Més no sempre és millor

BenzoRed

Es possible la retirada de benzodiacepinas? Estudio **BENZORED**

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Grup de Investigació en salut mental rediAPP

XX Jornada de la Societat Catalana de farmàcia Clínica.

Barcelona, 17 de Juny de 2014

redIAPP
Red de Investigación en Actividades Preventivas y Promoción de la Salud

Antonio

- Acude a la consulta para recoger medicación.
- Ha cambiado de domicilio y de centro de salud y acude por primera vez a la consulta.
- Esta tomando

"Orfidal" 1 comp/8h

- Desde hace 12 años..
- Pregunto….

Algo de historia

Leo Sternbach (1908-2005) en 1955 desarrolló la primera benzodiacepina: Clordiazepoxido, la denominó "***Librium***" de la palabra latina equilibrium…

La patentó en 1960

En 1963 patentó el diazepam como **"Valium"** y a finales de los 60 y 70 fue el fármaco más prescrito del mundo.

Para que se utilizan?

Las benzodiazepinas están indicadas en:

- Tratamiento a corto plazo de la ansiedad
- Tratamiento a corto plazo del insomnio
- Coadyuvantes en el tratamiento de los síntomas ansiosos en la depresion.
- Coadyuvantes en la desintoxicación alcoholica.
- Relajantes musculares, anticonvulsivantes.

Indicaciones y duración tratamiento con benzodiacepinas.

Guia para el manejo ansiedad, insomnio, GuiaSalud, Guias NICE anxiety and depression, Guia de prescripción terapéutica.

	Indicaciones de las benzodiacepinas	Consideraciones duración tratamiento
Trastornos del sueño	Manejo del **insomnio severo e incapacitante** que interfiere con las actividades de la vida diaria. Fracaso de medidas no farmacológicas	Cuando se utilicen hipnóticos, éstos deben ser utilizados durante un **breve periodo (2-4 semanas)** y de acuerdo con las indicaciones aprobadas.
Ansiedad	Tratamiento sintomático de las **manifestaciones ansiosas intensas o invalidantes.**	La duración global del tratamiento no debería **exceder las 8-12 semana.**
Depresión	Como coadyuvante en la depresión con síntomas de ansiedad importantes al iniciar el tratamiento.	Durante un breve periodo **no superior a las 2 semanas.**
Desintoxicación alcohólica	Prevención del delirium tremens	Tratamiento breve del orden **de 8-10 días**, individualizar.

Tabla 2
Criterios STOPP[a]: herramienta para la detección de prescripciones potencialmente inapropiadas en personas mayores. Las siguientes prescripciones de medicamentos son potencialmente inapropiadas en personas de 65 o más años

Medicación potencialmente inapropiada en personas mayores (>65)
Criterios de Beers
Criterios START-STOPP

MEDICAMENTOS POTENCIALMENTE INAPROPIADOS[1] EN PACIENTES DE 65 O MÁS AÑ

Medicamento potencialmente inadecuado (Grupo terapéutico)	Situación clínica	Comentario	
Antimuscarínicos vesicales (oxibutinina, solifenacina,			
BS)		la úlcera péptica, esofagitis o reflujo gastroesofágico	
Benzodiazepinas de acción prolongada o con metabolitos de acción prolongada (bromazepam, clobazam, clordiazepóxido, diazepam, flurazepam, flunitrazepam, clorazepato dipotásico, ketazolam, nitrazepam) (Ansiolíticos benzodiazepinas – N05BA)	Uso prolongado (p. e.: más de 1 mes)	Riesgo de sedación prolongada, confusión, trastornos del equilibrio, caídas	Evitar su utilización
Benzodiazepinas de acción prolongada o con metabolitos de acción prolongada (bromazepam, clobazam, clordiazepóxido, diazepam, flurazepam, flunitrazepam, clorazepato dipotásico, ketazolam, nitrazepam) (Ansiolíticos benzodiazepinas – N05BA)	Pacientes con riesgo de caídas (1 o más en últimos 3 meses)	En el tratamiento del insomnio las benzodiazepinas no deben superar las 2 semanas (4 si se incluye la retirada del tratamiento). Como hipnóticos son preferibles los fármacos de vida media corta o media. En el trastorno de ansiedad generalizada, como tratamiento prolongado, se utilizan los antidepresivos ISRS.	Evitar su utilización

7. Uso prolongado (i.e. más de 1 mes) de benzodiazepinas de vida media larga (como clordiazepóxido, flurazepam, nitrazepam, clorazepato) o benzodiazepinas con metabolitos de larga acción (como diazepam) (*riesgo d sedación prolongada, confusión, trastornos del equilibrio, caídas*)

CUÁNTO SE UTILIZAN?

Encuesta Nacional de Salud 2011-2012

MINISTERIO DE SANIDAD Y CONSUMO

Instituto Nacional de Estadística

Volver al Índice general

UTILIZACIÓN DE SERVICIOS SANITARIOS Y CONSUMO DE MEDICAMENTOS

(Distribución Porcentual)

	Tranquilizantes, relajantes, pastillas para dormir		
	Total	Sí	No
AMBOS SEXOS			
Total	100	16,86	83,14
De 0 a 14 años	100	2,29	97,71
De 15 a 24 años	100	3,74	96,26
De 25 a 44 años	100	11,34	88,66
De 45 a 64 años	100	19,6	80,4
De 65 y más años	100	28,71	71,29
HOMBRES			
Total	100	11,56	88,44
De 0 a 14 años	100	2,76	97,24
De 15 a 24 años	100	2,2	97,8
De 25 a 44 años	100	10,33	89,67
De 45 a 64 años	100	13,22	86,78
De 65 y más años	100	17,43	82,57
MUJERES			
Total	100	20,97	79,03
De 0 a 14 años	100	1,79	98,21
De 15 a 24 años	100	4,82	95,18
De 25 a 44 años	100	12,12	87,88
De 45 a 64 años	100	24,73	75,27
De 65 y más años	100	36,57	63,43

SI: 16,9%

SI: 36,6%

Prevalencia de consumo prolongado

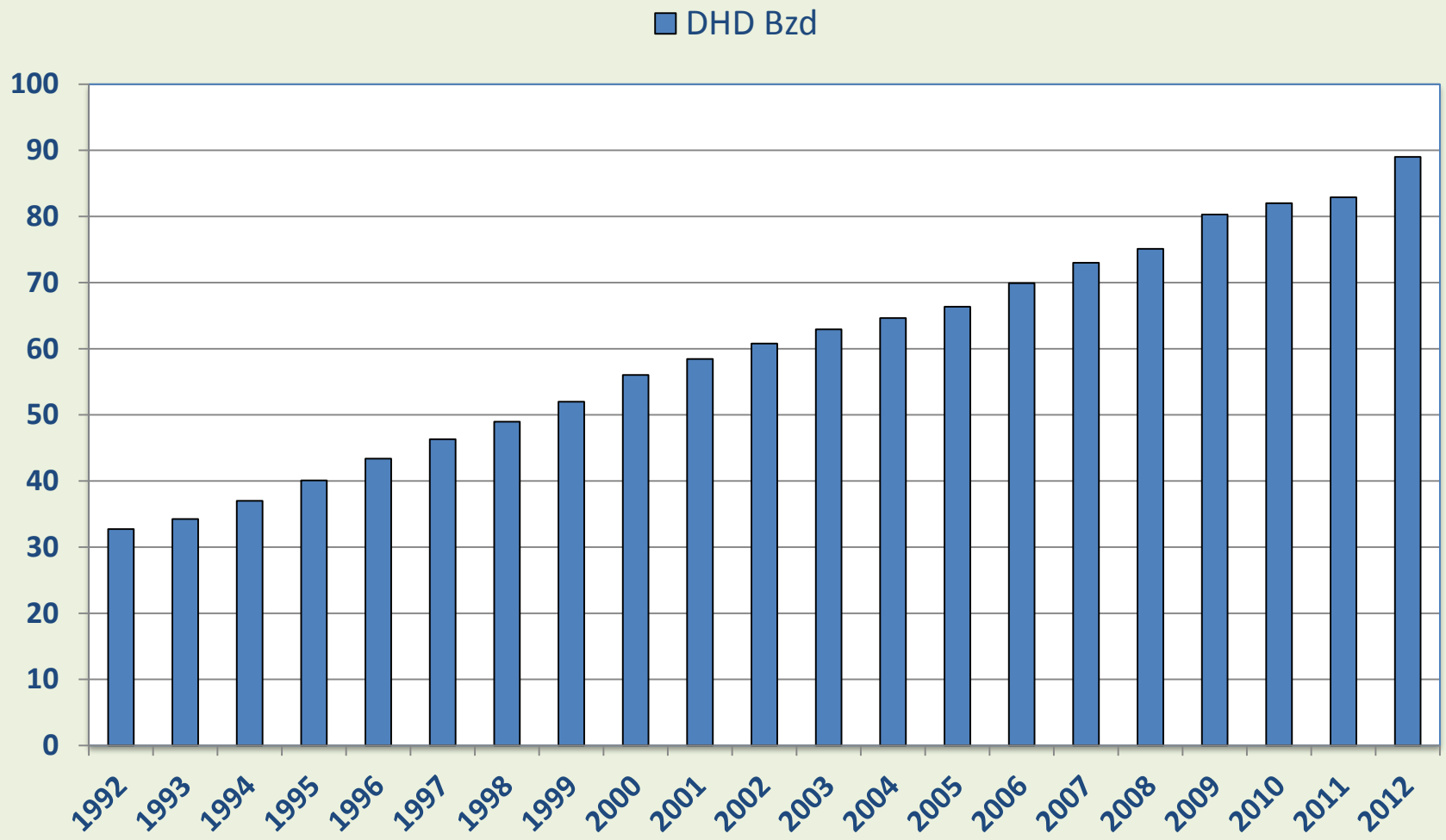
Elevada prevalencia de consumo prolongado.

España:

- **Reus: 6,9%** población consumo > 3 meses y 30% si son mujeres de más de 65 años *(Bejarano et al. 2008)*
- **Asturias: 5,8%** población de forma regular *(Secades et al. , 2003)*
- **Mallorca**: Del total de consumidores ¾ partes lo hacen durante mas de 6 meses *(Cañellas et al., 1998)*

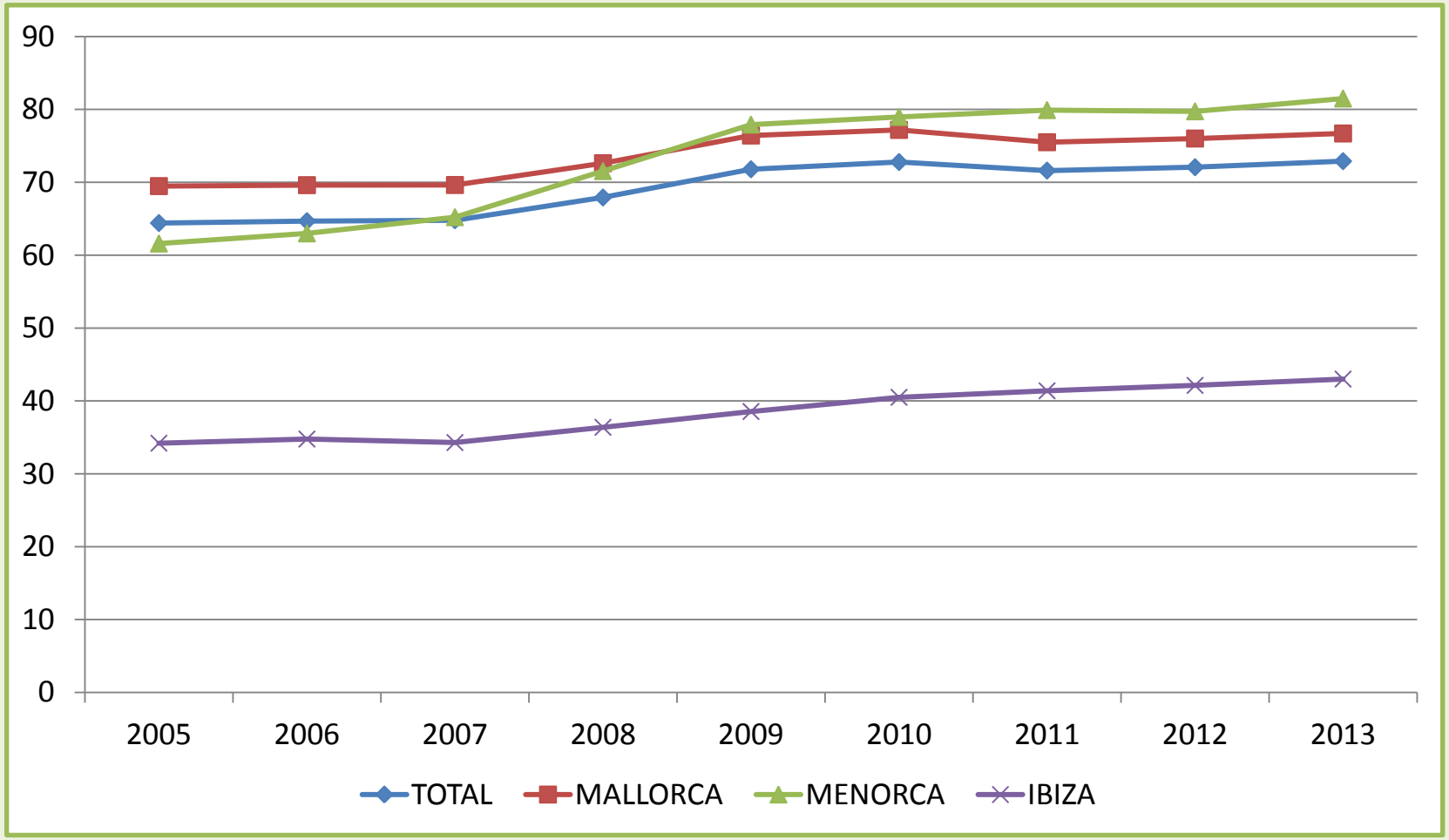
Mayor consumo **mujeres y creciente con la edad**.

