Kliiniline küsimus nr 7
Kas alkoholivõõrutusravile peaks parema ravitulemuse saavutamiseks järgnema alati spetsiifiline sõltuvushäire farmakoteraapia vs mittefarmakoloogiline ravi vs kombineeritult mittefarmakoloogiline ravi ja spetsiifiline sõltuvushäire farmakoteraapia vs toetavad teenused vs kõik eelnevad sekkumised koos?

Kliiniline küsimus nr 8
Kas kõigi alkoholi kuritarvitavate ja alkoholisõltuvusega patsientide esmaseks raviks kasutada alati spetsiifilist sõltuvushäire farmakoloogilist ravi vs mittefarmakoloogilist ravi vs spetsiifiline sõltuvushäire farmakoloogiline ravi koos mittefarmakoloogilise raviga?

Kriitilised tulemusnäitajad: *abstinents, tagasilangus, alkoholi tarvitamise vähenemine, patsiendi rahulolu, patsiendi elukvaliteet, kvaliteetselt elatud eluaastate lisandumine, haiguse/vaegurluse tõttu kaotatud päevade arv, ravisoostumus, ravi katkestamine mistahes põhjusel, ravi katkestamine ravimite kõrvaltoimete tõttu, osalemine ravijärgsetes programmides või ravijärgsete programmide lõpetanute arvu osakaal alustanutest, juhuslik alkoholi tarvitamine*

Ravijuhendid

Kokkuvõte tõendusmaterjali kvaliteedist

Käesolevaid kliinilisi küsimusi nr 7 ja nr 8 käsitletakse koos, kuna tõendusmaterjal ning küsimuste sisu on väga suures osas kattuv. Küsimuste vastamiseks on teemad jaotatud 4 alakategooriasse:

1. ravi alustamine peale võõrutusravi ja ravi eesmärk

2. farmakoloogiline ravi

3. mittefarmakoloogiline ravi

4. kombineeritud ravi (farmakoteraapia+psühhosotsiaalsed sekkumised)

5. toetavad teenused

Farmakoloogilisele ravile on pühendatud eraldi kliinilised küsimused (K11- K16) ja mittefarmakoloogiline ravi on põhjalikumalt käsitletud kliinilise küsimuse nr 9 raames, mistõttu käesolevas kokkuvõttes tuuakse ära kõige põhilisemad uuringud.

1. Ravi alustamine peale võõrutusravi ja ravi eesmärk

2 hea kvaliteediga juht-kontrolluuringut ja üks kohortuuring näitasid, et pikkade ootejärjekordade puhul jätsid patsiendid ravile tulemata. (Rees et al., 1984, 1985; Leigh et al., 1984). Ühes randimiseeritud platseebokontrollitud uuringus (Mason et al., 2002) leiti, et akamprosaadiga ravi alustamine kohe peale võõrutusravi on soovitav, kuna esimestel päevadel peale võõrutust on tagasilanguseks oht väga suur. Kirjanduse ülevaade (Edwards, et al., 2003) leiab, et kõik mõõduka ja raske alkoholisõltuvusega patsiendid peaksid kohe peale võõrutusravi saama võimaluse õppida tagasilangusi ennetavaid strateegiaid. APA 2006 leiab, et tagasilangust ennetavate ravimitega tuleks kohe peale võõrutusravi alustada.

Ravi eesmärk ja ravivalik:

NICE 2011 süstemaatiline ülevaade astmelise ravi (stepped care) kohta (3 RCT, N=496), kus tulemusnäitajateks olid abstinents ja tarvitatud alkoholi kogus, ei leitud statistiliselt olulist erinevust astmelise ravi grupi ja tavaravi (kontrollgrupp) vahel.

2 hea kvaliteediga randomiseeritud platseebokontrollitud uuringut (Project MATCH Research Group 1993 ja UKATT 2005) tõdevad, et on palju erinevaid ravisekkumisi alkoholitarvitamise häire ravis, kuid ei leidu ühte kindlat ravisekkumist, mis sobiks kõigile alkoholiprobleemidega inimestele. Ravivalik varieerub patsientide seas ning muutub ka ühe patsiendi jaoks ravi erinevatel etappidel, kuna haigus on krooniline ning vajab erinevatel etappidel erineva intensiivsusega sekkkumisi. Alkoholitarvitamise häire ravivalik (farmakoloogiline või psühhosotsiaalne sekkumine) sõltub patsiendi seisundist, vajadustest ja olemasolevatest võimalustest. Lisaks diagnoosi püstitamisele ning õige ravivaliku tegemisele on väga oluline võtta arvesse patsiendi soove ja ootusi ravi

suhtes. Uuringud näitavad, et andes patsiendile võimaluse kaasa rääkida ravi valikutes paraneb ka ravisoostumus.

Abstinents või alkoholi tarbimise vähendamine?

Mõõdukas alkoholi tarbimine võib olla ravieesmärgiks patsientidele, kel ei ole alkoholisõltuvust ja olulisi alkoholist tingitud kahjustusi (Sitharthan et al. 1997; Heather 1995). Abstinents ravieesmärgina on soovitav patsientidele, kel esineb raske alkoholisõltuvus ja/ või esineb alkoholist tingitud organkahjustus (kirjanduse ülevaade, Tilg and Day 2007), kognitiivne defitsiit või kaasuv psüühikahäire (kirjanduse ülevaade, Edwards 2003, Tilg and Day 2007). Mitmed randomiseeritud platseebokontrollitud uuringud (Anton et al., 2006; Mason and Lehert, 2010; Koeter et al., 2010, Valliant et al., 1996) on näidanud, et abstinents kui ravieesmärk annab parimaid pikaaegseid ravitulemusi. Alkoholi tarvitamise vähendamine kui ravieesmärk on efektiivne ohustava alkoholi tarbimise ja alkoholi kuritarvitamise puhul (Heather et al 2006). Uuringud (Vaillant et al., 1996, Marlatt et al., 1993) ei kinnita kontrollitud joomise efektiivsust keskmise ja raske alkoholisõltuvuse korral. Siiski, kui abstinents ei ole esialgu võimalik, siis tarbimise vähendamine ja sellega seoses riskikäitumise maandamine võib olla realistlik eesmärk (Miller et al., 1991; Hodgins 1997).

Farmakoloogiline ravi

NICE 2011 süstemaatiline ülevaade, mis hõlmas hea kvaliteediga 19 randomiseeritud platseebokontrollitud uuringut ning kokku 4629 patsienti leidis, et akamprosaat võrreldes platseeboga on efektiivne abstinetnsi säilitamisel (RR 0.83; 95% CI 0.77 - 0.88). Akamprosaadi efekt oli kõige suurem 6. ravikuul, kuid püsis olulisena kuni 12. ravikuuni.

Meta-analüüs (Mann et al., 2004, 16 RCT, N=4500) keskendus akamprosaadi, naltreksooni ja disulfiraami efektiivsuse uurimisele alkoholisõltuvuse ravis. Akamprosaat andis häid tulemusi abstinentsi saavutamisel. Naltrexone oli efektiivne alkoholitungi vähendamisel ning pigem vähendas tagasilanguste arvu kui aitas säilitada kainust. Meta-analüüs soovitab antud ravimeid kasutada koos psühhosotsiaalsete sekkumistega.

Akamprosaat

NICE 2011 süstemaatiline ülevaade, mis hõlmas hea kvaliteediga 19 randomiseeritud platseebokontrollitud uuringut ning kokku 4629 patsienti leidis, et akamprosaat võrreldes platseeboga on efektiivne abstinetnsi säilitamisel (RR 0.83; 95% CI 0.77 - 0.88). Akamprosaadi efekt oli kõige suurem 6. ravikuul, kuid püsis olulisena kuni 12. ravikuuni.

1 süstemaatiline ülevaade (Bouza et al., 2004, 33 RCT, N=4000) hõlmas alkoholisõltuvusega patsienti, kes kõik olid eelnevalt läbinud võõrutusravi. 13 uuringut võrdlesid akamprosaati platseeboga, 19 uuringut naltreksooni platseeboga ja 1 uuring võrdles akamprosaati naltreksooniga. Akamprosaat oluliselt tõstis abtinentsis veedetud päevade arvu. Naltreksoon vähendas relapside arvu, kuid ei aidanud oluliselt kaasa abstinentsi hoidmisele, mistõttu sobib naltreksoon, kui ravieesmärgiks on kontrollitud alkoholi tarvitamine. Metaanalüüsid (Rosner et al. 2008, 2010), mis võrdlesid akamprosaati naltreksooniga, leidsid, et mõlemal ravimil on spetsiifilised terapeutilised eelised, kuna nende toimemehhanism on erinev. Akamprosaat on efektiivsem abstinentsi säilitamisel ja naltreksoon efektiivsem alkoholitungi vähendamisel. Hea kvaliteediga süstemaatilised ülevaated ja metaanalüüsid (Slattery et al., 2003; Berglund et al., 2003; Kranzler et al.,2001; Mason et al., 2000; Mason et al., 2010) tulevad järeldusele, et akamprosaat võrreldes platseeboga on mõõdukalt efektiivne abstinentsi saavutamisel peale võõrutusravi. Randomiseeritud platseebokontrollitud uuring (Anton et al., 2006) ei suutnud tõestada akamprosaadi efektiivsust üksi või komineerides naltreksooniga relapside ärahoidmisel. Akamprosaat võib olla kõige sobilikum mõõduka kuni raske alkoholisõltuvusega patsientidele, kes on rahuldavas üldseisundis, motiveeritud raviks ja psühholoogiliseks nõustamiseks. (Shand et al., 2003).

Naltreksoon

NICE 2011 süstemaatiline ülevaade, mis hõlmas 27 randomiseeritud platseebokontrollitud uuringut ja kokku 4296 alkoholisõltuvusega patsienti, leidis, et

naltreksoon võrreldes platseeboga vähendas oluliselt joomasööstude arvu (RR = 0.83, 95% CI = 0.75–0.91). Hea kvaliteediga Cochrane süstemaatiline ülevaade (Rösner et al., 2010), leidis, et naltreksoon vähendas joomasööstu riski 83%ni võrreldes platseebogrupiga (RR = 0.83 (95% CI 0.76–0.90) ja vähendas joomispäevi 4% võrra (MD -3.89 (95% CI -5.75 to -2.04). Süstemaatiline ülevaade (Bouza et al. 2004), mis hõlmas 19 randomiseeritud uuringut ja kokku 3205 alkoholisõltuvusega patsienti, hindas naltreksooni võrreldes platseeboga joomasööstude arvu vähendamises. Leiti, et naltreksoonraviga vähenes risk joomasööstuks 38%. (OR 0.62 [95% CI 0.52, 0.75,PB0.00001]). Naltreksoon ei saavutanud statistiliselt olulist efekti abstinentsi osas. (OR 1.26; 95% CI 0.97, 1.64, P 0.08).

Metaanalüüsid (Streeton et al., 2001; Srisurapanont et al., 2005; Garbutt et al., 1999) leiavad, et naltreksoon on võrreldes platseeboga efektiivsem abstinents saavutamisel, joomasööstude vähendamises ja relapside vähendamises. Olenevalt uuringust ja tulemusnäitajast, naltreksoonil on leitud väike kuni mõõdukas kasu (efekti suurus 0.1–0.5 ja suhtelise riski vähenemine 10%–14%). Lisaks tuleb arvestada patsientide individuaalse varieeruvusega, ning mõningane tõendusmaterjal väidab, et alkoholisõltuvuse esinemine perekonnas ja suur tung alkoholi järele võib ennustada paremat ravivastust naltreksoonile.

Platseebokontrollitud randimiseerutid uuring (Anton et al., 2006) võrdles kombineeritud käitumuslikke sekkumisi üksi, naltreksooni üksi ja naltreksoon+ käitumuslikud sekkumised ning leidis, et kõigel kolmel sekkumisviisil olid sarnased tulemused. Seetõttu võib osutuda, et inimesed, kellel ei ole võimalik või kes ei soovi farmakoteraapiale lisaks intensiivset psühhosotsiaalset sekkumist, kasutada naktreksooni üksi, mille juurde kuulub nö meditsiiniline jälgimine (MM medical management) lühikontaktid meditsiiniõega ravisoostumuse jälgimine ja abstinentsi toetus. (Anton et al., 2006; O'Malley et al., 2003)

Nalmefeen

Randomiseeritud platseebokontrollitud uuring (Karhuvaara et al., 2007) leidis, et nalmefeen (10mg või 40mg) koos minimaalse psühhosotsiaalse sekkumisega, võttes enne oodatavad joomisepisoodi, vähendab oluliselt joomasööstude arvu ja alkoholi kogutarbimist. Ühes randomiseeritud platseebokontrollitud uuringus (Mason et al. 1999) ei leitud efekti nii 20mg kui 80mg juures, kuid kombineeritult, siis nalmefeeniga ravitud grupis leidus oluliselt vähem joomasööste kui platseebogrupis. Multi center study (Anton et al., 2004) ei leidnud nalmefeenil efekti olevat 5, 20 või 40mg juures ühegi tulemusnäitaja osas.

Disulfiraam

Tõenduspõhisus disulfiraami osas on väiksem võrreldes akamprosaadi või naltreksooniga. Selle peamine põhjus on, et disulfiraamiga teostatud uuringud ei saanud olla topeltpimedad eetilistel põhjustel, kuna patsient peab teadlik olema disulfiraami ja alkoholi koostoime ohtlikkusest.

NICE 2011 süstemaatiline ülevaade disulfiraami kohta hõlmas mõõduka kuni raske alkoholisõltuvusega patsiente ning kokku 7 mõõduka kvaliteediga randomiseeritud uuringut: disulfiraam vs platseebo (3 RCT N = 859), disulfiraam vs akamprosaat (1 RCT N= 243), disulfiraam vs naltreksoon (2 RCT N=343), disulfiraam vs topiramaat (1 RCT N=100). Disulfiraam ei olnud erinev platseebost hoidmaks ära alkoholi tarvitamist. (RR 1.05; 95% CI, 0.96 to 1.15). Küll aga oli disulfiraam efektiivsem naltreksoonist vähendamaks aega esimese dringini (RR 0.18; 95% CI, 0.08 to 0.42) või joomasööstuni (RR 0.28; 95% CI, 0.13 to 0.59). Disulfiraam võrreldes topiramaadiga oli oluliselt efektiivsem joomasööstude ennetamisel kui topiramaat (RR 0.23; 95% CI, 0.09 to 0.55). Antud tulemused on avatud uuringute põhjal.

Disulfiraam on sobilik patsientidele, kes on kõrgelt motiveeritud abstinentsile ja kelle ravimi võtmist on võimalik jälgida. (Shand et al., 2003)

Mitmekeskusega koostööuuring (Fuller et al., 1986) leidis, et patsientidel, kes said 250mg disulfiraami päevas, oli oluliselt vähem joomispäevi kui neil, kes said disulfiraami 1mg või platseebot.

Patiendid, kes on intelligentsed, motiveeritud ja mitte impulssiivsed ja kelle joomine on tavaliselt tingitud ootamatutest sisemistest või välistest stiimulitest (tõstavad alkoholihimu), on parimad kandidaadid disulfiraami raviks. Patsiendid, kes on impulssiivsed, kel on kehv otsustusvõime või tõsine psüühikahäire, mis võib patsiendi muuta ennast ohustavaks, on kehvad kandidaadid disulfiraami raviks.

On vähe tõendusmaterjali selle kohta, milline on parim ravim alkoholisõltuvusega patsientide erinevatele alagruppidele. Enne kui otsustada milline ravim millisele patsiendile sobib, tuleks kaaluda järgnevat (SAMHSA 2009):

- varasem kogemus alkoholisõltuvuse ravimitega
- Motivatsioonitase abstinentsiks
- tervise üldseisund ja vastunäidustused
- varasemravisoostumus

Exhibit 6-4
AUD Medication Decision Grid

Pretreatment Indicators	Medications			
	Acamprosate (Campral®)	Disulfiram (Antabuse®)	Oral Naltrexone (ReVia®, Depade®)	Injectable Naltrexone (Vivitrol®)
Renal failure	X	A	A	A
Significant liver disease	A	C	C	C
Coronary artery disease	A	C	A	A
Chronic pain	A	A	C	C
Current opioid use	A	A	X	X
Psychosis	A	C	A	A
Unwilling or unable to sustain total abstinence	A	X	A	A
Risk factors for poor medication adherence	C	C	C	A
Diabetes	A	C	A	A
Obesity that precludes IM injection	A	A	A	X
Family history of AUDs	A	A	+	+
Bleeding/other coagulation disorders	A	A	A	C
High level of craving	A	A	+	+
Opioid dependence in remission	A	A	+	+
History of postacute withdrawal syndrome	+	A	A	A
Cognitive impairment	A	X	A	A

A = Appropriate to use C = Use with caution
X = Contraindicated + = Particularly appropriate

Mittefarmakoloogiline ravi

Hea kvaliteediga süstemaatiline ülevaade (Slattery et al., 2003) uuris milline ravi või ravikombinatsioonid (farmakoloogiline ja psühhosotsiaalne) annavad häid tulemusi alkoholisõltuvate patsientide käsitlemisel peale võõrutusravi. Autorid leidsid, et kõige enam kliinilist efektiivsust ja kulutõhusust on näidanud järgmised psühhosotsiaalsed sekkumised: Coping Skills (toimetulekuoskuste õpetamine); Behavioural Self Control Training (enesekontrolli käitumise õpetamine); motiveeriv intervjuu; paari- või pereteraapia. Teised psühhoteraapia vormid olid vähem efektiivsed. Lühinõustamine ei ole efektiivne alkoholisõltuvusega patsientide ravis.

