Tõendusmaterjali kokkuvõte - EvSu

Kliiniline küsimus nr 18

Kas kõikide hilja suunatud (*late referral*) kroonilise neeruhaigusega patsientide ravitulemusi mõjutab eelnevate kroonilise neeruhaiguse komplikatsioonide ravimata jätmine vs mitte?

Tulemusnäitajad: kroonilise neeruhaiguse ravi tulemuslikkus, kroonilise neeruhaiguse progresseerumine, neeruasendusravi, aneemia, kõrgvererõhktõbi, sekundaarne hüperparatüreoidism, patsiendi elukvaliteet, hospitaliseerimine, südame-veresoonkonna tüsistused, ravikulu, elulemus, üldsuremuse vähenemine

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

- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. **KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease** (Kidney inter., Suppl. 2013; 3: 1-150; http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf) **(KDIGO)**

- National Clinical Guideline Centre; National Institute for Health and Care Excellence. **Chronic kidney disease (artial 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)**

Täiendavalt otsisime viimasel viiel aastal (alates 2011.a) avaldatud uuringuid, mille täistekstid olid kättesaadavad. Järgnevalt on otsingud, leitud artiklite arv ning kliinilisele küsimusele vastamiseks sobinud artiklite arv.

Sumsearch: chronic kidney disease and late referral -0
Chronic kidney disease and predialysis and late referral – 0
Chronic kidney disease and late consultation- 7 systematic reviews:
chronic kidney disease and pre-dialysis care: 12 systematic reviews – 0
PubMed: chronic kidney disease and late referral + piirang (syst. Rev., meta-anal.) 13 →6?
chronic kidney disease and late referral and complications 4→2
chronic kidney disease and late referral and anemia 1 (Nazar)
chronic kidney disease and late referral and hyperkalemia 0
chronic kidney disease and late referral and acidosis 0
chronic kidney disease and late referral and hyperphosphatemia 0
chronic kidney disease and late referral and hyperparathyroidism 3→0

chronic kidney disease and late referral and cardiovascular complications 2
chronic renal failure and late referral 13→6
chronic kidney disease and pre-dialysis care and late referral 21→ 2 (piirangutega ainult 1 süst. ülevaade 2006 a)
chronic kidney disease and late referral and diabetes mellitus 3 → 1
chronic kidney disease and late referral and hypertension 2 → 1?
Chronic kidney disease and late referral and glomerulonephritis 1 - ei sobi
Chronic kidney disease + pre-end-stage +
chronic kidney disease + late referral + heart ishaemic disease 6 →0
chronic kidney disease+late referral+coronary heart disease 12→1
chronic kidney disease + late referral+ atherosclerosis 0
chronic kidney disease+ late referral+ coronary artery disease 10→0

Süstemaatilised ülevaated

Leitud üks süstemaatiline ülevaade (**Neil A. Smart et al. 2011)**, mille eesmärgiks oli hinnata kliinilisi tulemusi varakult vs hilja nefroloogile suunatud haigetel. Süstemaatiline ülevaade põhineb 27 kohortuuringu tulemustel (viidatud KDIGO ravijuhendis).
Üks meta-analüüs **(Micah R. Chan et al. 2007)**, mis põhineb 22 uuringu andmetel. Küsimused: Suremuse risk varakult vs hilja suunatud ESRDga haigetel? Hospitaliseerimise pikkus? (viidatud KDIGO ja Malaysia ravijuhendites).
Prospektiivses kohortuuringus **(Dinanda J. de Jager. 2011)** hinnati seost nefroloogile suunamise aja ja elulemuse vahel diabeetikutel ja vanuritel (vanus ≥ 70) 1 aasta jooksul peale dialüüsravi alustamist.
Ühe keskuse andmetel põhinevas retrospektiivses uuringus (**Satoko Nakamura et al. 2007)** uuriti varajase suunamise mõju õigeaegsele dialüüsravi ajastamisele ja elulemusele kroonilse neeruhaiguse ja südame-veresoonkonna haigustega patsientidel.
Retrospektiivse vaatlusuuringu eesmärgiks **(Chris Jones et al. 2006)** oli välja selgitada kas 3-5 staadiumi KNHga patsientide rutiinne nefroloogiline kontroll aeglustab KNH progresseerumist ja on seotud parema patsientide elulemusega (viidatud Malaysia ravijuhendis).
Ühe keskuse retrospektiivses uuringus **(Frimat L et al. 2004 saadaval ainult abstrakt)** hinnati prognoosi 3 kuu ja 1 aasta möödudes peale NAR ravi algust 2 tüübi diabeetikutel.
Sankar D Navaneethan et al. (2008) süstemaatiline ülevaade oli koostatud selleks, et hinnata haigete hilinenud suunamise põhjusi (patsiendi- ja tervishoiusüsteemi poolsed) (viidatud KDIGO ravijuhendis).

