

# Efficacy of Brief Interventions for Hazardous Drinkers in Primary Care: Systematic Review and Meta-Analyses

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**Background:** Because recent research in primary care has challenged the findings of previous reviews on the efficacy of brief interventions (BIs) on hazardous drinkers, we conducted a systematic review and meta-analysis to update the evidence of BIs as applied in the primary care setting.

**Methods:** We obtained source material by searching electronic databases and reference lists and hand-searching journals. We selected randomized trials providing frequency data that allowed assessment of the efficacy of BIs on an intention-to-treat basis. Results were summarized by the odds ratio (OR) of response. When appropriate, risk difference (RD) and its inverse (number needed to treat [NNT] to achieve a positive result) were also computed. Fixed and/or random effect models were fitted according to heterogeneity estimates.

**Results:** Thirteen studies provided data for a dose-effect analysis, 12 for comparison of BIs with reference categories. No clear evidence of a dose-effect relationship was found. BIs outperformed minimal interventions and usual care (random effects model OR = 1.55, 95% confidence interval [CI] = 1.27–1.90; RD = 0.11, 95% CI = 0.06–0.16; NNT = 10, 95% CI = 7–17). Similar results were obtained when two influential studies were removed (fixed effect model OR = 1.57, 95% CI = 1.32–1.87; RD = 0.11, 95% CI = 0.07–0.15; NNT = 9, 95% CI = 7–15). The heterogeneity between individual estimates was accounted for by the type of hazardous drinkers (heavy versus moderate) and by the characteristics of the included individuals (treatment seekers versus nontreatment seekers). The funnel plot did not show evidence of publication bias.

**Conclusion:** Our results, although indicating smaller effect sizes than previous meta-analyses, do support the moderate efficacy of BIs. Further research is outlined.

**Key Words:** Brief Interventions, Hazardous Drinkers, Primary Care, Systematic Review, Meta-Analysis.

PREVIOUS META-ANALYSES HAVE produced positive findings on the efficacy of brief interventions (BIs) on hazardous drinkers in several health care settings (Bien et al., 1993; Moyer et al., 2002; Poikolainen, 1999; Wilk et al., 1997), but more recent studies conducted in primary care have challenged their results mainly on the basis of issues related to long-term efficacy and program implementation (Aalto et al., 2000, 2001; Beich et al., 2002). It was therefore considered appropriate to attempt to update the evidence regarding the efficacy of BIs in the primary care

setting and to overcome certain limitations that were present in previous analyses. For example, the issue of a dose-effect trend by intensity of BIs previously has been suggested (Poikolainen, 1999; Wilk et al., 1997) but not formally tested. Previous effect size estimates also could be flawed because of the use of inappropriate weights when pooling individual estimates (Bien et al., 1993) or because the outcomes were disparate quantities combined to give a unique mean effect for each study (Bien et al., 1993; Moyer et al., 2002). Moreover, earlier meta-analyses have pooled endpoint estimates as reported in the original studies without provision for the types of analyses described: either by endpoint protocol completers or by intention-to-treat analyses (ITT). Because the problem of subjects lost to follow-up is not negligible in these studies (Edwards and Rollnick, 1997), the use of results based on protocol completers could overestimate the efficacy of BIs as recently reported in a Spanish study (Ballesteros et al., 2003). Also little is known on the differential effect of BIs on different types of hazardous drinkers. This is an important issue because there seems to be a trend in the type of drinkers recruited to BI studies since the late 1980s (mainly heavy drinkers) up to the present, with the criterion for alcohol consumption cutoff levels decreasing through the period so that initially moderate hazardous drinkers are also in-

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cluded. Finally, some previous meta-analyses included studies not conducted specifically in primary care but in diverse health settings (Bien et al., 1993; Moyer et al., 2002; Wilk et al., 1997) limiting their application to BIs conducted in primary care practices by primary care providers.

To overcome these limitations and update the evidence, we performed a systematic review and further meta-analyses. Our objective was to assess the efficacy of BIs as applied in primary care settings by using estimates for the decrease in the proportion of hazardous drinkers, which could be calculated by an ITT approach even if ITT analyses were not reported in the primary studies. We also took into account the intensity of interventions and the type of drinkers to whom the interventions were applied.

## METHODS

### *Eligibility and Coding Criteria*

Studies were included if (a) they reported a parallel trial with two or more intervention arms and randomized subjects to interventions, (b) hazardous drinkers not satisfying criteria for alcohol dependence were included, (c) the BIs were applied in primary care settings, (d) outcome assessment was available at follow-up of 6 to 12 months, and (e) enough information was given in text or tables to extract data to carry out an ITT analyses. Studies were excluded if conducted in other health settings than primary care or, if conducted in primary care, the BIs were applied within other health programs (i.e., hypertension control, pregnancy). Also excluded were those studies that used cognitive interventions on the grounds that this approach is not part of the primary care providers' usual work.

Because there is a range of types of BIs (Heather, 1995; Poikolainen, 1999) and our first objective was to analyze the feasibility of a dose-effect trend, we coded the interventions as follows: control (CTRL, no specific advice on alcohol consumption to participants from their primary care providers except if required by the health problem reported or if requested by the patient); minimal intervention (MI, a unique session of general advice on alcohol consumption lasting ~3–5 min but without stressing strategies to decrease consumption); brief intervention (BI, a specific intervention lasting ~10–15 min in one session concerning alcohol consumption, health risks, and strategies to decrease alcohol intake, with possible simple reinforcing visits through follow-up of ~3–5 min each); and extended brief interventions (EBI, which had the characteristics of a BI but also included several specific reinforcement sessions through follow-up, ~10–15 min each).

A coding scheme was developed to categorize the main characteristics of the studies or participants we thought might be related with heterogeneous results: length of follow-up (6 months = 0, 12 months = 1), type of hazardous drinkers recruited (moderate drinkers = 0, heavy drinkers = 1), type of patients included (nontreatment seekers = 0, treatment seekers = 1), and quality score (low quality = 0, high quality = 1). We defined a study as including moderate drinkers if its inclusion criteria for ethanol consumption were >132 to 168 g/week in men and >96 to 132 g/week in women, whereas for the definition of heavy drinkers the inclusion criteria were >280 g/week in men and >160 g/week in women. The studies were categorized as including nontreatment seekers if all the population registered within the practices was targeted for screening for hazardous drinking and as including treatment seekers if screening was restricted to patients attending medical consultation. The quality score was based on a four-item scale with a total score ranging from 0 to 8, which was dichotomized as representing low- (score ≤4) and high-quality studies (score ≥5). Three items were borrowed with some minor modifications from an internal validity scale previously reported (Kahan et al., 1995): potential adequacy of sample size attained by the studies by rating 0 if previous power analysis was not included in the methods section of the selected

studies, and 2 if it was included; blinding of assessor to treatment allocation of subjects (0 = no, 2 = yes); and percentage of subjects lost to follow-up (0 = >20%, 1 = 10–20%, 2 = <10%). The fourth item was related with the type of randomization (0 = pseudorandomization, 1 = blocked, 2 = individual).

### *Outcome Selected*

We were aware from the beginning that many studies reporting quantitative outcomes (e.g., alcohol consumption, biochemical markers) were not primarily analyzed—and reported—by an ITT approach but according to endpoint protocol completers. This rendered their information inadequate for our aim of analyzing ITT data. We selected the decrease in the frequency of hazardous drinkers as it was reported in the original articles—or inferred from them—as the outcome to extract because it would permit us to compute the necessary data to obtain an ITT estimate from the number of individuals randomized at baseline to treatment arms conservatively assuming that subjects lost to follow-up did not change their baseline consumption levels. For each independent study, data were extracted to conform to a two-by-two table or a two-by-k table.