Alkoholiprobleemide ravi tõendusmaterjali ülevaates (Proude et al. 2009) leiti, et kõige enam kasutatavad psühhosotsiaalsed sekkumised on lühinõustamine, motiveeriv intervjuu ja KKT, enesekontrolli õpetamine, tagasilanguse ennetamine ja paariteraapia. Psühhosotsiaalseid sekkumisi võib kasutada üksi või koos farmakoteraapiaga. Sekkumiste tulemusena väheneb oluliselt alkoholitarbimine, suureneb kainete päevade arv ja paraneb üldine toimetulek. Leiti, et madala intensiivsusega psühhosotsiaalsed

sekkumised (lühinõustamine) on näidustatud alkoholi liig-ja kuritarvitamise korral. Intensiivsemad psühhosotsiaalsed sekkumised (KKT, paariteraapia) sobivad raske alkoholisõltuvuse ja komorbiidsete psüühikahäirete korral.

NICE 2011 süstemaatiline ülevaade psühhosotisaalsetest sekkumistest koosnes keskmise kvaliteediga randomiseeritud uuringutest. Kõige parem tõendus alkoholi kuritarvitamise ja alkoholisõltuvuse raviefektiivsuse kohta oli paariteraapial (behavioural couples therapy [BCT], kognitiiv-käitumuslikul teraapial, sotsiaalse võrgustiku ja keskkonnapõhisel teraapial (social network and environment-based therapies) ja käitumuslikel teraapiatel (behavioural therapies). Vt. tõenduspõhised uuringud K9 täpsemalt.

Tõenduspõhisus rehabilitatsiooni programmide kohta on väiksem. Ühes metaanalüüsis (Smith et al., 2006), kus uuriti rehabilitatsiooniprogrammide efektiivsust sõltuvushäirete (sealhulgas alkohol) ravis, leiti vähe tõendust, et ravi lõpetanute arv või alkoholi kasutamisega seotud tulemusnäitajad oleksid paremad rehabilitatsiooniprogrammide korral võrreldes kogukonnapõhiste sekkumistega (residential treatments (community residence). Rehabilitatsiooniprogrammid on efektiivsed inimestele, kes vajavad struktureeritud pikaajalist sotsiaalset toetust, kel on mõõdukas kuni raske alkoholisõltuvus ja vähene sotsiaalne toetus. (Moos et al 1999) leidis, et programmid, mis olid konkreetsele ravisuunale orienteeritud, olid efektiivsemad kui programmid, mis olid diferentseerumata lähenemisega (nt.turvalisusele, toitlustamisele suunatud, limiteeritud nõustamise ja aktiivse ravita programmid.) NICE 2011 süstemaatiline ülevaade alkoholisõltuvuse ravist rehabilitatsiooniprogrammides vs ambulatoorses ravis, mis hõlmas keskmise kvaliteediga 14 randomiseeritud uuringut ja 2679 patsienti ja võttis arvesse järgmisi tulemusnäitajaid: tagasilangus, joomise sagedus ja alkoholikogus, leidis, et ambulatoorne ravisekkumine on sama efektiivne ja vähem kulukam kui rehabilitatsiooniprogrammid.teenuse Kõige enam uuritud patsiendipoolsed näitajad, mis mõjutavad raviteenuse valikut (ambul. või rehab. programm) on alkoholisõltuvuse raskusaste ja sotsiaalne stabiilsus. Raskema alkohlisõltuvusega ja sotsiaalselt ebastabiilsed patsiendid sobivad paremini raviks reh. programmides. Abielus, stabiilse elamiskohaga, lühema kestusega alkoholisõltuvusega patsiendid sobivad paremini ambul. raviks. (Kissin et al. , 1970; McLellan et al. , 1983; Orford et al. , 1976; Smart et al. , 1977; Stinson, 1970; Willems et al. , 1973). (Pettinati et al., 1999). Väikesele osale raske alkoholisõtltuvusega patsientidele, kes on kodutud, võib rohkem kasu olla rehabilitatsiooniprogrammidest. Süstemaatiline ülevaade (Roozen et al., 2004), mis hindas Community Reinforcement Approach ravi alkoholisõltlastel leidis vähese kuni mõõduka tõenduse community reinforcement approach (koos või ilma ravimita) efektiivsuse kohta.

<u>Kombineeirtud ravi (farmakoteraapia + psühhosotisaalsed sekkumised)</u>

Alkoholisõltuvuse farmakoteraapia peaks olema alati koos psühhosotsiaalsete sekkumistega. (Mann et al. 2004; Bauza et al. 2004 Laaksonen et al. 2008). Farmakoteraapia vs psühhoteraapia uuringuid, kus oleks võrreldud ainult ravimit psühhoteraapilise sekkumisega on vähe. Üheks selliseks uuringuks on platseebokontrollitud randomiseeritud uuring COMBINE (Anton et al., 2006). Suur osa alkoholisõltuvuse farmakoloogilise ravi uuringuid (naktreksoon, akamprosaat, disulfiraam) on kaasanud lisaks farmakonile ka psühhoterapetulisi sekkumisi nagu lühinõustamine, motiveeriv intervjuu, toimetuleku oskuste õpetamine, kognitiiv-käitumuslik teraapia ja teised psühhoteraapiad. NICE 2011 süstemaatiline ülevaade naltreksooni efektiivsusest, koosneb 27st randomiseeritud platseebokontrollitud uuringust naktreksooni kohta, millest 26 uuringul on lisaks naltreksoonile rakendatud ka mõnda psühhoterapeutilist sekkumist võrreldes platseebogrupiga. Samuti on psühhosotsiaalsed sekkumised (individuaalne teraapia, AA, psühhosotsiaalne toetus, käitumuslik teraapia ja võrgustiku teraapia) lisatud disulfiraam vs platseebo uuringutesse (Fuller et al., 1979,1983,1986; Chick et al., 1992; Berglund et al., 2003; Slattery 2003; Miller 1992; Laaksonen 2008). NICE 2011 süstemaatiline ülevaade akamprosaadi efektiivsusest kaasas 19 randomiseeritud uuringut, kus lisaks uuritavale ravimile (akamprosaat) oli lisatud psühhosotsiaalne sekkumine alkoholiteemaline nõustamine, raviprogrammid). Slattery et al., 2003 süstemaatiline ülevaade leidis, et akamprosaat ja superviseeritud võtmisega disulfiraam on soovitatav lisada psühhoterapeutilistele sekkumistele. Süstemaatilised ülevaated, meta-analüüsid ja randomiseeritud uuringud (Berglund et al., 2003; Kranzler et al., 2001; Rubio et al., 2002) leidsid, et opioidi antagonist selgelt parandas ravitulemusi võrreldes platseeboga,

kui ravimile oli lisatud kognitiiv-käitumuslik teraapia või motiveerivad tehnikad. Ledgerwood et al. 2005 analüüsib kliinilises juhendis psühhoteraapia ja farmakoteraapia kombineeirtud ravi alkoholitarvitamise häire ravis. Nad võtsid aluseks 6 erinevat psühhoteraapiat, mida on kasutatud koos alkoholisõltuvuse farmakoteraapiaga: lühinõustamine, motiveerivad tehnikad, KKT, käitumuslikud teraapiad (e.g., contingency management), käitumuslik paariteraapia ja 12 sammu programm. Autor leiab, et kuigi paljud psühhoteraapiad on sageli kasutuses alkoholisõltuvuse ravis koos farmakoteraapiaga, on vähe uuringuid, mis on uurinud nende omavahelisi mõjusid alkoholisõltuvuse ravis. Anton et al. 2006 randomiseeritud platseebokontrollitud uuring, mis hõlmas kokku 1393 alkoholisõltuvusega patsienti uuris akamprosaatravi+ platsebo, naltreksoon +platseebo, Naltreksoon + kombineeritud käitumuslikud sekkumised, akamrpsaat+kombineeritud käitumuslikud sekkumised ja käitumuslikud sekkumised ilma farmakoteraapiata. Olulised tulemusnäitajad olid abistinents (mitu % päevadest veedetud abstinentsis) ja aeg esimese joomasööstuni. Leiti, et patsientidel, keda raviti naltreksooni, kombineeritud käitumuslike sekkumiste või nende omavahelise kombinatsiooniga, olid paremad tulemusnäitajad kui akamorisaadil koos või ilma käitumusliku teraapiaga. Kui kaasatud oli meditsiiniline jälgimine (ingl. k medical management), siis kombineeritud ravi ei olnud tõhusam kui naltreksoon või käitumuslik teraapia eraldi võttes. Patsientidele, kes said platseebot ja olid meditisiinipersonaliga regulaarses kontaktis, oli suurem efekt kui patsientidel, kes said ainult käitumuslikku teraapiat. Uuringud on näidanud, et farmakoteraapia üksi on limiteeritud efektiivsusega sõltuvushäirete ravis. Fuller et al., 1986 leidis, et disulfiraami efektiivsus on tunduvalt parem kui ravisse on kaasatud pereliige või keegi teine oluline inimene. Uuringud on näidanud, et isegi kõige efektiivsemad sõltuvusravi farmakonid on limiteeritud tõhususega ning ei suuda katta kõiki sõltuvushäire sümptomeid. Siinkohal tulebki appi psühhoteraapia, millega on võimalik neid puudusi leevendada. Psühhosotsiaalsete sekkumistega saab: 1)suurendada patsiendi motivatsiooni ravimit võtma, 2)juhendada patsienti ravimi kasutamisel ja nende kõrvaltoimetega tegelemisel 3)hoida alal patsiendi motivatsiooni ravimiga jätkata peale algset saavutatud abstinentsi 4)toetav terapeutiline suhe hoiab ära enneaegse ravi katkestamise 5)aitab arendada oskusi, et tulla toime alkoholivaba eluga. Kuna farmakoteraapial ja psühhosotisaalsel ravil on erinev toimemehhanism, siis nende komibeerimisel saab kummagi raviviisi puudusi vähendada ning seetõttu ka efekti suurendada. Psühhoteraapiaga saab mõjutada sõltuvuse psühhosotsiaalseid aspekte nagu motivatsioon, toimetuleku oskused, düsfunktsionaalsed mõtted või sotsiaalsed suhted. Kui käitumuslike teraapiate toime võib tulla aeglaselt, sest vajab praktiseerimist ning läbitöötamise protsessi, siis farmakoteraapia tugevateks külgedeks on (Garbutt, West, Carey, Lohr, & Crews, 1999; Kranzler & Van Kirk, 2001; O'Malley & Kosten, 2006):

1) pikendab abstinentsi perioodi, mis suurendab inimese toimetulekut pikemaks tervistumiseks

2) ennetab ühekordset alkoholi tarvitamist, mis muidu võib viia relapsini

3) annab võimaluse ajurakkudel readapteeruda tagasi normaalsele mittealkohoolsele seisundile, aitab patsiente stabiliseerida, mõelda selgelt, omada rohkem positiivseid emotsionalseid vastuseid, tugevdab toimetuleku mehhanisme, tõstab valmidust muutusek

4) leevendab võõrutusnähtude sümptomeid (akamprosaadi toimemehhanismi hüpotees)

5) toetab psühhosotsiaalsete sekkumiste efektiivsust

Kombineeritud ravi kohta uuringuid on küll vähe, kuid üldiselt kombineeritud ravi on toetatud nii ravijuhendite kui ka uuringute poolt. On oluline märkida, et uuringud ei ole näidanud, et kombineeritud ravi oleks vähem efektiivne kui farmakotertaapia või psühhoteraapia üksi. (APA 2006).

Meditsiiniline juhtimine/jälgimine (Medical management - MM) on sageli kasutatav perearstisüsteemis diabeedi ja hüpertensiooni korral. NIAAA on arendanud välja koostöös COMBINE uuringuga meditsiinilise juhimise ka alkoholitarvitamise häiretele (NIAAA, 2004). MM pakub struktuuri ja materjali klinitsistidele, et teostada järgnevat: pakub patsientidele erinevaid strateegiaid ravimite võtmiseks ja ravisse jäämiseks; pakub hariduslikke materjale alkoholisõltuvuse ning farmakoteraapia kohta; toetab patsiendi pingutusi muutmaks oma joomisharjumusi; teeb otseseid soovitusi joomiskäitumise muutmiseks.

Toetavad teenused:

Proude et al., 2009 tõendusmaterjali ülevaade AA efektiivsuse kohta leiab, et patsiendid, kes lisaks ambulatoorsele ravile käivad ka AA rühmades ja liituvad rühmaga kohe ravi alguses, demonstreerivaid paremaid ravitulemusi kui need kes käivad vaid AA-s või saavad ainult ambulatoorset alkoholisõltuvuse ravi. Sage valeuskumus on, et 12 sammu programmiga liitunud peavad olema religioossed, et programmist kasu saada. Winzelberg et Humphreys 1999 näitasid oma uuringus, milles osales kokku 3018 meespatsiendist sõltlast, et hoolimata sellest, kas patsiendid omasid või ei omanud konkreetseid religioosseid tõekspidamisi, paranesid AA-s osalenute ravitulemused. Patsiendid, kellel on raskemad sõltuvuse sümptomid on altimad liituma AA-ga (Tonigan et al. 2006) ja saavad enam kasu, mida suurem on nende aktiivne kaasatus (Morgenstern et al, 2003). AA annab sõltlasele uue, kainust toetava keskkonna, mis on abistav sõltuvusest paranemisel (Litt et al. 2007). Süstemaatiline ülevaade Ferri et al., 2006, mille eesmärgiks oli hinnata AA või 12sammu programmi efektiivsust 3417 alkoholisõltuvate patsientide ravis, leidis, et vaadeldud 8 uuringut ei demonstreerinud üksmeelselt AA või 12SM efektiivsust alkoholisõltuvuse korral ning edasised uuringud on vajalikud.

Kokkuvõte ravijuhendites leiduvatest soovitustest

1. Ravi alustamine peale võõrutusravi ja ravi eesmärk

Kõik ravijuhendid kajastavad aklholivõõrutusravi kui üht osa kogu alkoholisõtuvuse ravist, millele kohe järgneb relapsi ennetusele suunatud ravitaktikad. Alkoholisõltuvuse raviga tegelvad asutused peaksid kohe alustama tagasilangust ennetava raviga (SIGN2003, NICE 2011, Australia 2009, APA 2006) ning vältima selle hilinemist peale võõrutusravi (SIGN 2003). Farmakoteraapiaga, mis on suunatud tagasilanguse ennetamiseks, tuleb alustada kohe peale võõrutusravi või selle ajal (NICE 2011, APA 2006). Psühhosotisaalsete sekkumistega on parim alustada kohe peale võõrutusravi (Australia 2009). Alkoholisõltuvaid patsiente tuleb informeerida ravi võimalustest. Patsiendi vajadused, eelistused ja sotsiaalsed olud tuleb ravi valikul arvesse võtta. Ravisekkumiste valik sõltub mitmetest teguritest: patsiendi käesolevatest probleemidest, alkoholitarvitamise ja teiste nakootiliste ainete tarvitamise muster, kaasuv psüühiline või kehaline haigus, motivatsioon ja ravieelistused, sotsiaalsed võimalused ja olemasolevad vahendid. Ravi eesmärgi ja ravisekkumise valik on patsiendi ja terapeudi jagatud otsus. (SIGN 2003, NICE 2011, Australia 2009,) *Abstinents* on ravi eesmärgiks enamustele mõõduka kuni raske alkoholisõltuvusega patsientidele. Lisaks patsientidele, kes liigtarvitavad alkoholi ja esineb muu psüühikahäire või kehaline haigus (SIGN 2003, Soome 2010, NICE 2011, Australia 2009, BAP 2012, WFSBP 2008, APA 2006, SAMHSA2009.) Lisaks soovitab SAMHSA 2009 ravijuhend abstinentsi veel patsientidele, kes: on, või planeerivad rasedaks jääda, tarvitavad ravimeid, mille korral on alkohol vastunäidutatud, kellel on diagnoositud alkoholitarvitamise häire. Kui patsiendile on näidustatud abstinents (mõõdukas kuni raske alkoholisõltuvus), kuid viimane ei soovi seda, vaid soovib jätkata mõõduka alkoholi tarbimisega, siis mitte loobuda alkoholisõltuvuse ravimisest. Tugeva alkoholisõltuvusega patsientide korral, alkoholi kuritarvitavate ja kaasuva komorbiidsusega patsientidele, kes ei soovi abstinentsi, kaalu kahjusid vähendavat ravilähenemist (NICE 2011, WFSBP 2008) või mõõdukat alkoholi tarbimist kui ajutine ravieesmärk, motiveerides patsienti siiski abstinentsile (APA 2006, SAMHSA 2009). Valides ravieesmärki, tuleb silmas pidada, et mõnede patsientide puhul on abstinents nõutud kohtuotsusega (NICE 2011).

