Six articles from four studies made up our final study population, with four articles evaluating different screening methodologies and two reporting cost-effectiveness analyses. The qualities of the included articles ranged from fair to high. Spot urine albumin concentration and spot urine albumin:creatinine ratio had a similar diagnostic performance for microalbuminuria screening in the general population. **Screening for microalbuminuria in high-risk populations,**	Ren Fail. 2013;35(5):607-14. **Microalbuminuria screening for detecting chronic kidney disease in the general population: a systematic review.** Wu HY, Huang JW, Peng YS, Hung KY, Wu KD, Lai MS, Chien KL.

such as patients with diabetes, hypertension, or old age, was cost-effective. However, there was no consensus regarding the cost-effectiveness for microalbuminuria screening in the general population. **CONCLUSIONS:** **Microalbuminuria screening in high-risk populations is cost-effective. However, the cost-effectiveness of screening for microalbuminuria in the general population deserves further study**. To keep costs low, spot urine albumin concentration may be preferable than the albumin:creatinine ratio. Antud süstemaatilises ülevaates kasutatud uuringutest oli kulutõhususe analüüs teostatud ainult kahes. Ühes neist jõuti järeldusele, et üldpopulatsiooni sõelumine mikroalbuminuuria suhtes ja järgnev mikroalbuminuuriaga patsientide ravi AKEI-ga on kulutõhus (PREVEND uuring). Teises kasutatud uuringus aga leiti, et kulutõhus on sõeluda vaid riskigrupi patsiente. Seega ei anna antud süstemaatilise ülevaate autorid lõplikku otsust üldpopulatsiooni sõelumise kulutõhususe kohta – mainitakse, et see võib siiski olla kulutõhus, eriti juhul, kui sõelumise meetodina kasutatakse uriini albumiini kontsentratsiooni määramist. Siiski on vaja teostada lisauuringuid, s.h. ülpopulatsiooni sõelumise negatiivsete mõjude kohta.	
BACKGROUND: Chronic kidney disease (CKD) is a major health problem with an increasing incidence worldwide. Data on the cost-effectiveness of CKD screening in the general population have been conflicting. **STUDY DESIGN** Systematic review. General, hypertensive, and diabetic populations. Studies that evaluated the cost-effectiveness of screening for CKD. **INTERVENTION:** Screening for CKD by proteinuria or estimated glomerular filtration rate (eGFR). **OUTCOMES:** Incremental cost-effectiveness ratio of screening by proteinuria or eGFR compared with either no screening or usual care. **RESULTS:** 9 studies met criteria for inclusion. 8 studies evaluated the cost-effectiveness of proteinuria screening and 2 evaluated screening with eGFR. For proteinuria screening, incremental cost-effectiveness ratios ranged from $14,063-$160,018/quality-adjusted life-year (QALY) in the general population, $5,298-$54,943/QALY in the diabetic population,	Am J Kidney Dis. 2014 May;63(5):789-97. **Cost-effectiveness of primary screening for CKD: a systematic review.** Komenda P, Ferguson TW, Macdonald K, Rigatto C, Koolage C, Sood MM, Tangri N.

