

# Reduction of Alcohol Consumption by Brief Alcohol Intervention in Primary Care

## Systematic Review and Meta-analysis

Nicolas Bertholet, MD; Jean-Bernard Daeppen, MD; Vincent Wietlisbach, BA†; Michael Fleming, MD; Bernard Burnand, MD, MPH

**Background:** Numerous trials of the efficacy of brief alcohol intervention have been conducted in various settings among individuals with a wide range of alcohol disorders. Nevertheless, the efficacy of the intervention is likely to be influenced by the context. We evaluated the evidence of efficacy of brief alcohol interventions aimed at reducing long-term alcohol use and related harm in individuals attending primary care facilities but not seeking help for alcohol-related problems.

**Methods:** We selected randomized trials reporting at least 1 outcome related to alcohol consumption conducted in outpatients who were actively attending primary care centers or seeing providers. Data sources were the Cochrane Central Register of Controlled Trials, MEDLINE, PsycINFO, ISI Web of Science, ETOH database, and bibliographies of retrieved references and previous reviews. Study selection and data abstraction were performed independently and in duplicate. We assessed the validity of the studies and per-

formed a meta-analysis of studies reporting alcohol consumption at 6 or 12 months of follow-up.

**Results:** We examined 19 trials that included 5639 individuals. Seventeen trials reported a measure of alcohol consumption, of which 8 reported a significant effect of intervention. The adjusted intention-to-treat analysis showed a mean pooled difference of -38 g of ethanol (approximately 4 drinks) per week (95% confidence interval, -51 to -24g/wk) in favor of the brief alcohol intervention group. Evidence of other outcome measures was inconclusive.

**Conclusion:** Focusing on patients in primary care, our systematic review and meta-analysis indicated that brief alcohol intervention is effective in reducing alcohol consumption at 6 and 12 months.

*Arch Intern Med.* 2005;165:986-995

**Author Affiliations:** Alcohol Treatment Center (Drs Bertholet and Daeppen) and Clinical Epidemiology Center (Drs Bertholet and Burnand), University Hospital, Lausanne, Switzerland; Health Care Evaluation Unit, Institute of Social and Preventive Medicine, University of Lausanne (Mr Wietlisbach and Dr Burnand); and Department of Family Medicine, University of Wisconsin-Madison Medical School (Dr Fleming).  
**Financial Disclosure:** None.  
†Deceased.

**E**XCESSIVE ALCOHOL USE IS A major public health concern<sup>1</sup> associated with an increased risk of morbidity and mortality.<sup>2</sup> Numerous trials of the efficacy of brief alcohol intervention (BAI) have been conducted in various settings among individuals with a wide range of alcohol disorders. It has been suggested that BAI has the potential to reduce serious adverse consequences of alcohol consumption.<sup>3</sup> Between 1993 and 2002, 8 systematic reviews<sup>4-11</sup> including between 7 and 56 studies were published; 4 of these aggregated data in a meta-analysis.<sup>5,9-11</sup>

*See also pages 1016 and 1022*

While BAI applies to various settings, the efficacy of the intervention is likely to be influenced by the context. Admission to an emergency department or hospital differs from an opportunistically delivered intervention among primary care patients. Furthermore, because primary care encoun-

ters include a large proportion of the community and because of a low threshold of access, it is important to focus on BAI conducted among primary care patients. Several projects aimed at implementing brief alcohol counseling in primary care are ongoing (eg, the World Health Organization brief intervention project, phase IV<sup>12</sup>). Although conditions for optimal implementation strategies of BAI are yet to be determined,<sup>13,14</sup> a summary of the efficacy of BAI in primary care on non-treatment-seeking patients is needed.

The purpose of this systematic review was to evaluate the evidence of efficacy of BAI aimed at reducing long-term alcohol use and related harm among individuals actively attending primary health care centers but not seeking help for alcohol problems.

## METHODS

### LITERATURE SEARCH

Studies included in this review were drawn from different sources: (1) the Cochrane Central Reg-

ister of Controlled Trials, MEDLINE, and PsycINFO from inception to January 2003, completed with searches in the ISI Web of Science and ETOH databases; (2) bibliographies of retrieved references and previous reviews; and (3) our own bibliographic resources. No restrictions were applied to language or year of publication.

## STUDY SELECTION

Eligible studies were randomized controlled trials reporting at least 1 outcome related to change in alcohol intake, drinking status, health-related quality of life or functional status, laboratory markers related to alcohol use, utilization of health care resources, or cost data.

