Kliiniline küsimus nr 20

Kas raviefekti puudumisel tuleb kõigil alkoholi kuritarvitamise ja alkoholisõltuvusega patsientidel ravi muutmiseks hinnata raviplaani 1 vs 3 vs 6 kuu pärast?

Kriitilised tulemusnäitajad: *Tulemusnäitajad: abstinents, tagasilangus, alkoholi tarvitamise vähenemine, patsiendi rahulolu, patsiendi elukvaliteet, ravisoostumus, ravi katkestamine mistahes põhjusel, ravi katkestamine ravimite kõrvaltoimete tõttu, juhuslik alkoholi tarvitamine*

Kliiniline küsimus nr 21

Kas kõigil alkoholi kuritarvitavate ja alkoholisõltuvusega patsientidel lõpetada ravi vs mitte lõpetada järgmistel juhtudel:
- soovitud ravitulemus on kestnud 3 kuud vs 6 kuud vs 12 kuud
- patsiendi vähene ravikoostöö?

Kriitilised tulemusnäitajad: *Tulemusnäitajad: abstinents, tagasilangus, alkoholi tarvitamise vähenemine, patsiendi rahulolu, patsiendi elukvaliteet, ravisoostumus, ravi katkestamine mistahes põhjusel, ravi katkestamine ravimite kõrvaltoimete tõttu, juhuslik alkoholi tarvitamine*

SMD - The standardized mean difference within groups

RR - relative risk (RR) A relative risk of 1 means there is no difference in risk between the two groups. An RR of < 1 means the event is less likely to occur in the experimental group than in the control group. An RR of > 1 means the event is more likely to occur in the experimental group than in the control group.

Effect Size –Cohen's *d* This means that if we see a *d* of 1, we know that the two groups' means differ by one standard deviation; a *d* of 0.5 tells us that the two groups' means differ by half a standard deviation; and so on. Cohen suggested that *d*=0.2 be considered a 'small' effect size, 0.5 represents a 'medium' effect size and 0.8 a 'large' effect size. This means that if two groups' means don't differ by 0.2 standard deviations or more, the difference is trivial, even if it is statistically signficant.

Risk difference –absolute risk reduction, risk difference or excess risk is the change in risk of a given activity or treatment in relation to a control activity or treatment.[1] It is the inverse of the number needed to treat.[2] RD = RR intervention group-RR placebo

Mean difference - The mean difference is the average difference between the intervention group and the control group across studies.

PDA - the percentage of days during the follow up period that patients remained abstinent from alkohol, percent days abstinence

CAPD - Cumulative Abstinence Duration Proportion

RB - relative benefit

Ravijuhendid

Kokkuvõte tõendusmaterjali kvaliteedist vt. tabel 1.

Kokkuvõte ravijuhendites leiduvatest soovitustest

Alkoholsõltlaste patsientide medikamentoosset ravi soovitatakse lõpetada juhul, kui patsient jätkab rohket alkoholi tarbimist pärast 4-6 nädalast ravi ning ei soostu psühhosotsiaalsete sekkumistega. Raviskeemi soovitatakse täielikult üle vaadata juhul, kui patsient saab medikamentoosset ravi, psühhosotisaalset ravi ning vaatamata sellele jätkab rohket alkoholi tarbimist. Komorbiidsete psühhiaatriliste haiguste puhul soovitatakse esmalt loobuda alkoholi tarbimisest ning hinnata patsiendi seisundit 3-4 nädala pärast uuesti. Kaasuva psühhiaatrilise haiguse sümptimite püsimisel patsient tasub suunata eriarsti vastuvõtule. Tõrguva suhtumisega patsiendid, kes ei soostu raviprotsessi kaasamisega, võiksid saada kasu biblioteraapiast, sealhulgas alkopäeviku pidamisest ning motiveerivast intervjueerimisest. Kõige suuremad muutused alkoholi tarbimises toimuvad esimese 3 ravikuu jooksul ning enamikes uuringutes raviefektiivsust on hinnatud 3 kuud kestnud ravi järel. Kui patsient soostub raviga, siis ravikuur (medikamentoosne ravi ja psühhosotsiaalsed sekkumised) peaks kestma vähemalt 3 kuud, alles siis on võimalik hinnata kas raviga on saavutatud püstitatud eesmärke või mitte. Iga konkreetse patsiendi puhul on vaja hinnata tagasilanguse riski (toetava sotsiaalse võrgustiku olemasolu, stressirohked elusituatsioonid, patsiendi motiveeritus). Kuna tagasilanguste risk on sage, siis medikamentoosne ravi koos psühhosotsiaalsete sekkumistega peaks kestma naltreksooni puhul vähemalt 6 kuud ning akamposaadi puhul kuni 6-12 kuud, ravikuuri võib pikendada patsiendi soovil seni kuni kõik püstitatud ravieesmärgid on saavutatud. Disulfiraami puhul ravisoostumust tuleb hinnata esimesel 2 kuul iga 2 nädala tagant ning seejärel kord kuus. Patsiendi terviseseisundit (kas tekkisid vastunäidustused ?) tuleb uuesti hinnata iga poole aasta tagant.

Otsust ravi lõpetamise või regulaarse jälgimise katkestamise suhtes peaks langetama suure ettevaatusega ning koostöös patsiendiga, lähtudes tema ootustest ja eesmärkidest ning jättes talle võimaluse tagasipöördumiseks. Suure relapsi riskiga patsientide puhul võib planeerida regulaarseid kohtumisi sõltumata sellest kas patsient saab ravi või mitte. Patsiendile peaks pakkuma edasisuunamist juhul, kui kõik ravieesmärgid ei ole saavutatud. Madala intensiivsusega monitoring 1-3 aasta jooksul pärast aktiivse ravi lõppu (nt. telefonikõne või lühike visiit) võib vähendada tagasilanguste arvu.

SIGN 2003

Akamposaati soovitatakse kasutada 6-12 kuu jooksul juhul, **kui on märgata selle positiivset mõju.** Kuid kuna on teada, et akamposaat ei ole efektiivne kõikide patsientide puhul, siis **patsiente soovitatakse hinnata alkoholi tarbimise vähenemise suhtes regulaarsete intervallidega ning lõpetada ravi akamposaadiga juhul, kui alkoholi tarbimine ei ole vähenenud olulisel määral.** Disulfiraami soovitatakse kasutada vähemalt 6 kuud ja ainult **regulaarse kontakti puhul raviarstiga** (supervised use), selleks et tagada ravimi võtmist ka ambivalentsuse perioodidel (Ludbrook A et al. 2001; . Berglund M at al. 2001; . Slattery J at al. 2003; Garbutt JC at al. 1999; . Kranzler HR at al. 2001)

Motiveerivat teraapiat soovitatakse kasutada eriti nende patsientide puhul, kes esialgu suhtuvad tõrksalt ravisse. Kaasuva psühhiaatrilise diagnoosiga patsiente soovitatakse suunata eriarsi vastuvõtule (Project MATCH posttreatment drinking outcomes, 1997 a; Project MATCH secondary a priori hypotheses, 1997 a, Longabaugh R, 1998 a) Madala intensiivsusega monitooring (telefonikõne patsiendile või lühike kokkusaamine) 1-3 aasta jooksul pärast aktiivse ravi lõppu näitas efektiivsust relapside arvu langetamises. (Hilton ME, 2001; Stout RL , 1999 a)

NSW 2009

Arst peaks langetama kliinilise otsuse raviplaani suhtes , lähtudes järgnevatest aspektidest: erakorralise sekkumise vajadus, probleemi tõsidus, patsiendi valmidus muutumiseks ning raviks. Üldiselt soovitatakse jätkata patsiendi jälgimist teatud aja jooksul ka pärast ravi lõpetamist, sest tagasilangused on sagedased.