Mõõdukat alkoholi tarbimist võib kaaluda patsientidel, kellel on alkoholi kuritarvitamine või kerge alkoholisõltuvus ilma komorbiidsete haigusteta ja adekvaatse sotsiaalse tugivõrgustikuga(NICE 2011, Australia 2009, BAP 2012).

3 ravijuhenidt (NICE 2011, Australia 2009 ja NSW 2008) soovitavad ravi valikul silmas pidada astmelise ravi (stepped care) printsiipi. Astmelise ravi korral alustatakse vähem intensiivsematest sekkumistest (nt. lühinõustamine), kui need osutuvad ebaefektiivseks liigutakse suurema intensiivsusesega sekkumiste poole (nt. KKT, farmakoteraapia).

2. farmakoloogiline ravi

Patsiendid peavad olema abstinentsis, kui alustatakse farmakoloogilise raviga(NICE 2011). Kõikidel alkoholisõltuvuse ravimitel on abistav roll psühhosotsiaalsete sekkumiste kõrval (SIGN 2003, NICE 2011, Australia 2009,WFSBP 2008, NSW 2008,

APA 2006,SAMHSA 2009,Soome 2010) ning neid ei tohiks kirjutatada üksi ilma psühhosotisaalsete sekkumisteta (NICE 2011). Alkoholisõltuvuse ravimitena soovitatakse akamprosaati (SIGN2003, NICE 2011,Australia 2009, BAP 2012, WFSBP 2009, NSW 2008,APA 2006, SAMHSA 2009, Soome 2010), naltreksooni (NICE 2011, Australia 2009, BAP 2012, WFSBP 2008,NSW 2008, APA 2006, SAMHSA 2009, Soome 2010), jälgitud kasutamisega disulfiraami (SIGN 2003,Australia 2009, NICE 2011,BAP 2012, WFSBP 2008, NSW 2008, APA 2006,SAMHSA 2009, Soome 2010) ja nalmefeeni (Soome 2010, . Nende ravimitega alustatakse kohe peale võõrutusravi.(NICE 2011, Australia 2009). SAMHSA 2009 toob välja patsientide alagrupid, kellele milline farmakon paremini sobida võib:

Akamprosaat – sobib patsientidele, kelle ravieesmärgiks on abstinents. Sobib kaasuva opiodsõltuvuse korral, patsientidele, kellel on mitmeid kaasuvaid kehalisi haigusi, mille tõttu tarvitavad mitmeid ravimeid, kuna akamprosaadil on vähe koostoimeid teiste ravimitega.

Disulfiraam - patiendid, kes on motiveeritud raviks ning ravieesmärgiks on abstinents. Patsiendid, kes on suutelised aru saama tagajärgedest, mis tekivad ravimi kooskasutamisel alkoholiga, patsiendid, kelle ravimi võtmist on võimalik jälgida, kaasuva kokaiini kuritarvitamise korral.

Naltreksoon – motiveeritud patsiendid, opioide mittekasutavad patsiendid, tugeva alkoholitungiga patsiendid.

Pikatoimeline süstitav naltreksoon - patsientidele, kes ei ole abi saanud teistest alkoholivastastest ravimitest või psühhosotsiaalsetest sekkumitest, patsiendid, kellel põhiprobleemiks on kehv ravireziimist kinnipidamine.

Ükski ravijuhend ei anna konkreetset soovitust kasutada nalmefeeni. Mitmed ravijuhendid (BAP 2012, NICE 2011, Soome 2010) on analüüsinud nalmefeeni efektiivsust, kuid uuringuid nalmefeeni kohta oli vähe, et nende põhjal anda soovitusi.

3. mittefarmakoloogiline ravi

Käitumuslik enesekontrolli treening (Behavioural Self Control Training – BSCT, SIGN 2003, Australia 2009), (Motivational Enhancement Therapy – MET, SIGN 2003, NSW 2008,Soome 2010, Australia 2009, NICE 2011, APA 2006), paari-või pereteraapia (Marital/Family Therapy SIGN 2003, NICE 2011,Soome 2010, Australia 2009, APA 2006) ja sotsiaalsete-ja toimetulekuoskuste treening (Coping/Social Skills Training SIGN 2003, Australia 2009) on soovitavad psühhosotsiaalsete sekumistena alkoholisõltuvuse ravis. Lühinõustamine on soovitav alkoholi liigtarvitamise korral, kuid ei ole soovitav alkoholisõltuvuse korral. (SIGN 2003, Australia 2009, NSW 2008, APA 2006) Psühhosotsiaalsed sekkumised on soovitavad kõigile mõõduka kuni raske alkoholisõltuvate patsientide korral kohe peale võõrutusravi (Australia 2009). Rehabilitatsiooniprogrammid on soovitatavad mõõduka kuni raske alkoholisõtluvusega inimestele, kes vajavad struktureeritud elamis-ja raviteenuseid, nt kodutud.(NICE 2011, Australia 2009) Kõikidele alkoholi liigtarvitavatele patsientidele rakenda motiveerivat intervjuud kui üht osa üldisest seisundi hindamisest. (NICE 2011) Alkoholi kuritarvitajatele ja kerge sõltuvusega patsientidele soovitatakse psühhosotisaalseid sekkumisi (kognitiiv-käitumuslik teraapia NICE 2011, NSW 2008, Soome 2010, APA 2006) käitumuslikud teraapiad(NICE 2011, APA 2006) või sotsiaalse võrgustiku ja keskkonnapõhised teraapiad NICE 2011) ning kellel on partner, siis paariteraapiat (NICE 2011). Mõõduka ja raske alkoholisõltuvusega patsientidele paku farmakoteraapia koos psühhosotsiaalsete sekkumistega (kognitiiv-käitumuslik teraapia, käitumuslikud teraapiad või sotsiaalse võrgustiku ja keskkonnapõhised teraapiad, paariteraapia, kui on parner, kes soovib ravis osaleda). Cue exposure soovitab Australia 2009 ravijuhend.

4. kombineeritud ravi (farmakoteraapia+psühhosotsiaalsed sekkumised)

Kõik ravijuhendid on seisukohal, et alkoholisõltuvuse ravi nurgakiviks on psühhosotsiaalsed sekkumised. Farmakoteraapia lisamine psühhoteraapiale suurendab ravi efektiivsust keskmiselt 15-25% (Soome 2010). Farmakopteraapia ja psühhosotisaalsete sekkumiste kombineerimist soovitatakse mõõduka ja raske alkoholisõltuvuse korral. Alkoholi kuritarvitamise korral võib piisata vaid

psühhosotsiaalsetest sekkumistest. Kuigi uuringuid kombineeritud ravist versus psühhosotsiaalsed sekkumised üksi vs farmakoteraapia üksi on vähe, on käesolev seisukoht siiski kombineeritud ravi pooldav. APA 2006 ja SAMHSA 2009 toovad välja põhjused, miks kombineeritud ravi võiks eelistatud olla:

Farmakoteraapia:

*vähendab võõrutusjärgseid sümptome, mis võiks põhjustada uut relapsi (akamprosaadi toime hüpotees glutamaatergilisse süsteemi)

* vähendab tungi (e.g., naltrexone)

*vähendab impulssiivset või olukorrast tulenevat alkoholi tarvitamist (disulfiraam)

Pühhosotisaalsed sekkumine:

*parandab patsiendi motivatsiooni muutuseks

*täiustab, suurendab motivatsiooni

*hõlbustab ravisoostumust ja ravist kinni pidamist, osalemist tugigruppides

5. toetavad teenused

9 ravijuhendist 7 (SIGN 2003, NICE 2011, Australia 2009, NSW 2008, APA 2006, Soome 2010,SAMHSA 2009) soovitavad alkoholisõltuvusega patsiendi ravimeeskonnal soovitada patsiendile AA grupiga liitumist. Ravimeeskonnal või raviasutusel peaks olema korralik ülevaade kohalisest eneseabigruppidest (AA, SMART recovery) ja nende kontaktandmed. Patsientidele tuleks aktiivselt soovitada AA rühmades osalemist. Osalemine on patsiendile vabatahtlik.

Ravijuhendite soovituste tekstid (inglise keeles):

1. Ravi alustamine peale võõrutusravi ja ravieesmärk:

SIGN 2003: Alcohol services should aim to reduce the delay between detoxification and interventions for the prevention of relapse. This would be facilitated by joint working between specialist mental health services, primary care, social work addiction services and non-statutory agencies, as recommended by the Joint Futures Group.
People who are alcohol dependent should be informed about treatment choices. Their needs, preferences and social circumstances should be considered. As a result, the choice of interventions should be a shared decision between the health professional and the patient.

NICE 2011: The SPC recommends that 'treatment with acamprosate should be initiated as soon as possible after the withdrawal period and should be maintained if the patient relapses'. Advice to start as soon as possible was made because studies that allowed more than 2 to 3 weeks after assisted withdrawal resulted in more people drinking again before initiating acamprosate, with consequent reduced efficacy. In the initial assessment in specialist alcohol services of all people who misuse alcohol, agree the goal of treatment with the service user. Abstinence is the appropriate goal for most people with alcohol dependence, and peoplewho misuse alcohol and have significant psychiatric or physical comorbidity(for example, depression or alcohol-related liver disease). When a service user prefers a goal of moderation but there are considerable risks, advise strongly that abstinence is most appropriate, but do not refuse treatment to service users who do not agree to a goal of abstinence. For harmful drinking or mild dependence, without significant comorbidity, and if there is adequate social support, consider a moderate level of drink-ing as the goal of treatment unless the service user prefers abstinence or there are other reasons for advising abstinence. For people with severe alcohol dependence, or those who misuse alcoholand have significant psychiatric or physical comorbidity, but who areunwilling to consider a goal of abstinence or engage in structured treat-ment, consider a harm reduction programme of care. However, ultimately the service user should be encouraged to aim for a goal of abstinence. When developing treatment goals, consider that some people who misusealcohol may be required to abstain from alcohol as part of a court order or sentence.

Australia 2009: Psychosocial relapse prevention strategies are best delivered as soon as acute withdrawal symptoms have subsided. Patients should be involved in goal setting and treatment planning.The choice of interventions for addressing alcohol use disorders will depend on a number of factors, including the patient's presenting problems, pattern of alcohol and other drug use, medical and psychiatric comorbidity, motivation and treatment preferences, and social circumstances, as well as available resources. Treatment plans should be modified according to reassessment and response to interventions (stepped care approach). For patients with no or low levels of dependence, and who are not experiencing significant alcohol related harms, a goal of moderation may be achievable. For patients with severe alcohol dependence, and/or those presenting with associated problems such as organ damage, cognitive impairment and co-existing mental health problems, the most realistic drinking goal is likely to be abstinence.

APA 2006: Relapse prevention medications should always be considered after detoxification. Currently available medications are naltrexone, disulfiram and acamprosate. The goals of treatment and the specific therapies chosen to achieve these goals may vary among patients and even for the same patient at different phases of an illness [I]. Because many substance use disorders are chronic, patients usually require long-term treatment, although the intensity and specific components of treatment may vary over time. The treatment plan includes the following components: 1) psychiatric management; 2) a strategy for achieving abstinence or re-ducing the effects or use of substances of abuse; 3) efforts to enhance ongoing adherence with the treatment program, prevent relapse, and improve functioning; and 4) additional treatments nec-essary for patients with a co-occurring mental illness or general medical condition. The long-term goals of treatment for patients with an alcohol use disorder are identical to those for patients with any type of substance use disorder and include abstinence (or reduction in use and effects), relapse prevention, and rehabilitation. There is some controversy in the lit-erature, however, regarding the possible benefits of striving for a reduction in alcohol intake, as opposed to total abstinence, for those who are unlikely to achieve the latter. A comprehensive review of the issue (951) concluded that a lower severity of pretreatment alcohol dependence and an individual's belief that he or she could control his or her drinking were associated with the individual's achieving controlled drinking after treatment. Interventions aimed at achieving moderate drinking have also been used with patients in the early stages of alcohol abuse. Controlled drinking may be an acceptable outcome of treatment for a select group of pa-tients when it is accompanied by substantial improvements in morbidity and psychosocial functioning. However, abstinence is the optimal goal that achieves the best long-term overall functioning.

BAP 2012: For those with cirrhosis and decompensated liver failure any drink-ing, even small amounts, is likely to be harmful. In addition, for those who have lost control of their drinking, reductions maybe hard to achieve and maintain, so a period of abstinence is also gen-erally advocated. For those that are unwilling or unable to become abstinent, reduced drinking may be an appropriate intermediate goal on the way to abstinence, although ideally clinical benefit should also be evident. For others with less adverse health conse-quences or not dependent, some drinking may be acceptable.

WSFBP 2008: Following a harmreduction strategy for patients not motivated for abstinence-oriented interventions to promote a reductionin drinking is acceptable in such situations (Good Clinical Practice), but abstinence from alcohol remains the primary long-term goal for moderate-to-severe alcohol dependence.

NSW 2008: In the stepped care approach to treatment, a set of empirically-based guidelines determine what treatment to start with and when to progress to an additional or more intensive treatment. The principle of Stepped Care as outlined by Schippers states that "a more intensive or different form of care or treatment is offered only when a less intensive form has been insufficient". For drug and alcohol treatment, this would involve monitoring the results of interventions and changing the intervention in some way if the outcome in relation to treatment goals was poor.

SAMHSA 2009: Decisions about care level, setting, and type of treatment should be based

on patient assessment and commitment to change, as well as treatment availabil ity. Another patient may be motivated for total absti-nence If a patient with an AUD is unwilling to be completely abstinent, he or she may be willing to cut down on alcohol use. Practitioners can work with this while noting that abstinence is the safer strat-egy and has greater chance of long-term success. Certain conditions warrant advising a patient to abstain from rather than reduce drinking. As noted in the NIAAA (2006) clinician's guide, these conditions include when drinkers: Are or may become pregnant Are taking a contraindicated medication Have a medical or psychiatric disorder caused or exacerbated by drinking Have an AUD. For those who drink heavily and who do not have an AUD, the practitioner should use professional judgment to determine whether cutting down or abstaining is more appropriate, based on factors such as (NIAAA, 2006): A family history of alcohol problems Advanced age Injuries related to drinking.

2. Farmakoteraapia

SIGN 2003: Acamprosate and supervised oral disulfiram are treatment options recommended as adjuncts to psychosocial interventions. Naltrexone does not have a Marketing Authorisation for the treatment of alcohol dependence in the UK and is not recommended for routine use in NHS Scotland.

NICE 2011: People should be abstinent from alcohol at the time of starting medication for relapse prevention. All medications should be used as an adjunct to psychosocial treatment and not prescribed in isolation. Delivering pharmacological interventions. Before starting treatment with acamprosate, oral naltrexone or disulfi-ram, conduct a comprehensive medical assessment (baseline urea and elec-trolytes and liver function tests including gamma glutamyl transferase [GGT]). In particular, consider any contraindications or cautions (see the SPC), and discuss these with the service user.

Acamprosate - If using acamprosate, start treatment as soon as possible after assisted

withdrawal. Usually prescribe at a dose of 1,998 mg (666 mg three times a day) unless the service user weighs less than 60 kg, and then a maximum of 1,332 mg should be prescribed per day. Acamprosate should: usually be prescribed for up to 6 months, or longer for those benefiting from the drug who want to continue with it be stopped if drinking persists 4–6 weeks after starting the drug. Service users taking acamprosate should stay under supervision, at least monthly, for 6 months, and at reduced but regular intervals if the drug is continued after 6 months. Do not use blood tests routinely, but consider them to monitor for recovery of liver function and as a motivational aid for service users to show improvement.

Naltrexone - If using oral naltrexone start treatment after assisted withdrawal. Start prescribing at a dose of 25 mg per day and aim for a maintenance dose of 50 mg per day. Draw the service user's attention to the information card that is issued with oral naltrexone about its impact on opioid-based anal-gesics. Oral naltrexone should: usually be prescribed for up to 6 months, or longer for those benefiting from the drug who want to continue with it Service users taking oral naltrexone should stay under supervision, at least monthly, for 6 months, and at reduced but regular intervals if the drug is continued after 6 months. Do not use blood tests routinely, but consider them for older people, for people with obesity, for monitoring recovery of liver function and as a motivational aid for service users to show improve-ment. If the service user feels unwell advise them to stop the oral naltrex-one immediately.

