# Verslaving en co-morbiditeit

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# 1. Prevalentie

# Voorkomen van psychiatrische stoornissen :

- Algemene bevolking:  22.5 %
  - Depressieve stoornis (life time) 18,7 %
  - SUD (life time): 19,1 %
- Bij mensen met alcoholproblemen: 36.5 %
- Bij mensen met drugsproblemen: 53 %

| Stoornis | % met verslaving | % bij verslaving |
|---|---|---|
| -Persoonlijkheid | 40-50% | 40-50% |
| -ADHD | 15-25% | 20-30% |
| -Depressie | 15-20% | 25-30% |
| -PTSS | 30-40% | 25-30% |
| -Angst | 10-20% | 20-30% |
| -Bipolair | 30-40% | 10-15% |
| -Psychose | 45-50% | 5-15% |

Co-occurring addictive and psychiatric disorders
A practice-based handbook from a European Perspective

# USA: Epidemiology of concurrent disorders

**Table 4** Prevalence of specific SUDs in patients in specific psychiatric categories

| Psychiatric disorder (total *n*) | Substance use disorder | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Alcohol (%) | Opioids (%) | Cannabis (%) | Sedatives (%) | Cocaine (%) | Psycho-stimulants (%) | Hallucinogens (%) | Any SUD (%) |
| Schizophrenia (53,035) | 27.6 | 5.3 | 13.2 | 4.7 | 1.8 | 3.6 | 1.2 | 36.6 |
| Schizotypal disorder (5640) | 25.0 | 3.5 | 11.6 | 4.3 | 1.7 | 2.3 | 0.4 | 34.9 |
| Other psychoses (56,065) | 22.7 | 3.5 | 4.9 | 4.5 | 0.8 | 1.4 | 0.4 | 28.3 |
| Bipolar disorder (24,567) | 27.6 | 2.6 | 3.3 | 4.9 | 0.7 | 0.9 | 0.1 | 31.9 |
| Depression (197,057) | 20.9 | 2.8 | 2.1 | 3.9 | 0.4 | 0.7 | 0.1 | 25.4 |
| Anxiety (40,552) | 20.0 | 2.4 | 2.9 | 4.1 | 0.6 | 0.9 | 0.1 | 24.8 |
| OCD (5953) | 8.8 | 1.2 | 2.3 | 1.0 | 0.2 | 0.6 | 0.02 | 11.4 |
| PTSD (7343) | 12.5 | 2.9 | 3.0 | 1.4 | 0.7 | 0.8 | 0.1 | 17.0 |
| Personality disorders (72,791) | 38.6 | 7.2 | 5.6 | 7.6 | 0.8 | 1.8 | 0.6 | 46.4 |

**Fig. 1** Comparison of the subgroups of SUDs in the different psychiatric categories

Bron: naar https://www.niaaa.nih.gov/alcohols-effects-health/alohols-effects-body

**Tabel 23.2 Meest voorkomende somatische ziektebeelden als gevolg van chronische tabaksconsumptie; per orgaansysteem in aflopende rangorde**

| *Orgaansysteem* | *Aandoeningen* |
|---|---|
| Cardiovasculair systeem | Atherosclerose, aneurysma aortae, cardiomyopathie, cerebrovasculaire aandoeningen, perifere vaatziekten |
| Kanker | Orofarynx, larynx, oesofagus, long, hersenen, nier, blaas, leukemie, pancreas, maag |
| Respiratoir systeem | Chronische bronchitis, COPD, exacerbatie astma, pneumonie |

**Tabel 23.3 Meest voorkomende somatische ziektebeelden als gevolg van chronisch opioïdengebruik; per orgaansysteem in aflopende rangorde**

| *Orgaansysteem* | *Aandoeningen* |
|---|---|
| Respiratoir systeem | COPD |
| Gastro-intestinaal systeem | Obstipatie |
| Zenuwstelsel | Hyperalgesie |
| Immuunsysteem | Hiv, hepatitis B en C |
| Cardiovasculair systeem | QT-tijdverlenging, torsade de pointes |

