



Benzodiazepine dependence and treatment strategies; myths versus reality

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Workshop "De schrik van je leven", Leuven, 17-10-2019

Indicaties voor benzodiazepinen

Indicaties	Opmerkingen
1. Slaapstoornissen	• Twee keus na slaaphygiëne en CGT-I • Enkel kortdurend i.v.m. tolerantie
2. Angststoornissen	• Mogelijk minder effectief dan antidepressiva • Risico op afhankelijkheid • Wel rol bij therapieresistente angststoornissen
3. Alcoholdetoxificatie	• Bewezen effectief in tegengaan onthoudingsverschijnselen, verkleind risico op insulten, delier en cognitieve problemen
4. Katatonie	• Zeer effectief, m.n. lorazepam
5. Delier	• Enkel wanneer sedatie vereist is.
6. Acute opwindning	• Psychiatrie: In combinatie met antipsychotica • Intensive care: Anaestheticum (propofol) eerste keuze
7. Status epilepticus	• Tolerantie bij onderhoudsbehandeling
8. Start antidepressiva	• Initiële angsttoename bij start antidepressiva

Contra-indicaties benzodiazepinen

Absolute contra-indicaties:

- Myasthenia Gravis
- Overgevoeligheid voor benzodiazepinen

Relatieve contra-indicaties:

- Ademhalingsdepressie (m.n. bij risicopatiënten zoals COPD of slaapapneu)
- Alcohol- of drugsverslaving in de voorgeschiedenis
- Ernstige leverproblemen (enkel voor BZD die gemetaboliseerd worden)

Long-term benzodiazepine use

Year prevalence in the population¹:

- Incidental usage: 6.2 – 17.6%
- Long-term use (> 6 months): 3.1 – 3.8%

Associated with many adverse effects:

- Increased risk on falls, hip fracture and traffic accidents
- Memory problems (and decline over time?!)
- Dependence

¹ Zandstra et al, Soc Psychiatry Psychiatr Epidemiol 2002

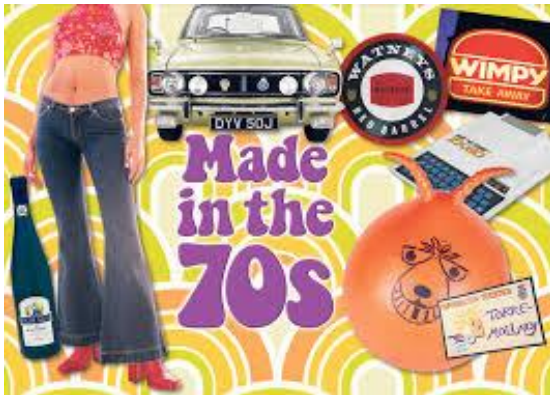
A historical perspective



Introduction chloordiazepoxide ('60) & diazepam ('63)

First case reports:

- Withdrawal symptoms after dose-escalation (e.g. Hollister, 1961)



First scientific discussions

- Marks (1978): 1 in 5 million patients will become addicted *versus*
- Lader (1978): "Benzodiazepine – The opium of the masses?"
- Tyrer (1974): "Benzodiazepine Bonanza"

Dose escalation therapeutic users¹

Variable	1–6 months		7–12 months		13–18 months		19–24 months	
	N or median	% or range ^a	N or median	% or range	N or median	% or range	N or median	% or range
Median dosage								
New recipients (N=460)	9.1	5.9–13	10.1	6.2–14.6	10.2	6.1–15	10.1	6.4–15.5
Continuing recipients (N=1,980)	9.7	6.4–13.8	10.1	6.6–14.6	10.2	6.5–14.6	10.0	6.5–14.9
Number of recipients with a high dosage ^b								
New recipients	— ^c	—	10	2.2	17	3.7	14	3
Continuing recipients	—	—	14	.71	24	1.2	26	1.3

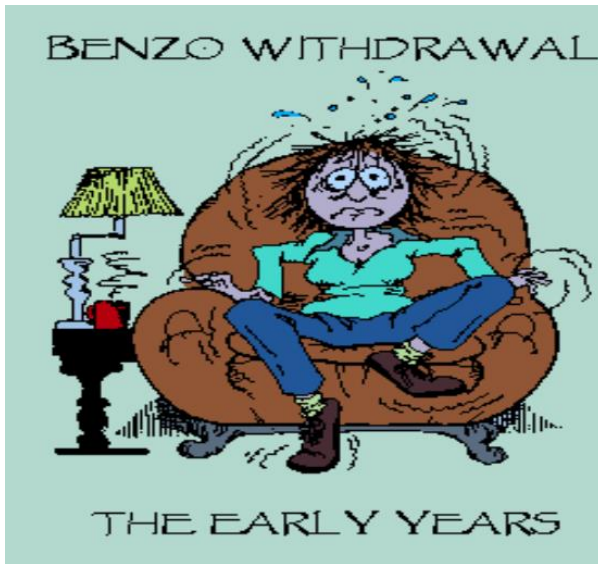
^a Interquartile range

^b Average daily dosage at least 20 DMEs for recipients aged 65 years or older and at least 40 DMEs for those aged less than 65 years

^c Cohort defined as starting on dosages within the therapeutic range; escalation to a high dosage can occur during the next three periods

Withdrawal after long-term therapeutic use¹

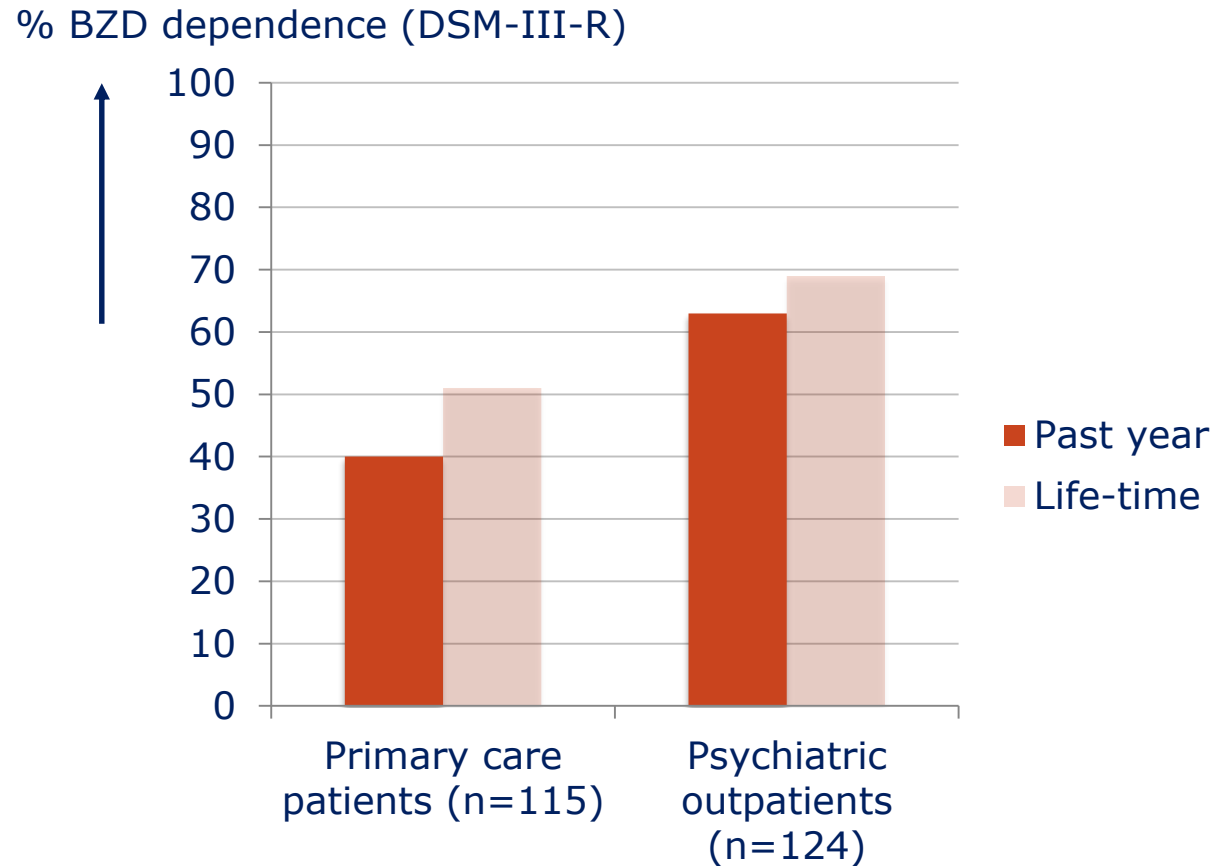
Double-blind, placebo controlled trial (n=40) of placebo versus diazepam tapering



Results:

- More (withdrawal) symptoms in placebo group
- More dropouts in placebo group
- Some withdrawal symptoms different from anxiety (e.g. tinnitus, involuntary movement, perceptual changes)

1997: First prevalence study



Other side-effects of benzodiazepines

- Traffic accidents
- Falls & hip fractures
- Cognitive side-effects & dementia
- Mortality

Verkeersongevallen



- Meta-analyses^{1,2}
 - RR=1.6 (patient-controle onderzoek)^{1,2}
 - OR= 1.6 – 1.8 (cohort studies)^{1,2}
 - OR= 7.8 wanneer gecombineerd met alcohol²
 - Experimentele studies: laterale afwijking (SMD=0.8, $p<.001$)¹
- Methodologisch beste studie (Barbone et al, Lancet 1998)
 - OR = 1.6 [95% CI: 1.4 – 2.1] (within-person design)
 - Dosisresponse effect, zowel kort als lange halfwaardetijd.

¹ Rapaport et al, J Clin Psychiatry 2009

² Dassanayake et al, Drug Safty 2011

BZD: falls & hip fractures



- Meta-analyse of impact BZD on hip fractures (n=18 studies)¹:
 - Short-term use: RR=2.4 [95% CI: 1.9 – 3.1]
 - Medium-term use: RR=1.5 [95% CI: 1.2 – 1.9]
 - Long-term use: RR=1.2 [95% CI: 1.1 – 1.3]
- Population Attributable Risk (PAR):
 - Varies between 1.8% (Germany) and 8.2% (Spain)²
 - Modified by age: 28% when age ≥ 80 years³
- Even in low dosages (≤ 3 mg diazepam equivalent)^{4,5}

¹ Donnelly et al, PLoS One 2017

² Khong et al, Calcif Tissue Int 2012

³ Pariente et al, Drugs Aging 2008

⁴ Chang et al, Am J Geriatr Psychiatry 2008

⁵ Yu et al, BMC Geriatr 2017

Fractures: Are BZD the worst of all?

	Osteoporotic fractures		Hip fractures	
	HR	[95% CI]	HR	[95% CI]
Benzodiazepines	1.15	[1.04 – 1.26]	1.24	[1.05 – 1.47]
<i>Antidepressants (AD):</i>				
• SSRI	1.43	[1.27 – 1.60]	1.48	[1.18 – 1.85]
• TCA	1.05	[0.93 – 1.19]	1.21	[0.96 – 1.51]
• Other AD	1.27	[1.06 – 1.52]	1.06	[0.71 – 1.58]
Lithium	0.80	[0.45 – 1.41]	-	-
Mood stabilizers	1.41	[1.12 – 1.77]	1.24	[0.80 – 1.92]
Antipsychotics	1.43	[1.15 – 1.77]	2.14	[1.52 – 3.02]

Hip fracture in nursing home residents

- Valrisico mogelijk hoger in verpleeghuissetting¹
- Valrisico m.n. gevolg van sedatie en cognitieve beperkingen²
- Stoppen BZD-hypnotica gebruik in VHP (n=26, gem 79 jaar)²:
 - Betere stabiliteit
 - Verbetering cognitieve maten
 - Geen verslechtering slaap

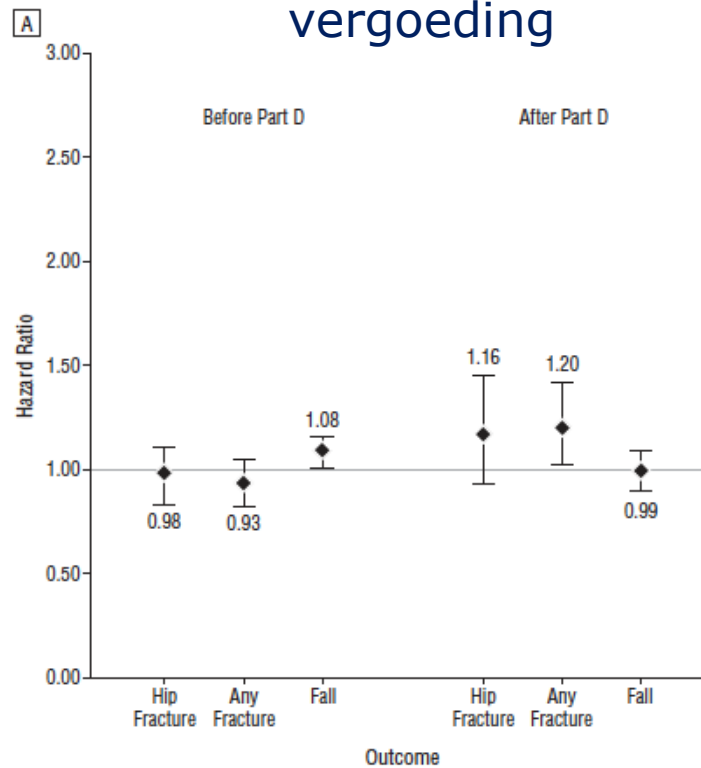


1 Ray et al, Drug Saf 2002

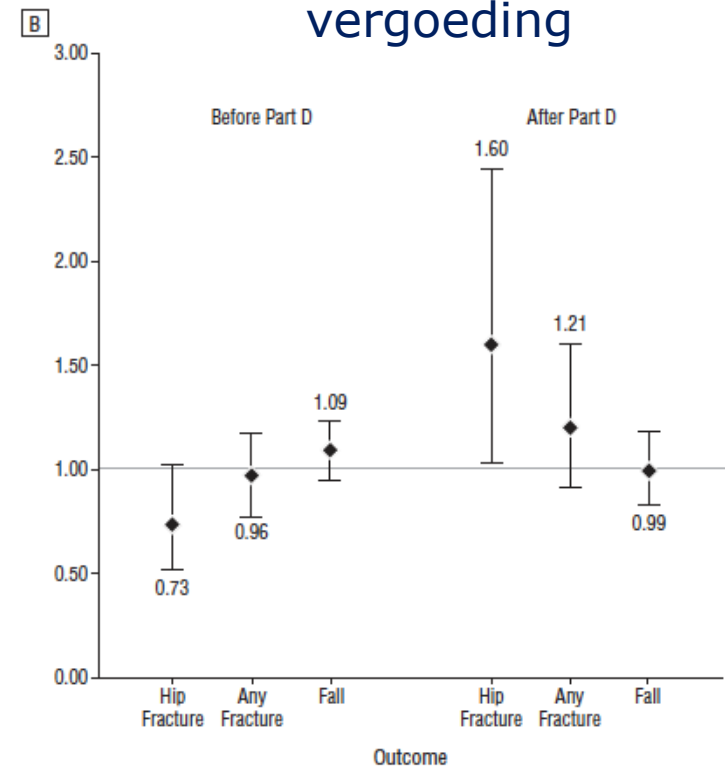
2 Tsunado et al, Int J Geriatr Psychiatry 2010

Paradox: Valrisico ↑ na staken BZD in VPH¹

Verminderde vergoeding



Volledige afschaffing vergoeding



Cognitive functioning

wat ben ik nou vergeten?