Disulfiram - If using disulfiram, start treatment at least 24 hours after the last alco-holic drink consumed. Usually prescribe at a dose of 200 mg per day. For service users who continue to drink, if a dose of 200 mg (taken regularly for at least 1 week) does not cause a sufficiently unpleasant reaction to deter drinking, consider increasing the dose in consultation with the service user. Before starting treatment with disulfiram, test liver function, urea and electrolytes to assess for liver or renal impairment. Check the SPC for warnings and contraindications in pregnancy and in the following conditions: a history of severe mental illness, stroke, heart disease or hypertension. Make sure that service users taking disulfiram: stay under supervision, at least every 2 weeks for the first 2 months, then monthly for the following 4 months if possible, have a family member or carer, who is properly informed about the use of disulfiram, oversee the administration of the drug are

medically monitored at least every 6 months after the initial 6 months of treatment and monitoring. Warn service users taking disulfiram, and their families and carers, about: the interaction between disulfiram and alcohol (which may also befound in food, perfume, aerosol sprays and so on), the symptoms of which may include flushing, nausea, palpitations and, more seriously, arrhythmias, hypotension and collapse the rapid and unpredictable onset of the rare complication of hepatotoxicity; advise service users that if they feel unwell or developa fever or jaundice that they should stop taking disulfiram and seek urgent medical attention. be stopped if drinking persists 4–6 weeks after starting the drug.

Australia 2009: Pharmacotherapy should be considered for all alcohol-dependent patients, in association with psychosocial supports. Naltrexone should be started as soon as possible after completion of withdrawal (usually 3 to 7 days after last drink) Acamprosate should be started as soon as possible after completion of withdrawal (usually 3 to 7 days after last drink). Disulfiram is recommended in closely supervised alcohol-dependent patients motivated for abstinence and with no contraindication.

BAP 2012: Acamprosate can be used to improve abstinence rates. It should be continued if the person starts drinking, since there is evidence that acamprosate reduces alcohol consumption, at least for a period to assess whether there is overall patient benefit attributable to acamprosate. Naltrexone can be used to reduce risk of lapse becoming a relapse, but there is less evidence to support its use in maintaining abstinence. Naltrexone may therefore be a better choice if someone is 'sampling' alcohol regularly but wishes to be abstinent. For acamprosate and naltrexone there is no consistent evi-dence to suggest which types of patient will respond, and relapse prevention medication should be offered to/con-sidered for everyone who is alcohol dependent wanting to be abstinent. Disulfiram is effective if intake is witnessed. Disulfiram can be offered as a treatment option for patients who intend to maintain abstinence, and for whom there are no contraindications.

WSFBP 2008: Pharmacotherapy can be used in conjunction with psychosocial treatment to increase abstinence rates or reduce relapse rates, treat other alcohol-related disorders (see above), or treat comorbid psychiatric disorders. In this context, psychotherapeutic or psychosocial interventions have been used to increase motivation for abstinence, improve motivation for medication compliance, and to enhance outcomes generally.

NSW 2008: Naltrexone is an anti-craving drug that acts on the brain's opiate receptors and reduces the likelihood of relapse to alcohol dependence (28). Acamprosate is thought to reduce drinking by moderating the brain's response to withdrawal from alcohol, and may be most suitable for people who are moderately to severely alcohol dependent and medically stable, provided they are also willing to comply fully with the medication regimen and engage in regular counselling. There is less evidence for the use of disulfiram among people with alcohol dependence. It is most commonly indicated for clients who are highly motivated to abstain from alcohol, and good outcomes can be achieved with close supervision. Disulfiram works by interacting with alcohol to create an intensely aversive reaction when alcohol is consumed, however is not currently subsidised by the pharmaceutical benefits scheme.

APA 2006: Naltrexone may attenuate some of the reinforcing effects of alcohol. Acamprosate, a γ -aminobutyric acid (GABA) analog that may decrease alcohol craving in abstinent individuals, may also be an effective adjunctive medication in motivated patients who are concomitantly receiving psychosocial treatment. Disulfiram is an effective adjunct to a comprehensive treatment program for reliable, motivated patients whose drinking may be triggered by events that suddenly increase alcohol craving.

SAMHSA 2009: evidence exists that acampro-sate is most effective for patients who, at treatment onset, are motivated for complete abstinence rather than decreased drinking

(Mason et al., 2006). As noted earlier, acamprosate does not affect endogenous or exogenous opioids, so it may be particularly appropriate for patients who are receiving opioid main-tenance therapy (reviewed by Myrick and Anton, 2004), at risk of relapsing to opioid use, or undergoing treatment with opioids for pain. Because there are no clinically significant drug interactions with acam-prosate, it can be a safe medication for patients who are coping with multiple medical issues and are taking many other medications.

3. Mittefarmakoloogiline ravi

SIGN 2003: Behavioural Self Control Training (BSCT), Motivational Enhancement Therapy (MET), Marital/Family Therapy and Coping/Social Skills Training are clinically and cost effective psychosocial interventions and are recommended treatment options for the prevention of relapse in alcohol dependence. Brief Interventions are not recommended, as trials in alcohol dependent people have failed to show any benefit. However, this guideline recommends Brief Interventions for hazardous drinkers (a less severely affected group than those who are considered to be alcohol dependent). Other psychosocial interventions are not recommended as their clinical effectiveness is unproven.

Australia 2009: 6.7 Psychosocial relapse prevention strategies are recommended for use with all moderately to severely alcohol-dependent patients. 6.9 Residential rehabilitation programs can be effective for patients with moderate to severe dependence who need structured residential treatment settings. 6.8 Psychosocial relapse prevention strategies are best delivered as soon as acute withdrawal symptoms have subsided.

NICE 2011: For people with alcohol dependence who are homeless, consider offering residential rehabilitation for a maximum of 3 months. Help the service user find stable accommodation before discharge. For all people who misuse alcohol, carry out a motivational intervention as part of the initial assessment. The intervention should contain the key elements of motivational interviewing including: helping people to recognise problems or potential problems related to

their drinking, helping to resolve ambivalence and encourage positive change and

belief in the ability to change, adopting a persuasive and supportive rather than an argumentative and confrontational position. For all people who misuse alcohol, offer interventions to promote absti-nence or moderate drinking as appropriate and prevent relapse, in community-based settings. Consider offering interventions to promote abstinence and prevent relapse as part of an intensive structured community-based intervention for people with moderate and severe alcohol dependence who have: very limited social support (for example, they are living alone or have

very little contact with family or friends) or complex physical or psychiatric comorbidities or not responded to initial community-based interventions. All interventions for people who misuse alcohol should be delivered by appropriately trained and competent staff. Pharmacological interventions should be administered by specialist and competent staff.

For harmful drinkers and people with mild alcohol dependence, offer a psychological intervention (such as cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) focused specifically on alcohol-related cognitions, behaviour, problems and social networks. For harmful drinkers and people with mild alcohol dependence who have a regular partner who is willing to participate in treatment, offer behav-ioural couples therapy. For harmful drinkers and people with mild alcohol dependence who have not responded to psychological interventions alone, or who have specifi cally requested a pharmacological intervention, consider offering acamprosate or oral naltrexone in combination with an individual psychological inter-vention (cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) or behavioural couples therapy. After a successful withdrawal for people with moderate and severe alcohol dependence, consider offering acamprosate or oral naltrexone in combi-nation with an individual psychological intervention (cognitive behavioural therapies, behavioural therapies or social network and environment-based therapies) focused specifically on alcohol misuse.

Soome 2010: Psychosocial treatment is more effective than leaving the patient untreated [128–145]A. Psychosocial therapies form the cornerstone of treatment in alcohol dependence, but the results may be significantly enhanced (by 15-25%, on an average) with drug therapies. So far, insufficient results are available from comparative studies of various drugs or of their concomitant use.

NSW 2008: CBT, Motivational Enhancement Therapy and Brief Interventions have a strong evidence base for their effectiveness in treating alcohol use. Psychodynamic, Interpersonal Therapies and 12-step treatments have received less research attention, but may well be effective for some clients with alcohol use disorders (eg. suicidality, acute psychosis, etc, 16). The decision about which specific psychosocial intervention is to be used with the drug and Alcohol client should be made by both the client and D&A professional, and be related to the list of problems and goals generated in the above phases (52). Where possible, the choice of intervention should be based on supporting evidence suggesting its effectiveness for the client's issues, along with the skill and expertise of the D&A professional in delivering the intervention. Adjunctive therapies should also be considered (eg. pharmacotherapy, etc) and appropriate referrals made at this time. Both the client's and D&A professional's expectations for treatment should be clarified, including a discussion about each client's role/boundaries for treatment. These issues should be documented in the clinical notes.

APA 2006: The major psychotherapeutic treatments that have been studied in patients with sub-stance use disorders are cognitive-behavioral, behavioral, psychodynamic/interpersonal, and re-covery-oriented therapies. A growing body of efficacy data from controlled clinical trials suggests that psychotherapy is superior to control conditions as a treatment for patients with a substance use disorder. However, no particular type of psychotherapy has been found to be consistently superior when compared with other active psychotherapies for treating substance use disorders.

4. Kombineeritud ravi (farmakoteraapia+psühhosotsiaalsed sekkumised)

*SIGN 2003***:** Acamprosate and supervised oral disulfiram are treatment options recommended as adjuncts to psychosocial interventions.

Soome 2010: Psychosocial therapies form the cornerstone of treatment in alcohol dependence, but the results may be significantly enhanced (by 15-25%, on an average) with drug therapies. So far, insufficient results are available from comparative studies of various drugs or of their concomitant use. • Naltrexone (50 mg daily) increases the number of non-drinking days and reduces relapses compared with placebo. Concomitant behavioural or motivational therapy greatly improves the treatment results

BAP 2012: In addition, all pharmacotherapies discussed here have been studied as an adjunct to psychosocial interventions, and use of medication alone is not currently advocated. Whether there is an optimal combination of a particular type of psychosocial intervention and pharmacotherapy has not been widely studied, so patients should engage with which-ever psychosocial approach they find beneficial or is available

SAMHSA 2009: Any pharmacologic treatment for alcohol dependence should be used as an adjunct to, not a replacement for, psychosocial treatment.

5. Toetavad teenused:

SIGN 2003: Introduction to AA and non-statutory agencies such as local Councils on Alcohol (Alcohol Focus Scotland) should be part of the overall strategy of specialist NHS services for the prevention of relapse. As with other psychosocial treatments, attendance is most likely to be beneficial if it is an informed voluntary decision.

Austraalia 2009 : Long-term participation in Alcoholics Anonymous can be an effective strategy to maintain abstinence from alcohol for some patients. Assertive referral practices to Alcoholics Anonymous increase participation and improve outcome.

NICE 2011: For all people seeking help for alcohol misuse:give information on the value and availability of community support networks and self-help groups (for example, Alcoholics Anonymous or SMART Recovery) and help them to participate in community support networks and self-help groups by encouraging them to go to meetings and arranging support so that they can attend.

APA 2006: Thus, most patients should be encouraged to attend at least sev-eral AA meetings to ascertain the appropriateness and utility of AA in helping them remain al-cohol free. Individual patient needs and concerns should, however, be taken into consideration when making this recommendation.

SAMHSA 2009: Providers should encourage patients to try different group meetings if they meet with negativity. Other mutual- or self-help groups include Self Management and Recovery Training (http://www.smartrecovery.org) and Women for Sobriety, Inc. (http://www. womenforsobriety.org). Although groups other than AA are not available in every community, they do offer a number of online resources. For patients' family members, there are Al-Anon and Alateen meetings (http://www.al-anon.alateen. org). Providers should have a working knowledge of the most common groups so that they can suggest these groups to their patients and discuss patients' participation.

Viited

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The management of harmful drinking and alcohol dependence in primary care, a national clinical guideline, Scottish Intercollegiate Guidelines Network, 2003	SIGN 2003
Alcohol-Use Disorders: Diagnosis, Assessment and Management of Harmful Drinking and Alcohol Dependence, National Institute for Health & Clinical Excellence, 2011	NICE 2011
Guidelines for the Treatment of Alcohol Problems, Australian Government Department of Health and Ageing, 2009	Austraalia 2009
Treatment of Alcohol Abuse, Current Care Guideline**,** The Finnish Medical Society Duodecim and the Finnish Society of Addiction Medicine,2010	Soome 2010
Evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from The British Association for Psychopharmacology,2012	BAP 2012
World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Substance Use and Related Disorders, Part 1: Alcoholism, 2008	WFSBP 2008
NSW Health Drug and Alcohol Psychosocial Interventions Professional Practice Guidelines, 2008	NSW 2008
Practice Guideline For The Treatment of Patients With Substance Use Disorders, 2nd Edition, American Psychiatric Association, 2006	APA 2006
Incorporating Alcohol Pharmacotherapies Into Medical Practice . Treatment Improvement Protocol (TIP) Series, Substance Abuse and Mental Health Services	SAMHSA 2009

Administration, 2009.	
Alcohol-use disorders: preventing harmful drinking, NICE public health guidance 24, 2010	NICE 2010b
Screening and Behavioral Counseling Interventions in Primary Care to Reduce Alcohol Misuse: U.S. Preventive Services Task Force Recommendation Statement, U.S. Preventive Services Task Force, 2013	USPSTF 2013

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Kokkuvõtte (abstract või kokkuvõtlikum info)	**Viide kirjandusallikale**
SIGN 2003	
This study examined the health beliefs and attitudes of patients seen in an alcoholism treatment clinic and investigated the relationship between these beliefs and attitudes and patient compliance as defined by length of time in treatment contact. Results showed that health beliefs and attitudes measured at the onset of treatment were predictive of patient adherence to treatment. Elements of the Health Belief Model found to be strongly associated with compliance included patients' perceived severity of their drinking problem, their expectations of improvement by remaining in treatment, and their levels of satisfaction with aspects of the doctor-patient relationship during the initial visit. The Health Belief Model offers a fruitful approach to understanding patients' compliance with alcoholism treatment and indicates possible areas for intervention to improve adherence.	Rees DW. Health beliefs and compliance with alcoholism treatment. J Stud Alcohol 1985;46(6):517-24. **Cohort study**
SIGN 2003	
The investigation set out to examine the extent of problems of low compliance at an alcoholism clinic, to investigate some variables that might differentiate referral failures and initial clinic attenders as well as categories of patients who attend for treatment, and to generate hypotheses concerning these differences as a means of developing a compliance-enhancement strategy. Information, including sociodemographic and personality variables, patient self-reports of drinking behaviour, self-perceptions of their need for help and of drinking problem severity, and therapist ratings of drinking problem severity, was gathered on one hundred referrals to a clinic for new patients. Results showed that 46% of patients were referral failures and that, in comparison with attenders, the former group had both waited longer for the initial appointment and were younger. Few variables differentiated the categories of attenders. A greater proportion of those remaining in treatment contact for longer than a month rated the change in their drinking problem over the previous year as 'worse' and more of them had been arrested for public drunkenness. Those who made five or more clinic visits had waited a shorter time for their initial appointment, and a greater proportion rated the effects of their drinking on their work as 'serious' and the change in their social life as 'worse' than patients who had made fewer visits. The findings suggest that variables related to personal perceptions of drinking problems offer a better account of compliance behaviour than the sociodemographic variables which have been the focus of previous research	Rees DW, Beech HR, Hore BD. Some factors associated with compliance in the treatment of alcoholism. Alcohol Alcohol 1984;19(4):303-7. **Case control study**
SIGN 2003	
Treatment dropout was studied in 172 patients (40 women) of an outpatient alcoholism treatment program. The best predictors of dropout were the length of delay between appointments, and	Leigh G, Ogborne AC, Cleland P. Factors associated with patient

variables related to symptom levels such as the number of prior alcohol-related arrests, the use of illicit drugs and scores on the Michigan Alcoholism Screening Test. Of lesser importance, but in line with previous findings, were sociodemographic variables such as age, the level of social stability and the presence of dependents at home. No personality variables were found to be relevant. It is suggested that treatment programs can improve attendance by reducing the delay with which services are offered and by changing certain characteristics of treatment personnel.	dropout from an outpatient alcoholism treatment service. J Stud Alcohol 1984;45(4):359-62. **Case control study**
NICE 2011	
Acamprosate and naltrexone have each demonstrated safety and efficacy for alcohol dependence in placebo-controlled clinical trials. There is scientific and clinical interest in evaluating these drugs in combination, given their high tolerability, moderate effect sizes, different pharmacological profiles and potentially different effects on drinking outcomes. Thus, this is the first human pharmacokinetic and pharmacodynamic drug interaction study of acamprosate and naltrexone. Twenty-four normal, healthy adult volunteers participated in a double-blind, multiple dose, within subjects, randomized, 3-way crossover drug interaction study of the standard therapeutic dose of acamprosate (2 g/d) and the standard therapeutic dose of naltrexone (50 mg/d), given alone and in combination, with seven days per treatment condition and seven days washout between treatments. Blood samples were collected on a standardized schedule for pharmacokinetic analysis of naltrexone, 6-beta-naltrexol, and acamprosate. A computerized assessment system evaluated potential drug effects on cognitive functioning. Coadministration of acamprosate with naltrexone significantly increased the rate and extent of absorption of acamprosate, as indicated by an average 33% increase in acamprosate maximum plasma concentration, 33% reduction in time to maximum plasma concentration, and 25% increase in area under the plasma concentration-time curve. Acamprosate did not affect the pharmacokinetic parameters of naltrexone or 6-beta-naltrexol. A complete absence of negative interactions on measures of safety and cognitive function supports the absence of a contraindication to co-administration of acamprosate and naltrexone in clinical practice	Mason, B. J., Goodman, A. M., Dixon, R. M., et al.(2002) A pharmacokinetic and pharmacodynamic drug interaction study of acamprosate and naltrexone. Neuropsychopharmacology , 27, 596–606. **RCT**
NICE 2011, Austraalia 2009	
Not available	Edwards, G, EJ Marshall and CCH Cook 2003, The treatment of drinking problems: A guide for the helping professions. Cambridge: Cambridge University Press. **Literature review**
NICE 2011	
(3 RCT: Breslin 1999, Bischof 2008; Drummond 2009 N=496) Studies assessing stepped-care methods found that there may be a smalleffect in favour of stepped care for hazardous drinkers. There were no significant differences found on alcohol outcomes for more harmful and dependent drinkers, which are the population covered by this guideline.	**NICE systematic review (stepped care)**
NICE 2011	
Not available	Project MATCH Research Group (1993) Project MATCH: rationale and

