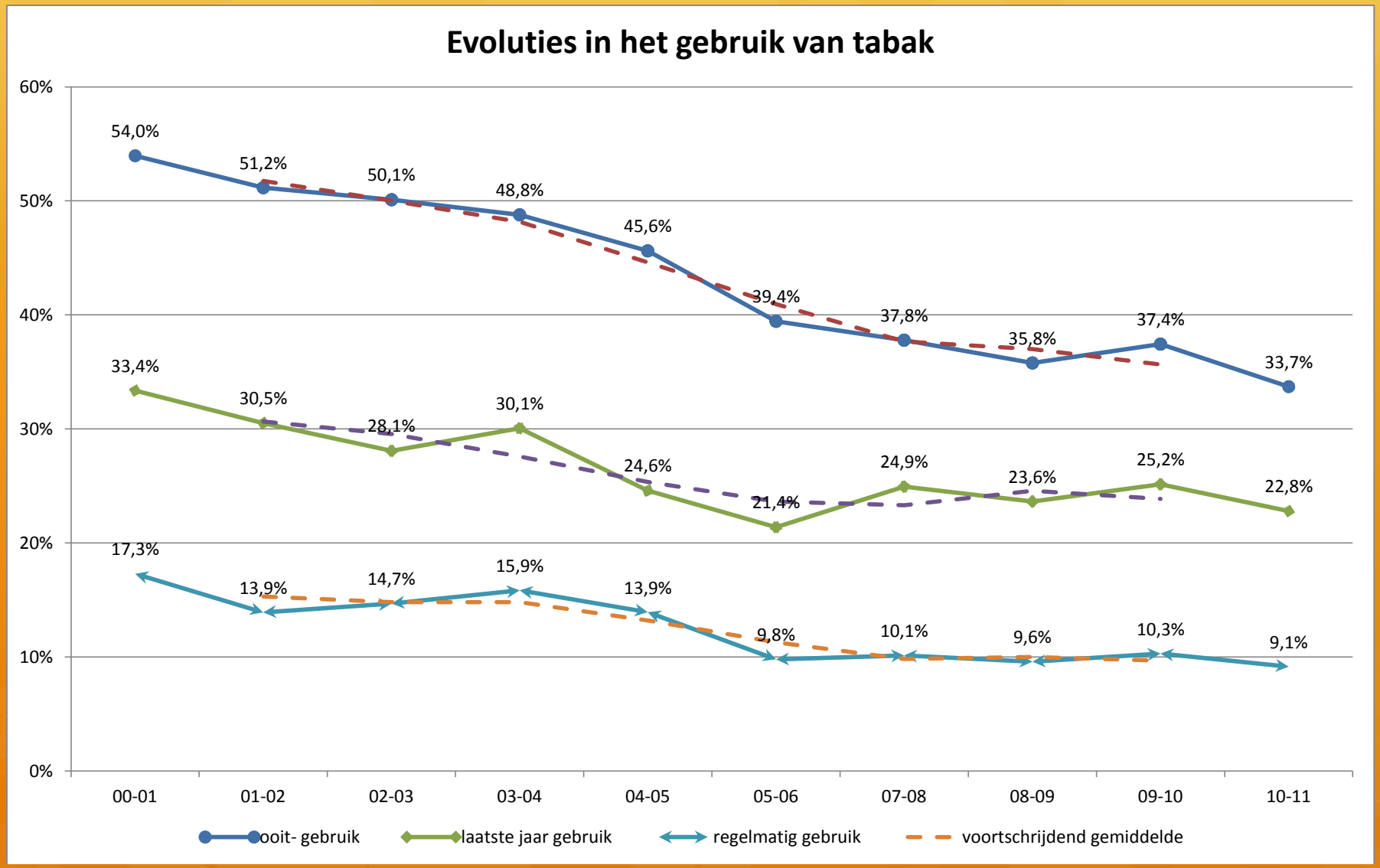
Alcoholproblemen: hoe verder ?

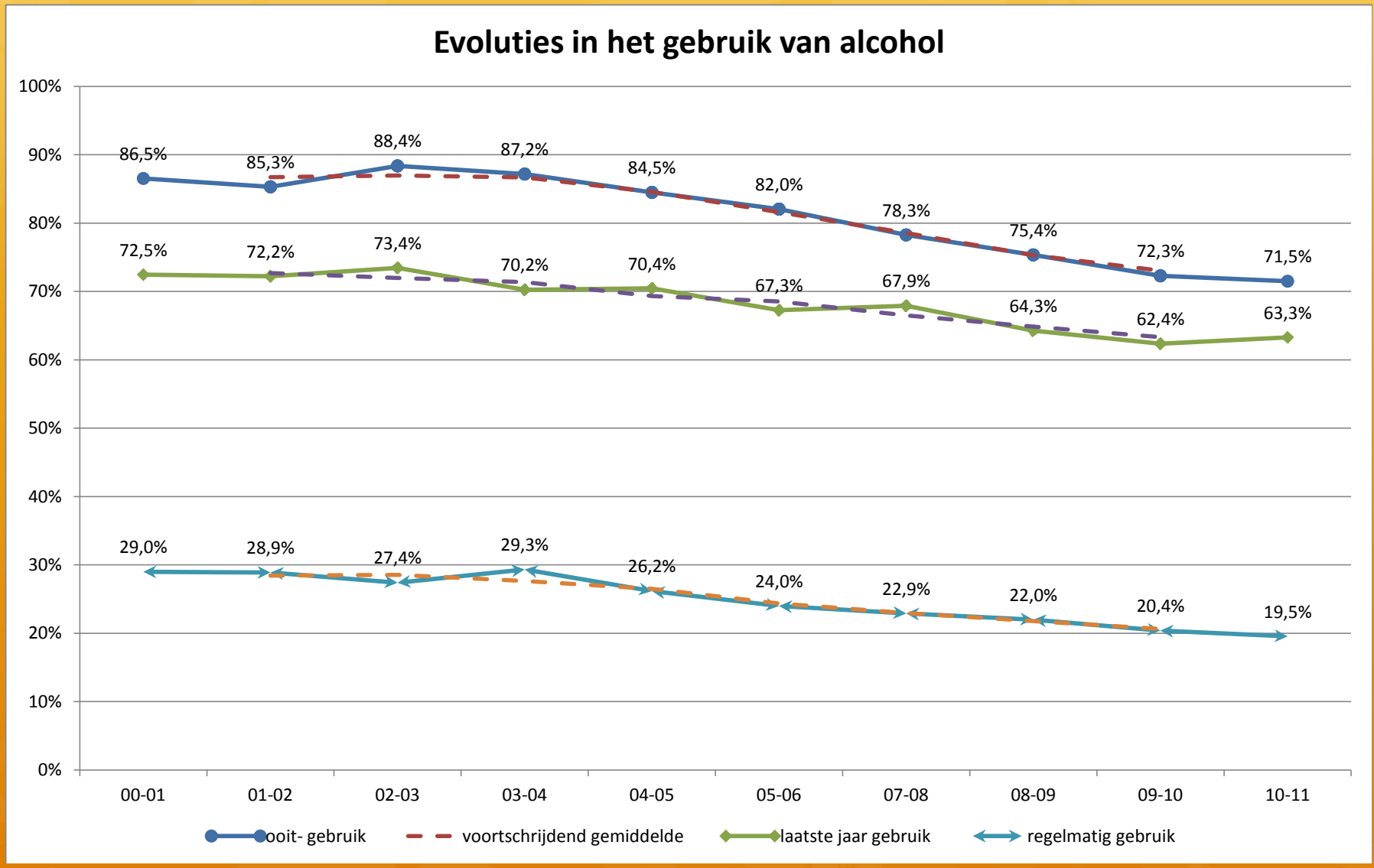
Breinwijzer 07-03-2013

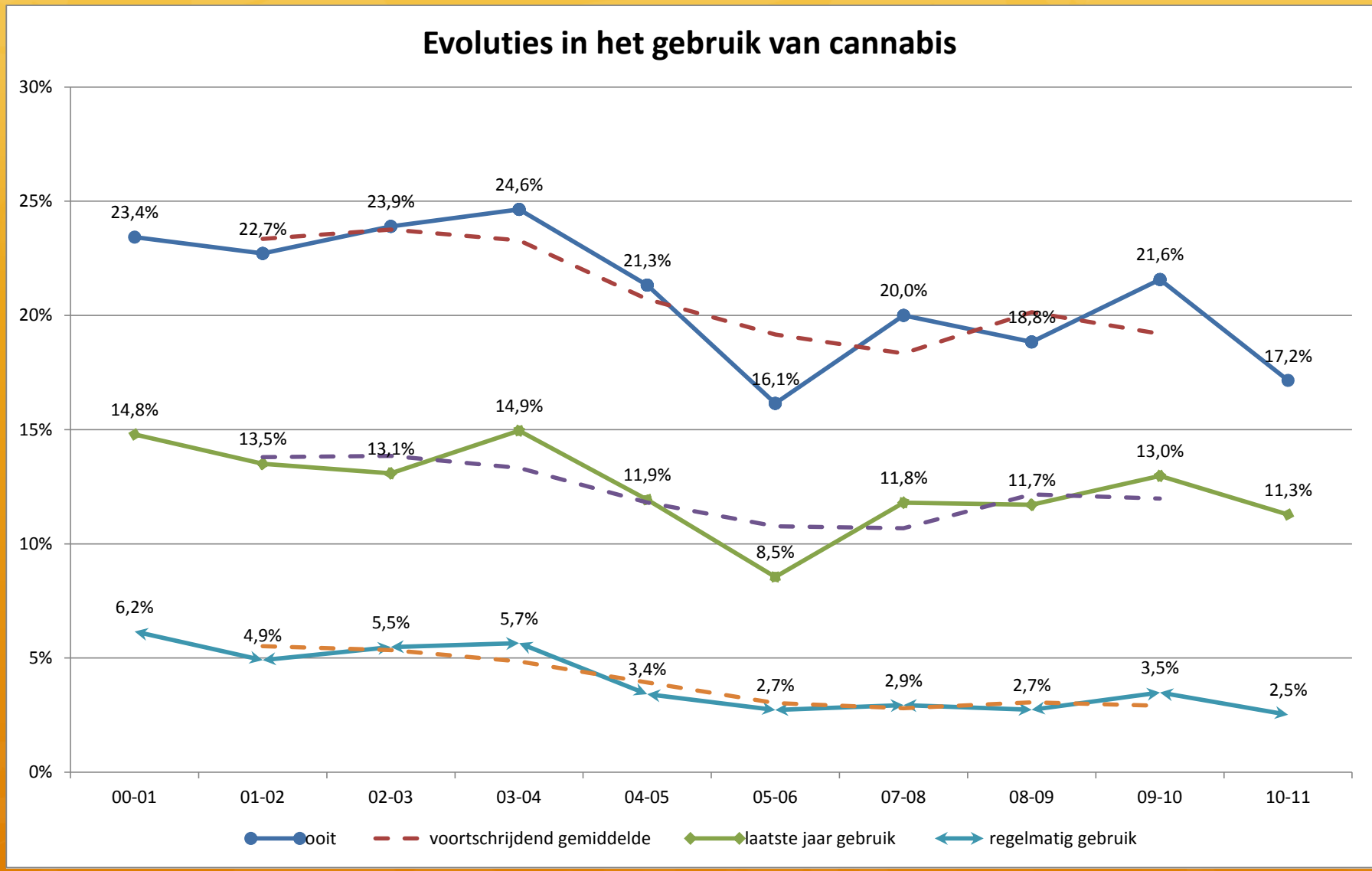
presentatie

- Alcohol gebruik: nadelen en voordelen.
- Behandelingen:
- Natuurlijk verloop
- Effectiviteit
- Huidige behandelingen en hoe die te verbeteren.
- De toekomst:
- besluit

Goed nieuws ;-)

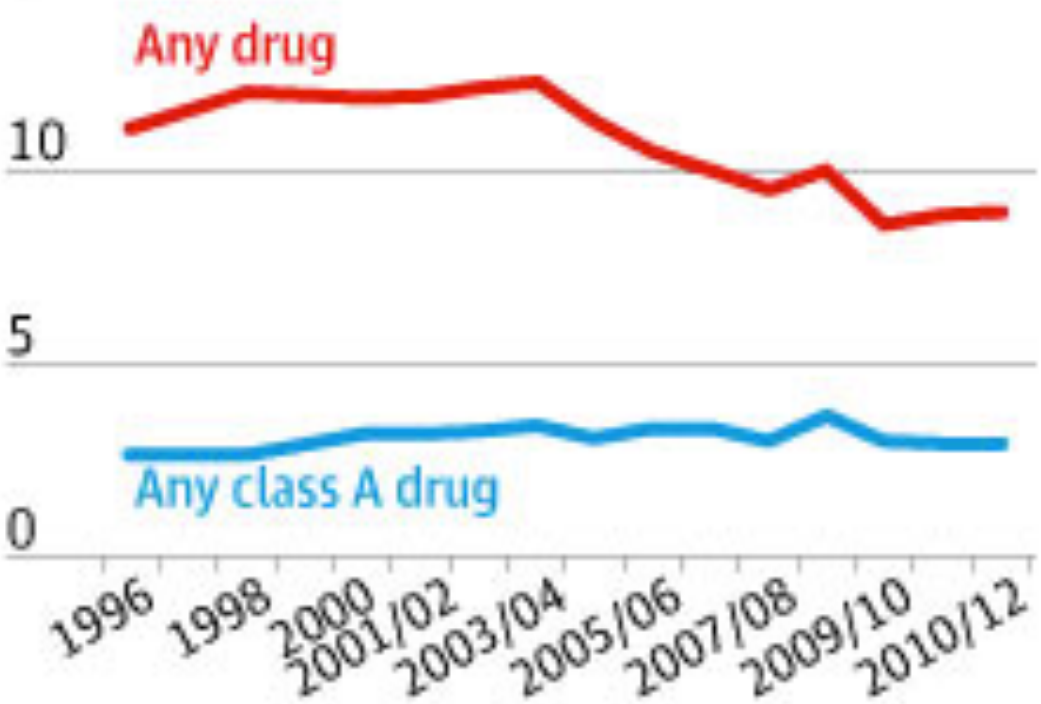

Evoluties in het gebruik van tabak
60%
50%
40%
30%
20%
10%
0%
54,0%
51,2%
50,1%
48,8%
45,6%
39,4%
37,8%
35,8%
37,4%
33,7%
33,4%
30,5%
28,1%
30,1%
24,6%
21,4%
24,9%
23,6%
25,2%
22,8%
17,3%
13,9%
14,7%
15,9%
13,9%
9,8%
10,1%
9,6%
10,3%
9,1%
00-01
01-02
02-03
03-04
04-05
05-06
07-08
08-09
09-10
10-11
ooit- gebruik
laatste jaar gebruik
regelmatig gebruik
voortschrijdend gemiddelde


Evoluties in het gebruik van alcohol
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
86,5%
85,3%
88,4%
87,2%
84,5%
82,0%
78,3%
75,4%
72,3%
71,5%
72,5%
72,2%
73,4%
70,2%
70,4%
67,3%
67,9%
64,3%
62,4%
63,3%
29,0%
28,9%
27,4%
29,3%
26,2%
24,0%
22,9%
22,0%
20,4%
19,5%
00-01
01-02
02-03
03-04
04-05
05-06
07-08
08-09
09-10
10-11
ooit- gebruik
voortschrijdend gemiddelde
laatste jaar gebruik
regelmatig gebruik


Evoluties in het gebruik van cannabis
30%
25%
20%
15%
10%
5%
0%
23,4%
22,7%
23,9%
24,6%
21,3%
16,1%
20,0%
18,8%
21,6%
17,2%
14,8%
13,5%
13,1%
14,9%
11,9%
8,5%
11,8%
11,7%
13,0%
11,3%
6,2%
4,9%
5,5%
5,7%
3,4%
2,7%
2,9%
2,7%
3,5%
2,5%
00-01
01-02
02-03
03-04
04-05
05-06
07-08
08-09
09-10
10-11
ooit
voortschrijdend gemiddelde
laatste jaar gebruik
regelmatig gebruik

Illicit drug use

Among adults 16 to 59, England and Wales, %



SOURCE: HOMEOFFICE

- Slecht nieuws ;-((

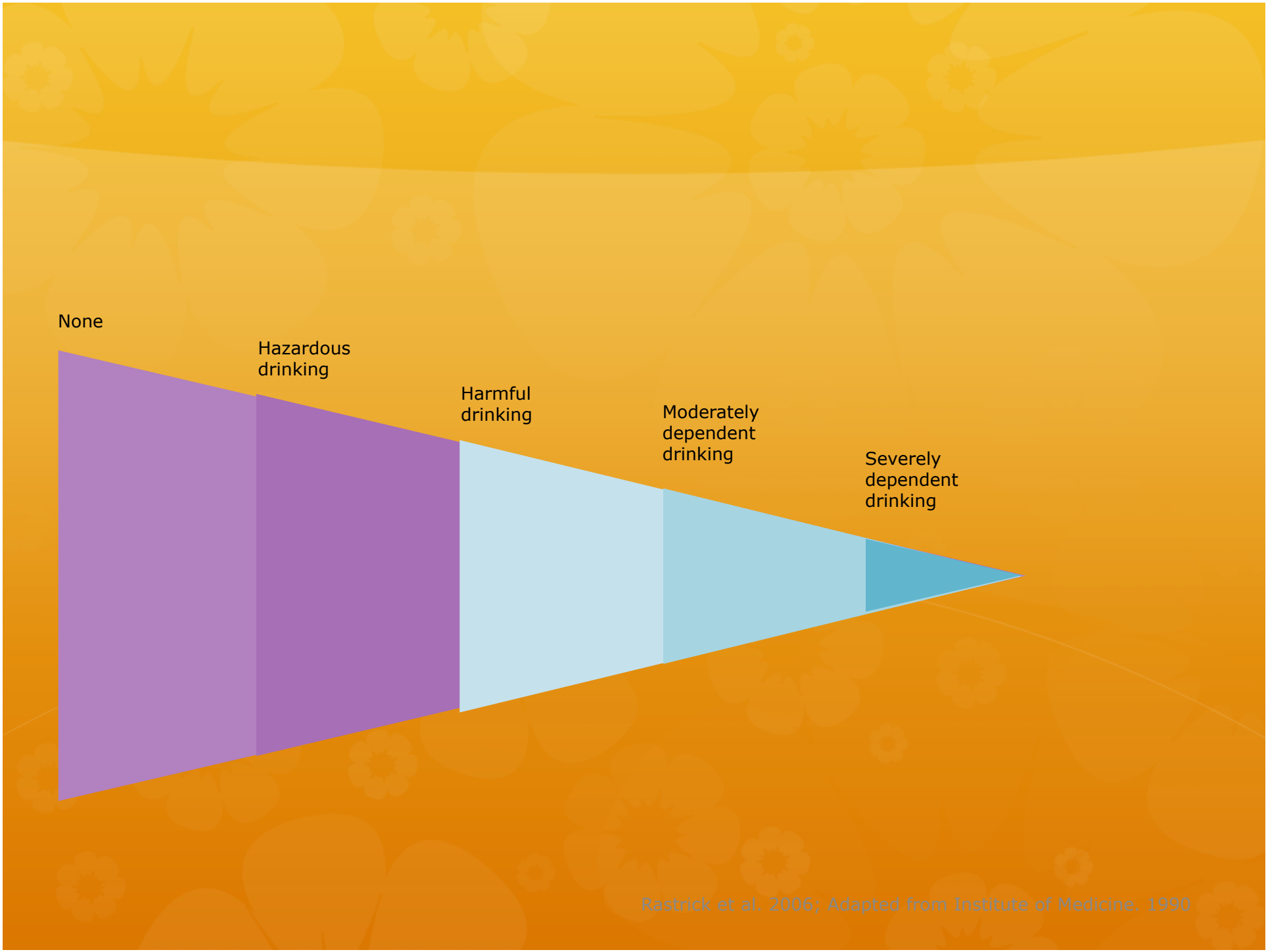
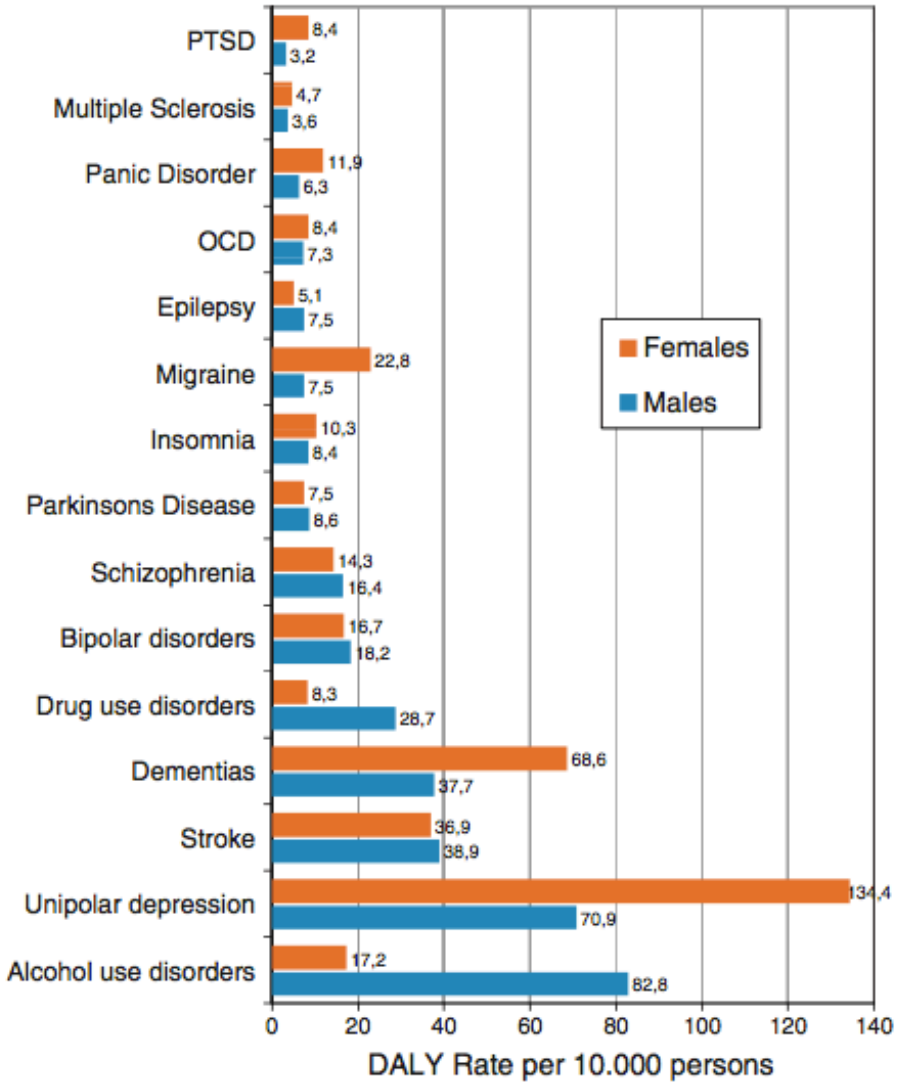

None
Hazardous drinking
Harmful drinking
Moderately dependent drinking
Severely dependent drinking
Rastrick et al. 2006; Adapted from Institute of Medicine. 1990

Table 4 Comparison of 2005 and 2011 estimates and overall number of cases affected by mental disorders in the EU (in millions).