Cognitive effects of chronic use¹:

- Meta-analyse (13 studies) of 12 cognitive domains
- Mean effect size: -0.74 (SD +/- 0.25), range (-1.30 through -0.42)

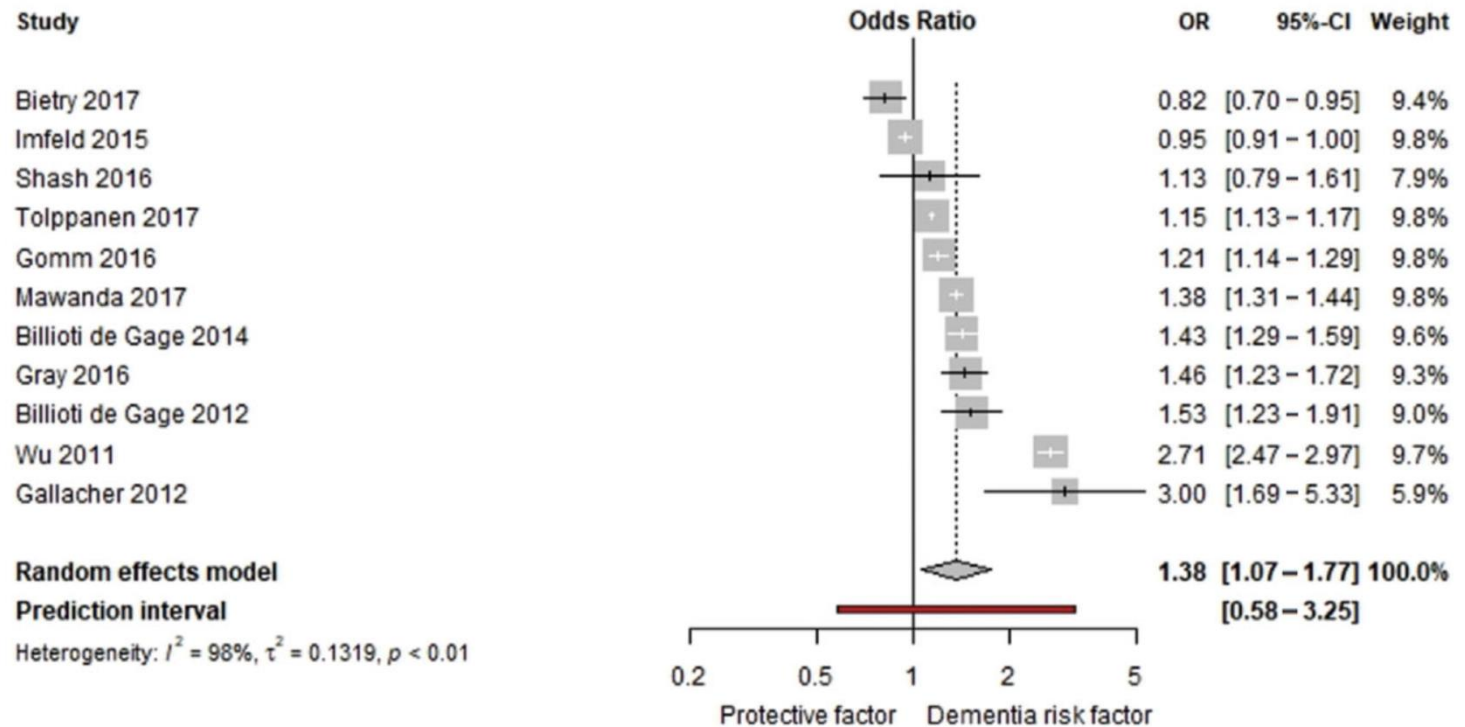
Long-term effects (LASA)²:

- 435 / 2105 BZD-users
- Duration of use and cumulative dose predicts cognitive decline.
- Small effect-size ($F^2 < 0.01$)

¹ Barker et al, CNS Drugs, 2004

² Biermans, Int J Geriatr Psychiatry 2005

BZD-related risk of dementia

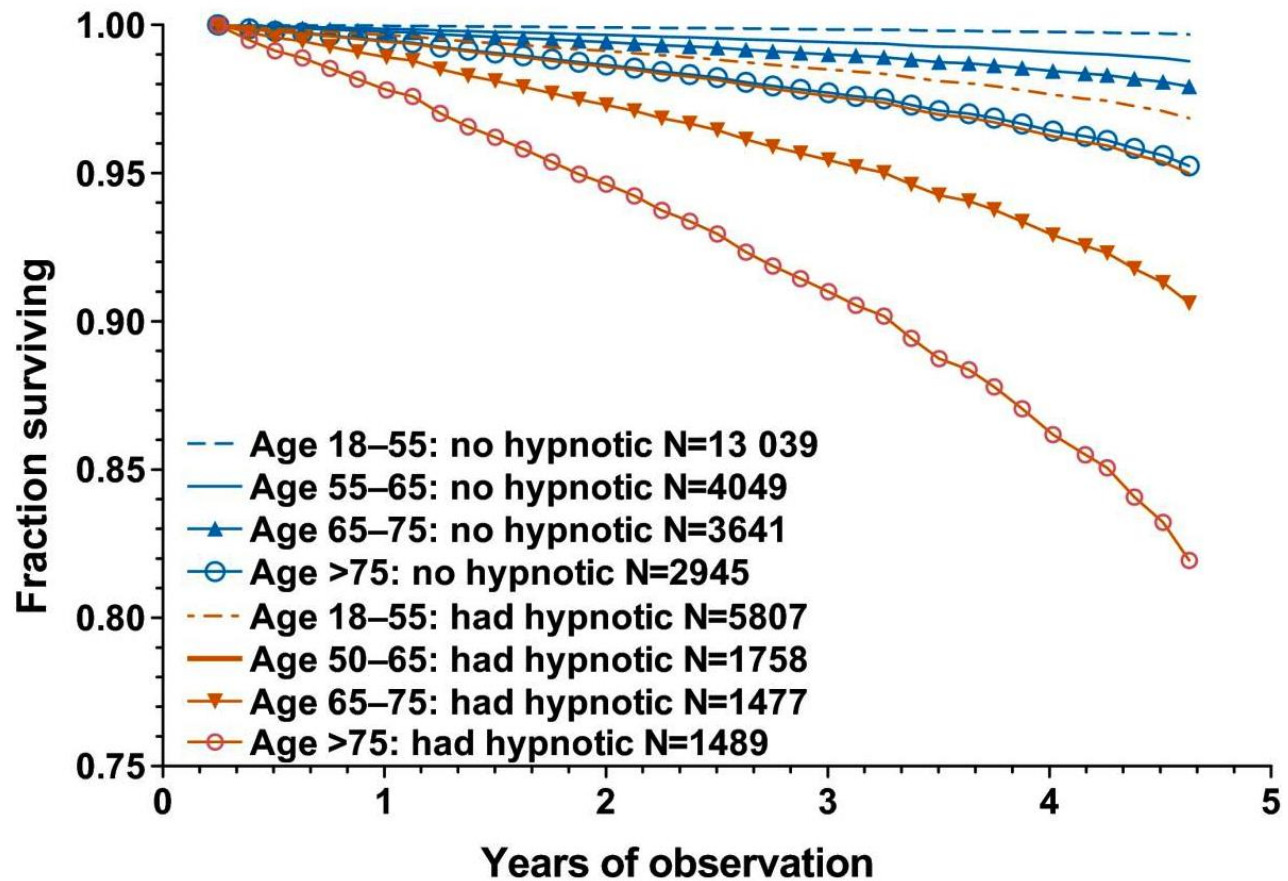


BZD-related mortality risk¹

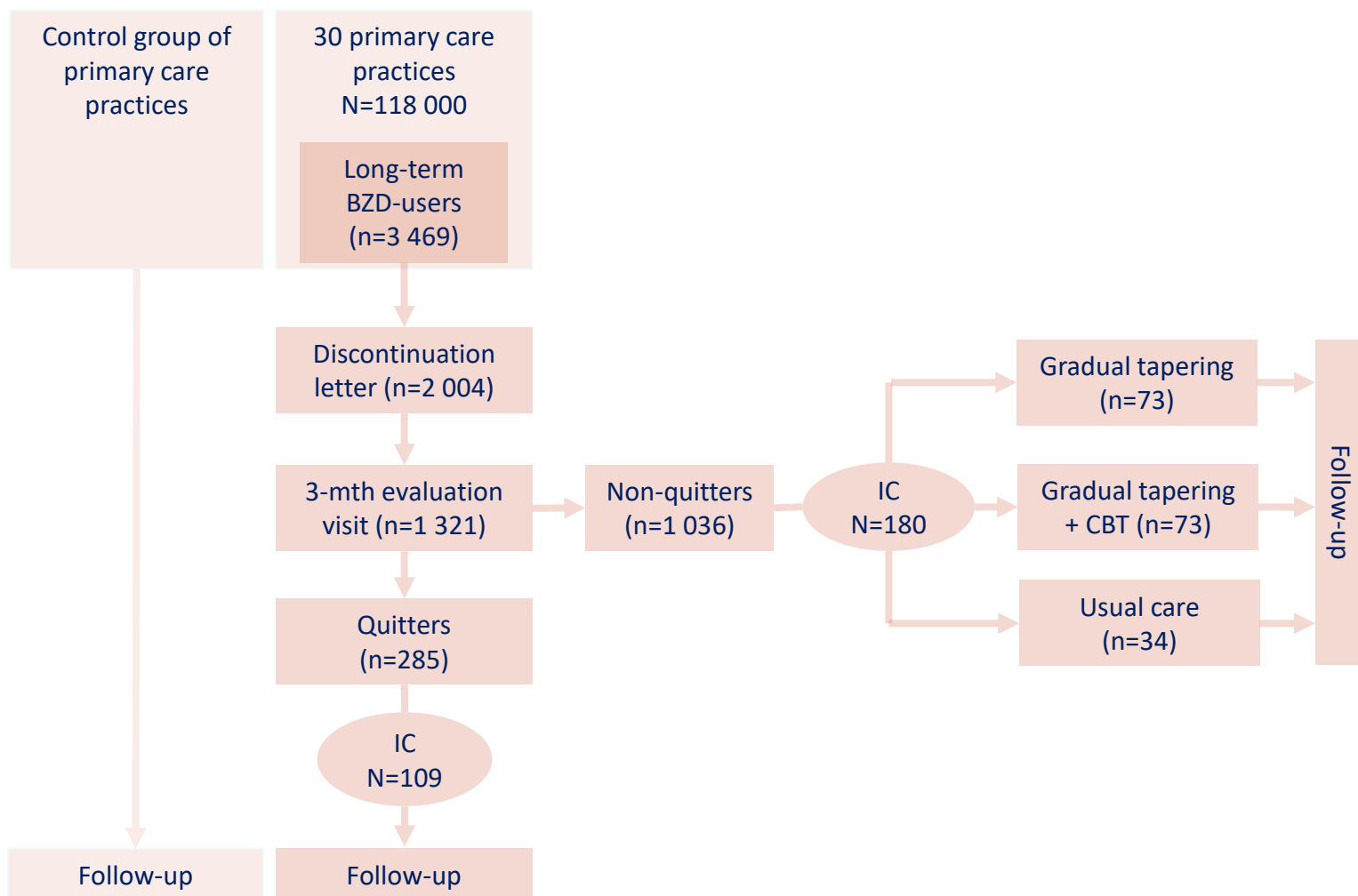


- 18/24 positive studies
- Kripke et al (BMJ 2012)
 - N = 10 529 with a follow-up of 2.5 years
 - Well-adjusted for confounders, especially chronic disease
 - Dosis-effect response:
 - 0.4 – 18 doses / year: HR = 3.6
 - 18 – 132 doses / year: HR = 4.4
 - > 132 doses / year: HR = 5.3

Hypnotic use and age: effects on survival



BenzoRedux project:



Not only patients worry.....

Some worries of the general practitioner:

- Feel ashamed to advise discontinuation after 20 years
- Feasible for the oldest old (>90 years)?
- Patients will request other, more toxic pills
- Medical consumption will increase



BenzoRedux project: Part I



Results discontinuation letter^{1,2}

Main effects discontinuation letter in primary care¹:

- Quitters at 6 months: 24% vs 12% (RR=2.1 [95% CI: 1.8–2.4])
- Full abstinence over 21 months: 13% vs 5% (RR=2.6 [95% CI: 2.0–3.4])
- Mean dose reduction vs control: 21.5 PDD [95% CI: 8.2–16.8]

Secondary effects^{2,3}:

- No increase in medical consumption²
- No substitution for other (psychotropic) drugs³

¹ Gorgels et al, Drug Alc Dependence 2005

² Gorgels et al, Scand J Prim Health Care 2008

³ Gorgels et al, Fam Pract 2007

Predictors of effectiveness¹

Adjusted hazard rate [95% CI]:

Predictors of long-term discontinuation²:

- Male sex 1.7 [1.3 – 2.5], $p < .001$
- Dosage

≤ 65 PDD	<i>Reference</i>
$> 65 \leq 130$ PDD	0.3 [0.2 – 0.4], $p < .001$
> 130 PDD	0.2 [0.1 – 0.4], $p < .001$
- Duration of use:

≤ 24 months	<i>Reference</i>
$> 24 \leq 120$ months	0.5 [0.3 – 0.8], $p < .001$
> 120 months	0.2 [0.1 – 0.4], $p < .001$
- Use of a BZD with a half-life < 24 h 1.7 [1.1 – 2.5], $p = .01$

Predictors of effectiveness¹

Adjusted hazard rate [95% CI]:

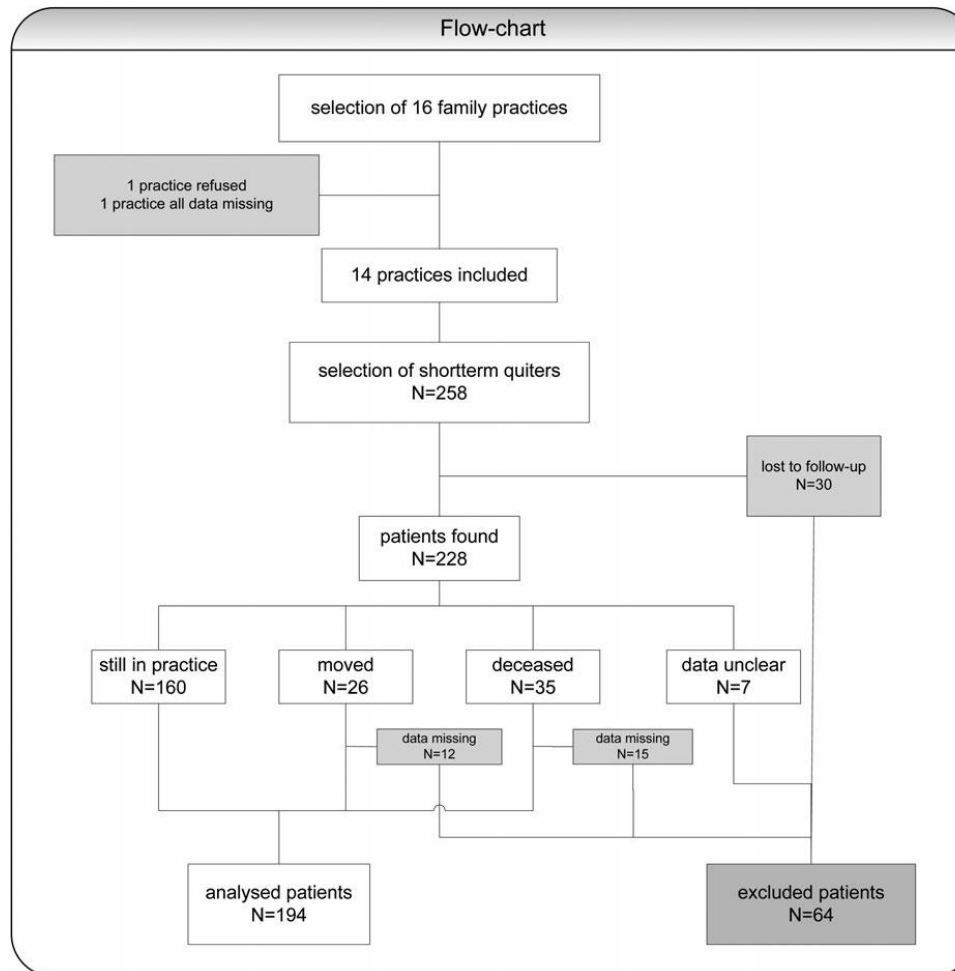
Predictors of long-term discontinuation²:

- Male sex 1.7 [1.3 – 2.5], p<.001
- Dosage
 - ≤65 PDD Reference
 - >65 ≤130 PDD 0.3 [0.2 – 0.4], p<.001
 - >130 PDD 0.2 [0.1 – 0.4], p<.001
- Duration of use: ≤24 months Reference
 - >24 – 120 months 0.5 [0.3 – 0.8], p<.001
 - >120 months 0.2 [0.1 – 0.4], p<.001
- Use of a BZD with a half-life ≤24h 1.7 [1.1 – 2.5], p=.01

No negative impact of old age!

Even not in those over 75 years of age!