Evolución del consumo de benzodiacepinas en España 1992-2012 (DHD).

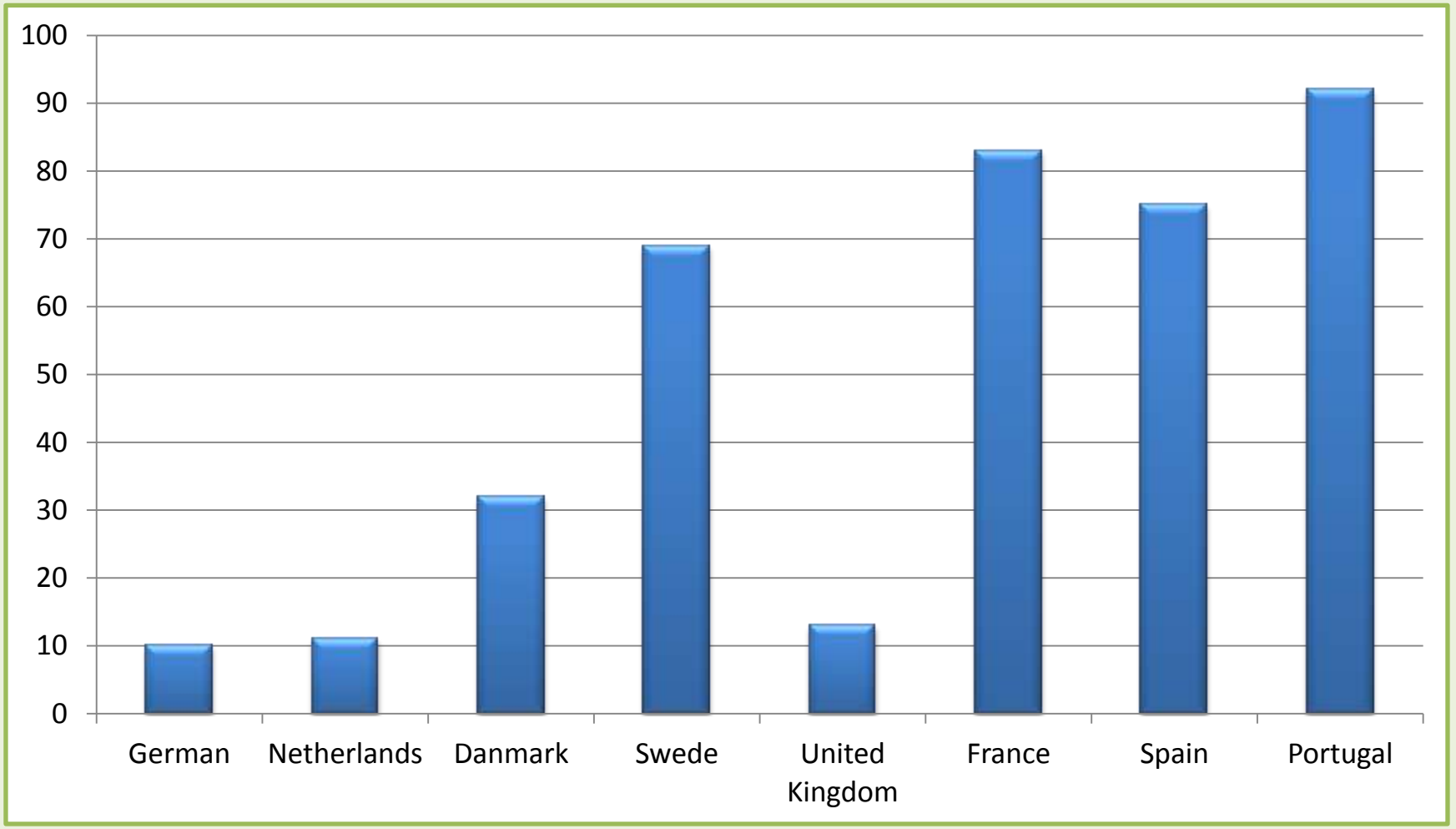


Observatorio. Agencia Española de medicamentos y productos sanitarios AGEMED. Sistema Nacional de Salud.

Evolución del consumo de benzodiacepinas en Baleares 2005-2013 (DHD)



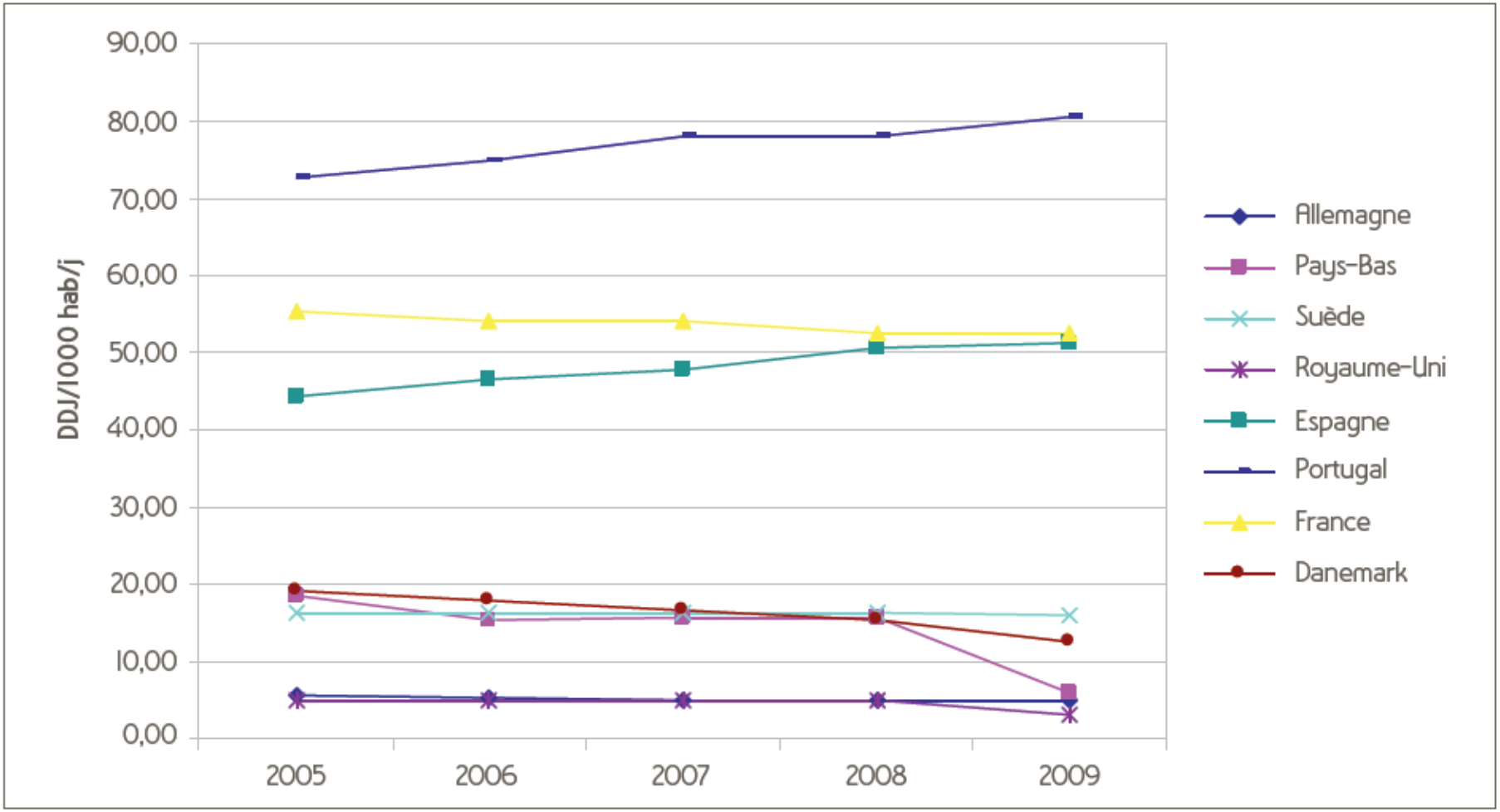
Variabilidad en el consumo de benzodiacepinas en Europa 2009 (DHD)



Evolución del uso de ansiolíticos en Europa 2005-2009 (DHD)

afssaps
Agence française de sécurité sanitaire des produits de santé

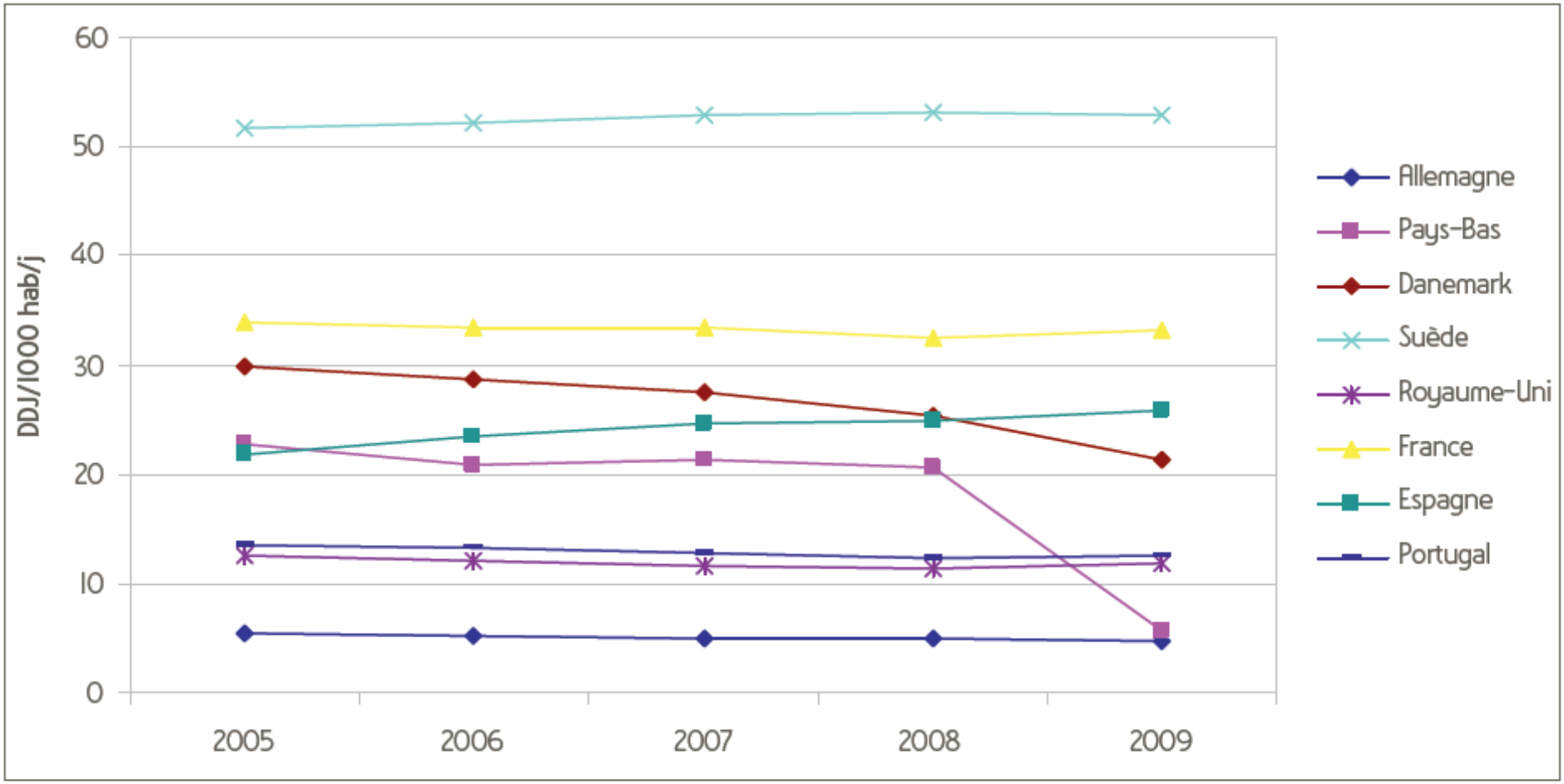
Figure 3: Évolution des niveaux de consommation des anxiolytiques (N05B) dans certains pays européens, en DDJ/1 000 hab./J, 2005-2009