	methods fora multisite clinical trial matching patients to alcoholism treatment. Alcoholism:Clinical and Experimental Research, 17, 1130–1145.**RCT**
NICE 2011, Australia 2009, Soome 2010	
OBJECTIVE: To compare the effectiveness of social behaviour and network therapy, a new treatment for alcohol problems, with that of the proved motivational enhancement therapy.DESIGN: Pragmatic randomised trial.SETTING: Seven treatment sites around Birmingham, Cardiff, and Leeds.PARTICIPANTS: 742 clients with alcohol problems; 689 (93.0%) were interviewed at three months and 617 (83.2%) at 12 months.INTERVENTIONS: Social behaviour and network therapy and motivational enhancement therapy.MAIN OUTCOME MEASURES: Changes in alcohol consumption, alcohol dependence, and alcohol related problems over 12 months.	UKATT Reaearch Team 2005, Effectiveness of treatment for alcohol problems: findings of the randomised UK alcohol treatment trial (UKATT) BMJ 331: 331-541. **RCT**
NICE 2011, Australia 2009	
To date, the published controlled trials on exposure to alcohol cues have had an abstinence treatment goal. A modification of cue exposure (CE) for moderation drinking, which incorporated priming doses of alcohol, could train participants to stop drinking after 2 to 3 drinks. This study examined the effects of modified CE within sessions, combined with directed homework practice. Nondependent problem drinkers who requested a moderation drinking goal were randomly allocated to modified CE or standard cognitive-behavior therapy (CBT) for alcohol abuse. Both interventions were delivered in 6 90-min group sessions. Eighty-one percent of eligible participants completed treatment and follow-up assessment. Over 6 months, CE produced significantly greater reductions than CBT in participants' reports of drinking frequency and consumption on each occasion. No pretreatment variables significantly predicted outcome. The modified CE procedure appears viable for nondependent drinkers who want to adopt a moderate drinking goal.	Sitharthan, T, Sitharthan G, Hough MJ et al. 1997, Cue exposure in moderation drinking: A comparison with cognitive-behavioural therapy. J Consult Clin Psychol 65: 878-882. **RCT**
Australia 2009	
Not available	Heather, N. 1995, Brief intervention strategies. In: Hester, R and WR Miller (eds), Handbook of Alcoholism Treatment Approaches (pp. 105-122). Boston: Allyn and Bacon**.Literature review**
BAP 2012	
Alcoholic liver disease (ALD) and its complications is still one of the most frequent causes of death in the Western world. Treatment modalities for both alcoholic steatohepatitis (ASH; the major inflammatory complication of ALD) and alcoholic liver cirrhosis are insufficient. Severe ASH is associated with a high mortality; although glucocorticoid treatment has been reported to improve survival, meta-analyses of clinical trials performed to date have failed to show a convincing benefit of such an approach. Most of the progress in understanding these diseases, especially ASH, has come from studies of cytokines. Various proinflammatory cytokines, such as tumor necrosis factor (TNF), have been proposed to have an important role in the pathophysiology of ALD and its complications. Pilot studies on the	Nat Clin Pract Gastroenterol Hepatol. 2007 Jan;4(1):24-34. Management strategies in alcoholic liver disease. Tilg H[1], Day CP. **Review**

use of anti-TNF drugs, such as pentoxifylline or infliximab, in the treatment of ASH have now been performed with various levels of success. The treatment of patients with alcohol-related cirrhosis is mainly symptomatic and no therapies are currently available except orthotopic liver transplantation for end-stage liver disease. Independent of the stage of disease, abstinence from alcohol is the cornerstone of management. New treatment modalities for these diseases are eagerly awaited.	
BAP2012, Austria 2009, NICE 2011, Soome 2010	
OBJECTIVES: To evaluate the efficacy of medication, behavioral therapies, and their combinations for treatment of alcohol dependence and to evaluate placebo effect on overall outcome.DESIGN, SETTING, AND PARTICIPANTS: Randomized controlled trial conducted January 2001-January 2004 among 1383 recently alcohol-abstinent volunteers (median age, 44 years) from 11 US academic sites with Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, diagnoses of primary alcohol dependence.INTERVENTIONS: Eight groups of patients received medical management with 16 weeks of naltrexone (100 mg/d) or acamprosate (3 g/d), both, and/or both placebos, with or without a combined behavioral intervention (CBI). A ninth group received CBI only (no pills). Patients were also evaluated for up to 1 year after treatment.MAIN OUTCOME MEASURES: Percent days abstinent from alcohol and time to first heavy drinking day.RESULTS: All groups showed substantial reduction in drinking. During treatment, patients receiving naltrexone plus medical management (n = 302), CBI plus medical management and placebos (n = 305), or both naltrexone and CBI plus medical management (n = 309) had higher percent days abstinent (80.6, 79.2, and 77.1, respectively) than the 75.1 in those receiving placebos and medical management only (n = 305), a significant naltrexone x behavioral intervention interaction (P = .009). Naltrexone also reduced risk of a heavy drinking day (hazard ratio, 0.72; 97.5% CI, 0.53-0.98; P = .02) over time, most evident in those receiving medical management but not CBI. Acamprosate showed no significant effect on drinking vs placebo, either by itself or with any combination of naltrexone, CBI, or both. During treatment, those receiving CBI without pills or medical management (n = 157) had lower percent days abstinent (66.6) than those receiving placebo plus medical management alone (n = 153) or placebo plus medical management and CBI (n = 156) (73.8 and 79.8, respectively; P<.001). One year after treatment, these between-group effects were similar but no longer significant.CONCLUSIONS: Patients receiving medical management with naltrexone, CBI, or both fared better on drinking outcomes, whereas acamprosate showed no evidence of efficacy, with or without CBI. No combination produced better efficacy than naltrexone or CBI alone in the presence of medical management. Placebo pills and meeting with a health care professional had a positive effect above that	Anton RF, O'Malley SS, Ciraulo DA, et al. (2006) Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. JAMA 295: 2003–2017. **RCT**

of CBI during treatment. Naltrexone with medical management could be delivered in health care settings, thus serving alcohol-dependent patients who might otherwise not receive treatment	
BAP 2012	
This secondary analysis of the first U.S. acamprosate trial (N = 601) for alcohol dependence examines the effects of subsyndromal psychiatric symptoms or history of severe psychopathology on alcoholism treatment outcomes and any mitigating effects of acamprosate. Psychiatric antecedents were documented using a protocol-specific interview. Current psychiatric symptoms were assessed using Hamilton Anxiety and Depression (HAM-A, HAM-D) rating scales. Predictors of good response, defined as abstinence for > or =90% of trial duration, were identified using logistic regression. Subsyndromal anxiety (as determined by HAM-A "Anxious Mood" item) and the presence of > or =1 psychiatric antecedent were significant negative predictors of good response. Lower pretreatment drinking intensity, baseline motivation to have abstinence as a goal, and treatment with acamprosate were significant positive predictors of good response. No significant interactions among predictors were detected, indicating that they are independent, additive factors. Thus, the beneficial effects of acamprosate treatment in combination with motivational therapy may offset the liabilities for alcoholism recovery that are associated with current anxiety symptoms and/or a significant past psychiatric history. (Am J Addict 2010;00:1-8).	Mason BJ and Lehert P (2010) The effects of current subsyndromal psychiatric symptoms or past psychopathology on alcohol depen-dence treatment outcomes and acamprosate efficacy. Am J Addict 19: 147–154
APA 2006, WFSBP 2008,BAP 2012	
BACKGROUND: This study attempted to determine the course of male alcohol abuse from the age of 40 years to 60 or 70 years, to estimate the duration of abstinence required for stable remission and to study the hypothesis of progression of symptoms in chronic alcohol abuse.METHODS: The subjects were 268 former Harvard University (Cambridge, Mass) undergraduates (college sample) and 456 nondelinquent inner-city adolescents (core city sample) who had been repeatedly studied in multidisciplinary fashion since 1940. Since 47 years of age, these men have been followed up biennially by questionnaire and every 5 years by physical examination. At some point during their lives, 55 (21%) of the college and 150 (33%) of the core city men met DSM-III criteria for alcohol abuse. The college cohort has been followed until the age of 70 years, the core city cohort until age 60 years. The dependent variables were mortality and alcohol abuse status every 5 years.RESULTS: By 60 years of age, 18% of the college alcohol abusers had died, 11% were abstinent, 11% were controlled drinkers, and 59% were known to be still abusing alcohol. By 60 years of age, 28% of the core city alcohol abusers had died, 30% were abstinent, 11% were controlled drinkers, and only 28% were known to be still abusing alcohol.CONCLUSIONS: In three respects the two socially divergent samples resembled each other. After abstinence had been maintained for 5 years, relapse was rare. In contrast, return to controlled drinking without eventual relapse was unlikely. Alcohol abuse could continue for decades without remission or progression of symptoms. The samples differed in that the core city men began to abuse alcohol when younger and, although they were more likely than the college men to become alcohol dependent, the core city men were twice as likely to achieve stable abstinence	Vaillant GE: A long-term follow-up of male alcohol abuse. Arch Gen Psychiatry 1996; 53:243–249 **Cohort study**
BAP 2012	
BACKGROUND: The aim of this study is to assess the influence of early and late compliance of acamprosate on attendance and abstinence duration in the treatment of alcohol	Koeter MW, van den Brink W and Lehert P (2010)

dependence.METHODS: Individual patient data of 2,305 patients from 11 randomized controlled trials comparing acamprosate (n = 1,128) with placebo (n = 1,177) were used to predict early and late compliance and to study the effect of early and late compliance on attendance and abstinence duration using regression analysis and structural equation modeling.RESULTS: Early compliance was predicted by baseline motivation to become fully abstinent and baseline abstinence (R(2) = .26); late compliance was predicted by early compliance (R(2) = .13); treatment discontinuation was predicted by young age, marital status, compliance, and treatment condition (R(2) = .26); and abstinence duration was predicted by motivation to become fully abstinent early compliance and the interaction of early compliance and treatment condition (R(2) = .27). Structural equation modeling showed that abstinence duration was significantly associated with motivation at baseline, late compliance, and treatment condition (Goodness of Fit Index [GFI] chi(2)/df = 1.56; Parsimonious Goodness of Fit Index [PGFI] = 0.69).CONCLUSIONS: Motivation to become fully abstinent and abstinence at the start of treatment are important for early compliance. Early compliance in turn predicts late compliance. Late compliance, in combination with motivation to become fully abstinent, and treatment condition (acamprosate vs. placebo) predict duration of abstinence. This suggests that motivational interventions directed toward full abstinence motivation and abstinence at the start of treatment are crucial for both compliance with acamprosate and successful treatment outcome	Effect of early and late compliance on the effectiveness of acamprosate in the treatment of alcohol dependence. J Subst Abuse Treat 39: 218–226. **Review**
NSW 2008	
Not available	Heather, N. 'Controlled Drinking, Harm Reduction and Their Roles in the Response to Alcohol-related Problems'. Addiction Research and Theory 2006; 14(1): p7-18.
APA 2006	
The requirement of immediate and abrupt quitting ("cold turkey") can be an obstacle to the acceptance and accomplishment of abstinence as a long-term outcome. Three alternative "warm turkey" routes to abstinence are discussed: (a) sobriety sampling, (b) tapering down, and (c) trial moderation. Clinical research evidence and case examples are provided in support of these alternative approaches.	Miller WR, Page AC: Warm turkey: other routes to abstinence. J Subst Abuse Treat 1991; 8:227–232
APA 2006	
The relationship between individuals' choice of abstinence or moderate drinking during outpatient behavioral management treatment and outcome over 12 months' posttreatment was examined. At the initial assessment, 46% of 106 chronic alcoholic subjects chose abstinence, 44% chose moderate drinking, and 9% were unsure. Over the course of treatment, subjects were more likely to move from moderation to abstinence goals, and after the first 4 weeks of treatment, two-thirds chose abstinence. These subjects were older, had more severe alcohol problems (i.e., higher MAST scores), and were more likely to maintain their weekly alcohol consumption goals during the 16-week treatment period. Moreover, these subjects reported less alcohol use in the 12 month follow-up period, and a greater proportion were judged as having successful outcomes. The implications of these findings are discussed.	Hodgins DC, Leigh G, Milne R, Gerrish R: Drinking goal selection in behavioral self-management treatment of chronic alcoholics. Addict Behav 1997; 22:247–255
NICE 2011	
19 RCT (ANTON2006 BALTIERI2003 BARRIAS1997 BESSON1998 CHICK2000A GEERLINGS1997 GUAL2001 KIEFER2003	**NICE Systematic review**

LADEWIG1993 MORLEY2006 NAMKOONG2003 PAILLE1995 PELC1992 PELC1997 POLDRUGO1997 ROUSSAUX1996 SASS1996 TEMPESTA2000 WHITWORTH1996) total 4629 patients. There was a significant but small effect of acamprosate in promoting abstinencein participants when compared with placebo (RR 0.83; 95% CI 0.77 to 0.88).The effect was most pronounced at 6 months, but remained significant up to 12months. In the one trial that continued up to 2 years (WHITWORTH1996) this smalleffect continued for up to 12 months after the termination of treatment. The numberof individuals relapsing to heavy drinking was also significantly less in the acam-prosate group. This effect was also small (RR 0.90; 95% CI 0.81 to 0.99) but suggests participants were more likely to stay in treatment if randomised to acam-prosate instead of placebo. However, more participants left the trials due to adverse events in the acamprosate group, although this was not statistically significant.The quality of the evidence for acamprosate is high , therefore further research isunlikely to have an important impact on confidence in the estimate of the effect.	**(acamprosate)**
NICE 2011, Austraalia 2009, APA 2006, BAP 2012, WFSBP 2008	
Over the last 20 years, the role of adjuvant pharmacotherapy in optimising outcome in rehabilitation programmes for alcohol-dependent patients has become increasingly evident. New avenues for rational drug treatment have arisen from better understanding of the neurobiological substrates of alcohol dependence, including adaptive changes in amino acid neurotransmitter systems, stimulation of dopamine and opioid peptide systems, and, possibly, changes in serotonergic activity. Disulfiram, naltrexone and acamprosate are currently the only treatments approved for the management of alcohol dependence. However, there is still no unequivocal evidence from randomised controlled clinical trials that disulfiram improves abstinence rates over the long term. Aversive therapy with disulfiram is not without risk for certain patients, and should be closely supervised. Both naltrexone and acamprosate improve outcome in rehabilitation of alcohol-dependent patients, but seem to act on different aspects of drinking pathology. Naltrexone is thought to decrease relapse to heavy drinking by attenuating the rewarding effects of alcohol. However, data from the naltrexone clinical trial programme are somewhat inconsistent, with several large studies being negative. Acamprosate is believed to maintain abstinence by blocking the negative craving that alcohol-dependent patients experience in the absence of alcohol. The clinical development programme has involved a large number of patients and studies, of which the vast majority have shown a beneficial effect of acamprosate on increasing abstinence rates. Both drugs are generally well tolerated; nausea is reported by around 10% of patients treated with naltrexone, while the most frequent adverse effect reported with acamprosate is diarrhoea. Another opioid receptor antagonist,	Mann, K. (2004) Pharmacotherapy of alcohol dependence: a review of the clinical data. CNS & Neurological Disorders Drug Trials, 18, 485–504. **Meta-analysis**