and $23,028-$73,939/QALY in the hypertensive population. For eGFR screening, one study reported a cost of $23,680/QALY in the diabetic population and the range across the 2 studies was $100,253-$109,912/QALY in the general population. The incidence of CKD, rate of progression, and effectiveness of drug therapy were major drivers of cost-effectiveness. **LIMITATIONS:** Few studies evaluated screening by eGFR. Performance of a quantitative meta-analysis on influential assumptions was not conducted because of few available studies and heterogeneity in model designs. **CONCLUSIONS:** **Screening for CKD is suggested to be cost-effective in patients with diabetes and hypertension. CKD screening may be cost-effective in populations with higher incidences of CKD, rapid rates of progression, and more effective drug therapy.**	
BACKGROUND: Hyperuricemia has been reported to be associated with chronic kidney disease (CKD). However whether an elevated serum uric acid level is an independent risk factor for new-onset CKD remained controversial. **METHODS:** A systematic review and meta-analysis using a literature search of online databases was conducted. Summary adjusted odds ratios with corresponding 95% confidence intervals (95% CI) were calculated to evaluate the risk estimates of hyperuricemia for new-onset CKD. **RESULTS:** Thirteen studies containing 190,718 participants were included. A significant positive association was found between elevated serum uric acid levels and new-onset CKD at follow-up (summary OR, 1.15; 95% CI, 1.05-1.25)**. Hyperuricemia was found be an independent predictor for the development of newly diagnosed CKD in non-CKD patients (summary OR, 2.35; 95% CI, 1.59-3.46).** This association increased with increasing length of follow-up. No significant differences were found for risk estimates of the associations between elevated serum uric acid levels and developing CKD between males and females. **CONCLUSIONS:** With long-term follow-up of non-CKD individuals, elevated serum uric acid levels showed an increased risk for the development of chronic renal dysfunction. Antud süstemaatilises ülevaates ei ole nimetatud küll hüperurikeemiaga patsientide sõelumise vajadust KNH suhtes, kuid samas kirjeldatakse hüperurikeemiat kui iseseisvat KNH riskifaktorit ning antakse soovitusi KNH	BMC Nephrol. 2014 Jul 27;15:122. **Is hyperuricemia an independent risk factor for new-onset chronic kidney disease?: A systematic review and meta-analysis based on observational cohort studies.** Li L, Yang C, Zhao Y, Zeng X, Liu F, Fu P.

ennetamiseks hüperurikeemia ravi näol.	
BACKGROUND: Studies of the association of prehypertension with the incidence of end-stage renal disease (ESRD) after adjusting for other cardiovascular risk factors have shown controversial results. **STUDY DESIGN:** Systematic review and meta-analysis of prospective cohort studies. **SETTING & POPULATION:** Adults with prehypertension. **SELECTION CRITERIA FOR STUDIES:** Studies evaluating the association of prehypertension with the incidence of ESRD **PREDICTOR:** Prehypertension. **OUTCOMES:** The relative risks (RRs) of ESRD were calculated and reported with 95% CIs. Subgroup analyses were conducted according to blood pressure (BP), age, sex, ethnicity, and study characteristics. **RESULTS:** Data from 1,003,793 participants were derived from 6 prospective cohort studies. **Compared with optimal BP, prehypertension significantly increased the risk of ESRD (RR, 1.59; 95% CI, 1.39-1.91).** In subgroup analyses, prehypertension significantly predicted higher ESRD risk across age, sex, ethnicity, and study characteristics. Even low-range (BP, 120-129/80-84 mm Hg) prehypertension increased the risk of ESRD compared with optimal BP (RR, 1.44; 95% CI, 1.19-1.74), and the risk increased further with high-range (BP, 130-139/85-89 mm Hg) prehypertension (RR, 2.02; 95% CI, 1.70-2.40). The RR was significantly higher in the high-range compared with the low-range prehypertensive population (P = 0.01). **LIMITATIONS:** No access to individual patient-level data. **CONCLUSIONS:** **Prehypertension is associated with incident ESRD. The increased risk is driven largely by high-range prehypertension.**	Am J Kidney Dis. 2014 Jan;63(1):76-83. **Prehypertension and Incidence of ESRD: a systematic review and meta-analysis.** Huang Y, Cai X, Zhang J, Mai W, Wang S, Hu Y, Ren H, Xu D.
BACKGROUND AND OBJECTIVES: Observational studies have reported an association between metabolic syndrome (MetS) and microalbuminuria or proteinuria and chronic kidney disease (CKD) with varying risk estimates. We aimed to systematically review the association between MetS, its components, and development of microalbuminuria or proteinuria and CKD. **DESIGN, SETTING, PARTICIPANTS AND MEASUREMENTS AND POPULATION:** We searched MEDLINE (1966 to October 2010), SCOPUS, and the Web of Science for prospective cohort confidence interval (CI) studies that reported the development of microalbuminuria or	Clin J Am Soc Nephrol. 2011 Oct;6(10):2364-73. **Metabolic syndrome and kidney disease: a systematic review and meta-analysis.** Thomas G, Sehgal AR, Kashyap SR, Srinivas TR, Kirwan JP, Navaneethan SD.