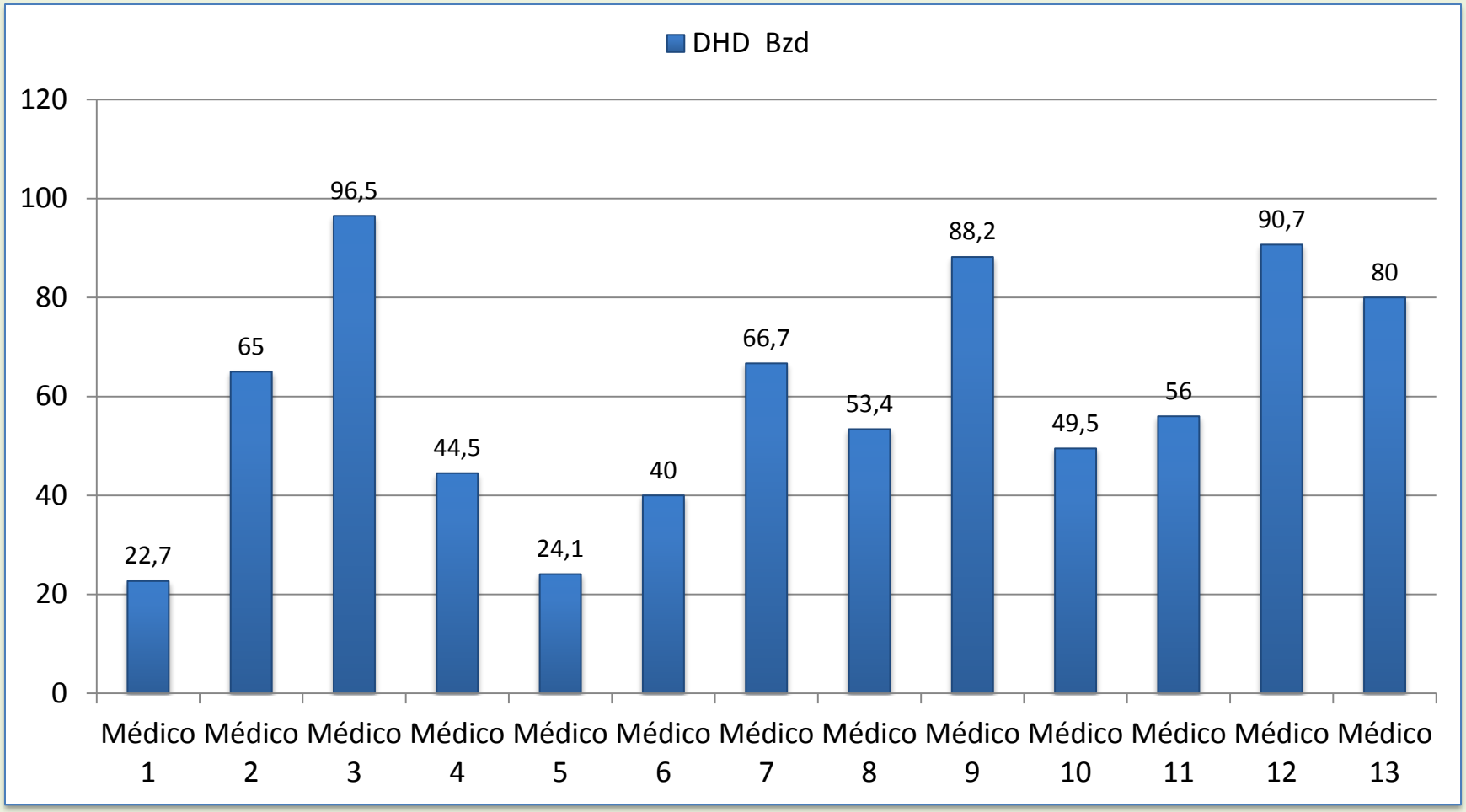
Evolución del uso de hipnóticos en Europa 2005-2009 (DHD)

afssaps
Agence française de sécurité sanitaire des produits de santé

Figure 4 : Évolution des niveaux de consommation des hypnotiques (N05C) dans certains pays européens, en DDJ/1 000 hab./J, 2005–2009



Variabilidad en la prescripción de benzodiacepinas por MF (Enero-Diciembre 2013)



Prescription de bzd por MF del CS Son Serra-La Vileta. Palma de Mallorca. Ib-salut. Base de datos Farmacia.

CONSECUENCIAS CONSUMO PROLONGADO

Consecuencias del uso prolongado de benzodiacepinas.

No se ha podido establecer con claridad su eficacia a largo plazo, a partir de las 4-6 semanas no parece superior a placebo.

Tras pocas semanas de tratamiento producen dependencia (adaptación fisiológica del organismo que induce a perpetuar el consumo)

Consecuencias del uso prolongado de benzodiacepinas.

El consumo prolongado de benzodiacepinas se ha **relacionado con:**

- Alteraciones de la **memoria y cognitivas, incremento del riesgo de demencia** *(Billoti de Gage et al., 2012; Baker et al., 2004; Neutel et al., 2002)*
- Aumento de **caídas y fracturas de cadera** *(Khong et al., 2012; Cuming y Le Couteur 2003; Herrings et al., 1995)*
- Incremento del **riesgo de accidentes de trafico** *(Barbone et al., 1998; Orriols et al., 2011)*
- Aumento de **mortalidad global** *(Kripke et al., 2012, 1998; Mallon et al., 2009; Belleville et al., 2010, Weich et al, 2014)*

Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits

Jennifer Glass, Krista L Lanctôt, Nathan Herrmann, Beth A Sproule, Usoa E Busto

Abstract

Objectives To quantify and compare potential benefits (subjective reports of sleep variables) and risks (adverse events and morning-after psychomotor impairment) of short term treatment with sedative hypnotics in older people with insomnia.

Data sources Medline, Embase, the Cochrane clinical trials database, PubMed, and PsychLit, 1966 to 2003; bibliographies of published reviews and meta-analyses; manufacturers of newer sedative hypnotics (zaleplon, zolpidem, zopiclone) regarding unpublished studies.

Selection criteria Randomised controlled trials of any pharmacological treatment for insomnia for at least five consecutive nights in people aged 60 or over with insomnia and

Conclusions

Although the improvements in sleep variables obtained from prescription sedative hypnotics are statistically significant, the effect size is small, and the clinical benefits may be modest at best. The added risk of an adverse event may not justify these benefits, particularly in a high risk elderly population. These factors should be considered when sedative hypnotics are prescribed for older patients. Non-pharmacological therapies such as cognitive behaviour therapy have been shown to be as efficacious as pharmacotherapy for insomnia in older people.[44 55] Because fewer risks are associated with behavioural therapies,[21 44 56] they may be a viable treatment alternative in a healthy elderly population with no cognitive impairment.

risk-benefit relation is not known. This meta-analysis aims to study the benefits of sedative use, as determined by subjective reported changes in sleep variables, and the risks, as determined by adverse events.

Methods

Identification of studies

We searched Medline, Embase, the Cochrane clinical trials database, PubMed, and PsychLit from 1966 to 2003, using the keywords "elderly" *or* "aged" (Medline and Cochrane database only) *and* "sedatives" *or* "hypnotics" *or* "benzodiazepines" *or* "zolpidem" *or* "zaleplon" *or* "zopiclone" *or* "antihistamines" (PsychLit and Cochrane database only) *or* "diphenhydramine" *or* "sleep" (Cochrane database only) *or* "sleep disorders" (PsychLit and Cochrane database only). For each citation identified, we scanned titles or abstracts, or both, to identify randomised controlled trials that excluded patients under 60 years old. If studies included some patients who were under 60 years old, the mean age of participants had to be over 60. We searched bibliographies of publis[illegible]t titles and asked Se[illegible]eplon), Sanofi-Synthelab[illegible]anada (maker of zopicl[illegible]

Inclusion criteri[illegible]

We considered [illegible]ials of sedative hypnoti[illegible]atment against placebo[illegible] active treatment phases of included studies were double blind.

In the included studies, participants had a mean age of at least 60 years and met predetermined diagnostic criteria for

NNT: 13

NNH: 6

What is already known on this topic

Prescription of benzodiazepines in elderly people is widespread and often chronic in many developed countries, regardless of good practice guidelines

Benzodiazepines can have delayed adverse effects on cognition (cognitive decline and dementia), as reported in several case-control studies and a few cohort studies

What this study adds

Benzodiazepine exposure was associated with dementia, even after a long follow-up period

Adjustment for factors strongly associated with starting benzodiazepines or considered to be markers for a prodrome of early dementia did not alter the association

RESEARCH

Benzodiazepine use and risk of dementia: prospective population based study

Sophie Billioti de Gage *PhD student*[12], Bernard Bégaud *professor*[123], Fabienne Bazin *researcher*[12], Hélène Verdou
Tobias Kurth *d*

[1]Université Bordeaux
Hospitalier Charles Pe
Hospital, Boston, MA,

Abstract

Objective To evaluate
and incident dementia

Design Prospective, p

Setting PAQUID study

Participants 1063 me

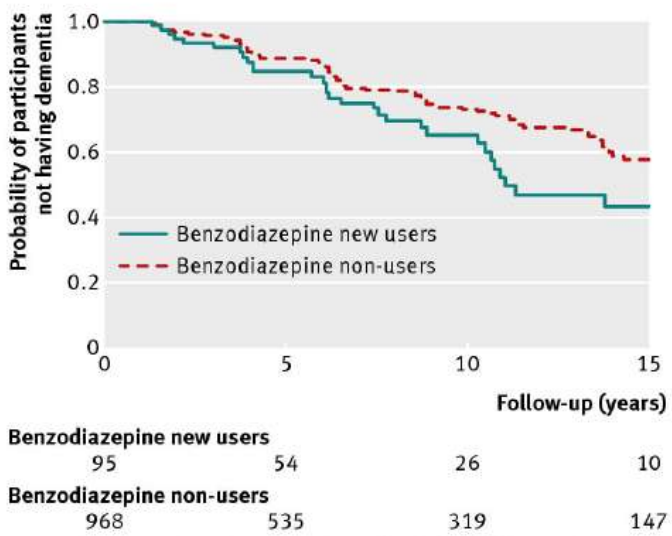


Fig 3 Dementia-free survival in PAQUID study, in new benzodiazepine users and non-users at baseline (T_5)

Calcif Tissue Int (2012) 91:24–31
DOI 10.1007/s00223-012-9603-8

ORIGINAL RESEARCH

Potential Impact of Benzodiazepine Use on the Rate of Hip Fractures in Five Large European Countries and the United States

T. P. Khong · F. de Vr
O. H. Klungel · N. J. R
H. Petri

Received: 19 January 2012/

Abstract Benzodiazep
and has been associate
fractures. Our aim was t
impact of the use of be
fracture in France, Ge
Kingdom, and the Unite
review to estimate the pooled relative risk (RR) for hip fractures were 1.8 %, 95 % CI 1.1–2.6 (Germany); 2.0 %,

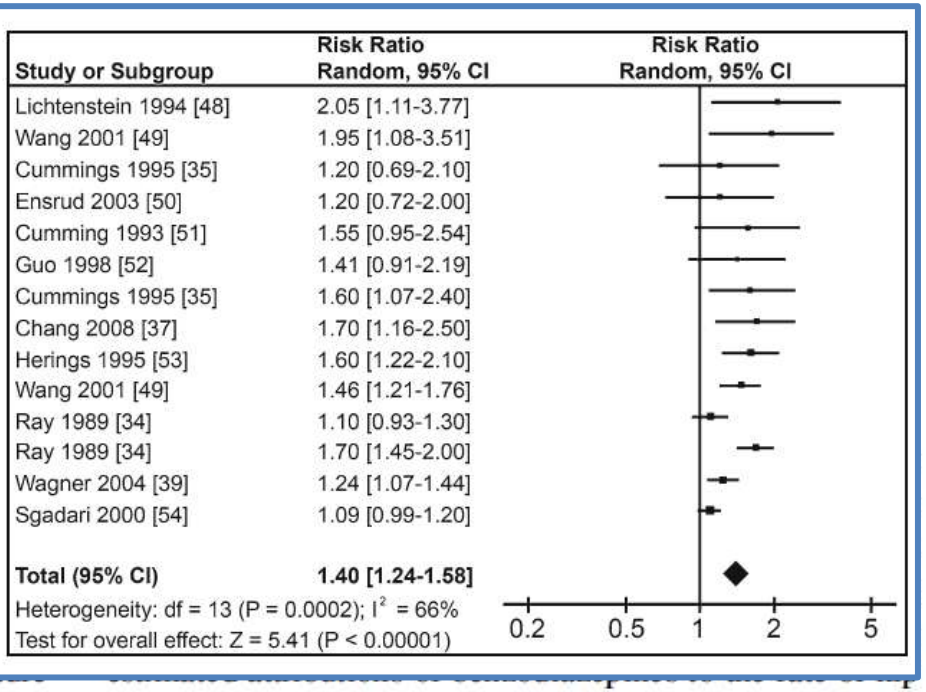
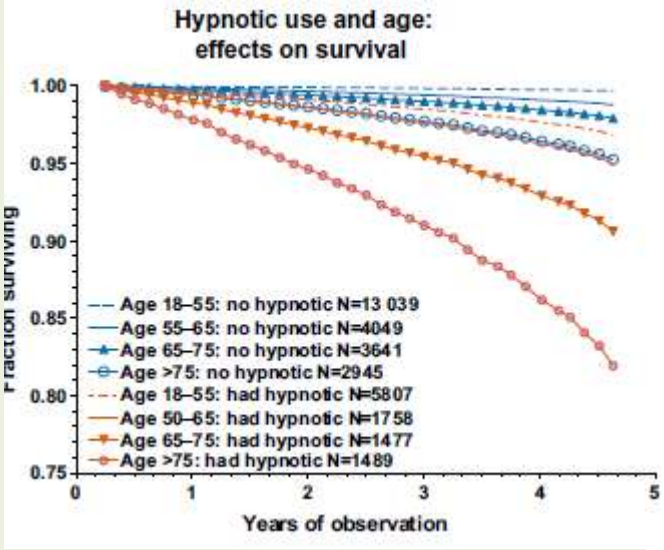


Fig. 1 Forest plot of relative risks for hip fractures and use of benzodiazepines versus nonuse. *Squares* represent the relative risk in each study; their sizes are proportional to their weights. *Horizontal lines* represent 95 % confidence intervals. *Black diamonds* represents the pooled relative risk (calculated with a random-effects model). Studies are ordered according to their weights



Conclusions: Receiving hypnotic prescriptions was associated with greater than threefold increased hazards of death even when prescribed <18 pills/year. This association held in separate analyses for several commonly used hypnotics and for newer shorter-acting drugs. Control of selective prescription of hypnotics for patients in poor health did not explain the observed excess mortality.

BMJ open

Hypnotics' association with mortality or cancer: a matched cohort study

Daniel F Kripke,[1] Robert D Langer,[2] Lawrence E Kline[1]

PRESS RELEASE

To cite: Kripke DF, Langer RD, Kline LE. Hypnotics' association with mortality or cancer: a matched cohort study. *BMJ Open* 2012;**2**: e000850. doi:10.1136/bmjopen-2012-000850

► Prepublication history and additional materials for this paper are available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2012-000850).