### *Searching Strategy*

Electronic searching was performed by using a combination of the following keywords—either as free text or mapping them to appropriate thesaurus terms: (drink\* or heavy drink\* or harmful drink\* or excessive drink\* or excessive alcohol) and (treatment or prevention or counsel\* or brief intervention\* or minimal intervention\* or early intervention\*) and (randomized controlled trial or clinical trial or controlled clinical trial) and (primary care). Because we were aware of several studies published in other languages than English (Ballesteros et al., 2003), no language restriction was imposed. The searched databases and final searching date were Medline-Pubmed (up to March 2003), PsycINFO (up to February 2003), CINAHL (up to March 2003), EMBASE (up to March 2003), and the Cochrane Library (2003, issue 1). Throughout the study, secondary searching was done by hand-searching the reference lists from initially selected studies and previous meta-analyses and reviews and also main journals in the field of alcohol-related problems. All retrieved references were managed with the Reference Manager program (ISI ResearchSoft, Berkeley, CA).

### *Statistical Analyses*

The results are primarily expressed as odds ratios (OR) to assess the strength of the effect, but to indicate their clinical significance we also report, for some selected results, the risk difference (RD) and its inverse, the number of patients needed to treat to obtain a success (NNT). Our first analysis tried to assess the efficacy of BIs in a multitreatment frame (Hasselblad, 1998) (CTRL as reference – MI – BI – EBI), to investigate whether there was a dose-effect relationship or if interventions of different intensity could be grouped to simplify further analyses. This analysis was performed by first fitting a fixed effects logistic regression model. If there was evidence of heterogeneity, a random effects logistic regression was then fitted (Hasselblad, 1998). We sought a parsimonious model compatible with the reference model that included as factors the four intervention levels and the selected studies. Comparisons with reduced nested models (intervention as a variate instead of a four-level factor and intervention as a two-level factor by grouping interventions) were performed by the likelihood ratio test (LRT). Because the results showed the feasibility of grouping CTRL+MI and BI+EBI, these groups were further analyzed by usual procedures (Normand, 1999). We combined the individual ORs by using either a fixed or a random effects model with inverse variance weights and considered the relationship with between-studies heterogeneity of a selected set of variables (length of follow-up, type of hazardous drinkers, and patients included in the studies, and quality score) using a procedure similar to the analyses of variance method (Hedges, 1994) and by checking the LRT obtained when comparing nested logistic regression models: a model with the corresponding variable included as a factor and

another with a term for its interaction with the treatment. The between-studies heterogeneity was assessed by the usual Cochran's test and the recently reported  $I^2$  statistic, which is interpreted as the percentage of variation in the effect size estimate attributable to heterogeneity (Higgins and Thompson, 2002). As a tentative rule,  $I^2$  values of 25%, 50%, and 75% have been respectively ascribed to low, moderate, and high heterogeneity (Higgins et al., 2003). Post hoc influence or sensitivity analysis was done by leaving out from the meta-analysis one study at the time and checking the consistency of the combined effect estimate. The influence of publication bias was assessed by Egger's method, which is based on the asymmetry of the funnel plot (Egger et al., 1997). Finally, a cumulative meta-analysis was also done to present the history of the available evidence of BI efficacy on hazardous drinkers since the late 1980s. All statistical analyses were performed either with EGRET (CYTEL Software Corporation, Cambridge, MA) or with available macros written for Stata (Stata Corporation, College Station, TX).

## RESULTS

### *Study Inclusion and Characteristics*

The electronic and manual searches yielded a preliminary set of 739 studies, of which 67 were judged suitable for inclusion. Eighteen of these studies did not fit the criteria for a randomized trial (reviews and former meta-analyses), included cognitive interventions, or recruited subjects with a diagnosis of alcoholism (see flowchart in Fig. 1). Another 36 studies were excluded because they duplicated results reported elsewhere, did not provide information to perform an ITT analyses, or were conducted in other health care settings or in primary care within another intervention program. This left 13 studies (4353 participants), with 1788 subjects randomized to CTRL group, 580 to MI group, 1410 to BI group, and 575 to EBI group (Altisent et al., 1997; Anderson and Scott, 1992; Curry et al., 2003; Díez et

al., 2002; Fernández et al., 1997; Fleming et al., 1997, 1999; Heather et al., 1987; Ockene et al., 1999; Richmond et al., 1995; Scott and Anderson, 1990; Senft et al., 1997; Wallace et al., 1988). We included the 12-month data from the study of Richmond et al. (1995) and coded the intervention reported by Curry et al. (2003) as MI instead of EBI, because although the reported intervention seemed similar to our definition of EBI, the direct physician-patient contact was only 5 min and related to simple advice. In four studies that did not report frequencies for the outcome of interest, frequency was calculated by percentages reported in the article and rounded to the nearest unit (Altisent et al., 1997; Curry et al., 2003; Richmond et al., 1995; Senft et al., 1997). Table 1 shows the main characteristics of included studies, whereas the Appendix lists those excluded and the reasons for their exclusion.

The set of 13 studies covered more than a decade of research, from the late 1980s to early 2000s. Four studies were from the United Kingdom, five from the United States, one from Australia, and three from Spain. Most studies recruited patients in the age range 18 to 70 years except one that was conducted in older patients ( $\geq 65$  years). Four studies included only men and one study included only women. Six studies included heavy drinkers and seven used a criterion of moderate consumption for inclusion. Only three studies were conducted on nontreatment seekers. Eleven of the 13 studies presented comparisons between two arms (six BI versus CTRL, one MI versus CTRL, two BI versus MI, two EBI versus CTRL), whereas two reported a three-arm comparison (one BI versus MI versus CTRL, one EBI versus MI versus CTRL). Ten

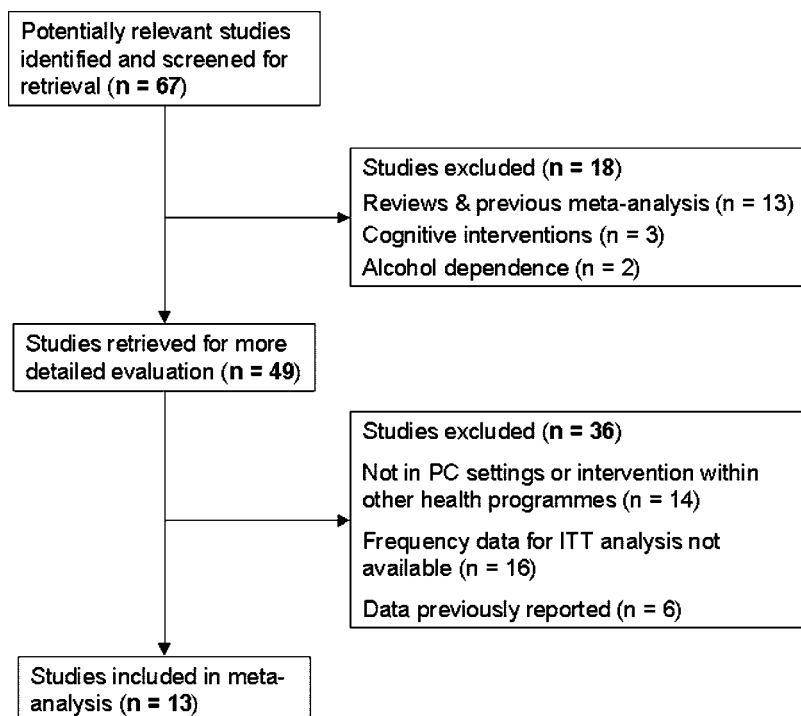


Fig. 1. Meta-analysis flowchart for selected studies.