Viited

Kokkuvõtte (abstract või kokkuvõtlikum info)	**Viide kirjandusallikale**
1. Neil A. Smart et al. Outcomes of Early versus Late Nephrology Referral in Chronic Kidney Disease: A Systematic Review. Am J Med. 2011 Nov;124(11):1073-80.e2. doi: 10.1016/j.amjmed.2011.04.026. **Abstract:** **BACKGROUND:** As late provision of specialist care, before starting dialysis therapy, is believed to be associated with increased morbidity and mortality, a systematic review was undertaken to evaluate clinical outcomes relating to early versus late referral of patients to nephrology services. **AIM**: The aim of	**http://www.amjmed.com/article/S0002-9343(11)00412-8/abstract** **täisteksti saab www.researchgate.com 'st**

this study was to conduct a broader systematic review, examining whether early versus late referral of adult chronic kidney disease patients to nephrology services also im- pacted on choice of dialysis modality, placement of relevant dialysis access, and other measures such as serum biochemistry. **METHODS:** Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE were searched up until September 2008 for studies of early versus late nephrology referral in adult (>18 years) patients with chronic kidney disease. Early referral was defined by the time period at which patients were referred to a nephrologist. **FINDINGS:** No randomized controlled trials were found. Twenty-seven longitudinal cohort studies were included in the final review, providing data on 17,646 participants; 11,734 were referred early and 5912 (33%) referred late. Comparative mortality was higher in patients referred to a specialist late versus those referred early. Odds ratios (OR) for mortality reductions in patients referred early were evident at 3 months (OR 0.51; 95% confidence interval [CI], 0.44-0.59) and remained at 5 years (OR 0.45; 95% CI, 0.38-0.53), both *P* <.00001. Initial hospitalization was 8.8 days shorter with early referral (95% CI, -10.7 to -7.0 days; *P* <.00001). Differences in mortality and hospitalization data between the 2 groups were not explained by differences in prevalence of diabetes mellitus, previous coronary artery disease, blood pressure control, serum phosphate, and serum albumin. However, early referral was associated with better preparation and placement of dialysis access. **CONCLUSION:** Our analyses show reduced mortality and hospitalization, better uptake of peritoneal dialysis, and earlier placement of arteriovenous fistula for hemodialysis with early nephrology referral. **Süstemaatilise ülevaate eesmärgiks oli hinnata kliinilisi tulemusi varakult vs hilja nefroloogile suunatud haigetel. Süstemaatiline ülevaade põhineb 27 kohortuuringu tulemustel (osalejate arv 17,646). Varakult suunatud: 1-3 kuud enne dialüüsravi. 11,734 suunatud varakult, 5912 (33%) hilja suunatud.** **Tulemused:** **- suremus oli kõrgem hilja suunatud patsientide seas. Hinnati 3, 6, 12 kuul ja 5 aasta pärast.** **- hospitaliseerimine: 6 uuringus oli vaadatud hospitaliseerimise pikkust. Meta-analüüs näitas, et varakult suunatud haigete rühmas hospitaliseerimine oli lühem 8,8 päeva võrra. Nende uurigute seas, kus varajane suunamine oli defineeritud kui 3-4 kuu enne dialüüsravi alustamist tulemus oli sama.** **- peritoneaaldialüüs: 14 uuringus uuriti dialüüsi valikut. Varem suunatud patsientide seas PD haigete arv oli suurem.** **- 11 uuringu andmetel varakult nefroloogile suunatud haigete seas ajutisi dialüüsi kateetreid kasutati vähem.** **- permanentne dialüüsi tee: AVF oli rohkem varakult nefroloogile suunatud haigetel.**	