DFK and RDL contributed equally to the research. Author responsibility: all authors had access to all the data and can take responsibility for the integrity of the data and the accuracy of the data analysis.

ABSTRACT

Objectives: An estimated 6%–10% of US adults took a hypnotic drug for poor sleep in 2010. This study extends previous reports associating hypnotics with excess mortality.

Setting: A large integrated health system in the USA.

Design: Longitudinal electronic medical records were extracted for a one-to-two matched cohort survival analysis.

Subjects: Subjects (mean age 54 years) were 10 529 patients who received hypnotic prescriptions and 23 676 matched controls with no hypnotic prescriptions, followed for an average of 2.5 years between January 2002 and January 2007.

Main outcome measures: Data were adjusted for age, gender, smoking, body mass index, ethnicity, marital status, alcohol use and prior cancer. Hazard ratios (HRs) for death were computed from Cox proportional hazards models controlled for risk factors and using up to 116 strata, which exactly matched cases and controls by 12 classes of comorbidity.

Results: As predicted, patients prescribed any hypnotic had substantially elevated hazards of dying compared to those prescribed no hypnotics. For groups prescribed 0.4–18, 18–132 and >132 doses/year, HRs (95% CIs) were 3.60 (2.92 to 4.44), 4.43 (3.67 to 5.36) and 5.32 (4.50 to 6.30), respectively, demonstrating a dose–response association. HRs were elevated in separate analyses for several common hypnotics, including zolpidem, temazepam, eszopiclone, zaleplon, other benzodiazepines, barbiturates and sedative antihistamines. Hypnotic use in the upper third was associated with a significant elevation of incident cancer; HR=1.35 (95% CI 1.18 to 1.55). Results were robust within groups suffering each comorbidity, indicating that the death and cancer hazards associated with hypnotic drugs were not attributable to pre-existing disease.

Conclusions: Receiving hypnotic prescriptions was associated with greater than threefold increased hazards of death even when prescribed <18 pills/year

ARTICLE SUMMARY

Article focus

- Estimate the mortality risks associated with specific currently popular hypnotics in a matched cohort design, using proportional hazards regression models.
- Estimate the cancer risks associated with specific currently popular hypnotics.
- Explore what risk associated with hypnotics can be attributed to confounders and comorbidity.

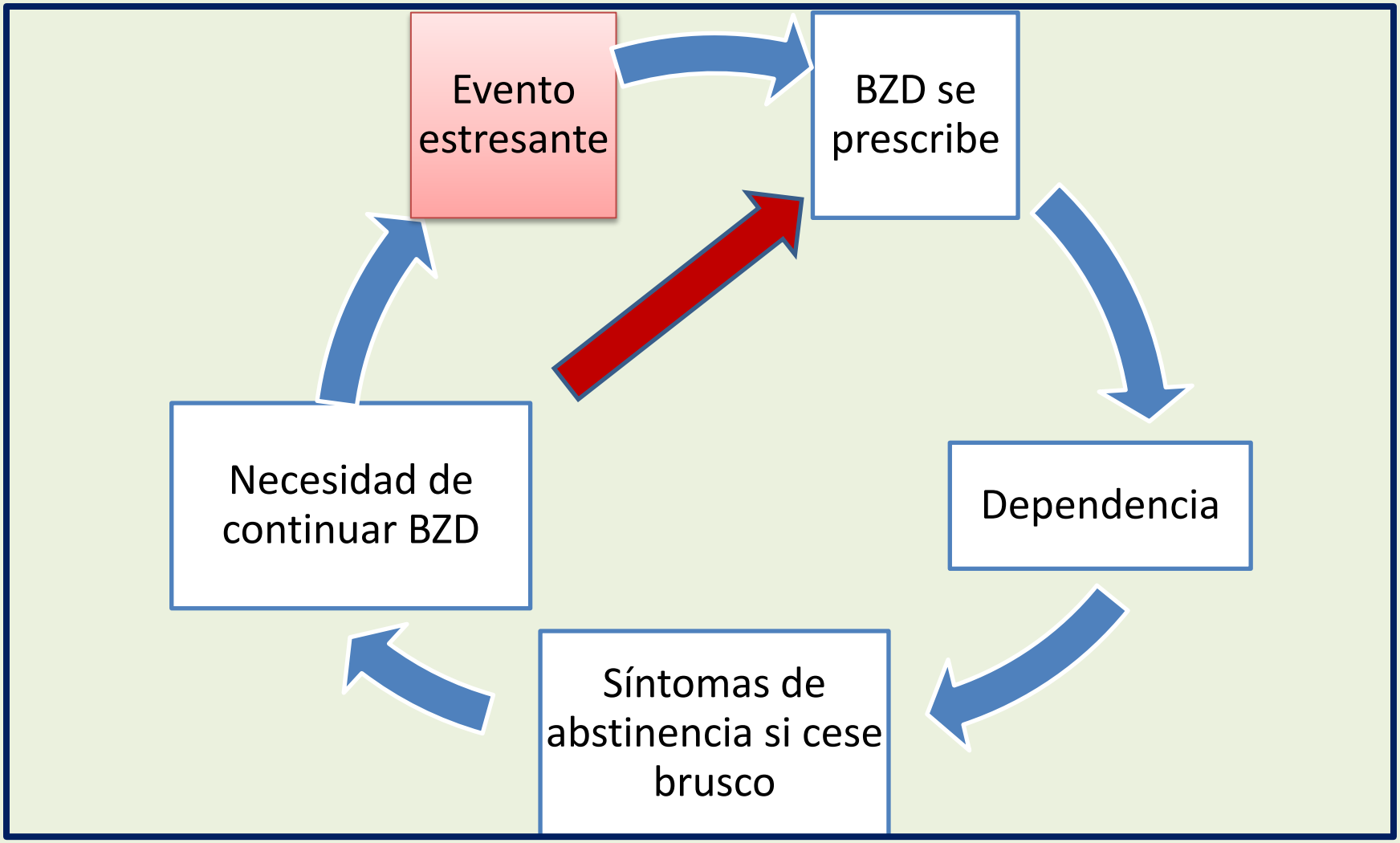
Key messages

- Patients receiving prescriptions for zolpidem, temazepam and other hypnotics suffered over four times the mortality as the matched hypnotic-free control patients.
- Even patients prescribed fewer than 18 hypnotic doses per year experienced increased mortality, with greater mortality associated with greater dosage prescribed.
- Among patients prescribed hypnotics, cancer incidence was increased for several specific types of cancer, with an overall cancer increase of 35% among those prescribed high doses.

Strengths and limitations of this study

- Design strengths included matching patient and control cohorts by age, gender and smoking. Through stratified statistical analyses, patients using hypnotics were matched with controls diagnosed with the exactly the same combination of 12 categories of comorbidity in up to 116 strata.
- The major limitation was that residual confounding could not be fully excluded, due to possible biases affecting which patients were prescribed hypnotics and due to possible imbalances in surveillance.
- Cohort studies demonstrating association do not necessarily imply causality, but the preferable randomised controlled trial method for assessing hypnotic risks may be impractical due to ethical

Rueda de la dependencia



Errores o puntos débiles más comunes….

- Al inicio del tratamiento: **no se suele explicar riesgos ni establecer la duración**.
- Como coadyuvante del tratamiento antidepresivo se suele mantener de **forma prolongada.**
- **Escasa revisión de tratamientos crónicos,** se cuestiona poco la pertinencia.
- En tratamientos prolongados: dificultades para abordar la retirada el profesional y el paciente lo ven como "**misión imposible**"

ESTRATEGIAS PARA REDUCIR EL CONSUMO DE BENZODIACEPINAS

Estrategias evaluadas para la retirada de benzodiacepinas

Intervención mínima por carta

(Bashir et al., 1994; Cormack et al., 1994; Gorgels et al., 2005).

Intervención breve en consulta médica

(Bashir et al., 1994; Belleville et al., 2007).

Estrategias aumentadas con medidas psicológicas

(Baillageron et al., 2003; Morin et al., 2004; Oude Voshaar et al., 2003b)

Estrategias aumentadas con terapia farmacológica

(Denis et al., 2006; Rickels et al., 1999).

Addiction

REVIEW

doi:10.1111/j.1360-0443.2008.02364.x

Effectiveness of current treatment approaches for benzodiazepine discontinuation: a meta-analysis

Jannette M. Parr[1], David J. Kavanagh[2], Lareina Cahill[3], Geoffrey Mitchell[1] & Ross McD. Young[2]

School of Medicine, University of Queensland, Herston, Queensland, Australia,[1] Institute of Health and Biomedical Innovation, Queensland University of Technology, Queensland, Australia[2] and Far North Queensland Rural Division of General Practice, Innisfail, Queensland, Australia[3]

ABSTRACT

Aims To assess the effectiveness of current treatment approaches to assist benzodiazepine discontinuation. benzodiazepine discontinuation in general practice and out-patient pared with three treatment approaches: brief interventions, gradual tions. GDR was compared with GDR plus psychological interventions clusion criteria were met by 24 studies, and a further eight were) = 5.96, confidence interval (CI) = 2.08–17.11] and brief interven- erior cessation rates at post-treatment to routine care. Psychological ine care (OR = 3.38, CI = 1.86–6.12) and GDR alone (OR = 1.82, otherapies did not add to the impact of GDR (OR = 1.30, CI = 0.97– ines by other pharmacotherapy was less effective than GDR alone y technique had significantly greater benzodiazepine discontinuation ing an intervention is more effective than routine care. Psychological e GDR alone. While some substitutive pharmacotherapies may have ort their use.

CONCLUSIONS

Evidence for the use of substitutive pharmacotherapy in the management of benzodiazepine dependence remains relatively weak. However, raising the issue of cessation of benzodiazepine use systematically with every patient who has been prescribed benzodiazepines for longer than 3 months and recommending that they gradually reduce the benzodiazepine dosage is likely to result in better cessation rates when compared with continuation of routine care. Linking patients with psychological assistance may further increase the chances of ceasing use successfully.

BRITISH JOURNAL OF PSYCHIATRY (2006), 189, 213–220. doi: 10.1192/bjp.189.3.213

Strategies for discontinuing long-term benzodiazepine use

Meta-analysis

Cualquier intervención tiene **eficacia superior a la consulta habitual**
Con **apoyo psicológico puede aportar** beneficio especialmente en pacientes con insomnio aunque precisa mayor inversión de recursos.
Con **apoyo farmacológico a día de hoy** no existe evidencia suficiente para recomendarla de forma sistemática.
La **intervención breve con reducción escalonada de dosis es efectiva y coste-efectiva** .

Method Meta-analysis of comparable intervention studies.

Results Twenty-nine articles met inclusion criteria. Two groups of

Conclusions Evidence was found for the efficacy of stepped care (minimal intervention followed by systematic discontinuation alone) in discontinuing long-term benzodiazepine use.

estimated to be stable or slightly decreasing (Stillwell & Fountain, 2002), but remains at levels varying between 2% and 3% of the general population (Zandstra *et al*, 2002). Although long-term therapeutic use of benzodiazepines is controversial, limited evidence suggests long-term efficacy in specific diagnostic groups such as panic disorder and social phobia (Schweizer *et al*, 1993; Otto *et al*, 2000). The prevalence of these disorders among people who are long-term benzodiazepine users, however, is relatively low (Zandstra *et al*, 2004).

Problems experienced by patients stopping long-term benzodiazepine use initiated the development of treatment strategies for discontinuing these drugs. Russell & Lader (1993) proposed a stepped care approach to address the problem of long-term use. They advised starting with a minimal intervention and, if this failed, gradually intensifying treatment from

Library in December 2004, using the keywords BENZODIAZEPINE(S) in combination with WITHDRAWAL, DETOXIFICATION, DEPENDENCE, DISCONTINUATION *or* LONG-TERM. This search was extended by a manual

months.

Excluded were case series, review papers, double publications, experimental research or clinical trials evaluating the efficacy of benzodiazepine treatment for a fixed period, and animal research. Authors R.C.O.V. and J.E.C. independently checked the inclusion and exclusion criteria of the identified studies.

Selection procedure, data extraction and quality assessment

Included studies were coded twice by R.C.O.V. and J.E.C. Discrepancies in the two coding forms were resolved by consensus after discussion or by referring to the data in the original article. This method yielded one coding form per article. The intervention type was added to the coding form by distinguishing between minimal interventions and systematic discontinua-

study OR=6.1, 95% CI 2.0–18.6).
Augmentation of systematic
discontinuation with imipramine (two

BenzoRed

Eficacia comparativa de dos intervenciones del médico de familia para el abandono del consumo prolongado de benzodiacepinas
Estudio BENZORED

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Estudio BENZORED

Objetivo:

Evaluar la eficacia de dos intervenciones en Atención Primara para el cese del consumo prolongado de benzodiazepinas.

Vicens et al. BMC Family Practice 2011, 12:23
http://www.biomedcentral.com/1471-2296/12/23

BMC Family Practice

STUDY PROTOCOL Open Access

Comparative efficacy of two primary care interventions to assist withdrawal from long term benzodiazepine use: A protocol for a clustered, randomized clinical trial

Caterina Vicens[1*], Isabel Socias[2], Catalina Mateu[3], Alfonso Leiva[3], Ferran Bejarano[4], Ermengol Sempere[5], Josep Basora[6], Vicente Palop[7], Marta Mengual[8], Jose Luis Beltran[8], Enric Aragonès[9], Guillem Lera[10], Silvia Folch[11], Josep Lluis Piñol[12], Magdalena Esteva[13], Miguel Roca[14], Arturo Arenas[15], Maria del Mar Sureda[16], Francisco Campoamor[17] and Francisca Fiol[1]

Abstract

Background: Although benzodiazepines are effective, long-term use is not recommended because of potential adverse effects; the risks of tolerance and dependence; and an increased risk of hip fractures, motor vehicle accidents, and memory impairment. The estimated prevalence of long-term benzodiazepine use in the general population is about 2.2 to 2.6%, is higher in women and increases steadily with age. Interventions performed by General Practitioners may help patients to discontinue long-term benzodiazepine use. We have designed a trial to evaluate the effectiveness and safety of two brief general practitioner-provided interventions, based on gradual dose reduction, and will compare the effectiveness of these interventions with that of routine clinical practice.