Only studies conducted in outpatients who were actively attending a primary health care center or provider were considered. Studies involving alcohol treatment-seeking patients were excluded. We considered individuals who responded to advertisements or who were referred for alcohol treatment to be alcohol treatment seekers. Studies conducted in a hospital ward or in an emergency department were not eligible. Studies that selected patients by means of registers or patient lists or that specifically convened individuals for alcohol screening were also excluded. At least 75% of the study population consisted of primary care patients; for samples with less than 75% primary care patients, subanalyses must have been performed according to population type.

Eligible interventions were as follows: (1) intervention delivered individually that focused on alcohol consumption with a face-to-face component during the initial session, and (2) intervention defined as "brief intervention" or "motivational intervention" or reporting the use of feedback or advice to reduce alcohol consumption. No restrictions were applied to repeated interventions or reinforcement sessions.

Two of us (N.B. and B.B.) reviewed the titles and abstracts independently and in duplicate. Abstracts were selected for full text reading whenever selected by 1 or 2 authors. The same 2 then read the preselected articles independently and in duplicate, and applied inclusion and exclusion criteria. When no consensus was obtained, articles that were not fully rejected or accepted were discussed and submitted to a third author (J.-B.D.).

## DATA ABSTRACTION

For each selected article, 2 of us alternatively performed data abstraction in-

dependently and in duplicate. Disagreements over the abstraction were discussed and submitted to a third author (N.B., B.B., then J.-B.D., or N.B., J.-B.D., then B.B.) when necessary.

## SYSTEMATIC REVIEW ANALYSES

We analyzed several components of treatment and control interventions (contents, provider, duration, and repetition), outcomes, and methods (design and inclusion and exclusion criteria) to understand and evaluate the impact of these elements on our results. Two of us (N.B. and B.B.) assessed trial quality independently and in duplicate and obtained a quality score (by consensus when needed) for each trial by using an instrument adapted from Ferri et al.<sup>15</sup> We added elements derived from the Consolidated Standards of Reporting Trials statement<sup>16</sup> and from Jüni et al.<sup>17</sup> For each trial, a quality score ranging from 0 (low) to 18 (high) was assigned. The instrument evaluated randomization, concealment of allocation, blinding in assessment of outcomes, attrition during follow-up, presence of an intention-to-treat analysis, and additional criteria (clear definition of intervention, selection and performance bias, and presence of a measure of intervention exposure).

## META-ANALYSIS

In the framework of this systematic review, a meta-analysis was deemed feasible only for the principal outcome of alcohol consumption. Studies reporting alcohol consumption or differences in alcohol consumption at 6 or 12 months of follow-up containing corresponding confidence intervals (CIs), standard deviations, or standard errors at baseline and other follow-up measures were included in the meta-analysis. The magnitude of effect (effect size) was expressed in terms of mean net reduction in alcohol consumption (in grams of ethanol per week) observed in the BAI group compared with the control group. For example, an effect size of -10 g means that, on average, subjects in the BAI group reduced their weekly alcohol consumption by 10 g more than the controls. When data on weekly alcohol consumption were missing (eg, no description of the content of a standard drink in absolute alcohol or description of corresponding equivalences of various alcoholic beverages such as beer, wine, or spirits), we used the definition of the absolute ethanol content in a standard drink used in the country where the study was performed, according to Babor and Higgins-Biddle<sup>18</sup> and Dufour.<sup>19</sup> The varia-

tion between countries and studies of a "standard" drink's ethanol content is also the reason for expressing results in grams of ethanol and not in drinks.