	Prevalence estimate		No. of persons affected	
	2005	2011	2005	2011
	% (95% CI)	%	Million	Million
Group A: 2005 report diagnoses				
Alcohol dependence	2.4 (0.2–4.8)	3.4	7.2 (5.9–8.6)	14.6
Opioid dependence (*drug dep*)	*0.5 (0.1–0.6)*	0.1–0.4	2.0 (1.5–2.2)	1.0
Cannabis dependence (*drug dep*)	*See above*	0.3–1.8	*See above*	1.4
Psychotic disorders	0.8 (0.2–2.0)	1.2	3.7 (2.8–5.4)	5.0
Major depression	6.9 (4.8–8.0)	6.9	18.4 (17.2–19)	30.3
Bipolar disorder	0.9 (0.5–0.9)	0.9	2.4 (1.7–2.4)	3.0
Panic disorder	1.8 (0.7–2.2)	1.8	5.3 (4.3.–5.3)	7.9
Agoraphobia	1.3 (0.7–2.0)	2.0	4.0 (3.3–4.7)	8.8
Social phobia	2.3 (1.1–4.8)	2.3	6.7 (5.4–9.3)	10.1
Generalized anxiety dis.	1.7 (0.8–2.2)	1.7–3.4	5.9 (5.3–6.2)	8.9
Specific phobias	6.4 (3.4–7.6)	6.4	18.5 (14.4–18.6)	22.7
OCD	0.7 (0.5–1.1)	0.7	2.7 (2.5–3.1)	2.9
PTSD	–	1.1–2.9	–	7.7
Somatoform disorders [d]	6.3 (2.1–7.8)	4.9	18.9 (12.7–21.2)	20.4
Anorexia nervosa *(eating dis.)*	*0.4 (0.3–0.7)*	0.2–0.5	1.2 (1.0–1.7)	0.8
Bulimia nervosa *(eating dis.)*	*See above*	0.1–0.9	*See above*	0.7
Subtotal any Group A	27.4%	27.1%	82.7	118.1
Group B: additional 2011 diagnoses				
Borderline personality dis [a]	–	*0.7*	–	*2.3*
Dissocial personality dis [a]	–	*0.6*	–	*2.0*
Hyperkinetic dis./ADHD [b]	–	(5.0) 0.6	–	3.3
Pervasive dev. dis./autism	–	0.6	–	0.6
Conduct disorders [b]	–	(3.0) 0.4	–	2.1
Mental retardation	–	1.0	–	4.2
Insomnia [c]	–	(7.0) 3.5	–	(29.1) 14.6
Hypersomnia	–	0.8	–	3.1
Narcolepsy	–	0.02	–	0.1
Sleep apnoea	–	3.0	–	12.5
Dementias [b]	–	(5.4) 1.2	–	6.3
Total any Group B	–	*27.1*		*51.0*
Subtotal any adjusted	–	11.1%	–	46.7
Total A and B	**27.4%**	**38.2%**	**82.7**	**164.8**



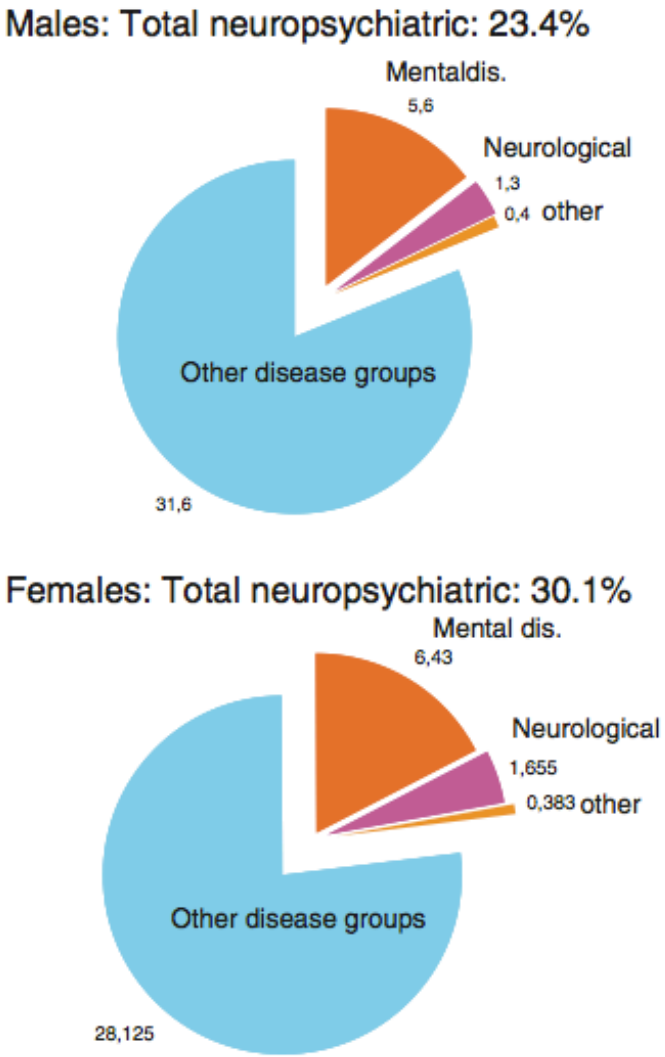


Fig. 2 Summary of DALY estimates.

Alcohol gevolgen

Voordelen

- Sociaal
- Gastronomisch
- Cardiovasculair J-curve
- ?cognitief

Nadelen

- Sociaal
- Maatschappelijk: werk/ criminaliteit/agressie/..
- Psychiatrisch: suicide/ depressie/zelfdestructief/…
- Lichamelijk:

Complications of and associations with alcohol misuse

Physical complications

Gastroenterological disorders

- Alcoholic liver disease – fatty liver, alcoholic hepatitis, cirrhosis
- Pancreatitis
- Gastric and peptic ulceration
- Mallory–Weiss syndrome

Musculoskeletal disorders

- Gout
- Osteoporosis
- Avascular necrosis
- Acute and chronic skeletal muscle myopathy

Endocrine disorders

- Alcohol-induced pseudo-Cushing's syndrome
- Male hypogonadism
- Increased risk of infertility
- Diabetes

Cancer

- Increased risks of oropharyngeal, laryngeal, oesophageal, liver, breast and colorectal cancer

Cardiovascular

- Arrhythmias
- Hypertension
- Cerebrovascular disease
- Coronary heart disease
- Alcoholic cardiomyopathy

Respiratory

- Immune suppression and self-neglect lead to greater incidence of lower respiratory tract infections
- Inhalation of vomit while in stupor may result in pneumonia, with bronchiectasis as a possible sequela

Metabolic

- Hypoglycaemia

Neurological

- Seizures
- Neuropathy
- Marchiafava–Bignami syndrome
- Central pontine myelinosis
- Alcoholic cerebellar degeneration

Skin

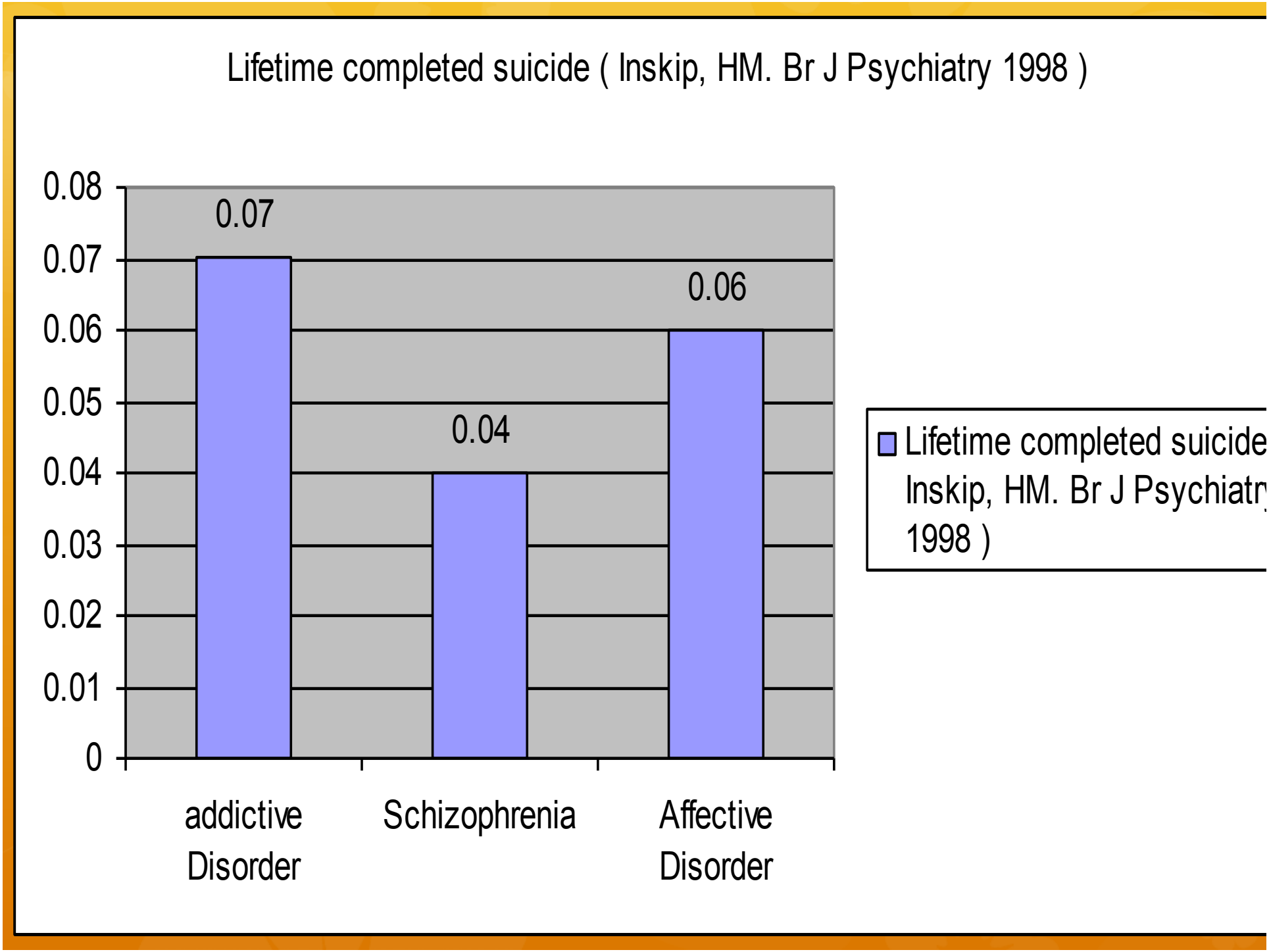
- Psoriasis
- Discoid eczema
- Rosacea

Neuropsychiatric complications

- Transient hallucinatory experiences
- Alcoholic hallucinosis
- Wernicke–Korsakoff syndrome
- Alcoholic dementia
- Delirium tremens

Co-morbid disorders

- Depression
- Anxiety
- Post-traumatic stress disorder
- Psychotic disorders (e.g. schizophrenia)
- Bipolar disorder
- Personality disorder
- Eating disorders
- Other substance abuse


Lifetime completed suicide (Inskip, HM. Br J Psychiatry 1998)
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0.07
0.04
0.06
addictive Disorder
Schizophrenia
Affective Disorder
Lifetime completed suicide Inskip, HM. Br J Psychiatr 1998)

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Sleep apnoea	–	3.0	–	12.5
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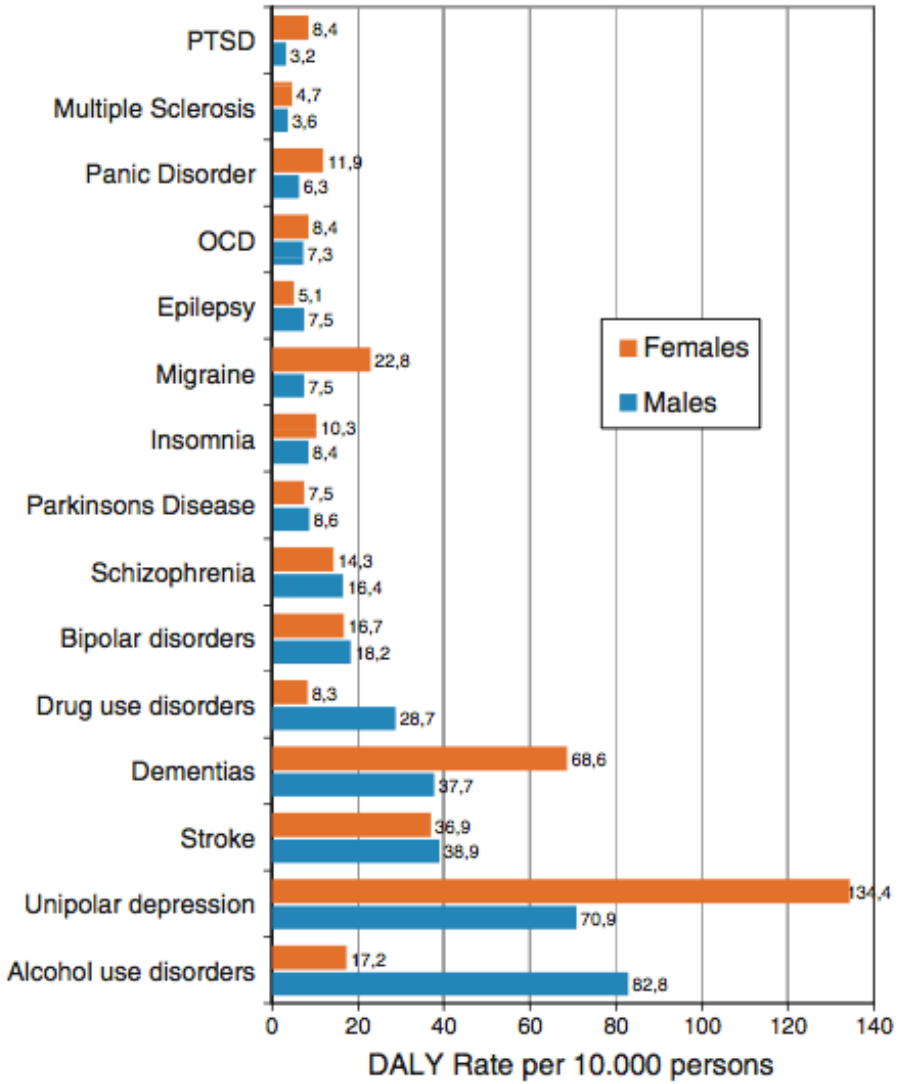


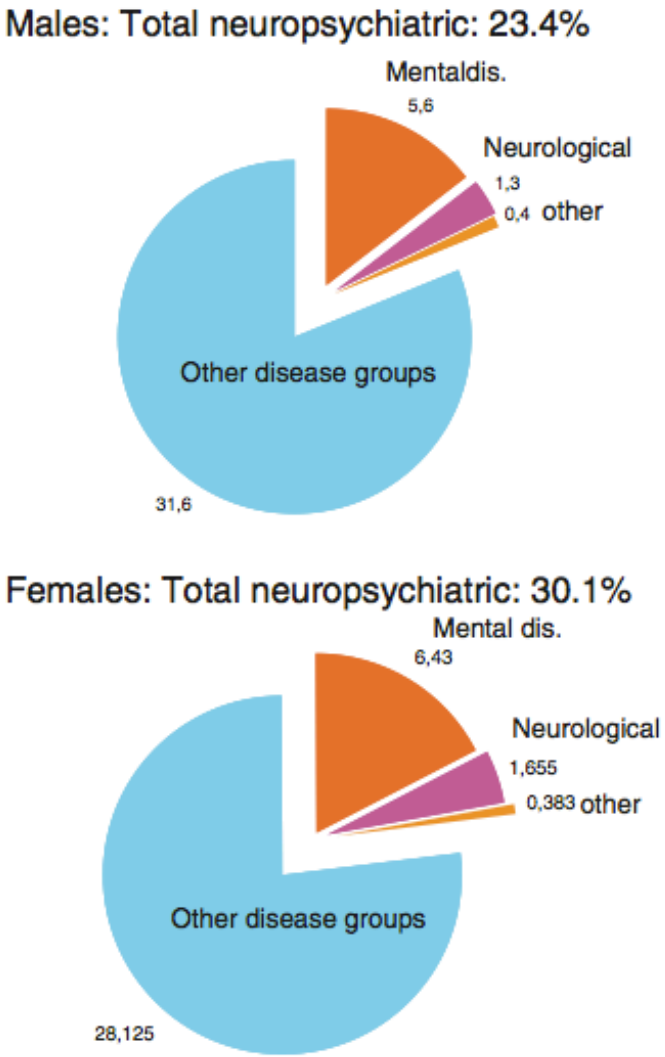


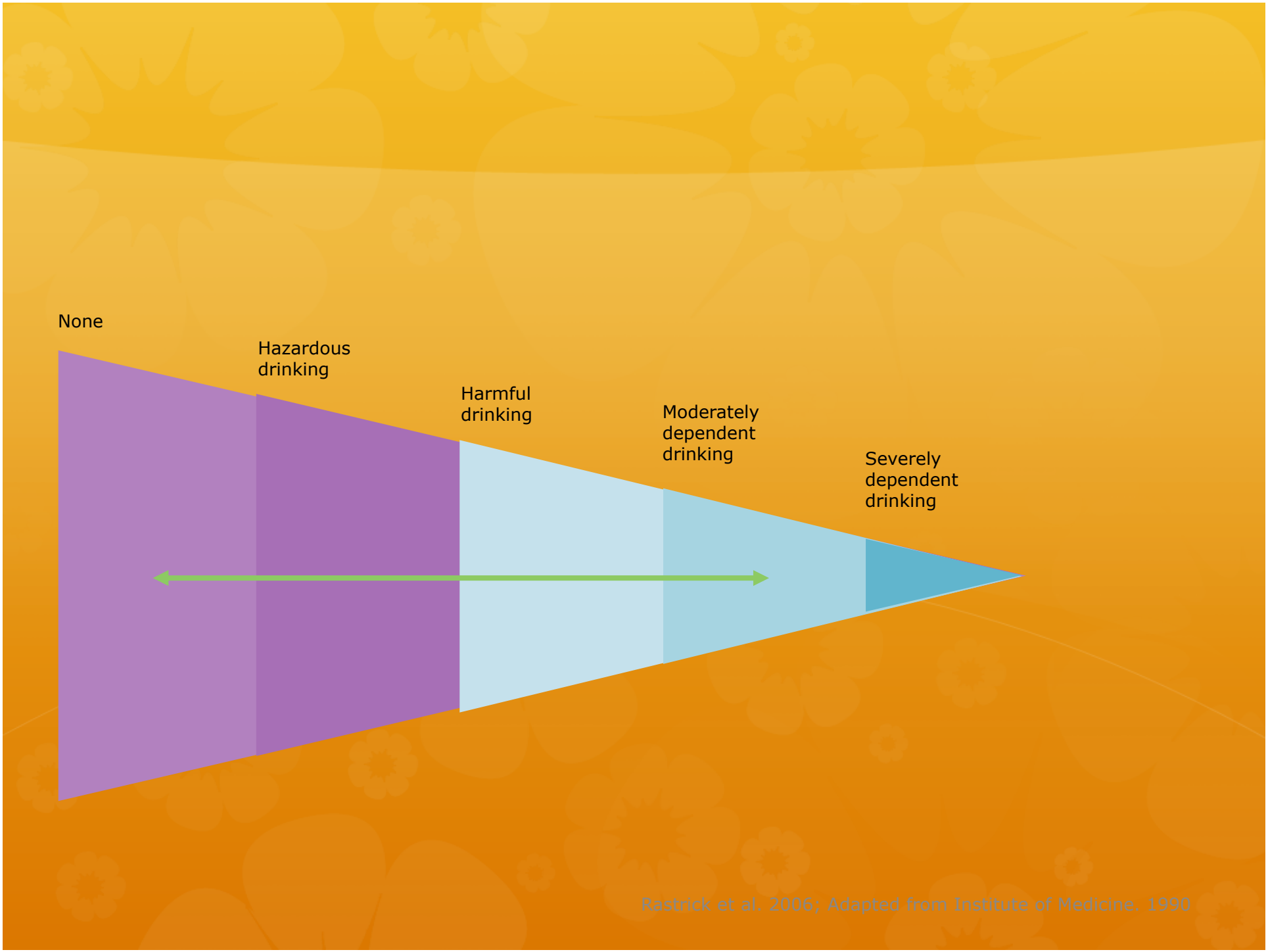
Fig. 2 Summary of DALY estimates.

Alcohol problemen

verloop

Probleem !!

- Verloop alcohol problematiek binnen de algemene bevolking….
- Is heel anders dan van diegenen die in behandeling zijn….


None
Hazardous drinking
Harmful drinking
Moderately dependent drinking
Severely dependent drinking
Rastrick et al. 2006; Adapted from Institute of Medicine. 1990

The three year course of alcohol use disorders in the general population: DSM-IV, ICD-10 and the Craving Withdrawal Model

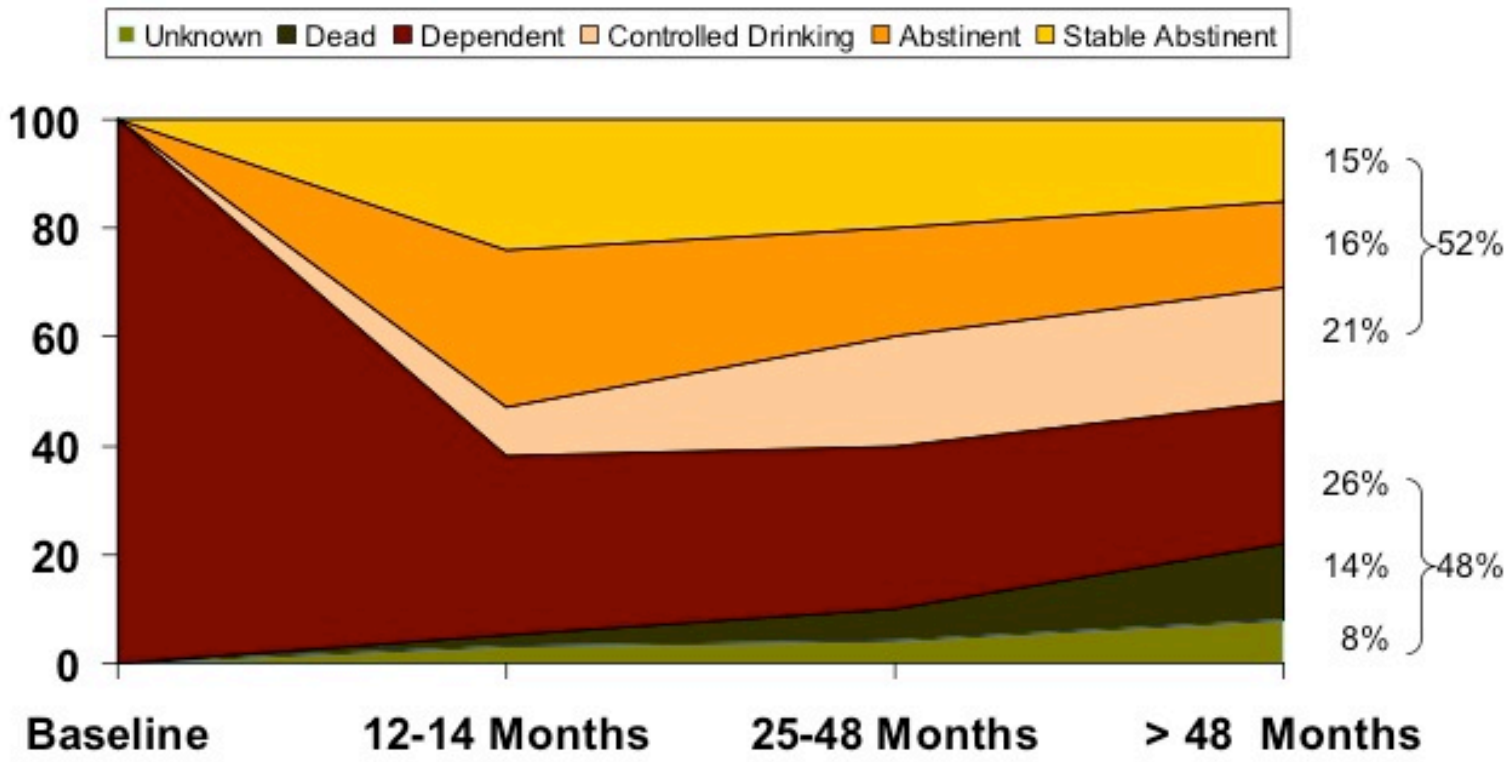
Carla de Bruijn[1], Wim van den Brink[2,3], Ron de Graaf[4] & Wilma A. M. Vollebergh[4]

University Medical Centre Utrecht, Department of Psychiatry Utrecht, the Netherlands,[1] Academic Medical Centre, Department of Psychiatry Amsterdam, the Netherlands,[2] Amsterdam Institute for Addiction Research, Amsterdam, the Netherlands[3] and Netherlands Institute of Mental Health and Addiction, Utrecht, the Netherlands[4]

Algemene Bevolking	Remissie		Terugval
	1 Jaar FU	3 Jaar FU	2 Jaar FU
DSM-IV Alcohol Misbruik	81%	85%	10%
ICD-10 Schadelijk gebruik	89%	92%	4%
DSM-IV Alcoholafhankelijkheid	67%	74%	14%

Diagnose/Beloop Alcohol

Schippers en Broekman, 2006

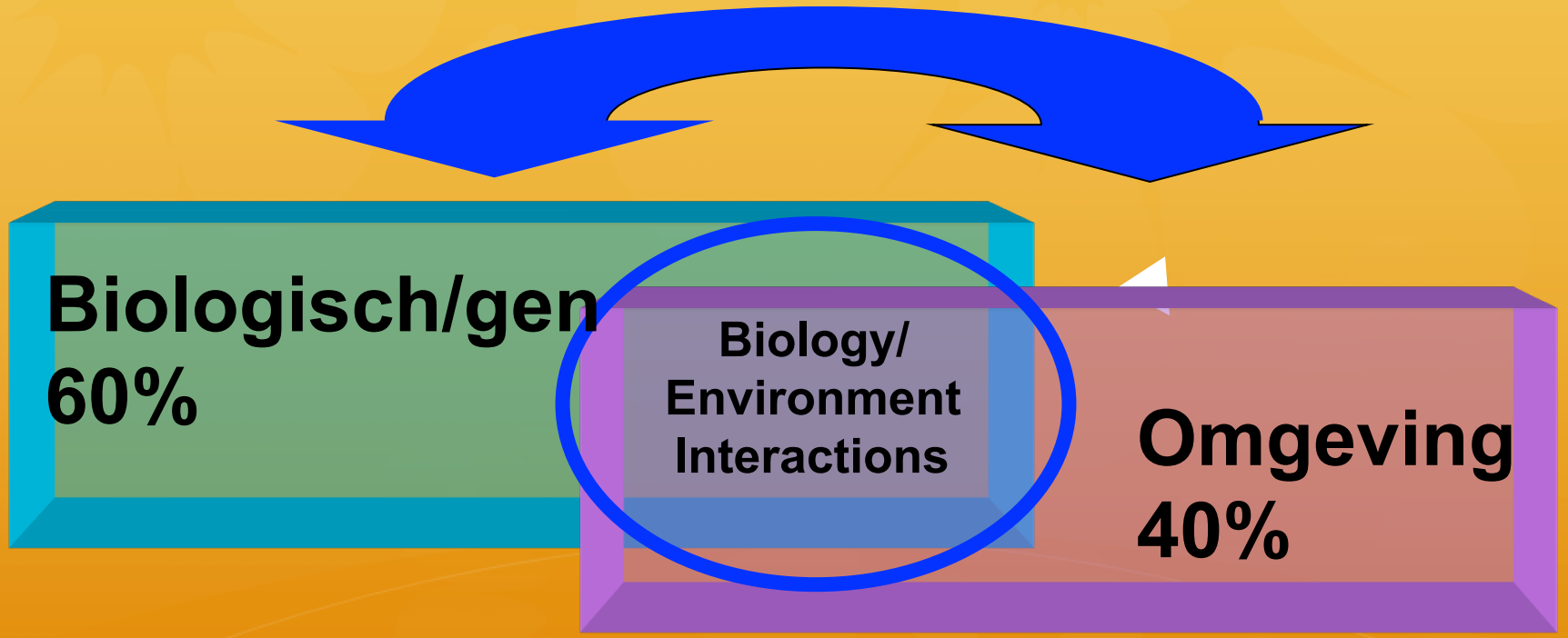


Alcohol afhankelijkheid kan een dodelijke ziekte zijn.