Methods/Design: In a three-arm cluster randomized controlled trial, general practitioners will be randomly allocated to: a) a group in which the first patient visit will feature a structured interview, followed by visits every 2-3 weeks to the end of dose reduction; b) a group in which the first patient visit will feature a structured interview plus delivery of written instructions to self-reduce benzodiazepine dose, or c) routine care. Using a computerized pharmaceutical prescription database, 495 patients, aged 18-80 years, taking benzodiazepine for at least 6 months, will be recruited in primary care health districts of three regions of Spain (the Balearic Islands, Catalonia, and Valencia). The primary outcome will be benzodiazepine use at 12 months. The secondary outcomes will include measurements of anxiety and depression symptoms, benzodiazepine dependence, quality of sleep, and alcohol consumption.

Discussion: Although some interventions have been shown to be effective in reducing benzodiazepine consumption by long-term users, the clinical relevance of such interventions is limited by their complexity. This randomized trial will compare the effectiveness and safety of two complex stepped care interventions with that of routine care in a study with sufficient statistical power to detect clinically relevant differences.

Trial Registration: Current Controlled Trials: ISRCTN13024375

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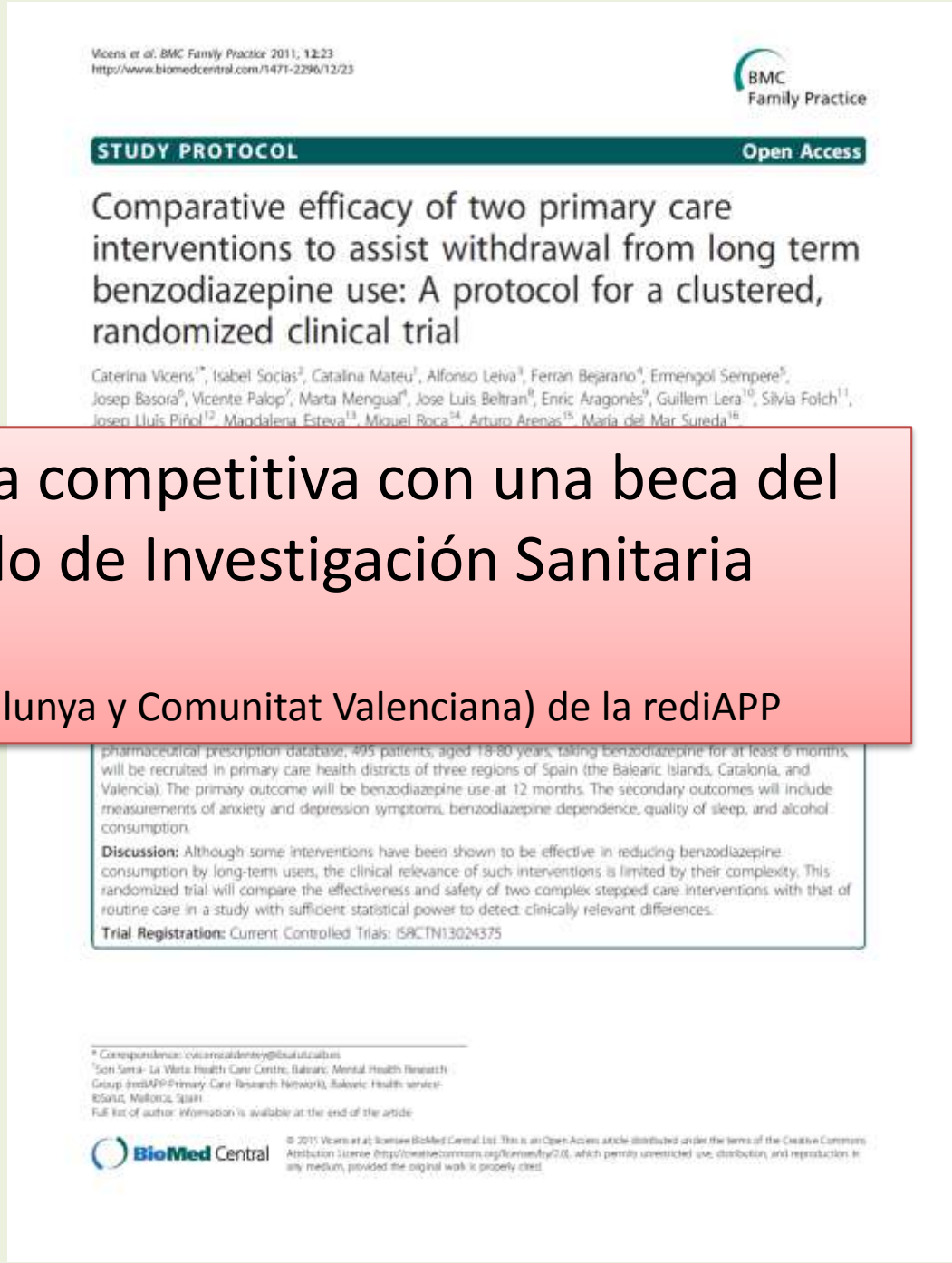
Estudio BENZORED

Objetivo:

el cese del consumo prolongado de benzodiazepinas.

Financiado en convocatoria competitiva con una beca del Instituto Carlos III del Fondo de Investigación Sanitaria (PS09/00947).

Proyecto multicéntrico (Illes Balears, Catalunya y Comunitat Valenciana) de la rediAPP



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BMC Family Practice

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Método

Diseño:

Ensayo clínico aleatoriado multicéntrico con **tres ramas** en Atención Primaria de tres Comunidades Autónomas de España (Illes Balears, Catalunya and Comunitat Valenciana).

Sujetos:

Pacientes entre 18 y 80 años que han consumido **BZD o similar (análogos) durante al menos 6 meses** y presentan ninguno de los criterios de exclusión del estudio.

Diseño:

Ensayo clíni
multicéntric
ramas en Ate
Primaria de tres Comunidades Autónomas de España (Illes Balears, Catalunya and Comunitat Valenciana).

durante a os 6 meses y presen ninguno de los criterios de exclusión del estudio.

CRITERIOS DE EXCLUSIÓN:

Trastorno depresivo ó ansioso severo, trastorno psicótico, trastorno de personalidad grave, y/o seguimiento por parte de psiquiatría.

Enfermedad médica severa incluyendo epilepsia y demencia

Consumidores de **drogas ilegales** ó consumo abusivo de alcohol.

Pacientes **institucionalizados o en fase terminal**

Cuando el MF considera que retirar la bzd en este momento puede no ser adecuado.

Limitada capacidad de comprensión para consentimiento.

Método. Aleatorización.

Aleatorización por conglomerados (MF)

Long term benzodiazepine users were identified from General Practitioner (GP) clinical records by prescription database.

30 patients were randomly selected from each GP patient list.

GP had to include systematically 8 patients

Once patients were included, GPs were randomly allocated to one of the three arms of the study

GPs received the specific training according to the group they belonged to.

Método. Intervención.

A. Grupo Intervención breve estructurada con seguimiento (SIF): Entrevista con mensaje estructurado + pauta de reducción escalonada de dosis + visitas de seguimiento (cada 2-3 semanas).

B. Grupo Intervención con soporte escrito sin visitas de seguimiento (SIW): Entrevista con mensaje estructurado + información escrita de refuerzo con pauta de retirada de la medicación. No se realizan visitas de seguimiento.

C. Grupo Control: Proceder como habitualmente en consulta.

Méto

CONTENIDOS MENSAJE ESTRUCTURADO:
Qué son las benzodiacepinas
Para qué sirven, tratamiento sintomático.
Concepto de dependencia
Reconocer síntomas de abstinencia/retirada.
Efectos desfavorables a largo plazo
- Disminución reflejos, riesgo caídas
- Alteración memoria....

A. Grupo Interve
seguimiento (SI: ...sta con mensaje estructurado + pauta de reducción escalonada de dosis + visitas de seguimiento (cada 2-3 semanas).

B. Grupo Intervención con soporte escrito sin visitas de seguimiento (SIW): Entrevista con mensaje estructurado + información escrita de refuerzo con pauta de retirada de la medicación. No se realizan visitas de seguimiento.

C. Grupo Control: Proceder como habitualmente en consulta.

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B. Grupo Intervención con soporte escri in visitas de seguimiento (SIW): Entrevista con n ie estructurado + información escrita de re con pauta de retirada de visitas de seguimient

Disminución del 10 al 25% de la dosis diaria inicial en intervalos de 2-3 semanas.
Individualizar pauta.
Posibilidad cambio a diazepam a dosis equivalentes.

C. Grupo Control: Proc consulta.

Méto

CONTENIDOS MENSAJE ESTRUCTURADO:
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A. Grupo Interve
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B. Grupo Interven[illegible]ón con soporte escri[illegible]in visitas
[illegible]**W):** Entrevista con n[illegible]ie
[illegible]rmación escrita de re[illegible]con
[illegible]e
[illegible]nt

Abordar síntomas de retirada
Establecer siguiente escalón de descenso de dosis.
Posibilidad cambio a diazepam a dosis equivalentes.

Disminución del 10 al 25% de la dosis diaria inicial en intervalos de 2-3 semanas.
Individualizar pauta.
Posibilidad cambio a diazepam a dosis equipotentes

C. Grupo Control: Proc
consulta.

Método. Intervención.

A. Grupo Intervención breve estructurada con seguimiento (SIF): Entrevista con mensaje estructurado + pauta de reducción escalonada de dosis + visitas de seguimiento (cada 2-3 semanas).

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C. Grupo Control: Proceder como habitualmente en consulta.

Anexo 4.1: INFORMACIÓN DE APOYO Y PAUTA DE RETIRADA (GIM)

- Las **benzodiacepinas** (*tranquilizantes)* son fármacos cuyas indicaciones principales son los trastornos de ansiedad y el insomnio. También se utilizan en las convulsiones y como relajantes musculares.
- Mejoran los síntomas. **No constituyen un tratamiento curativo** de la enfermedad.
- Son medicamentos muy eficaces cuando se consumen durante un breve período de tiempo o de forma intermitente, sin embargo **su uso prolongado no aporta beneficios** y expone a quien las consume a una serie de riesgos.
- Cuando la duración del tratamiento ha sobrepasado algunos meses se produce una adaptación fisiológica del organismo a esta sustancia que hace que **si se retira de forma brusca produzca un malestar significativo con síntomas desagradables** (ansiedad, irritabilidad, insomnio...) que refuerza su consumo. Esto es lo que llamamos dependencia y los síntomas desagradables son los **síntomas de abstinencia**. Estos síntomas suelen ser limitados en el tiempo pero pueden ser evitados si la retirada de la medicación se realiza de forma gradual y progresiva.
- Además, el consumo prolongado de estas sustancias se ha relacionado con **disminución de reflejos, incremento de riesgo de caídas y fracturas de cadera en personas mayores, de accidentes de tráfico y alteraciones de la memoria. El riesgo aumenta si la edad es avanzada**.
- Existen otros abordajes no farmacológicos que pueden ayudarle en el tratamiento del insomnio y de los trastornos de ansiedad (higiene del sueño, técnicas de relajación, yoga...).
- Lea atentamente esta información y proceda a realizar la reducción de las dosis tal y como su médico se lo indica en esta tabla.

Pauta de reducción de benzodiacepinas personalizada

Nombre: .....

Fecha	Medicación	Desayuno	Comida	Cena	Acostarse

Fdo. Dr. .....

Fecha: .....

Método. Intervención.

A. Grupo Intervención breve estructurada con seguimiento (SIF): Entrevista con mensaje estructurado + pauta de reducción escalonada de dosis + visitas de seguimiento (cada 2-3 semanas).

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C. Grupo Control: Proceder como habitualmente en consulta.

Método. Variables.

- **Variable principal** (endpoint):
  - **Consumo de benzodiacepinas** en el ultimo mes, autodeclarado y **confirmado** en base de datos de prescripción a los 12 meses.
- **Otras variables**:
  - **Ansiedad y depresion medido con la** Hospital Anxiety and Depression Scale (HAD)
  - **Calidad sueño** (Cuestionario de Oviedo COS)
  - **Consumo de Alcohol** declarado en unidades de alcohol por semana.
  - **Sintomas de abstinencia/retirada** u otros efectos adversos que puedan estar relacionados con la intervencion.