- hemoglobiini tase: varakult nefroloogile suunatud haigetel hemoglobiini tase oli kõrgem. **- erütropoetiin: ESA ravi kasutati rohkem varakult nefroloogile suunatud haigetel.** **- seerumi kreatiniin: varakult nefroloogile suunatud haigetel kreatiniini tase dialüüsravi alustamisel oli madalam.** **- seerumi fosfori, albumiini, lipiidide tase oli mõlemas rühmas ühesugune.**	
2. Micah R. Chan et al. Outcomes in Patients with Chronic Kidney Disease Referred Late to Nephrologists: A Meta-analysis. Am J Med (2007) 120, 1063-1070 **Abstract:** **PURPOSE:** The study purpose was to compare differences in mortality and the duration of hospitalization in patients with chronic kidney disease who are referred early versus late to nephrologists. **METHODS:** We searched English-language literature from 1980 through December 2005, along with national conference proceedings, the Web of Science Citation Index, and reference lists of all included studies. Twenty-two studies with a total sample size of 12,749 met inclusion criteria. The definition of the time factor "late" is somewhat arbitrary and varies in the literature, ranging from <1 month to 1 year before renal replacement therapy. In general, a patient is considered to have been referred late "when management could have been improved by earlier contact with renal services. The definition of timing varied from study to study. Late referral defined as < 3 months before initiation of renal replacement therapy had the highest cumulative frequency in the mortality studies. **RESULTS:** There was significantly increased overall mortality in the late referral group as compared with the early referral group (relative risk 1.99; 95% confidence interval [CI], 1.66 to 2.39, *P* <.0001). The duration of hospital stay, at the time of initiation of renal replacement therapy, was greater in the late referred group by an average of 12 days (95% CI, 8.0 to 16.1, *P* =.0007). Significant heterogeneity was detected for both outcomes. **CONCLUSION:** Timing of referral emerged to be a significant factor impacting homogeneity in the mortality outcome. Our results suggest significantly higher mortality and increased early hospitalization of chronic kidney disease subjects referred late to nephrologists as compared with earlier referred subjects. **Meta-analüüs põhineb 22 uuringu andmetel. Meta-analüüsi küsimused: Suremuse risk varakult vs hilja suunatud ESRDga haigetel? Hospitaliseerimise pikkus?** **Lisaks hinnati erinevused laboratoorsetes analüüsides: kreatiniin, kreatiniini kliirens, hemoglobiin, hematokrit, albumiin.** **Enamik uuringutest "hilja suunatud" < 3 kuud enne NAR alustamist.** **Tulemused:** **- hilja suunatud haigetel suremuse risk on oluliselt kõrgem.** **- hospitaliseerimine hilja suunatud haigete rühmas oli 12 päeva võrra pikem.**	**http://www.amjmed.com/article/S0002-9343(07)00664-X/pdf**

- hilja suunatud haigetel albumiini ja hematokriti tase oli oluliselt madalam.	
3. Dinanda J. de Jager et al. Association between time of referral and survival in the first year of dialysis in diabetics and the elderly. Nephrol Dial Transplant (2011) 26: 652–658 doi: 10.1093/ndt/gfq438 **Abstract:** **Objective.** The objective of the study was to estimate the association between time of referral and survival during dialysis in diabetics and patients aged ≥70 years. **Design, setting and subjects.** This study was a prospective follow-up study in 1438 incident dialysis patients (1996– 2004, 62% male, 60 ± 15 years) in The Netherlands. **Main outcome measures**. Referral (time between first pre-dialysis visit to a nephrologist and dialysis initiation) was classified as: late (<3 months), early (3–12 months) or very early (≥12 months). All-cause mortality risk within the first year of dialysis was calculated [HR (95% confidence interval, CI), adjusted for age, sex and primary kidney disease (PKD)]. Additive interaction between time of referral and diabetes mellitus (adjusted for age and sex) or age (adjusted for sex and PKD) was assessed by synergy index [S (95% CI)]. **Results.** Thirty-two percent were late referred, 12% early and 56% very early; 21% had diabetes; and 30% were ≥70 years. Early and late referrals were associated with increased mortality compared with very early referral [HR_{adj}early: 1.5 (1.0, 2.4), late: 1.8 (1.3, 2.5)]. The cumulative incidence of mortality during the first year of dialysis in patients referred late, early and very early was 18%, 15% and 9%, respectively (P < 0.001). A similar trend was observed in diabetics and non-diabetics. However, no interaction between time of referral and diabetes was present [S_{late} 0.8 (0.4, 1.9), S_{early} 1.2 (0.4, 3.6)]. Likewise, in patients aged < 70 and ≥ 70 years, time of eferral was associated with increased mortality, without interaction [S_{late} 0.9 (0.4, 1.8), S_{early} 0.8 (0.3, 2.0)]. **Conclusion.** Late referral is associated with increased mortality in the first year of dialysis. Diabetes or high age does not have an additional worsening effect, implying that timely referral is important in future dialysis patients irrespective of diabetes or high age. **Prospektiivse kohortuuringu eesmärgiks oli hinnata seost nefroloogile suunamise ja elulemuse vahel diabeetikutel ja vanuritel (vanus ≥ 70) 1 aasta jooksul peale dialüüsravi alustamist.** **1438 pts, diabeetikuid - 21%, vanus ≥ 70 - 30%.** **Hilja suunatud < 3 kuud enne dialüüsi alustamist, vara suunatud 3-6 kuud enne dialüüsi alustamist, väga vara suunatud ≥ 12 kuud.** **32% - hilja suunatud, 12% - vara suunatud, 56% - väga vara suunatud.** **Tulemused: üldine suremus esimesel dialüüsravi aastal on kõrgem hilja suunatud patsientide rühmas. Seost kõrgema suremuse ja kaasuva DM**	**http://ndt.oxfordjournals.org/content/26/2/652.full.pdf+html**