Uuringutes oma efektiivsust näitasid struktureeritud nn "continued care" programmid , mille puhul patsientidele olid tagatud regulaarsed kohtumised ravimeeskonnaga (keskmiselt kord kuus) sõltumata sellest, kas nad saavad parasjagu ravi või tarbivad alkoholi. Selles programmis osalemine langetas oluliselt nii relapsi riski, kui ka kuriteo panemise ning töötuks jäämise riski võrreldes programmiga, milles patsientidele oli tagatud kohtumine ravimeeskonnaga kutse alusel (Ahles, T., et al 1983 a; Shand, F., et al. 2003 a). Regulaarsed kohtumised võimaldavad korduvalt hinnata patsiendi seisundit ning vajadusel kaasata ta uuesti raviprogrammi (step up or

step-down treatment). Uuringutes need patsiendid, kes said järelravi pärast statsionaarset ravi, näitasid paremaid ravitulemusi võrreldes nendega, kes ei osalenud järelravi programmides. (*Practice Guideline for the Treatment of Patients with Substance Use Disorders: Second edition*. American Journal of Psychiatry 2006). Otsust ravi lõpetamise või regulaarse jälgimise katkestamise suhtes peaks langetama suure ettevaatusega ning koostöös patsiendiga, lähtudes tema ootustest ja eesmärkidest ning jättes talle võimaluse tagasipöördumiseks. Patsiendile peaks pakkuma edasisuunamist juhul, kui kõik tema ravieesmärgid ei ole saavutatud (Marsh, A., et al., 2000 a) Patsientide ravisse kaasamise kergendamiseks ning ravisoostumuse parandamiseks soovitatakse kasutada motiveeriva intervjueerimise tehnikaid (Handmaker, N., et al., 2002 a) Tõrguva suhtumisega patsiendid, kes ei soostu raviprotsessi kaasamisega, võiksid saada kasu biblioteraapiast, sealhulgas alkopäeviku pidamisest (Duckert, F 1988 a, Heather, N. , 2002 a).

BAP 2012:

Ühes uuringus (Longabaugh et al., 2009) leiti, et nendel alkoholsõltlastel patsientidel kes said ravi naltreksooniga 24 nädalat olid paremad ravitulemused võrreldes nendega, kes said ravi ainult 12 nädalat. **Optimaalset ravikuuri pikkust ei ole teada**. Mõistlik on teha 6 kuulist ravikuuri naltreksooniga ja **lõpetada medikamentoosse ravi juhul, kui patsient jätkab rohket alkoholi tarbimist 4-6 nädalat pärast ravi ordineerimist**. Anton et al., 2001 ja O'Malley et al., 1996 uuringud näitasid, et naltreksooni positiivne mõju (alkoholi tarbimise vähenemine) kestab **täpselt nii kaua kui kaua patsient saab ravi naltreksooniga** ja kaob juba pärast 1 kuu kestvat jälgimisperioodi. Donovan et al 2008 uuring näitas, et naltreksooni positiivne mõju püsib ka aasta pärast medikamentoosse ravi lõppu, siiski see tulemus ei olnud statistiliselt oluline.

NICE 2011

Suurimad muutused alkoholi tarbimise mustris ning kogustes toimuvad tavaliselt esimese 3 ravikuu jooksul. Esimesi ravitulemusi, nagu nt tarbitava alkoholi koguse vähenemine ning alkoholivabade päevade arvu tõus, on näha juba esimesel kolmel ravikuul (Mann at al. 2004), kuid sotsiaalse funsktsioneerimise paranemine ning üldtervisega seotud ravitulemused vajavad pikemat jälgimisperioodi.

Sõltuvuse puhul antakse soovitust teha 6-kuulist ravikuuri akamposaadi –või naltreksooniga, **ravikuuri võib pikendada juhul kui on märgata ravimi positiivset mõju ning patsient soovib jätkata raviga.** Medikamentoosse ravi soovitatakse **lõpetada juhul, kui patsient jätkab rohket alkoholi tarbimist pärast 4-6 nädalast medikamentoosset ravi ning ei soostu psühhosotsiaalse raviga**. Raviskeemi soovitatakse **täielikult üle vaadata juhul, kui patsient kasutab medikamentoosset ravi, teda on kaasatud psühhosotsiaalsesse ravisse ning vaatamata sellele ta jätkab rohket alkoholi tarbimist.**

Disulfiraami soovitatakse kasutada ainult superviseeritut – patsiendi ravisoostumust tukeb hinnata esimesel kahek kuul iga kahe nädala tagant ja seejärel kord kuus. Patsiendi terviseseisundit (kas tekkisid vastunäidustused ?) tuleb uuesti hunnata iga poole aasta tagant. Komorbiidsete psühhiaatriliste haiguste puhul soovitatakse esmalt loobuda alkoholi tarbimisest ning hinnata patsiendi seisundit 3-4 nädala pärast uuesti. Kaasuva psüjhhiaatrilise haiguse sümptimite püsimisel patsient tasub suunata eriarsti vastuvõtule. Alkoholi kuritarvitajate puhul soovitatakse alustada psühhosotsiaalsete sekkumistega ning rakendada medikamentoosset ravi alles siis, kui patsient ei vasta viimastele (kognitiiv-käitumuslik teraapia, teised käitumuslikud teraapiad, paariteraapia). Psühhoteraapia kuuri pikkuseks on enamikes uuringutes 12 nädalat (1 kuni 6 nädalat motivatsiooniteraapia jaoks, 2 nädalat kuni 6 kuud kognitiiv-käitumisteraapia jaoks - enamikes uuringutes siiski 12 nädalat, muud käitumuslikud teraapiad – 12 nädalat, paariteraapia – 4 kuni 12 nädalat).

AUSTRALIAN 2009

Ei ole teada medikamentoosse ravikuuri optimaalset pikkust (naltreksoon, akamposaat). Tavaks on rakendada ravi 3 kuni 6 kuud. Raviarst peab langetama otsuse ravikuuri pikkuse üle vastavalt konkreetsele ravijuhtumile, võttes arvesse kõrvaltoimete esinemist, tagasilanguste sagedust, patsiendi sotsiaalset tausta ning muid patsiendipoolseid tegureid (Evidence D). Arvatakse, et **suuremat kasu medikamentoossest ravist saavad kõrgelt motiveeritud patsiendid, mistõttu ei ole mõtet jätakata medikamentoosse raviga juhul, kui patsient jätkab rohket alkoholi tarbimist ravi foonil. Suureks probleemiks on ravisoostumus**, mille võimalikuks põhjuseks on hirm kõrvaltoimete eest, stigma ravimite võtmise eest, kohese ravitulemuse puudumine (O'Malley 1998; Kranzler et al. 2000). Disulfiraami soovitatakse võtta 3-6 kuu jooksul, pärast seda peaks julgustama patsienti abstinentsile ilma selle ravimita.