nalmefene, has shown promising activity in pilot studies, and may have a similar profile to naltrexone. Data from studies of SSRIs in alcohol dependence are somewhat heterogeneous, but it appears that these drugs may indirectly improve outcome by treating underlying depression rather than affecting drinking behaviour per se. Similarly, the anxiolytic buspirone may act by ameliorating underlying psychiatric pathology. Dopaminergic neuroleptics, benzodiazepines and antimanic drugs have not yet demonstrated evidence of activity in large controlled clinical trials. Trials with drugs acting at serotonin receptors have yielded disappointing results, with the possible exception of ondansetron. Because the biological basis of alcohol dependence appears to be multifactorial, the future of management of alcoholism may be combination therapy, using drugs acting on different neuronal pathways, such as acamprosate and naltrexone. Pharmacotherapy should be used in association with appropriate psychosocial support and specific treatment provided for any underlying psychiatric comorbidities.	
NICE 2011, Australia 2009 , BAP2012, WFSBP 2008	
Two pharmacological agents have repeatedly been shown to be efficacious for relapse prevention in alcohol dependence: The putative glutamate-antagonist acamprosate and the opioid-antagonist naltrexone. Clinical evidence for both drugs is based on various outcome criteria. Whereas for acamprosate primarily abstinence maintenance has been demonstrated, studies with naltrexone have mostly emphasised the prevention of heavy drinking. The remaining effects of both drugs are not always reported; accordingly the corresponding database is fragmentary. Thus, the primary objective of the present meta-analysis was to complete the efficacy profiles for acamprosate and naltrexone and to compare them with each other. Unreported results, requested from the study investigators and the drug manufacturers, were integrated in the computation of effect sizes. For the meta-analysis, emphasis was placed on the conceptual distinction between having a first drink and returning to heavy drinking. Naltrexone was found to have a significant effect on the maintenance of abstinence as well as the prevention of heavy drinking. Acamprosate was shown only to support abstinence; it did not influence alcohol consumption after the first drink. When the efficacy profiles of the two drugs were compared, acamprosate was found to be more effective in preventing a lapse, whereas naltrexone was better in preventing a lapse from becoming a relapse. The superiority of either one drug or over the other one cannot be determined as a general rule, it rather depends on the therapeutic target. Benefits in the treatment of alcohol dependence might be optimized by matching the efficacy profiles of specific antidipsotropics with the motivational status of alcohol-dependent patients.	Rosner, S., Leucht, S., Lehert, P., et al. (2008) Acamprosate supports abstinence, naltrexone prevents excessive drinking: evidence from a meta-analysis with unreported outcomes. Journal of Psychopharmacology, 22, 11–23. **Meta-analysis**
APA 2006	
BACKGROUND: Renewed interest in medications to prevent relapse in alcoholics (i.e., antidipsotropics) resulted in approval by the Food and Drug Administration of naltrexone to treat alcohol dependence. Acamprosate, although not approved in the United States, is used in alcoholism treatment in many other parts of the world. In the absence of studies that compare the effects of these medications, we used a meta-analytic approach to the literature to	Kranzler HR, Van Kirk J: Efficacy of naltrexone and acamprosate for alcoholism treat-ment: a meta-analysis. Alcohol Clin Exp Res 2001; 25:1335–

compare their efficacy in alcoholism treatment.METHODS: All published placebo-controlled trials of naltrexone or acamprosate for alcohol dependence were examined, and, when suitable, data were extracted for calculation of a mean effect size. A sample of studies of selective serotonin reuptake inhibitors for treatment of major depression conducted over the last two decades served as a comparator for the antidipsotropics.RESULTS: Both antidipsotropics exerted significant, but modest, effects on treatment retention and/or drinking outcomes. There was significant variability among the studies for the measure on which the largest effect was exerted by each of these medications. Based on limited comparisons of the two medications, there appears to be no statistical difference in their efficacy in the treatment of alcohol dependence. In contrast, there was a consistent effect of selective serotonin reuptake inhibitors on depressive symptoms in major depression, which was significantly greater than the effects observed for the antidipsotropics.CONCLUSIONS: Both naltrexone and acamprosate are efficacious in reducing alcohol consumption in alcoholics. However, their specific role in alcoholism treatment remains to be more clearly defined. New approaches to the use of these medications and development of new medications are needed if pharmacotherapy is to play a substantial role in the treatment of alcoholism.	1341 **Meta-analysis**
BAP 2012, SIGN 2003	
The objectives of this health technology assessment were to answer the following questions:1. Which treatment or combination of treatments (pharmacological and psychosocial) will yield the maximum maintenance of recovery amongst the population of those with alcohol dependence who have undergone detoxification? 2. What is the most effective and efficient approach to delivering the individual interventions (or combination of interventions) taking into account the different risk groups, locations, durations of treatment, etc? Authors' conclusions1. The following treatments are recommended because they are clinically effective and cost-effective: Coping Skills;Behavioural Self Control Training; Motivational Interviewing; Marital/Family Therapy. Suitably trained andcompetent professionals should administer them using standardized protocols. 2. Other therapies are less effective and are not recommended. In particular, Brief Interventions are not effective forpeople with established alcohol dependence. The Classical Relapse Prevention model of treatment is also unproven.3. Specialist services must make themselves aware of non-NHS agencies (such as Councils on Alcohol and AlcoholicsAnonymous) operating in their area and co-ordinate their approach, making this information available to individualswithin their care. Informing people about these agencies should be part of the overall relapse prevention strategy.4. Disulfiram (given under supervision) and acamprosate are recommended as options for treatment in addition totalking therapies. Acamprosate is the most cost effective. As these medicines work differently and have different sideeffects the choice of treatment should be considered carefully on an individual patient basis.5. Naltrexone is not recommended because it does not have Marketing Authorisation in the UK for this use and is notas cost effective as acamprosate.6. Specialist	Slattery J, Chick J, Cochrane M, et al. (2003) Prevention of relapse in alcohol dependence. Health Technology Assessment Report 3. Glasgow: Health Technology Board for Scotland. (BAP) **Systematic review**

unit protocols should be available for all treatment options to ensure standardised and consistenttreatment. Clear patient information leaflets should be available for each intervention.7. Patients value group and one-to-one therapies. Certain people - such as young people, the homeless and those withother mental health problems - have special service needs and providers should ensure services are responsive andaccessible to all.8. Collection of longer-term audit data, evaluating patient outcome and resource consequences of alcohol relapse, invarious Scottish settings, is needed to refine further these recommendations.	
Austraalia 2009	
This article represents the proceedings of a symposium at the 2002 annual meeting of the Research Society on Alcoholism in San Francisco, CA, organized and cochaired by Mats Berglund and Sten Thelander. The presentations were (1) Preventive interventions against hazardous consumption of alcohol, by Mikko Salaspuro; (2) Treatment of alcohol withdrawal, by Johan Franck; (3) Psychosocial treatment for alcohol problems, by Sven Andréasson and Agneta Ojehagen; and (4) Pharmacological treatment of alcohol dependence, by Mats Berglund.	Berglund, M, Thelander S, Salaspuro M et al. 2003, Treatment of alcohol abuse: an **evidence-based review**. Alcohol Clin Exp Res 27(10): 1645-56.
NICE 2011	
27 RCT, total patients 4296 The comparison of oral naltrexone versus placebo showed a small but significanteffect favouring naltrexone on rates of relapse to heavy drinking (RR 0.83; 95% CI, 0.75 to 0.91). The mean DDD within the trial duration was less in the naltrexone group when compared with placebo, with a small but significant effect (SMD −0.28; 95% CI, −0.44 to −0.11). A significant but small effect favouring naltrexone was also found on days of heavy drinking during the trial (SMD − 0.43; 95% CI, − 0.82 to − 0.03). Although overall discontinuation rates favoured naltrexone over placebo, there was no significant difference between the two groups.	NiCE 2011 **systematic review** (naltrexone)
Ausralia 2009 , BAP 2012, APA 2006, WFSBP 2008	
A systematic review and analysis of 33 studies was carried out by Bouza et al (2004). The number of patients involved was 4000 with DSM-III or DSM-IV criteria for dependence (all had undergone detoxification). Thirteen trials compared acamprosate with placebo; 19 compared naltrexone with placebo, and 1 compared acamprosate with naltrexone. The main findings were that acamprosate was associated with a significant improvement in abstinence rate and days of cumulative abstinence, and that short-term administration of naltrexone reduced the relapse rate significantly but was not associated with significant improvement in the abstinence rate. The side-effects of naltrexone were more numerous, but it was tolerated acceptably without compromising adherence to treatment. The overall conclusions were that acamprosate appeared to be better in achieving abstinence, whereas naltrexone seemed to be better directed at treatments where controlled drinking is the goal.	Bouza, C, Angeles M, Magro A et al. 2004, Efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence: a systematic review. Addiction 99(7): 811-828. **Systematic review**
APA 2006	
The objective of this study was to review the evidence for the efficacy and toxicity of naltrexone, a treatment of alcohol dependence. A systematic review and meta-analysis of randomized controlled trials of naltrexone used in the treatment of alcohol dependence was conducted. We searched MEDLINE, EMBASE, PsychLIT and the Cochrane Controlled Trials Registry for articles published between 1976 to January 2001. The manufacturer of	Streeton C, Whelan G: Naltrexone, a relapse prevention maintenance treatment of alcohol dependence: a meta-analysis of randomized controlled trials. Alcohol Alcohol

naltrexone was asked to submit additional complete trial reports not in the literature. We analysed data from seven studies that compared naltrexone to placebo. The meta-analysis of benefit indicates that naltrexone is superior to placebo. Subjects treated with naltrexone experience significantly fewer episodes of relapse, and significantly more remain abstinent when compared to placebo-treated subjects [risk difference of relapse rates = -14% [95% confidence interval (CI): -23%, -5%]; and risk difference of abstinence rates = 10% (95% CI: 4%, 16%)] after 12 weeks of treatment. The naltrexone-treated subjects also consume significantly less alcohol over the study period than do placebo-treated subjects. There is no significant difference between naltrexone and placebo in terms of the number of subjects with at least one adverse event or the number of subjects who discontinued the trial due to an adverse event.	2001; 36:544–552 **Meta-analysis**
APA 2006	
OBJECTIVE: To evaluate the efficacy of 5 categories of drugs used to treat alcohol dependence--disulfiram, the opioid antagonists naltrexone and nalmefene, acamprosate, various serotonergic agents (including selective serotonergic reuptake inhibitors), and lithium.STUDY SELECTION: We included all studies on alcohol-dependent human subjects aged 18 years or older from all inpatient and outpatient settings between 1966 and December 1997 that met our inclusion criteria.DATA EXTRACTION: We abstracted the following information: study design and blinding, diagnostic instrument and severity assessment, drug interventions and cointerventions, demographic and comorbidity details about patients, compliance, and numerous outcome measures (eg, relapse, return to drinking, drinking or nondrinking days, time to first drink, alcohol consumed per unit of time, craving). We graded quality of the individual articles (scale, 0-100) independently from the strength of evidence for each drug class (A, strong and consistent evidence of efficacy in studies of large size and/or high quality; B, mixed evidence of efficacy; C, evidence of lack of efficacy; and I, insufficient evidence).DATA SYNTHESIS: Of 375 articles evaluated, we abstracted and analyzed data from 41 studies and 11 follow-up or subgroup studies. Naltrexone (grade A) reduces the risk of relapse to heavy drinking and the frequency of drinking compared with placebo but does not substantially enhance abstinence, ie, avoidance of any alcohol consumption. Acamprosate (grade A, from large-scale studies in Europe) reduces drinking frequency, although its effects on enhancing abstinence or reducing time to first drink are less clear. Controlled studies of disulfiram (grade B) reveal a mixed outcome pattern--some evidence that drinking frequency is reduced but minimal evidence to support improved continuous abstinence rates. The limited data on serotonergic agents were not very promising (grade I), although most studies were confounded by high rates of comorbid mood disorders. Lithium lacks efficacy (grade C) in the treatment of primary alcohol dependence.CONCLUSIONS: Recent reports documenting that naltrexone and acamprosate are more effective than placebo in the treatment of alcoholism justify clinical interest in use of these medications for alcohol-dependent patients. Use of disulfiram is widespread but less clearly supported by the clinical trial evidence; however, targeted studies on supervised administration of disulfiram may be warranted. Use of existing serotonergic agents or lithium for patients with primary alcohol dependence does not appear to be supported by the efficacy data available at this time; these medications may still have a positive effect **in patients with coexisting psychiatric disorders.**	Garbutt JC, West SL, Carey TS, Lohr KN, Crews FT: Pharmacological treatment of alcohol dependence: a **review of the evidence.** JAMA 1999; 281:1318–1325
APA 2006	

BACKGROUND: Opioid antagonists can decrease alcohol consumption in animals. Their harms and benefits have been examined in many clinical trials.OBJECTIVES: To determine the effectiveness of opioid antagonists in attenuating or preventing the recommencement of alcohol consumption in patients with alcohol dependence in comparison to placebo, other medications and psychosocial treatments. In addition, discontinuation rate, death, patient satisfaction, functioning, health-related quality of life and economic outcomes were also evaluated.SEARCH STRATEGY: The specialised register of the Cochrane Group on Drugs and Alcohol was searched until September 2003. The search was integrated with previous searches of Cochrane Controlled Trials Register (Cochrane Library 2001, issue 4), MEDLINE (1966 - October 2001), EMBASE (1980 - December 2001) and CINHAL (1982 - December 2001). Du Pont Pharmaceutical and Ivax Corporation were contacted for information regarding unpublished trials. The reference lists of the obtained papers were also examined.SELECTION CRITERIA: All relevant randomised controlled trials (RCTs) were included. Participants were people with alcohol dependence. Naltrexone (NTX), nalmefene (NMF) and other opioid antagonists with/without other biological or psychosocial treatments were examined. Two primary outcomes were number of participants with relapses (including those who return to heavy drinking) and number of participants who return to drinking. Other outcomes of interest were time to first drink, percentage or number of drinking days, number of standard drinks, craving, percentage or number of days or episodes of heavy drinking, amount of alcohol consumed, discontinuation rate, patient satisfaction, impaired function, health-related quality of life, economic and death.DATA COLLECTION AND ANALYSIS: Two reviewers evaluated and extracted the data independently. The dichotomous data were extracted on an intention-to-treat basis. The Relative Risk with the 95% confidence interval was used to assess the dichotomous data. A weighted (or standardised) mean difference (WMD or SMD) with 95% confidence interval was used to assess the continuous data.MAIN RESULTS: The review included 29 RCTs presented in 36 articles. Except two RCTs of nalmefene, all others investigated NTX. In comparison to placebo, a short-term treatment of NTX significantly decreased the relapse [RR (95% CI) = 0.64 (0.51 to 0.82)] and was likely to decrease the return to drinking [RR (95% CI) = 0.87 (0.76 to 1.00). In the respect of acceptability, NTX treatment significantly diminished treatment withdrawal [RR (95% CI) = 0.82 (0.70 to 0.97). While a medium-term treatment of NTX gave no benefit in the respect of relapse prevention, it was found to be beneficial on two of four secondary outcomes by increasing time to first drink and diminishing craving. A medium-term treatment of NTX was superior to acamprosate in reducing relapses, standard drinks and craving. NTX plus an intensive psychosocial treatment (PST) was not superior to NTX plus a simple PST on any primary and secondary short-term outcomes. For a medium-term treatment, NTX plus an intensive PST was superior to NTX plus a simple PST in increasing time to first drink and decreasing craving.AUTHORS' CONCLUSIONS: The review findings support that short-term treatment of NTX decreases the chance of alcohol relapses for 36% (number-needed-to-treat or NNT = 7) and likely to reduce the chance of returning to drinking for 13% (NNT = 12). In comparison to placebo group, NTX treatment can lower the risk of treatment withdrawal in alcohol-dependent patients for 28% (NNT = 13). Some major limitations of the available evidence include short study duration in many trials, small sample sizes in most trials and lack of data on psychosocial benefits. In conclusion, NTX	Srisurapanont M, Jarusuraisin N: Opioid antagonists for alcohol dependence. **Coch-rane Database Syst Rev 2005**