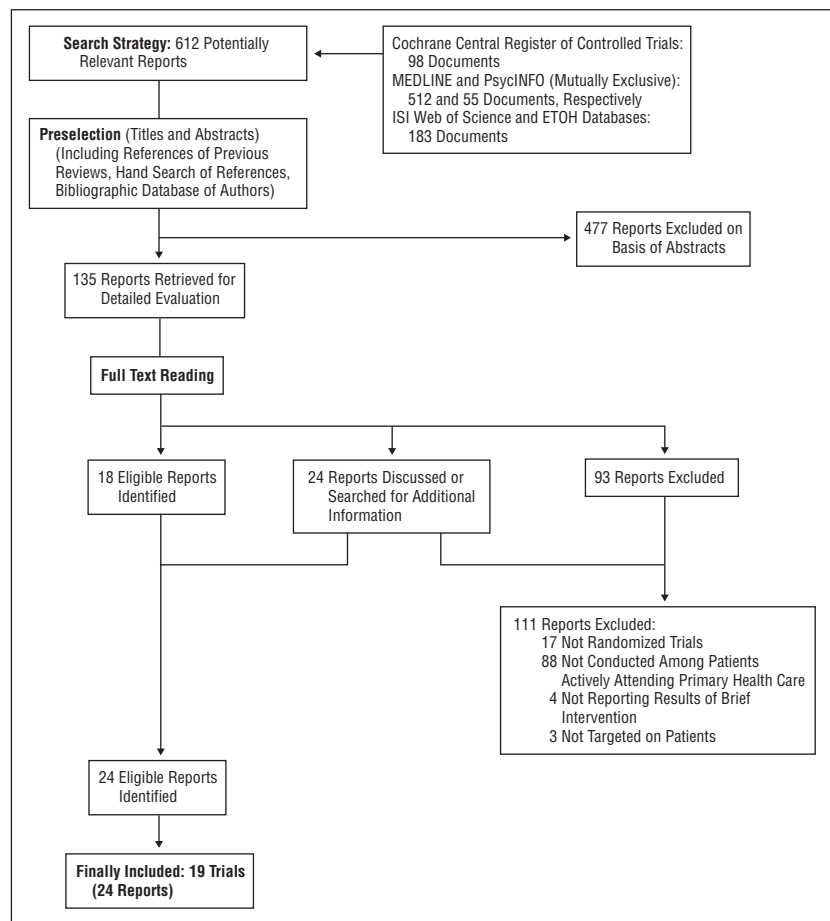
To obtain an intention-to-treat analysis across all studies, we considered all randomized individuals. We chose a conservative option and assigned the mean group baseline alcohol consumption value to randomized individuals excluded from the analyses at follow-up. For studies reporting change in alcohol consumption, missing individuals were counted as showing no change.

## STATISTICAL METHODS FOR META-ANALYSIS

Meta-analysis was performed by using the commands "metan" and "meta" of the statistical software Stata 8 (Stata Corp, College Station, Tex). A random effects model was used to examine the heterogeneity between the studies and combined their results. The overall pooled effect was estimated by the weighted average of individual study effects by means of the DerSimonian and Laird weighting method. Between-studies heterogeneity in outcome was tested using the Cochran  $\chi^2$   $Q$  statistic. The  $I^2$  measure proposed by Higgins et al<sup>20</sup> was used to estimate the percentage of total variation in outcome that is due to heterogeneity rather than chance. The extent to which study-level variables explained heterogeneity in the effect size was explored by fitting meta-regression models. The following variables were considered: year of study publication, sex of study population, mean alcohol consumption in the BAI group at baseline, length of follow-up, response rate to follow-up, duration of intervention, technique used in intervention, score of methodologic quality, and subscore related to quality of randomization, allocation concealment, and blinding. Publication bias was examined by means of the Begg and Mazumdar adjusted rank correlation test<sup>21</sup> and the Egger regression asymmetry test.<sup>22</sup>

## RESULTS

A total of 612 references were obtained after exclusion of redundant references from various sources, from which 135 reports were selected for detailed evaluation. The selection process is summarized in **Figure 1**. Of the 24 selected articles, all but 1 was retrieved for further evaluation during the abstract selection process by one reviewer (N.B.) and all but 1 by the other (B.B.) (agreement, 92%;  $\kappa=0.65$ ).



**Figure 1.** Flow diagram of literature searches and study selection resulting in identification of 19 eligible trials (see “Methods” section). For the number of reports excluded, one study was counted twice because there could be more than 1 reason for exclusion.

## STUDY CHARACTERISTICS

The 24 retained reports represent the results of 19 trials<sup>23-46</sup>, 9 conducted in North America, 7 in Europe, 2 in Africa, and 1 in Australia. Two reports were published in Spanish, 1 in French, and 21 in English. Four reports were related to Project TrEAT (Trial for Early Alcohol Treatment),<sup>30,32,33,40</sup> 1 was an ancillary report connected to the study conducted by Senft et al<sup>44</sup> that focused on health care utilization,<sup>34</sup> and 2 reported results of men and women separately.<sup>23,24</sup> Inclusion and exclusion criteria are summarized in **Table 1** and **Table 2**. All but 4 (26%)<sup>27,44-46</sup> of the 19 selected studies used customary alcohol consumption as an inclusion criterion, and 14 studies (74%) excluded alcohol-dependent individuals.

Study size ranged from 80 to 774 subjects, with a total of 5639. Thirteen trials (74%) included subjects of both sexes, 3 (16%) were males only, and 3 (16%) were initially conducted among male and females in-

dividuals but females were not included in the analyses.<sup>25,26,38</sup> One study focused specifically on elderly patients ( $\geq 65$  years old).<sup>31</sup>

Three trials were cluster randomized,<sup>28,36,42</sup> 1 was randomly allocated to groups in weekly blocks,<sup>43</sup> and the remaining 15 were individually randomized. Two of the cluster-randomized trials<sup>28,42</sup> used the primary care center as the unit of randomization and the patient as the unit of analysis. The third one<sup>36</sup> used the physician as the unit of randomization. The length of follow-up ranged from 6 to 48 months.