Süstemaatilised ülevaated

Kokkuvõte süstemaatilistest ülevaadetest, meta-analüüsidest, juht-kontrolluuringutest

1 meta-analüüs **(Mann at al 2004 a** , 17 RCT of acamposate , N 4087) leidis, et pikem ravikuur akamposaadiga on seotud suurema raviefektiga (abtinentsi saavutanutevarv on suurem ning 3-, 6- ja 12 –kuud kestva ravikuuri effect size ehk RB on vastavalt 1.33, 1.50, and 1.95; Cumulative Abstinence Duration Proportion ehk CADP 3 kuud kestva ravi puhul on 10.88, p <0.001 (95% CI 6.74–15.02), 6 kuu ravi puhul 11.15, p<0.001 (95% CI 6.91–15.38) ja 12-kuu ravi puhul 12.63 , p < 0.001 (95% CI 8.97–15.33).Nende seas, kes said ravi akamposaadiga 6 kuud abtsinentsi saavutas 53,5 % võrreldes 43,3%-ga platseebo-rühmas (RB 1.28 (95% CI, 1.17–1.39; p < 0.001; homogeneity p < 0.557). 12 kuud kestnud ravi puhul abstinensti saavutatas ja säilitas 45% patsientidest võrreldes 23%-ga platseebo-rühmas (RB 1.73 (95% CI, 1.41–2.11; p <0.001; homogeneity p < 0.896) . Enamikes uuringutes raviefekti on mõõdetud mitte varem kui 3 kuni 6 kuud kestnud ravi järel (kõikides uuringutes koos psühhosotdsisaalsete sekkumistega).

1 meta analüüs (**Hopkins at al 2002 a**, 15 RCT of acamprosate, N 3979) leidis, et akamposaadi ja platseebo saanud patsiendirühmade tagasilanguse (relapse) riskivahe on suurim esimese kolme ravikuu järel. RD ehk risk difference (riskivahe) ravimi – ja platseebo rühma vahel 3-, 6-, ja 12 kuud kestva ravi puhul on vastavalt 0.15, 0.09 ja 0.11, vastav NNT-ga 6.6, 11.2, and 9.0. See uuring toetab arvamust, et kõige drastilisemad muutused alkoholi tarbimises toimuvad esimesel kolmel ravikuul.

Ühes RCT-s (**Weisner at al 2006** , N 784) jälgiti 5 aasta jooksul alkoholsiõltuvaid patsiente, kes uuringusse haaramisel said medikamentoosse ravi 8-10 nädala jooksul. Uuringus leiti, et nendel, kes püsisid karsklasena 6 kuud pärast ravi on oluliselt suuremad šanssid jääda karsklaseks ka 5 aasta pärast. Oluliseks teguriteks, mis ennustas karsklaseks jäämist pärast 5 aastast jälgimisperioodi nende seas, kes püsisid karsklasena 6. jälgimiskuul oli kõrgem patsiendi vanus, naissugu ja toetava sotsiaalvõrgustiku olemasolu**.** Need patsiendid, kes ei püsinud karsklasena 6. jälgimskuul, kuid näitasid ennast karsklasena pärast 5 aastast jälgimisperioodi, olid suurema tõenäosusega monosõltuvusega patsiendid, samuti need, kes pöördusid tagasi ravi saamiseks ning toetava sotsiaalvõrgustikuga patsiendid. Autor leiab olulist seost lühiajaliste (6 kuud) ja pikaajaliste (5 aastat) ravitulemuste vahel ning seda, et sotsiaalse toetusvõrgustiku olemasolu ning tagasipöördumine ennustab suuremat tõenäosust jääda karsklaseks ka pikema jälgimisperioodi järel. Mõned patsiendid, kes ei saavutanud või ei säilitanud abstinentsi kohe pärast esimest ravikuuri, kuid pöördusid tagasi ravi saamiseks, näitasid ennast karsklasena pärast pikemat jälgimisperioodi. Oma uuringus autor toetub varasemalt läbi viidud uuringutele ja järeldab, et sageli pikaajalist ravitulemust ei ole võimalik saavutada ühekordse raviepisoodiga. Üks süstemaatiline ülevaade (**Berglund at al 2001,** 139 RCT) hindas, kas patsiendi seisundi raskusest peaks sõltuma psühhosotsiaalse ravi intensiivsus ning pikkus. Ei ole tõendeid selle kohta, et ühe ja sama psühhosotsiaalse intervensiooni pikem rakendamine oluliselt parandaks ravitulemust võrreldes lühema ravikuuriga. Samas uuringud näitavad (Holder et al. (2000) , Rychtarik et al. (2000), et kerge- ja mõõduka sõltuvusega patsiendid saavad võrdselt kasu kergematest psühhosotisaalsetest inerventsioonidest (nt biblioteraapia) ja intensiivsematest interventsioonidest (nt. kognitiiv-käitumisteraapia). Kulu-efektiivsuse uuring näitas, et komorbiidsete psühhiaatriliste haigustega ning kõrge sõltuvustasemega patsiendid saavad rohkem kasu intensiivsematest psühhoteraapia meetoditest (nt kognitiiv-käitumisteraapia). Üks süstemaatiline ülevaade ning meta-analüüs, mis koosnes 19 RCT-st (**Bouza at al 2004**, N 3205 naltrexone vs control group) võrdles omavahel ravitulemused vastavalt ravikuuri pikkusele. Tulemusi oli jagatud vastavalt ravikuuri pikkusele (3 -, 6- või 12 kuud ravi naltreksooniga). Lühiajalise teraapia korral (3 kuud) naltreksoon näitas olulist efektiivsust alkoholi tarbimise vähenemisel (relapse rate during treatment : naltrexone vs placebo: PetoOD (95% CI) 0,62 (0.52;0,75), p < 0,00001), jälgimisperioodi järgselt (6-18 kuud) see tulemus oli võrdne aktiivse ravi perioodiga, kuid statistiliselt ebaoluline (Relapse during follow- up:; naltrexone vs placebo – OD (95%CI) 0.65 (0.44, 0.97), p 0.03. Kuigi analüüs näitas, et ravirühmas abstinensi saavutanute arv oli suurem võrreldes platseebo rühmaga, siiski see tulemus ei olnud statistiliselt oluline. 6 kuud kestva ravi puhul naltreksoon näitas samuti olulist efektiivsust alkoholi tarbimise vähenemisele ning abstinentsi saavutanute määr oli nüüd statistiliselt oluline (abstinence [OR (95% CI): 7, 49 (1.94, 32.52), P = 0.004] and relapse rates [OR (95% CI): 0.18 (0.04, 0.78), P = 0.02]. Kahjuks ei ole andmeid jälgimisperioodi kohta selle grupi jaoks. Need patsiendid, kes said ravi naltreksooniga 12 kuud ei näidanud statistiliselt olulist alkoholi tarbimise vähenemist võrreldes platseebo rühmaga, kahjuks selles rühmas andmed olid saadaval ainult sekundaarsete ravitulemuste kohta