- Park et al., 2013, opvolging patienten na opname voor alcohol behandeling:
- 29% overlijden tijdens studie periode (vooral ten gevolge van lever problemen).
- = risico van overlijden vergeleken met de algemene bevolking sterk verhoogd: x7,12 voor mannen,x 2,62 voor vrouwen.

verslaving

Een complexe, genetische problematiek


Biologisch/gen
60%
Biology/
Environment
Interactions
Omgeving
40%

Heritability Of Psychiatric Disorders

Heritability	Psychiatric Disorders	Other Important Familial Traits
~zero		Language Religion
20-40%	Anxiety disorders, Depression, Bulimia, Personality Disorders	Myocardial Infarction, Normative Personality, Breast Cancer, Hip Fracture
40-60%	Alcohol Dependence Drug Dependence	Blood Pressure, Asthma Plasma cholesterol, Prostate Cancer, Adult-onset diabetes
60-80%	Schizophrenia Bipolar Illness	Weight, Bone Mineral Density
80-100%	Autism	Height, Total Brain Volume

Rates of alcoholism among adoptees with and without biological alcoholic parents

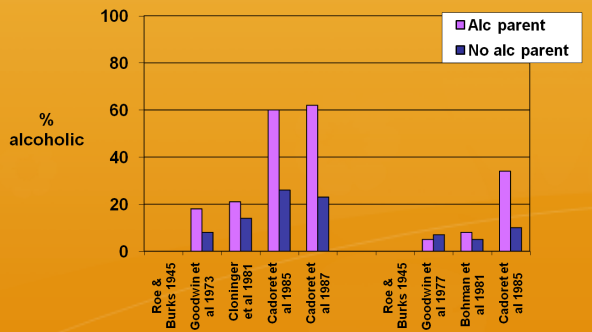


Figure 1,
Prescott, Maes & Kendler, 2005

Studies of male adoptees

Studies of female adoptees

Agrawal & Linskey, 2008 erfelijkheid verslaving

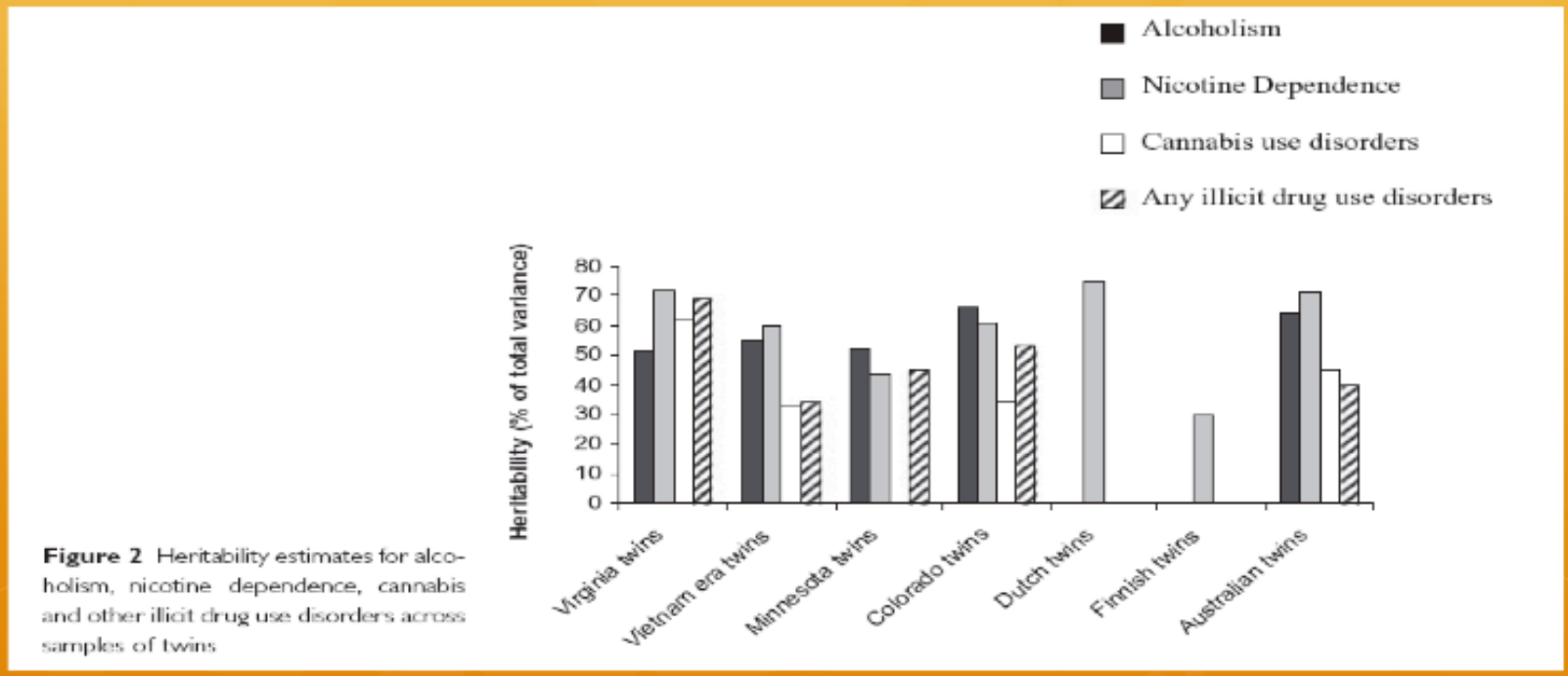
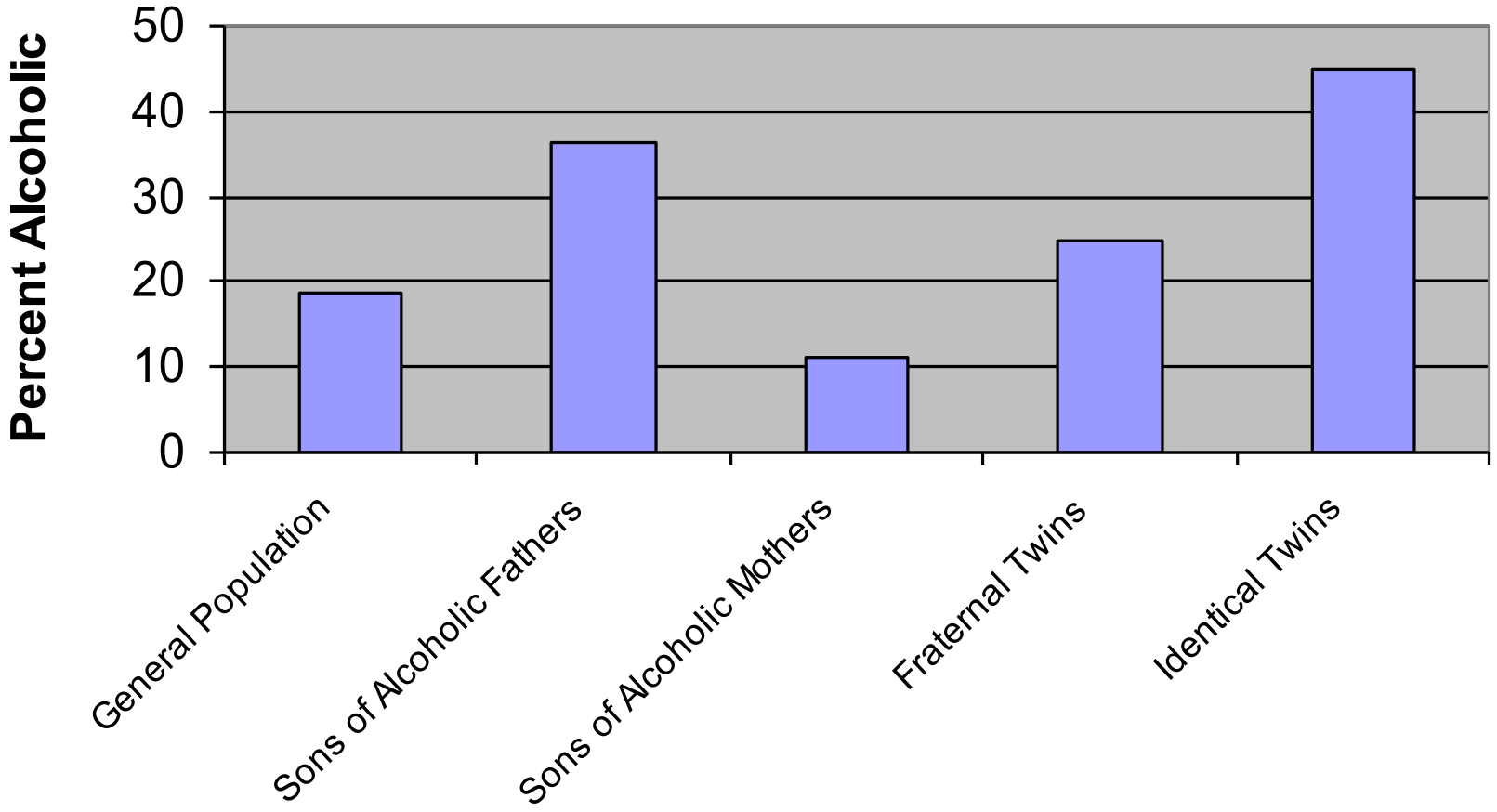


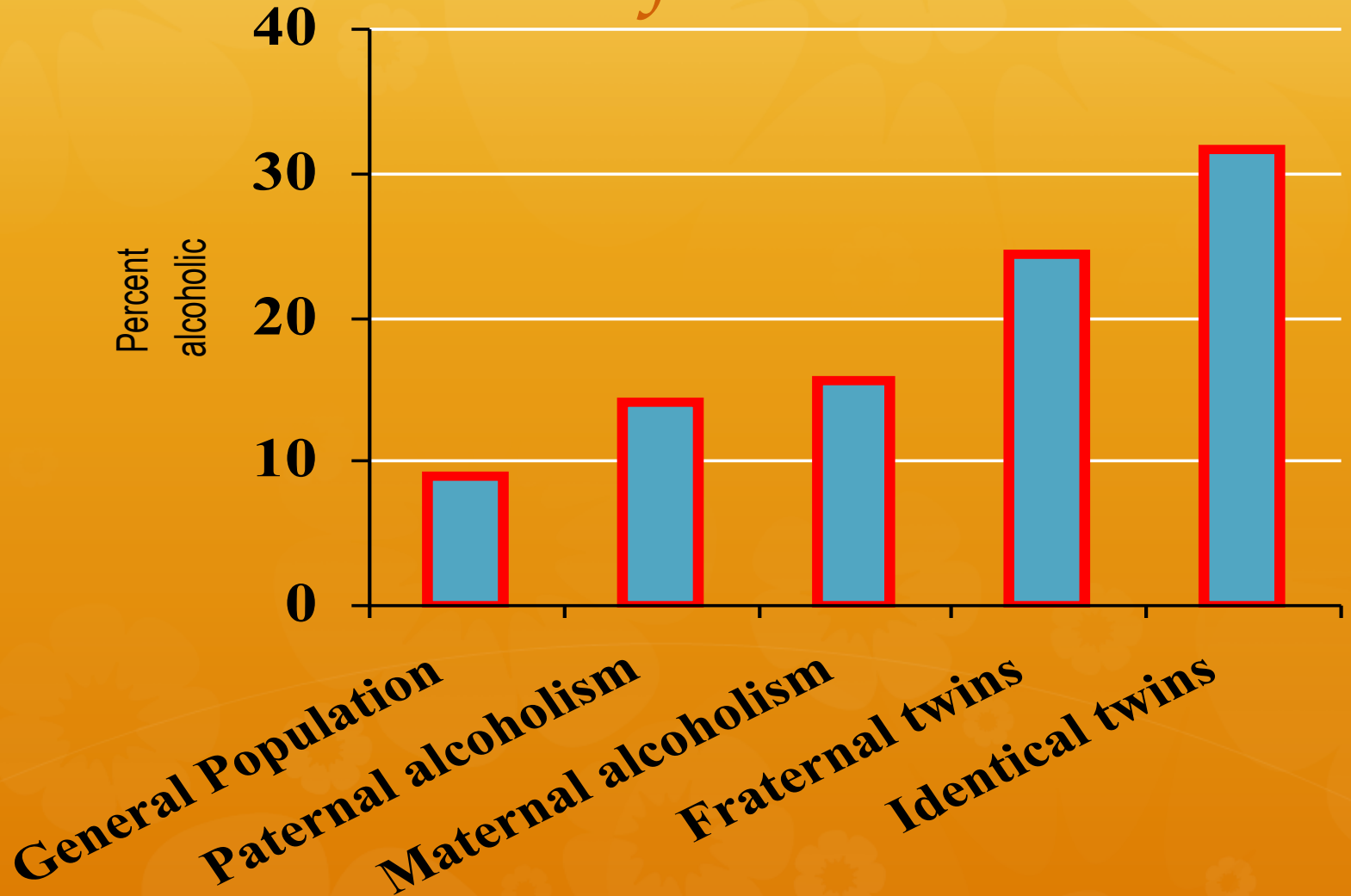
Figure 2 Heritability estimates for alcoholism, nicotine dependence, cannabis and other illicit drug use disorders across samples of twins

Genetische bijdrage	alcohol afhankelijkheid	50-70%
	nicotine afhankelijkheid	50-75%
	cannabis afhankelijkheid	35-75%
	cocaine afhankelijkheid	35-80%
	heroine afhankelijkheid	40-60%

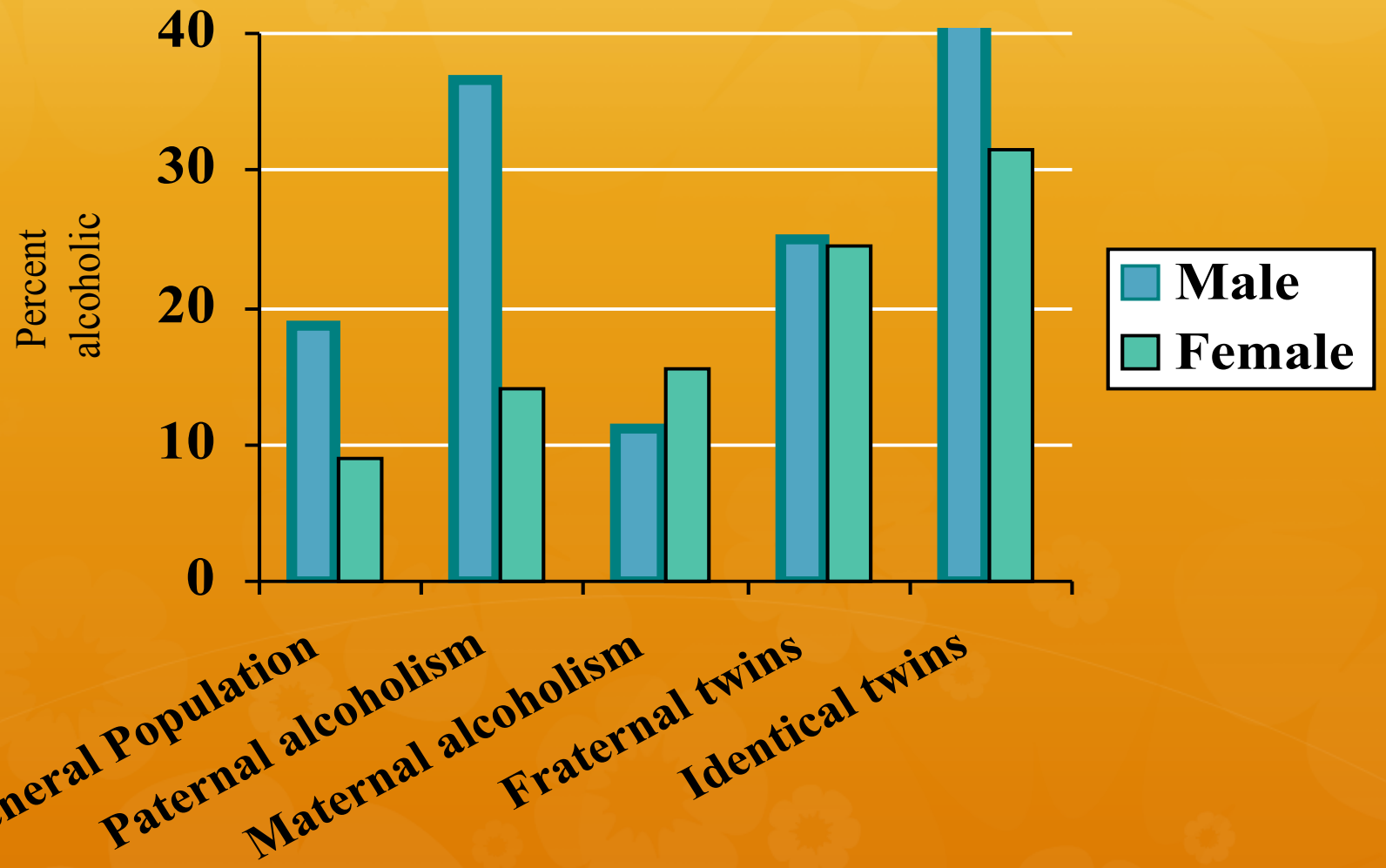
Estimated Rate of Alcoholism in Men Among Relatives of an Alcoholic