Continued abstinence: a 10 year follow-up¹

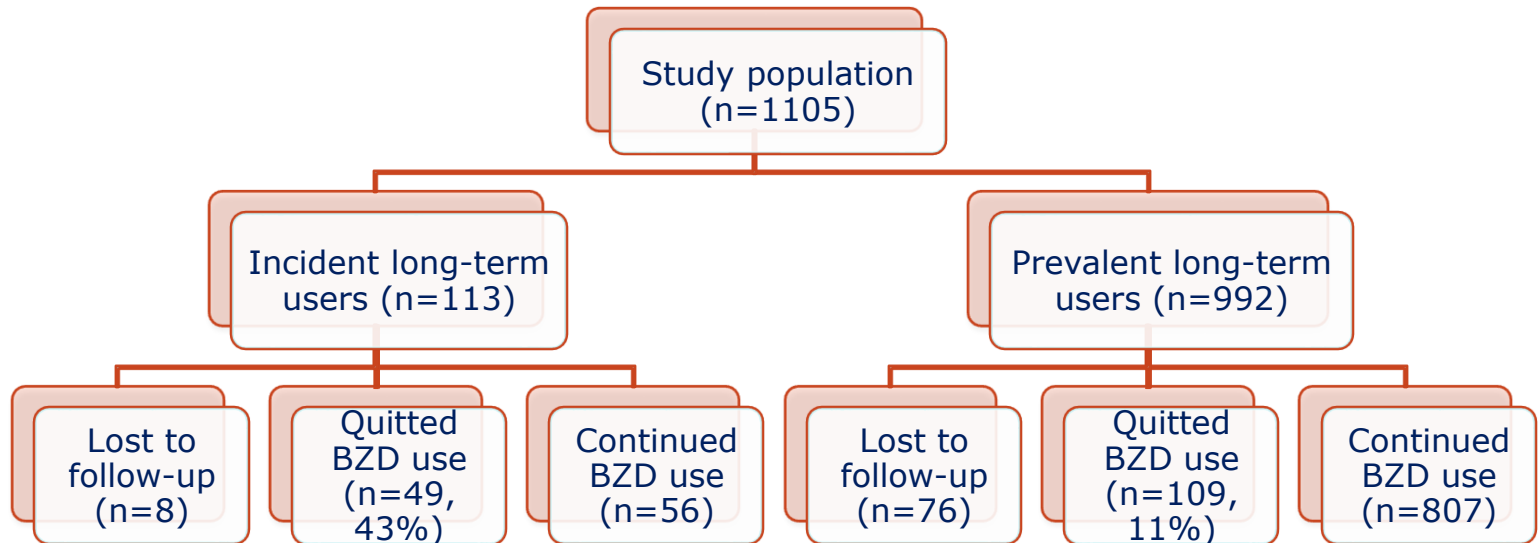


Only two predictors of continued abstinence over 10 years:

- Continued abstinence during first 21 months (OR=4.4 [2.2-8.7], $p<.001$)
- Visitor of evaluation visit 3 months after the letter (OR=2.1 [1.0 - 4.3], $p=.044$)

The natural course of long-term BZD use¹

Does tolerance to BZD use lead to dose-escalation in primary care?



The natural course of long-term BZD use¹

Control group of the BenzoRedux project:

	Regression coefficient (SEM)	P-value
Total group of BZD users (n=863)	0.034 (0.148)	.817
• Incident long-term users (n=56)	0.639 (0.543)	.240
• Prevalent long-term users (n=807)	-0.008 (0.153)	.960

No impact of:

- Old age (<50, 50-75, > 75 years)
- Sex
- High dose usage (use of more than 2 DDD per day)

BenzoRedux project: Part II



Part II: Gradual tapering of BZD

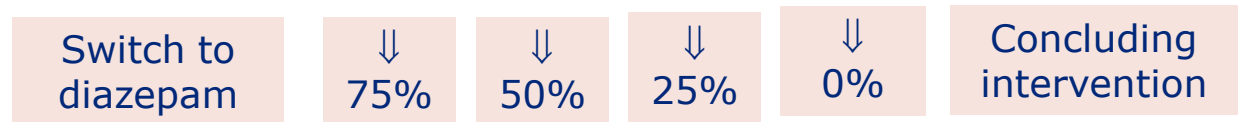
Time span (weeks):



Visits to the GP:



Dose reduction (by GP):



CBT group meetings:



TABLE

35.1

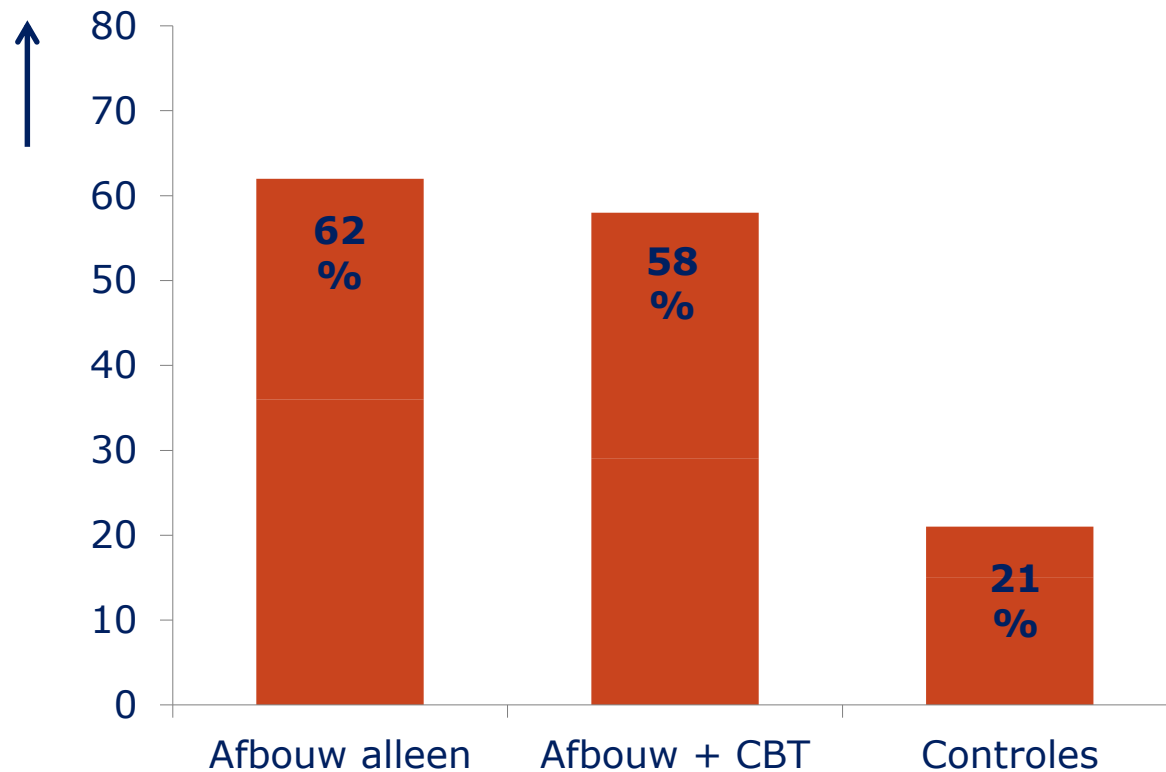
**Conversion factors for benzodiazepine agonists
in diazepam equivalents**

Benzodiazepine agonist	Equivalent dosages	Conversion factor to diazepam equivalents
■ Alprazolam	0.5–1 mg	×10–20
■ Bromazepam	5–10 mg	×1–2
■ Brotizolam	0.25 mg	×40
■ Chlordiazepoxide	20–25 mg	×0.4–0.5
■ Clobazam	15–20 mg	×0.5–0.67
■ Clonazepam	0.5–8 mg	×1.25–20
■ Clorazepinezuur	10–15 mg	×0.67–10
■ Diazepam ^a	10 mg	×1
■ Flunitrazepam	1 mg	×10
■ Flurazepam	15–30 mg	×0.33–0.67
■ Ketazolam	15–60 mg	×0.16–0.67
■ Loprazolam	1–2 mg	×5–10
■ Lorazepam	1–2 mg	×5–10
■ Lormetazepam	1–2 mg	×5–10
■ Medazepam	10–20 mg	×0.5–1
■ Midazolam	7.5–10 mg	×1–1.33
■ Nitrazepam	10 mg	×1
■ Nordazepam	10 mg	×1
■ Oxazepam	20–50 mg	×0.2–0.5
■ Prazepam	10–20 mg	×0.5–1
■ Quazepam	20	×0.5
■ Temazepam	20–30 mg	×0.5–0.67
■ Triazolam	0.125–0.5 mg	×20–80
■ Zaleplon ^b	20 mg	×0.5
■ Zolpidem ^b	5–20 mg	×0.5–2
■ Zopiclon ^b	7.5–15 mg	×0.66–1.33

¹ Oude Voshaar, Chapter 35 Lowinson's & Ruiz's Substance Abuse: A comprehensive textbook (5th edition)

Abstinence at end-of-treatment¹

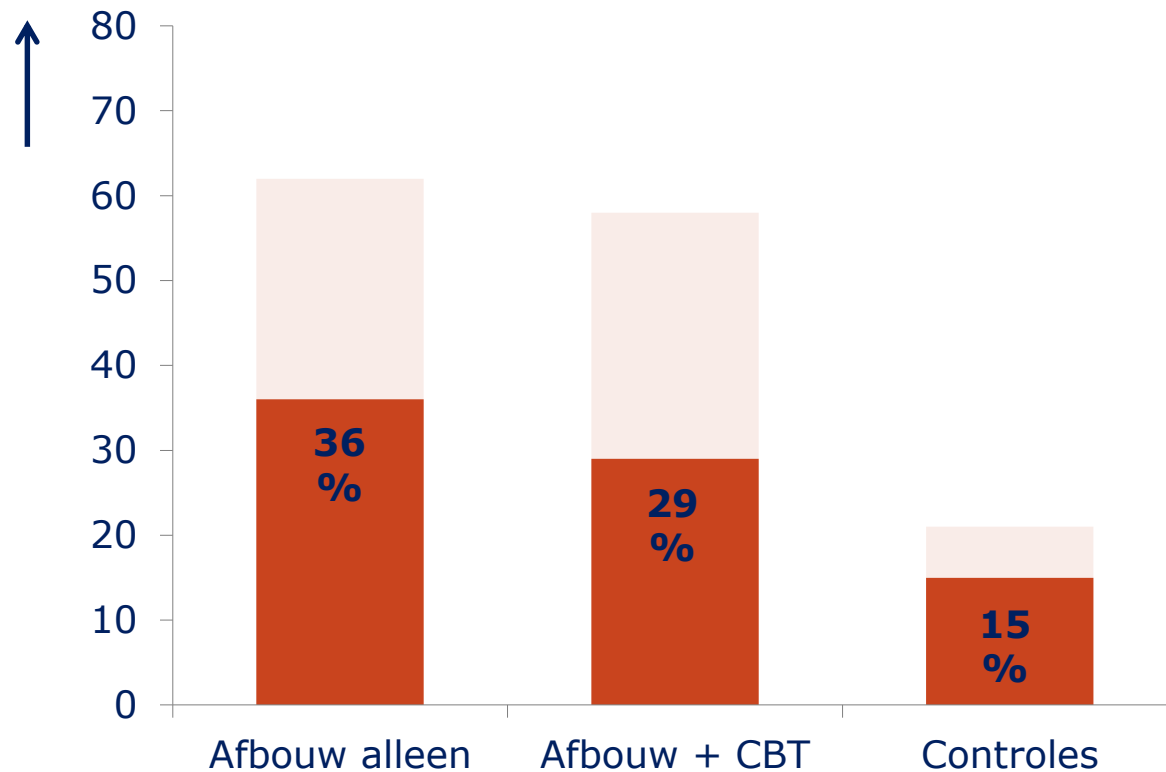
% of abstinent patients



¹ Oude Voshaar, Br J Psychiatry 2003

Abstinence at end-of-treatment¹

% of abstinent patients



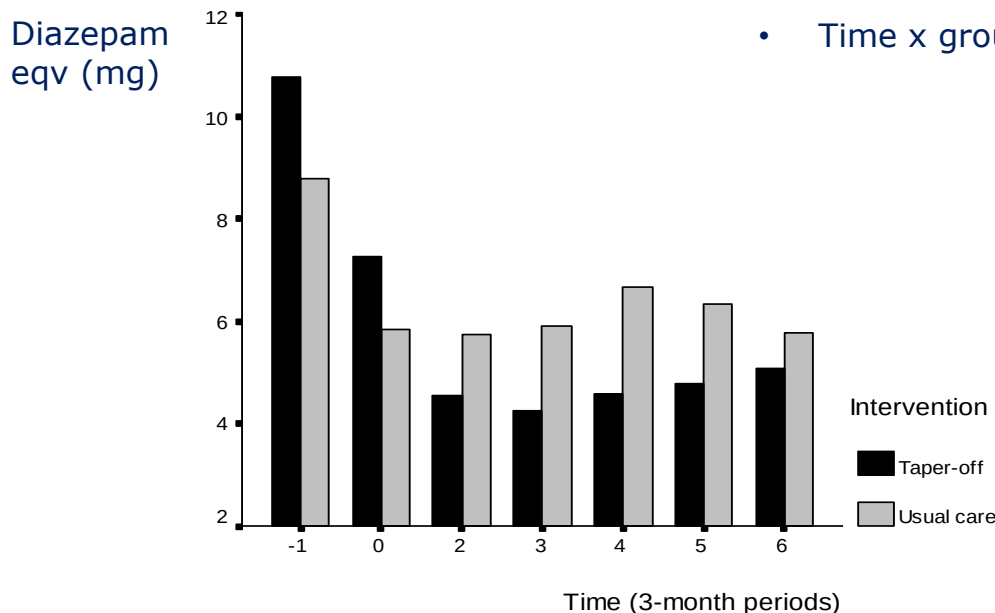
¹ Oude Voshaar, Br J Psychiatry 2003

Secondary outcome measures at follow-up

Dose reduction in non-quitters:

Intervention vs usual care (RM ANOVA):

- Group: $F=6.5$; $df=1$; $p=0.01$
- Time x group: $F=5.3$; $df=1$; $p=0.02$



Psychological functioning:

- No worsening of quality of life (HUI, EQ-5), depression (POMS), or anxiety (POMS) in quitters compared to non-quitters

Incremental cost-effectiveness ratio¹

Costs taken into account:

- Intervention
- Benzodiazepine prescription
- Other drug prescriptions
- Non-regular medicine
- Over-the-counter drugs
- Primary care
- Medical specialist/first aid
- Psychologist/social worker
- Physiotherapist
- Productivity loss
- Other

Limited pharmaceutical perspective:
• ICER = € 0.57 for TO alone

Comprehensive pharmaceutical perspective:
• ICER = € 10.30 for TO + CBT
• ICER = € 10.02 for TO alone

Societal perspective:
• ICER = € 62.53 for TO + CBT
• ICER = € 21.69 for TO alone

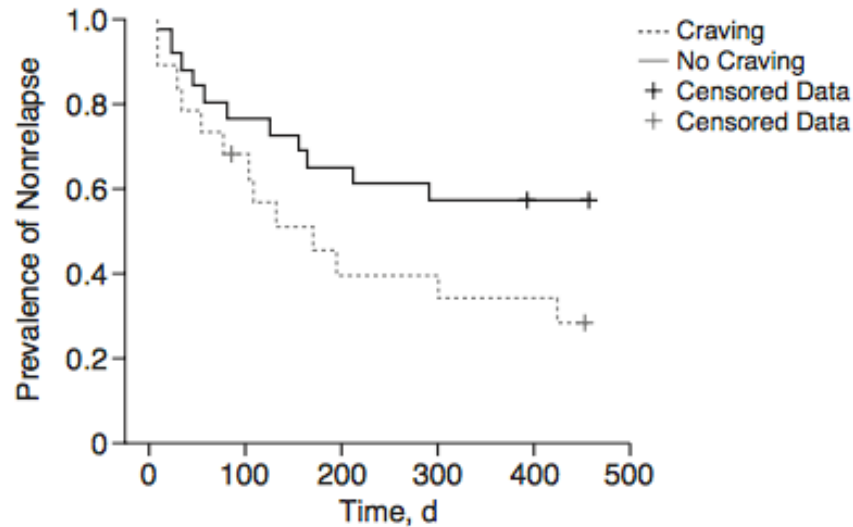
Predictors of long-term abstinence¹

	Crude ^a Hazard Rate [95% CI]	Adjusted Hazard Rate [95% CI]
Lower dosage (per 10 mg diazepam eqv)	1.7 [1.4–2.0]	1.5 [1.2–1.9]
>50% dose reduction after letter	2.3 [1.5–3.3]	2.1 [1.4–3.3]
Shorter duration of use (per 10 years)	1.2 [1.0–1.5]	-
Low potency BZD	1.7 [1.1–2.7]	-
Not smoking	1.5 [1.0–2.1]	-
No alcohol use	1.5 [1.0–2.1]	1.7 [1.2–2.5]
Withdrawal symptoms at baseline	1.0 [1.0–1.1]	-
Preoccupation with BZD use (Bendep-SRQ)	1.9 [1.3–2.7]	-
Lack of compliance (Bendep-SRQ)	4.5 [2.3–8.8]	2.4 [1.1–5.2]
Negativism (MMPI)	1.0 [1.0–1.1]	-
Tension (POMS)	1.0 [1.0–1.1]	-

^a Only corrected for treatment condition

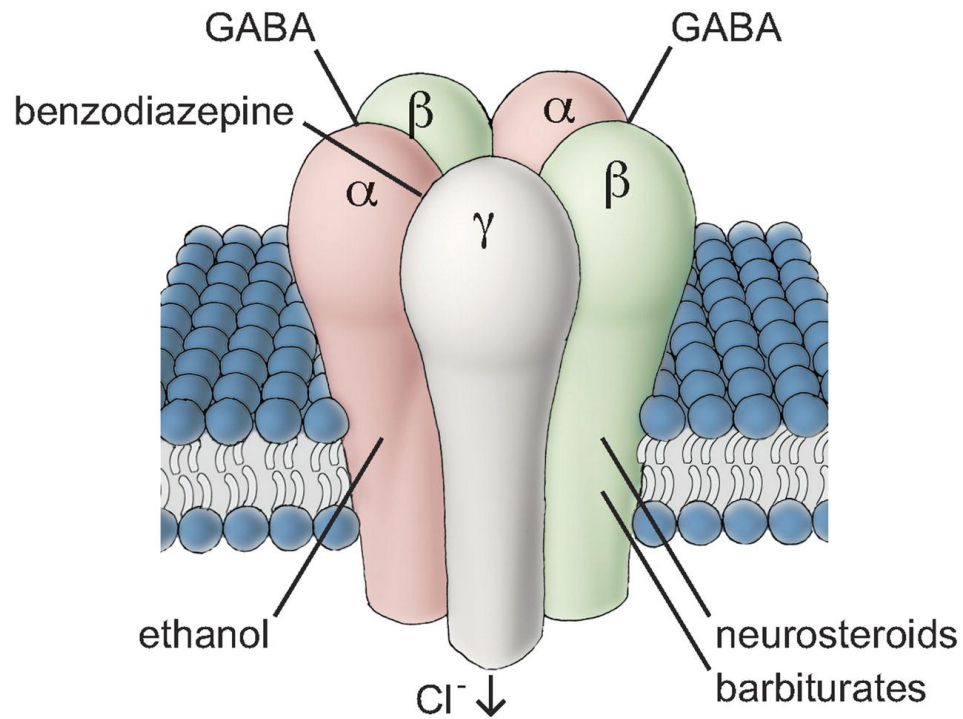
Impact of craving on relapse¹

- The Benzodiazepine Craving Questionnaire (BCQ) assesses craving reliably.
- Craving is a risk factor for relapse after BZD discontinuation.