või kõrge eaga pole leitud. **Kokkuvõte: hilja suunatud patsientidel suremuse risk on kõrgem sõltumata kaasuvast DMst või kõrgest east.**	
4. Satoko Nakamura et al. Effect of Early Nephrology Referral on the Initiation of Hemodialysis and Survival in Patients With Chronic Kidney Disease and Cardiovascular Diseases. Circ J 2007; **71:** 511 – 516 **Abstract:** **Background** The timing of referral to nephrologists is highly variable in patients with chronic kidney disease (CKD). The impact of early referral on the timing of hemodialysis (HD) and mortality in the patients with CKD and cardiovascular diseases (CVD) was evaluated in this present study. **Aim** The purpose of this study was to explore the impact of early nephrology referral (ER) before ESRD initiation on the timing of hemodialysis therapy and patient survival in Japanese patients. **Methods and Results** A total of 366 patients with CKD and CVD began HD at the National Cardiovascular Center between 1983 and 2003, and survival was followed until 2005. The times between the first evaluation by a nephrologist and the date of the first HD were categorized as late (LR <6 months) or early (ER □6 months) referral. Patients were classified into the ER (n=194) and LR (n=172) groups. Clinical data and renal function were not different. In the LR group, the renal function declined more rapidly and the duration between the first visit to the hospital and the first HD was shorter than the ER group. The survival rate after the initiation of HD was better in the ER group. Age, pre end-stage renal disease therapy and cardiac function had a significant impact on survival. **Conclusions** Early nephrology referral is important and necessary for patients with CKD and CVD in terms of a better renal prognosis and survival. **Retrospektiivne ühe keskuse uuring. Uuringu eesmärk: välja selgitada varajase suunamise mõju õigeaegsele dialüüsravi ajastamisele ja elulemusele kroonilse neeruhaiguse ja südame-veresoonkonna haigustega patsientidel.** **Varakult suunatud > 6 kuud enne dialüüsravi, hilja suunatud < 6 kuud enne dialüüsravi. Jälgimisperiood 41 kuud.** **Tulemused:** **- aeg esimesest visiidist nefroloogile esimese dialüüsi seansini oli pikem vara suunatud haigete rühmas** **- neerufunktsiooni alanemine oli aeglasem varakult suunatud haigete rühmas** **- hilja suunatud haiged jõudsid dialüüsi varem** **- atsidoosi, hüperkaleemia, hüperurikeemia, aneemia ravi oli paremini korraldatud varakult suunatud haigetel, ESA kasutati neid ka rohkem,**	**https://www.jstage.jst.go.jp/article/circj/71/4/71_4_511/_pdf**