Alcoholism among Female Relatives of an Alcoholic

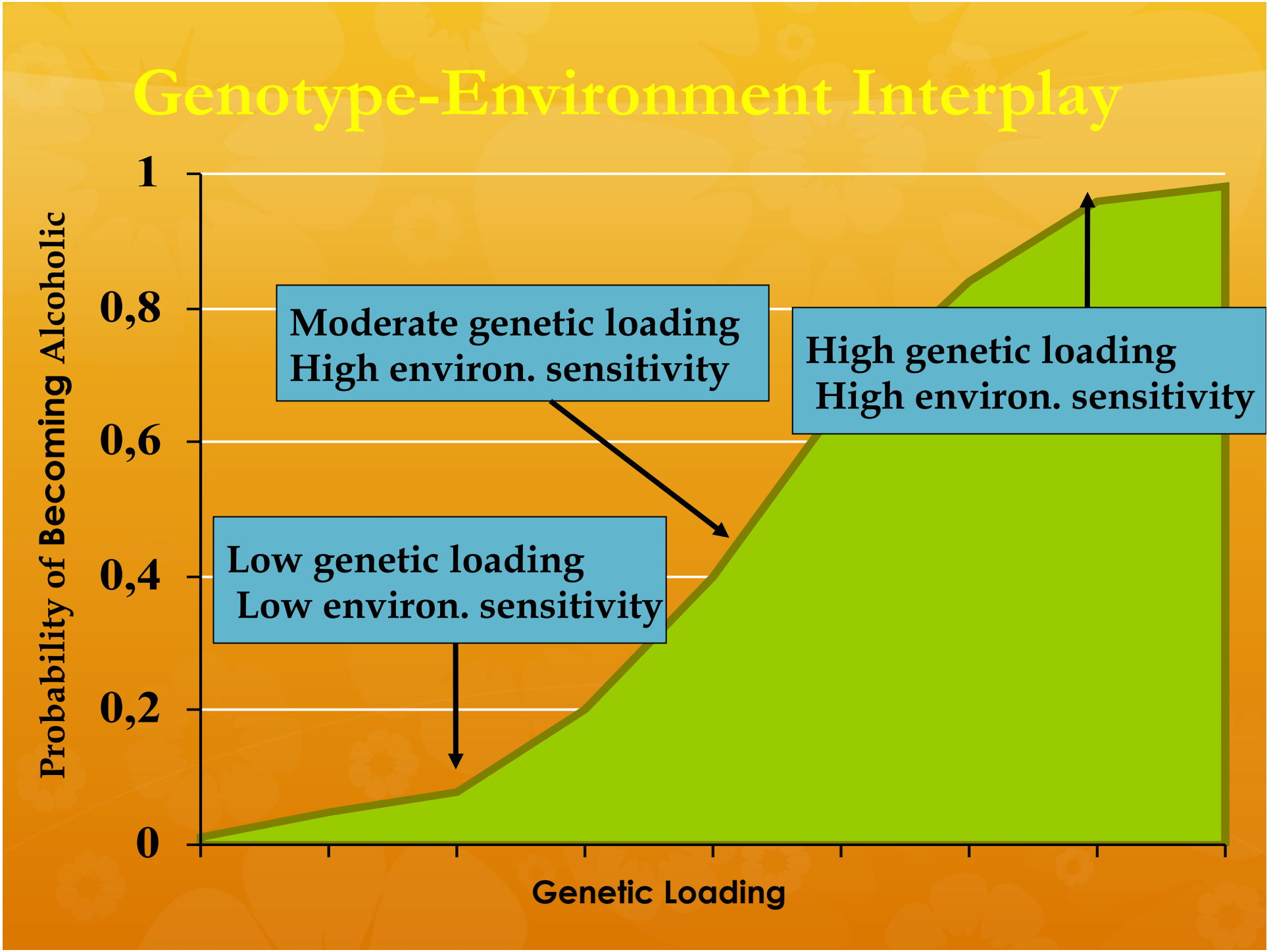


Alcoholism among Relatives of Alcoholic Probands

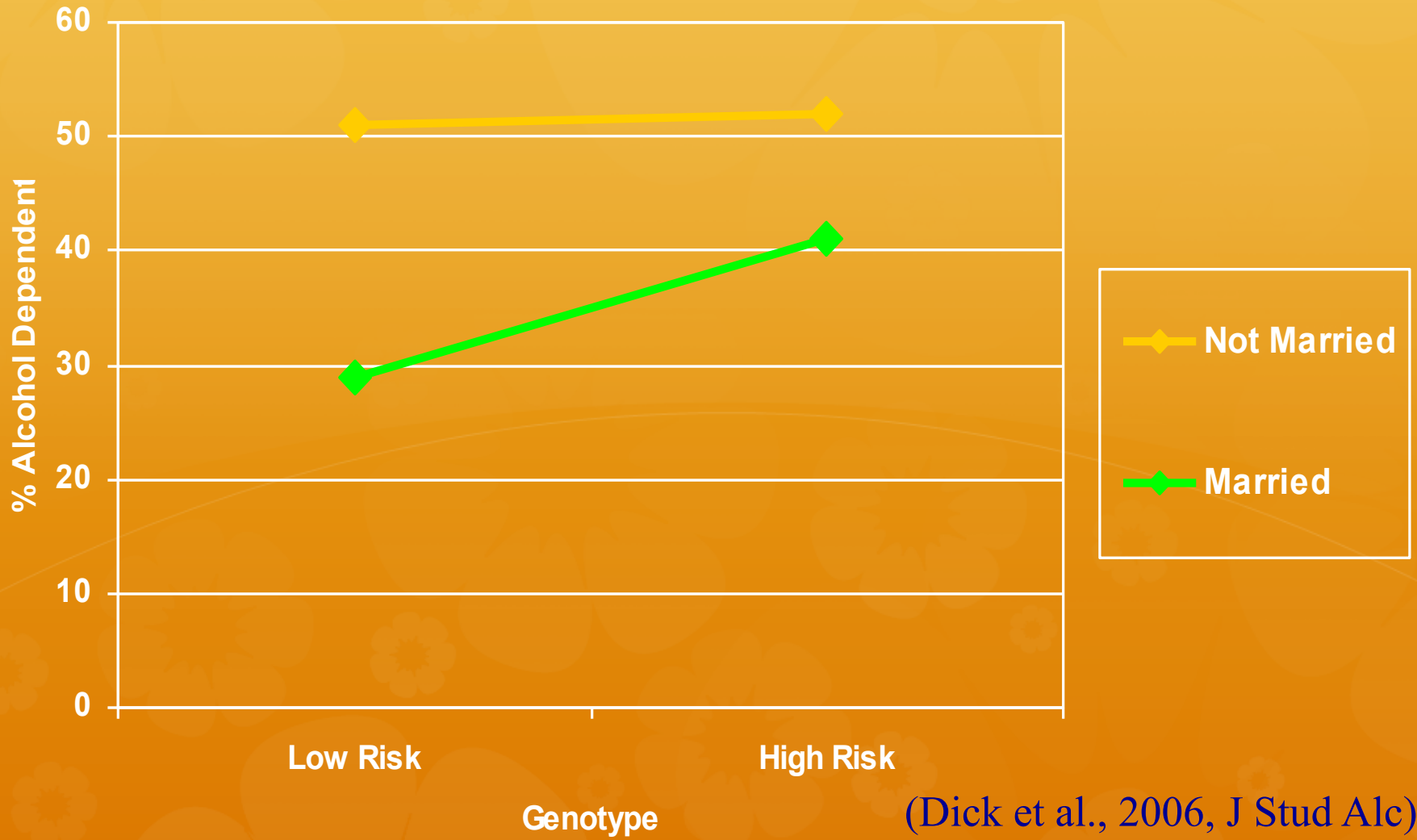


Interplay of Genes & Environment

Genotype-Environment Interplay

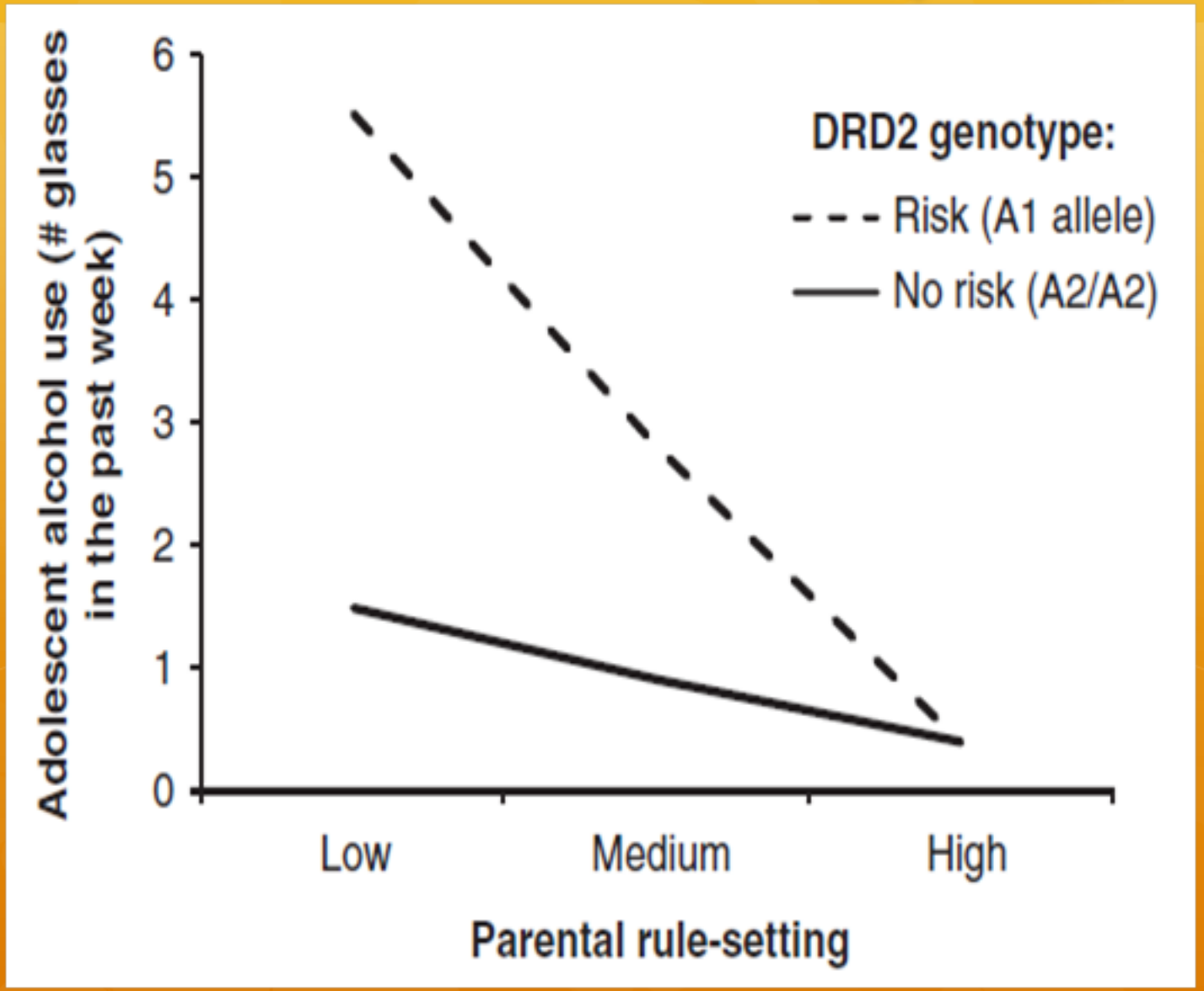


Rates of Alcohol Dependence, *GABRA2* and Marital Status

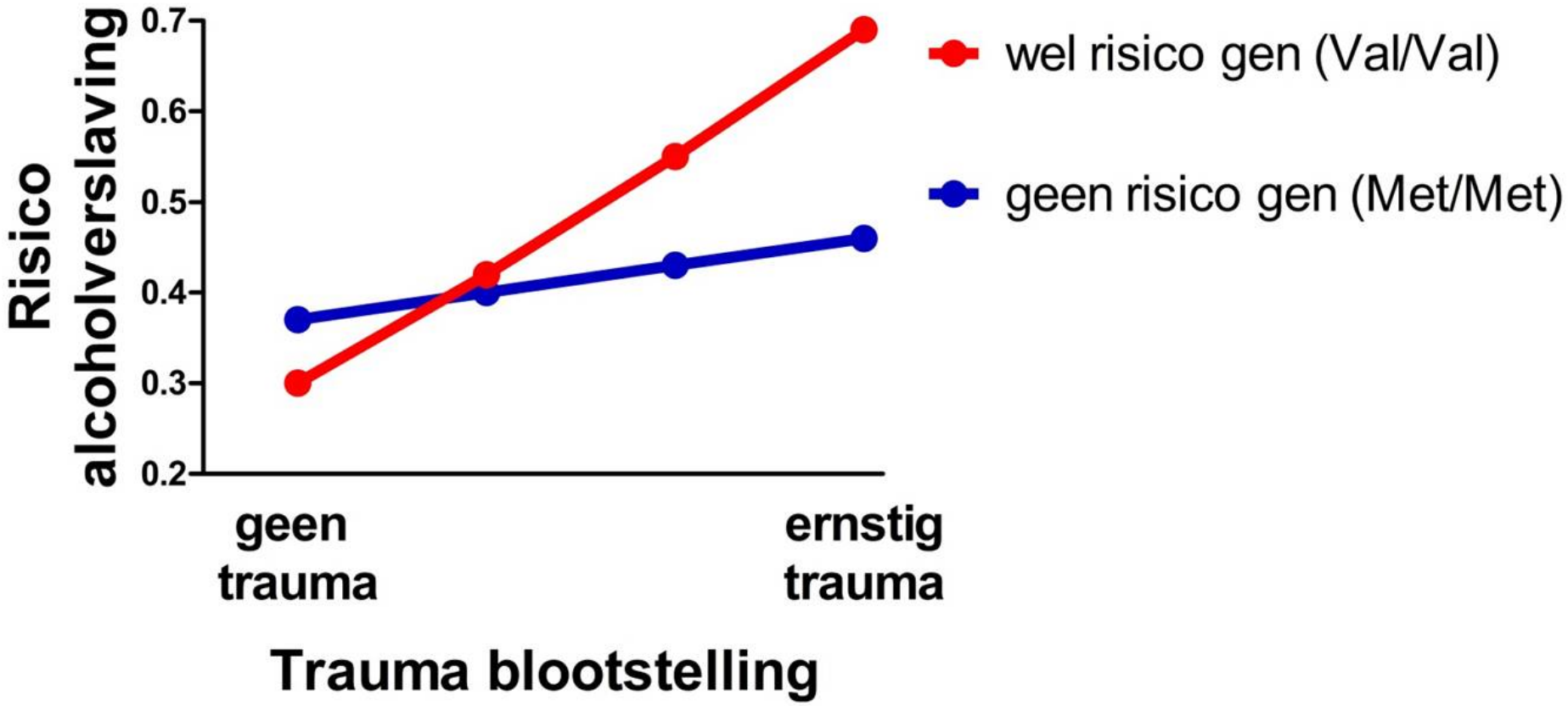


(Dick et al., 2006, J Stud Alc)

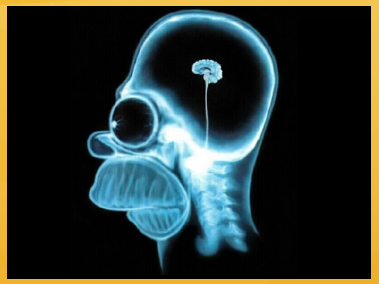
Schellekens et al., 2012



Schellekens et al., 2012



Verslavingsproces



Start gebruik:
1.Familie - gebruikscultuur
2.Temperament-karakter

Factoren die verband houden met transitie naar verslavingsgedrag:
1.Genetica
2.Effect van de middelen

Use

addiction

Relapse

Factoren geassocieerd transitie naar intensief gebruik:
1.Peers
2.Genetica /biologie
3.karakter

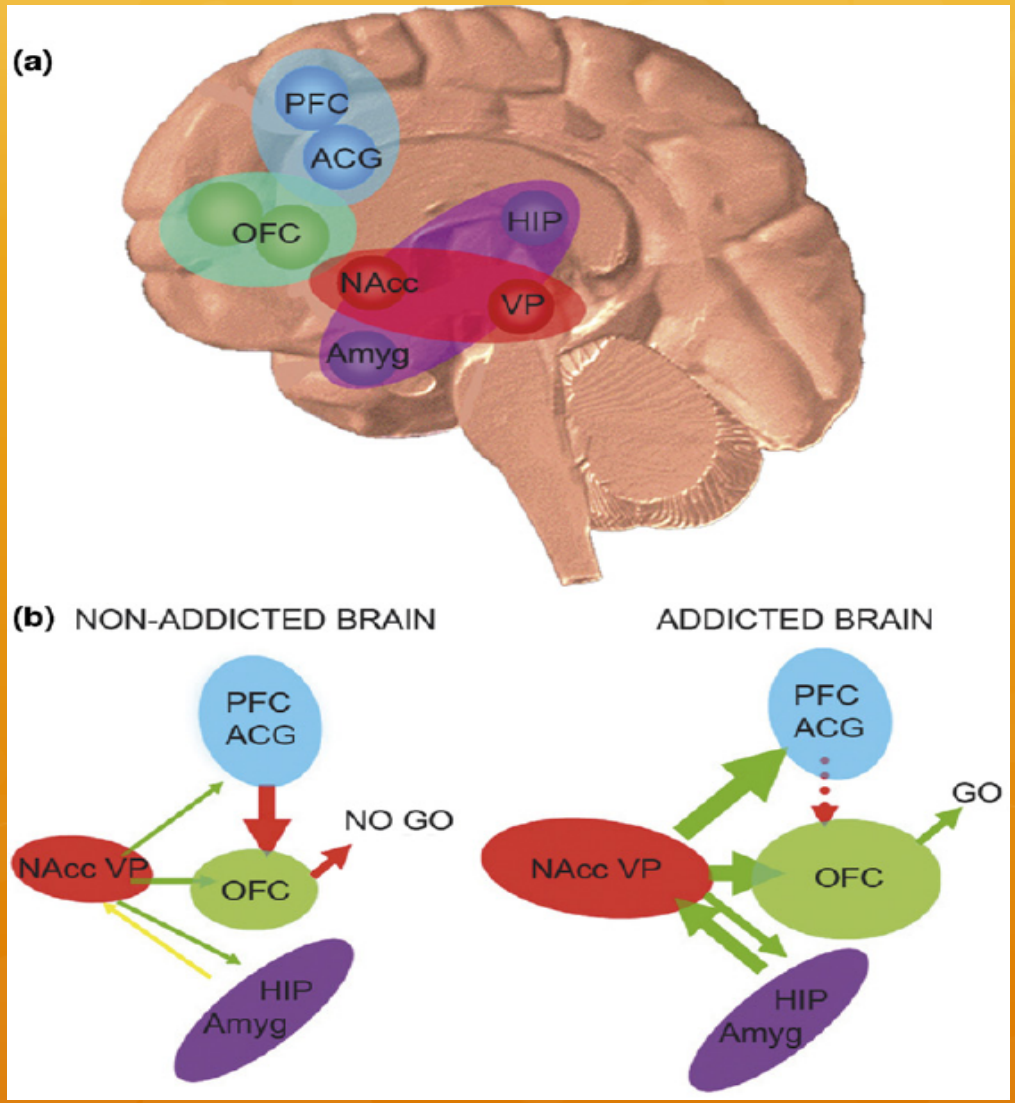
Factoren die verband houden met herval:
1.Craving
2.stress

Kenmerken ernstige verslaving

- Controle verlies
- Craving = zucht = verstoring aandacht

- >>>> ***Blijvend gebruik ondanks negatieve gevolgen***

Functioneel Model en Hersenstructuren



Volkow, 2006

presentatie

- Alcohol gebruik: nadelen en voordelen.
- Behandelingen:
- Natuurlijk verloop
- Effectiviteit
- Huidige behandelingen en hoe die te verbeteren.
- De toekomst:
- besluit

presentatie

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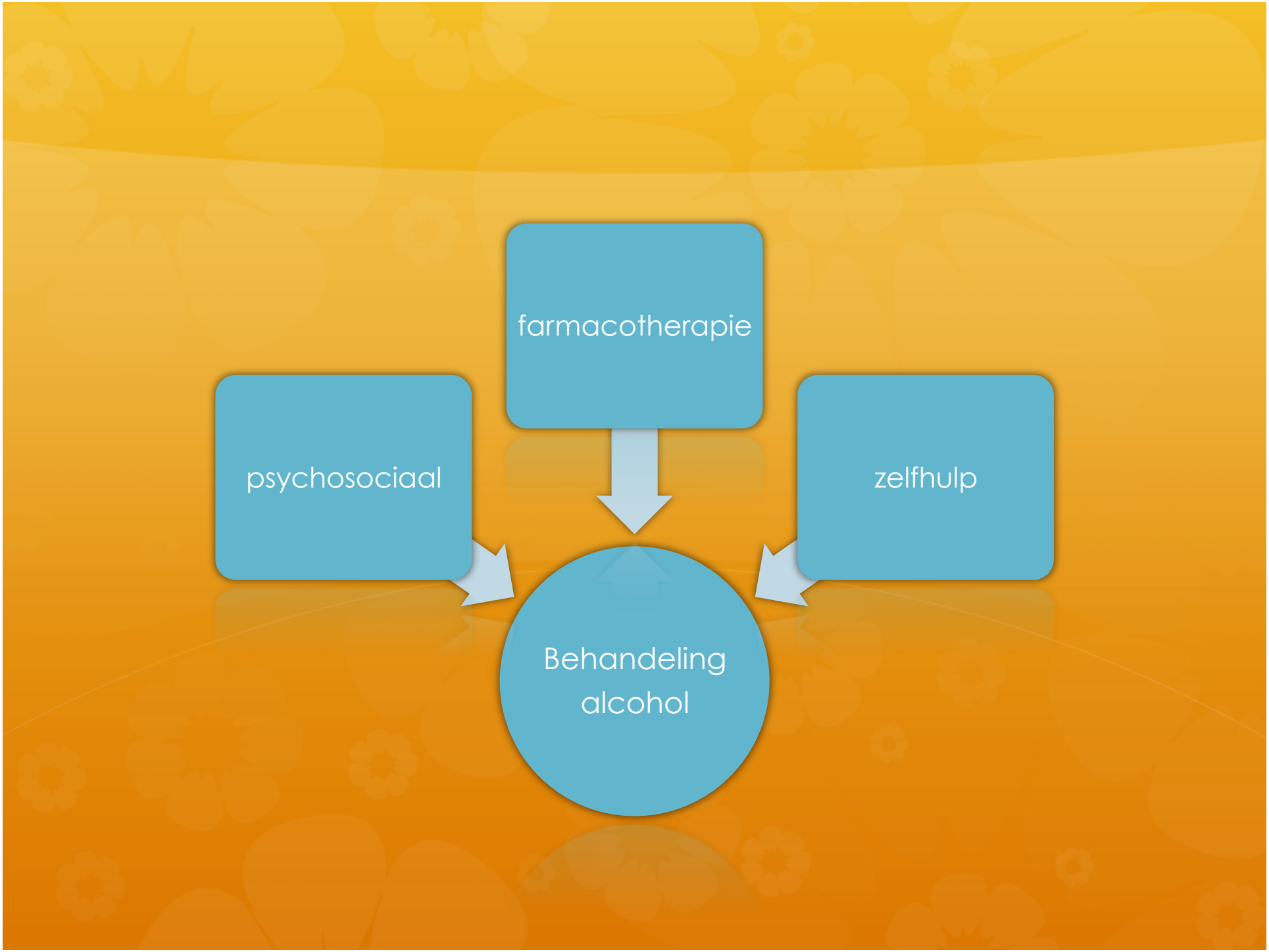
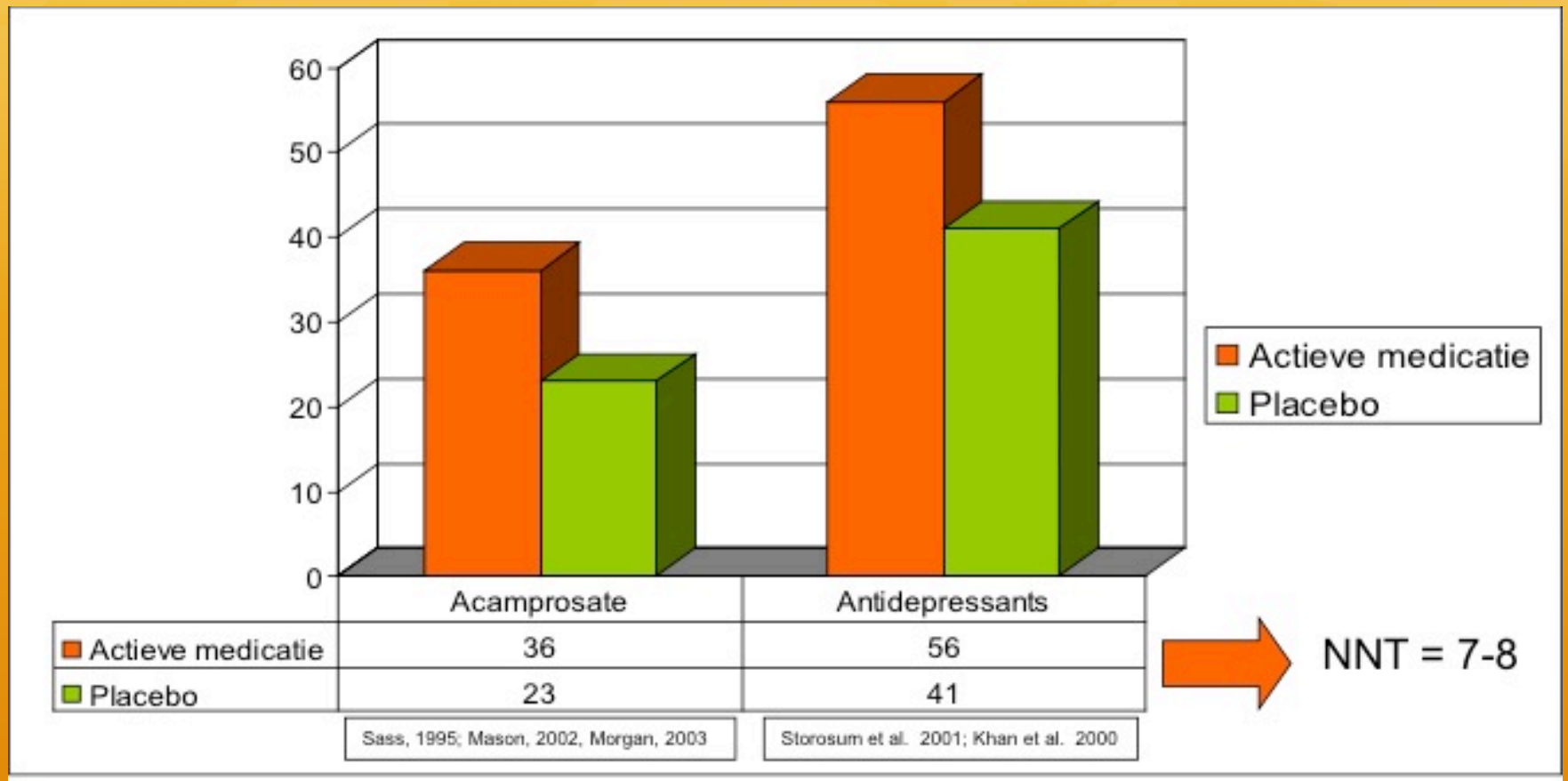

farmacotherapie
psychosociaal
zelfhulp
Behandeling alcohol

Knelpunten behandeling alcoholproblemen

- We weten enkel iets over de behandeling van zeer ernstig afhankelijke patienten.
- Behandelingen vooral gegroeid op basis trial en error
- Niet voortbouwend op kennis van onderliggende neurobiologische defecten.
- Behandeling voor iedereen hetzelfde = geen differentiatie = gepersonaliseerde behandeling.
- Heel klein behandelbereik.
- ***GEVOLG :*** behandelingen werken maar hebben een matige effectiviteit.