Treatment and control interventions are summarized in **Table 3**. The reported descriptions (eg, content and duration) varied across these studies. All selected studies included some advice being given to the BAI groups, and all except 1<sup>36</sup> reported the use of feedback regarding alcohol consumption levels and/or adverse effects of alcohol consumption. Six studies made explicit reference to the Moti-

vational Interview<sup>47</sup> by Miller and Rollnick,<sup>23,24,28,39,42-44</sup> 2 studies<sup>37,41</sup> to the cognitive-behavioral techniques developed by Sanchez-Craig,<sup>48</sup> and 3 studies<sup>30,31,36</sup> to the intervention developed by Wallace et al.<sup>49</sup> The length of intervention ranged from 5 to 45 minutes. The BAI was repeated or included a booster session in 10 studies, and in 4 additional studies a follow-up visit was offered to participants. The control intervention in 6 studies consisted of up to 5 minutes of advice. The remaining 13 studies had no intervention or usual care as the control group.

## QUALITATIVE DATA SYNTHESIS

Summary results of the systematic review are presented in **Table 4**. Follow-up rates ranged from 31.5% to 92.4% (mean, 72.4%; median, 77.2%). Nine (47%) of 19 studies had an attrition rate of less than 20%. The methodologic quality scores ranged from 5<sup>36</sup> to 14,<sup>30,39</sup> with a mean of 9.6 and a median of 9.0. Ten points was arbitrarily determined to be the cutoff between “high-quality” and “low-quality” studies. A low-quality rating was principally related to inadequate randomization or insufficient reporting of concealment of allocation. Only 2 of the selected studies<sup>39,46</sup> sufficiently reported concealment of allocation, whereas most of the remaining studies either reported it only partially, or documented inadequate concealment of allocation. High-quality studies were more likely than low-quality studies to report statistically significant positive effects of intervention ( $\chi^2 = 3.9$ ,  $P = .048$ ).

## EFFECTS OF THE COMPARED INTERVENTIONS

Among 17 trials reporting a quantified outcome measure of alcohol consumption, 8 reported statistically significant effects of BAI and 7 reported no significant effects. None of the studies reported negative effects of BAI. Two trials reported significant effects on secondary measures (number of drinking days per month<sup>38</sup> and usual drinking amount per occasion among women<sup>23</sup>) and nonsignificant principal quantity-frequency outcomes. Meta-analysis was restricted to those 10 trials for which the reduction of alcohol consumption could

**Table 1. Inclusion Criteria of Patients in 19 Selected Trials**

Resource	Sex	Age, y	Absolute Ethanol Consumption (Cutoff), g/wk	Binge Drinking	CAGE or AUDIT Score Cutoff*	Other
Heather et al, <sup>35</sup> 1987	M/F	18-65	M: >280 F: >160	NR	NR	Clinical suspicion according to GP
Acuda, <sup>25</sup> 1992	M	18-70	≥350†	100 g/occ, ≥2 times/mo†	NR	NA
Machona, <sup>38</sup> 1992	M	18-70	≥350†	100 g/occ, ≥2 times/mo†	NR	NA
Seppa, <sup>45</sup> 1992	M/F	NR	NR	NR	NR	MCV ≥100 fL (no other cause than alcohol consumption) and Malmö Modified MAST score ≥2‡
Richmond et al, <sup>43</sup> 1995	M/F	18-70	M: ≥350 F: >210	NR	NR	NA
Israel et al, <sup>37</sup> 1996	M/F	30-60	≥1080 g/4 wk	≥60 g/d, ≥8 d in previous 4 wk	CAGE: ≥2	NA
Fernandez San Martin et al, <sup>29</sup> 1997	M	18-64	>210	NR	NR	NA
Project TrEAT, <sup>30,32,33,40</sup> 1997-2002	M/F	18-65	M: >168 F: >132	>60 g on ≥4 occ in previous 30 d	CAGE: ≥2	NA
Altisent et al, <sup>26</sup> 1997	M§	15-70	M: >280 F: >168	NR	NR	NA
McIntosh et al, <sup>41</sup> 1997	M/F	>15	NR	≥54.4 g on any day in previous 28 d	CAGE: ≥1	NA
Senft et al, <sup>44</sup> 1997	M/F	≥21	NR	NR	AUDIT: 8-21	NA
Burge et al, <sup>27</sup> 1997	M/F	≥18	NR	NR	NR	Consumers in past 6 mo and DIS positive in past year
Cordoba et al, <sup>28</sup> 1998	M	14-50	>280	>80 g/d at least once/mo	NR	NA
Project GOAL, <sup>31</sup> 1999	M/F	≥65	M: >132 F: >96	M: >48 g/occ ≥2 times in past 3 mo F: ≥36 g/occ, ≥2 times in past 3 mo	CAGE: ≥2 NR	NA NA
Ockene et al, <sup>42</sup> 1999	M/F	21-70	M: >153.5 F: >115.2	M: ≥62 g on ≥1 occ in previous 1 mo F: ≥51.2 g on ≥1 occ in previous 1 mo	CAGE: ≥2	And regular appointment with GP
Aalto et al, <sup>23,24</sup> 2000-2001	M/F	20-60	M: ≥280 F: ≥190	NR	CAGE: ≥3 (M), ≥2 (F)	NA
Vinson and Devera-Sales, <sup>46</sup> 2000	M/F	≥18	NR	NR	AUDIT: ≥8	NA
Maisto et al, <sup>39</sup> 2001	M/F	≥21	M: ≥224 F: ≥168	NR	AUDIT: ≥8	NA
Huas et al, <sup>36</sup> 2002	M	18-65	≥280	NR	NR	And ≥5 d/wk with alcohol consumption