hilja suunatud haigete rühmas oli rohkem vere ülekandeid **- permanentse dialüüsi tee protsent oli kõrgem varakult suunatud haigete rühmas** **- elulemus neeruasendusravil oli parem varakult suunatud haigetel** **- vanus, ravi predialüüsi staadiumis, südame-veresoonkonna seisund oluliselt mõjutasid elulemust.**	
5. Chris Jones et al. Decline in kidney function before and after nephrology referral and the effect on survival in moderate to advanced chronic kidney disease. Nephrol Dial Transplant (2006) 21: 2133–2143 doi:10.1093/ndt/gfl198 **Abstract :** **Background.** The burden of chronic kidney disease (CKD) is high, but its natural history and the benefit of routine nephrology care is unclear. This study investigated the decline in kidney function prior to and following nephrology referral and its association with mortality. **Methods.** This study provides a retrospective review of the individual rates of glomerular filtration rate (GFR) decline (millilitre per minute per 1.73 m^2/year) for the 5 years before and after referral in 726 new referrals with stages 3–5 CKD to one renal unit between 1997 and 2003. Blood pressures are averages at referral, 1 and 3 years post referral. Logistic regression and Cox's models tested factors predicting post-referral GFR decline and the impact on mortality. **Results.** Mean (SD) age was 72 (14), and 389 (54%) patients had stages 4–5 CKD. GFR decline slowed significantly from -5.4 ml/min/1.73 m^2/year (-13. to -2) before to -0.35ml/min/1.73m^2/year (-3 to +3) after referral ($P < 0.001$). Blood pressure also reduced significantly (155/84 to 149/80, $P < 0.05$) with most changes occurring within 1 year of referral. Factors predicting a non-progressive post-referral decline included a lower systolic blood pressure at referrral and 1 year after referral, a CKD diagnosis other than diabetic nephropathy, less baseline proteinuria and a non-progressive pre-referral GFR decline. A non-progressive post-referral GFR decline was independently associated with significantly better survival (hazard ratio 0.55, 95% CI 0.40–0.75, $P <= 0.001$) after adjustment for known risk factors. **Conclusions.** Following nephrology referral, GFR decline slowed significantly and was associated with better survival. Earlier detection of patients with progressive CKD and interventions to slow progression may have benefits on both kidney and patient survival. **Retrospektiivse vaatlusuuringu eesmärgiks oli välja selgitada kas 3-5 staadiumi KNHga patsientide rutiinne nefroloogiline kontroll aeglustab KNH progresseerumist ja kas see on seotud parema patsientide elulemusega.** **Jälgimisperiood: 3 aastat.** **Osalejate arv: 726 pts.** **Tulemused:** **- GFR alanemise aeglustamine peale nefroloogile suunamist.**	**http://ndt.oxfordjournals.org/content/21/8/2133.full.pdf+html**

-stabiilne GFR tase peale suunamist nefroloogile on seotud kõrgema elulemusega (P <= 0.001). **- parem VR kontroll** **-kõrgem iga, südame-veresoonkonna haigused anamneesis, progresseeruv GFR alanemine enne nefroloogile suunamist, suurem proteinuuria tase olid seotud kõrgema suremuse riskiga.**	
6. Frimat L et al. Early referral to a nephrologist is associated with better outcomes in type 2 diabetes patients with end-stage renal disease. Diabetes Metab. 2004 Feb;30(1):67-74 **(abstract)** **Abstract:** **OBJECTIVE:** End-stage renal disease (ESRD) requiring renal replacement therapy (RRT) is a late complication of type 2 diabetes. The correlation between pre-ESRD medical care and outcome has been rarely studied in France. **METHODS:** Community-based study of case-incident ESRD patients. Medical care practices were described retrospectively when starting RRT. Medical status, mortality, morbidity, and quality-of-life were recorded prospectively. **RESULTS:** One hundred and fourty-eight ESRD patients with type 2 diabetes were included. Factors independently correlated with mortality within 3 Months of RRT onset were presence of physical impairment of ambulation at onset of RRT [odd ratio (OR): 5, (95%CI: 1.9-13.3)], and starting RRT in life-threatening circumstances [OR: 3.6, (95%CI: 1.2-10.7)]. Factors independently correlated with "poor outcome" 1 Year after the onset of RRT were BMI less than 20 kg/m2 [OR: 13.4, (95%CI: 1.5-120.2)] and presence of 2 [OR: 2.7, (95%CI: 0.9-8.4)], or 3 or more comorbid conditions [OR: 4, (95% CI: 1.4-11)]. Three Months after the first RRT session, survival was 16.4% better for patients who had had regular nephrological care versus none, and 9.1% better for those who had had late nephrological care versus none. Type 2 diabetes patients starting RRT in an emergency setting had had significant less regular nephrological care. Length of their first hospital stay was significantly longer. They were more likely to have lower residualrenal function, gastrointestinal symptoms, lower serum albumin, lower hematocrit, lower serum calcium, and higher serum phosphorus. **CONCLUSIONS:** During the course of chronic renal failure in type 2 diabetes patients, early implementation of nephrological well-established guidelines is associated with better outcome after starting RRT. **Retrospektiivne uuring Prantsusmaal: 148 2 tüübi suhkurhaigusega patsienti. 1 aasta peale NAR alustamist hinnati haigete prognoosi: halvem prognoos oli madalama (<20kg/m^2) KMIga, 2-3 kaasuva haigusega patsientidel. Liikuvuspiirang ja erakorraliselt alustatud NAR olid sõltumatud suremuse riskifaktorid. 3 kuud peale NAR algust elulemus oli 16,4% kõrgem nendel haigetel, kes regulaarselt külastasid nefroloogi enne NARi ning 9,1% parem hilja suunatud nefroloogile haigetel kui nendel, kes pole üldse käinud nefroloogi juures enne NAR. NAR oli alustatud erakorraliselt sagedamini nendel, kes pole käinud regulaarsel kontrollil. Samuti oli pikem hospitaliseerimine, madalam neerude jääkfunktsioon, rohkem sümptomeid seedetrakti poolt, madalam**	**http://www.ncbi.nlm.nih.gov/pubmed/15029100**