# 2. Impact van co-morbiditeit

- Meer en ernstigere symptomen, trager herstel
- Therapie- en medicatie-ontrouw
- Verhoogd risico op terugval en heropnames
- Meer interpersoonlijke conflicten en verlies sociale contacten
- Financiële problemen
- Verminderd functioneren, minder kans op herstel
- Agressie en suïcide
- Dakloosheid
- Somatische problemen
- Belang van diagnostiek

(Mueser, 2003)

# 3. Behandeling: algemene principes

- Sequentieel

- Parallel

- Geïntegreerde behandeling

IDDT Integrated Dual Disorder Treatment

- 1 multidisciplinair team, beide stoornissen
- outreachend
- aandacht functioneren op alle levensgebieden

# The efficacy of psychotherapies and pharmacotherapies for mental disorders in adults: an umbrella review and meta-analytic evaluation of recent meta-analyses

Falk Leichsenring[1,2], Christiane Steinert[1,3], Sven Rabung[4], John P.A. Ioannidis[5-7]



| Disorder, treatment | SMD (95% CI) | N. studies/patients | Risk of bias (% studies) |
|---|---|---|---|
| MDD, PHA[36] | 0.30 (0.26-0.34) | 522 / 116,477 | H: 9%, M: 73%, L: 18% |
| MDD, PSY[51] | 0.31 (0.24-0.38)** | 127 / NR | H or U: 78%, L: 22% |
| Panic disorder, PHA[53] | 0.44 (0.30-0.58) | 41 / 9,377 | H: 84%, U: 16%, L: 0% |
| Panic disorder, PSY[6] | 0.28 (0.07-0.49) | 7 / 398 | L: 17% |
| GAD, PHA[56] | 0.33 (0.28-0.37)° | 56 / 12,655 | H: 22%, U: 61%, L: 17% |
| GAD, PSY[55] | 0.44 (0.26-0.63) | 15 / 1,028 | L: 28-85% |
| SAD, PHA[64] | 0.35 (0.28-0.42)° | 52 / 12,153 | H: 63%, U: 25%, L: 12% |
| SAD, PSY[66] | 0.35 (0.21-0.49) | 11 / 1,207 | H: 100% |
| OCD, PHA[72] | 0.56 (0.43-0.70) | 22 / 4,350 | H: 73%, U: 18%, L: 9% |
| OCD, PSY[74] | 1.03 (0.61-1.46)° | 6 / 508 | H: 67%, L: 33% |
| PTSD, PHA[76] | 0.21 (0.13-0.29) | 58 / 3,137 | H: 26%, U: 41%, L: 33% |
| PTSD, PSY[54] | 0.54 (0.28-0.80) | 9 / 643 | H: 90%, L: 10% |
| Binge eating, PHA[82] | 0.45 (0.34-0.57) | 19 / 2,471 | H: 67%, U: 28%, L: 6% |
| Binge eating, PSY | - | - | |
| Anorexia nervosa, PHA[83] | 0.25 (0.06-0.44) | 17 / 830 | H: 72%, L: 28% |
| Anorexia nervosa, PSY[85] | 0.14 (0.00-0.29) | 13 / 1,074 | H: 23%, U: 23%, L: 54% |
| Bulimia nervosa, PHA[80] | 0.61 (0.31-0.91) | 21 / 1,316 | H: 97% |
| Bulimia nervosa, PSY[80] | - | - | |
| Insomnia, PHA[90] | 0.27 (0.17-0.38) | 31 / 3,820 | Jadad rating >4: 48% |
| Insomnia, PSY | - | - | |
| Somatoform disorder, PHA[91] | 0.50 (-0.24 to 1.24) | 7 / 804 | H: 84%, U: 12%, L: 4% |
| Somatoform disorder, PSY[92] | 0.19 (-0.04 to 0.43) | 5 / 624 | H: 100% |
| Borderline PD, PHA | - | - | |
| Borderline PD, PSY[93] | 0.57 (0.37-0.76) | 20 / 1,088 | H: 85%, U: 10%, L: 5% |
| Substance use disorders, PHA[95] | 0.26 (0.07-0.45) | 45 / 8,371 | High quality |
| Substance use disorders, PSY[96] | 0.23 (0.04-0.43) | 10 / 1,319 | L: 64% |
| ADHD, PHA[99] | 0.45 (0.37-0.52) | 44 / 9,952 | H: 9-27% |
| ADHD, PSY | - | - | |
| Schizophrenia, PHA[103] | 0.38 (0.34-0.42)** | 106 / 23,630 | H: 41%, U: 21%, L: 38% |
| Schizophrenia, PSY[111] | 0.33 (0.21-0.40) | 12 / 903 | H: 19%, U: 19%, L: 63% |
| Bipolar disorder, PHA | - | - | |
| Bipolar disorder, PSY[121] | 0.18 (0.03-0.34) | 8 / 683 | Low (GRADE) |
| Bipolar depression, PHA[113] | 0.42 (0.17-0.67) | 40 / 11,448 | H: 42%, L: 58% |
| Bipolar depression, PSY | - | - | |
| **Total PHA** | 0.36 (0.32-0.41) | | |
| **Total PSY** | 0.34 (0.26-0.42) | | |
| **Total overall** | 0.35 (0.31-0.39) | | |