(differences between naltrexone and placebo in terms of percentage of drinking days [WMD (95% CI): 3.00 (- 7.80, 1.80), P = 0.2] or number of drinks per drinking day [WMD (95% CI): 0.30 (- 1.35, 1.95), P = 0.7])

1 süstemaatiline ülevaade (**Lundbrook at al 2001a**, 44 RCT) näitas, et need patsiendid, kes said ravi akamposaadiga vähemalt 52 nädalat säilitasid abstinentsi ka 104-l jälgimisnädalal ehk 1 aasta pärast ravi lõppu. Need, kes said ravi akamposaadiga 6 kuud ja saavutasid abstinentsi (statistiliselt oluline tulemus) näitasid suuremat abstinentsi määra ka 12-ndal jälgimiskuul, kuid see tulemus ei olnud enam statistiliselt oluline.

Kõrge kvaliteediga meta-analüüs (**Srisurapanont at al 2004,** 24 double-blind RCT, N 2861) hindas naltreksooni raviefekti, selle kõrvaltoimeid ning ravi katkestamise põhjusi. Meta-analüüs haaras 24 topeltpimedat randomiseeritud kontroll-uuringut (N 2861). Kõik ravitulemused olid jagatud rühmadesse vastavalt ravikuuri pikkusele ning jälgimisperioodile (kuni 12 nädalat, kuni 12 kuud ja rohkem kui 12 kuud kestvad uuringud). Enamus uuringuid kestis 12 nädalat ning selle rühma kohta on saadud kõige rohkem andmeid. Kõikides uuringutes patsiendid said psühhoteraapiat lisaks medikamentoossele ravile. Esimese 12 ravinädala jooksul naltreksoon oluliselt vähendas tagasilanguse riski (RR 0.64, 95% CI 0.51–0.82), kuid ei mõjutanud olulisel määral riski hakata uuesti tarbima alkoholi (RR 0.91, 95% CI 0.81–1.02).

Kuus kuud kestva ravi puhul statistiliselt oluliseks oli aeg esimese dringini ning alkoholihimu vähenemine (time to first drink (Balldin et al., 2003) , N =55 , WMD 35.00 (95% CI 29.83 to 40.17); Craving (Balldin et al., 2003), N = 55, SMD -0.88 (95% CI -1.44 to -0.33). Autorid järeldasid, et ei ole teada optimaalset ravikuuri pikkust naltreksooniga nende alkoholsõltlaste patsientide jaoks, kes saavutasid positiivse ravitulemuse pärast lühiajalist ravikuuri. Andmed kõrvaltoimete ning ravi katkestanute kohta on saadaval ainult lühiajaliste uuringute jaoks (12 nädalat) ning kõrvaltoimete risk on oluliselt suurem naltreksoon-ravirühmas võrreldes platseeboga (nausea,dizziness, and fatigue RRs were of 2.14 ((95% CI)1.61–2.83), 2.09 ((95% CI)1.28–3.39), and 1.35 ((95% CI)1.04–1.75) respectively). Ravi katkestanute arv ei erinenud olulisel määral naltreksoon- ja platseebo ravirühmades. (RR 0.85, 95% CI 0.72–1.01). Nendest alkoholsõltlastest patsientidest kes alustasid ravi naltreksooiga 36% katkestas ravi erinevatel põhjustel esimese 12 nädala jooksul, mistõttu ravi planeerimisel on eriti oluline rakendada meetmeid ravi katkestamise riski vähendamiseks.

Moos at al 2003 a (N 473) viis läbi longitudinaalse uuringu, mille eesmärgiks oli võrrelda erineva pikkusega ravikuuride efekti püsimist pärast 1 aastast jälgimisperioodi. Uuringus osalesid alkoholi liigtarvitavad patsiendid (nii sõltlased kui ka mitte sõltlased), kes said nn standartravi (medikamentoosne ravi + psühhoteraapia). Uuringu tulemusena leiti, et need patsiendid, kes said ravi pikema perioodi jooksul (27 nädalat ja rohkem) näitasid oluliselt paremaid ravitulemusi võrreldes nendega, kes said lühemat ravikuuri.

Randomiseeritud kontroll uuringus (**Anton at al 2001** a, N 131) alkoholsõltlased patsiendid said ravi naltreksooniga ja psühhoteraapiat 12 nädala jooksul. Uuring näitas statistiliselt olulist alkoholi tarbimise vähenemist ravirühmas võrreldes placeboga. Siiski ravi lõppedes tagasilangenute arv drastiliselt suurenes ning muutused toimusid ka teistes nn sekundaarsetes ravitulemustes (tarbitava alkoholi kogused suurenesid). Jälgimisperioodil need patsiendid, kes said ravi naltreksooniga üldiselt tarbisid vähem alkoholi võrreldes platseebo rühmaga, kuid see erinevus ei olnud enam statistiliselt oluline. Uuringu autorid järeldavad, et mõned patsiendid vajavad kindlasti pikemat kui 3 kuud ravikuuri (kas ainult naltreksooniga või naltreksoon+ psühhoteraapia kombineeritud raviga) abstinentsi säilitamiseks.

1 RCT (Stephanie S. **O'Malley at al. 1996** a, N=97), milles alkoholsõltlased patsiendid said raviks kas naltreksooni- või psühhoteraapiat 12 nädala jooksul näitas, et naltreksooni positiivne mõju kestis mitte rohkem kui üks kuu pärast ravi lõpetamist. Uuringu autorid järeldavad, et mõned patsiendid vajavad pikemat ravikuuri naltreksooniga eesmärgiga pikendada abstinentsi perioodi.

Randomiseeritud kontroll-uuring (**Raymond F at al 2006 a,** N1383) oli läbi viidud eesmärgiga võrrelda naltreksooni ja akmposaadi toimet alkoholi tarbimisele koos või ilma psühhoteraapiata (kognitiiv-käitumisteraapia). Need patsiendid, kes said raviks kas naltreksooni, psühhoteraapia või mõlemat näitasid paremaid ravitulemusi võrreldes platseebo rühmaga (PDA ehk percent days abstinent 80.6%, 79.2%, and 77.1%, respectively with p = 0,009). Platseebo rühmas PDA oli vaid 75,1%. Selles uuringus akamposaat naitas statistiliselt olulist tulemust (efektiivsus alkoholi

tarbimise vähenemisel). **Ühe aastase jälgimisperioodi järel need tulemused olid protsentuaalselt sarnased, kuid statistilsielt ebaolulised (66.2 (31.62) 66.6 (31.85) 67.3 (31.62) with p=0.27.**

Tabel 1.