kaltsiumi tase, madalam hematokrit, kõrgem fosfaadi tase.	
7. Sankar D Navaneethan et al. A systematic review of patient and health system characteristics associated with late referral in chronic kidney disease. BMC Nephrology 2008, 9:3 doi:10.1186/1471-2369-9-3 **Abstract:** **Background:** To identify patient and health system characteristics associated with late referral of patients with chronic kidney disease to nephrologists. **Methods:** MEDLINE, CENTRAL, and CINAHL were searched using the appropriate MESH terms in March 2007. Two reviewers individually and in duplicate reviewed the abstracts of 256 articles and selected 18 observational studies for inclusion. The reasons for late referral were categorized into patient or health system characteristics. Data extraction and content appraisal were done using a prespecified protocol. **Results:** Older age, the existence of multiple comorbidities, race other than Caucasian, lack of insurance, lower socioeconomic status and educational levels were patient characteristics associated with late referral of patients with chronic kidney disease. Lack of referring physician knowledge about the appropriate timing of referral, absence of communication between referring physicians and nephrologists, and dialysis care delivered at tertiary medical centers were health system characteristics associated with late referral of patients with chronic kidney disease. Most studies identified multiple factors associated with late referral, although the relative importance and the combined effect of these factors were not systematically evaluated. **Conclusion:** A combination of patient and health system characteristics is associated with late referral of patients with chronic kidney disease. Overall, being older, belonging to a minority group, being less educated, being uninsured, suffering from multiple comorbidities, and the lack of communication between primary care physicians and nephrologists contribute to late referral of patients with chronic kidney disease. Both primary care physicians and nephrologists need to engage in multisectoral collaborative efforts that ensure patient education and enhance physician awareness to improve the care of patients with chronic kidney disease. **Süstemaatiline ülevaade oli koostatud selleks, et hinnata haigete hilinenud suunamise põhjusi (patsiendi- ja tervishoiusüsteemi poolsed). Ülevaate koostamiseks kasutatud 18 vaatlusuuringu tulemusi (dialüüsi- ja perearstide keskustest). Enamus uuringutest olid retrospektiivsed (2 prospektiivset kohortuuringut).** **Tulemused:** **Patsiendipoolsed põhjused hilinenud suunamiseks: kõrgem iga, kaasuvad haigused, kindlustuse puudus, madalam sotsiaalne status, madalam haridustase.** **Tervishoiusüsteemi poolsed põhjused: ebapiisavad teadmised sellest, millal on õige aeg suunata pt spetsialisti juurde, puudulik koostöö perearsti ja nefroloogi vahel, dialüüsravi võimalus ainult suurtes**	**http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2291456/pdf/1471-2369-9-3.pdf**

keskustes.	

Ravijuhendid

Kolmes ravijuhendis (KDIGO, Malaysia, NICE) leidub infot haige õigeaegse suunamise kohta nefroloogile. Enamik uuringutest, millele oli viidatud ravijuhendites on toodud ka antud dokumendis.

KDIGO CKD management (lk. 113)

Selle küsimuse kohta kirjanduses on järjekindlad andmed: uuringutest ja ülevaadetest on leitud hilise suunamise negatiivsed tagajärjed ja kasu seoses varajase suunamisega (Navaneethan et al., Chan et al., Smart et al.)
In this section we will briefly consider summaries of the evidence relating to timely referral for planning RRT in people with progressive CKD. In this aspect the literature concerning late referral in the last quarter of a century has been remarkably consistent; both studies and narrative reviews identifying a number of adverse consequences of late referral and related benefits of early referral (Table 35).