	Acamprosate	Antidepressants
Actieve medicatie	36	56
Placebo	23	41

Sass, 1995; Mason, 2002, Morgan, 2003

Storosum et al. 2001; Khan et al. 2000

NNT = 7-8

Acamprosaat is bewezen effectieve interventie met een beperkte effectgrootte:
Ongeveer 40% abstinent na 6-12 maanden en een NNT van 7-8

Medications tested in phase II Clinical Trials for reducing drinking severity (without taking into account pharmacogenetic heterogenity)

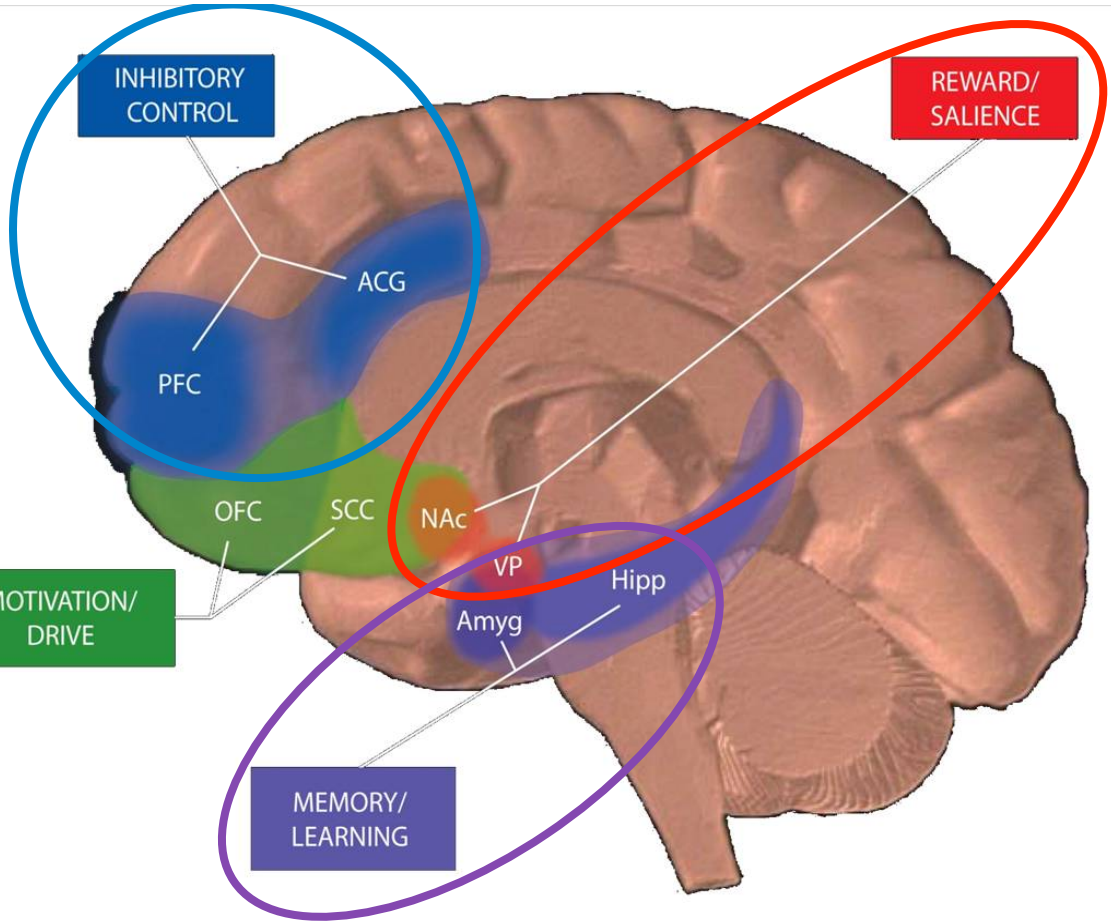
Transmittor system	Medication	Primary molecular target	Effect size
Opioid	Naltrexone	M-opioidreceptor antagonist	Small
GABA	Baclofen	GABA-B agonist	Mixed effects
Glutamate, GABA	Acamprosate	NMDA antagonist GABA-A agonist	Small
Serotonin	Sertraline	5-HT transporter	Small-medium
Serotonin	Ondansetron	5HT3 antagonist	Small-medium
GABA, glutamate	Topiramate	GABA-A antagonist	medium

Small effect size: 0.2-0.3 Medium: around 0.5; Large effect-size: > 0.8

After Bankole Johnson

Behandeling verbeteren

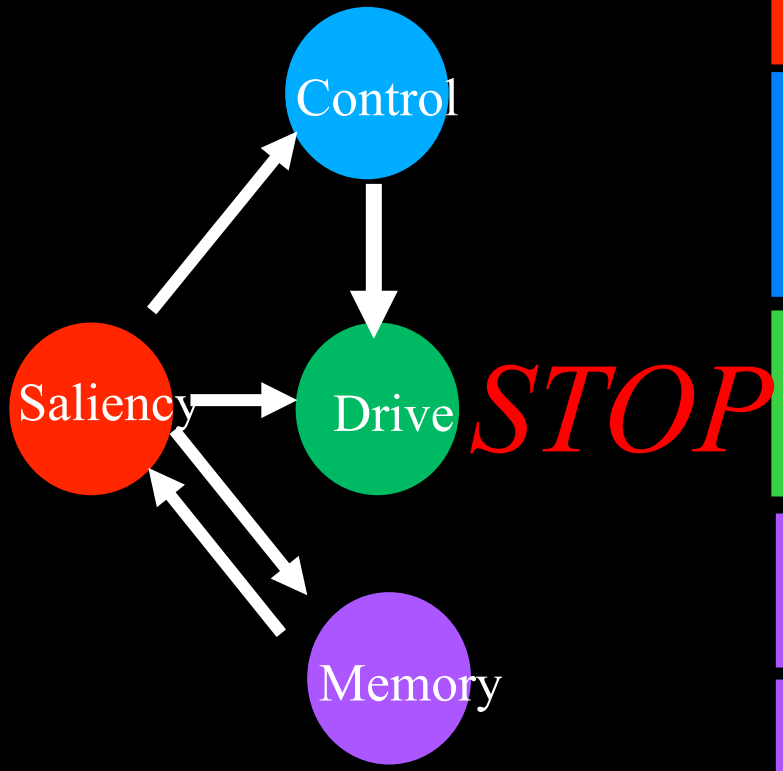
- Betere targetting = subgroepen die beter reageren op medicatie.
- Beter aansluiten op de neurobiologie:
  - Hedonische = craving regulatie
  - Betere zelfcontrole ontwikkelen
- Vergroten behandel bereik
- Hoe te veel gebruik aanpakken, maar sociaal gebruik haalbaar maken.
- Preventie:
  - Primair
  - secundair



be an important target for treating alcohol dependence.

Medications for Relapse Prevention

Non-Addicted Brain



Interfere with drug's reinforcing effects	*Vaccines* *Enzymatic degredation* *Naltrexone* *DA D3 antagonists* *CB_1 antagonists*
Executive function/ Inhibitory control	*Biofeedback* *Modafinil* *Bupropion* *Stimulants*
Strengthen prefrontal-striatal communication	*Adenosine* *A2 antagonists* *DA D3 antagonists*
Interfere with conditioned memories (craving)	*Antiepileptic GVG* *N-acetylcysteine*
Teach new memories	*Cycloserine*
Counteract stress responses that lead to relapse	*CRF antagonists* *Orexin antagonists*

Behandeling verbeteren

- Betere targetting = subgroepen die beter reageren op medicatie.
- Beter aansluiten op de neurobiologie:
  - Hedonische = craving regulatie
  - Betere zelfcontrole ontwikkelen
- Vergroten behandel bereik
- Hoe te veel gebruik aanpakken, maar sociaal gebruik haalbaar maken.
- Preventie:
  - Primair
  - secundair

A Simple Risk Scoring System for Prediction of Relapse after Inpatient Alcohol Treatment

Mads Uffe Pedersen, PhD, Morten Hesse, PhD

Center for Alcohol and Drug Research, Aarhus University, Århus C, Denmark

2009

TABLE 2. Variables Included in the RARS = Risk of Alcohol Relapse Scale

		Value in the original construction sample		
	Code	Mean or percentage (relapsers)	Mean or percentage (abstainers)	Probability*
Standard units of alcohol per day during intensive periods	One if >20	23.0	17.2	0.003
Economic problems (EuropASI Composite Score)	One if >0	0.66	0.54	0.04
Treatment on the initiative of the clients, their families or workplace	One if false	58%	75%	0.001
Treatment paid by the client and/or the clients family	One if false	18%	31%	0.02
Treated for alcohol problems before	One if true	74%	62%	0.047
Prescribed psychopharmacological medicine	One if true	44%	30%	0.04
Contemplated suicide	One if true	29%	16%	0.03
Attempted suicide	One if true	8%	2%	0.048
Troubled with social problems/conflicts	One if>2	1.42	0.92	0.03
Need for help physical problems	One if>2	1.40	0.96	0.04

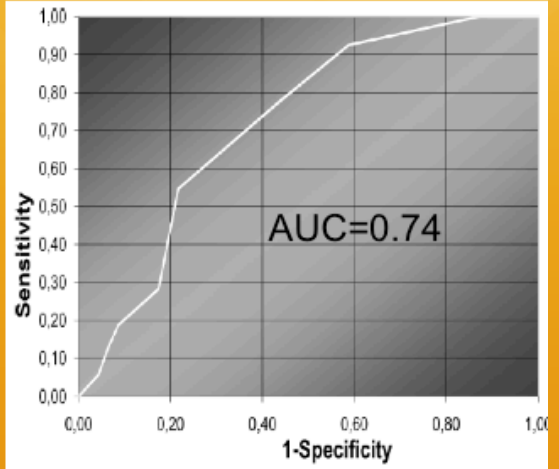


FIGURE 1. Receiver operating characteristics curve for validation sample 1 (RARS as a predictor of uncontrolled drinking during 6 months follow-up).

Voorspellers behandeluitkomst:
* ernst (alcoholconsumptie)
* sociale problemen (geld, conflicten)
* psychiatrische comorbiditeit
* somatische problemen
* motivatie voor behandeling
* eerdere alcoholbehandelingen

NS

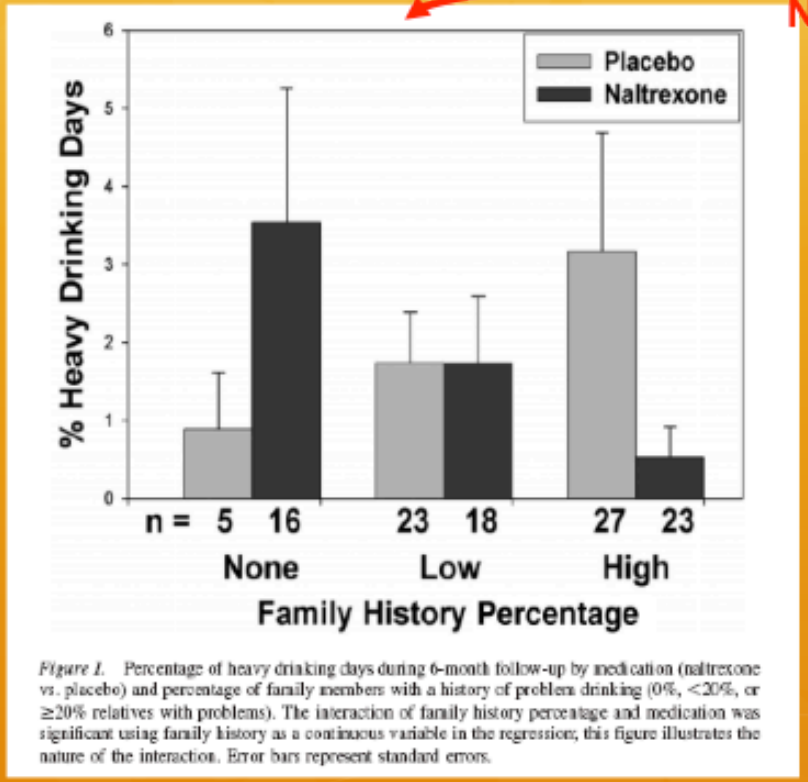


Figure 1. Percentage of heavy drinking days during 6-month follow-up by medication (naltrexone vs. placebo) and percentage of family members with a history of problem drinking (0%, <20%, or ≥20% relatives with problems). The interaction of family history percentage and medication was significant using family history as a continuous variable in the regression; this figure illustrates the nature of the interaction. Error bars represent standard errors.

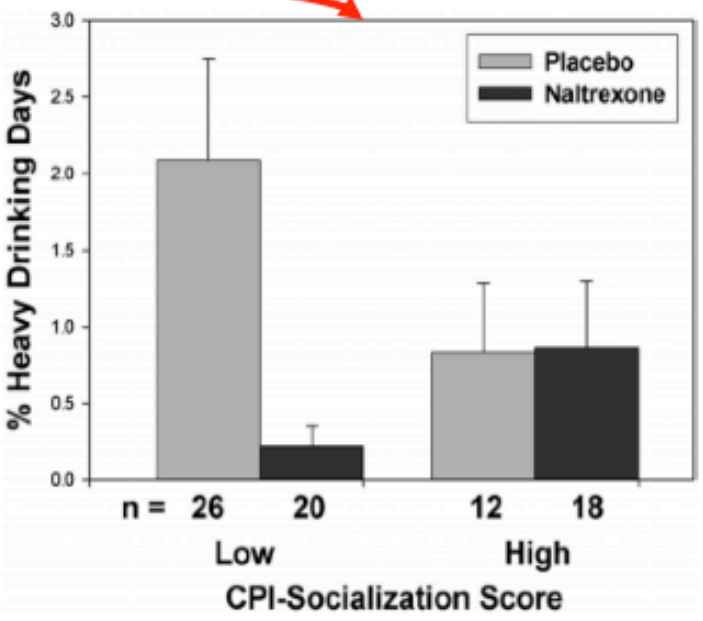


Figure 2. Among patients compliant with ≥70% of medication doses, percentage of heavy drinking days during 6-month follow-up by medication (naltrexone vs. placebo) and socialization (California Personality Inventory-Socialization scale [CPI-So] score ≤24 or >24). The interaction of CPI-Socialization with medication was significant using CPI-Socialization as a continuous variable in the regression; this figure illustrates the nature of the interaction. Error bars represent standard errors.

Experimental and Clinical Psychopharmacology
2007, Vol. 15, No. 3, 272–281

DOI: 10.1037/1064-1297.15.3.272

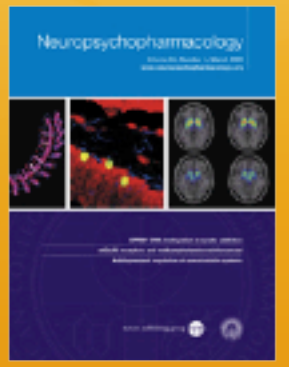
Family History and Antisocial Traits Moderate Naltrexone's Effects on Heavy Drinking in Alcoholics

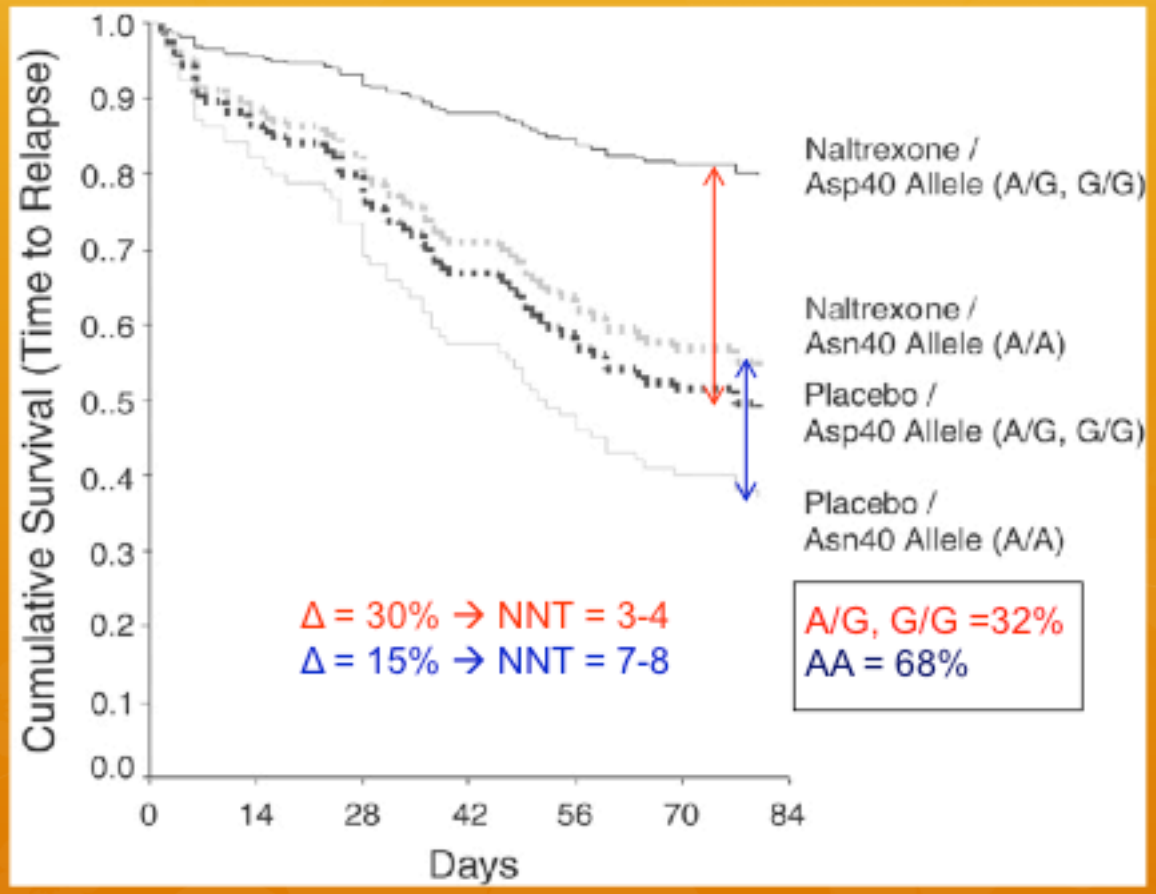
Damaris J. Rohsenow
Providence Veterans Affairs Medical Center and Brown University School of Medicine

Robert Miranda Jr.
Brown University School of Medicine

John E. McGeary and Peter M. Monti
Providence Veterans Affairs Medical Center and Brown University School of Medicine

Farmacogenomics



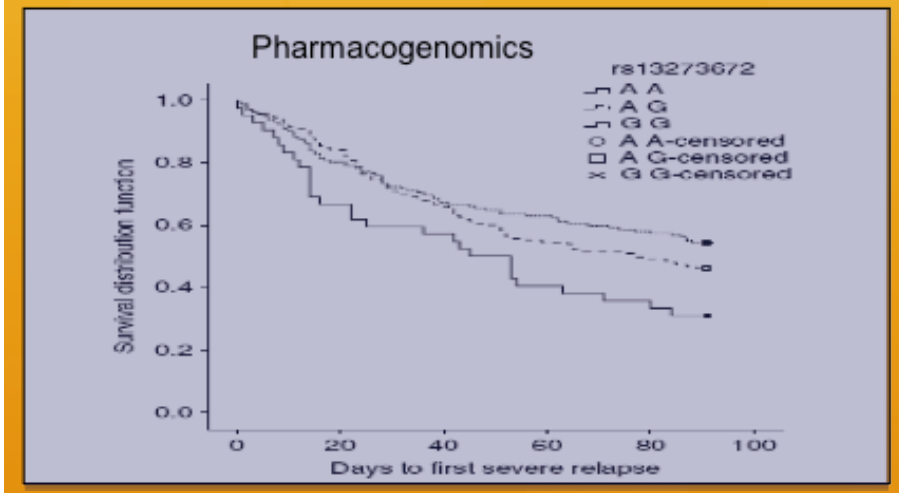


Oslin et al. 2003	+
McGeary et al. 2006	+
Anton et al. 2008	+
Kim et al. 2008	+
Ooteman et al. 2009	+
Gerlernter et al. 2007	-
Tidey et al. 2008	-

Table 2 Association tests between *GATA4* SNP rs13273672 and abstinence proportion after 90 days of pharmacological treatment

	Group size[a]	*P-value*[b]	*Allele A*	*Allele B*	*Frequency A Abstinent*	*Frequency A Relapsed*	*Odds ratio*	*CI (OR)*
Acamprosate	147	0.0013	A	G	0.725	0.539	2.255	1.385–3.670
Naltrexone	148	0.3006	A	G	0.717	0.665	1.281	0.780–2.105
Placebo	74	1.0000	A	G	0.676	0.676	1.000	0.502–1.990

Abbreviations: CI, confidence interval; OR, odds ratio; SNP, single nucleotide polymorphism.
[a]Effective sample size after excluding missing values.
[b]Cochran–Armitage test for trend.



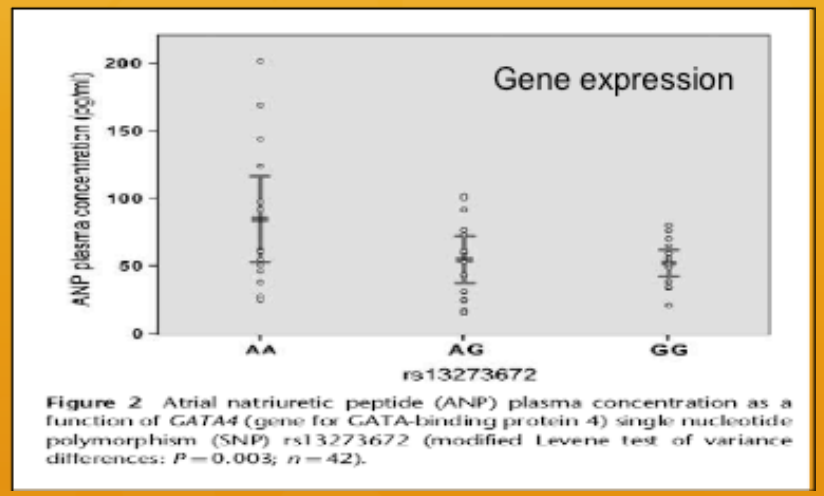


Figure 2 Atrial natriuretic peptide (ANP) plasma concentration as a function of *GATA4* (gene for GATA-binding protein 4) single nucleotide polymorphism (SNP) rs13273672 (modified Levene test of variance differences: $P = 0.003$; $n = 42$).

Involvement of the atrial natriuretic peptide transcription factor *GATA4* in alcohol dependence, relapse risk and treatment response to acamprosate

F Kiefer[1,12], SH Witt[2,12], J Frank[2], A Richter[1], J Treutlein[2], T Lemenager[1], MM Nöthen[3,4], S Cichon[3,4], A Batra[5], M Berner[6], N Wodarz[7], US Zimmermann[1,8], R Spanagel[9], K Wiedemann[10], MN Smolka[8], A Heinz[11], M Rietschel[2,12] and K Mann[1,12]

2010

Addiction Biology

REVIEW

doi:10.1111/j.1369-1600.2010.00287.x

Pharmacogenetics of alcohol, nicotine and drug addiction treatments

Jessica E. Sturgess[1], Tony P. George[2,3], James L. Kennedy[1,3], Andreas Heinz[4] & Daniel J. Müller[1,3]

Pharmacogenetics Research Clinic, Neurogenetics Section, Centre for Addiction and Mental Health, Canada[1], Addiction Psychiatry Program, Department of Psychiatry, University of Toronto, Schizophrenia Program, Centre for Addiction and Mental Health, Canada[2], Schizophrenia Program, Centre for Addiction and Mental Health, Canada[3] and Department of Psychiatry, University Medicine Berlin, Charité Campus Mitte, Germany[4]

Behandeling verbeteren

- Betere targetting = subgroepen die beter reageren op medicatie.
- Beter aansluiten op de neurobiologie:
  - ***Hedonische = craving regulatie***
  - Betere zelfcontrole ontwikkelen
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- Hoe te veel gebruik aanpakken, maar sociaal gebruik haalbaar maken.
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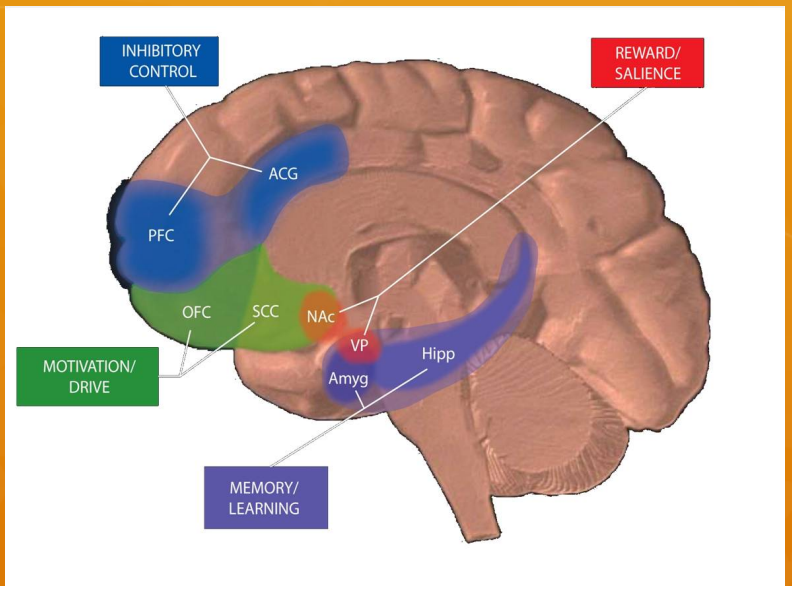


rTMS

- Repetitieve transcraniele magnetische stimulatie

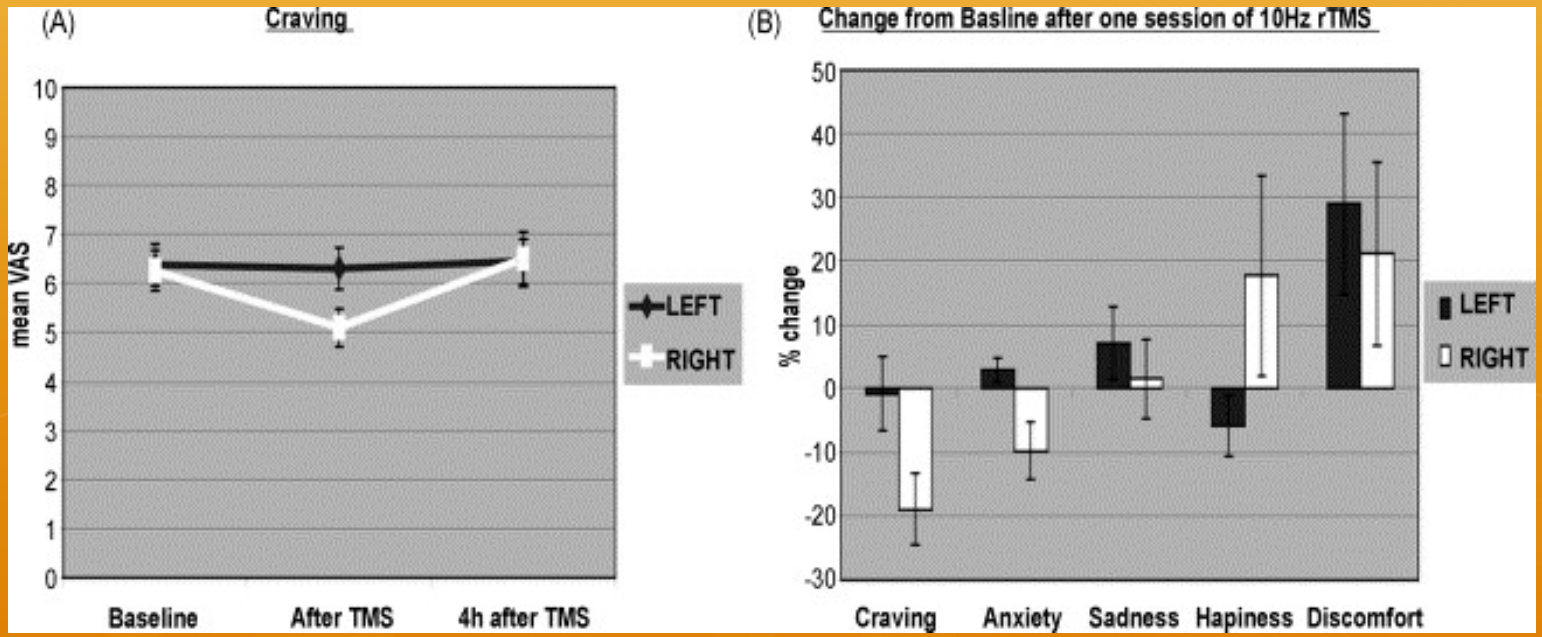
Transcraniele Magnetische Stimulatie bij Cocaineverslaafden

Available online at www.sciencedirect.com
ScienceDirect
Drug and Alcohol Dependence xxx (2006) xxx–xxx
DRUG and ALCOHOL DEPENDENCE
www.elsevier.com/locate/drugalcdep
ELSEVIER

Short communication

One session of high frequency repetitive transcranial magnetic stimulation (rTMS) to the right prefrontal cortex transiently reduces cocaine craving

Joan Albert Camprodon [a], José Martínez-Raga [b], Miguel Alonso-Alonso [a], Mei-Chiung Shih [c], Alvaro Pascual-Leone [a,*]



Een is misschien te weinig……..