Table 1. Main Characteristics of Included Studies on the Efficacy of BIs in Primary Care

Authors	Setting/subjects	Eligibility criteria	Treatment arms	LFU (months)	Lost subjects (%)	Outcomes selected ( <i>n/n</i> )	Comments/QS
United Kingdom Heather et al. (1987)	8 PCP 78 M/26 W Age: 18–65 years TS HHD	WAC > 35 units in M (280 g ethanol) or >20 units in W (160 g ethanol); questionnaire score $\geq 1$ or doctor's clinical suspicion of heavy drinking. Exclusion criteria: Diagnosis of AD, LD, dependence on opiate drugs, severe mental illness, on antidepressant medication, subnormal intelligence, pregnancy. WAC >35 units in M (280–350 g ethanol) or >21 units in W (168–210 g ethanol) or CAGE score $\geq 2$ .	BI ( <i>n</i> = 34) MI ( <i>n</i> = 32) CTRL ( <i>n</i> = 38)	6	Total: 12.5 BI: 14.7 MI: 6.2 CTRL: 15.8	WAC <35 units in M (280 g ethanol) or <20 units in W (160 g ethanol). BI: 14/34 MI: 14/32 CTRL: 13/38	QS: 5
	47 PCP 641 M/268 W Age: 17–69 years NTS HHD		BI ( <i>n</i> = 450) CTRL ( <i>n</i> = 459)	12	Total: 17.7	WAC <35 units in M (280–350 g ethanol) or <21 units in W (168–210 g ethanol). BI: 201/450 CTRL: 122/459 WAC <14 units (140 g ethanol). BI: 9/33 CTRL: 10/39	QS: 7
Scott and Anderson (1990)	8 PCP 72 W Age: 17–69 years NTS HHD	WAC >21 units (210 g ethanol). Exclusion criteria: Previous advice to cut down consumption or drinking >70 units/week (700 g ethanol).	BI ( <i>n</i> = 33) CTRL ( <i>n</i> = 39)	12	Total: 30.6 BI: 24.2 CTRL: 35.9		QS: 6
	8 PCP 154 M Age: 17–69 years NTS HHD	WAC >35 units (350 g ethanol). Exclusion criteria: Previous advice to cut down consumption or drinking >105 units/week (1050 g ethanol).	BI ( <i>n</i> = 80) CTRL ( <i>n</i> = 74)	12	Total: 35.1 BI: 31.2 CTRL: 39.2	WAC <22 units (220 g ethanol). BI: 14/80 CTRL: 4/74	QS: 6
Spain Altisent et al. (1997)	10 PCP 99 M Age: 15–70 years TS HHD	WAC >35 units (280 g ethanol). Exclusion criteria: On treatment for ARP, LD.	BI ( <i>n</i> = 54) MI ( <i>n</i> = 45)	12	Total: 35.4 BI: 37.0 MI: 33.3	WAC <35 units (280 g ethanol). BI: 28/54 MI: 14/45	Outcomes calculated from percentages reported in the article. QS: 4
	4 PCP 152 M Age: 18–64 years TS MHD	WAC >21 units (168 g ethanol). Exclusion criteria: AD diagnosis, on psychiatric treatment or on illegal drug consumption.	BI ( <i>n</i> = 67) CTRL ( <i>n</i> = 85)	6–18	Total: 42.1 BI: 43.3 CTRL: 41.2	WAC <35 units (280 g ethanol). BI: 23/67 CTRL: 24/85	Blocked randomization design. QS: 5
Díez et al. (2002)	1 PCP 293 M Age: 18–65 years TS MHD	WAC >21 units (168 g ethanol) and <95 units (760 g ethanol).	BI ( <i>n</i> = 158) CTRL ( <i>n</i> = 135)	6	Total: 28.3 BI: 27.8 CTRL: 28.9	WAC <35 units (280 g ethanol). BI: 65/158 CTRL: 41/135	Pseudo-randomization design. QS: 2
Australia Richmond et al. (1995)	40 PCP 159 M/126 W Age: 18–70 years TS HHD	WAC >35 drinks in M (350 g ethanol) or >21 drinks in W (210 g ethanol). Exclusion criteria: AD or treatment for ARP; abstinence indicated because illness; psychiatric disturbance or pregnancy.	EBI ( <i>n</i> = 96) MI ( <i>n</i> = 96) CTRL ( <i>n</i> = 93)	12	Total: 30.9 EBI: 31.3 MI: 27.1 CTRL: 34.4	WAC <28 drinks in M (280 g ethanol) or <14 drinks in W (140 g ethanol). EBI: 16/96 MI: 16/96 CTRL: 13/93	Blocked randomization design. Outcomes calculated from percentages reported in the article. QS: 5
	17 PCP 482 M/292 W Age: 18–65 years TS MHD	WAC >14 drinks in M (168 g ethanol) or >11 drinks in W (132 g ethanol). Exclusion criteria: On treatment for ARP in previous year; previous advice to cut down consumption; consumption >50 drinks/week (600 g ethanol); symptoms of alcohol withdrawal or suicide; pregnancy.	EBI ( <i>n</i> = 392) CTRL ( <i>n</i> = 382)	12	Total: 6.6 EBI: 9.9 CTRL: 3.1	WAC <20 drinks in M (240 g ethanol) or <13 drinks in W (156 g ethanol). EBI: 293/392 CTRL: 251/382	Subjects and physicians included in the study were paid for their participation. QS: 6



Table 1. Continued

Authors	Setting/subjects	Eligibility criteria	Treatment arms	LFU (months)	Lost subjects (%)	Outcomes selected (r/n)	Comments/QS
Senft et al. (1997)	3 PCP 364 M/152 W Mean age: 42 years TS	AUDIT score $\geq 8$ and $< 22$ .	BI (n = 260) CTRL (n = 256)	12	Total: 19.8	WAC $< 21$ drinks in M (250 g ethanol) or $< 14$ drinks in W (168 g ethanol). BI: 158/260 CTRL: 158/256	Outcomes calculated from percentages reported in the article. QS: 5
Fleming et al. (1999)	24 PCP 105 M/53 W Age: $\geq 65$ years TS MHD	WAC $> 11$ drinks in M (132 g ethanol) or $> 8$ drinks in W (96 g ethanol) or CAGE score $\geq 2$ or binge drinking. Exclusion criteria: On treatment for ARP in the previous year; advice to cut down drinking; consumption $> 50$ drinks/week (600 g ethanol); symptoms of alcohol withdrawal or suicide.	EBI (n = 87) CTRL (n = 71)	12	Total: 9.5 EBI: 12.6 CTRL: 5.6	WAC $< 20$ drinks in M (240 g ethanol) or $< 13$ drinks in W (156 g ethanol). EBI: 64/87 CTRL: 44/71	Subjects and physicians included in the study were paid for their participation. QS: 6
Ockene et al. (1999)	4 PCP 343 M/187 F Age: 21–70 years TS MHD	WAC $> 12$ drinks in M (160 g ethanol) or WAC $> 9$ drinks in W (120 g ethanol) or binge drinking. Exclusion criteria: Subjects enrolled in a alcohol program or with any psychiatric disorder other than substance abuse; pregnancy.	BI (n = 274) MI (n = 256)	6	Total: 9.0 BI: 9.0 MI: 9.0	WAC $< 12$ drinks in M (160 g ethanol) or $< 9$ drinks in W (120 g ethanol). BI: 102/274 MI: 66/256	Blocked randomization design. QS: 7
Curry et al. (2003)	1 PCP 198 M/109 W Mean age: 47 years TS MHD	WAC $\geq 14$ drinks (168 g ethanol) or binge drinking or drinking and driving and AUDIT score $\geq 15$ . Exclusion criteria: AD; pregnancy; terminally ill or cognitively impaired.	MI (n = 151) CTRL (n = 156)	12	Total: 28.0 MI: 33.8 CTRL: 22.4	WAC $< 14$ drinks (168 g ethanol). MI: 75/151 CTRL: 87/156	Outcomes calculated from percentages in the article. QS: 2