**Figure 2** Effect sizes in the largest meta-analyses of pharmacotherapies (squares) and psychotherapies (circles) in comparison to placebo or treatment-as-usual (TAU). PHA – pharmacotherapy; PSY – psychotherapy, SMD – standardized mean difference, * – adjusted for risk of bias, ° – adjusted for small-study effects, MDD – major depressive disorder, GAD – generalized anxiety disorder, SAD – social anxiety disorder, OCD – obsessive-compulsive disorder, PTSD – post-traumatic stress disorder, PD – personality disorder, ADHD – attention-deficit/hyperactivity disorder, H – high, M – medium, L – low, U – uncertain, NR – not reported. Where SMD is not provided, this means that no valid meta-analysis reporting this value was available.



Doorheen heel de psychiatrie (en de geneeskunde) effect size van de behandelingen gemiddeld matig
= Cohen d 0.3-0.4
= NNT 6 – 9

**Figure 4** Effect sizes in the largest meta-analyses for combined therapy vs. pharmacological (squares) or psychological (circles) monotherapy. SMD – standardized mean difference, ° – adjusted for small-study effects, COM – combined therapy, PHA – pharmacotherapy, PSY – psychotherapy, MONO – monotherapy, MDD – major depressive disorder, SAD – social anxiety disorder, OCD – obsessive-compulsive disorder, PTSD – post-traumatic stress disorder, ADHD – attention-deficit/hyperactivity disorder, H – high, M – medium, L – low, U – uncertain, NR – not reported

Beperkte aanwijzingen dat combinatie farmaca én psychosociaal beter vergeleken met enkelvoudige behandeling

- Kad

| Type | Doel | Proces | Medicatie | EBM |
|---|---|---|---|---|
| Crisisinterventie | Overleven | Reanimatie | Naloxon | +++ |
| Genezing | Abstinentie | Detoxificatie | Methadon afbouw | +++ |
| | | | Buprenorfine afbouw | ++ |
| | | | Clonidine/lofexidine | ++ |
| | | | Naltrexone | ++ |
| | | | BZD/anti-epileptica | ++ |
| | | | Nicotinevervanger/bupropion/varenicicline | ++ |
| | | Hervalpreventie | Naltrexone onderhoud | ++ |
| | | | Acamprosaat | ++ |
| | | | Disulfiram | +/- |
| Zorg | Stabilisatie | Verminderen | Methadon onderhoud | +++ |
| | | | Brupenorfine onderhoud | ++ |
| | Harm Reduction | Secundaire preventie | Methadon LD | + |
| | | | Heroine onderhoud | +/- |
| Palliatieve zorg | Vermindering lijden | Levenskwaliteit | Methadone/heroine | |