should be accepted as a short-term treatment for alcoholism. Strategies to improve adherence to NTX treatment, eg, PSTs and management of adverse effects, should be concomitantly given. We have not yet known so far how long alcohol-dependent patients who respond to NTX treatment should continue their treatment. Due to too little evidence, NMF should have no role for the treatment of alcohol dependence.	
NICE 2011	
METHODS: This multisite, randomized double-blind study investigated targeted nalmefene in reducing heavy drinking. Specialized alcohol treatment centers and private general practices enrolled 403 subjects (328 men, 75 women). Subjects were instructed to take nalmefene 10 to 40 mg (n=242) or placebo (n=161) when they believed drinking to be imminent. After 28 weeks, 57 subjects from the nalmefene group continued into a 24-week randomized withdrawal extension. Concomitant psychosocial intervention was minimal and no treatment goals were imposed. Alcohol consumption was recorded using the time-line follow-back method. Biochemical indicators of alcohol use were also measured.RESULTS: The mean monthly number of heavy drinking days (HDDs) during the 12-week period before inclusion was 15.5 (SD 6.9) in the nalmefene group and 16.2 (SD 6.9) in the placebo group. During treatment, the mean numbers of HDDs were 8.6 to 9.3 in the nalmefene group and 10.6 to 12.0 in the placebo group (p=0.0065). The levels of serum alanine aminotransferase and gamma-glutamyl transferase decreased in the nalmefene group compared with the placebo group (p=0.0088 and 0.0023). During the randomized withdrawal period, subjects randomized to placebo apparently returned to heavier drinking. Subjects receiving nalmefene reported more nausea, insomnia, fatigue, dizziness, and malaise than subjects on placebo.CONCLUSIONS: Nalmefene appears to be effective and safe in reducing heavy drinking, even when accompanied by minimal psychosocial support	Karhuvaara S, Simojoki K, Virta A, et al. (2007) Targeted nalmefene with simple medical management in the treatment of heavy drinkers: a ran-domized double-blind placebo-controlled multicenter study. Alcohol Clin Exp Res 31: 1179–1187. **RCT**
The opiate antagonist nalmefene has been shown in 2 single-site studies to reduce alcohol consumption and relapse drinking in alcohol-dependent individuals. This safety and preliminary multisite efficacy study evaluated 3 doses of nalmefene (5, 20, or 40 mg) in a double-blind comparison to placebo over a 12-week treatment period in 270 recently abstinent outpatient alcohol-dependent individuals. Participants concomitantly received 4 sessions of a motivational enhancement therapy (with a medication compliance component) delivered from trained counselors. Although more subjects in the active medication groups terminated the study early secondary to adverse events, the rates did not differ significantly from that of placebo. The 20-mg/d group experienced more insomnia, dizziness, and confusion, while the 5-mg group also had more dizziness and the 40-mg group had more nausea than the placebo group. Most of these symptoms were mild and improved over time. Although all subjects had a reduction in heavy drinking days, craving, gamma-glutamyl transferase, and carbohydrate-deficient transferrin concentrations over the course of the study, there was no difference between the active medication and placebo groups on these measures. The time to first heavy drinking day was also not significantly different between the	Anton RF, Pettinati H, Zweben A, et al. (2004) A multi-site dose ranging study of nalmefene in the treatment of alcohol dependence. J Clin Psychopharmacol 24: 421–428. **RCT**

placebo and the active treatment groups. This relatively small multisite trial showed that nalmefene was reasonably well tolerated in recently abstinent alcoholics. However, possibly because of variation among the sites or the comparatively small sample size, there was no evidence of superior efficacy outcomes with nalmefene treatment.	
METHODS: A double-blind, placebo-controlled trial was conducted to evaluate the safety and efficacy of 2 doses of oral nalmefene for alcohol dependence. The 105 outpatient volunteers were abstinent for a mean of 2 weeks prior to random assignment to the placebo or 20- or 80-mg/d dose nalmefene groups for 12 weeks. Cognitive behavioral therapy was provided weekly during treatment. Self-reported drinking or abstinence was confirmed by determinations of breath alcohol concentration and by collateral informant reports. RESULTS: Outcomes did not differ between the 20- and 80-mg dose nalmefene groups. Significantly fewer patients treated with nalmefene than patients given placebo relapsed to heavy drinking through 12 weeks of treatment (P<.02), with a significant treatment effect at the first weekly study visit (P<.02). The odds ratio of relapsing to heavy drinking was 2.4 times greater with placebo compared with nalmefene (95% confidence interval, 1.05-5.59). Patients treated with nalmefene also had fewer subsequent relapses (P<.03) than patients given placebo.CONCLUSIONS: Treatment with nalmefene was effective in preventing relapse to heavy drinking relative to placebo in alcohol-dependent outpatients and was accompanied by acceptable side effects.	Mason BJ, Salvato FR, Williams LD, et al. (1999) A double-blind, pla-cebo-controlled study of oral nalmefene for alcohol dependence. Arch Gen Psychiatry 56: 719–724. **RCT**
NICE 2011	
Oral disulfiram was not significantly different from placebo in preventing partic-ipants lapsing to alcohol consumption (RR 1.05; 95% CI, 0.96 to 1.15). There was also no difference in rates of discontinuation between the two groups. However, LAAKSONEN2008 showed that, in comparison with acamprosate, disulfiram was significantly more likely to increase the time until participants first drank any alcohol (SMD └0.84; 95% CI, └1.28 to └0.40) and drank heavily (SMD └1.17; 95% CI, └1.66 to └0.68), and also decreased the amount of alcohol consumed and the number of drinking days. In comparison with naltrexone, disulfiram was also signif-icantly more likely to increase the time to first heavy drinking day and the number of abstinent days. Participants in the naltrexone group were significantly more likely to return to any drinking (RR 0.18; 95% CI, 0.08 to 0.42) or relapse to heavy drink-ing (RR 0.28; 95% CI, 0.13 to 0.59) when compared with the oral disulfiram group, although this was based on two open-label studies (DESOUSA2004; LAAK-SONEN2008). The comparison of disulfiram and topiramate also showed a significant difference in the number of participants relapsing to heavy drinking (RR 0.23; 95% CI, 0.09 to 0.55), time to first drink and time to first relapse in favour of disulfiram, but this was based on just one open-label study (DESOUSA2008). It may be that the psycho-logical effects of knowing they were taking disulfiram may have contributed signifi-cantly to the results. The comparison of disulfiram with counselling versus counselling alone showed no significant differences between the groups on numbers of participants returning to drinking (RR 0.86; 95% CI, 0.55 to 1.34).	**NICE 2011 systematic review (disulfiram)**
NICE 2011	
Not available	Fuller, R. K., Branchey, L., Brightwell, D. R., et al.(1986) Disulfiram

	treatment of alcoholism: a veterans administration cooperative study. Journal of the American Medical Association, 256, 1449–1455.
Austrlia 2009	
Despite these limitations, a substantial body of methodologically sound naturalistic research suggests that AA is beneficial in promoting abstinence and facilitates the maintenance of long-term sobriety (see Moos and Timko, 2008, for a review). In a 16 year longitudinal study, Moos and Moos (2006a; see also Moos and Moos, 2005 and 2006b) examined how the duration of various treatment approaches in the first year of help-seeking behaviour influenced drinking outcomes. Whilst both professional treatment and AA affiliation for a period of 27 weeks or more in the first year of recovery were associated with better 16 year abstinence rates, the improvements gained by professional treatment were mediated by AA attendance; only participants who concurrently participated in AA showed better long-term outcomes. Further, continued involvement in AA (yrs 2-8) was associated with a higher likelihood of remission at each follow up point.	The Treatment of Alcohol Problems A Review of the Evidence Elizabeth Proude, Olga Lopatko, Nicholas Lintzeris and Paul Haber, 2009 Evidence for AA effectiveness
Australia 2009	
OBJECTIVES: To determine the effectiveness of TC versus other treatments for substance dependents, and to investigate whether effectiveness is modified by client or treatment characteristics. SELECTION CRITERIA: Randomised controlled trials comparing TC with other treatments, no treatment or another TC. MAIN RESULTS: Seven studies were included. Differences between studies precluded any pooling of data, results are summarised for each trial individually: TC versus community residence: no significant differences for treatment completion; Residential versus day TC: attrition (first two weeks), and abstinence rates at six months significantly lower in the residential treatment group; Standard TC versus enhanced abbreviated TC: number of employed higher in standard TC RR 0.78 (95% CI 0.63, 0.96). Three months versus six months programme within modified TC, and six months versus 12 months programme within standard TC: completion rate higher in the three months programme and retention rate (40 days) significantly greater with the 12 months than 6 months programme. Two trials evaluated TCs within a prison setting: one reported significantly fewer re incarcerated 12 months after release from prison in the TC group compared with no treatment, RR 0.68 (95% CI 057, 0.81). In the other, people treated in prison with TC compared with Mental Health Treatment Programmes showed significantly fewer re incarcerations RR 0.28 (95% CI 0.13, 0.63), criminal activity 0.69 (95% CI 0.52, 0.93) and alcohol and drug offences 0.62 (95% CI 0.43, 0.90) 12 months after release from prison. AUTHORS' CONCLUSIONS: There is little evidence that TCs offer significant benefits in comparison with other residential treatment, or that one type of TC is better than another. Prison TC may be better than prison on it's own or Mental Health Treatment Programmes to prevent re-offending post-release for in-mates. However, methodological limitations of the studies may have introduced bias and firm conclusions cannot be drawn due to limitations of the existing evidence.	Smith, LA, S Gates and D Foxcroft 2006, Therapeutic communities for substance related disorder. **Cochrane Database Syst Review**
Australia 2009	
OBJECTIVE: Treatment approaches used in community residential facilities for patients with substance use disorders were identified, and patients' participation in treatment and case-mix-adjusted	Moos, RH, Moos BS, Andrassy JM 1999, Outcomes of four

one-year outcomes for substance use, symptoms, and functioning in facilities with different treatment approaches were examined. METHODS: A total of 2,376 patients with substance use disorders treated in a representative sample of 88 community residential facilities were assessed at entry to and discharge from the facility and at one-year follow-up. The community residential facilities were classified into four types based on the major emphasis of the treatment program: therapeutic community, psychosocial rehabilitation, 12-step, and undifferentiated.RESULTS: Patients in programs that used the therapeutic community, psychosocial rehabilitation, and 12-step approaches had comparable one-year outcomes in symptoms and functioning that were better than those of patients in undifferentiated programs. A more directed treatment orientation, a longer episode of care, and completion of care were independently related to better one-year outcomes. These findings held for patients with only substance use disorders and for patients with both substance use and psychiatric disorders.CONCLUSIONS: Community residential programs that have a more directed treatment orientation and that motivate patients to complete treatment have better substance use outcomes. As an increasingly important locus of specialized care, community residential facilities need to develop and maintain more differentiated and distinctive treatment orientations	treatment approaches in community residential programs for patients with substance use disorders. Psychiatr Serv 50(12): 1577-83.
APA 2006	
The community reinforcement approach (CRA) has been applied in the treatment of disorders resulting from alcohol, cocaine and opioid use. The objectives were to review the effectiveness of (1) CRA compared with usual care, and (2) CRA versus CRA plus contingency management. Studies were selected through a literature search of RCTs focusing on substance abuse. The search yielded 11 studies of mainly high methodological quality. The results of CRA, when compared to usual care: there is strong evidence that CRA is more effective with regard to number of drinking days, and conflicting evidence with regard to continuous abstinence in the alcohol treatment. There is moderate evidence that CRA with disulfiram is more effective in terms of number of drinking days, and limited evidence that there is no difference in effect in terms of continuous abstinence. Furthermore, there is strong evidence that CRA with "incentives" is more effective with regard to cocaine abstinence. There is limited evidence that CRA with "incentives" is more effective in an opioid detoxification program. There is limited evidence that CRA is more effective in a methadone maintenance program. Finally, there is strong evidence that CRA with abstinence-contingent "incentives" is more effective than CRA (non-contingent incentives) treatment aimed at cocaine abstinence.	Roozen HG, Boulogne JJ, van Tulder MW, van den Brink W, De Jong CA, Kerkhof AJ: A systematic review of the effectiveness of the community reinforcement approach in alcohol, cocaine and opioid addiction. Drug Alcohol Depend 2004; 74:1–13
NICE 2011	
This study investigated whether selected patients have better outcomes with inpatient than outpatient treatment. There were 93 inpatients and 80 outpatients with alcohol dependence who were evaluated at treatment entry to a private healthcare setting. Patients with multiple drinking-related consequences were less likely to return to significant drinking in the first 3 months after treatment ended if they had attended inpatient compared to outpatient treatment. Thus, inpatient appeared to have some advantage over outpatient treatment in the early recovery period for patients with multiple drinking-related consequences. The gap between inpatient and outpatient costs was also reduced when computed as a cost-effectiveness ratio, although treatment costs continued to remain proportionally higher with inpatient than outpatient treatment.	Pettinati, H. M., Meyers, K., Evans, B. D. et al.(1999) Inpatient alcohol treatment ina private healthcare setting: which patients benefit and at what cost? TheAmerican Journal on Addictions, 8, 220–233. **Cost-effectivness review**

Not found	Ledgerwood D, McCaul ME, Petry NM. 2005. Psychotherapyand pharmacotherapy in treatment of substance use disorders. In: Kranzler HR, Ciraulo DA, editors. Clinical manual of addiction psychopharmacology. Washington, DC: American Psychiatric Press. pp 339 363.
http://pubs.niaaa.nih.gov/publications/MedicalManual/MMManual.pdf	National Institute on Alcohol Abuse and Alcoholism. (2004). Medical manage-ment treatment manual: A clinical research guide for medically trained clinicians providing pharmacotherapy as part of the treatment for alcohol dependence. COMBINE Monograph Series, Vol. 2. Bethesda, MD: Author.
NICE 2011	
Not found	Morgenstern, J., Bux, D. A., Labouvie, E., et al.(2003) Examining mechanisms of action in 12-step community outpatient treatment. Drug and Alcohol Dependence, 72, 237–247.
	Shand, F., et al., the Treatment of Alcohol Problems: a Review of the Evidence. 2003, Canberra: Australian Commonwealth Department of Health and Ageing
Australia 2009	
Twelve Steps (TS) has demonstrated effectiveness; induction into Alcoholics Anonymous (AA) is a primary objective of TS and is a pivotal mechanism explaining its effectiveness. However, evidence suggests that, after treatment, dropout from AA is high. This study investigated whether alcohol problem severity predicted both AA affiliation and disaffiliation among clients receiving TS. This study of a Project MATCH sample included 453 alcohol-dependent clients randomly assigned to TS who reported AA attendance during treatment. Greater alcohol problem severity predicted AA attendance; opposite to prediction, less alcohol-impaired clients were more than twice as likely to discontinue AA attendance after treatment. When sustained AA attendance is desired, the evaluation of client pretreatment alcohol involvement may be useful for identifying potential AA dropout after TS treatment. Findings also indicate that, among treatment-seeking problem drinkers, AA dropout and disaffiliation are distinct, albeit correlated, constructs that require future investigation.	Tonigan, JS, MP Bogenschutz and WR Miller 2006, Is alcoholism typology a predictor of both Alcoholics Anonymous affiliation and disaffiliation after treatment? J Subst Abuse Treat 304: 323-330.

NICE 2011	
The aim of this study was to determine whether a socially focused treatment can effect change in the patient's social network from one that reinforces drinking to one that reinforces sobriety. Alcohol dependent men and women (N = 210) recruited from the community were randomly assigned to 1 of 3 outpatient treatment conditions: network support (NS), network support + contingency management (NS + CM), or case management (CaseM; a control condition). Analysis of drinking rates for 186 participants at 15 months indicated a significant interaction effect of Treatment x Time, with both NS conditions yielding better outcomes than the CaseM condition. Analyses of social network variables at posttreatment indicated that the NS conditions did not reduce social support for drinking relative to the CaseM condition but did increase behavioral and attitudinal support for abstinence as well as Alcoholics Anonymous (AA) involvement. Both the NS variables and AA involvement variables were significantly correlated with drinking outcomes. These findings indicate that drinkers' social networks can be changed by a treatment that is specifically designed to do so, and that these changes contribute to improved drinking outcomes.	Litt, M. D., Kadden, R. M., Kabela-Cormier, E., et al. (2007) Changing network support drinking: initial findings from the network support projects. Journal of Consulting and Clinical Psychology, 77, 229–242. **RCT**
	Zarkin, G. A., Bray, J. W., Aldridge, A., et al.(2008) Cost and cost-effectiveness of the COMBINE study in alcohol-dependent patients. Archives of General Psychiatry, 65, 1214–1221 **Cost-effectivness review**