LFU, length of follow-up; r, no. of positive outcomes; n, no. of subjects initially randomized to treatment conditions; QS, quality score; PCP, primary care practices; M, men; W, women; NTS, nontreatment-seekers; TS, treatment-seekers; HHD, heavy hazardous drinkers; MHD, moderate hazardous drinkers; WAC, weekly alcohol consumption; AD, alcohol dependence; ARP, alcohol-related problems; LD, liver disease; EBI, extended brief intervention; BI, brief intervention; MI, minimal intervention; CTRL, control.

studies presented data at 12 months follow-up, and only three were rated as low quality. Most studies used an individual randomization design, but three used blocked randomization either by weeks or centers and one used a pseudorandomization design in which only the first patient each day was randomized to the interventions reported (CTRL or BI) and the next patients were systematically assigned to interventions by a consecutive A–B sequence. Two studies reported that subjects and physicians were paid for their participation.

#### Efficacy of BIs by Intensity (Four Levels of Intervention)

Table 2 presents a summary of results obtained by fitting logistic regression models including the four intervention categories. A logistic random effects model seemed appropriate due to the heterogeneity in the fixed effects model ( $\chi^2 = 21.16$  on 12 *df*,  $p = 0.048$ ). The random effects model estimates favored BI (OR = 1.6, 95% CI = 1.33–1.93) and EBI (OR = 1.5, 95% CI = 1.12–1.95) compared with CTRL. However, MI was not significantly different from control (OR = 0.95, 95% CI = 0.72–1.25). A test for linear trend did not show an adequate fit when compared with the four-level treatment random model (LRT  $\chi^2 = 6.24$  on 2 *df*,  $p = 0.044$ ), whereas the two-level treatment model fit (obtained by joining adjacent treatment groups, CTRL+MI and BI+EBI) was adequate (LRT  $\chi^2 = 0.42$  on 2 *df*,  $p = 0.81$ ). As a consequence we selected this grouping for further analyses.

#### Efficacy of BIs (Two-Level Intervention)

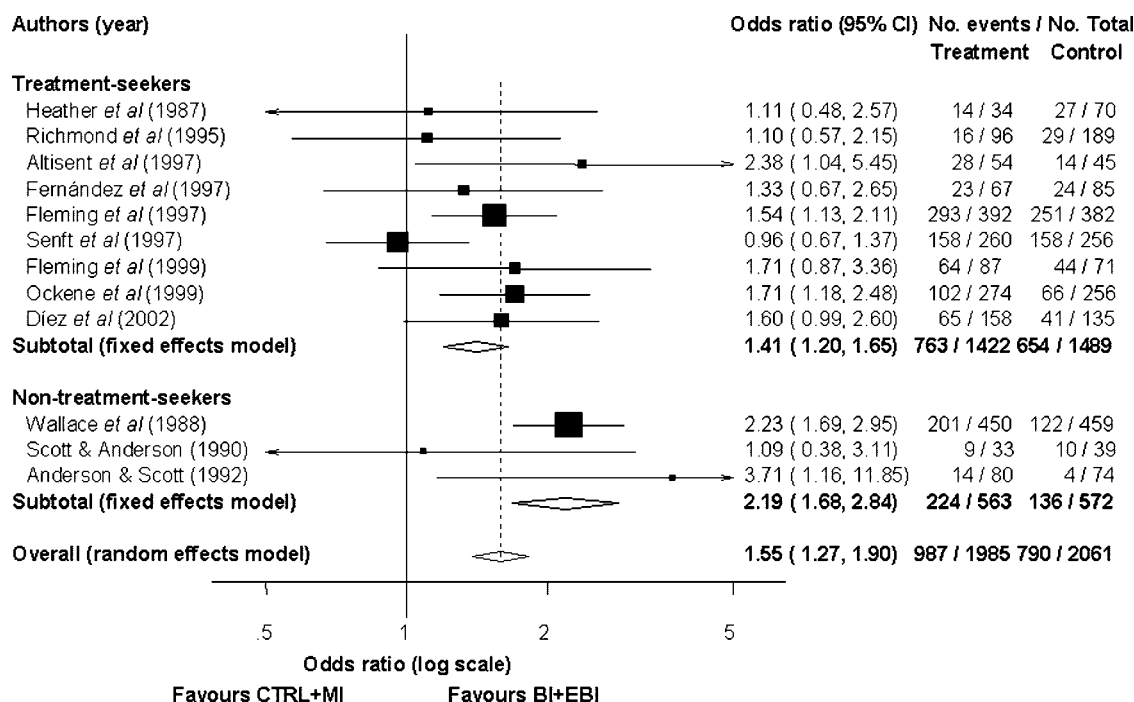
Figure 2 displays a summary of the main results for the 12 studies included. The study by Curry et al. (2003) was excluded because it presented only an MI/CTRL comparison. The comparison of BIs (defined as BI and/or EBI) with the control category (defined as CTRL and/or MI) by a fixed effects model showed sufficient heterogeneity ( $\chi^2 = 19.24$  on 11 *df*,  $p = 0.06$ ,  $I^2 = 42.8\%$ ) to warrant a random effects approach, which indicates the efficacy of BIs (OR = 1.55, 95% CI = 1.27–1.90) with an improvement of 11% in the success rate (RD = 0.11, 95% CI = 0.06–0.16; NNT = 10, 95% CI = 7–17). Of the four factors selected as likely to be related to heterogeneity, two were able to account for a significant part of the variability between groups, the type of hazardous drinkers (LRT for its interaction with the treatment,  $\chi^2 = 7.38$  on 1 *df*,  $p = 0.007$ ; between-groups  $\chi^2 = 4.92$  on 1 *df*,  $p = 0.03$ ; within-groups  $\chi^2 = 13.98$  on 10 *df*,  $p = 0.17$ ), and the type of patients included in the studies (LRT  $\chi^2 = 5.77$  on 1 *df*,  $p = 0.02$ ; between-groups  $\chi^2 = 7.91$  on 1 *df*,  $p = 0.005$ ; within-groups  $\chi^2 = 10.99$  on 10 *df*,  $p = 0.36$ ). Both factors reduced the overall moderate heterogeneity (42.8%) to low heterogeneity regarding either the type of included patients ( $I^2$  for nontreatment seekers = 20.5% and 9.4% for treatment seekers) or type of hazardous drinkers (37.6% for heavy and 22.5% for moderate drinkers). BIs seem to have greater efficacy when applied in

**Table 2.** Summary of Multitreatment Analyses by Logistic Regression Models ( $n = 13$ )<sup>†</sup>

Treatment	Fixed effects OR (95% CI)	Random effects OR (95% CI)	Random effects OR (95% CI)
CTRL (reference)	—	—	CTRL+MI (reference)
MI	0.95 (0.73–1.24)	0.95 (0.72–1.25)	—
BI	1.62 (1.36–1.92)	1.60 (1.33–1.93)	BI+EBI
EBI	1.48 (1.14–1.92)	1.48 (1.12–1.95)	1.58 (1.36–1.83)
Deviance ( <i>df</i> )	21.16 (12) <sup>‡</sup>	20.93 (11)	21.35 (13)
Between-studies variance	—	0.005	0.006

OR, odds ratio; CI, confidence interval; CTRL, control; MI, minimal intervention; BI, brief intervention; EBI, extended brief intervention. Results from the random effect model with treatment fitted as a variate: OR = 1.20, 95% CI = 1.12–1.30, deviance = 27.17 on 13 *df*, between-studies variance = 0.018.