# Alcohol

## Why is alcohol dependence treatment successful?

- It reduces level of consumption either to abstinence or by sizable reduction of heavy drinking

Typical risk curve for alcohol (e.g., liver cirrhosis mortality)

Relative gain in risk for mortality of reducing by three drinks/day for different levels of drinking

Roerecke & Rehm, 2013 Alc.Alc

Wat zijn goede outcome variabelen: totale abstinentie of reductie gebruik. Beide lijken waardevol

# Mental and Substance Use Disorders: High Prevalence/Huge Treatment Gaps

* No Treatment for SUD is defined as not receiving treatment at any location, such as a hospital (inpatient), rehabilitation facility (inpatient or outpatient), mental health center, emergency room, private doctor's office, self-help group, or prison/jail.

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CRITICAL REVIEW

ALCOHOL CLINICAL & EXPERIMENTAL RESEARCH

# Medications for treating alcohol use disorder: A narrative review

Henry R. Kranzler[1,2] | Emily E. Hartwell[1,2]

TABLE 2 Non-FDA-approved medications for treating alcohol use disorder.

| Medication | Nalmefene (oral formulation) | Baclofen | Gabapentin | Topiramate |
|---|---|---|---|---|
| Indication(s) | European Union: Help reduce alcohol consumption in adults with alcohol dependence who consume => 60 g (~4 drinks) per day (men) or > 40 g (~3 drinks/day; women). | To alleviate signs and symptoms of spasticity resulting from multiple sclerosis | Manage postherpetic neuralgia in adults and adjunctive therapy in treating partial seizures in patients aged 3 and older | Monotherapy for partial onset or primary generalized tonic–clonic seizures; adjunctive therapy for partial onset seizures or primary generalized tonic–clonic seizures and seizures associated with Lennox–Gastaut syndrome; migraine prophylaxis; weight loss and chronic weight management (combined with phentermine) |
| Dosage for AUD | Dosage approved in the European Union: 18 mg/day, as needed<br>Dosage in clinical trials: 5–80 mg/day in a single or twice daily dose | Dosage in clinical trials: 30–180 mg/day in up to four divided doses | Dosage in clinical trials: 600–1800 mg/day in three divided doses | Dosage in clinical trials: 75–300 mg/day in two divided doses |
| Effects | Meta-analysis of five RCTs ($N$ = 2567 participants; Palpacuer et al., 2018) showed a small effect on binge drinking at both 6 months and 1 year of treatment. Nalmefene was associated with a reduction in total alcohol consumption by 20% at 6 months. | A Cochrane meta-analysis of 12 RCTs ($N$ = 1128 participants; Minozzi et al., 2018) showed no difference between baclofen and placebo for return to any drinking, percentage of days abstinent or percentage of heavy drinking days. In a second meta-analysis of 13 RCTs ($N$ = 1492 participants; Pierce et al., 2018), baclofen was associated with a small-to-moderate effect on both the time to first drinking lapse and a likelihood of abstinence during treatment. The drug effect was evident at a dosage of ≤60 mg/day, with no effect at a higher dosage. | Meta-analysis of seven RCTs ($N$ = 751 participants; Kranzler et al., 2019) showed that for all six outcome measures effect estimates favored gabapentin over placebo, though only percentage of heavy drinking days was significant. | In a meta-analysis of seven RCTs ($N$ = 1125), there were small-to-medium effects of topiramate on abstinent days (Hedges' $g$ = 0.468) and binge drinking days (Hedges' $g$ = 0.406). |
| Most common adverse effects | Nausea (22.1%), dizziness (18.2%), insomnia (13.4%), headache (12.3%), vomiting (8.7%), fatigue (8.3%), somnolence (5.2%) (van den Brink et al., 2015) | With low-dose treatment (30 mg/day): drowsiness (39.1%), dizziness (26.4%), headache (25.3%), confusion (23.0%), muscle stiffness (16.1%), excessive perspiration (14.9%), itching/pruritis (14.9%), abnormal muscle movements (13.8%), numbness (12.6%), slurred speech (10.3%) (Hauser et al., 2017) | Dizziness (19.1%), somnolence (14.1%), ataxia or gait disorder (14.0%), peripheral edema (6.6%) (Wiffen et al., 2017) | Paresthesia (50.8%), dysgeusia (23.0%), anorexia (19.7%), difficulty with concentration/attention (14.8%), nervousness (14.2%), dizziness (11.5%), pruritis (10.4%) (Johnson et al., 2007). Transient mental slowing and modest reductions in verbal fluency and working memory are generally dose related (Smith et al., 2016) |
| Clinical notes | Not approved in the United States for treating AUD | Approved in France for use in the management of alcohol dependence at a maximum recommended dosage of 80 mg/day | Additional studies needed to validate medication effects | To reduce risk/severity of adverse effects, begin treatment at 25–50 mg/day, with increases of 25–50 mg/day at weekly intervals to a maximum of 200 mg/day.<br>Contraindicated in patients with a predisposition or history of metabolic acidosis, renal calculi, or angle-closure glaucoma. |