- Clinicians should explore the patients' expectations of the effects of BZDs and focus on how to cope with craving.

Z-drugs: Selective for the alpha1 subunit

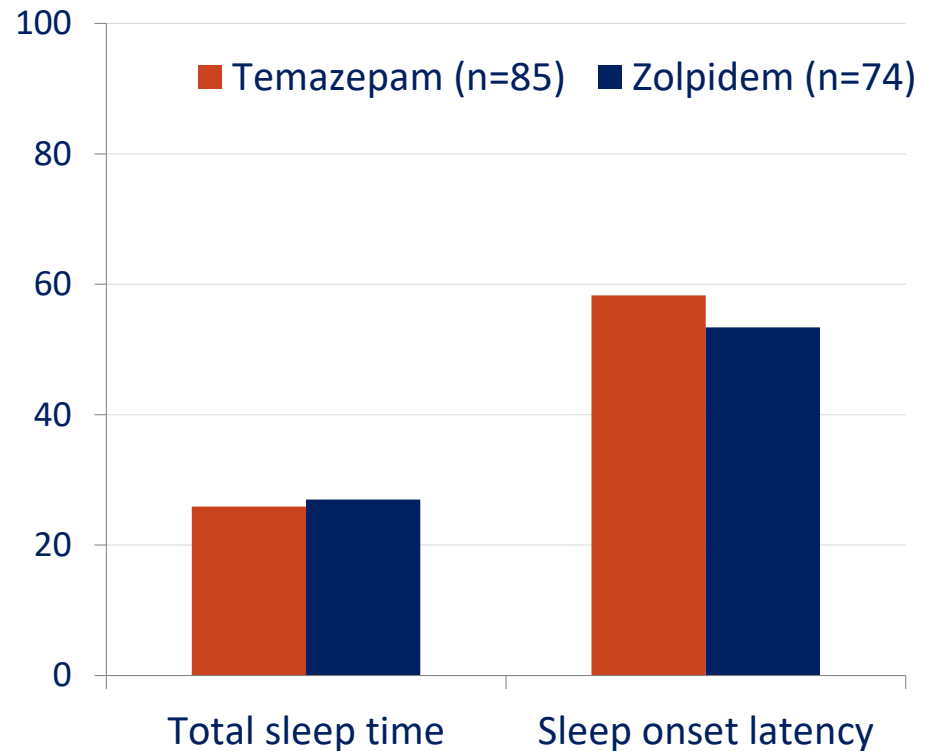


Withdrawal symptoms

after 4 week treatment of insomnia (RCT)¹

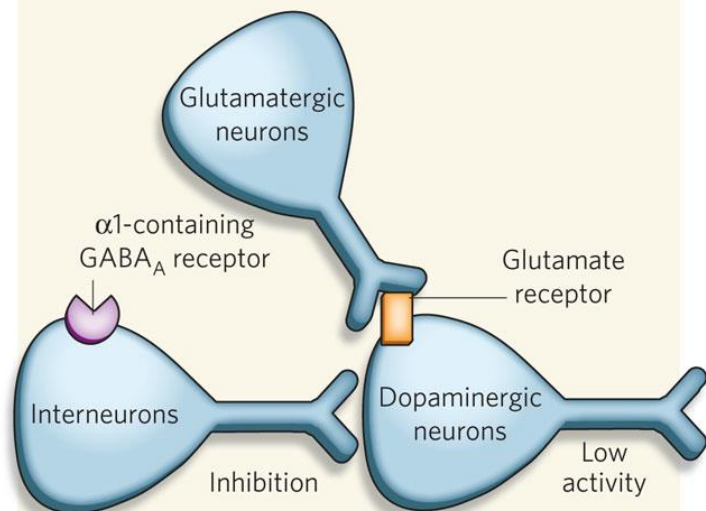
Prevalence (%)
of withdrawal
symptoms

(>40% change
from baseline)

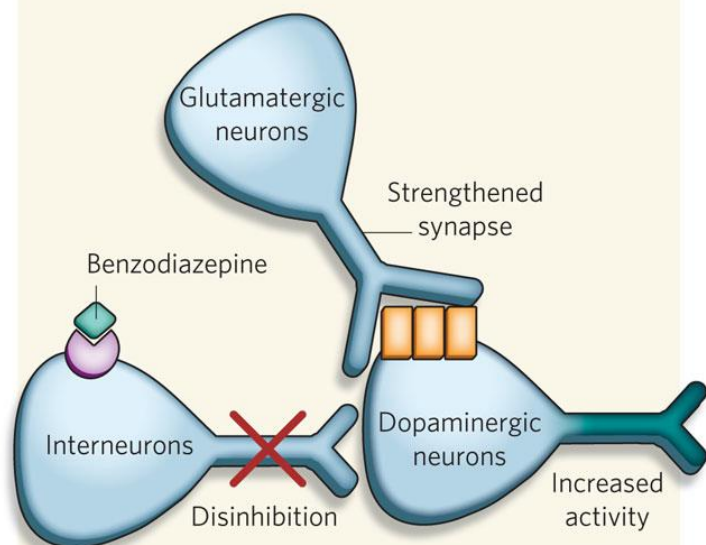


¹ Oude Voshaar et al, Eur Neuropsychopharmacol 2004

a No benzodiazepines



b Benzodiazepines bound



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nature

ARTICLES

Neural bases for addictive properties of benzodiazepines

Kelly R. Tan¹, Matthew Brown^{1*}, Gwenaël Labouèbe^{1*}, Cédric Yvon^{1*}, Cyril Creton¹, Jean-Marc Fritschy², Uwe Rudolph³ & Christian Lüscher^{1,4,5}

Benzodiazepines are widely used in clinics and for recreational purposes, but will lead to addiction in vulnerable individuals. Addictive drugs increase the levels of dopamine and also trigger long-lasting synaptic adaptations in the mesolimbic reward system that ultimately may induce the pathological behaviour. The neural basis for the addictive nature of benzodiazepines, however, remains elusive. Here we show that benzodiazepines increase firing of dopamine neurons of the ventral tegmental area through the positive modulation of GABA_A (γ-aminobutyric acid type A) receptors in nearby interneurons. Such disinhibition, which relies on α1-containing GABA_A receptors expressed in these cells, triggers drug-evoked synaptic plasticity in excitatory afferents onto dopamine neurons and underlies drug reinforcement. Taken together, our data provide evidence that benzodiazepines share defining pharmacological features of addictive drugs through cell-type-specific expression of α1-containing GABA_A receptors in the ventral tegmental area. The data also indicate that subunit-selective benzodiazepines sparing α1 may be devoid of addiction liability.

Meta-analysis on achieving BZD abstinence¹

	OR	[95% CI]	p-value
Ten controlled withdrawal studies:			
• Withdrawal with psychotherapy (n=4):	5.1	[2.7–9.6]	p<.001
• Withdrawal with pharmacotherapy (n=4):	1.3	[0.7–1.5]	p=.42
• Withdrawal with prescribing intervention (n=2):	1.4	[1.0–2.0]	p=.04
Eight prescribing RCTs:			
• Multifaceted intervention (n=5):	1.4	[1.1 – 1.7]	p=.006
• Single prescribing intervention (n=3):	0.9	[0.7 – 1.1]	p=.27

¹ Gould et al, Br J Psychiatry 2014

Meta-analysis of subgroups¹

Antidepressants	Studies	Patients	Odds Ratio [95% C.I.]
• Paroxetine	2	167	1.6 [0.8 – 3.0]
• Imipramine	2	75	3.0 [1.2 – 7.8]
• Dothiepin	1	87	0.6 [0.3 – 1.6]
• Trazodone	2	108	2.6 [1.1 – 6.4]
Pooled analysis	7	437	1.6 [1.1 – 2.4]

¹ Oude Voshaar, Chapter 35 Lowinson's & Ruiz's Substance Abuse: A comprehensive textbook (5th edition)

Meta-analysis of subgroups¹

Anticonvulsants:	Studies	Patients	Odds Ratio [95% C.I.]
• Carbamazepine	3	99	1.0 [0.4 – 2.7]
• Valproate	1	37	4.8 [1.1 – 20.3]
Pooled analysis	4	136	1.7 [0.8 – 3.8]

¹ Oude Voshaar, Chapter 35 Lowinson's & Ruiz's Substance Abuse: A comprehensive textbook (5th edition)

Meta-analysis of subgroups¹

Anti-anxiety agents	Studies	Patients	Odds Ratio [95% C.I.]
• Buspirone	5	217	1.1 [0.7 – 1.9]
• Progesterone	1	35	0.8 [0.2 – 3.2]
• Alpidem	1	25	0.2 [0.0 – 0.9]
Pooled analysis	7	277	0.9 [0.6 – 1.4]

¹ Oude Voshaar, Chapter 35 Lowinson's & Ruiz's Substance Abuse: A comprehensive textbook (5th edition)

Meta-analysis of subgroups¹

Sedatives-hypnotics	Studies	Patients	Odds Ratio [95% C.I.]
• Melatonin	2	72	2.5 [1.0 – 6.4]
• Hydroxyzine	1	139	1.1 [0.4 – 2.9]
• Cyamemazine	1	168	0.4 [0.2 – 0.8]
Pooled analysis	4	379	0.9 [0.6 – 1.5]

¹ Oude Voshaar, Chapter 35 Lowinson's & Ruiz's Substance Abuse: A comprehensive textbook (5th edition)

Meta-analysis of subgroups¹

Other drugs	Studies	Patients	Odds Ratio [95% C.I.]
• Propranolol	2	71	0.8 [0.3 – 1.9]
• Aspartate	1	144	0.9 [0.4 – 2.1]
• Homeogene	1	41	2.0 [0.5 – 7.5]
• Sedatif PC	1	46	1.5 [0.5 – 4.9]
• Flumazenil	1	40	3.7 [1.0 – 14.0]

¹ Oude Voshaar, Chapter 35 Lowinson's & Ruiz's Substance Abuse: A comprehensive textbook (5th edition)

Meta-analysis of subgroups¹

	Patients	Odds Ratio [95% C.I.]
CBT for anxiety disorders		
• Otto et al (1993)	33	9.8 [2.0 – 47.9]
• Spiegel et al (1994)	21	1.1 [0.1 – 9.9]
• Gosselin et al (2006)	61	5.0 [1.7 – 14.8]
Pooled analysis	115	4.7 [2.1 – 10.7]
CBT for insomnia		
• Baillargeon et al (2003)	52	6.2 [1.7 – 23.3]
• Morin et al (2004)	65	5.0 [1.7 – 14.4]
Pooled analysis	117	5.5 [2.4 – 12.5]
CBT for BZD dependence		
• Vorma et al (2002)	76	0.4 [0.1 – 1.3]
• Oude Voshaar et al (2003)	146	0.8 [0.4 – 1.5]
Pooled analysis	222	0.7 [0.4 – 1.2]
Overall pooled analysis	499	1.8 [1.3 – 2.6]

¹ Oude Voshaar, Chapter 35 Lowinson's & Ruiz's Substance Abuse: A comprehensive textbook (5th edition)

Thank you
for your
attention!

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Dokter, mag ik 1 pilletje extra?



Challenge study BZD (side)effects¹

Gerandomiseerde, dubbelblinde, cross-over trial:

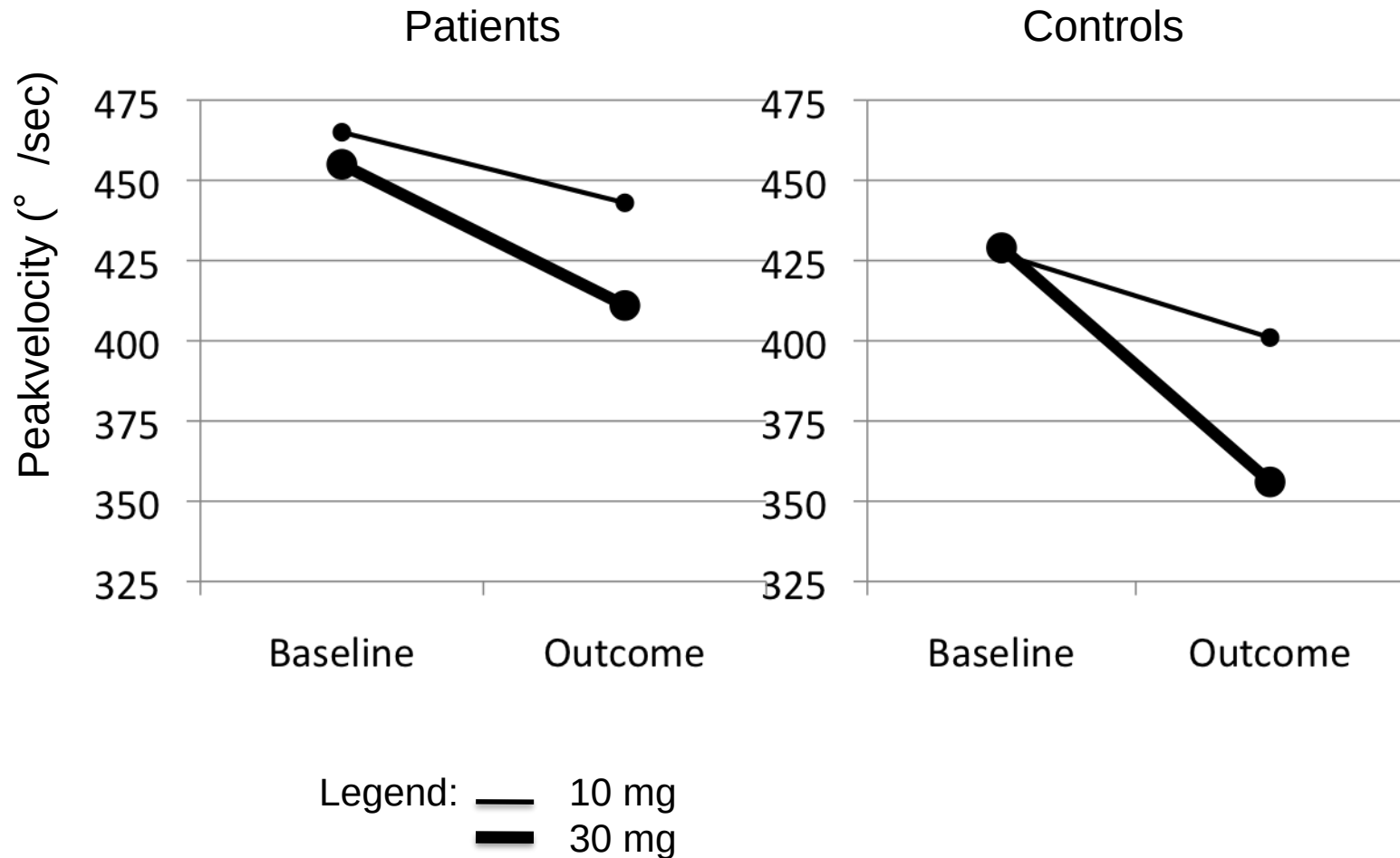
- Overslaan ochtenddosering oxazepam voor komst naar ziekenhuis
- Inname van 10 mg, respectievelijk 30 mg oxazepam
- Patiënten dachten beide dagen 30 mg oxazepam te krijgen