Abbreviations: AUDIT, Alcohol Use Disorder Identification Test; CAGE, a questionnaire for alcoholism evaluation (Have you ever felt the need to cut down on your drinking? Have you ever felt annoyed by criticism of your drinking? Have you ever felt guilty about your drinking? Have you ever taken a drink (eye opener) first thing in the morning?); DIS, Diagnostic Interview Schedule for Alcohol Abuse and Dependence; GOAL, Guiding Older Adult Lifestyles; GP, general practitioner; MAST, Michigan Alcoholism Screening Test; MCV, mean corpuscular volume; NA, not applicable; NR, not reported; occ, occasion(s); TrEAT, Trial for Early Alcohol Treatment.

\*Patients with CAGE or AUDIT scores above the cutoff (or within the interval in the study by Senft et al<sup>44</sup>) were included. See also exclusion criteria in Table 2.

†If the patient perceived a problem or had tried to cut down in the past 3 years, the inclusion criteria were lower (at least 300 g/wk or 100 g on 1 occasion per month or more).

‡Medical history and alcohol-induced increase in serum  $\gamma$ -glutamyltransferase were also taken into account.

§Women were included in the trial but excluded from the analyses.

||If the sum of the AUDIT frequency and quantity item scores was 5 or more, or if the patient reported having 6 or more drinks per occasion at least weekly, the patient was included even if the total AUDIT score was less than 8 (15% of subjects).

be calculated to assess the efficacy of the intervention.

In studies reporting results at both 6 and 12 months of follow-up, the net reduction in alcohol consumption was similar at 6 and 12 months (intention-to-treat analysis,  $P=.91$ ). Similarly, only a small difference in effect size

(intention-to-treat analysis,  $P=.75$ ) was found between men and women in studies reporting sex differences. Therefore, meta-analysis was performed on all studies reporting data with either 6 or 12 months of follow-up (12 months if both) independent of sex. For the 3 trials that evaluated

2 different intervention modalities, each intervention group was considered separately to examine its contribution to the effect size. Intention-to-treat analyses were possible for only 12 of 13 intervention groups because the number of subjects randomized in each group at baseline was not reported