Abbreviations: NNT, number needed to treat; RCT, randomized clinical trial.
*Source*: Table adapted from Kranzler and Soyka (2018).





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TABLE 1 Medications approved by the US Food and Drug Administration (FDA) for treating alcohol use disorder.

| Medication | Disulfiram | Naltrexone | Extended-release naltrexone | Acamprosate |
|---|---|---|---|---|
| Indication | Management of selected chronic alcohol patients who want to remain in a state of enforced sobriety | Treatment of alcohol dependence | Treatment of alcohol dependence in outpatients who can abstain from alcohol | Maintenance of abstinence from alcohol in patients with alcohol dependence |
| FDA- Approved Dosage | 250–500 mg/day | 50 mg/day | 380 mg intramuscularly/month | 1998 mg/day |
| Dosage in clinical trials | 125–500 mg/day | Initially 25–50 mg/day with increases to 50–100 mg/day | 190 or 380 mg intramuscularly/month | 1000–3000 mg/day |
| Efficacy | In meta-analysis (Skinner et al., 2014; $N$ = 22 studies and 2414 subjects), open-label disulfiram treatment ($N$ = 15 studies) showed a medium-to-large effect on sustained abstinence from alcohol compared with control conditions. Blinded trials ($N$ = 7 studies) showed no effect of disulfiram. Large effect compared with control conditions when medication compliance was supervised ($N$ = 13 studies), but nonsignificant in unsupervised studies ($N$ = 9; Skinner et al., 2014) | Meta-analysis of placebo-controlled trials (Jonas et al., 2014; $N$ = 16 studies and 2347 subjects) showed a small effect of naltrexone 50 mg/day on the risk of any drinking (number needed to treat [NNT] = 20) and a small effect on the risk of binge drinking [$N$ = 19 studies and 2875 subjects (NNT = 12) | In the only published placebo-controlled trial of extended-release naltrexone (Garbutt et al., 2005), the median monthly number of binge drinking days declined from 19.3/month at baseline to 6.0/month in the placebo group, 4.5/month in the 190-mg group, and 3.1 in the 380-mg group. | Meta-analysis of placebo-controlled trials (Jonas et al., 2014; $N$ = 16 studies and 4847 subjects) showed a small effect on reducing the risk of any drinking among abstinent subjects (NNT = 12), but no significant effect on the likelihood of binge drinking. |
| Most common adverse effects | Moderate or severe drowsiness is most common; severe adverse events, which include hepatitis, neuropathy, optic neuritis, psychosis, and confusional states, are rare (Chick, 1999) | Somnolence, nausea, vomiting, decreased appetite, abdominal pain, insomnia, and dizziness (Rösner, Hackl-Herrwerth, Leucht, Vecchi, et al., 2010) | Same adverse events as oral naltrexone plus injection site reactions (swelling, pain, and induration) | Diarrhea was common, but the only adverse event that was more common with acamprosate than placebo (Rösner, Hackl-Herrwerth, Leucht, Lehert, et al., 2010) |
| Clinical notes | Should only be used in patients who are aware of the potential for adverse effects and who have a goal of complete abstinence from alcohol | Can block the effects of opioid analgesics and precipitate withdrawal in a patient physically dependent on opioids | Can block the effects of opioid analgesics and precipitate withdrawal in a patient physically dependent on opioids | Not metabolized (renally excreted), so can be used in patients with hepatic disease |