<sup>†</sup> Fitted models included treatment and study and a random effects term when appropriate; <sup>‡</sup> interpreted as a test of heterogeneity,  $p = 0.048$ .

**Fig. 2.** Meta-analysis. Individual and combined estimates.

general screening programs (nontreatment seekers, fixed effect model OR = 2.19, 95% CI = 1.68–2.84) than at consultation (treatment seekers, fixed effect model OR = 1.41, 95% CI = 1.20–1.65). Also, BIs seem to work better when applied to heavy drinkers (fixed effect model OR = 1.94, 95% CI = 1.55–2.43) than when applied to moderate drinkers (fixed effect model OR = 1.42, 95% CI = 1.19–1.68). The corresponding RD and NNT estimates for nontreatment seekers were RD = 0.20 (95% CI = 0.13–0.26), NNT = 6 (95% CI = 4–8); for treatment seekers RD = 0.09 (95% CI = 0.05–0.12), NNT = 12 (95% CI = 9–22); for heavy drinkers RD = 0.16 (95% CI = 0.11–0.22), NNT = 7 (95% CI = 5–10); and for moderate drinkers RD = 0.09 (95% CI = 0.05–0.13), NNT = 12 (95% CI = 8–23).

### Sensitivity Analyses

The studies with most influence on the overall estimate were those of Wallace *et al.* (1988), which included heavy drinkers and nontreatment seekers, and Senft *et al.* (1997), which included moderate drinkers but also treatment seekers. Excluding Wallace *et al.*, homogeneity was achieved ( $\chi^2$

= 11.71 on 10 *df*,  $p = 0.31$ ,  $I^2 = 14.6\%$ ) and we obtained the most conservative estimate of BIs efficacy (fixed effect model OR = 1.43, 95% CI = 1.22–1.67; RD = 0.09, 95% CI = 0.05–0.13; NNT = 12, 95% CI = 8–19). By deleting the results of Senft *et al.*, the combined estimate increased somewhat (fixed effect model OR = 1.73; 95% CI = 1.50–2.01; RD = 0.14, 95% CI = 0.10–0.17; NNT = 8, 95% CI = 6–10) and homogeneity was also achieved ( $\chi^2$  = 10.17 on 10 *df*,  $p = 0.43$ ,  $I^2 = 1.7\%$ ). On deleting both studies, the pooled estimate was homogeneous ( $\chi^2$  = 5.78 on 9 *df*,  $p = 0.76$ ,  $I^2 = 0.0\%$ ) with an OR = 1.57 (95% CI = 1.32–1.87), RD = 0.11 (95% CI = 0.07–0.15), and NNT = 9 (95% CI = 7–15).

### Publication Bias

The set of studies analyzed here did not showed clear evidence for publication bias when OR estimates were plotted against their precision (see funnel plot in Fig. 3). As expected, the two extreme studies were Wallace *et al.* (1988) and Senft *et al.* (1997).

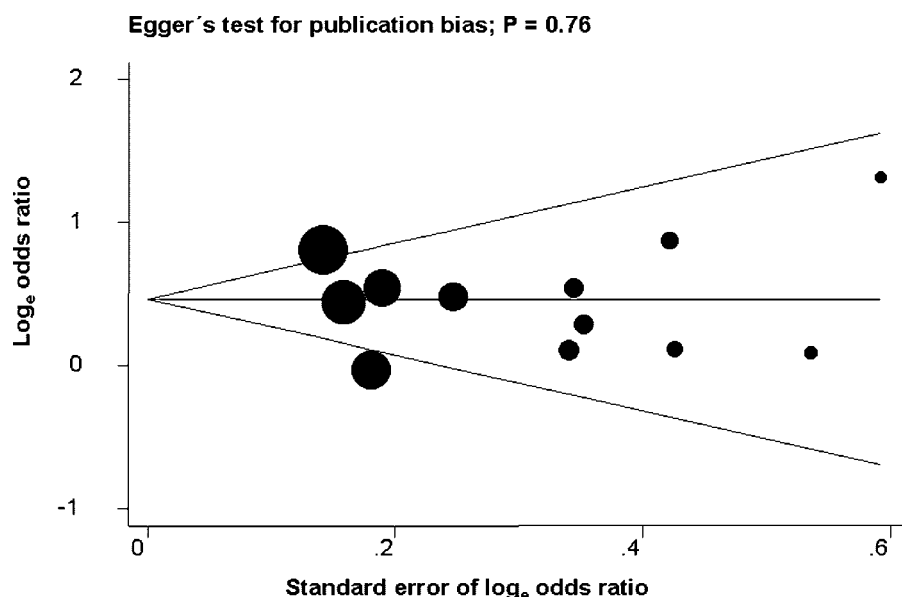


Fig. 3. Examination of publication bias.

### Cumulative Meta-Analysis

Figure 4 displays the change in the overall estimate (random effects model OR) as studies were accumulated by year of publication. The efficacy of BIs was clearly established by the early 1990s, but stability of estimates was not achieved until late 1990s, by which time new studies were mainly conducted in samples including moderate drinkers recruited at consultation.

### DISCUSSION

Our results support the efficacy of BIs for hazardous drinkers in primary care using more demanding criteria than formerly used. As previously reported (Heather et al., 1987; Richmond et al., 1995), we have not found clear evidence of a dose-effect relationship linking the intensity of BIs with outcome. Nevertheless, we have shown that MI

(simple advice) is not better than usual care, and because there are few studies including an EBI arm, further research is needed to establish whether EBIs differ in efficacy from BIs.

Wilk et al. (1997), analyzing a set of eight studies, also included in our review, reported an OR estimate of 1.95 favoring BIs. Our estimates are somewhat lower but consistent whether combining the whole set of 12 studies or deleting the two most influential studies: OR = 1.6, which translates to a 11% difference in success rate between BIs and usual care or simple advice, or to the necessity to treat nine hazardous drinkers to obtain one additional success. The disagreement between our result and that of Wilk et al. can be explained by the different approaches followed to extract individual estimates (also apparent in the tabulated data). We have used an ITT approach, whereas Wilk et al. did not.