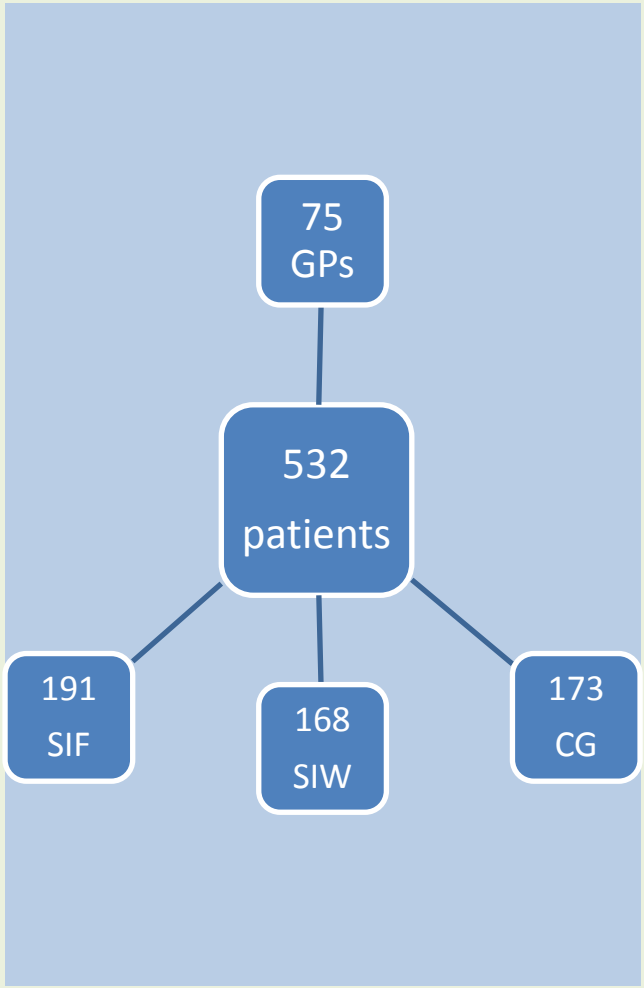
Table 1 Measures, variables, and timeline

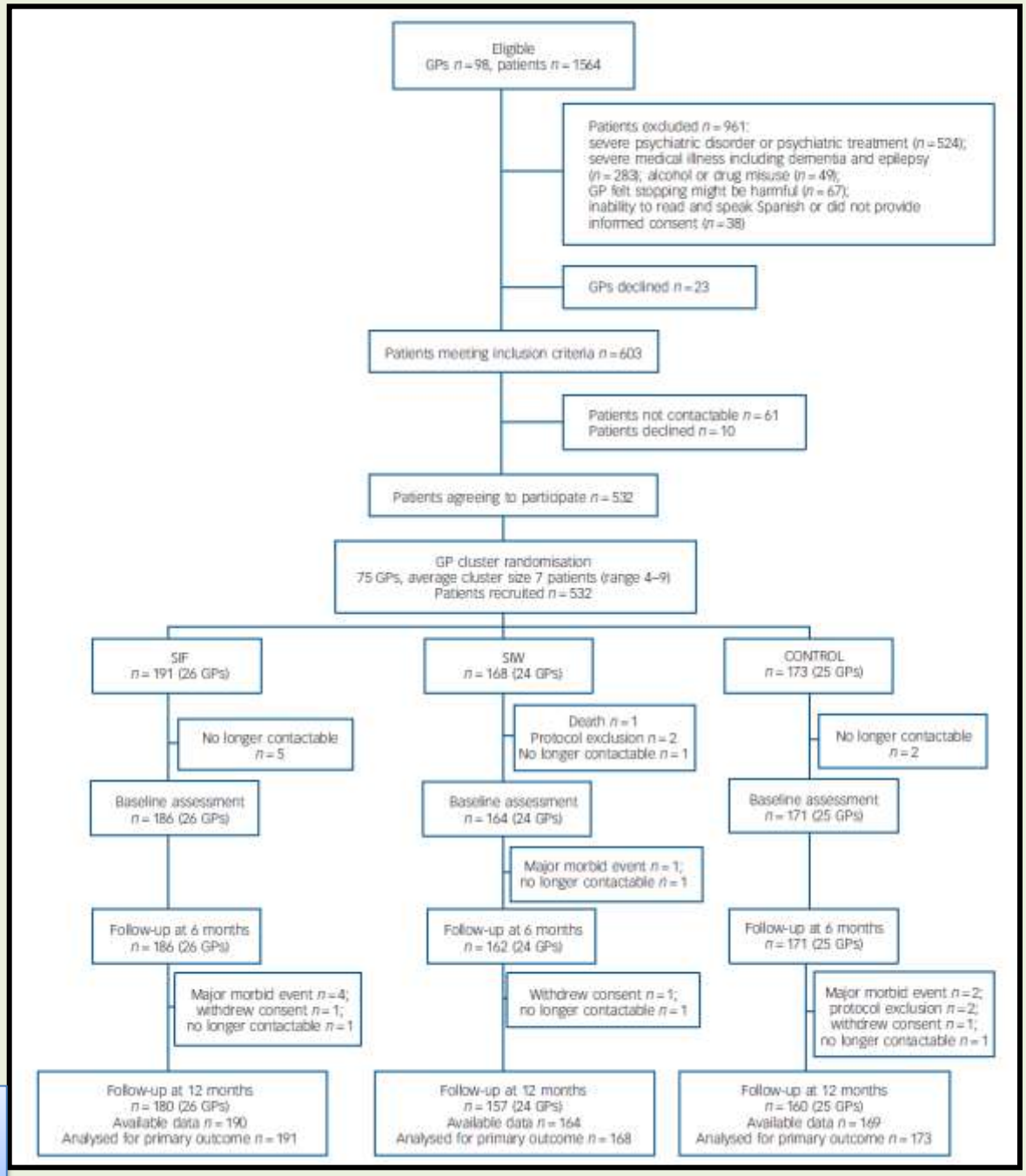
Instrument	Assessment area	Time(s) of assessments
Sampling form	Inclusion/exclusion criteria	Before randomization
Sociodemographic data form	Sociodemographic data: age, gender, educational level, labor status, marital status, number of persons living in the home, disabled persons under his/her care.	At baseline
Baseline clinical data form	Identification of consumed benzodiazepines Dosage and duration of benzodiazepines consumed Original reason for taking benzodiazepines Comorbid chronic physical or psychological diseases	At baseline
Benzodiazepine Severity of Dependence Scale (SDS)	Severity of benzodiazepine dependence	At baseline
Hospital Anxiety and Depression Scale (HADS)	Symptoms of anxiety and depression	At baseline, 6 and 12 months
Oviedo Sleep Quality Scale (COS)	Sleep quality and features	At baseline, 6 and 12 months
Alcohol consumption form	Alcohol consumption	At baseline, 6 and 12 months
Antidepressant consumption form	Current consumption of antidepressants	At baseline, 6 and 12 months
Current use of benzodiazepine form	Current consumption of benzodiazepines	At baseline, 6 and 12 months
Adverse effects form	Adverse effects related to benzodiazepine withdrawal	At 6 and 12 months
Use of health resources questionnaire	Number of primary care visits related to tapering of benzodiazepines	At 12 months

Método. Análisis.

- Comprobar si los tres grupos son homogéneos.
- Variables categóricas expresadas en números y porcentajes y variables continuas en medianas y quartiles (IQR)
- Análisis por intención de tratar.
- Riesgo Relativo (RR), Reducción absoluta de riesgo (RAR) y el NNT, utilizando la Generalized Estimation Equation (GEE) para aleatorización por conglomerados con su 95% IC.
- Seguridad de las intervenciones: Cambios entre grupos y dentro del grupo a los 6 y 12 meses.

Resultados. Flow-chart





Perdidas: 35/532 (6.6%) pacientes.
Non-available final data: 9/532 (1.7%)

Resultados. Caracteristicas MF

Table 1 Characteristics of participating general practitioners

	Control group	SIW group	SIF group
Total GPs, *n*	25	24	26
Age, years: median (IQR)	53 (47–55)	51 (41–54)	46 (42–54)
Gender, *n/N* (%)			
Men	16/25 (64)	8/24 (33)	9/26 (35)
Women	9/25 (36)	16/24 (67)	17/26 (65)
Patients attending PCC, *n*: median (IQR)	22 000 (9800–30 000)	22 000 (9000–26 000)	13 000 (6000–30 000)
GPs working in a teaching PCC, *n/N* (%)			
Yes	14/25 (56)	17/24 (71)	15/26 (58)
No	11/25 (44)	7/24 (29)	11/26 (42)
Speciality, *n/N* (%)			
Family doctor	25/25 (100)	22/23 (96)	26/26 (100)
Other	0/25 (0)	1/23 (4)	0/26 (0)
Professional experience, years: median (IQR)	26 (18–30)	22 (14–24)	18 (15–28)
Previous training in benzodiazepine withdrawal, *n/N* (%)			
Yes	11/22 (50)	11/19 (68)	19/26 (73)
No	11/22 (50)	8/19 (42)	7/26 (27)
Previous participation in clinical trials, *n/N* (%)			
Yes	11/20 (55)	7/17 (41.2)	12/25 (48)
No	9/20 (45)	10/17 (58.8)	13/25 (52)

GP, general practitioner; IQR, interquartile range; PCC, primary care centre; SIF, intervention group with follow-up visits; SIW, intervention group with written instructions.

Resultados.
Características basales de los pacientes

Table 2 Patients' characteristics at baseline

	Control group	SIW group	SIF group
Age, years: median (IQR)	62 (54–70)	65 (56–72)	65 (56–72)
Gender, women, *N/n* (%)	116/171 (67.8)	120/163 (73.6)	139/187 (74.3)
Marital status, *N/n* (%)			
Married, cohabiting	114/170 (67.1)	118/165 (71.5)	134/186 (72.0)
Single, divorced, widowed	56/170 (33.0)	47/165 (28.5)	52/186 (28.0)
Education status, *N/n* (%)			
<6 years	53/171 (31.0)	64/164 (39.0)	79/186 (42.5)
Primary education	84/171 (49.1)	76/164 (46.3)	79/186 (42.5)
Secondary or higher education	34/171 (19.9)	24/164 (14.6)	28/186 (15.0)
Employment, *N/n* (%)			
Employed	53/171 (31.0)	50/164 (30.5)	39/186 (21.0)
Unemployed, homeworker	48/171 (28.0)	34/164 (20.7)	60/186 (32.3)
Retired	70/171 (40.9)	80/164 (48.8)	87/186 (46.8)
Reason for initial prescription, *N/n* (%)			
Anxiety	122/171 (71.3)	104/164 (63.4)	113/185 (61.1)
Depression	46/171 (26.9)	54/162 (33.3)	53/185 (28.6)
Insomnia	128/171 (74.9)	109/163 (66.9)	121/186 (65.1)
Pain	20/171 (11.7)	17/163 (10.4)	21/185 (11.3)
Who prescribed benzodiazepine, *N/n* (%)			
GP	135/170 (79.4)	121/162 (74.7)	125/184 (67.9)
Psychiatrist	17/170 (10.0)	17/162 (10.5)	27/184 (14.7)
Time taking benzodiazepines, months: median (IQR)	48 (24–96)	60 (24–120)	60 (28–120)
Short benzodiazepine half-life, *N/n* (%)	149/173 (86.1)	143/168 (85.1)	159/191 (83.2)
Equivalent dose >10 mg diazepam, *N/n* (%)	55/173 (31.8)	46/168 (27.4)	53/191 (27.7)
Currently taking antidepressants, *N/n* (%)	62/171 (36.3)	53/164 (32.3)	55/185 (29.7)
Alcohol drinker, *N/n* (%)	71/171 (41.5)	52/161 (32.3)	72/185 (38.9)
Insomnia,[a] *N/n* (%)	37/167 (22.2)	27/159 (17)	27/186 (14.5)
Scores: median (IQR)			
SDS	5 (3–8)	5 (3–7)	5 (3–8)
HADS Anxiety	7.5 (4–11)	7 (4–12)	9 (6–12)
HADS Depression	5 (2–7)	5 (2–8)	5 (2–8)
Sleep satisfaction[a]	4 (3–6)	4 (3–5)	4 (3–5)
Alcohol consumption: median (IQR)[b]	6 (2–11)	7 (2–11.5)	7 (2.5–11)

GP, general practitioner; HADS, Hospital Anxiety and Depression Scale; IQR, interquartile range; SDS, Severity Dependence Scale; SIF, intervention group with follow-up visits; SIW, intervention group with written instructions.
a. Oviedo Sleep Questionnaire.
b. Standard alcohol units per week among drinkers.

Resultados.
Características basales de los pacientes

Mediana edad: 64 años
Sexo: 72% mujeres
73% prescrito por MF
Mediana duración: 60 meses
Semivida corta: 85%
Dosis elevadas: 29%

Table 2 Patients' characteristics at baseline

	Control group	SIW group	SIF group
Age, years: median (IQR)	62 (54–70)	65 (56–72)	65 (56–72)
	116/171 (67.8)	120/163 (73.6)	139/187 (74.3)
	114/170 (67.1)	118/165 (71.5)	134/186 (72.0)
	56/170 (33.0)	47/165 (28.5)	52/186 (28.0)
	53/171 (31.0)	64/164 (39.0)	79/186 (42.5)
	84/171 (49.1)	76/164 (46.3)	79/186 (42.5)
	34/171 (19.9)	24/164 (14.6)	28/186 (15.0)
	53/171 (31.0)	50/164 (30.5)	39/186 (21.0)
	48/171 (28.0)	34/164 (20.7)	60/186 (32.3)
	70/171 (40.9)	80/164 (48.8)	87/186 (46.8)
	122/171 (71.3)	104/164 (63.4)	113/185 (61.1)
	46/171 (26.9)	54/162 (33.3)	53/185 (28.6)
	128/171 (74.9)	109/163 (66.9)	121/186 (65.1)
	20/171 (11.7)	17/162 (10.4)	21/185 (11.3)
	135/170 (79.4)	121/162 (74.7)	125/184 (67.9)
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Alcohol drinker, *N/n* (%)	71/171 (41.5)	52/161 (32.3)	72/185 (38.9)
Insomnia,[a] *N/n* (%)	37/167 (22.2)	27/159 (17)	27/186 (14.5)
Scores: median (IQR)			
SDS	5 (3–8)	5 (3–7)	5 (3–8)
HADS Anxiety	7.5 (4–11)	7 (4–12)	9 (6–12)
HADS Depression	5 (2–7)	5 (2–8)	5 (2–8)
Sleep satisfaction[a]	4 (3–6)	4 (3–5)	4 (3–5)
Alcohol consumption: median (IQR)[b]	6 (2–11)	7 (2–11.5)	7 (2.5–11)

GP, general practitioner; HADS, Hospital Anxiety and Depression Scale; IQR, interquartile range; SDS, Severity Dependence Scale; SIF, intervention group with follow-up visits; SIW, intervention group with written instructions.
a. Oviedo Sleep Questionnaire.
b. Standard alcohol units per week among drinkers.