Procedure:

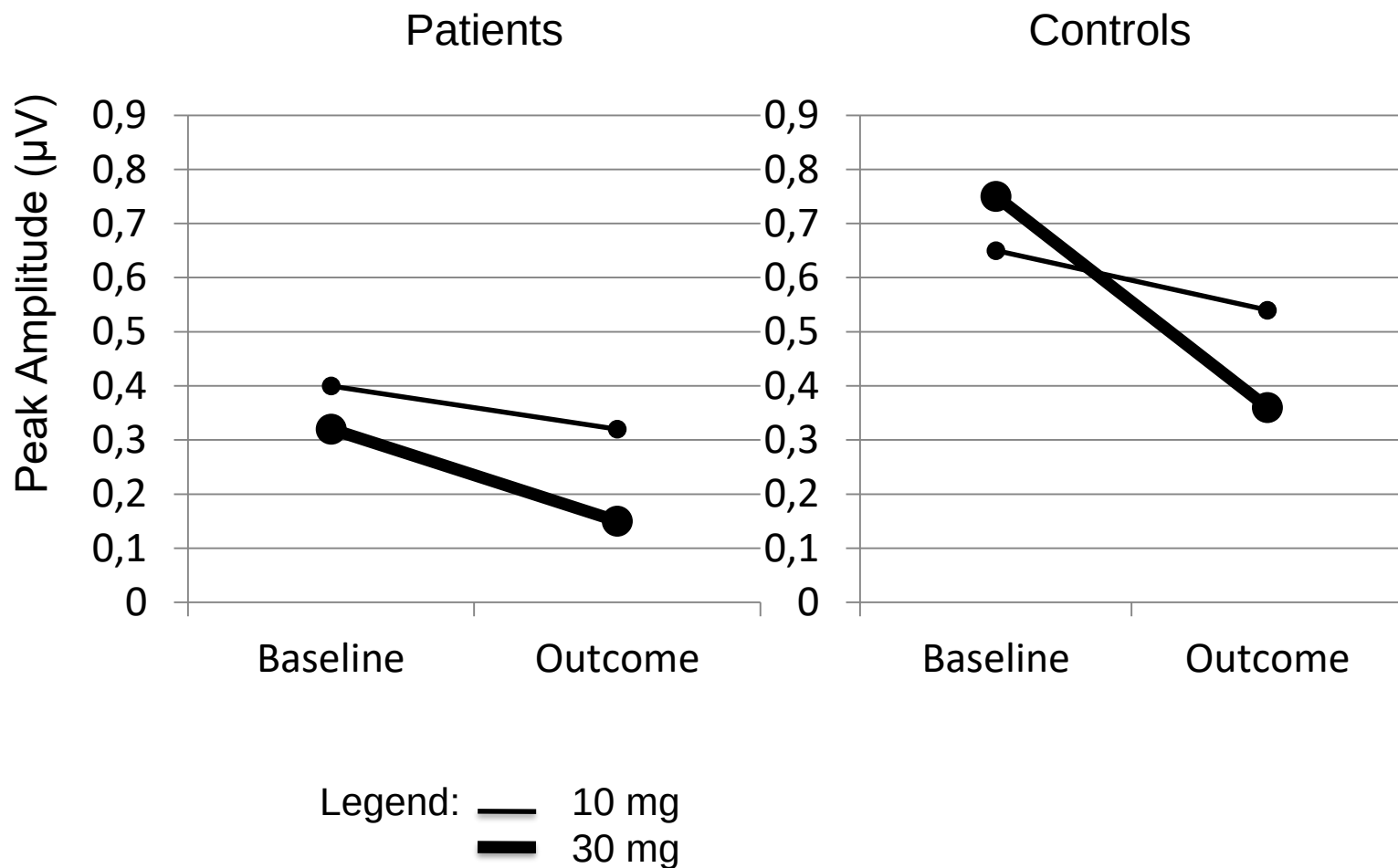
- Baseline meting
- Inname van oxazepam (10 / 30 mg)
- Effect meting na 2.5 uur ($T_{\max}$ oxazepam)

¹ Oude Voshaar et al, Hum Psychopharmacol 2005

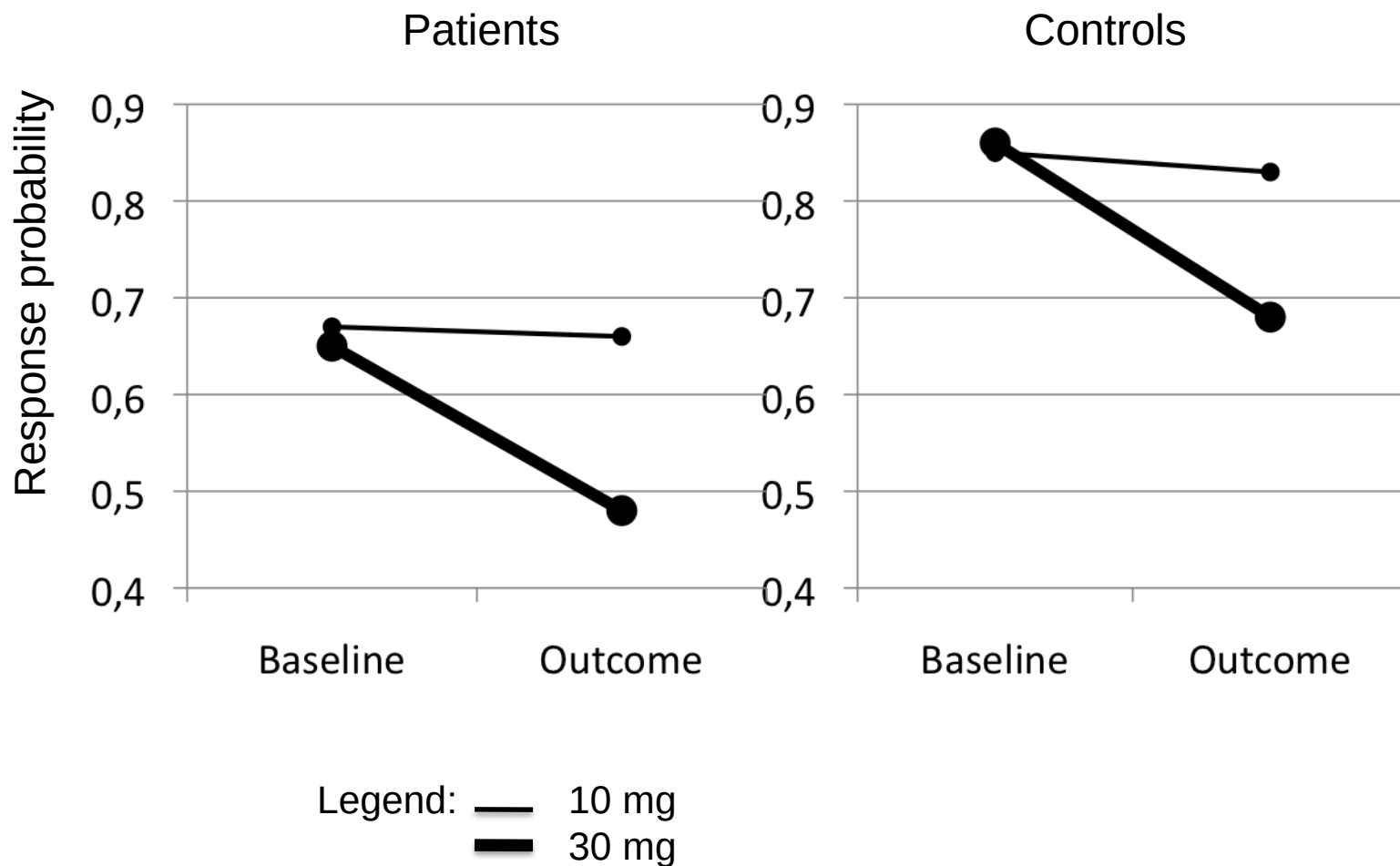
Saccadic eye movements



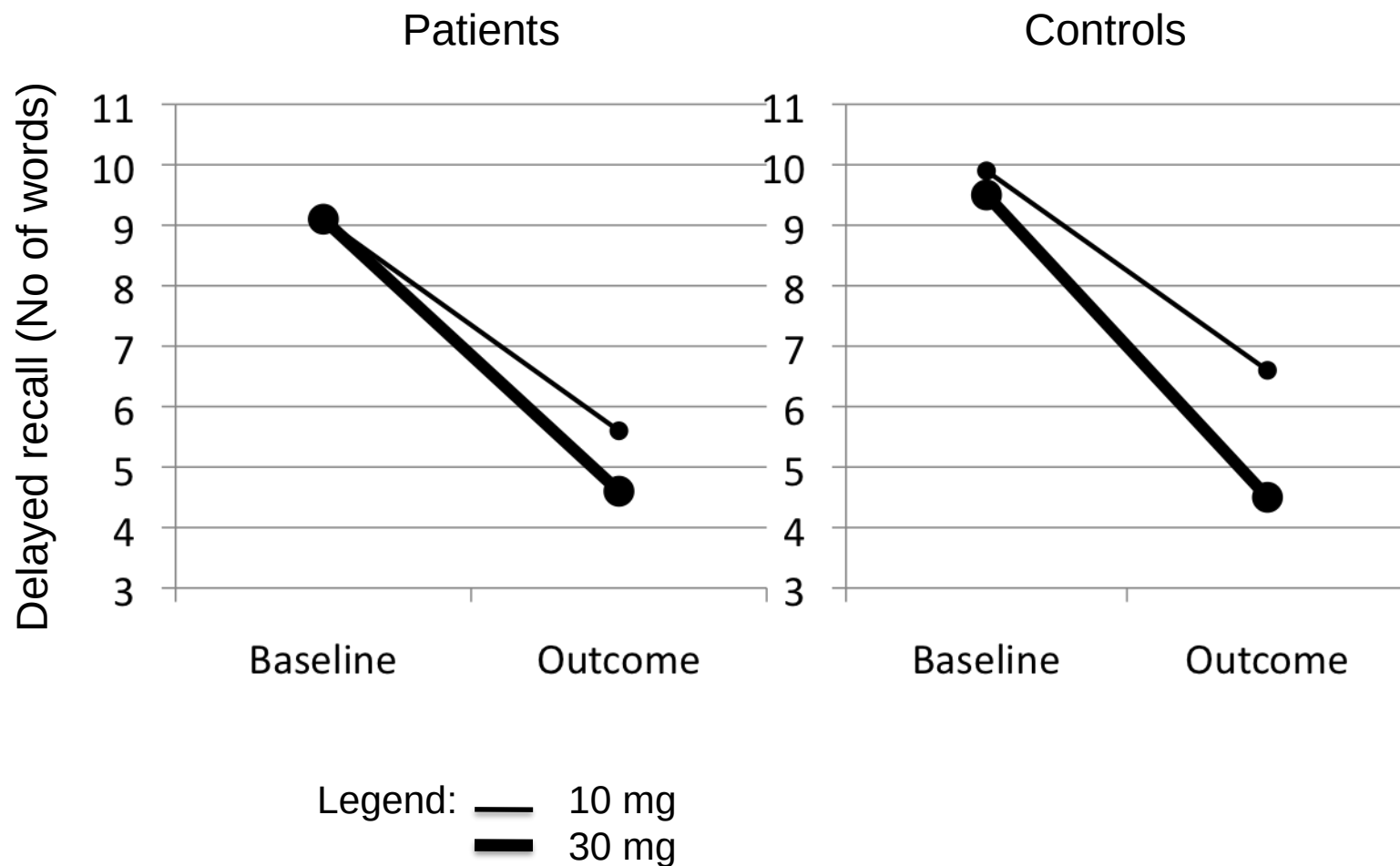
Acoustic Startle Response



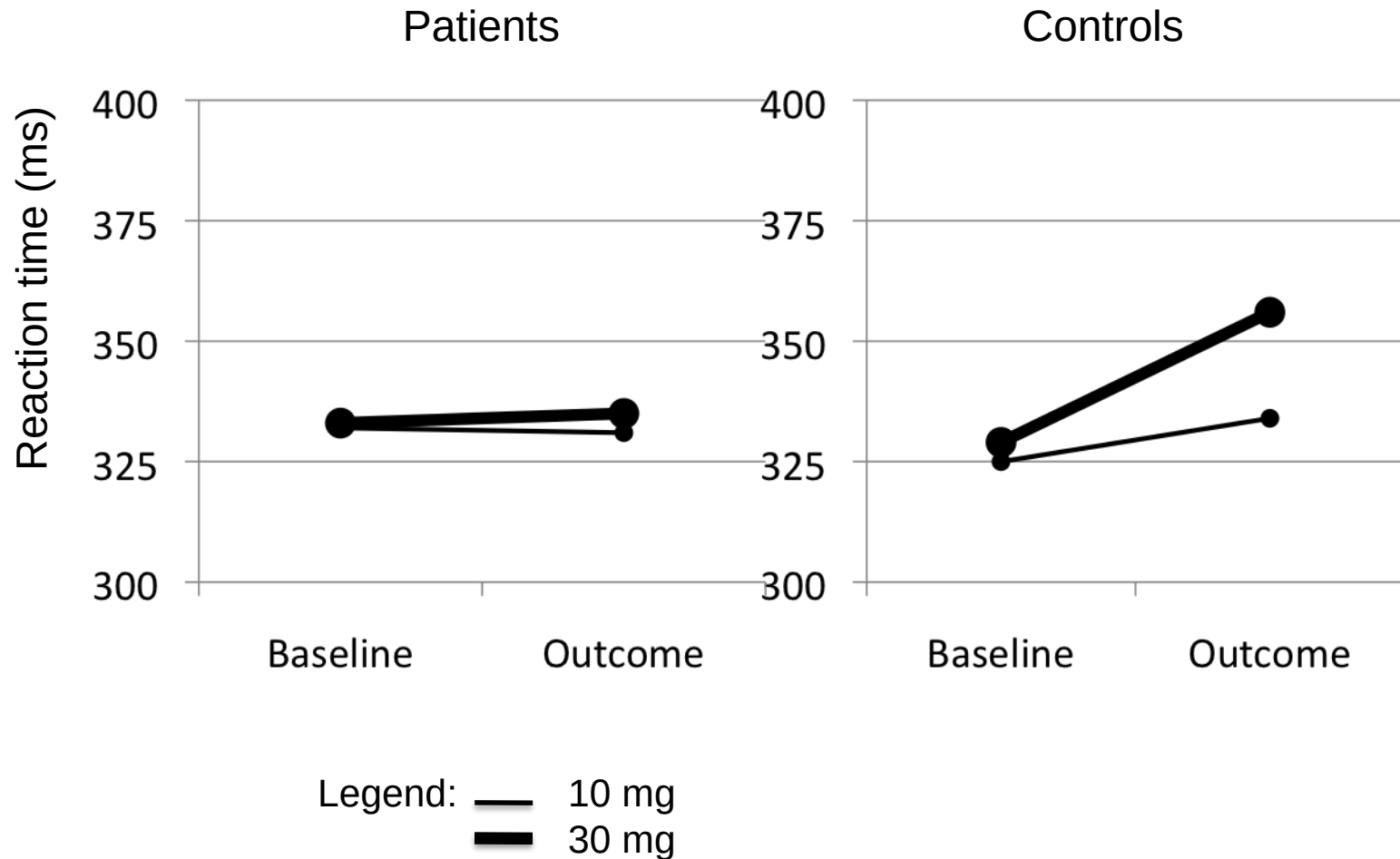
Acoustic Startle Response I



15-words test (memory)



Complex reaction time task



Samenvatting challenge studie

	<i>Effect</i>	<i>Interpretatie</i>
Sedatie	JA	Tolerantie; onderdrukken onttrekking? (Potokar 1999, Van Steveninck 1997)
Anxiolyse	JA	Geen tolerantie (Lucki 1986)
Psychomotore effecten	NEE	Volledige tolerantie (Rickels 1986, 1999)
Geheugen effecten	NEE	Geen tolerantie; klinische relevantie? (Lucki 1986)

Effectiviteit BZD bij slaapstoornissen

Effectiviteit^{1,2}:

- Number Needed to Treat (NNT): **13** [95% CI: 7 - 63]
- ES verbetering slaapkwaliteit: **0.14** [95% CI: 0.05 – 0.23]
- Toename totale slaaptijd: **25 min.** [95% CI: 13 - 38]
- Geen verschil BZD vs Z-drugs (zolpidem, zopiclone, zaleplon)

¹ Glass, BMJ 2005: n= 24 studies

² Huedo-Medina et al, 2012

Bijwerkingen BZD bij slaapstoornissen

Bijwerkingen¹:

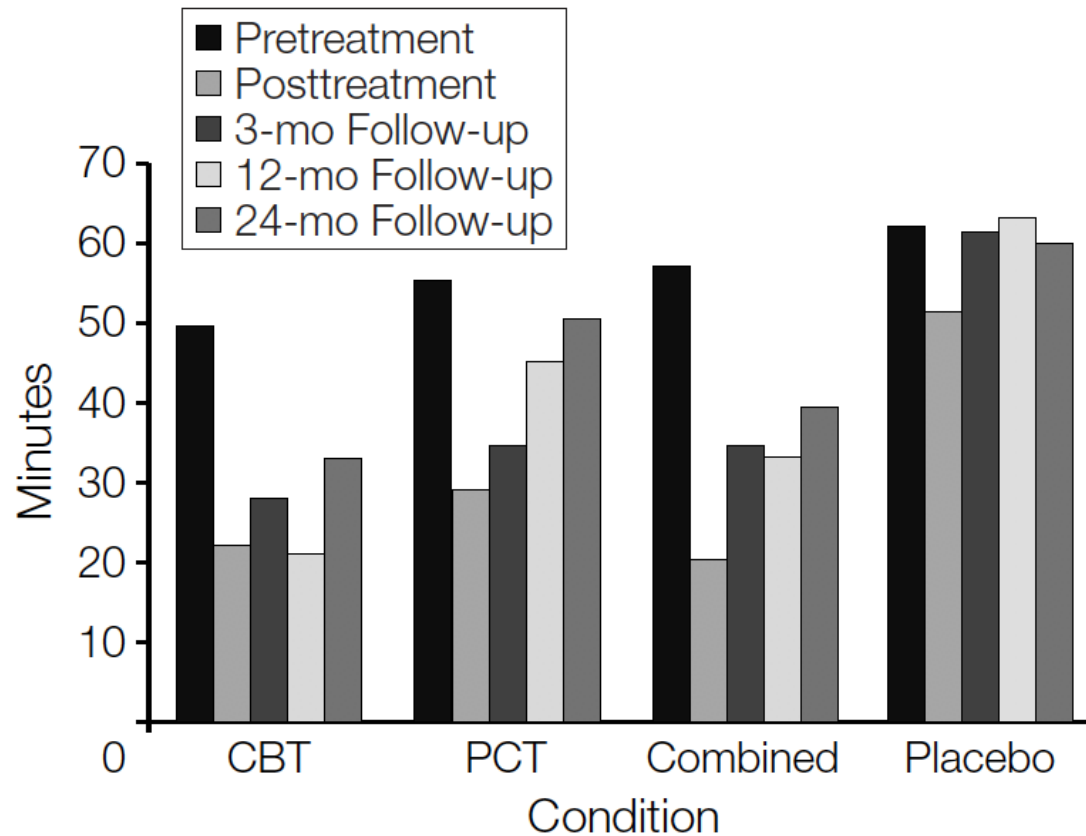
Number Needed tot Harm (NNH):	6	[95% CI: 5 – 7]
• OR cognitieve bijwerkingen:	4.8	[95% CI: 1.5 – 15.5]
• OR sedatie overdag / sufheid:	3.8	[95% CI: 1.9 – 7.8]
• OR psychomotore bijwerkingen:	2.3	[95% CI: 0.9 – 5.4]

Hoezo CGT?

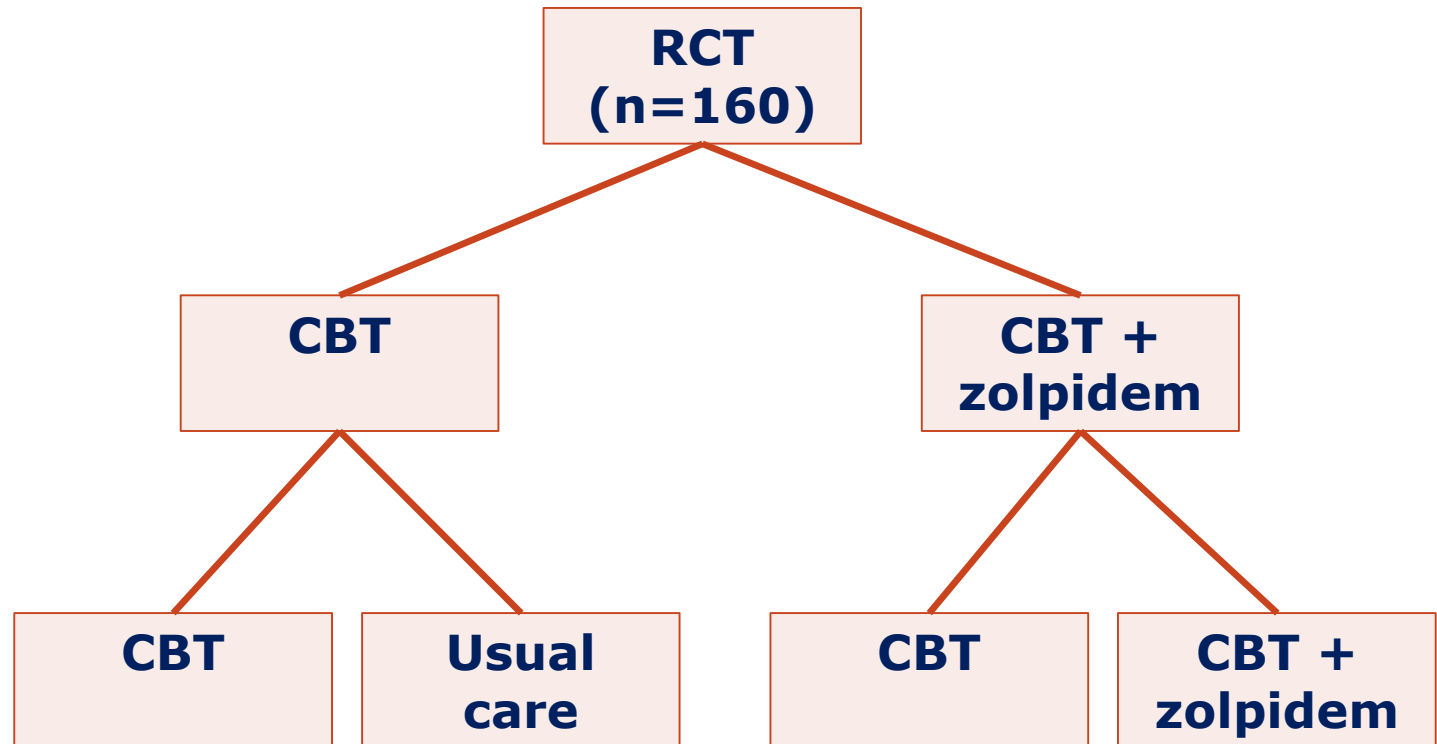
vandaag eten we weer gewoon!



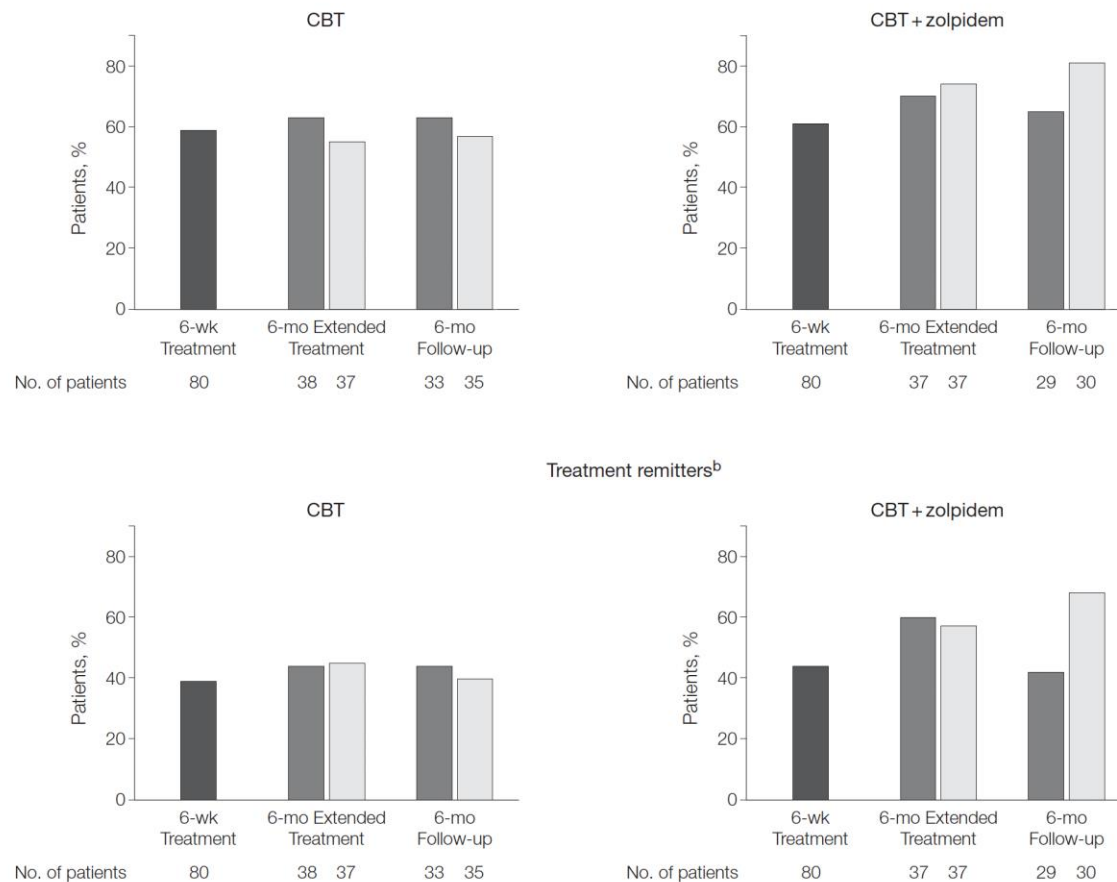
BZD, CGT of combinatie voor insomnia



CGT met/zonder BZD voor insomnia



CGT met/zonder BZD voor insomnia



Quebec Survey on the Health of Older Persons¹

2,782 persons randomly selected persons aged 65 years or older in Quebec

└→ 707 (25.4%) report benzodiazepine usage

└→ **67 (9.5%) meet DSM-IV criteria for BZD dependence**
└→ 304 (43%) consider themselves dependent on BZDs

¹ Voyer et al, Can J Aging 2010



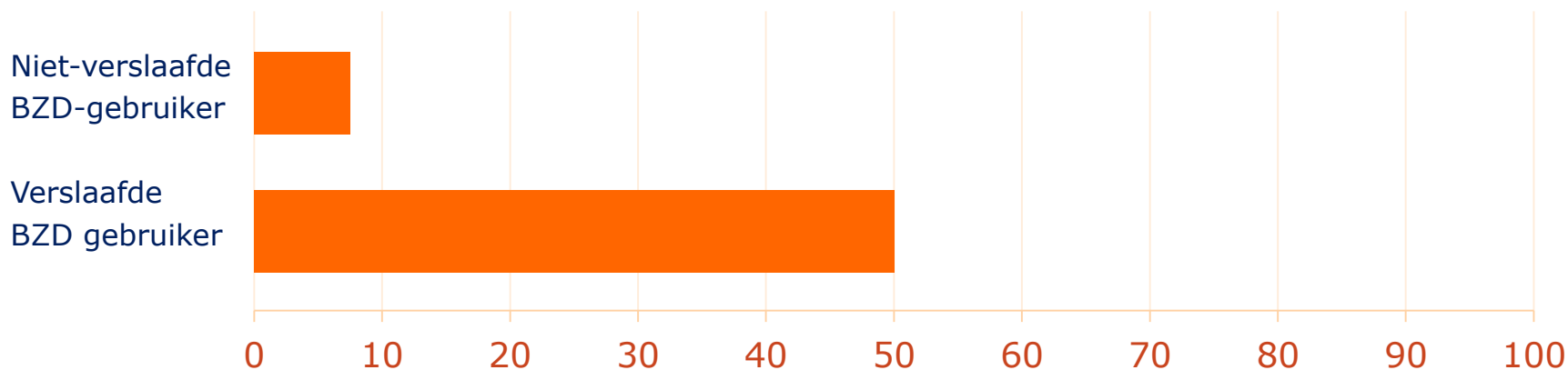
DSM-criteria for substance use dependence

DSM-IV criterion	Dependent BZD users (n=67)	None- dependent users (n=639)
1. Tolerance		
2. Withdrawal		
3. Increases in quantity or duration/ tolerance		
4. Ongoing resolution or fruitless efforts to reduce or cease medication		
5. Takes time to recover from drug effects		
6. Reduction or abandonment of important activities		
7. Continued drug use despite problems caused by use		

Criterium 1: Tolerantie

Heeft u een afname van het effect van deze medicijnen ervaren
(slaap, angst of somberheid)?

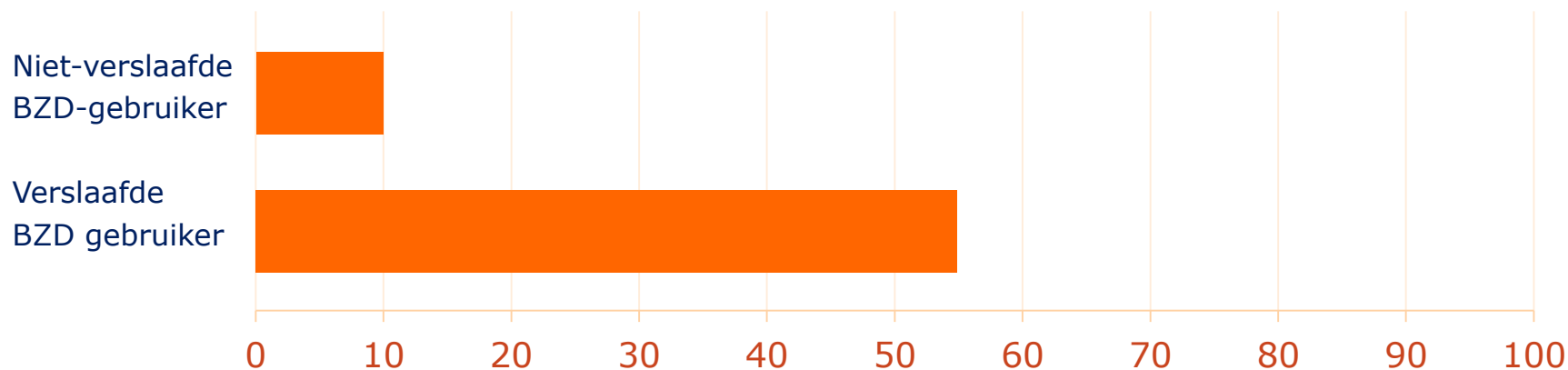
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterion 2: Onthouding (1)

Kreeg u lichamelijke klachten (zoals slapeloosheid, beven, zweten, angst) toen u probeerde deze medicatie te stoppen of te minderen?

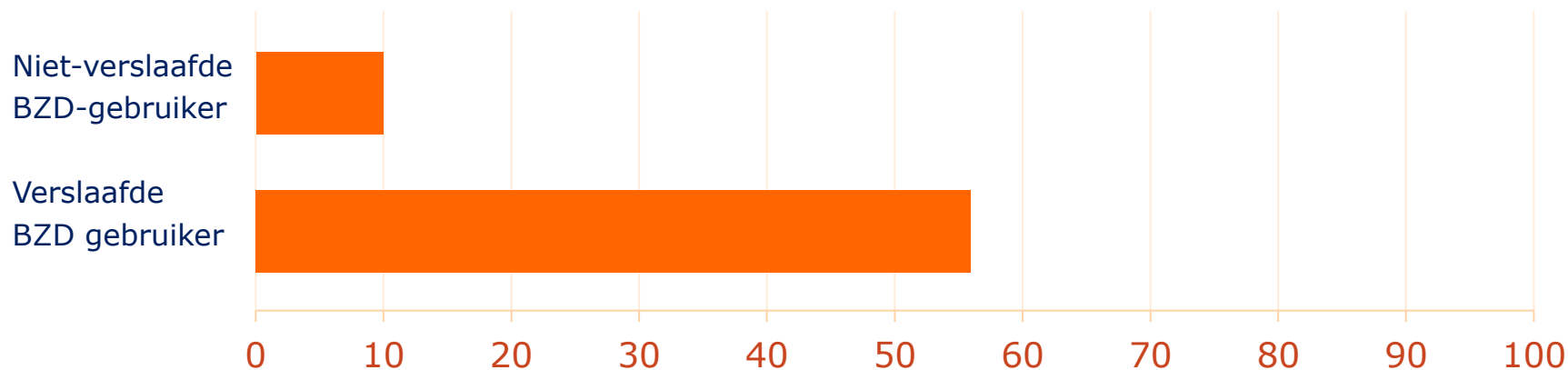
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterion 2: Onthouding (2)

Heeft u alsnog BZD of andere stoffen, zoals alcohol, genomen omdat stoppen of minderen te moeilijk bleek?