**Table 2. Exclusion Criteria in 19 Selected Trials**

Resource	Alcohol Dependence	Treatment for Alcohol Problems	Absolute Ethanol Consumption	Pregnancy	Drug Use	Somatic Disease	Psychiatric Disease	Previous Advice to Cut Down	Other
Heather et al, <sup>35</sup> 1987	Yes	NA	NA	Yes	Dependence on opiate drugs	Known liver disease	Yes	NA	NA
Acuda, <sup>25</sup> 1992	Yes	Yes	≥150 g/d	Yes	Yes	Liver damage	Yes	Yes	NA
Machona, <sup>38</sup> 1992	Yes	Yes	≥150 g/d	Yes	Yes	Liver damage	Yes	Yes	NA
Seppa, <sup>45</sup> 1992	NA	NA	NA	NA	NA	NA	NA	NA	NA
Richmond et al, <sup>43</sup> 1995	Yes	Yes	NA	Yes	NA	Presence of disease in which alcohol consumption is contraindicated	Yes	NA	MAST >20
Israel et al, <sup>37</sup> 1996	Yes	AA	NA	NA	Yes	NA	Yes	NA	GGT 4 times or higher than normal (>200 U/L)
Fernandez San Martin et al, <sup>29</sup> 1997	NA	Yes	NA	NA	Yes	NA	Yes	NA	NA
Project TrEAT, <sup>30,32,33,40</sup> 1997-2002	Yes	Yes	>600 g/wk	Yes	NA	NA	Suicidal ideation	If in previous 3 mo	NA
Altisent et al, <sup>26</sup> 1997	Yes*	Yes	NA	NA	NA	Liver damage or other pathology for which abstinence is recommended	Yes	NA	MALT ≥11
McIntosh et al, <sup>41</sup> 1997	NA	NA	NA	NA	NA	NA	NA	NA	NA
Senft et al, <sup>44</sup> 1997	Yes	NA	NA	Yes	NA	NA	NA	NA	AUDIT >21
Burge et al, <sup>27</sup> 1997	NA	Yes	NA	NA	If in treatment	NA	NA	NA	NA
Cordoba et al, <sup>28</sup> 1998	NA	NA	NA	NA	NA	Pathology or treatment >3 mo that suggests alcohol abstinence	NA	If for ≥2 y	CAGE score >1, exclusively weekend drinkers
Project GOAL, <sup>31</sup> 1999	Yes	Yes	>600 g /wk	NA	NA	NA	Suicidal ideation	If in previous 3 mo	NA
Ockene et al, <sup>42</sup> 1999	Yes	NA	NA	NA	Yes	NA	Yes	NA	NA
Aalto et al, <sup>23,24</sup> 2000-2001	Yes	Yes	NA	NA	NA	Severe disease	Yes	NA	Positive CAGE because of earlier heavy drinking but who had now stopped or reduced
Vinson and Devera-Sales, <sup>46</sup> 2000	Yes	Yes	NA	Yes	If in treatment or if treatment scheduled	NA	Yes	NA	NA
Maisto et al, <sup>39</sup> 2001	Yes	Including AA	NA	NA	Yes	NA	Unstable psychiatric status	NA	NA
Huas et al, <sup>36</sup> 2002	Yes	Yes	NA	NA	NA	NA	NA	NA	MAST ≥3

Abbreviations: See Table 1; AA, Alcoholics Anonymous; MALT, Munich Alcoholism Test.  
\*A MALT result of 11 or more indicated alcohol dependence.

in 1 study.<sup>28</sup> The forest plot of the effect sizes observed in the 12 trials and sub-trials included in the meta-analysis is shown in **Figure 2**. Based on follow-up observations without adjustment for dropout, the overall pooled effect size of the trials consisted of a net change of -50 g of ethanol (about 5 drinks) per week (95% CI, -65 to -34). In relative terms, this net change of

-50 g of ethanol corresponds to an additional relative mean reduction of 15% in alcohol consumption when the intervention groups (relative mean reduction, 34%) are compared with the control groups (relative mean reduction, 19%). When only trials for which intention-to-treat analysis was possible are considered, the unadjusted pooled effect size was similar (-47 g/wk; 95%

CI, -62 to -31 g/wk) and the adjusted effect size after correction for lost subjects was smaller (-38 g/wk; 95% CI, -51 to -24 g/wk) yet still significantly different from 0. Between-studies heterogeneity in effect size was not significant according to the Cochran  $\chi^2$  test ( $Q_{12} = 15.1, P = .24$ ). The measure of heterogeneity recommended by Higgins et al<sup>20</sup> indicated a low level of

**Table 3. Characteristics of Interventions**

Resource	Intervention in Study Groups: Length, min, and Presence of Repeated Intervention or Booster Session				Provider (Principal)	Written Material*
	Control	BAI1	BAI2	BAI3		
Heather et al, <sup>35</sup> 1987	UC	5	Time?	NA	GP	BAI2
Acuda, <sup>25</sup> 1992	UC	5	Probably 15-20	NA	Psychologists, social workers, advanced medical students	BAI1, BAI2
Machona, <sup>38</sup> 1992	UC	5	Probably 15-20	BAI2 + general health counseling	Nurse	BAI1, BAI2
Seppa, <sup>45</sup> 1992	UC	Time?†	NA	NA	GP	No
Richmond et al, <sup>43</sup> 1995	UC	5	15-20†	NA	GP	BAI1, BAI2
Israel et al, <sup>37</sup> 1996	≤5	30†	NA	NA	Nurse	Control, BAI1
Fernandez San Martin et al, <sup>29</sup> 1997	UC	10	NA	NA	GP	BAI1
Project TrEAT, <sup>30,32,33,40</sup> 1997-2002	UC	15†	NA	NA	GP	Control, BAI1
Altisent et al, <sup>26</sup> 1997	≤5	5†	NA	NA	GP	BAI1
McIntosh et al, <sup>41</sup> 1997	≤5	30†	30†	NA	Physician (BAI1) or nurse (BAI2)	Control, BAI1, BAI2
Senft et al, <sup>44</sup> 1997	UC	15	NA	NA	Researchers (training in motivational interviewing)	No
Burge et al, <sup>27</sup> 1997	UC	10-15	90†	BAI1 + BAI2	GP	No
Cordoba et al, <sup>28</sup> 1998	≤5	15	NA	NA	GP	BAI1
Project GOAL, <sup>31</sup> 1999	UC	15†	NA	NA	GP	Control, BAI1
Ockene et al, <sup>42</sup> 1999	UC	5-10	NA	NA	Physician and nurse practitioner	Control, BAI1
Aalto et al, <sup>23,24</sup> 2000-2001	≤5	10-20† (3 times)	10-20† (7 times)	NA	GP	BAI1, BAI2
Vinson and Devera-Sales, <sup>46</sup> 2000	UC	Time?	NA	NA	Computer	No
Maisto et al, <sup>39</sup> 2001	≤5	10-15	30-45†	NA	Trained interventionist	No
Huas et al, <sup>36</sup> 2002	UC	5	NA	NA	GP	No