Table 3 Comparison of benzodiazepine discontinuation between the control and intervention groups after 6 months and 12 months of follow-up

	6 months				12 months			
	Discontinued benzodiazepines *n/N* (%)	RR	95% CI	*P*	Discontinued benzodiazepines *n/N* (%)	RR	95% CI	*P*
Control group	25/173 (14.4)				26/173 (15.0)			
SIW group	72/168 (42.9)	2.97	2.07–4.26	<0.0001	76/168 (45.2)	3.01	2.03–4.46	<0.0001
SIF group	71/191 (37.2)	2.58	1.77–3.75	<0.0001	86/191 (45.0)	3	2.04–4.40	<0.0001

RR, relative risk; SIF, intervention group with follow-up visits; SIW, intervention group with written instructions.

NNT: 4 (SIF and SIW)

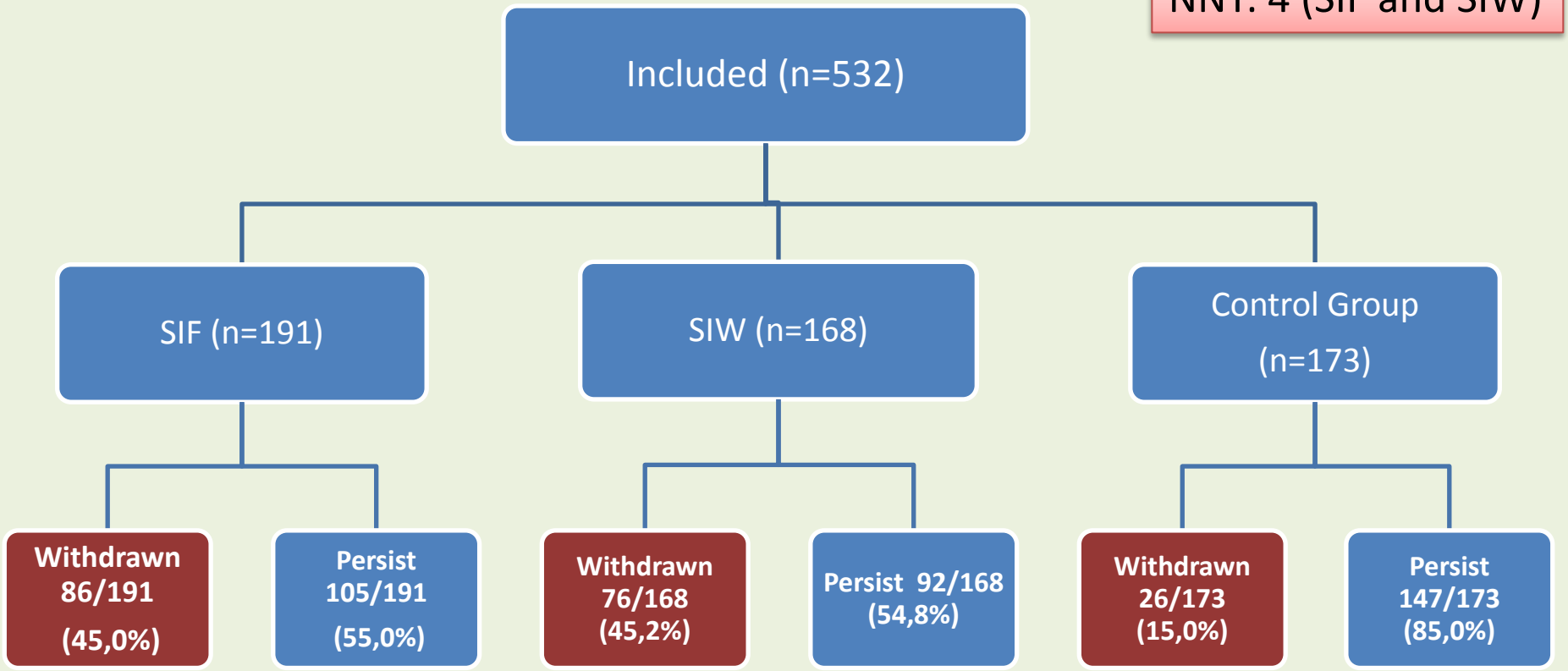


Table 3 Comparison of benzodiazepine discontinuation between the control and intervention groups after 6 months and 12 months of follow-up

	6 months				12 months			
	Discontinued benzodiazepines *n/N* (%)	RR	95% CI	*P*	Discontinued benzodiazepines *n/N* (%)	RR	95% CI	*P*
Control group					26/173 (15.0)			
SIW group		2.07–4.26	<0.0001		76/168 (45.2)	3.01	2.03–4.46	<0.0001
SIF group		1.77–3.75	<0.0001		86/191 (45.0)	3	2.04–4.40	<0.0001

RR, relative risk; … vention group with written instructions.

Análisis Subgrupos:

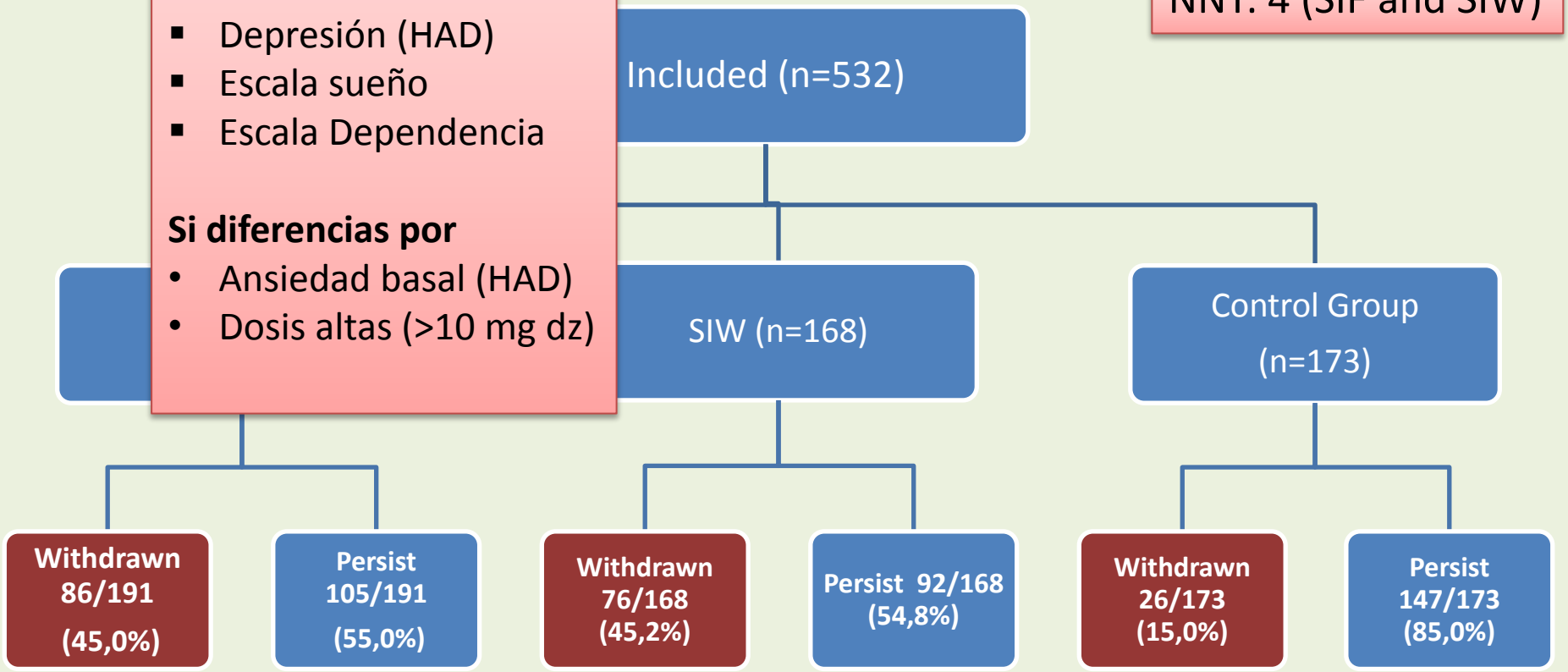
No diferencias por:

- Edad
- Sexo
- Semivida bzd
- Depresión (HAD)
- Escala sueño
- Escala Dependencia

Si diferencias por

- Ansiedad basal (HAD)
- Dosis altas (>10 mg dz)

NNT: 4 (SIF and SIW)



	Between-group analysis: median differences (95% CI)[a]					
	Control *v.* SIW group	*P*	Control *v.* SIF group	*P*	SIW *v.* SIF groups	*P*
At 6 months						
HADS Anxiety	−1 (−2 to 0)	0.280	0 (−1 to 1)	0.394	0 (−1 to 1)	0.748
HADS Depression	0 (−1 to 1)	0.941	0 (−1 to 0)	0.244	0 (−1 to 0)	0.346
Sleep satisfaction	−1 (−1 to 0)	0.002	0 (0 to 0)	0.993	1 (0 to 1)	0.003
Alcohol consumption[c]	0 (−1 to 1)	0.423	0 (−1 to 1)	0.393	0 (−1 to 1)	0.933
At 12 months						
HADS Anxiety	0 (−2 to 1)	0.442	0 (−1 to 1)	0.762	0 (−1 to 1)	0.673
HADS Depression	0 (−1 to 0)	0.373	0 (−1 to 0)	0.659	0 (0 to 1)	0.574
Sleep satisfaction	0 (−1 to 0)	0.095	0 (0 to 0)	0.749	0 (0 to 1)	0.034
Alcohol consumption[c]	0 (−1 to 1)	0.854	0 (−1 to 1)	0.390	0 (−1 to 1)	0.669

HADS, Hospital Anxiety and Depression Scale; SIF, intervention group with follow-up visits; SIW, intervention group with written instructions.
a. Hodges–Lehmann median difference.
b. Von Mises median difference, Somers' *D* rank statistics *P* values.
c. Standard alcohol units per week among drinkers.

Between-group and within-group analysis

	Within-group analysis: median differences (95% CI) from baseline[b]					
	Control group	*P*	SIW group	*P*	SIF group	*P*
At 6 months						
HADS Anxiety	0 (−1 to 1)	0.150	−1 (−2 to 0)	0.001	−2 (−3 to −1)	<0.0001
HADS Depression	−1 (−2 to 0)	<0.0001	−1 (−2 to 0)	<0.0001	−2 (−3 to −1)	<0.0001
Sleep satisfaction	0 (0 to 1)	0.073	0 (−1 to 0)	0.242	0 (0 to 1)	0.009
Alcohol consumption[c]	0 (0 to 1)	0.243	0 (−1 to 1)	0.932	0 (−1 to 1)	0.555
At 12 months						
HADS Anxiety	−1 (−2 to 0)	0.003	−1 (−2 to 0)	<0.0001	−2 (−3 to −1)	<0.0001
HADS Depression	−1 (−2 to 0)	0.001	−2 (−3 to 1)	<0.0001	−2 (−3 to −1)	<0.0001
Sleep satisfaction	0 (0 to 0)	0.347	0 (0 to 0)	0.864	0 (0 to 1)	0.011
Alcohol consumption[c]	0 (−1 to 1)	0.645	−1 (−1 to 0)	0.963	−1 (−2 to 0)	0.080

Table 4 Intervention safety outcomes

	6 months				12 months			
	Control group	SIW group	SIF group	*P*	Control group	SIW group	SIF group	*P*
Clinical assessment scores: median (IQR)								
HADS A				0.473	6 (3–9)	5.5 (2–9)	6 (3–9)	0.749
HADS D				0.473	3 (1–6)	2 (1–6)	3 (1–6)	0.662
Sleep sa				0.005	5 (2–6)	4 (3–5)	5 (4–6)	0.084
Alcohol				0.607	7 (3–14)	7 (1–12)	5 (2–10)	0.288
Withdrawa								
Tremor								
None					153/164 (93.3)	148/159 (93.1)	171/184 (92.9)	
Mild					9/164 (5.5)	10/159 (6.3)	7/184 (3.8)	
Moderate	2/170 (1.2)	9/159 (5.7)	11/186 (5.9)		2/164 (1.2)	1/159 (0.6)	5/184 (2.7)	
Severe	3/170 (1.8)	1/159 (0.6)	7/186 (3.8)	0.025	0/0 (0)			0.987
Irritability								
None		117/159 (73.6)	144/186 (77.4)		144/164 (8			
Mild		23/159 (14.5)	16/186 (8.6)		12/164 (7			
Modera		14/159 (8.8)	12/186 (6.5)		5/164 (3			
Severe		5/159 (3.1)	14/186 (7.5)	0.005	3/164 (1			0.868
Insomnia								
None		76/159 (47.8)	99/186 (53.2)		117/164 (71.3)	106/159 (66.7)	118/184 (64.1)	
Mild	10/170 (5.9)	26/159 (16.3)	32/186 (17.2)		21/164 (12.8)	17/159 (10.7)	29/184 (15.8)	
Moderate	7/170 (4.1)	32/				8/159 (17.6)	23/184 (12.5)	
Severe	13/170 (7.6)	25/				8/159 (5.0)	14/184 (7.6)	0.509
Anxiety								
None	149/170 (87.6)	95/				2/159 (70.5)	136/184 (73.9)	
Mild	10/170 (5.9)	31/				5/159 (15.7)	18/184 (9.8)	
Moderate	6/170 (3.5)	23/				1/159 (6.9)	21/184 (11.4)	
Severe	5/170 (2.9)	10/				1/159 (6.9)	9/184 (4.9)	0.288
Convulsions								
None	169/170 (99.4)	158/				9/159 (100)	184/184 (100)	
Mild	1/170 (0.6)	1/				0/0 (0)	0/0 (0)	
Moderate	0/0 (0)					0/0 (0)	0/0 (0)	
Severe	0/0 (0)					0/0 (0)	0/0 (0)	NA

HADS, Hospital Anxiety and Depression Scale; IQR, interquartile range; SIF, intervention group with follow-up visits; SIW, intervention group with written instructions.
a. Standard alcohol units per week among drinkers.