Drug and Alcohol Dependence 120 (2012) 209–213

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

No influence of one right-sided prefrontal HF-rTMS session on alcohol craving in recently detoxified alcohol-dependent patients: Results of a naturalistic study

S.C. Herremans[a], C. Baeken[a,b,*], N. Vanderbruggen[a], M.A. Vanderhasselt[c], D. Zeeuws[a], L. Santermans[a], R. De Raedt[c]

[a] University Hospital (UZBrussel), Psychiatric Department, University Hospital, UZBrussel Vrije Universiteit Brussel (V.U.B.), Laarbeeklaan 101, 1090 Brussels, Belgium
[b] Center for Neurosciences, Vrije Universiteit Brussel (V.U.B.), Laarbeeklaan 101, 1090 Brussels, Belgium
[c] Ghent University, Department of Experimental Clinical and Health Psychology, Ghent, Henri Dunantlaan 2, 9000 Ghent, Belgium

Neuroscience Letters 496 (2011) 5–10

Contents lists available at ScienceDirect

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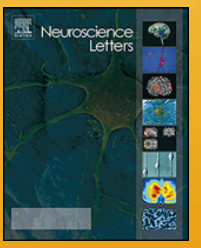
journal homepage: www.elsevier.com/locate/neulet



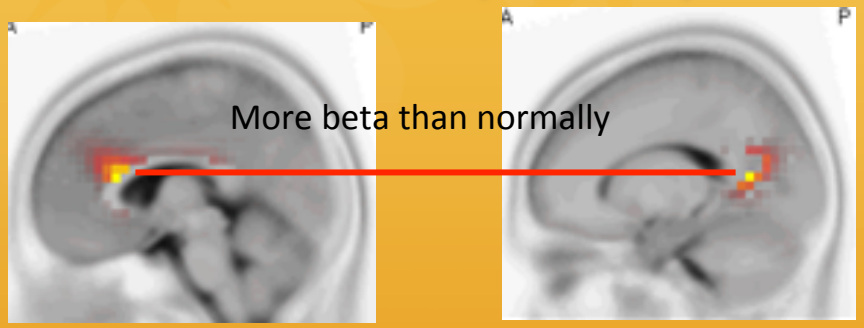
Transient alcohol craving suppression by rTMS of dorsal anterior cingulate: An fMRI and LORETA EEG study☆

Dirk De Ridder[a,*], Sven Vanneste[a], Silvia Kovacs[b], Stefan Sunaert[b], Geert Dom[c]

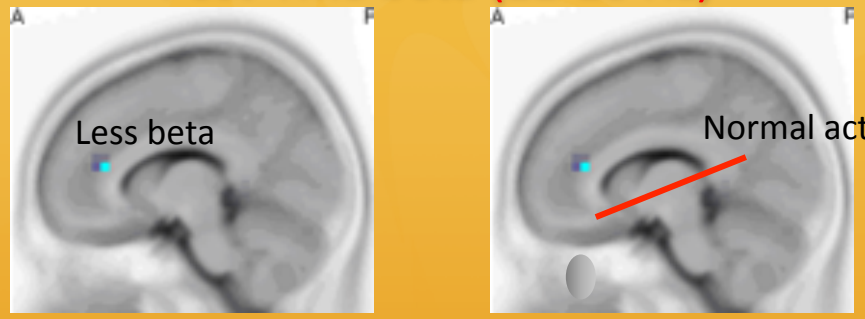
[a] *Brai²n, TRI & Department of Neurosurgery, University Hospital Antwerp, Belgium*
[b] *Department of Radiology, University Hospital Leuven, Belgium*
[c] *Collaborative Antwerp Psychiatry Research Institute, Antwerp University, Belgium*

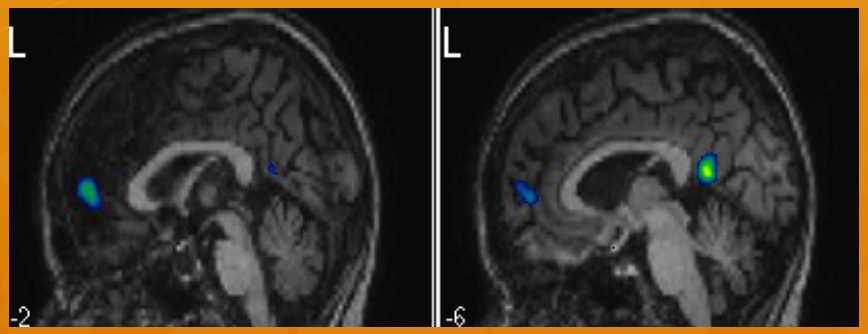
rTMS for alcohol addiction

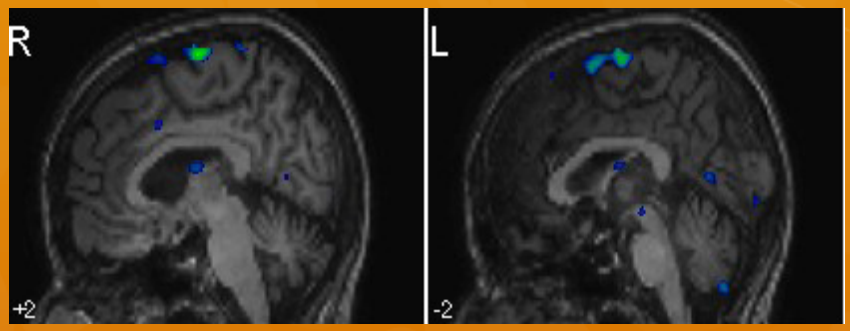
Pre-TMS beta (22-23 Hz)



Post-TMS beta (22-23 Hz)



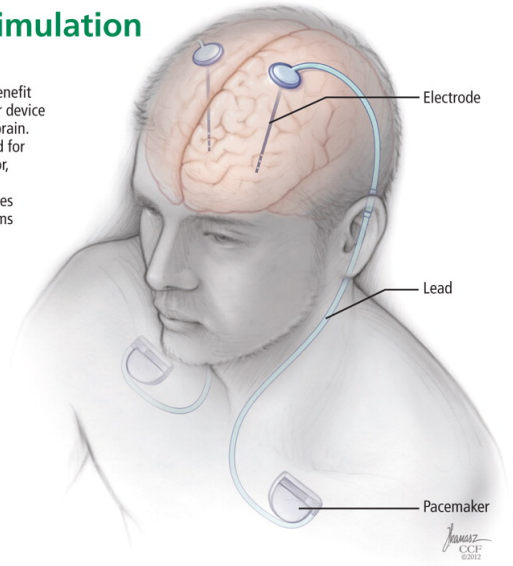


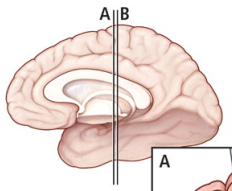


Deep brain stimulation

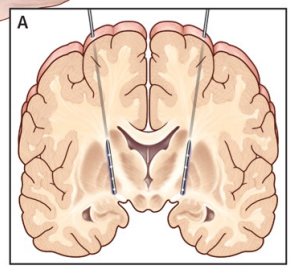
Carefully selected patients may benefit from implantation of a pacemaker device to stimulate precise areas of the brain. This treatment, currently approved for Parkinson disease, essential tremor, primary dystonia, and intractable obsessive-compulsive disorder, does not cure but can improve symptoms and quality of life.

The pacemaker is implanted in the chest, with a lead tunneled beneath the skin of the neck to the scalp and an electrode implanted in the target area of the brain. Batteries last 3–5 years.

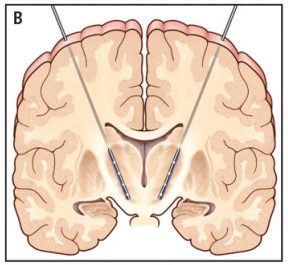




Millimeters matter. The leads are inserted under stereotactic guidance with computed tomography and magnetic resonance imaging, and their location is confirmed by "listening" to brain activity.



Placement for dystonia or Parkinson disease



Placement for Parkinson disease

Medical Illustrator: Joseph Kanasz CCF ©2012

MACHADO A et al. Cleveland Clinic Journal of Medicine 2012;79:113-120

Cleveland Clinic Journal of Medicine

Damage to the Insula Disrupts Addiction to Cigarette Smoking

Nasir H. Naqvi,[1] David Rudrauf,[1,2] Hanna Damasio,[3,4] Antoine Bechara[1,3,4]*

A number of brain systems have been implicated in addictive behavior, but none have yet been shown to be necessary for maintaining the addiction to cigarette smoking. We found that smokers with brain damage involving the insula, a region implicated in conscious urges, were more likely than smokers with brain damage not involving the insula to undergo a disruption of smoking addiction, characterized by the ability to quit smoking easily, immediately, without relapse, and without persistence of the urge to smoke. This result suggests that the insula is a critical neural substrate in the addiction to smoking.

2007

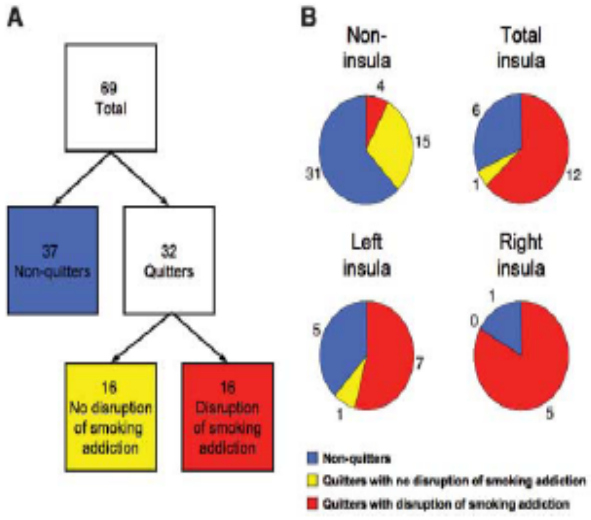


Fig. 2. Patients who quit smoking after lesion onset and patients who underwent a disruption of smoking addiction after lesion onset. (A) Tree diagram showing the behavioral classification of patients. (B) Pie charts illustrating the proportion of patients in each anatomical group who fell into each of the behavioral categories. The colors correspond to the behavioral group depicted in (A). These actual proportions are shown in the Materials and Methods. The proportion of patients with a disruption of smoking addiction was higher among both left insula–lesioned patients and right insula–lesioned patients compared with among noninsula-lesioned patients.

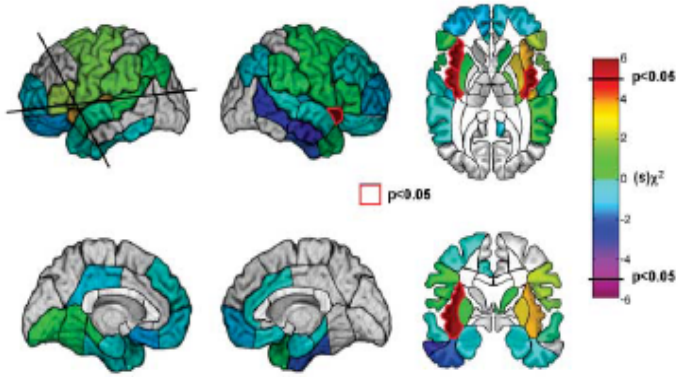


Fig. 3. Whole-brain region-by-region logistic regression analysis. The color of each region corresponds to a χ^2 statistic given the sign of regression coefficient obtained from the logistic regression analysis. The only regions that were assigned a color were those for which the number of patients was sufficient to detect a statistically significant effect (Materials and Methods). Regions for which there was a statistically significant association between a lesion and a disruption of smoking addiction ($P < 0.05$, uncorrected) are highlighted in red. The insula is the only region on either side of the brain where a lesion was significantly associated with a disruption of smoking addiction. There were nonsignificant effects in regions on the left side that are adjacent to the insula; however, patients with damage in these regions also tended to have damage in the insula (Materials and Methods). The likelihood of having a disruption of smoking addiction was not increased after damage in the orbitofrontal cortex.

Addiction Biology

BRIEF REPORT: PRECLINICAL RESEARCH

doi:10.1111/j.1369-1600.2011.00337.x

Successful deep brain stimulation of the nucleus accumbens in severe alcohol dependence is associated with changed performance monitoring

Jens Kuhn[1]*, Theo O. J. Gründler[2,3]*, Robert Bauer[4], Wolfgang Huff[1], Adrian G. Fischer[2], Doris Lenartz[5], Mohammad Maarouf[5], Christian Bührle[5] Joachim Klosterkötter[1], Markus Ullsperger[2,6] & Volker Sturm[5]

Department of Psychiatry and Psychotherapy, University of Cologne, Germany[1], Max Planck Institute for Neurological Research, Germany[2], Department of Psychology, University of Trier, Germany[3], International Centre for Ethics in the Sciences and Humanities, Eberhard Karls University of Tübingen, Germany[4], Department of Functional Neurosurgery and Stereotaxy, University of Cologne, Germany[5] Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, the Netherlands[6]

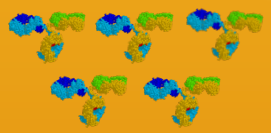
Future Research

Immunotherapies for Addiction Treatment (i.e., Vaccines)

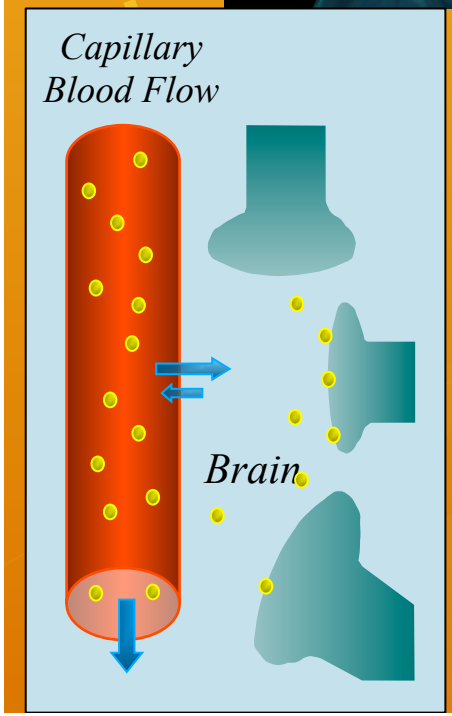
Antibodies Can Reduce Brain Concentrations

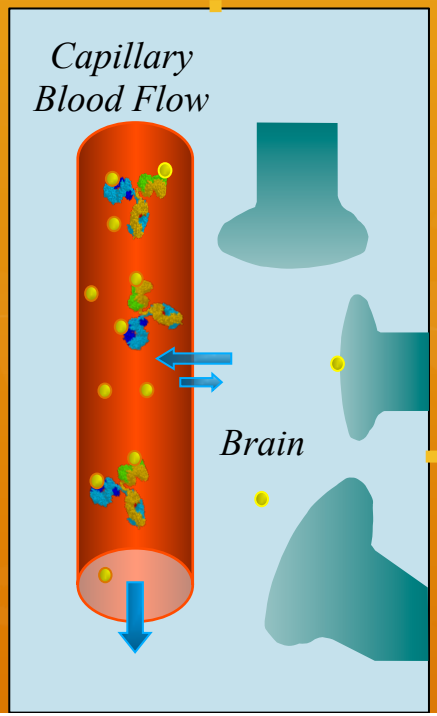
VACCINE

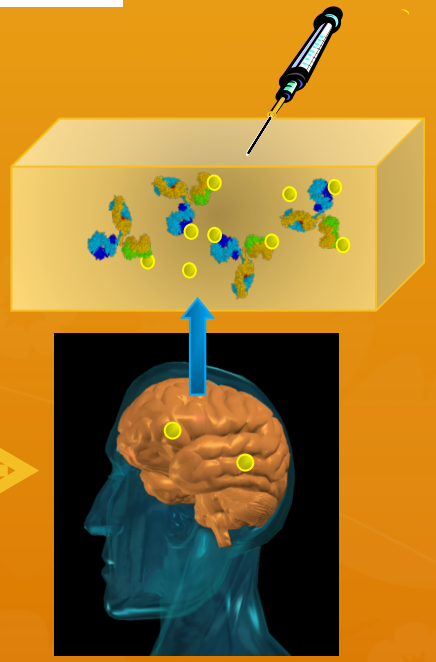
Antibodies



Targeting the drugs, not the receptors







Maar ook niet technische interventies kunnen alcohol cravingsysteem veranderen

De kracht van training

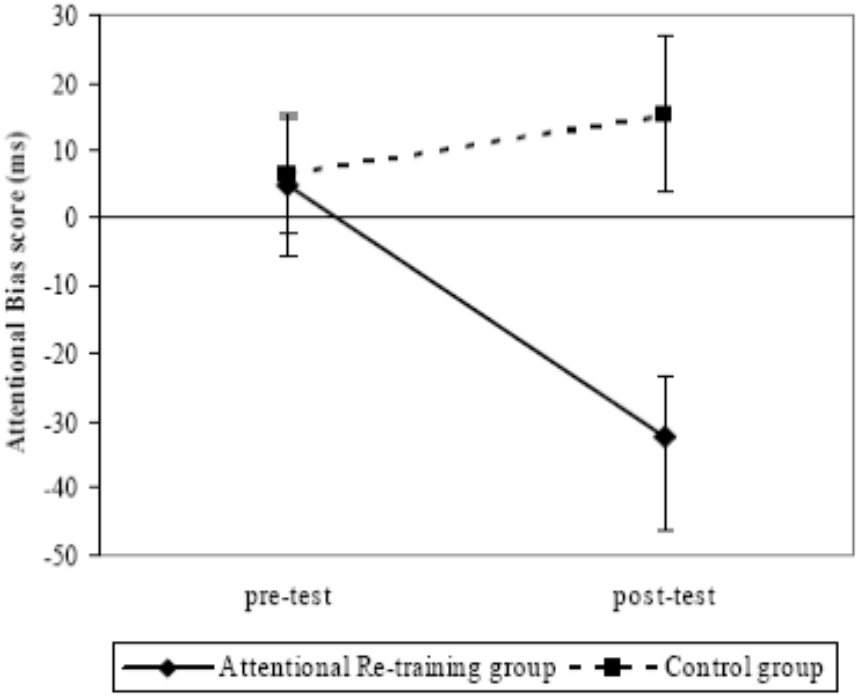
Klinische Re-training

(Schoenmakers et al. submitted)

37 alcoholisten: 4 x trainen in alcohol-kliniek (Attentional Retraining of placebo-training).

* Effecten op Attentional Bias

+ voorzichtige indicaties
Klinische effecten (minder Terugval; kortere succesvolle behandelduur



Andere training: AACTP (Fadardi & Cox) nu op www.impliciet.eu

Training om alcohol te negeren en achtergrondkleur te noemen.

Eerste resultaten:

Verminderen zucht bij alcoholisten en vergroot gevoel van controle.

Recent ontwikkeld alternatief:

Her-training Automatische Actie-tendensen

(met Mike Rinck, RUN e.a.)

Clinical effectiveness of attentional bias modification training in abstinent alcoholic patients

Tim M. Schoenmakers[a,b,*], Marijn de Bruin[c], Irja F.M. Lux[a,d], Alexa G. Goertz[a,d], Dorieke H.A.T. Van Kerkhof[e,f], Reinout W. Wiers[a,g]

2010

Table 2
Post-test and follow-up mean (SD) scores per group.

Variable	Attention modification	*n*	Control	*n*	Cohen's *d*
Attentional bias (ms)					
Speeded detection old pictures[a]	−18.06 (42.08)	21	−3.15 (54.68)	22	.32
Speeded detection new pictures[b]	−10.19 (32.95)	12	12.90 (47.57)	14	.57
Difficulty to disengage—old pictures[a]	−32.33 (64.19)	21	15.30 (53.94)	22	.87**
Difficulty to disengage—new pictures[b]	−51.43 (79.68)	12	27.79 (73.44)	14	1.06*
Craving (scale range 1–7)					
Mild desires[a]	1.80 (1.29)	21	1.78 (1.29)	22	–
Strong desires[a]	1.36 (.78)	21	1.32 (.83)	22	–
Reinforcement[a]	2.74 (1.99)	21	2.73 (1.74)	22	.01
Subjective control[a,c]	5.48 (2.02)	21	5.06 (1.95)	22	.29
Follow-up					
Time to relapse (in months)	2.75 (.50)	4	1.50 (.58)	4	–
Time to discharge after the intervention (in days)[a]	42.44 (24.28)	9	70.75 (18.39)	8	2.16*

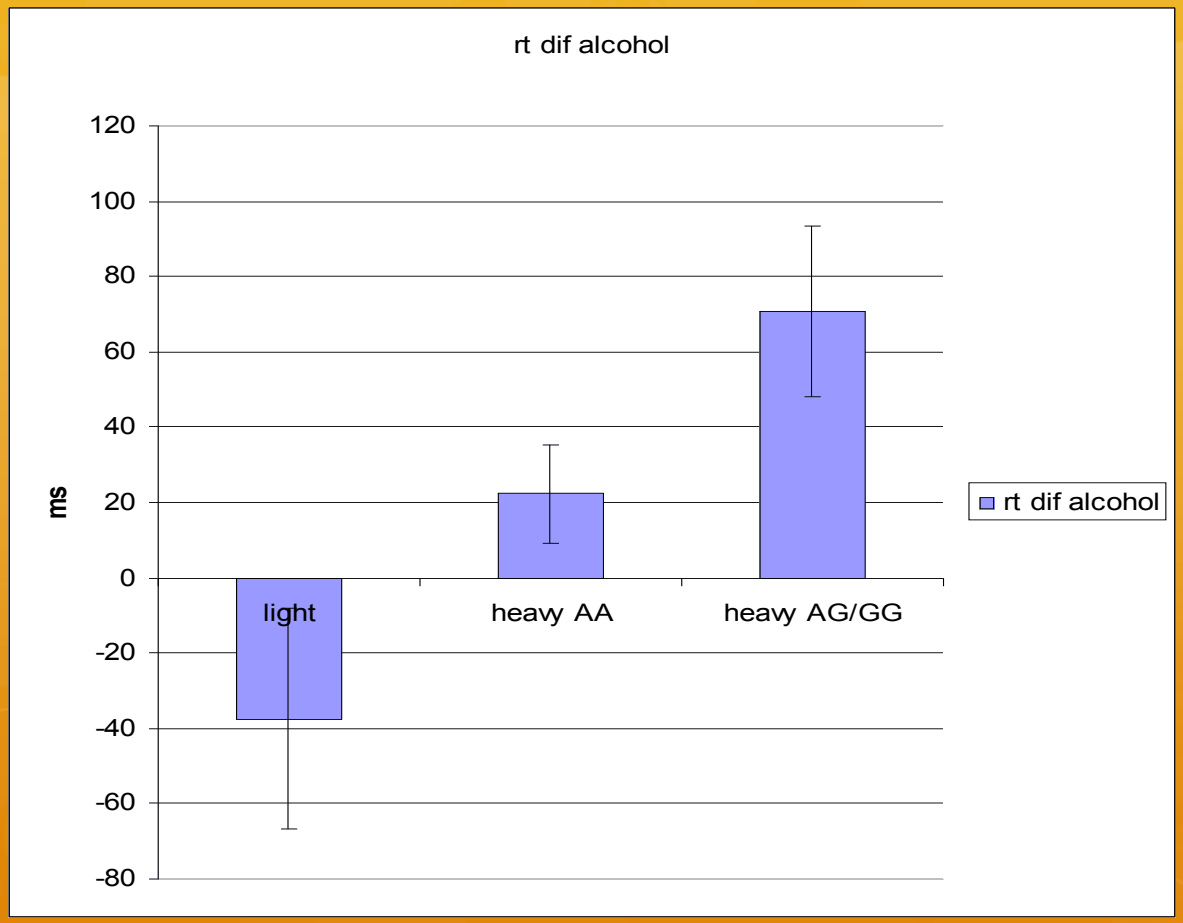
Effect sizes (Cohen's *d*) are given for parametric analyses only.
[a] Missing data imputed as last observation (data from pre-test) carried forward for 6 participants.
[b] Of the 37 participants who had finished the intervention, we lost data for new pictures of 11 participants due to a technical error.
[c] A higher score indicates lower perceived control.
* Significant at $p < .05$.
** Significant at $p < .01$.