Abbreviations: See Table 1; BAI, brief alcohol intervention group; UC, usual care without explicit mention of advice regarding alcohol use, or no intervention.

\*Written material (self-help booklet, general health booklet, "how to cut down" booklet) varied across studies and groups.

†Repeated intervention or booster session.

heterogeneity accounting for about one fourth of the total variance in outcome ( $I^2=25.8\%$ ). In the intention-to-treat analysis, the heterogeneity was smaller ( $Q_{11}=6.7, P=.82; I^2=0\%$ ).

There was no evidence of publication bias according to either the Begg and Mazumdar adjusted rank correlation test ( $P$  for null bias = .58) or the Egger regression asymmetry test ( $P=.66$ ). Although no correlation was found between the publication year of the studies and effect size by meta-regression ( $P=.85$ ), a significantly greater effect size was found in trials published after 1996 than in those published earlier (effect,  $-54.8$  vs  $6.6; P=.02$ ). Cumulative meta-analysis according to date of publication (**Figure 3**) clearly displays this time trend in scientific evidence from absence of ef-

fects toward statistically significant favorable effects of BAI.

There was no linear association between effect size and quality scores according to meta-regression using quality scores as an explanatory variable (per protocol analysis,  $P=.31$ ). However, all high-quality trials (score  $>10$ ) were from the United States, and baseline BAI mean alcohol consumption was less than 300 g/wk. By contrast, all low-quality trials were not from the United States and baseline BAI mean alcohol consumption was greater than 300 g/wk. The heterogeneity was higher among low-quality studies ( $Q=12.8; P=.08; I^2=82.9\%$ ) than among high-quality studies ( $Q=2.1; P=.71; I^2=0\%$ ). Meta-regression models showed that the correlation between mean alcohol consumption at baseline and effect size was weak ( $P=.71$ ) in high-

quality trials, but very strong ( $P<.001$ ) in low-quality studies. When both a dichotomous indicator of low vs high quality and the initial drinking level were included in meta-regression, each variable had an independent and significant contribution to effect size. A high-quality study increased effect size by an additional reduction of  $-110$  g/wk (95% CI,  $-208$  to  $-11$  g/wk;  $P<.03$ ) in alcohol consumption at follow-up, while each increment of 10 g/wk in mean alcohol consumption at baseline corresponded to an additional reduction of  $-6.0$  g/wk (95% CI,  $-11.3$  to  $-0.6$  g/wk;  $P=.03$ ) at follow-up. These 2 variables explained about 67% of the between-trials heterogeneity in effect size.

Meta-regression on intervention modalities (type of provider, duration, motivational technique used,

**Table 4. Sample Size, Response Rate to Follow-up, Follow-up Period, Methodologic Score, and Reported Effects of Included Studies**