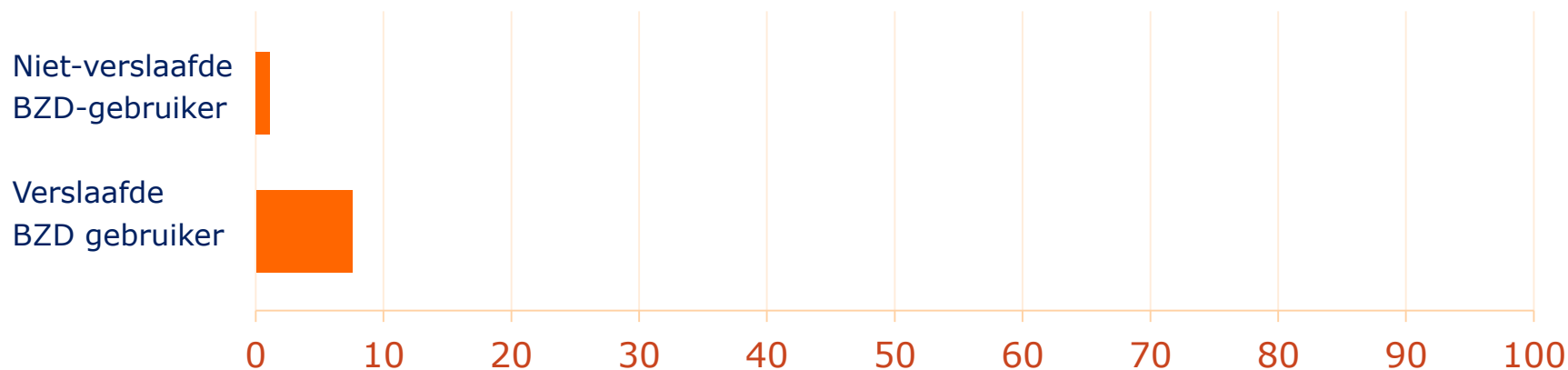
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterion 2: Onthouding (3)

Leidde uw poging tot mindering of stoppen tot problemen met familieleden of vrienden óf in het uitvoeren van voor u gebruikelijke activiteiten?

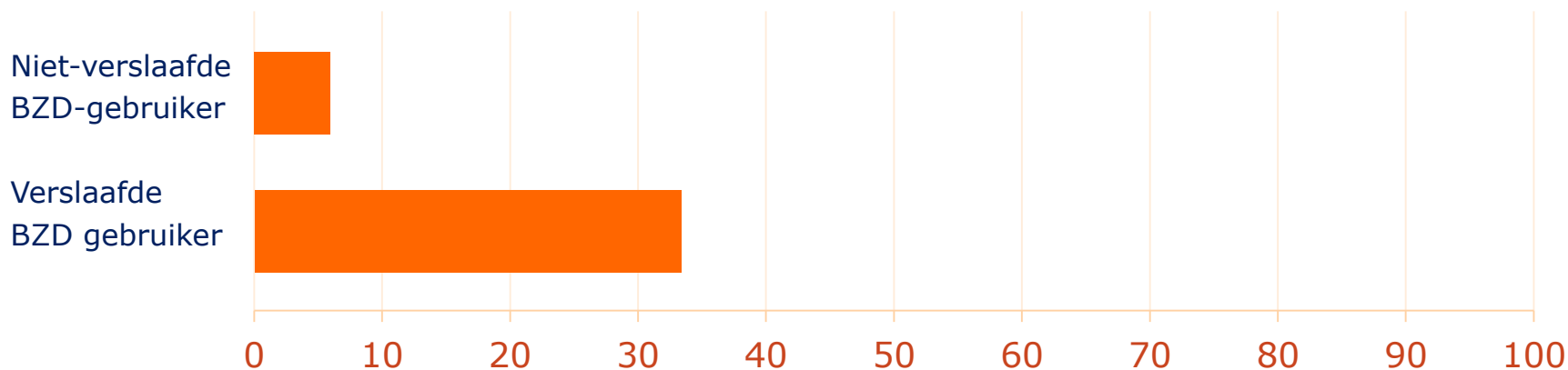
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterion 3: Meer of langer gebruikt

Heeft u een grotere hoeveelheid meidcatie (meer pillen of een hogere dosering) moeten nemen om het effect te krijgen wat u graag wilde?

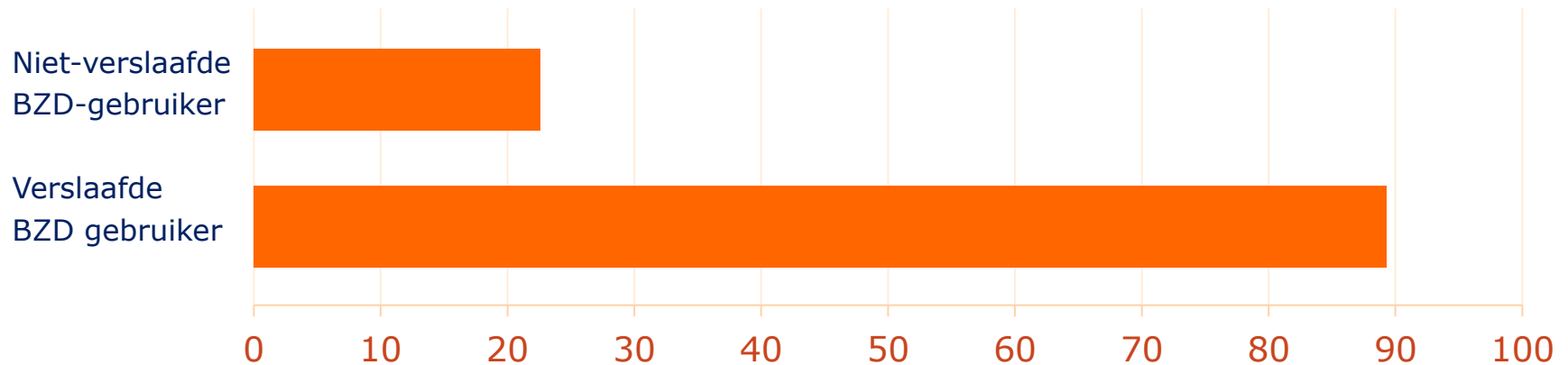
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterion 4: Stopwens?

Heeft u geprobeerd te stoppen?

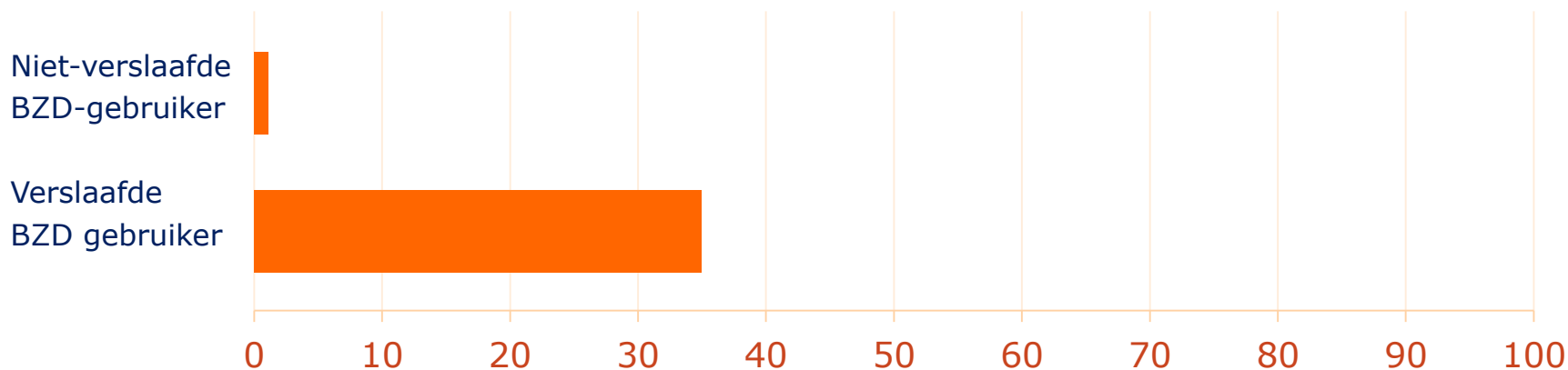
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterion 5: Tijdsinvestering?

Heeft u rustperiodes of rusttijden moeten inlassen om te herstellen van de effecten van deze medicatie?

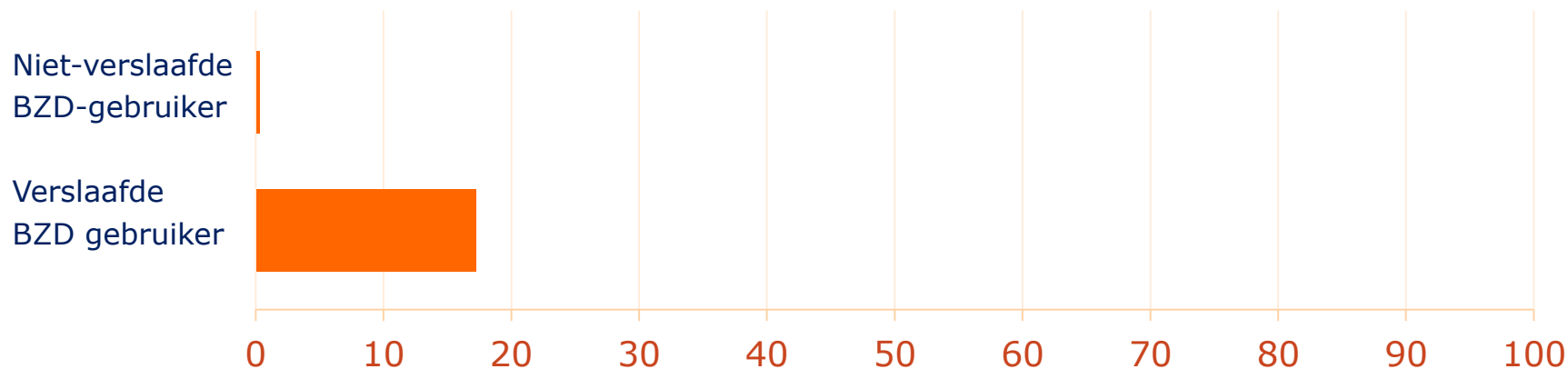
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterium 6: Reductie belangrijke activiteiten?

Heeft het gebruik van deze medicatie ertoe geleid dat u bepaalde activiteiten of vrijetijdsbehandeling die belangrijk voor u zijn moeten verminderen of staken?

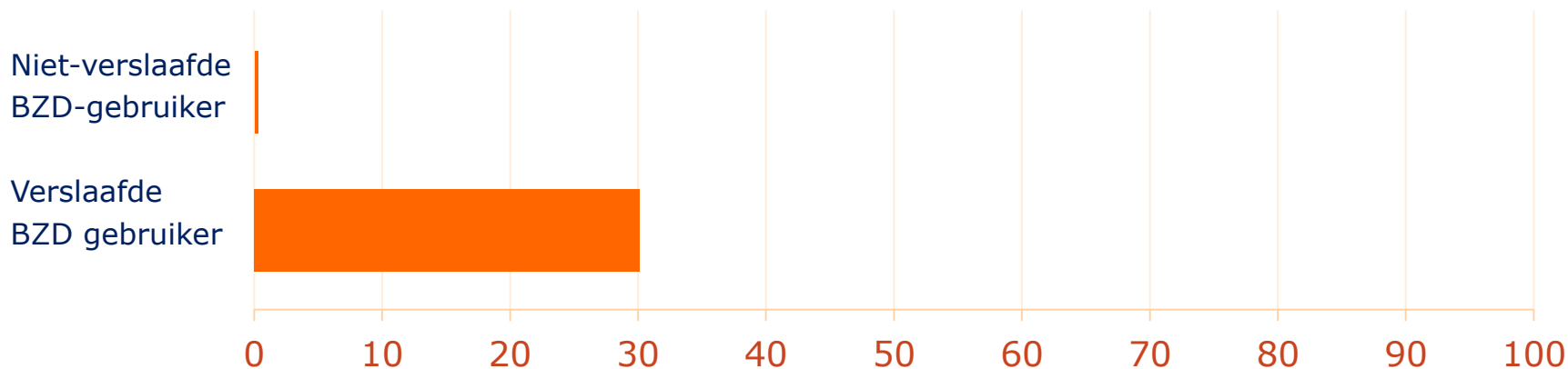
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterium 7: Continuering ondanks problemen (1)

Hebben deze medicijnen gezondheidsproblemen bij u veroorzaakt?

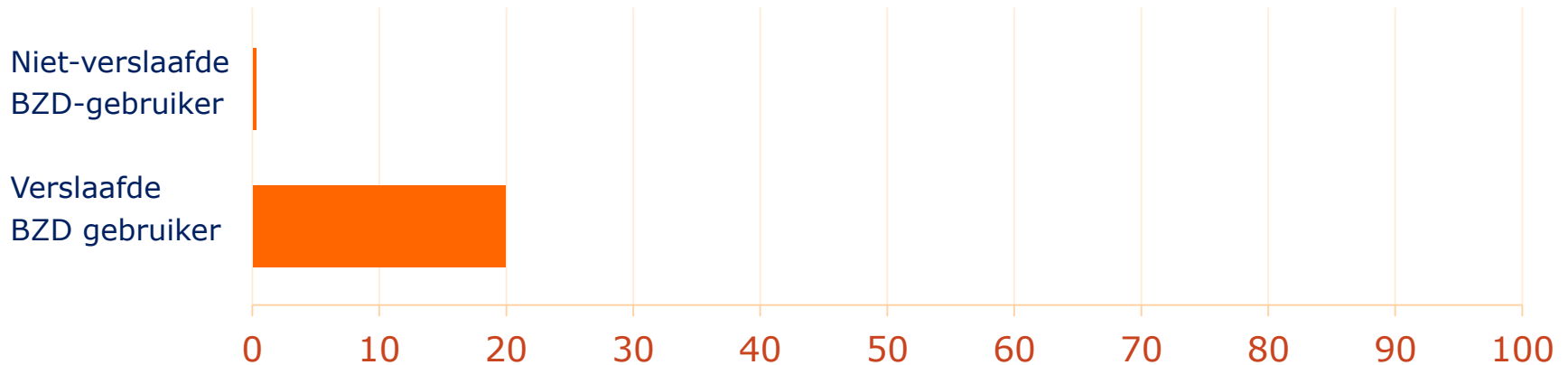
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Criterium 7: Continuering ondanks problemen (2)

Hebben deze medicijnen u problemen opgeleverd zoals ongelukken of bijwerkingen?

Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



DSM-criteria for substance use dependence

DSM-IV criterion	Dependent BZD users (n=67)	None- dependent users (n=639)
1. Tolerance	50 %	7 %
2. Withdrawal	56 %	10 %
3. Increases in quantity or duration/ tolerance	33 %	6 %
4. Ongoing resolution or fruitless efforts to reduce or cease medication	89 %	23 %
5. Takes time to recover from drug effects	35 %	2 %
6. Reduction or abandonment of important activities	17 %	0 %
7. Continued use of drug despite problems caused by use	30%	1 %

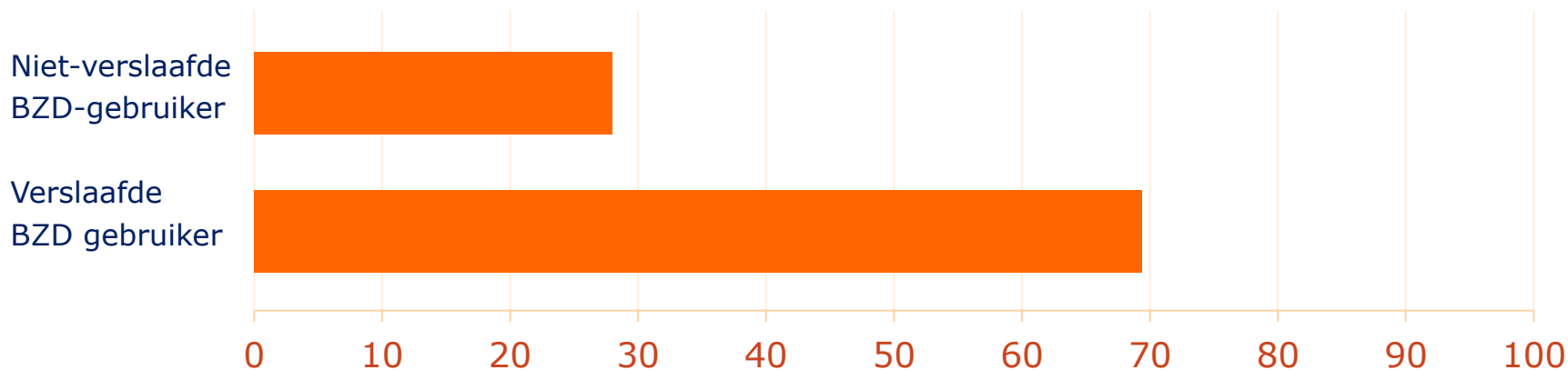
BZD: a typical type of dependence?