Attentional Bias Modification Training results in reduced attentional bias en a reduction of relapse in alcohol use (Wiers et al., 2011).

Meten (50% duw, 50% trek alcohol) Resultaten Wiers, Rinck et al, in press)

zware drinkers trekken alcohol gemakkelijker naar zich toe

vooral zware drinkers met risico-variant



mu-opioid receptor gen, ook gerelateerd aan cue-induced craving (van den Wildenberg et al., 2007, ACER)

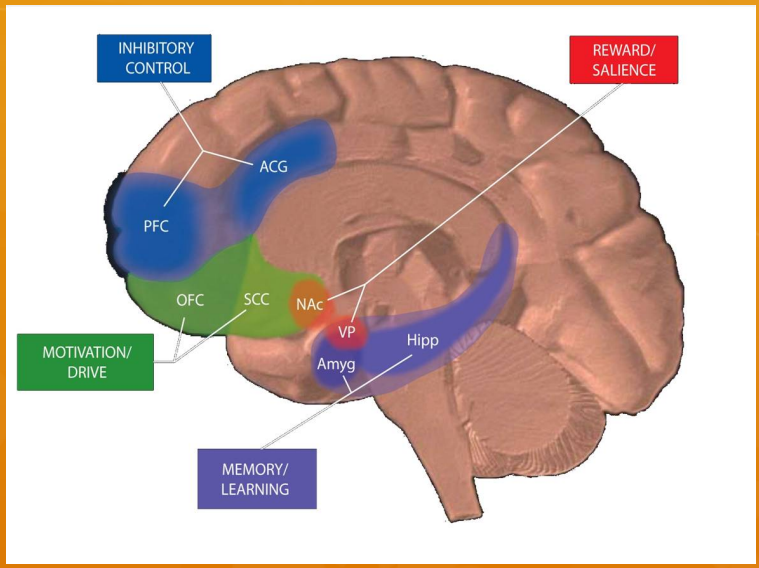
Hertraining

- helft naar bier toe getraind (bier: 90% trekken), helft er vanaf (bier, 90% duwen; fris andersom).

  - effect op automatische impulsen
  - eerste effect op gedrag (studenten)
- Eerste indicaties van klinisch relevante effecten (lopende studie kliniek)

Behandeling verbeteren

- Betere targetting = subgroepen die beter reageren op medicatie.
- Beter aansluiten op de neurobiologie:
  - Hedonische = craving regulatie
  - ***Betere zelfcontrole ontwikkelen***
- Vergroten behandel bereik
- Hoe te veel gebruik aanpakken, maar sociaal gebruik haalbaar maken.
- Preventie:
  - Primair
  - secundair



De kracht van training !

- Alfonso et al.; executive functioning and mindfulness training (polydrug users).
- Wiers et al. (2012): werkgeheugen training en outcome alcohol behandeling.

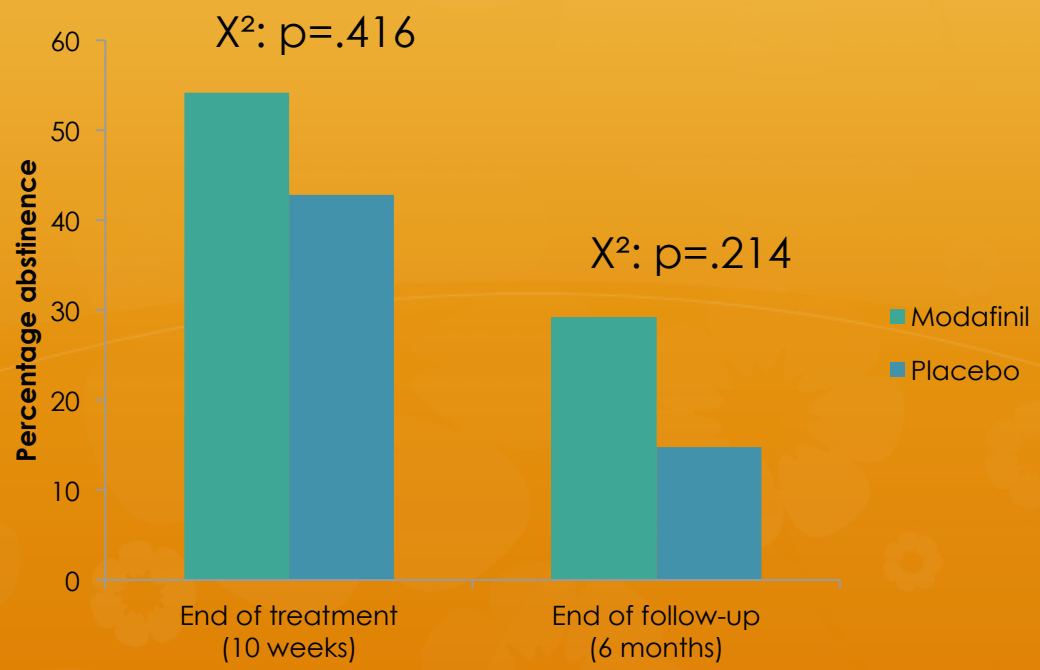
HET VERSTERKEN VAN COGNITIEVE ZELFCONTROLE MET MODAFINIL EN DE RELATIE TOT HERVAL BIJ ALCOHOLAFHANKELIJKE PATIENTEN

Capri COLLABORATIVE ANTWERP PSYCHIATRIC RESEARCH INSTITUTE
PSYCHIATRISCH CENTRUM BROEDERS ALEXIANEN
amc

Results: Complete abstinence

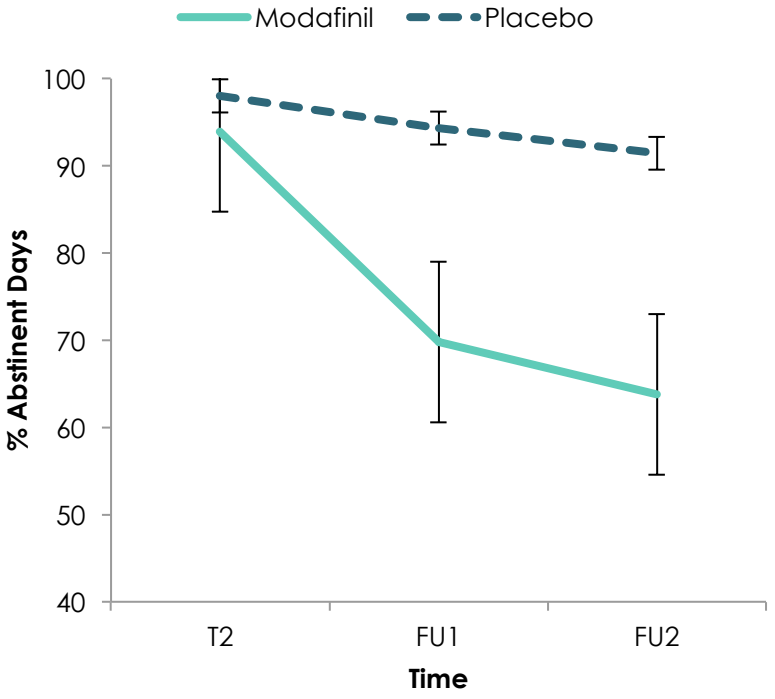
Groups did not significantly differed in abstinence rates

- Abstinence rates

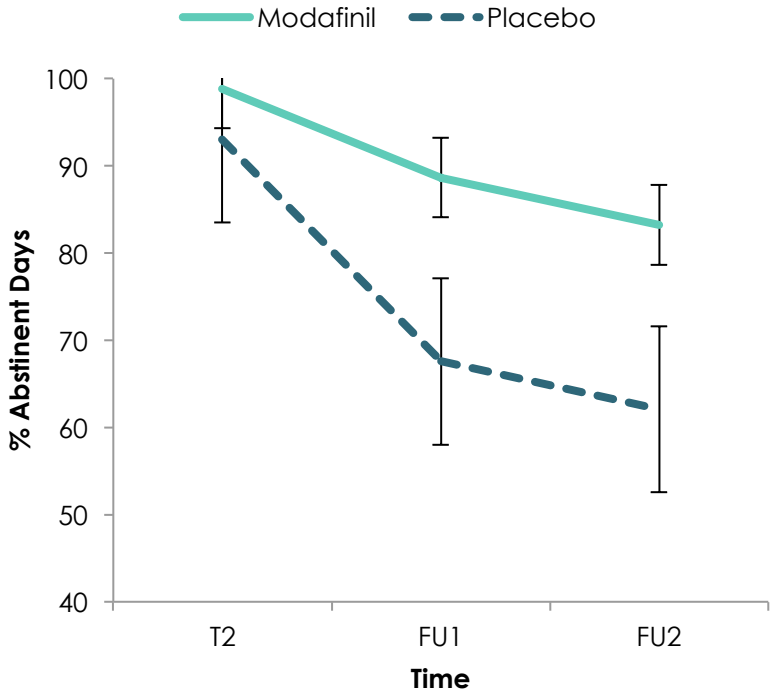


Bi-directional effects in subgroups

Percentage Abstinent Days (MMRM 3-way: p<.001)



MMRM: time by treatment: p=.002



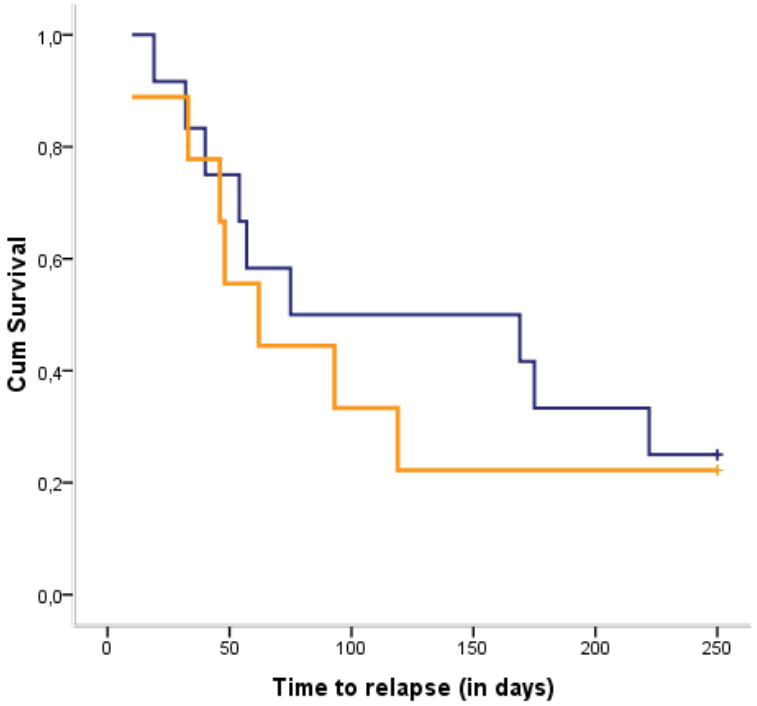
MMRM: time by treatment: p=.066

Bi-directional effects in subgroups

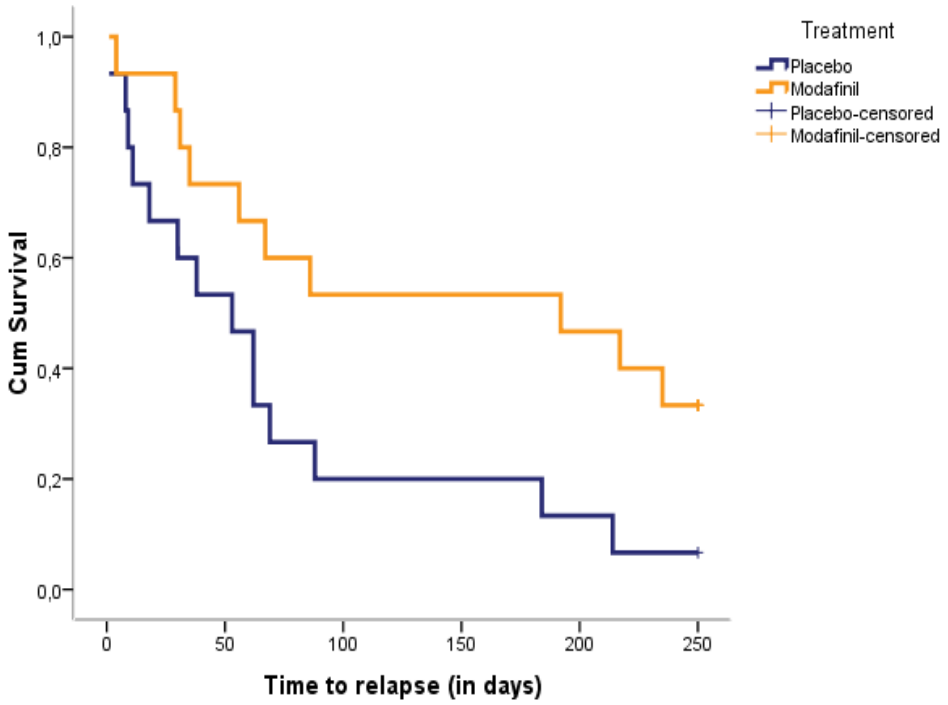
Postponed relapse in ADP with poor response inhibition with MOD

Only completers were included

Good Response Inhibition (n=21)



Poor Response Inhibition (n=30)



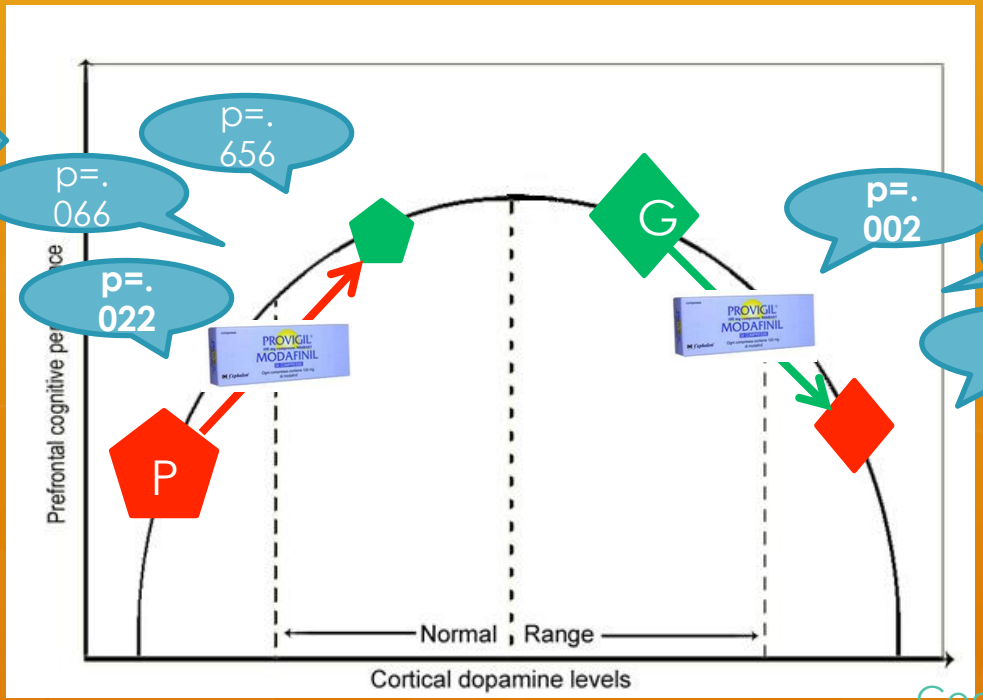
Log Rank (Kaplan-Meier): p=.708

Log Rank (Kaplan-Meier): p=.022

Discussion: bi-directional effects

- ✓ **Patients with poor response inhibition at baseline** might benefit from modafinil.
- ✓ D**etrimental effects** might occur in patients with good baseline response inhibition.

Inverted-U-shape function



Cools & D'Esposito, 2011

Behandeling verbeteren

- Betere targetting = subgroepen die beter reageren op medicatie.
- Beter aansluiten op de neurobiologie:
  - Hedonische = craving regulatie
  - Betere zelfcontrole ontwikkelen
- Vergroten behandel bereik
- Hoe te veel gebruik aanpakken, maar sociaal gebruik haalbaar maken.
- Preventie:
  - Primair
  - secundair

Middel	Jaarprevalentie gebruikers		Jaarprevalentie verslaafden		Verslavingszorg		Verslaafden in huisartsenpraktijk	
	% 12+	Aantal 12+	%18+	Aantal 18+	Aantal	% van ver-slaafden	Per 2500	Per 150
Tabak	34	4.400.000	17	2.000.000	Nihil	Nihil	425	25
Alcohol	73	9.800.000	3,7	280.000	28.000	10	90	6
Benzodia-zepinen	4	500.000	3,3	250.000	Nihil	Nihil	80	5
Cannabis	3	400.000	0,5	35.000	3.500	9	10	< 1
XTC	0,3	65.000	?	?	< 300	?	?	?
Heroïne	0,2	28.000	0,3	25.000	17.500	70	5-10	< 1
Cocaïne	> 0,4	> 50.000	> 0,3	> 20.000	7.000	< 30	> 10	1

Use of mental health services in Europe: results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project

Proportion of individuals consulting any type of formal health services in the previous 12 months, according to 12-month mental disorder status

Mental health state	Unweighted, n	Weighted, %	95% CI
Overall sample	21,425	6.4	5.9–6.8
No 12 month mental disorders	19,349	4.3	3.9–4.7
Any disorder	2,076	25.7	23.3–28.1
Any mood	972	36.5	32.5–40.5
Any anxiety	1,325	26.1	23.1–29.1
Any alcohol disorder	209	8.3	3.8–12.8
Only one 12 month mental disorder	1,435	19.6	17.1–22.2
More than one	641	40.0	35.0–45.0

In 2004 in Europe, 37% of persons with a mood disorder and 26% of persons with an anxiety disorder were consulting formal health services in the previous 12 months, whereas this was only **8%** for persons with an alcohol use disorder!!

CI=confidence interval

Alonso et al. Acta Psychiatr Scand Suppl 2004; 420: 47-54

behandelbereik

- 38,2% van de Europese bevolking (= 164,8 milj.) lijden aan een psychische stoornis (12-maand prevalentie).
- 13 % alcohol en 6% drugs lifetime
- Slechts 25% van de mensen met een psychische stoornis krijgen een vorm van hulp.
- Slechts 10 % krijgt de gepaste vorm van hulp
- ….Wittchen et al., 2011.

Behandeling verbeteren

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  - Hedonische = craving regulatie
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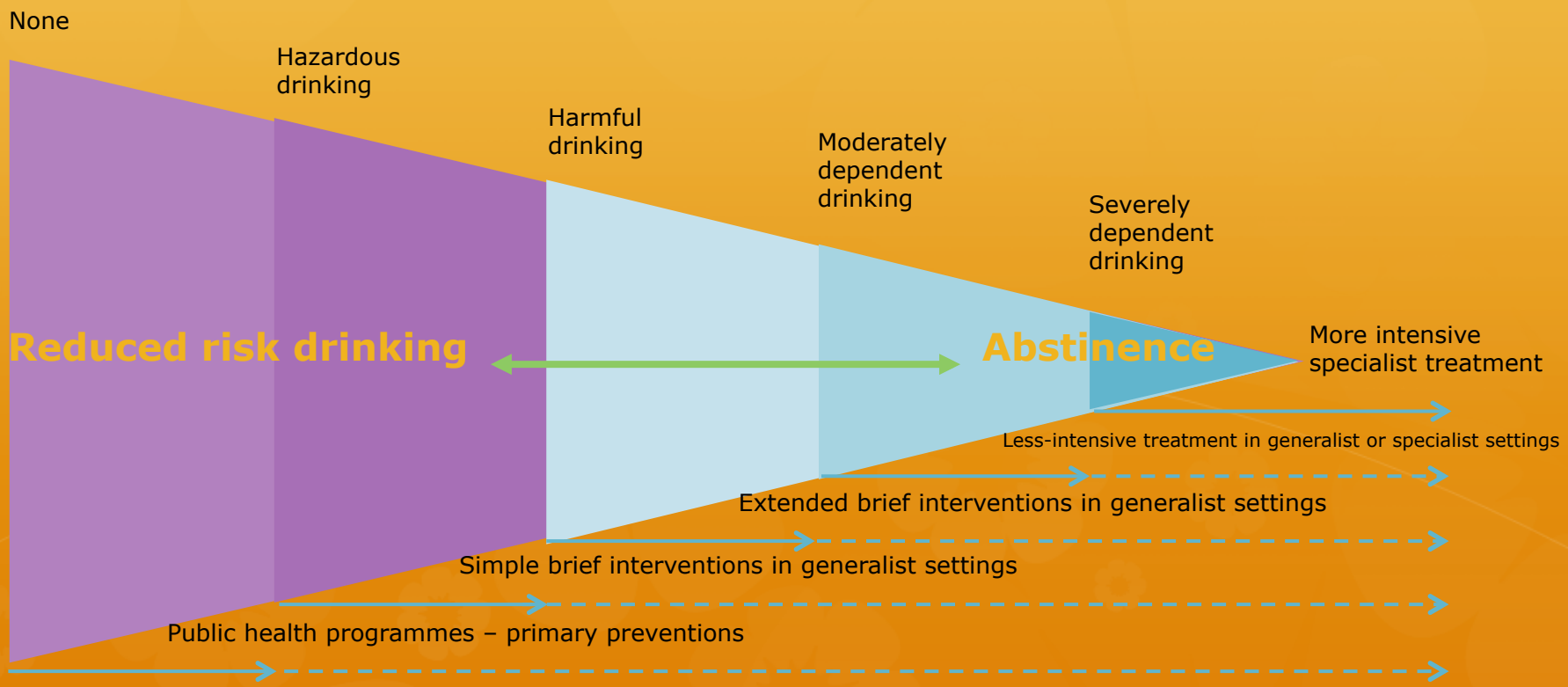
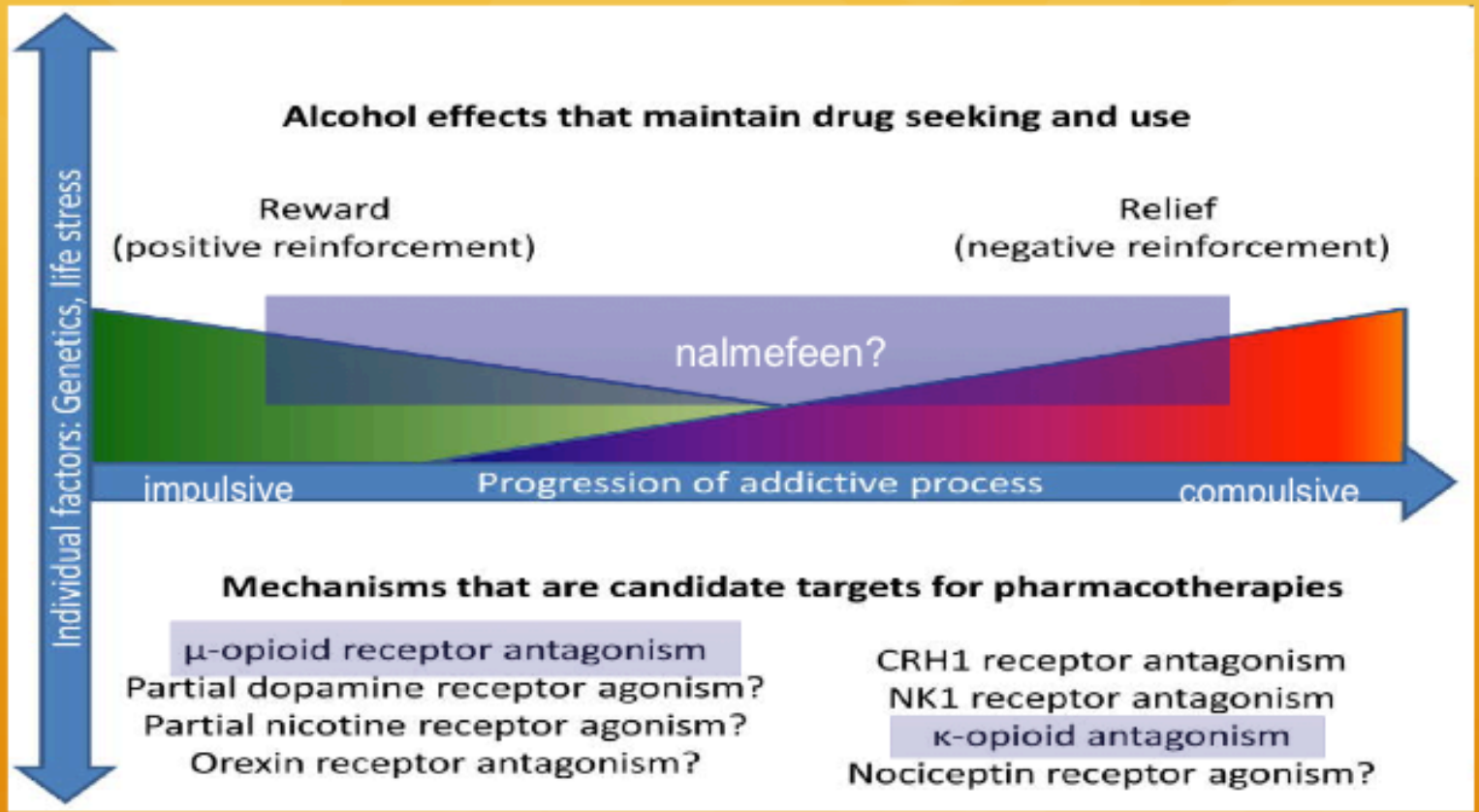
Alcohol problem severity and interventions