Hilise suunamise tagajärjed	**Kasu varajasest suunamisest**
Aneemia ja luuhaigus	Hilisem NAR alustamine
Raske hüpertensioon ja vedeliku ülekoormus	Suurem permanentse dialüüsiteega haigete arv
Permanentne dialüüsitee	Suurem ravivõimaluste valik
Hiline suunamine siirdamisele	Väiksem vajadus erakorraliseks dialüüsiks
Pikem hospitaliseerimise kestvus	Lühem hospitaliseerimine, odavam
Kõrgem 1-aasta suremus	Parem toitumus
Pt NAR valik	Parem südame-veresoonkonna ja teiste kaasuvate haiguste käsitlus
Halvem psühhosotsiaalne kohanemine	Kõrgem elulemus

Hilise suunamise definitsioon väga varieerub, ilmselt 3 kuud on lühike aeg selleks, et hinnata, õpetada, valmistada dialüüsraviks ette, dialüüsitee rajamiseks, kui see on kõige levinum definitsioon.

Patients who are aged >75 years, female, non-Caucasian, uninsured, of lower socioeconomic or educational status, or have multiple comorbidities are most at risk for non-referral for CKD care.[671,672] **(Navaneethan 2011, 2007)** Patients with kidney disease have never been randomized to early or late referral to nephrology services and the definition of late referral in the published studies varies; three months is probably less than the absolute minimum amount of time required for assessment, education, preparation for RRT and creation of access but is the most frequently employed definition. Overall there are more than 50 studies in the published literature and a meta-analysis of 22 of these studies from 10 different countries serves to underline some of the key messages (Table 36), giving an indication of the size of the differences in mortality and hospital length of stay and also highlighting the significantly lower serum albumin level in late referred patients.[673] **(Chan, 2007)**

A systematic review considered twenty-seven longitudinal cohort studies providing data on 17,646 participants of whom 11,734 were referred early and 5912 (33%) were referred late.[674] **(Smart, 2011)** OR for mortality reductions in patients referred early were evident at 3 months (OR 0.51; 95% CI 0.44-0.59; Po0.0001) and remained significant at 5 years (OR 0.45; 95% CI 0.38-0.53; Po0.0001). Initial hospitalization was 8.8 days shorter with early referral (95% CI -10.7 to -7.0 days; Po0.0001). Differences in mortality and hospita- lization data between the 2 groups were not explained by differences in prevalence of diabetes mellitus, previous CAD, BP control, serum phosphate, and serum albumin. Early referral was associated with better preparation and earlier placement of dialysis access and better uptake of peritoneal dialysis.

Over a decade ago McLaughlin et al. evaluated the cost implications of early versus late referral.[675] Outcomes of interest were total cost of patient care, patient life-years, patient life-years free of RRT and hospital length of stay. Mean total costs per patient over five years were US$87,711 and US$110,056 for early and late referrals, respectively. The mean patient life-years were 3.53 and 3.36 years, respectively, and the patient life-years free of RRT were 2.18 and 1.76 years, respectively. Those patients referred early spent significantly less time in hospital (length of stay 25 days versus 41 days). Klebe et al. subsequently investigated the annualized cost of implementation of referral guidelines for CKD.[676] Although CKD guideline implementation resulted in significant increases in nephrology referral and additional investigation, they estimated that the associated costs could be recouped by delaying dialysis requirement by 1 year in one individual per 10,000 patients managed according to guidelines.

NICE CKD guideline (lk. 258)

NICE ravijuhendis leidub üldist infot õigeaegse suunamise olulisuse kohta, kasutatud kirjandus on suhteliselt vana. Samuti on välja toodud töörühma soovitused selle kohta, keda peab suunama nefroloogile (info ei ole otseselt seotud antud küsimuse teemaga):
-Soovitav suunata nefroloogile diabeetikuid ja mittediabeetikuid GFRga < 30 ml/min/1,73m^2 (G4-5)

-ACR ≥ 70mg/mmol välja arvatud diabeedist põhjustatud albuminuuria korral, millega on juba tegeletud
-ACR ≥ 30mg/mmol (A3) koos hematuuriaga
-Püsiv GFR alanemine 25% võrra GFR kategooria muutusega või GFR alanemine 15ml/min/,73m^2 12 kuu jooksul
-Haruldase geneetilise haigusega (teadaolev või kahtlus)