Medinfokeskuse lisaotsingud

Kokkuvõtte (abstract või kokkuvõtlikum info)	**Viide kirjandusallikale**
BACKGROUND: Alcohol dependence belongs to the globally leading health risk factors. Therapeutic success of psychosocial programs for relapse prevention is moderate and could be increased by an adjuvant treatment with the opioid antagonists naltrexone and nalmefene.OBJECTIVES: To determine the effectiveness and tolerability of opioid antagonists in the treatment of alcohol dependence.SEARCH STRATEGY: We searched the Cochrane Drugs and Alcohol Group (CDAG) Specialized Register, PubMed, EMBASE and CINAHL in January 2010 and inquired manufacturers and researchers for unpublished trials.SELECTION CRITERIA: All double-blind randomised controlled trials (RCTs) which compare the effects of naltrexone or nalmefene with placebo or active control on drinking-related outcomes.DATA COLLECTION AND ANALYSIS: Two authors independently extracted outcome data. Trial quality was assessed by one author and cross-checked by a second author.MAIN RESULTS: Based on a total of 50 RCTs with 7793 patients, naltrexone reduced the risk of heavy drinking to 83% of the risk in the placebo group RR 0.83 (95% CI 0.76 to 0.90) and decreased	Rösner S[1], Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Coch-rane Database Syst Rev 2010 **Systematic Review**

drinking days by about 4%, MD -3.89 (95% CI -5.75 to -2.04). Significant effects were also demonstrated for the secondary outcomes of the review including heavy drinking days, MD - 3.25 (95% CI -5.51 to -0.99), consumed amount of alcohol, MD - 10.83 (95% CI -19.69 to -1.97) and gamma-glutamyltransferase, MD -10.37 (95% CI -18.99 to -1.75), while effects on return to any drinking, RR 0.96 (95 CI 0.92 to 1.00) missed statistical significance. Side effects of naltrexone were mainly gastrointestinal problems (e.g. nausea: RD 0.10; 95% CI 0.07 to 0.13) and sedative effects (e.g. daytime sleepiness: RD 0.09; 95% CI 0.05 to 0.14). Based on a limited study sample, effects of injectable naltrexone and nalmefene missed statistical significance. Effects of industry-sponsored studies, RR 0.90 (95% CI 0.78 to 1.05) did not significantly differ from those of non-profit funded trials, RR 0.84 (95% CI 0.77 to 0.91) and the linear regression test did not indicate publication bias (P = 0.765).AUTHORS' CONCLUSIONS: Naltrexone appears to be an effective and safe strategy in alcoholism treatment. Even though the sizes of treatment effects might appear moderate in their magnitudes, these should be valued against the background of the relapsing nature of alcoholism and the limited therapeutic options currently available for its treatment.	
AIMS: Although debates over the efficacy of oral naltrexone and acamprosate in treating alcohol use disorders tend to focus on their global efficacy relative to placebo or their efficacy relative to each other, the underlying reality may be more nuanced. This meta-analysis examined when naltrexone and acamprosate are most helpful by testing: (i) the relative efficacy of each medication given its presumed mechanism of action (reducing heavy drinking versus fostering abstinence) and (ii) whether different ways of implementing each medication (required abstinence before treatment, detoxification before treatment, goal of treatment, length of treatment, dosage) moderate its effects.METHODS: A systematic literature search identified 64 randomized, placebo-controlled, English-language clinical trials completed between 1970 and 2009 focused on acamprosate or naltrexone.RESULTS: Acamprosate had a significantly larger effect size than naltrexone on the maintenance of abstinence, and naltrexone had a larger effect size than acamprosate on the reduction of heavy drinking and craving. For naltrexone, requiring abstinence before the trial was associated with larger effect sizes for abstinence maintenance and reduced heavy drinking compared with placebo. For acamprosate, detoxification before medication administration was associated with better abstinence outcomes compared with placebo.CONCLUSIONS: In treatment for alcohol use disorders, acamprosate has been found to be slightly more efficacious in promoting abstinence and naltrexone slightly more efficacious in reducing heavy drinking and craving. Detoxification before treatment or a longer period of required abstinence before treatment is associated with larger medication effects for acamprosate and naltrexone respectively.	Addiction. 2013 Feb;108(2):275-93. doi: 10.1111/j.1360-0443.2012.04054.x. Epub 2012 Oct 17. Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? Maisel NC1, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. **Meta-analysis**

Lisa 1

K7-8 rehabilitatsiooni mõiste täpsustamine

Rehabilitatisooni mõiste täpsustamiseks kasutatud järgmisi allikaid: WHO lexicon 1994, NICE 2011, Austraalia 2009, NSW 2008 ravijuhendid ja nendes ravijuhendites viidatud allikatele: Models of care for Alcohol Misusers (MoCAM 2006) ja NSW Health, drug and alcohol treatment Guidelines for Residential Settings . 2007, NSW Department of Health (MHDAO 070010) Sydney.

WHO lexicon mõistab rehabilitatsiooni all protsessi, mille käigus sõltuvushäirega patsient saavutab optimaalse tervisliku seisundi, psühholoogilise funktsioneerimise ja sotsiaalse heaolu. Rehabilitatsioon järgneb aktiivravile (võõrutusravi,somaatiline, psühhiaatriline ravi). Rehabilitatsioon hõlmab erinevaid lähenemisi sisaldades grupiteraapiaid, käitumisteraapiaid relapsi ennetamiseks, tugigruppidesse kuulumist, ravikogukondades elamist, erialakutse õppimist, töötamise kogemust. Rehabilitatsiooni lõpptulemusena peaks inimene olema suuteline naasma taas ühiskonda.

Kõige põhjalikuma ülevaate rehabilitatisooni mõistest ja selle asetusest üldises alkoholisõltuvuse käsitluses annab MoCAM 2006. Ravi planeerimise seisukohalt jagab MoCAM alkoholiprobleemidega patsiendid 4 kategooriasse: ohustava (hazardous) tarvitamisega, kuritarvitamisega (harmful users), mõõduka alkoholisõltuvusega ja raske alkoholisõtluvusega patsiendid.
Alkoholiprobleemidega patsientidele mõeldud sekkumised on samuti jaotatud 4 kategooriasse vastavalt sellele, millised on patsiendi ravivajadused: esimese, teise, kolmanda ja neljanda rea sekkumised. Vt tabel allpool!
Esimese ja teise rea sekkumised on mõeldud ohustava ja kuritarvitava alkoholi tarbimisega patsientidele. Sekkumisteks on skriinimine ja lõhinõustamine ning triaaz, välja selgitamaks alkoholisõtluvaid patsiente, kes peaks minema põhjalikumale hindamisele. Sekkumiste ostuajateks on esmatasandi arstiabi, sotsiaaltöötajad, etc.
Teise ja kolmanda rea sekkumised on mõeldud mõõduka või raske alkoholisõltuvusega patsientidele. Nende sekkumiste alla käib ka rehabilitatsioon, mis võib olla ambulatoorne (community rehabilitation) või statsionaarne (residential rehabilitation, residential units, residential programmes, therapeutic communities). Rehabilitatisooni programmid on tavaliselt pikaajalised (1-12 kuud), kus inimesed elavad ja töötavad koos teiste sõltlastega ning professionaalse personaliga. Programmi eesmärk on aidata leida oskused ja käitumine alkoholivabaks elustiiliks. Arendatakse tööoskusi, antakse haridust, õpetatakse eluks vajalikke oskusi (söögi tegemine, finantsoskused), nõustatakse, tehakse grupiteraapiaid, ennetatakse relapse. (Austraalia 2009). Mõned ravijuhendid (NSW 2007) toovad välja erinevused terapeutiliste kogukondade (therapeutic communities) vahel ja statsionaarse ravirehabilitatsiooni programmide (residential treatment programs) vahel. Terapeutilised kogukonnad kasutavad holistilist ravilähenemist otsides sõltuvuse tekkimise taga

psühhosotsiaalseid või muid põhjusi. Kogukond ise on nii ravimeetod kui ravikontekst. Ravirehabilitatsiooniprogrammid pakuvad regulaarset ravi nagu nõustamine, oskuste treenimine, relapsi ennetamine, et tegeleda sõltuvuse psühhosotsiaalsete probleemidega. Esineb lühiajalisi ja pikaajalisi rehabilitatsiooniproramme:

- lühiajalised programmid tavaliselt koos stats. võõrutusraviga.
- Pikaajalised programmid 12-52 nädalat.

Algtekstid *(ingl. keeles):*
MoCAM identifies four main categories of alcohol misusers who may benefit from some kind of intervention or treatment: hazardous drinkers; harmful drinkers; moderately dependent drinkers and severely dependent drinkers. The categorisation should be seen as a conceptual framework to assist commissioners in planning for a full range of services for a local area. Individual drinkers may move in and out of different categories over the course of a lifetime.

Hazardous drinkers
The World Health Organization (WHO) defines hazardous use of a psychoactive substance, such as alcohol, as 'a pattern of substance use that increases the risk of harmful consequences for the user… In contrast to harmful use, hazardous use refers to patterns of use that are of public health significance despite the absence of any current disorder in the individual user. Hazardous drinkers are drinking at levels over the sensible drinking limits, either in terms of regular excessive consumption or less frequent sessions of heavy drinking. However, they have so far avoided significant alcohol-related problems. Despite this, hazardous drinkers, if identified, may benefit from brief advice about their alcohol use.

Harmful drinkers
The WHO Inter national Classification of Diseases (ICD-10) defines har mful use of a psychoactive substance, such as alcohol, as 'a pattern of use which is already causing damage to health. The damage may be physical or mental.' This definition does not include those with alcohol dependence. Harmful drinkers are usually drinking at levels above those recommended for sensible drinking, typically at higher levels than most hazardous drinkers. Unlike hazardous drinkers, har mful drinkers show clear evidence of some alcohol-related harm. Many harmful drinkers may not have understood the link between their drinking and the range of problems they may be experiencing. Identification of and intervention for hazardous and har mful drinkers Simple and reliable instruments, such as the alcohol use disorders identification test (AUDIT) and derivatives such as the fast alcohol screening test (F AST) tool (see Review of the effectiveness of alcohol treatment), can be used to identify hazardous and harmful drinkers and provide an indication of the likely extent and severity of their alcohol-related problems. As these drinkers do not have significant evidence of alcohol dependence, advice and brief interventions are often suitable to meet the needs of both these groups.

The main groups of alcohol users who clearly may benefit from specialist alcohol treatment are those who are moderately and severely dependent. This categorisation into those with moderate and those with severe dependence is

supported in the NTA Review of the effectiveness of treatment for alcohol problems as a pragmatic classification. The review suggests that, for treatment planning purposes, the most useful categorisation is into 'moderate dependence' and into 'severe dependence/dependence with complex needs'. This is because the latter 'severe and complex' group is likely to require a higher level of intervention at the outset than those with moderate dependence. The actual level of intervention to be provided initially, or subsequently, in individual cases can only be determined following comprehensive assessment, but broadly this is suggested as a valuable pragmatic categorisation.

Moderately dependent drinkers
Moderately dependent drinkers may recognise that they have a problem with drinking, even if this recognition has only come about reluctantly thr ough pressure, for example from family members or employers.
The level of dependence of drinkers in this categor y is not sever e. For example, they may not have reached the stage of 'relief drinking' – which is drinking to relieve or avoid physical discomfort from withdrawal symptoms. This is a very broad category and includes a wide range of severities and types of problem. Nevertheless, in older terminology, drinkers in this category would probably not have been described as 'chronic alcoholics'. Moderately dependent drinkers' treatment can often be managed effectively in community settings, including medically assisted alcohol withdrawal in the community. The choice of setting in each individual cir cumstance will depend on the range of accompanying physical, psychological or social problems, including risks posed to the drinker and risks to others from the drinker's behaviour. Some in this category will beidentified as needing interventions mor e typically pr ovided to sever e or complex dependent drinkers.

Severely dependent drinkers
People in this category may have serious and long-standing problems. This category includes individuals described in older terminology as 'chronic alcoholics'. Typically, they have experienced significant alcohol withdrawal and may have formed the habit of drinking to stop withdrawal symptoms. They may have pr ogressed to habitual significant daily alcohol use or heavy use over pr olonged periods or bouts of drinking. Given adequate risk assessment and a comprehensive and intensive care plan, medically assisted alcohol withdrawal can safely be provided to many severely dependent drinkers in the home or in community settings. However, more drinkers in this category may be in need of inpatient assisted alcohol withdrawal and residential rehabilitation. Some may have special needs, such as treatment for co-existing psychiatric problems, polydrug dependence or complicated assisted alcohol withdrawal; others may need rehabilitation and strategies to address the level of their dependence, or to address other issues, such as homelessness or social dislocation. Some may have had multiple previous episodes of treatment. Some will respond to community interventions more typically successful when provided to moderately dependent drinkers.

4 Tiers

Within MoCAM, Tier 1 interventions include identification of alcohol misuse; provision of information on sensible drinking; simple brief interventions to reduce alcohol

related harm; and referral of those with alcohol dependence or harm for more intensive interventions. These can be delivered by a wide range of staff in a various settings, including accident and emergency departments, primary care, acute hospitals, mental health services, criminal justice services and social services.
Tier 2 interventions
include open-access facilities and outreach that provide:
alcohol-specific advice, information and support; extended brief interventions; and triage assessment and referral of those with more serious alcohol-related problems for 'care planned' treatment. Care-planned treatment refers to the process of planning and reviewing care within the context of structured alcohol treatment, and this is located within Tier 3. If staff have the appropriate competencies to deliver Tier 2 interventions, these can be delivered by the same range of agencies as Tier 1 interventions.

Tier 3 interventions
include the provision of community-based specialist alcohol-misuse assessment, and alcohol treatment that is coordinated and planned (see
below). These include comprehensive assessment, structured psychological interventions or pharmacological interventions which aim to prevent relapse, community-based assisted alcohol withdrawal, day programmes and specialist alcohol liaison provided to for example, acute hospitals by specialist staff. Tier 3 interventions are usually provided by staff working in specialist alcohol treatment agencies both NHS and non-statutory (although the latter are often funded by the NHS to provide these interventions). Important exceptions to this are GPs who may provide more specialised interventions within a Direct Enhanced Services contract (NHS Employers, 2008). Interventions provided by GPs often involve assisted alcohol withdrawal in the community or prescribing medication for relapse prevention. As with interventions in other tiers, staff need to have the relevant competence to be able to provide them safely and effectively.

Tier 4 interventions
include the provision of residential, specialised alcohol treat-ments that are planned and coordinated, to ensure continuity of care and aftercare.
These interventions include comprehensive assessment, inpatient assisted alcohol withdrawal and structured psychosocial interventions provided in a residential setting, including residential rehabilitation. 'Wet' hostels also fit within this tier, although they operate more on a 'harm reduction' than an abstinence-oriented model of care. Tier 4 interventions are usually provided by specialist alcohol inpatient or residential rehabilitation units. However, assisted alcohol withdrawal is often provided in other residential settings, including acute hospitals, mental health inpatient services, police custody and prisons, delivered by medical and other staff whose primary role is not specialist alcohol treatment.

Australia 2009: Residential rehabilitation programs (sometimes called therapeutic communities) are usually long-term programs where people live and work in a community of other substance users, ex-users and professional staff. Programs can last anywhere between 1 and 24 months (or more). The aim of residential rehabilitation programs is to help people develop the skills and attitudes to make long-term changes towards an alcohol- and drug-free lifestyle.Programs

usually include activities such as employment, education and skills training, life skills training (such as budgeting and cooking), counselling, group work, relapse prevention, and a 're-entry' phase where people are helped return to their community.

NSW Health, drug and alcohol treatment Guidelines for Residential Settings . 2007, NSW Department of Health (MHDAO 070010),Sydney:

The main distinction that has emerged among residential treatment programs is between therapeutic communities and other residential programs.
n Therapeutic communities emphasise a holistic approach to treatment and address the psychosocial and other issues behind substance abuse. The "community" is thought of as both the context and method of the treatment model, where both staff and other residents assist the resident to deal with his or her drug dependence.
n Other residential programs deliver regular treatment to residents, such as counselling, skills training and relapse prevention, to address the psychosocial causes of drug dependence. Types of residential programs include:
– Short term residential treatment, often provided in conjunction with a medically supervised withdrawal program
– Longer term residential treatment over 12–52 weeks
– Low intensity residential treatment and extended care, in which clients live semi-independently with support

Rida	Patsiendi tüüp	sekkumised	Teenuse osutajad	Eesti tingimustes (rakenduskavasse?)
Esimese rea sekkumine	*Ohustava alkoholi tarbimisega *alkoholi kuritarvitajad	*Skriinimine *Tagasiside ja *nõustamine alkoholi tarvitamise osas *lühisekkumine *alkoholisõltuvusega patsientide edasi saatmine intensiivsemateks sekkumisteks	*EMO *perearstid *(acute hospitals), *psühhiaatriakliinikud, *kinnipidamisasutused *sotsiaaltöötajad (social services)	Perearstid?, EMO?, sotsiaaltöötajad?, psühhiaatriakliinikud? Kinnipidamisasutused?
Teise rea sekkumine	*Ohustava alkoholi tarbimisega *alkoholi kuritarvitajad *alkoholisõltuvuse kahtlusega	*Alkoholialane informatsioon, nõustamine ja tugi *pikmad lühinõustamised * triaaz alkoholisõltuvate patsientide osas ja edasi saatmine põhjalikumale hindamisele/ raviplaani koostamiseks	*open-access facilities. * samad teenused osutajad, mis I rea sekkumiste korral kui personalil on vastav ettevalmistus.	Alko nõustamiskabinetid? Perearstid?
Kolmanda rea sekkumine	*mõõdukas alkoholisõltuvus	*ambulatoorne põhjalik hindamine spetsialisti (psühhiaatri) poolt. *alkoholisõltuvuse koordineeritud ravi, struktureeritud psühholoogilised või farmakol. Sekkumised, mille eesmärk on tagasilanguse ennetamine *ambul. võõrutusravi *päevravi programmid *alkoravi osas teiste haiglate/osakondade nõustamine.	*psühhiaatriakliinikud (ambul. teenus) avalik kui ka (non-statutory sector)	Ambul. psühhiaatri teenus avalikõiguslikus või erasektoris.
Neljanda rea sekkumine	*raske alkoholisõltuvus	*statsionaarse planeeritud ja kordineeritud ravi, et tagada ravijärjepidevus ka järelravi (aftercare) * põhjalik hindamine *statsionaarne võõrutusravi Ja struktureeritud psühhosotsiaalsed sekkumised, mida pakutakse statsionaaris või rehabilitatsiooniprogrammides.	* provided by specialist alcohol inpatient or residential rehabilitation units.	Eestis puudub...