Uuring	Valimikogusuurus	*Abstinents*	Alkoholitarvitamise vähenemine	Lapsed (participants returning to any drinking)	Relapsed to heavy drinking		Heavy drinking episodes during study period	Discontinuation due to adverse events	Discontinuation for any reason
NICE 2011 Metaanalüüs 19 RCTs Acamposate vs placebo	N 4629	Cumulative abstinence duration At 3 months: SMD –2.75 (–7.51, 2.01) K 2, N 241 At 6 months: SMD –0.29 (–0.41, –0.17) K 4, N 1134 At 9 months: SMD –0.24 (-0.46, –0.03) K 1, N 330 PDA At 2 months: SMD –0.10 (–0.43, 0.23) K 1, N	DDD SMD –0.05 (–0.29,0.20 K2,N 258	At 2 months RR 1.19 (0.76, 1.88) K 1, N 142 At 3 months: RR 0.88 (0.75, 1.04) K 1, N 350 **At 6 months: RR 0.83** (0.77, 0.88) K 17, N 3964 At 12 months: RR 0.88 (0.80, 0.96) K 4, N 1332	**At 3 months: RR 0.95 (0.86, 1.05)** K 1, N 612 **At 6 months: RR 0.81 (0.72, 0.92)** K 10, N 2654 At 12 months: RR 0.96 (0.89, 1.04) K 1, N 612		No data	RR 1.36 (0.99, 1.88) K12, N 3774	RR 0.90 (0.81, 0.99) K15, N4037

		142 At 3 months: SMD 0.00 (–0.16, 0.15) K 1, N 612 At 12 months: SMD 0.00 (–0.20, 0.20) K 1, N 612							
NICE 2011 Metaanalüüs Naltrexone vs placebo 27 RCTs	N 4296	*Cumulative abstinence duration* SMD -0.12 (-0.39, 0.15) K 2, N 217 *PDA (procent day abstinent)* At 3 months: SMD –0.22 (–0.37, –0.07) K 9, N 1607 **At 6 months: SMD -0.25 (-0.51, 0.00)** K 1, N 240 At 12 months: SMD -0.11	DDD SMD -0.28 (-0.44,-0.11) K10, N 1639	**At 3 months: RR 0.92 (0.86, 1.00)** K17, N 1893 At 6 months RR 0.79 (0.60, 1.05) K 1, N 113	**At 3 months: RR** **0.83 (0.76, 0.91)** K22, N 3320 At 6 months (endpoint): RR 0.96 (0.79, 1.17) K 1, N 240 At 6 months (maintenance treatment): RR 0.46 (0.24, 0.89) K 1, N 113		SMD -0.43 (-0.82 ,-0.03) K 7, N 797	RR 1.79 (1.15, 2.77) K12, N 1933	RR 0.94 (0.84, 1.05) K 25, N 3926

		(-0.42, 0.20) K 1, N 618							
NICE 2011 Metaanalüüs Disulfiram vs placebo 3 RCT	N 859	Cumulative abstinence duration SMD -0,45 (-0.86, -0.04) K 1, N 93	No data	At 12 months: RR 1.05 (0.96, 1.15) K 2, N 492	No data		No data	No data	RR 1.15 (0.43, 3.12) K 1, N 406
NICE 2011 Metaanalüüs 2 RCTs Acamposate /naltrexone vs placebo	(N 694)	PDA At 3 months: SMD -0.09 (-0.42, 0.25) K 1, N 614 At 12 months SMD -0.09 (-0.25, 0.06) K 1, N 614			At 3 months RR 0.78 (0.56, 1.09) K 2, N 694 At 6 months: RR 0.44 (0.28, 0.69) K 1, N 80 At12 months: RR 0.97 (0.90, 1.05) K 1, N 614			RR 3.16 (1.03,9.7) K 1, N614	

Mann 2004	17 RCT, N - 4087	*Effect size* (treatment duration in months) 3 m - 1.39 6 m – 1.5 **12 m – 1.95** *Abstinence rate acamposate vs placebo* <u>3 month</u> - 45,7% vs 33,7% (pooled RB estimate 1.33 (95% CI, 1.20–1.47; *p* <0.001), <u>6 month</u> 36.1%; vs 23.4%; RB,							

		1.47; [95% confidence intervals (CI): 1.29 – 1.69]; *p* <0.001). <u>12 month</u> **27,3% vs 12,6% (pooled RB estimate 1.95** (95% CI, 1.58–2.42; *p* <0.001) CAD 3 months 10.88 (2.1) *p* < 0.001 (CI 6.74–15.02) 6 months 11.15 (2.2) *p* < 0.001 (CI 6.91–15.38)							

		12 months 12.63 (1.9) $p <$ 0.001 (CI 8.97–15.33 NTT 6 months 7,78 12 months 7,5							
Bouza 2004		3 months *Abstinence during treatment*: OD (95% CI) 1,26 (0,97;1,64), p 0,08 During follow-up: OD(95%CI) 1.67 (0.92, 3.02), p 0.09			3 months During treatment: OD (95% CI) – 0,62 (0.52;0,75), p < 0,00001 During follow-up:				

		6 months OR (95% CI): 7, 49 (1.94, 32.52), *P* = 0.004]			OD (95%CI) 0.65 (0.44, 0.97), p 0.03 6 months [OR (95% CI): 0.18 (0.04, 0.78), *P* = 0.02].				
Lundbrook 2003		Acamposate Rate of continuous abstinence at 6 months 20% vs 10% p=0.024 Rate of continuous abstinence at 12 months 11% vs 5% p=0.173	Acamposate Alcohol free days over 3 months 57 days (higher dose) 52 days (lower dose) versus placebo 34 days Alcohol free days over 6 months 61		Naltrexone vs placebo 3 months: 23% vs 54%, 70 patients 40% vs80% 104 patients 35% vs 53% 97 patients				

			days versus placebo 43 days p=0.025						

Viited

Kokkuvõtte (abstract või kokkuvõtlikum info)	Viide kirjandusallikale
For acamprosate, Mann (2004) reported from their meta-analysis that the effect sizes increased with time (the effect sizes on abstinence at 3, 6 and 12 months were 1.33, 1.50 and 1.95, respectively). This suggests that a clinically relevant benefit of treatment may be observed as early as 3 months, which gradually increases up to 1 year and possibly beyond.	***Mann, K. (2004)*** *Pharmacotherapy of alcohol dependence: a review of the clinical data. CNS & Neurological Disorders Drug Trials, 18, 485–504* ***Meta-analyses (NICE)***
N/A	*Hopkins J S , Garbutt J C , , , Poole C L, West S L, Carey T S (2002) Naltrexone and acamprosate: meta-analysis of two medical treatments for alcoholism.* *Alcohol Clin Exp Res 26 (Suppl)* ***Meta-analyses (NICE)***
Methods: The sample (N 784) is from an outpatient (day hospital and traditional outpatient) managed care chemical dependency program. Subjects were interviewed at baseline, 6 months, and 5 years. Logistic regression analysis was used to assess which individual, treatment and extra-treatment characteristics predicted alcohol and drug abstinence at 5 years. **Results:** Abstinence at 6 months was an important predictor of abstinence at 5 years. Among those abstinent at 6 months, predictors of abstinence at 5 years were older age, being female, 12-step meeting attendance, and recovery-oriented social networks. Among those not abstinent at 6 months, being alcohol dependent rather than drug dependent, 12-step meeting attendance, treatment readmission, and recovery-oriented social networks predicted abstinence at 5 years. **Conclusion:** Our findings demonstrate a clear association between short-term and long-term treatment success. In addition, these results strongly support the importance of recovery-oriented social networks for those with good short-term outcomes, and the beneficial impact of readmission for those not initially successful in treatment.	***Weisner, C****., Ray, G. T. & Mertens, J. R. et al. (2003) Short-term alcohol and drug treatment outcomes predict long-term outcome. Drug & Alcohol Dependence, 71,* *281–294.* **RCT** **(NICE)**
Babor et al 2003 oma raamatus kirjutab, et suurimad muutused alkoholi tarbimise mustris ning tarbitava alkoholi kogustes toimuvad tavaliselt esimesel 3	***Babor,*** *T. F., Steinberg, K., Zweben, A., et al. (2003) Treatment effects across multiple dimensions of outcome. In Treatment Matching in Alcoholism (eds*