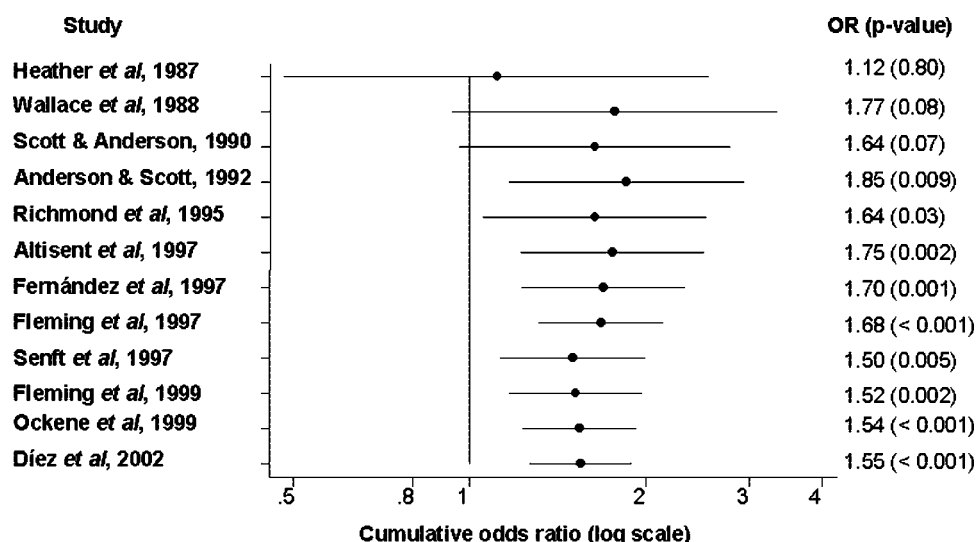


Fig. 4. Cumulative meta-analysis by publication year.

Our results agree with those of Moyer et al. (2002) on the lower but significant efficacy attained by BIs directed to people attending consultations in primary care (treatment seekers) than in those conducted within general screening programs on the population at large (nontreatment seekers). If we consider the estimates of BIs on treatment seekers to reflect more closely what could be expected of their routine implementation, our results—although lower than those reported in a recent meta-analysis that combined just eight studies (Beich et al., 2003)—support the efficacy of BIs at consultation in primary care (OR = 1.41, RD = 0.09, NNT = 12).

Previous meta-analyses did not differentiate between the types of hazardous drinkers included in the primary studies. When this is done, some evidence appears favoring the efficacy of BIs for heavy drinkers, but because this evidence relies on opposing effects of two highly influential studies, which also represent the two sampling schemes of nontreatment seekers and treatment seekers, it also requires reassessment by further research.

We have not considered the effect that gender could have on the efficacy of BIs because some of the included studies were conducted only in males and for some others data were not reported separately by gender. However, the results of a recent meta-analysis (Ballesteros et al., 2004), conducted to update the inconclusive evidence previously reported (Poikolainen, 1999), showed similar reductions of alcohol consumption and on the frequency of individuals who drank above harmful levels in men and women.

Due to our interest in reanalyzing all available primary studies by an ITT approach, the only reliable outcome we were able to extract was the change in the proportion of hazardous drinkers 6 to 12 months after subjects were randomized to treatment arms. This means that other outcomes customarily reported and meta-analyzed, such as changes in alcohol consumption, biochemical markers, use of medical services, and psychosocial outcomes, were not used in our meta-analysis. Our selected outcome—also used previously by Wilk et al. (1997)—singles out what we consider to be the strongest outcome for the evidence of efficacy of BIs, because biochemical markers lack sufficient sensitivity and specificity to be considered main outcomes in primary care (Conigrave et al., 2002), and medical or psychosocial outcomes, although showing an association with alcohol intake, do not permit its direct assessment and can be indirectly related to alcohol intake by other non-measured confounding variables. On the other hand, most quantitative changes in alcohol consumption were reported in the literature only for endpoint protocol completers, which made it impossible to compute reliable ITT estimates. Despite this, our results are shown to be robust by sensitivity analyses and also do not seem prone to publication bias, although due to our demanding inclusion criteria, studies combined in other meta-analyses were not included in ours.

## CONCLUSIONS

Our results, although lower than reported in former meta-analyses (Beich et al., 2003; Bien et al., 1993; Moyer et al., 2002; Poikolainen, 1999; Wilk et al., 1997), support the moderate efficacy of BIs as applied to hazardous drinkers in the primary care setting showing consistent estimates since the late 1990s. Nevertheless, several issues merit further research. Among these are the investigation of a dose-effect relationship by including arms with EBIs and the comparative efficacy of BIs when applied to different types of hazardous drinkers (heavy or moderate). We also need further naturalistic studies to investigate the reasons for the recently reported lack of long-term efficacy of BIs (Aalto et al., 2000, 2001; Wutzke et al., 2002) and the perceived barriers to their general implementation in primary care (Aalto et al., 2003; Beich et al., 2002).

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## APPENDIX

Studies excluded from the meta-analyses and main reasons for their exclusion

Aalto M, Saksanen R, Laine P, Forsström R, Raikaa M, Kiviluoto M *et al* (2000) Brief interventions for female heavy drinkers in routine general practice: a 3-year randomised, controlled study. *Alcohol Clin Exp Res* 24:1680–1686. [Frequency data for ITT analyses not available].

Aalto M, Seppä K, Mattila P, Mustonen H, Ruuth K, Hyvärinen H *et al* (2001) Brief interventions for male heavy drinkers in routine general practice: a three-year randomised controlled study. *Alcohol Alcohol* 36:224–230. [Frequency data for ITT analyses not available].

Acuda W. Nairobi, Kenia (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care*. Geneva: World Health Organization 113–128. [Not conducted specifically in primary care settings].

Adams A, Ockene JK, Wheeler EV, Hurley TG (1998) Alcohol counselling: physicians will do it. *J Gen Intern Med* 13:692–698. [Data previously reported].

Agosti V (1994) The efficacy of controlled trials of alcohol misuse treatments in maintaining abstinence: a meta-analysis. *Int J Addict* 29:759–769. [Meta-analysis including alcohol dependence].

Andréasson S, Hansagi H, Österlund B (2002) Short-term treatment for alcohol-related problems: four-session



guided self-change versus one session of advice. A randomised controlled trial. *Alcohol* 28:57–62. [Cognitive intervention].

Babor TF, Lauerma R, Kranzler H, McRee B, Korner P, Wilber C *et al.* Farmington, USA (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care.* Geneva: World Health Organization 191–210. [Not conducted specifically in primary care settings].

Babor TF, Grant M, Acuda W, Burns FH, Campillo C, Del Boca FK *et al.* (1994) A randomised trial of brief interventions in primary care: summary of a WHO project. *Addiction* 89:657–660. [Review].

Bien TH, Miller WR, Tonigan JS (1993) Brief interventions for alcohol problems: a review. *Addiction* 88:315–335. [Previous meta-analysis].

Boyadjieva M. Pleven, Bulgaria (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care.* Geneva: World Health Organization 91–102. [Not conducted specifically in primary care settings].

Burge SK, Amodei N, Elkin B, Catala S, Andrew SR, Lane PA *et al.* (1997) An evaluation of two primary care interventions for alcohol abuse among Mexican-American patients. *Addiction* 92:1705–116. [Alcohol dependence].

Campillo C, Martínez DRD, Mendoza MMR, Sánchez JC, Velásquez JV. Mexico City, México (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care.* Geneva: World Health Organization 129–42. [Frequency data for ITT analyses not available].

Chang G, Wilkins HL, Berman S, Goetz MA (1999) Brief intervention for alcohol use in pregnancy: a randomised trial. *Addiction* 94:1499–1508. [Intervention within other health programmes].

Chang G, Goetz MA, Wilkins-Haug L, Berman S (2000) A brief intervention for prenatal alcohol use: an in-depth look. *J Subst Abuse Treat* 18:365–369. [Intervention within other health programmes].

Chang G (2002) Brief interventions for problem drinking and women. *J Subst Abuse Treat* 23:1–7. [Review].