Referral criteria

9.1 Indications for referral to specialist care

- **9.1.1 Clinical introduction** What do nephrologists do for patients with CKD? The answer to this predominantly lies in 3 main areas: diagnosis and treatment of treatable kidney disease, identification and control of risk factors for progression of CKD and planning for renal replacement therapy in patients progressing to end stage kidney disease. The area that has deservedly received the most attention is planning for renal replacement therapy. There is abundant literature detailing the negative effect of late referral of patients with advanced CKD. Late referral leads to increased morbidity and mortality, increased length of hospital stay, and increased costs.[184(2006),185(1993),223(2002),269(GFR measurement,2006)336(1984),370(1996)] Several factors contribute to the adverse outcomes associated with late referral, including untreated anaemia, bone disease, hypertension and acidosis. The dominant factor though is insufficient time to prepare the patient for dialysis, particularly the establishment of permanent vascular access for haemodialysis. A CKD management programme encompasses blood pressure control and reduction of proteinuria, treatment of hyperlipidaemia, smoking cessation and dietary advice, treatment of anaemia, treatment of acidosis and metabolic bone disease, and just as importantly, the provision of timely and understandable information and education. The converse question though is how much of what nephrologists do could be done just as safely and effectively in primary care, and how much of an overlap is there between nephrology, diabetes, cardiology and the care of older people?

- **What are the criteria for referral to specialist care?**

- **9.1.2 Methodology** Due to the difficulty in searching this question, the results of a broad literature search were reviewed for systematic reviews on criteria for referral to specialist care in a CKD population. Seven papers were identified and all were excluded as they were narrative reviews or guidelines.

- **9.1.3 Health economics methodology** There were no health economics papers found to review.

- **9.1.4 Evidence statements** There are no evidence statements.

- **9.1.5 From evidence to recommendation** The GDG noted that there was no evidence to guide recommendations on who should be referred. The GDG considered the recommendations in other guidelines on who should be referred and also considered the aims and benefits of referral from their own professional standpoint. The GDG consensus was that the principles guiding referral should be: early identification of

people likely to require renal replacement therapy, the need for additional input to the management of CKD,

- e.g. for uncontrolled hypertension, the need for specialist advice about rare or genetic causes of CKD and the need to access specialist investigations such as magnetic resonance angiography.

- The GDG noted that section 5 and section 6 of the guideline had reviewed evidence relating to level of eGFR, proteinuria and risk factors for CKD and progression of CKD. From this evidence a consensus was reached regarding appropriate referral criteria in these areas.

- The GDG agreed that all people with a rapidly declining GFR and those with stage 4 and 5 CKD (with or without diabetes) should be referred, as well as those with heavy proteinuria unless this was already known to be due to diabetes and was being appropriately treated.

- The GDG agreed that specialist care can be provided by GPs, specialist nurses, renal nurses, geriatricians, diabetologists, cardiologists and nephrologists and that referral did not necessarily mean that the individual had to attend an out-patient clinic. In some situations advice could be obtained by correspondence. Furthermore, once an individual had been seen in a specialist clinic and a management plan agreed it may be possible for their future care to be carried out by the referring clinician rather than the specialist.

- The GDG recommended that if people with lower urinary tract symptoms required referral, this should initially be to urological services.

Recommendations

Take into account the individual's wishes and comorbidities when considering referral. [2008]

People with CKD in the following groups should normally be referred for specialist assessment:

o **GFR less than 30 ml/min/1.73 m^2 (GFR category G4 or G5), with or without diabetes**

o **ACR 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated**

o **ACR 30 mg/mmol (ACR category A3) or more, together with haematuria**

o **sustained decrease in GFR of 25% or more, and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m^2 or more within 12 months**

o **hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see also Hypertension [NICE clinical guideline 127])**

o **known or suspected rare or genetic causes of CKD**

Malaysia CKD management (lk. 31)

Ravijuhendis leidub infot õigeaegse suunamise kohta. Õigeaegne suunamine on seotud neerufunktsiooni alanemise aeglustamise, madalama suremuse riskiga (Jones et al., Chen et al. level III, Chan et al. level II).

Referral to a nephrologist is important to establish the diagnosis and formulate a plan of management for shared care to retard progression of CKD. The nephrologist would also monitor and manage the complications of CKD and plan for timely initiation of renal replacement therapy. Jones C et al. reported that following nephrology referral, there was a significantly slower decline in GFR and a 45% reduction in mortality.[167, level III] In another study, Chen SC et al. showed that nephrology referral was the most significant factor associated with retardation of renal disease progression.[168, level III] In fact, appropriate referral is associated with reduced hospitalisation, decreased patient morbidity and mortality, timely preparation of dialysis access and reduced cost of care.[169] A recent meta-analysis of cohort studies had shown that timing of referral was a significant factor affecting mortality.[170, level II-2]

SIGN Guideline: infot ei ole

KHA-CARI Guideline: infot ei leidu