Abbreviations: NNT, number needed to treat; RCT, randomized clinical trial.
*Source*: Table adapted from Kranzler and Soyka (2018).



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Samenvattend: farmacologische mogelijkheden behandeling alcohol uitgebreid !
Echter, slechts 10% van de mensen komen in behandeling en daarvan krijgt slechts ongeveer 10-20% farmacologie aangeboden…!!Treatment gap !!

# Behandeling: Algemene principes

- Herstelondersteunende zorg
- Biopsychosociaal model
  - Biologisch
    - Adequaat behandelen verslaving, co-morbiede psychiatrische stoornis en somatiek
  - Psychologisch
    - Motiverende gespreksvoering
    - ACT
    - Contingency management
    - Groepsbehandeling vaardigheden/terugvalpreventie
  - Sociaal
    - Betrekken familie, uitbreiden netwerk
    - Community Reinforcement Approach

# Behandeling: Algemene principes

- Belang van zorgcontinuïteit, casemanager, ZAG
- Gedeelde visie/behandelplan
- Therapeutische relatie
- Langdurig, weinig evidentie voor kortdurende programma’s
- Actieve benadering, aanklampend
- Op maat (motivationeel proces)

# Behandeling: Algemene principes

- Over het algemeen is geïntegreerde intensieve (ambulante) behandeling van dubbele diagnose geïndiceerd, meerwaarde van een klinische behandeling dient nog te worden aangetoond
- Verslaving is een onafhankelijk psychiatrisch ziektebeeld dat behandeling behoeft naast de behandeling van de andere psychiatrische problematiek.
- Behandelen van de psychiatrische problematiek alleen heeft doorgaans weinig invloed op het verloop van het verslavingsprobleem
- Er zijn wel aanwijzingen dat het behandelen van een verslavingsprobleem een significante invloed heeft op het beloop van de psychiatrische problematiek.
- Na behandeling van een verslavingsprobleem zijn diagnoses als depressie, angststoornis of borderline persoonlijkheidsstoornis soms niet meer van toepassing

# Behandeling: Algemene principes

- Voor veel dubbeldiagnosepatiënten zijn kleine hoeveelheden drugs of alcohol al ontregelend. Abstinentie is daarom een goed behandeldoel, zij het soms op lange termijn.
- Voorkomen moet worden dat de patiënt het contact met de hulpverlening verbreekt omdat er ten aanzien van het MM te hoge eisen worden gesteld
- Motiverende gespreksvoering heeft altijd een plaats in het behandelaanbod, ongeacht het stadium van motivatie van de patiënt.

# Wanneer opname nodig?

- Mogelijke criteria
  - Type van drug
  - Kans op ontwenningssymptomen, delier of E insult in VG
  - Ernst van gebruik (hoeveelheid, frequentie)
  - Verwante somatische, psychiatrische, cognitieve en sociale problemen
  - Eerdere ontwenningen (verloop, niet succesvol afronden detox)
  - Polygebruik met meervoudige detoxificatie
  - Agressie in VG
  - Netwerk
  - Zwangerschap