Córdoba R, Delgado MT, Pico V, Altisent R, Fores D, Monreal A *et al.* (1998) Effectiveness of brief intervention on non-dependent alcohol drinkers (EBIAL): a Spanish multi-centre study. *Fam Pract* 15:562–568. [Frequency data for ITT analyses not available].

Edwards AGK, Rollnick S (1997) Outcome studies of brief alcohol intervention in general practice: the problem of lost subjects. *Addiction* 92:1699–1704. [Review].

Fleming MF, Mundt MP, French MT, Manwell LB, Stauffacher EA (2000) Benefit-cost analysis of brief physician advice with problem drinkers in primary care settings. *Med Care* 38:7–18. [Data previously reported].

Fleming MF, Mundt MP, French MT, Manwell LB, Stauffacher EA, Barry KL (2002) Brief physician advice for problem drinkers: long-term efficacy and benefit-cost analysis. *Alcohol Clin Exp Res* 26:36–43. [Data previously reported].

Freeborn DK, Polen MR, Hollis JF, Senft RA (2000) Screening and brief intervention for hazardous drinking in an HMO: effects on medical care utilization. *J Behav Health Serv Res* 27:446–453. [Data previously reported].

Freemantle N, Song F, Sheldon T, Long A (1993) *Brief interventions and alcohol use.* York: NHS Centre for Reviews and Dissemination (NHSCRD), no 13. [Review].

Israel Y, Hollander O, Sanchez-Craig M, Booker S, Miller V, Gingrich R *et al.* (1996) Screening for problem drinking and counseling by the primary care physician-nurse team. *Alcohol Clin Exp Res* 20:1443–1450. [Cognitive intervention].

Ivanets NN, Lukomskaya MI. Moscow, USSR (1992). In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care.* Geneva: World Health Organization 157–174. [Not conducted specifically in primary care settings].

Kahan M, Wilson L, Becker L (1995) Effectiveness of physician-based interventions with problem drinkers: a review. *Can Med Assoc J* 152:851–859. [Review].

Kristenson H, Trell E, Hood B (1981) Serum-gamma-glutamyltransferase in screening and continuous control of heavy drinking in middle-aged men. *Am J Epidemiol* 114:862–872. [Frequency data for ITT analyses not available].

Kristenson H, Öhlin H, Hultén-Nosslin MB, Trell E, Hood B (1983) Identification and intervention of heavy drinking in middle-aged men: results and follow-up of 24–60 months of long-term study with randomized controls. *Alcohol Clin Exp Res* 7:203–209. [Frequency data for ITT analyses not available].

Kristenson H, Hood B, Peterson B, Trell E (1985) Prevention of alcohol-related problems in urban middle-aged males. *Alcohol* 2:545–9. [Frequency data for ITT analyses not available].

Kristenson H, Österling A, Nilsson JA, Lindgärde F (2002) Prevention of alcohol-related deaths in middle-aged heavy drinkers. *Alcohol Clin Exp Res* 26:478–84. [Frequency data for ITT analyses not available].

Kristenson H, Hood B (1984) The impact of alcohol on health in the general population: a review with particular reference to experience in Malmö. *Br J Addict* 79:139–45. [Frequency data for ITT analyses not available].

Larrosa P, Vernet M, Sender MJ, Simó E (2000) Intervención antialcohólica en bebedores crónicos en atención primaria. *Aten Primaria* 25:489–92. [Alcohol dependence].

Machona AM. Harare, Zimbabwe (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care.* Ge-

neve: World Health Organization 211–21. [Not conducted specifically in primary care settings].

Maheswaran R, Beevers M, Beevers DG (1992) Effectiveness of advice to reduce alcohol consumption in hypertensive patients. *Hypertension* 19:79–84. [Intervention within other health programmes].

Maisto SA, Conigliaro J, McNeil M, Kraemer K, Conigliaro RL, Kelley ME (2001) Effects of two types of brief intervention and readiness to change on alcohol use in hazardous drinkers. *J Stud Alcohol* 62:605–614. [Frequency data for ITT analyses not available].

Manwell LB, Fleming MF, Mundt MP, Stauffacher EA, Barry KL (2000) Treatment of problem alcohol use in women of childbearing age: results of a brief intervention trial. *Alcohol Clin Exp Res* 24:1517–1524. [Data previously reported].

McIntosh MC, Leigh G, Baldwin NJ, Marmulak J (1997) Reducing alcohol consumption. Comparing three brief methods in family practice. *Can Fam Physician* 43:1959–1967. [Cognitive intervention].

Miller WR, Wilbourne PL (2002) Mesa Grande: a methodological analysis of clinical trials of treatments for alcohol use disorders. *Addiction* 97:265–77. [Review].

Modesto-Lowe V, Boornazian A (2000) Screening and brief intervention in the management of early problem drinkers: integration into healthcare settings. *Dis Management Health Outcomes* 8:129–137. [Review].

Montero S. San José, Costa Rica (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care*. Geneva: World Health Organization 103–112. [Not conducted specifically in primary care settings].

Moyer A, Finney JW, Swearingen CE, Vergun P (2002) Brief interventions for alcohol problems: a meta-analytic review of controlled investigations in treatment-seeking and non-treatment-seeking populations. *Addiction* 97:279–292. [Previous meta-analysis].

Nilssen O (1991) The Tromsø study: identification of and a controlled intervention on a population of early-stage risk drinkers. *Prev Med* 20:518–528. [Frequency data for ITT analyses not available].

Persson J, Magnusson PH (1989) Early intervention in patients with excessive consumption of alcohol: a controlled study. *Alcohol* 6:403–8. [Frequency data for ITT analyses not available].

Poikolainen K (1999) Effectiveness of brief interventions to reduce alcohol intake in primary care populations: a meta-analysis. *Prev Med* 28:503–9. [Previous meta-analysis].

Rollnick S, Hodgson RJ, Snail S. Cardiff, United Kingdom (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care*. Geneva: World Health Organization 175–190. [Not conducted specifically in primary care settings].

Romelsjö A, Andersson L, Barner H, Borg S, Granstrand C, Hultman O *et al* (1989) A randomised study of secondary prevention of early stage problem drinkers in primary health care. *Br J Addict* 84:1319–1327. [Frequency data for ITT analyses not available].

Saunders JB, Reznik RB, Hanratty SJ, Douglas A, Burns FH. Sydney, Australia (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care*. Geneva: World Health Organization 73–90. [Not conducted specifically in primary care settings].

Seppä K (1992) Intervention in alcohol abuse among macrocytic patients in general practice. *Scand J Prim Health Care* 10:217–222. [Frequency data for ITT analyses not available].

Skutle A. Bergen, Norway (1992) In Babor TF, Grant M, eds. *Project on identification and management of alcohol-related problems. Report on Phase II: A randomised clinical trial of brief interventions in primary health care*. Geneva: World Health Organization 143–56. [Frequency data for ITT analyses not available].

Smith AJ, Hodgson RJ, Bridgeman K, Shepherd JP (2003) A randomised controlled trial of a brief intervention after alcohol-related facial injury. *Addiction* 98:43–52. [Intervention within other health programmes].

Stein MD, Anderson B, Charuvastra A, Maksad J, Friedmman PD (2002) A brief intervention for hazardous drinkers in a needle exchange program. *J Subst Abuse Treat* 22:23–31. [Intervention within other health programmes].

Stein MD, Charuvastra A, Maksad J, Anderson BJ (2002) A randomised trial of a brief alcohol intervention for needle exchangers (BRAINE). *Addiction* 97:691–700. [Intervention within other health programmes].