ravikuul. Sotsiaalse funsktsioneerimise- ning üldtervisega seotud ravitulemused vajavad pikemat jälgimisaega.	*T. F. Babor & F. K. Del Boca), pp. 50–165. Cambridge: Cambridge University Press.* ***Book***
Results: Generally, the association between the setting and intensity of treatment (inpatient, outpatient, amount, and duration) and outcome is weak. Comparisons of inpatient and outpatient treatment are inconclusive, as are results from treatments using the same method but with a different duration. However, the findings support adapting the extent of treatment to the problem severity. For persons with limited problems (moderate or low dependence), limited treatment yields the same effect as more extensive treatment. The value of a self-help manual, or bibliotherapy, has been analyzed in five studies, and all reported that bibliotherapy had the same effect as 6 to 10 therapist-managed treatment sessions. Brief treatment with a few sessions seems to have the same effect as more extensive treatment. For persons with greater problem severity, better results are seen with more treatment. For people with less pronounced dependence, the amount and duration of treatment seem to be of less importance. For this group, self-help manuals or a few treatment sessions seem to have as good or better effects than more extensive treatment. Rychtarik et al. (2000) reported on matching effects between problem severity and inpatient/outpatient care. Patients with greater problem severity had more sober days if they received more inpatient treatment, and vice versa: patients with lower alcohol involvement had more sober days if they were treated in outpatient care than in inpatient care. The study by Holder et al. (2000) shows that short treatment (motivational enhancement therapy) is cost-effective but that a higher cost-effectiveness is achieved by offering patients with certain prognostically unfavorable factors (e.g., a high level of alcohol dependence or psychiatric comorbidity) more extensive treatment (12-step treatment or cognitive behavioral therapy).	***Berglund*** *M, Andréasson S, Franck J, Fridell M, Håkanson I, Johansson B, et al. Treatment of alcohol and drug abuse: an evidence-based review [Swedish].* *Stockholm: The Swedish Council on Technology Assessment in Health Care; 2001.* ***Systematic Review*** ***(SIGN)***
Systematic review of the literature (1990–2002) and meta-analysis of full published randomized and controlled clinical trials assessing acamprosate or naltrexone therapy in alcohol dependence	**Bouza Carmen**, Magro Angeles, Muñoz Ana & Amate José María Efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence: a systematic review, Agency for Health Technology

	Assessment, Madrid, Spain, 2004
The aim of this study is to review evidence on the effectiveness and cost-effectiveness of interventions aimed at reducing alcohol misuse. A search of electronic databases for the period 1990-2001 has been conducted for the review of cost-effectiveness literature. **The majority of studies have shown brief interventions to be effective in changing drinking behaviour and reducing alcohol consumption for at least 12 months in patients who are not alcohol dependent**.	**Ludbrook** A, Godfrey C, Wyness L, Parrott S, Haw S, Napper M, et al. Effective and cost-effective measures to reduce alcohol misuse in Scotland: a literature review. Edinburgh: Scottish Executive; 2001. *(review)*
This paper is aimed to systematically review benefits, adverse effects, and discontinuation of treatment by naltrexone. **Outcomes** Two primary outcomes were subjects who *relapsed (including heavy drinking*) and those *who returned to drinking (lapsed)* . Secondary outcomes *were time to first drink, drinking days, number of standard drinks for a defined period, and craving*. All outcomes were reported for the short- (up to and including 12 wk), medium- (more than 12 wk and up to 12 months) and long-term naltrexone teratment (more than 12 months). **Methods** A total of 2861 subjects in 24 double-blind RCTs presented in 32 papers were included. With regard to study duration, only eight trials were carried out for longer than 12 naltrexone was given regulary for 12 weeks and then followed by other therapy (targeted naltrexone or psychotherapy during follow-up period). In The other 13 studies only naltrexone were given regulary for 12 weeks. All trials clearly defined the psychosocial treatment concomitantly given with naltrexone. While a trial gave a simple psychosocial treatment called medical advice (Latt et al., 2002), each of the remainder gave at least one form of intensive psychosocial treatment, e.g. coping skills and CBT. **Results** **Naltrexone vs placebo** ***Short-term*** In the first 12 wk of treatment, naltrexone significantly diminished the risk of relapse (RR 0.64, 95% CI 0.51–0.82), but not the risk of return to drinking (R0.91, 95% CI 0.81–1.02). No significant difference between groups and no significant heterogeneity of data were found in any secondary outcomes of short-term treatment (Time to first drink, N (number of patients in included studies) 511, WMD -0.06 (95% CI -1.04 to 0.93); Drinking days , N 489, WMD -1.96 (95% CI -5.47 to 1.56); Standard drinks, N 772, SMD -0.21 (95% CI -0.46 to 0.04); Craving, N 400, SMD -0.10 (95% CI -0.35, 0.15). ***Medium-term*** For medium-term treatment (Balldin 2003 – naltrexone treatment duration - 6 months), no significant difference between groups was found in respect of relapse (Relapses (Balldin et al., 2003), N = 118, RR 1.01 ((95% CI) 0.92 to 1.11)	**Srisurapanont M**, Jarusuraisin N. Naltrexone for the treatment of alcoholism: **a meta-analysis** of randomized controlled trials. Int J Neuropsychopharmacol 2005;2:267-80.