Síntomas de abstinencia más frecuentes:
Insomnio
Ansiedad
Irritabilidad
A los 12 meses no diferencias entre grupos

Inicio Antidepresivos:
SIF: 21%
SIW: 12,4%
Control: 13,6%

Cambio Diazepam:
SIF: 22%
SIW: 13%
Control: 7%

Duración intervención:
Visita intervención: 20 min
Visitas seguimiento: 12 min
Media visitas:
SIF: 4,6
SIW: 1,2
Control: 0,7

Conclusiones

- ✓ Ambas intervenciones son **tres veces más eficaces** que la consulta habitual.
- ✓ La intervención con visitas de seguimiento incrementa la complejidad de la intervención sin aumentar su eficacia.
- ✓ **Ambas intervenciones son seguras**, no aumentan el nivel de ansiedad ni los sintomas depresivos, la insatisfacción con el sueño y la cantidad de alcohol consumido.
- ✓ Los sintomas de abstinencia son mayormente leves o moderados y disminuyen a lo largo del tiempo.

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Comparative efficacy of two interventions to discontinue long-term benzodiazepine use: cluster randomised controlled trial in primary care

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Background
Benzodiazepines are extensively used in primary care, but their long-term use is associated with adverse health outcomes and dependence.

Aims
To analyse the efficacy of two structured interventions in primary care to enable patients to discontinue long-term benzodiazepine use.

Method
A multicentre three-arm cluster randomised controlled trial was conducted, with randomisation at general practitioner level (trial registration ISRCTN13024375). A total of 532 patients taking benzodiazepines for at least 6 months participated. After all patients were included, general practitioners were randomly allocated (1:1:1) to usual care, a structured intervention with follow-up visits (SIF) or a structured intervention with written instructions (SIW). The primary end-point was the last month self-declared benzodiazepine discontinuation confirmed by prescription claims at 12 months.

Results
At 12 months, 76 of 168 (45%) patients in the SIW group and 86 of 191 (45%) in the SIF group had discontinued benzodiazepine use compared with 26 of 173 (15%) in the control group. After adjusting by cluster, the relative risks for benzodiazepine discontinuation were 3.01 (95% CI 2.03–4.46, $P<0.0001$) in the SIW and 3.00 (95% CI 2.04–4.40, $P<0.0001$) in the SIF group. The most frequently reported withdrawal symptoms were insomnia, anxiety and irritability.

Conclusions
Both interventions led to significant reductions in long-term benzodiazepine use in patients without severe comorbidity. A structured intervention with a written individualised stepped-dose reduction is less time-consuming and as effective in primary care as a more complex intervention involving follow-up visits.

Declaration of interest
None.

Seguimiento proyecto

- Evaluación a largo plazo: Seguimiento a los 36 meses de la intervención
- Evaluación económica de la intervención mediante un análisis de coste-eficacia.
- Influencia de las características individuales del profesional en el éxito de la intervención (Empatía y Personalidad)

Antonio

- Vuelve a la consulta a las pocas semanas para hablar del tema.
- Estrategia:
- Información sobre dependencia y síntomas de abstinencia.
- Desmontar mitos
- Pauta reducción individualizada lenta.

Muchas Gracias!

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DOI 10.1007/s00228-004-0810-8

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

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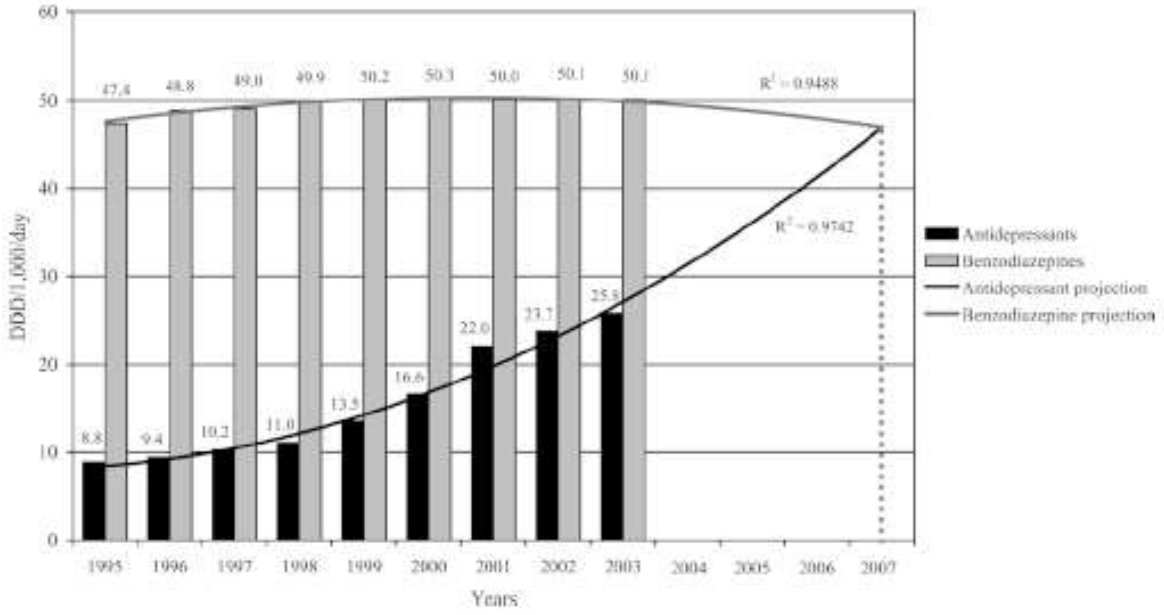
Letizia Corbari · Deborah Levi · Mersia Mirandola
Adriano Sorio · Corrado Barbui

Are we going to increase the use of antidepressants up to that of benzodiazepines?

Received: 29 April 2004 / Accepted: 3 July 2004 / Published online: 23 September 2004

Abstract *Objective*: The present study compared recent ther and, if the situation of the Italian market remains stable in the next few years, in 2007 the total sales of *Conclusions*: In Italy, the consumption of benzodiaze- is not affected by the increased prescribing of serotonin-reuptake inhibitors and newer essants.

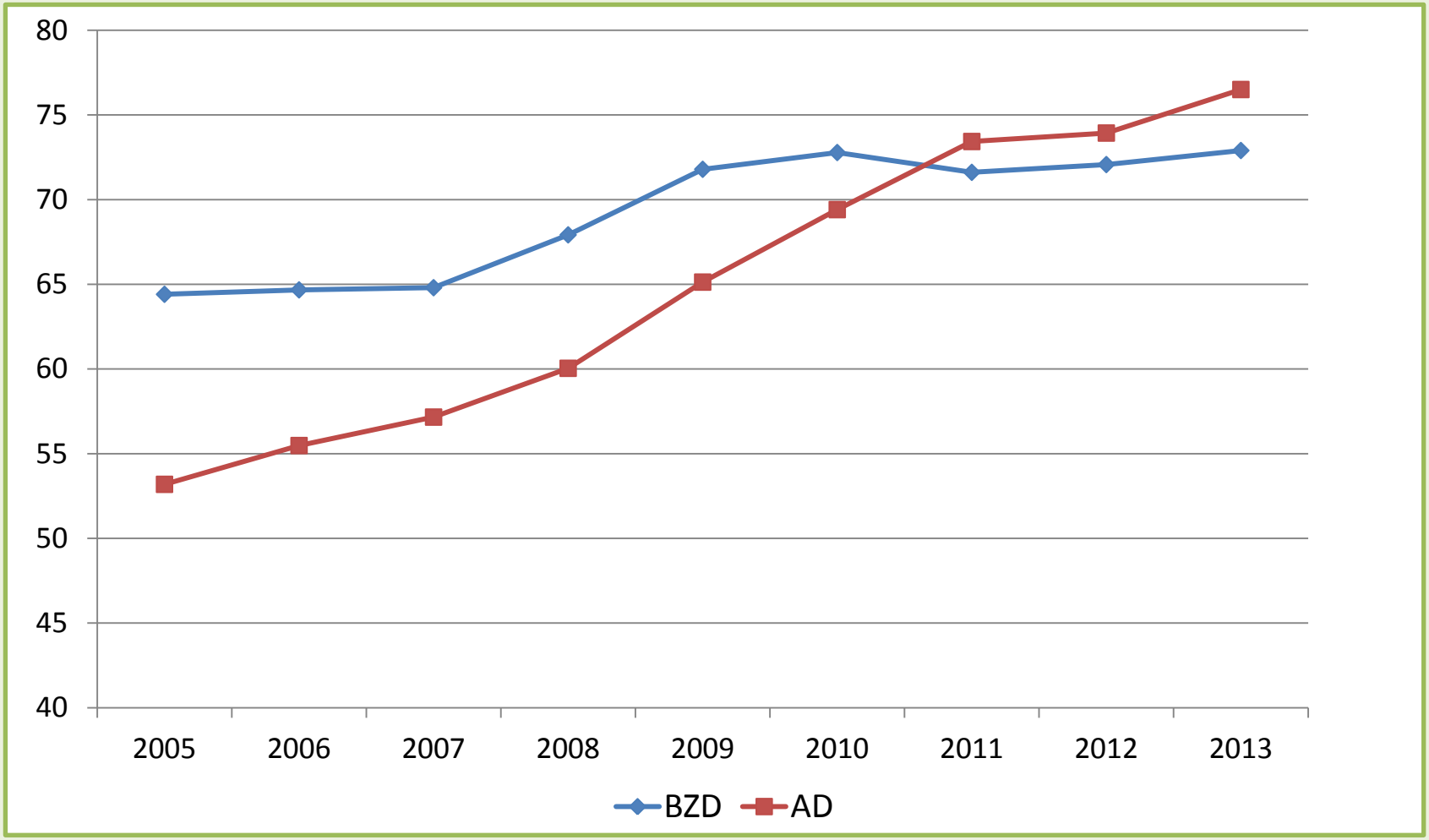
Fig. 1 Trends in antidepressant and benzodiazepine consumption in Italy from 1995 to 2003 and sale projections up to 2007



tion

h many adverse effects have been documented, g the risk of a discontinuation syndrome, for years, benzodiazepines have been widely d to tackle anxiety, insomnia and mild depres- s. In the early 1990s, however, the introduction ive serotonin-reuptake inhibitors has been seen cial breakthrough, since these agents were sug- ot only in the treatment of major depression, but the treatment of other psychiatric conditions, g obsessive-compulsive disorder, panic disorder, ed anxiety disorder, eating disorders, somato- sorder, premenstrual syndrome, subthreshold n and other mild depressive states that were ly treated with benzodiazepines [1–7]. It was , therefore, that the increasing use of antide-

Evolución del consumo de benzodiacepinas y antidepresivos en Baleares 2005-2012 (DHD)



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Trends in prescriptions and costs of drugs for mental disorders in England, 1998–2010

Stephen Ilyas and Joanna Moncrieff

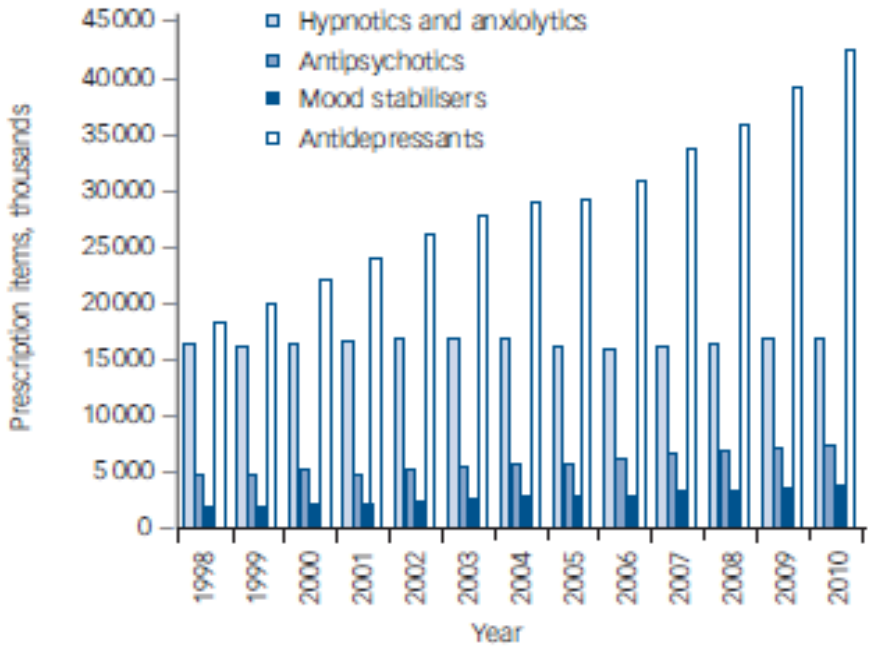

Fig. 1 Trends in prescriptions of major classes of psychiatric drugs 1998–2010.

anxiolytics and hypnotics (which did not change). Antidepressant prescriptions increased by 10% (95% CI 9.0–11) per year on average, and antipsychotics by 5.1% (95% CI 4.3–5.9). Antipsychotics overtook antidepressants as the most costly class of psychiatric medication, with costs rising 22% (95% CI 17–27) per year.

Conclusions

Rising prescriptions may be partly explained by longer-term treatment and increasing population. Nevertheless, it appears that psychiatric drugs make an increasing contribution to total prescription drug costs, with antipsychotics becoming the most costly. Low-dose prescribing of some antipsychotics is consistent with other evidence that their use may not be restricted to those with severe mental illness.

Declaration of interest

J.M. is co-chairperson of the Critical Psychiatry Network.

compare trends in different classes of medication to establish whether there has been an overall increase in the use of medications for psychiatric disorders. We also examine the costs of different classes of drugs, and analyse the contribution of individual drugs within the major classes of psychiatric medication.