proteinuria and/or CKD in participants with MetS. Risk estimates for eGFR <60 ml/min per 1.73 m(2) were extracted from individual studies and pooled using a random effects model. The results for proteinuria outcomes were not pooled because of the small number of studies. **RESULTS:** Eleven studies (n = 30,146) were included. **MetS was significantly associated with the development of eGFR <60 ml/min per 1.73 m(2) (odds ratio, 1.55; 95% CI, 1.34, 1.80). The strength of this association seemed to increase as the number of components of MetS increased (trend P value = 0.02).** In patients with MetS, the odds ratios (95% CI) for development of eGFR <60 ml/min per 1.73 m(2) for individual components of MetS were: elevated blood pressure 1.61 (1.29, 2.01), elevated triglycerides 1.27 (1.11, 1.46), low HDL cholesterol 1.23 (1.12, 1.36), abdominal obesity 1.19 (1.05, 1.34), and impaired fasting glucose 1.14 (1.03, 1.26). Three studies reported an increased risk for development of microalbuminuria or overt proteinuria with MetS. **CONCLUSIONS:** **MetS and its components are associated with the development of eGFR <60 ml/min per 1.73 m(2) and microalbuminuria or overt proteinuria.** Antud uuringu autorid rõhutavad, et lisaks kõrgenenud vererõhule või hüperglükeemiale kuuluvad iseseisvalt neerupuudulikkuse riskifaktorite hulka ka kõik teised metaboolse sündroomi komponendid. Sellest tulenevalt soovitatakse varasemast rohkem pöörata tähelepanu düslipideemia korrigeerimisele et seeläbi neerupuudulikkuse riski vähendada. Samuti tuuakse eraldi välja ülekaalulisus kui neerupuudulikkuse riskifaktor (risk võrreldes normkaalulistega 19% suurem) ja viidatakse elustiili nõustamise vajalikkusele KNH ennetamisel.	

Lisamaterjal ägeda neerukahjustusega patsiendi sõelumise kohta KNH suhtes

NICE, 2014

28. Offer testing for CKD using eGFRcreatinine and ACR to people with any of the following risk factors:
/..../ acute kidney injury (see recommendation 44)

lk. 145 – 159
Antud ravijuhendi raames teostati süstemaatiline ülevaade selgitamaks, kas äge neerukahjustus mõjutab KNH patsientidel haiguse prognoosi ja tulemusnäitajaid. Samas kattus antud teema osaliselt küsimusega, **kas ägeda neerukahjustuse episood mõjutab KNH progresseerumist.**
Kaasati 3 hea kvaliteediga retrospektiivset kohortuuringut. Kogutud andmeid analüüsides leiti, et **äge neerukahjustus suurendab KNH progresseerumise riski kõigi eGFR-i väärtuste juures. Seetõttu otsustas ravijuhendi töögrupp lisada ägeda neerukahjustuse KNH riskifaktorite hulka, mille puhul on näidustatud KNH suhtes sõelumine.**

lk.198 – 210
Lisaks teostati iseseisev süstemaatiline ülevaade hindamaks ägeda neerukahjustuse järgse KNH teket ja progresseerumist:
7.4.2 Review question: What is the risk of developing and/or progression of CKD after an episode of AKI?
Süstemaatilisse ülevaatesse kaasati 11 kohortuuringut, uuringute kvaliteeti hinnati mõõdukaks. **Süstemaatilisest ülevaatest selgus, et äge neerukahjustus suurendab KNH esmashaigestumise või progresseerumise riski (seda kinnitasid kõik kaasatud uuringud).** Ravijuhendi töögrupp rõhutas siinkohal, et risk jääb kõrgeks ka neil patsientidel, kellel neerufunktsiooni näitajad ägeda neerukahjustuse episoodi järgselt täielikult normaliseeruvad. Seega on vajalik ägeda neerukahjustuse järgselt regulaarne neerufunktsiooni näitajate monitoorimine vähemalt 2 – 3 aasta jooksul, et KNH tekkimisel avastada haigus varasemas staadiumis.
Eelnevast lähtuvalt sõnastati soovitused:
44. Monitor people for the development or progression of CKD for at least 2–3 years after acute kidney injury, even if serum creatinine has returned to baseline. [new 2014]
45. Advise people who have had acute kidney injury that they are at increased risk of CKD developing or progressing. [new 2014]