Two secondary outcomes were significantly different, in which naltrexone was superior in increased time (days) to first drink and decreased craving (Time to first drink (Balldin et al., 2003) , N =55 , WMD 35.00 (95% CI 29.83 to 40.17); Craving (Balldin et al., 2003), N = 55, SMD -0.88 (95% CI -1.44 to -0.33) ***Long-term*** (small sample size!) Only 1 study (Landabaso et al., 1999) 25 mg/d naltrexone+ intensive psychosocial treatment (in this study disulfiram!!) (n=15) for 6 months vs intensive psychosocial treatment (disulfiram!!) alone (n=15) for 12 months. Relapses : RR 0.60 (95% CI 0.40 to 0.91) Return to drinking RR 0.60 (95% CI 0.40 to 0.91) **Naltrexone+intensive psychosocial treatment (CBT) vs. naltrexone+simple psychosocial treatment** Both short- and medium-term outcomes were available in three placebo-controlled trials (Balldin et al., 2003; O'Malley et al., 1992, 2003). Intensive psychosocial treatment was CBT (cognitive-behavioural therapy), the simple psychosocial treatment was supportive psychotherapy (Balldin et al., 2003; O'Malley et al., 1992) and PCM (primary care management) (O'Malley et al., 2003). ***Short-term*** A short-term adjunct of intensive psychotherapy was not superior in any respect of primary or secondary outcomes. ***Medium-term*** No superiority was found on the risks of relapse and return to drinking. However, the intensive psychosocial adjunct significantly increased time (days) to first drink and decreased craving. **Conclusions** Naltrexone at the dose of 50 mg/d should be accepted as a short-term treatment for alcoholism. However, as yet, **we do not know the appropriate duration of treatment continuation in an alcohol-dependent patient who responds to short-term naltrexone administration.** Because psychosocial treatment was given in almost all trials included, to ensure that the real-world treatment would be as effective as the research findings, a form of psychosocial treatment should be concomitantly given to all alcohol-dependent patients receiving naltrexone administration. Although the adjunct of intensive psychosocial treatment, e.g. CBT, may not be superior to that of simple psychosocial treatment, its advantages in increasing time to first drink and decreasing craving may be seen after 12 wk of therapy. Naltrexone administration cannot lower the risk of discontinued treatment in alcohol-dependent patients. Approximately 36% of those taking naltrexone still discontinue their treatment in the first 12 wk. A naltrexone-treatment programme should, therefore, include strategies to improve treatment adherence, e.g. concomitant psychosocial treatment. In addition, management of the common adverse	

effects of naltrexone should be given, e.g. informing about naltrexone-induced nausea, dizziness, and fatigue.	
DESIGN, SETTING, PARTICIPANTS: A sample of alcoholic individuals (n = 473) was recruited at alcoholism information and referral centers and detoxification units and was surveyed at baseline and 1 year, 3 years and 8 years later. MEASUREMENTS: At each contact point, participants completed an inventory that assessed their treatment utilization since the last assessment and their current alcohol-related, psychological and social problems. FINDINGS: Compared with individuals who remained untreated, individuals who entered treatment relatively quickly and who obtained a longer duration of treatment had better short- and long-term alcohol-related outcomes and better short-term social functioning. Individuals who obtained a longer duration of additional treatment had better alcohol-related outcomes than individuals who obtained no additional treatment but, among individuals who delayed treatment entry, the duration of treatment was not associated with treatment outcomes. In general, the intensity of treatment was not related to better outcomes. CONCLUSIONS: Rapid entry into treatment and the duration of treatment for alcohol use disorders may be more important than the intensity of treatment. Treatment providers should consider structuring their programs to emphasize continuity, rather than intensity of care.	Moos,R.H. and Moos,B.S. (2003): Long-term influence of duration and intensity of treatment on previously untreated individuals with alcohol use disorders. *Addiction*, 98(3):325-337.
Objective: This study examined whether substance abuse patients self-selecting into one of three aftercare groups (outpatient treatment only, 12-step groups only, and outpatient treatment and 12-step groups) and patients who did not participate in aftercare differed on 1-year substance use and psychosocial outcomes. **Method:** A total of 3,018 male patients filled out a questionnaire at intake and 1 year following discharge from treatment. Patients were classified into aftercare groups at follow-up using information from VA databases and self-reports. **Results:** Patients who participated in both outpatient treatment and 12-step groups fared the best on 1-year outcomes. Patients who did not obtain aftercare had the poorest outcomes. In terms of the amount of intervention received, patients who had more outpatient mental health treatment, who more frequently attended 12-step groups or were more involved in 12-step activities had better 1-year outcomes. In addition, patients who kept regular outpatient appointments over a longer time period fared better than those who did not. **Conclusions:** Encouraging substance abuse patients to regularly attend both outpatient aftercare and self-help groups may improve long-term outcomes.	**Influence of Outpatient Treatment and 12-Step Group Involvement on One-Year Substance Abuse Treatment Outcomes** Paige Crosby Ouimette, Rudolf H. Moos, John W. Finney (J. Stud. Alcohol 59: 513-522, 1998)

An article by Allsop and Saunders (1997) reports a study carried out in Scotland in which 60 patients with a diagnosis of alcohol dependence were 'randomised' to Relapse Prevention (RP) or to a relapse discussion treatment or to no additional treatment. Allocation was in fact not random but alternated in pairs. The RP therapy consisted of eight 1-hour sessions intended to (1) develop, enhance and sustain commitment to change (2) identify individual relapse precipitants (3) develop coping skills (4) increase self-efficacy (5) encourage recognition that strategies are available to prevent relapse in case of lapse. The discussion group used the same exercises as RP for enhancing commitment but otherwise shared the patients' personal strategies for avoiding relapse. Outcome was assessed immediately post treatment, at 6 months and at 1 year. Number of weeks abstinent, drinking moderately, drinking heavily or functioning poorly (> 1 day in prison or hospital) was assessed at 6 months and 1 year. Time to first drink and time to first heavy drinking session (relapse) were also examined. It was assumed that patients who could not be contacted had relapsed. The median times to relapse for the RP, discussion and no treatment groups were 189, 51.5 and 26.5 days. This was a statistically significant difference between survival curves (Log rank $p<0.03$). Thirty six (90%) of 40 patients in the two control arms relapsed over 1 year. This compares with 14 (70%) of 20 in the RP group. This is not a statistically significant difference.	Allsop S, Saunders B, Phillips M, Carr A. A trial of relapse prevention with severely dependent male problem drinkers. Addiction [Internet]. 1997;92:61-73, RCT
Not available.	MILLER, W.R.; WESTERBERG, V.S.; HARRIS, R.J.; AND TONIGAN, J.S. What predicts relapse? Prospective testing of antecedent models. *Addiction* 91(suppl):155–172, 1996.
Naltrexone, an opiate antagonist medication, has been reported to be efficacious in the treatment of alcohol dependence when added to psychosocial treatments. Although the within-treatment efficacy of naltrexone has received primary attention, there has been little published on the outcome of individuals once the medication is discontinued. Animal studies have led to concern regarding a quick rebound to heavy drinking. This report extends the data previously reported by evaluating the outcome in alcoholic subjects during the 14 weeks after a 12-week treatment with naltrexone or placebo in conjunction with cognitive behavioral therapy. Of the 131 subjects evaluated during the treatment phase, 124 (95%) had up to 14 weeks of posttreatment drinking data available for analysis. Measures of craving and blood markers of heavy drinking were also evaluated. By the end of treatment, naltrexone demonstrated significantly greater efficacy than placebo. However, once the medication was discontinued, there was a gradual increase in relapse rates, heavy drinking days, and drinks per drinking day,	Anton RF, Moak DH, Latham PK, Waid LR, Malcolm RJ, Dias JK, Roberts JS. Posttreatment results of combining naltrexone with cognitive-behavior therapy for the treatment of alcoholism. J Clin Psychopharmacol. 2001 Feb;21(1):72-7. (only in abstract form)