A spectrum of responses to alcohol problems



Rastrick et al. 2006; Adapted from Institute of Medicine. 1990



Heilig et al., 2010

Behandeling verbeteren

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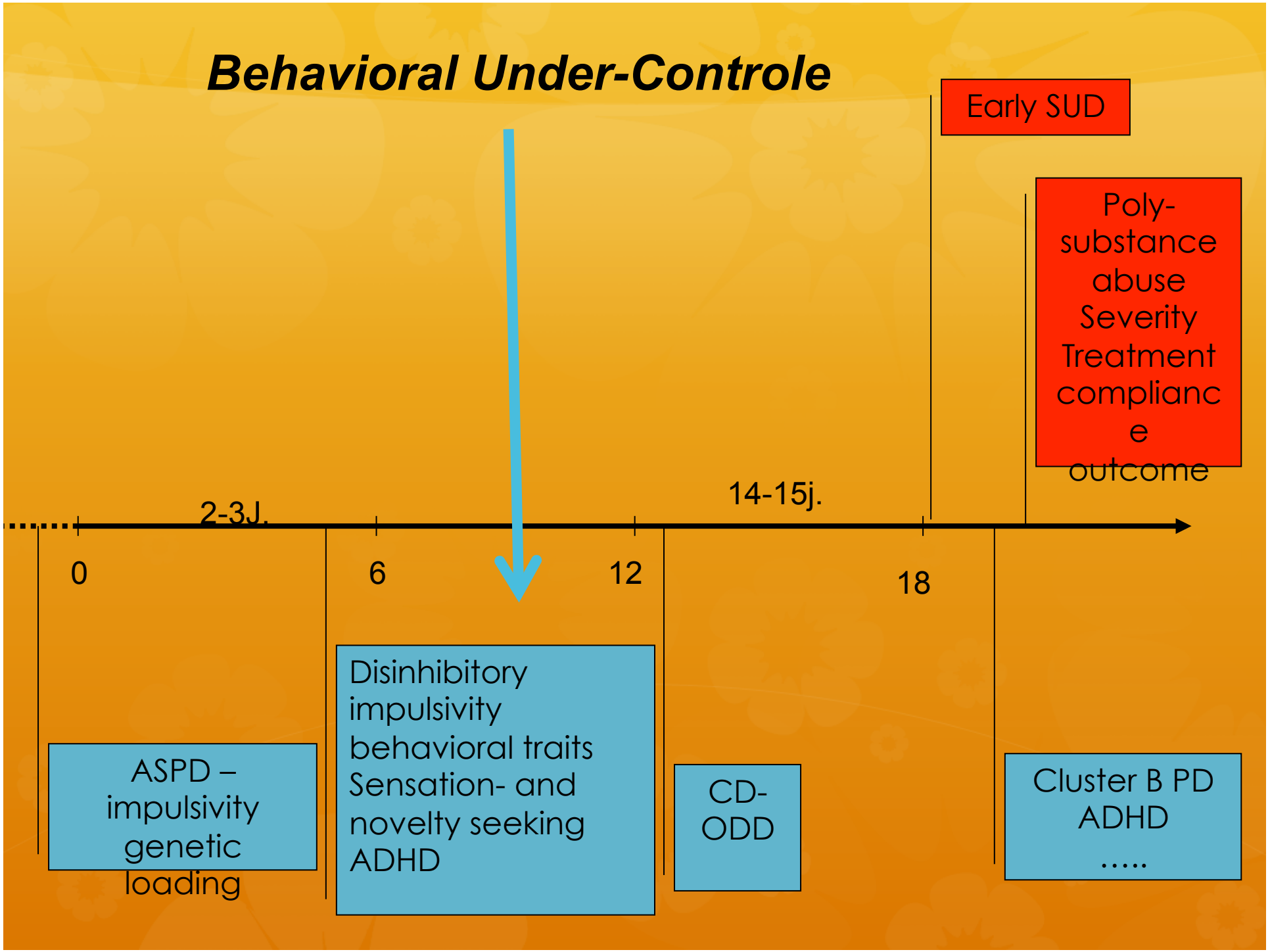
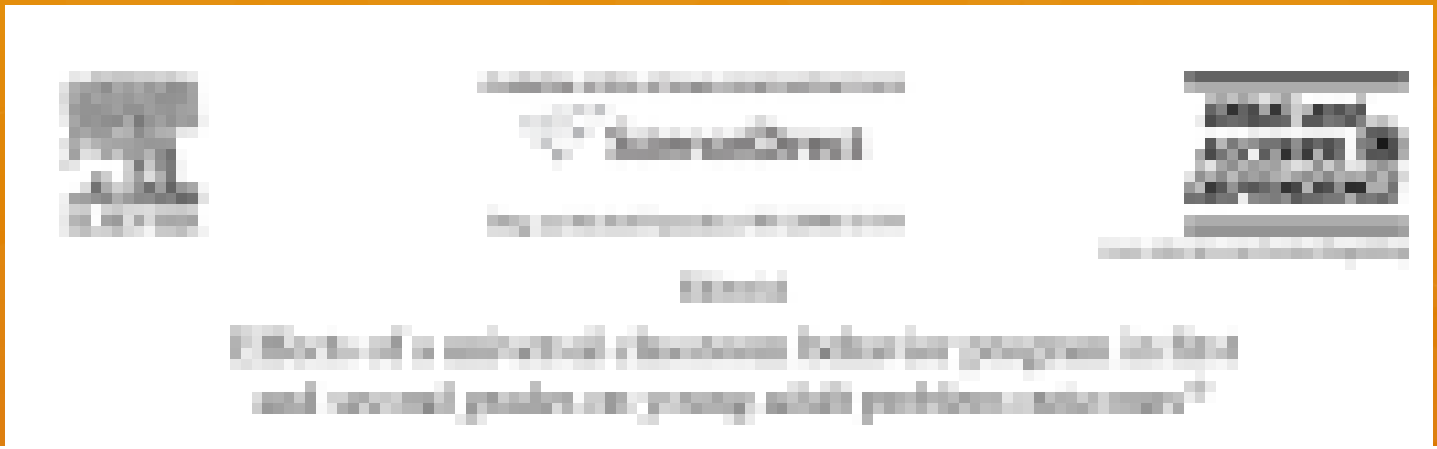
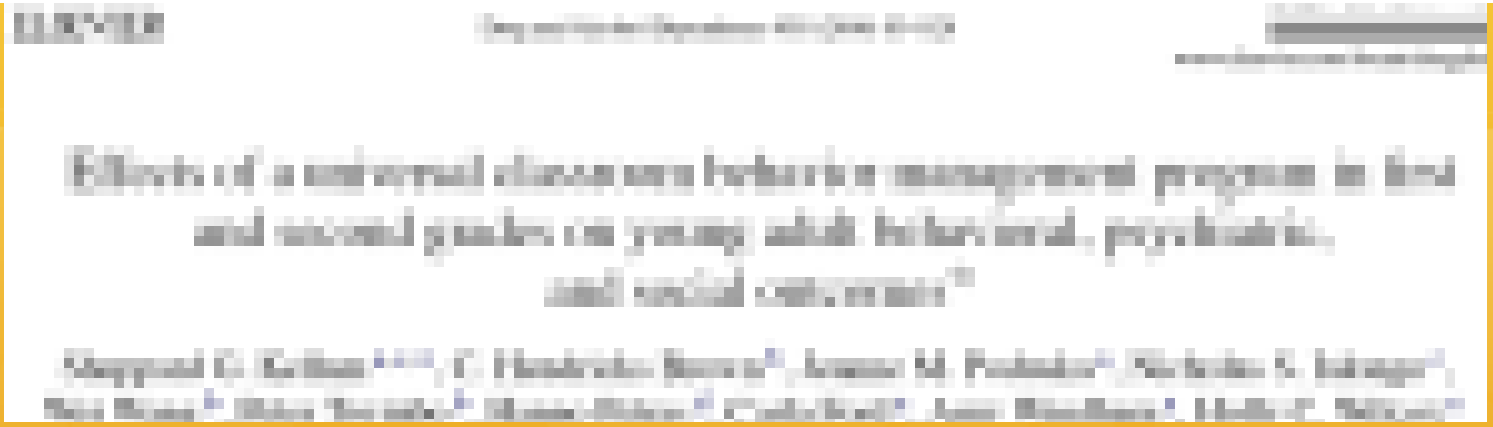

Behavioral Under-Controle
Early SUD
Poly-substance abuse Severity Treatment compliance outcome
2-3J.
14-15j.
0
6
12
18
ASPD – impulsivity genetic loading
Disinhibitory impulsivity behavioral traits Sensation- and novelty seeking ADHD
CD-ODD
Cluster B PD ADHD …..

Interventions

Early-class room interventions

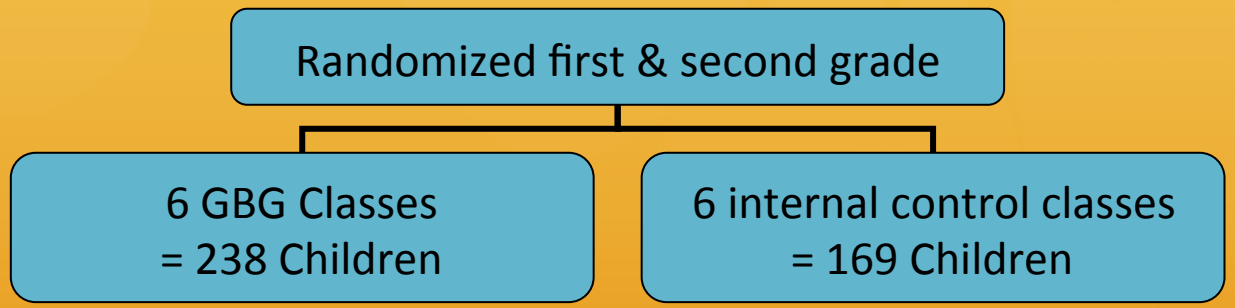
May 2008 - Vol. 103 s1, Destiny Matters: Childhood and Adolescent Prediction of Adult Alcohol Use and Abuse in Six Multi-decade Longitudinal Studies Page 1-109





1. Good Behavior Game (GBG): “classroom behavior manegement”” used by teachers in first- and second grade classrooms …….follow-up impact ages 19-21.
2. Intervention aimed to socialize children to student role and reduce aggressive, disruptive behaviors (antecedents of later SUD and ASPD).

Design



2 year GBG implementation

Results after 1 year = diminishment
aggressive/disruptive behavior boys.

Follow-up 19-21 years

ELSEVIER

Effects of a universal classroom behavior management program in first and second grades on young adult behavioral, psychiatric, and social outcomes*

Sheppard G. Kellam, C. Hendricks Brown, Jeanne M. Poduska, Nicholas S. Ialongo, Wei Wang, Peter Toyinbo, Hanno Petras, Carla Ford, Amy Windham, Holly C. Wilcox

randomly assigned to intervention or control.

Results: By young adulthood significant impact was found among males, particularly those in first grade who were more aggressive, disruptive, in reduced drug and alcohol abuse/dependence disorders, regular smoking, and antisocial personality disorder. These results underline the value of a first-grade universal prevention intervention.

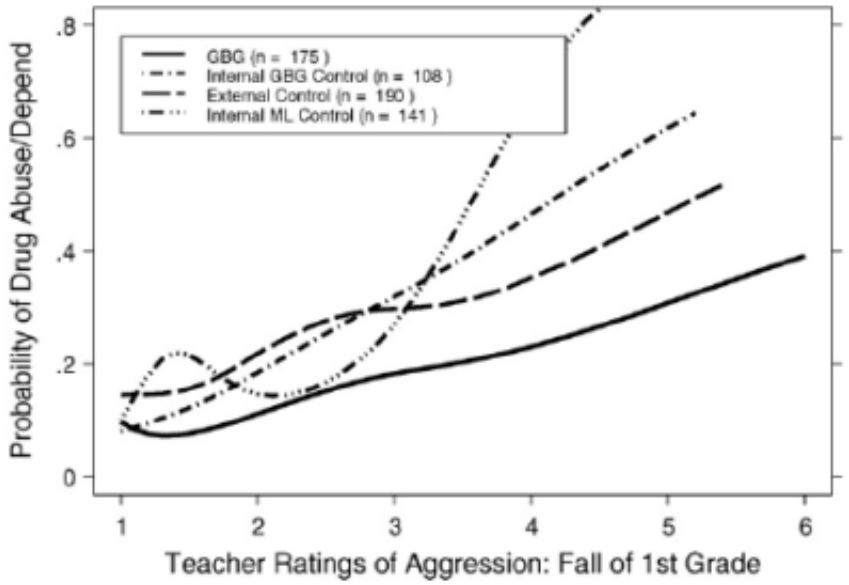


Fig. 1. Impact of GBG vs. all three controls on lifetime drug abuse/dependence disorders by baseline aggressive, disruptive behavior among Cohort 1 males and females.

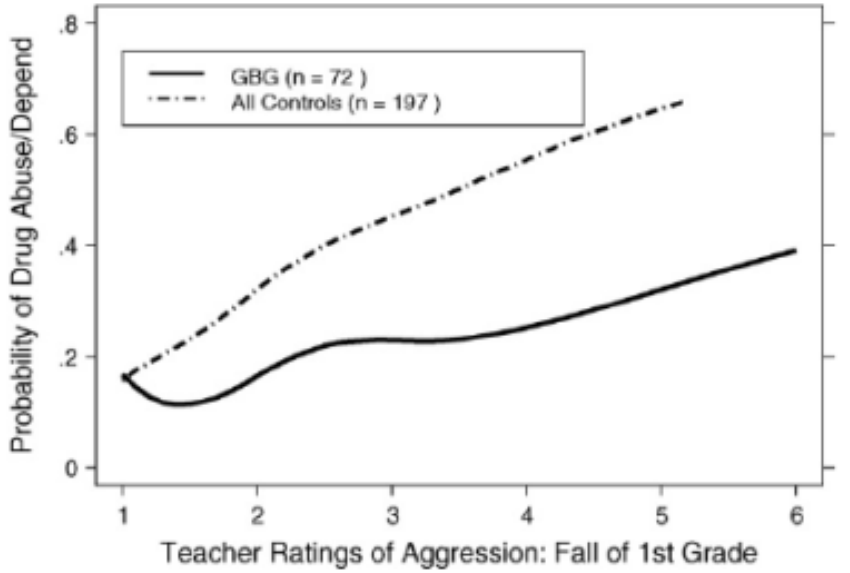


Fig. 2. Impact of GBG vs. all three controls combined on lifetime drug abuse/dependence disorders by baseline aggressive, disruptive behavior among Cohort 1 males.

ORIGINAL ARTICLE

Effectiveness of a Selective, Personality-Targeted Prevention Program for Adolescent Alcohol Use and Misuse

A Cluster Randomized Controlled Trial

Patricia J. Conrod, PhD; Maeve O'Leary-Barrett, BA; Nicola Newton, PhD; Lauren Topper, MSc; Natalie Castellanos-Ryan, PhD; Clare Mackie, PhD; Alain Girard, MSc

Context: Selective school-based alcohol prevention programs targeting youth with personality risk factors for addiction and mental health problems have been found to reduce substance use and misuse in those with elevated personality profiles.

Objectives: To report 24-month outcomes of the Teacher-Delivered Personality-Targeted Interventions for Substance Misuse Trial (Adventure trial) in which school staff were trained to provide interventions to students with 1 of 4 high-risk (HR) profiles: anxiety sensitivity, hopelessness, impulsivity, and sensation seeking and to examine the indirect herd effects of this program on the broader low-risk (LR) population of students who were not selected for intervention.

Design: Cluster randomized controlled trial.

Setting: Secondary schools in London, United Kingdom.

Participants: A total of 1210 HR and 1433 LR students in the ninth grade (mean [SD] age, 13.7 [0.33] years).

Intervention: Schools were randomized to provide brief personality-targeted interventions to HR youth or treatment as usual (statutory drug education in class).

Main Outcome Measures: Participants were assessed for drinking, binge drinking, and problem drinking before randomization and at 6-monthly intervals for 2 years.

Results: Two-part latent growth models indicated long-term effects of the intervention on drinking rates ($\beta = -0.320$, SE = 0.145, $P = .03$) and binge drinking rates ($\beta = -0.400$, SE = 0.179, $P = .03$) and growth in binge drinking ($\beta = -0.716$, SE = 0.274, $P = .009$) and problem drinking ($\beta = -0.452$, SE = 0.193, $P = .02$) for HR youth. The HR youth were also found to benefit from the interventions during the 24-month follow-up on drinking quantity ($\beta = -0.098$, SE = 0.047, $P = .04$), growth in drinking quantity ($\beta = -0.176$, SE = 0.073, $P = .02$), and growth in binge drinking frequency ($\beta = -0.183$, SE = 0.092, $P = .047$). Some herd effects in LR youth were observed, specifically on drinking rates ($\beta = -0.259$, SE = 0.132, $P = .049$) and growth of binge drinking ($\beta = -0.244$, SE = 0.073, $P = .001$), during the 24-month follow-up.

Conclusions: Findings further support the personality-targeted approach to alcohol prevention and its effectiveness when provided by trained school staff. Particularly novel are the findings of some mild herd effects that result from this selective prevention program.

Trial Registration: clinicaltrials.gov Identifier: NCT00776685

JAMA Psychiatry. 2013;70(3):334-342.
Published online January 23, 2013.
doi:10.1001/jamapsychiatry.2013.651

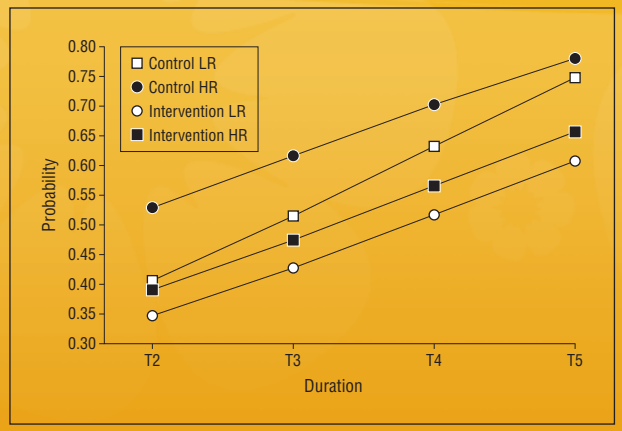


Figure 1. Estimated probability of reporting drinking × frequency of drinking in high-risk and low-risk youth attending intervention and control schools on the basis of 1217 respondents (53.1%) reporting nonuse at 6 months (T2), 1252 (54.6%) at 12 months (T3), 1020 (44.5%) at 18 months (T4), and 934 (40.7%) at 24 months (T5).

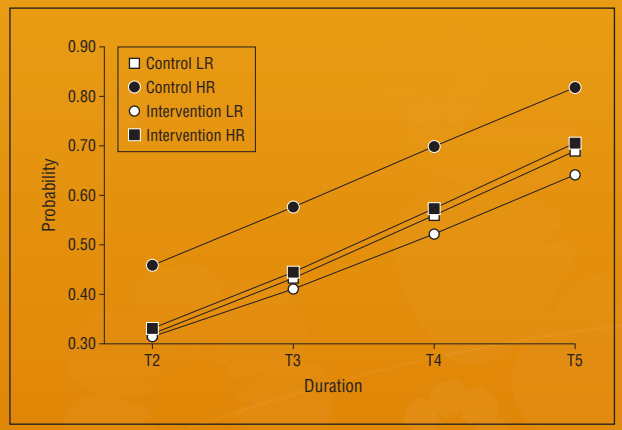


Figure 2. Estimated probability of reporting drinking × quantity of drinking in high-risk (HR) and low-risk (LR) youth attending intervention and control schools. T2 indicates 6 months after intervention; T3,12 months after intervention; T4, 18 months after intervention; and T5, 24 months after intervention.

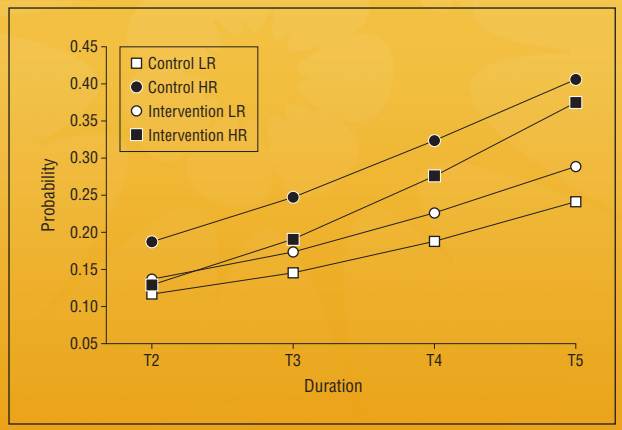


Figure 3. Estimated probability of reporting binge drinking × frequency of binge drinking in high-risk (HR) and low-risk (LR) youth attending intervention and control schools. T2 indicates 6 months after intervention; T3,12 months after intervention; T4, 18 months after intervention; and T5, 24 months after intervention.

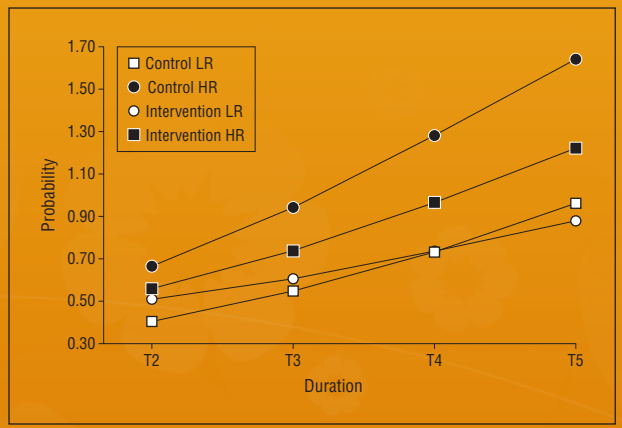


Figure 4. Estimated probability of reporting problem drinking symptoms × severity of problem drinking symptoms in high-risk (HR) and low-risk (LR) youth attending intervention and control schools. T2 indicates 6 months after intervention; T3,12 months after intervention; T4,18 months after intervention; and T5, 24 months after intervention.

Besluit

- Behandeling voor alcohol problemen werkt redelijk !!
- Het beste en goedkoopste wat we kunnen doen is de bestaande behandelingen bij meer patienten brengen !!
- Daarnaast kunnen we de behandel effectiviteit verbeteren door beter in te spelen op onze kennis van de neurobiologie
- Gepersonaliseerde behandeling wordt de toekomst o.m. farmacogenetica: 3-7j ?
- Neuromodulatie ook toekomst, maar nog niet voor nu: 5-15 jaar ?

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