Atypical dependence criteria	Dependent BZD users (n=67)	None- dependent users (n=639)
1. Expressing desire to stop		
2. Giving no reason or several reasons for using		
3. Downplaying effects of the BZD		
4. Perceiving medication as addictive		
5. Attributing unrealistic powers to medication		
6. Wanting to keep a supply of the medication in reserve		
7. Believing that one is dependent on the BZD		

Atypisch criterium 1: Stopwens?

Denkt u dat het goed zou zijn als u deze medicatie zou stoppen?

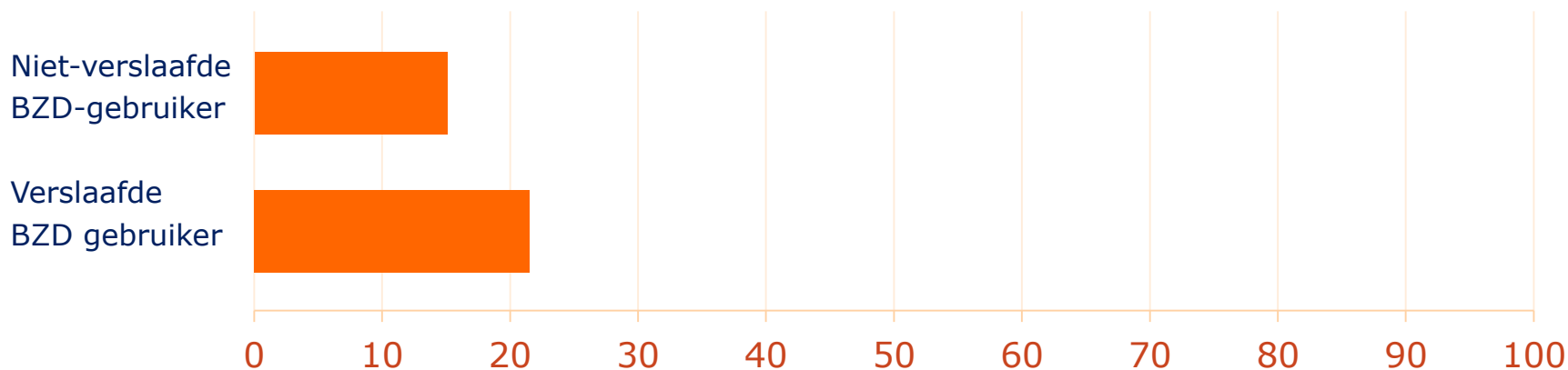
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Atypisch criterium 2: Geen/meer gebruiksredenen

Kunt u mij de reden(en) geven waarom u deze medicijnen gebruikt?

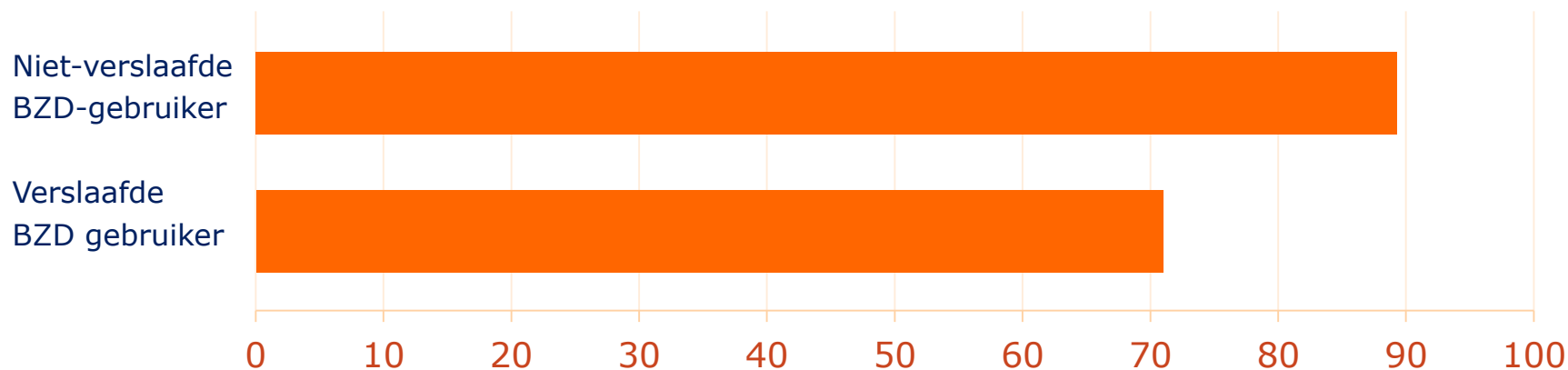
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Atypisch criterium 3: Afzwakken effecten

Klopt het dat de medicijnen die u gebruikt een tablet/capsule is die niet zo sterk of krachtig is?

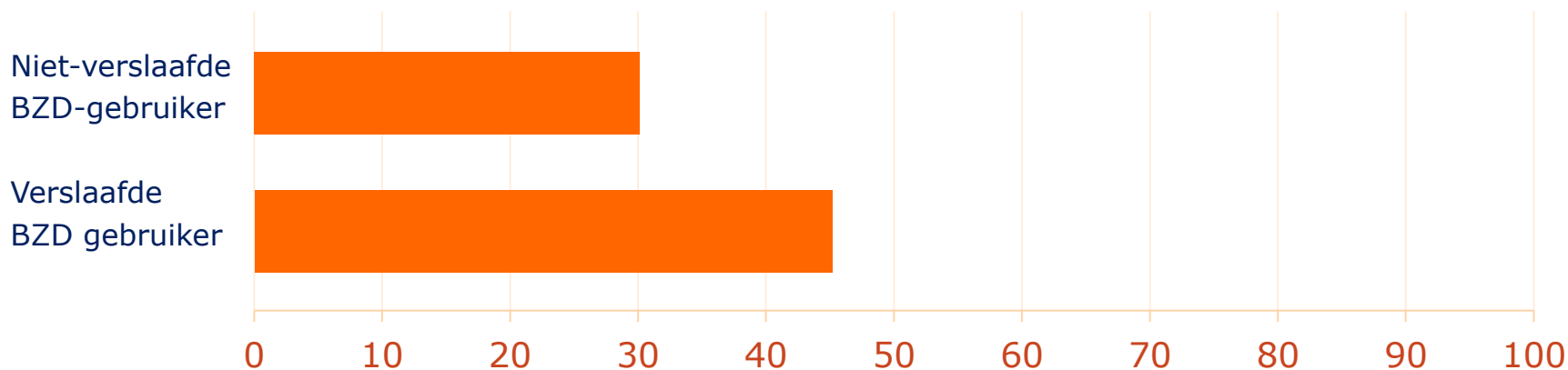
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Atypisch criterium 4: Ervaren als verslavend?

Lijkt de medicatie die u gebruikt op iets zoals een sigaret?

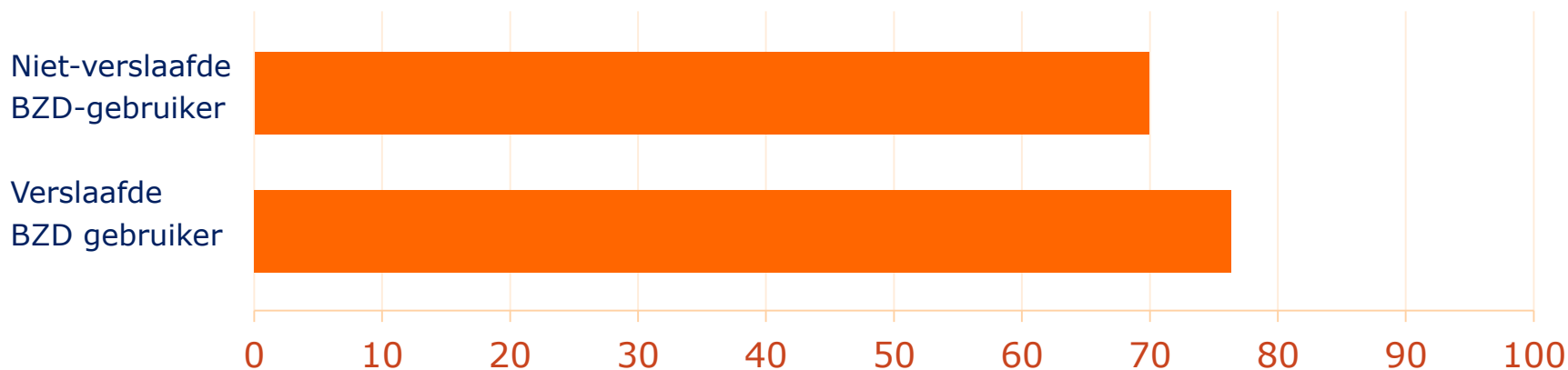
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Atypisch criterium 5: Onrealistische krachten

Kan deze medicatie bepaalde problemen, zoals conflicten met andere mensen, voorkomen?

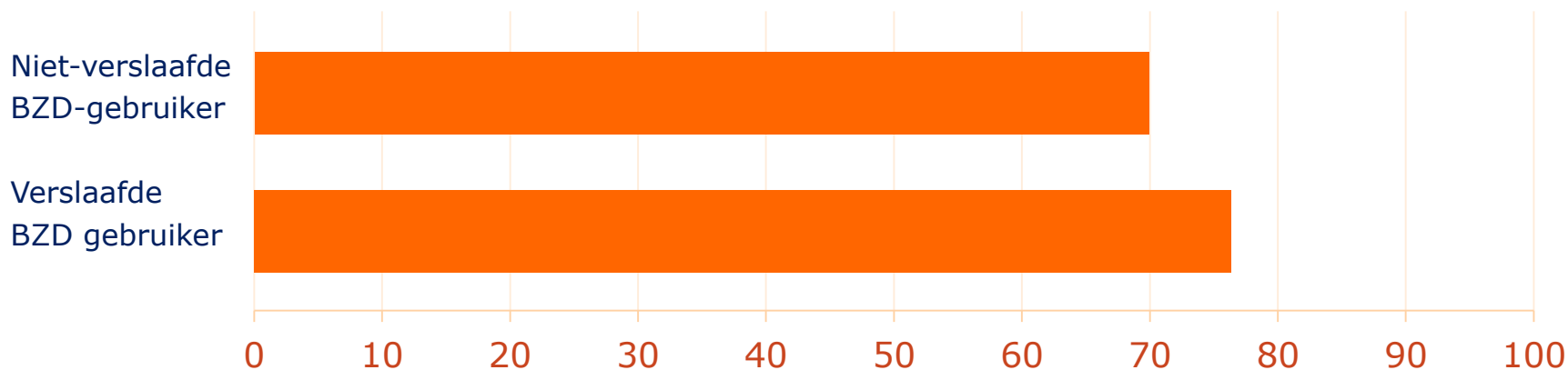
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Atypisch criterium 6: Voorraad / op safe?

Zelfs als u zou stoppen met deze medicatie, blijft het dan belangrijk voor u om er een aantal achter de hand te houden voor het geval dat?

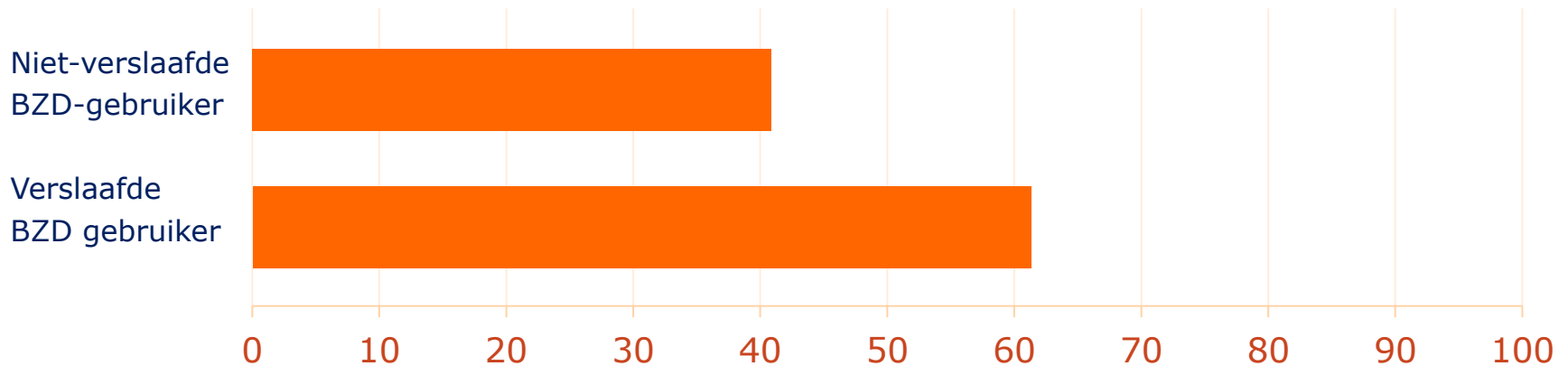
Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



Atypisch criterium 7: Overtuigd verslaafd?

Denkt u dat u verslaafd bent aan deze medicatie?

Proportie benzodiazepine-gebruikers die deze vraag bevestigend beantwoordt:



BZD: a typical type of dependence?

Atypical dependence criteria	Dependent BZD users (n=67)	None-dependent users (n=639)
1. Expressing desire to stop	69 %	28 %
2. Giving no reason or several reasons for using	22 %	15 %
3. Downplaying effects of the BZD	71 %	89 %
4. Perceiving medication as addictive	45 %	30 %
5. Attributing unrealistic powers to medication	17 %	22 %
6. Wanting to keep a supply of the medication in reserve	76 %	70 %
7. Believing that one is dependent on the BZD	41 %	61 %

Final conclusions BZD dependence

- Prevalence of dependence on benzodiazepines as well as dose-escalation in low-dose users is lower than originally thought
- Dependency characteristics, however, are prognostic determinants of successful outcome of discontinuation strategies.
- Multiple interventions are efficacious:
 - Even without treating underlying illness, psychological functioning does not worsen.
 - But targeted interventions also improve psychological outcome

Casus 1

- 86-jarige man
- Gebruikt sinds 36 jaar nitrazepam 5 mg
- Zo nodig temazepam 20 mg bij ontwaken (3-4x/week)
- Weigert te stoppen:
 - Nooit problemen gehad
 - Kan niet slapen zonder medicatie (wel geprobeerd)

Vraag 1: Moet deze man stoppen?

Vraag 1: Moet deze man stoppen?

- Redenen op te stoppen:
 - Mislukte stoppogingen vermoedelijk rebound insomnia
 - Slaapt verbeterd na staken
 - Helderder overdag
 - Geen risico op vallen ('s nachts) / heupfractuur
 - Geen risico op ongevallen / cognitieve stoornissen

Casus 2

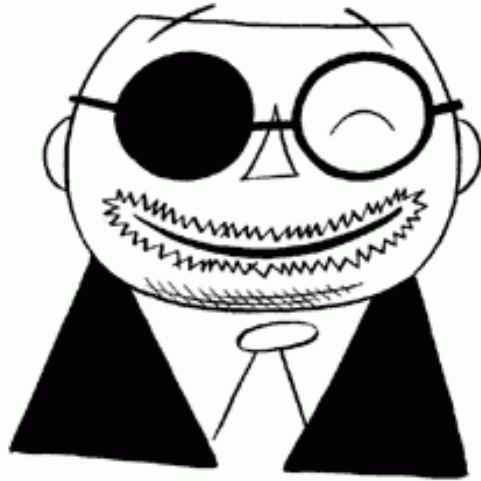
- 56-jarige vrouw
- Gebruikt sinds 18 jaar oxazepam, 3 dd 10 mg.
- Gebruikt z.n. 1-2 extra (gemiddeld 4x per week) bij piekeren of spanningsvolle (lees sociale) activiteiten
- Weigert te stoppen:
 - Nooit problemen gehad door oxazepamgebruik
 - Maakt zich onnodig zorgen (piekert) zonder oxazepam

Vraag 1: Moet deze vrouw stoppen?

Vraag 1: Moet deze vrouw stoppen?

- Redenen op te stoppen:
 - Lager risico op (onge)vallen
 - (beter cognitief functioneren)
 - Oxazepam is veiligheidsgedrag:
 - Ondermijnd zelfvertrouwen
 - Houdt klachten in stand

Motiverende gespreksvoering



Motiverende gespreksvoering

- Onvoorwaardelijke aanvaarding patient
- Contact met patient krijgen en houden
- Vermijden van discussie/onenigheid over wel/niet verslaafd (niet moraliseren, beschuldigen of confronteren)
- Samenwerken
- Objectieve informatie geven
- Actieve houding en werkrelatie stimuleren
- Gevoel van eigenwaarde vergroten
- Kennis van het probleem opdoen
- Gevoel van self-efficacy vergroten
- Laten nadenken over de ineffectiviteit van bZD m.b.t. eigen klachten gedurende het leven