and fewer days of abstinence were reported. By the end of the 14-week follow-up period, although naltrexone-treated subjects were, on average, still doing better than control subjects, the effectiveness of naltrexone was no longer statistically significant. There was no evidence that naltrexone subjects had an immediate return to heavy alcohol use as suggested in animals. These data suggest that, for a number of alcoholic subjects, continued treatment with naltrexone, or perhaps psychosocial intervention, for longer than 3 months is indicated. Future research should identify which alcohol-dependent individuals may need prolonged treatment to improve treatment success in the long term.	
Background: The goal of this study was to examine the persistence of naltrexone's effects on drinking outcomes among alcoholics following discontinuation of treatment and to determine whether coping skills therapy improves long-term outcomes compared with supportive therapy.**Methods:** Eighty of 97 alcohol-dependent subjects randomized to receive naltrexone or placebo and either coping skills therapy or supportive therapy for 12 weeks were assessed at a 6-month off-treatment follow-up. **Results:** Subjects who received naltrexone were less likely to drink heavily or to meet criteria for alcohol abuse or dependence than subjects who received placebo. The effect of naltrexone therapy on abstinence rates persisted only through the first month of follow-up. Coping skills therapy was associated with decreased levels of drinking among subjects who received placebo. Psychotherapy condition, however, did not predict alcohol diagnosis at follow-up. **Conclusions:** Some but not all of the benefits resulting from short-term naltrexone treatment persist after discontinuation of treatment. The findings suggest that continued treatment with naltrexone may be beneficial for some patients.	Stephanie S. O'Malley, PhD; Adam J. Jaffe, PhD; Grace Chang, MD; Sarah Rode, MA; Richard Schottenfeld, MD; Roger E. Meyer, MD; Bruce Rounsaville, MD . Six-Month Follow-up of Naltrexone and Psychotherapy for Alcohol Dependence . *Arch Gen Psychiatry.* 1996;53(3):217-224. (only in abstract form)
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. **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_behavioral intervention interaction (*P*=.009).	Raymond F, Anton RF, Miller WR, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence (The COMBINE Study): examination of posttreatment drinking outcomes. JAMA, May 3, 2006—Vol 295, No. 17

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 (66.2 (31.62) 66.6 (31.85) 67.3 (31.62) with p=0.27.**	
Aftercare to prevent relapse following alcohol treatment has not received adequate experimental investigation. The present study monitored alcohol intake of 50 patients following assignment to either an intensive aftercare recruitment procedure or regular clinic after-care. The results indicated that those who received the intensive aftercare procedure showed delayed relapse. In addition, regardless of group assignment those who attended aftercare had significantly more success as measured by alcohol intake. The implications of these results for the design of treatment and aftercare programs are discussed.	Ahles, T., et al. 'Impact of Aftercare Arrangements on the Maintenance of Treatment Success of Abusive Drinkers'. *Addictive Behaviors* 1983; 8: p53-58 (only abstract)

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Ahles, T., et al. 'Impact of Aftercare Arrangements on the Maintenance of Treatment Success of Abusive Drinkers'. *Addictive Behaviors* 1983; 8: p53-58

Shand, F., et al., *the Treatment of Alcohol Problems: a Review of the Evidence*. 2003, Canberra: Australian Commonwealth Department of Health and Ageing.
APA. *Practice Guideline for the Treatment of Patients with Substance Use Disorders: Second edition*. American Journal of Psychiatry 2006; 163(8): pS1-s82

Marsh, A., et al., *Addiction Counselling: Content and Process*. 2006, Melbourne: IP Communications.

Handmaker, N., et al., 'Motivational Interviewing in the Treatment of Dual Disorders', in *Motivational Interviewing: preparing People for Change* (second edition), W.R. Miller and S. Rollnick, editors. 2002, the Guildford Press: New York.

McLellan, A.T., et al. 'Contemporary Addiction Treatment: A Review of Systems Problems for Adults and Adolescents'. *Biological Psychiatry* 2004; 56(10): p764-770.

Duckert, F. 'Recruitment to Alcohol Treatment: a Comparison Between Male and Female Problem Drinkers Recruited to Treatment in Two Different Ways'. *British Journal of Addiction* 1988; 83: p285-293.

Heather, N. 'Effectiveness of Brief Interventions Proved Beyond Reasonable Doubt'. *Addiction* 2002; 97: p297-299.

SIGN

Matching Alcoholism Treatments to Client Group Heterogeneity: Project MATCH posttreatment drinking outcomes. J Stud Alcohol 1997;58(1):7-29

Project MATCH secondary a priori hypotheses. Project MATCH Research Group. Addiction 1997;92(12):1671-98.

Longabaugh R, Wirtz PW, Zweben A, Stout RL. Network support for drinking, Alcoholics Anonymous and long-term matching effects. Addiction 1998;93(9):1313-33.

Hilton ME, Maisto SA, Conigliaro J, McNiel M, Kraemer K, Kelley ME, et al. Improving alcoholism treatment across the spectrum of services. Alcohol Clin Exp Res 2001;25(1):128-35.

Stout RL, Rubin A, Zwick W, Zywiak W, Bellino L. Optimizing the costeffectiveness of alcohol treatment: a rationale for extended case monitoring. Addict Behav 1999;24(1):17-35.

Dunn C, Deroo L, Rivara FP. The use of brief interventions adapted from motivational interviewing across behavioural domains: a systematic review. Addiction 2001;96(12):1725-42.

Slattery J, Chick J, Cochrane M, Craig I, Godfrey C, Kohli H, et al. Prevention of relapse in alcohol dependence. Glasgow: Health Technology Board for Scotland; 2003. Health technology assessment report 3.

NICE

Mann, K. (2004) Pharmacotherapy of alcohol dependence: a review of the clinical data. CNS & Neurological Disorders Drug Trials, 18, 485–504

Hopkins J S , Garbutt J C , , , Poole C L, West S L, Carey T S (2002) Naltrexone and acamprosate: meta-analysis of two medical treatments for alcoholism.
Alcohol Clin Exp Res 26 (Suppl)

Weisner, C., Ray, G. T. & Mertens, J. R. et al. (2003) Short-term alcohol and drug treatment outcomes predict long-term outcome. Drug & Alcohol Dependence, 71,
281–294. RCT

Babor, T. F., Steinberg, K., Zweben, A., et al. (2003) Treatment effects across multiple dimensions of outcome. In Treatment Matching in Alcoholism (eds T. F. Babor & F. K. Del Boca), pp. 50–165. Cambridge: Cambridge University Press.

AUSTRALIAN

Stephanie S. O'Malley, PhD; Adam J. Jaffe, PhD; Grace Chang, MD; Sarah Rode, MA; Richard Schottenfeld, MD; Roger E. Meyer, MD; Bruce Rounsaville, MD . Six-Month Follow-up of Naltrexone and Psychotherapy for Alcohol Dependence, *Arch Gen Psychiatry.* 1996;53(3):217-224

Kranzler, H.R. and Van Kirk, J. (2001). Efficacy of naltrexone and acamprosate for alcoholism treatment:A meta-analysis. Alcohol Clin Exp Res, 22:1074–1079.