Tomson Y, Romelsjö A, Åberg H (1998) Excessive drinking – brief intervention by a primary health care nurse – a randomized controlled trial. *Scand J Prim Health Care* 16:188–192. [Frequency data for ITT analyses not available].

WHO Brief Intervention Study Group (1996) A cross-national trial of brief interventions with heavy drinkers. *Am J Public Health* 86:948–55. [Review].

Wilk AI, Jensen NM, Havighurst TC (1997) Meta-analysis of randomised control trials addressing brief interventions in heavy alcohol drinkers. *J Gen Intern Med* 12:274–283. [Previous meta-analysis].

Wutzke SE, Conigrave KM, Saunders JB, Hall WD (2002) The long-term effectiveness of brief interventions for unsafe alcohol consumption: a 10-year follow-up. *Addiction* 97:665–675. [Data previously reported].

## REFERENCES

- Aalto M, Pekuri P, Seppä K (2003) Primary health care professionals' activity in intervening in patients' alcohol drinking during a 3-year brief intervention implementation project. *Drug Alcohol Depend* 69:9–14.

- Aalto M, Saksanen R, Laine P, Forsström R, Raikaa M, Kiviluoto M, Seppä K, Sillanaukee P (2000) Brief interventions for female heavy drinkers in routine general practice: a 3-year randomized, controlled study. *Alcohol Clin Exp Res* 24:1680–1686.
- Aalto M, Seppä K, Mattila P, Mustonen H, Ruuth K, Hyvärinen H, Pulkkinen H, Alho H, Sillanaukee P (2001) Brief interventions for male heavy drinkers in routine general practice: a three-year randomized controlled study. *Alcohol Alcohol* 36:224–230.
- Altisent R, Córdoba R, Delgado MT, Pico MV, Melus E, Aranguren F, Alvira U, Barbera C, Moran J, Reixa S (1997) Estudio multicéntrico sobre la eficacia del consejo para la prevención del alcoholismo en atención primaria (EMPA). *Med Clin (Barc)* 109:121–124.
- Anderson P, Scott E (1992) The effect of general practitioners advice to heavy drinking men. *Br J Addict* 87:891–900.
- Ballesteros J, Ariño J, González-Pinto A, Querejeta I (2003) Eficacia del consejo médico para la reducción del consumo excesivo de alcohol. Metaanálisis de estudios españoles en atención primaria. *Gac Sanit* 17:116–122.
- Ballesteros J, González-Pinto A, Querejeta I, Ariño J (2004) Brief interventions for hazardous drinkers delivered in primary care are equally effective in men and women. *Addiction* 99:103–108.
- Beich A, Gannik D, Malterud K (2002) Screening and brief intervention for excessive alcohol use: qualitative interview study of the experiences of general practitioners. *Br Med J* 325:870–874.
- Beich A, Thorsen T, Rollnick S (2003) Screening in brief intervention trials targeting excessive drinkers in general practice: systematic review and meta-analysis. *Br Med J* 327:536–542.
- Bien TH, Miller WR, Tonigan JS (1993) Brief interventions for alcohol problems: a review. *Addiction* 88:315–335.
- Conigrave KM, Degenhardt LJ, Whitfield JB, Saunders JB, Helander A, Tabakoff B (2002) CDT, GGT and AST as markers of alcohol abuse: the WHO/ISBRA collaborative project. *Alcohol Clin Exp Res* 26:332–339.
- Curry SJ, Ludman EJ, Grothaus LC, Donovan D, Kim E (2003) A randomized trial of a brief primary-care-based intervention for reducing at-risk drinking practices. *Health Psychol* 22:156–165.
- Díez JF, Peña C, García E, Gaite L (2002) Intervención breve en Cantabria en problemas relacionados con el alcohol. *Adicciones* 14:13–24.
- Edwards AGK, Rollnick S (1997) Outcome studies of brief alcohol intervention in general practice: the problem of lost subjects. *Addiction* 92:1699–1704.
- Egger M, Smith GD, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. *Br Med J* 315:629–634.
- Fernández MI, Bermejo CJ, Alonso M, Herreros B, Nieto M, Novoa A, Marcelo MT (1997) Efectividad del consejo médico breve para reducir el consumo de alcohol en bebedores. *Aten Primaria* 19:127–132.
- Fleming MF, Barry KL, Manwell LB, Johnson K, London R (1997) Brief physician advice for problem alcohol drinkers. A randomized controlled trial in community-based primary care practices. *J Am Med Assoc* 277:1039–1045.
- Fleming MF, Manwell LB, Barry KL, Adams W, Stauffacher EA (1999) Brief physician advice for alcohol problems in older adults—A randomized community-based trial. *J Fam Pract* 48:378–384.
- Hasselblad V (1998) Meta-analysis of multitreatment studies. *Med Decis Making* 18:37–43.
- Heather N (1995) Interpreting the evidence on brief interventions for excessive drinkers: the need for caution. *Alcohol Alcohol* 30:287–296.
- Heather N, Campion PD, Neville RG, Maccabe D (1987) Evaluation of a controlled drinking minimal intervention for problem drinkers in general practice (the DRAMS scheme). *J R Coll Gen Pract* 37:358–363.
- Hedges LV (1994) Fixed effects models, in *The Handbook of Research Synthesis* (Cooper H, Hedges LV eds), pp 285–299. Russell Sage Foundation, New York.
- Higgins JPT, Thompson SG (2002) Quantifying heterogeneity in a meta-analysis. *Stat Med* 21:1539–1558.
- Higgins JPT, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. *Br Med J* 327:557–560.
- Kahan M, Wilson L, Becker L (1995) Effectiveness of physician-based interventions with problem drinkers: a review. *Can Med Assoc J* 152:851–859.
- Moyer A, Finney JW, Swearingen CE, Vergun P (2002) Brief interventions for alcohol problems: a meta-analytic review of controlled investigations in treatment-seeking and non-treatment-seeking populations. *Addiction* 97:279–292.
- Normand ST (1999) Meta-analysis: formulating, evaluating, combining and reporting. *Stat Med* 18:321–359.
- Ockene JK, Adams A, Hurley TG, Wheeler EV, Hebert JR (1999) Brief physician- and nurse practitioner-delivered counseling for high-risk drinkers. Does it work? *Arch Intern Med* 159:2198–2205.
- Poikolainen K (1999) Effectiveness of brief interventions to reduce alcohol intake in primary health care populations: a meta-analysis. *Prev Med* 28:503–509.
- Richmond R, Heather N, Wodak A, Kehoe L, Webster I (1995) Controlled evaluation of a general-practice-based brief intervention for excessive drinking. *Addiction* 90:119–132.
- Scott E, Anderson P (1990) Randomized controlled trial of general practitioner intervention in women with excessive alcohol consumption. *Drug Alcohol Review* 10:312–321.
- Senft RA, Polen MR, Freeborn DK, Hollis JF (1997) Brief intervention in a primary care setting for hazardous drinkers. *Am J Prev Med* 13:464–470.
- Wallace P, Cutler S, Haines A (1988) Randomised controlled trial of general practitioner intervention in patients with excessive alcohol consumption. *Br Med J* 297:663–668.
- Wilk AI, Jensen NM, Havighurst TC (1997) Meta-analysis of randomized control trials addressing brief interventions in heavy alcohol drinkers. *J Gen Intern Med* 12:274–283.
- Wutzke SE, Conigrave KM, Saunders JB, Hall WD (2002) The long-term effectiveness of brief interventions for unsafe alcohol consumption: a 10-year follow-up. *Addiction* 97:665–675.