Study, y	No. of Patients Randomized	Response Rate to Follow-up, %	Maximal Duration of Follow-up, mo	Methodologic Quality*	Effect of Intervention (Overall)†
Heather et al, <sup>35</sup> 1987	104	87.5	6	9	-
Acuda, <sup>25</sup> 1992	203	31.5	6	8	-
Machona, <sup>38</sup> 1992	129	92.0	6	9	-
Seppa, <sup>45</sup> 1992	178	53.4	12	7	-
Richmond et al, <sup>43</sup> 1995	378‡	69.0	12	6	-
Israel et al, <sup>37</sup> 1996	105	70.0	12	10	Yes
Fernandez San Martin et al, <sup>29</sup> 1997	152	57.9	6-18	8	-
Project TrEAT, <sup>30,32,33,40</sup> 1997-2002	774	83.0	48	14	Yes
Altisent et al, <sup>26</sup> 1997	139	46.0	12	8	Yes
McIntosh et al, <sup>41</sup> 1997	159	89.9	12	9	-
Senft et al, <sup>44</sup> 1997	516	80.2	12	13	-
Burge et al, <sup>27</sup> 1997	279	77.3	18	10	-
Cordoba et al, <sup>28</sup> 1998	499§	45.9	12	9	Yes
Project GOAL, <sup>31</sup> 1999	158	92.4	12	11	Yes
Ockene et al, <sup>42</sup> 1999	530§	90.8	6	13	Yes
Aalto et al, <sup>23,24</sup> 2000-2001 (M/F)	296/118	68.2/66.1	36	7	-
Vinson and Devera-Sales, <sup>46</sup> 2000	80	86.0	12	12	-
Maisto et al, <sup>39</sup> 2001	301	83.0	12	14	Yes
Huas et al, <sup>36</sup> 2002	541§	77.0	12	5	-

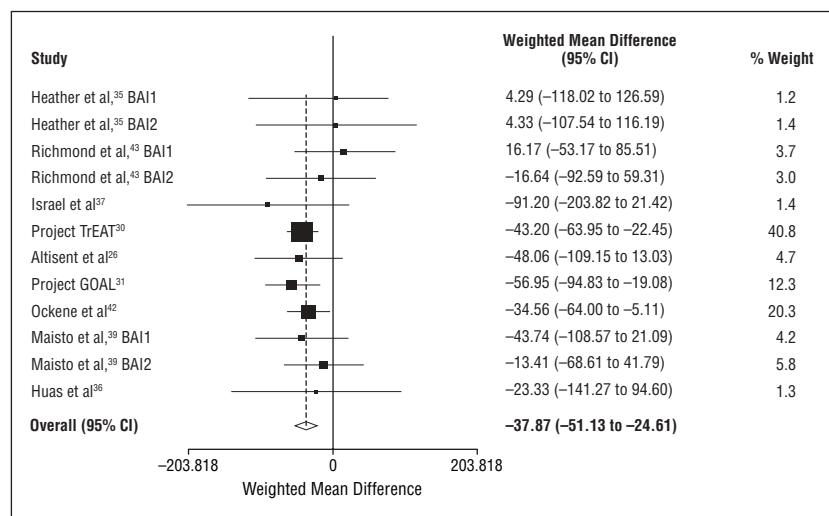
Abbreviations: See Table 1.

\*Maximum score, 18. Higher score means higher quality.

†Overall efficacy in favor of brief intervention group (yes) compared with control group contrasted with mainly not significant or inconclusive differences in reported outcomes (-).

‡Not randomized at individual level; alternate groups in weekly blocks.

§The unit of allocation is not the patient; cluster randomization.



**Figure 2.** Mean differences between brief alcohol intervention (BAI) and control groups in alcohol consumption: intention-to-treat results and meta-analysis. All weighted mean differences were calculated on an intention-to-treat basis (see "Methods" section). BAI indicates brief alcohol intervention; CI, confidence interval; GOAL, Guiding Older Adult Lifestyles; and TrEAT, Trial for Early Alcohol Treatment. Squares indicate means (size of square is related to size of the study); limit lines, 95% CIs.

written material, and repeated intervention) showed only a minor impact on effect size.

Eight studies used laboratory values as indicators of reduction in alcohol use, including 7 with  $\gamma$ -glutamyltransferase,<sup>23,24,26,27,35-37,43</sup> 5 with mean corpuscular volume,<sup>23,24,27,35,36,45</sup> 3 with aspartate aminotransferase and

alanine aminotransferase,<sup>23,24,26,27</sup> and 1 with carbohydrate-deficient transferrin.<sup>23,24</sup> Two trials<sup>26,37</sup> reported a statistically significant difference in improvement of  $\gamma$ -glutamyl transferase values between BAI and control groups. One reported an improvement of aspartate aminotransferase<sup>27</sup> and one an improvement of

alanine aminotransferase.<sup>23</sup> The remaining studies failed to report a significant effect of BAI on laboratory values compared with control groups.

Three studies<sup>32-34,37</sup> reported health care utilization measures to test the impact of BAI on health care costs. In an analysis conducted in a subsample of 29 patients, Israel et al<sup>37</sup> found a lower number of medical visits by the BAI group than the control group. In Project TrEAT, self-reports by patients indicated no significant group differences in emergency department visits during 6 and 12 months after BAI. However, there were significantly fewer emergency department visits at 48 months and fewer hospital days in the BAI group at 6, 12, and 48 months.<sup>33</sup> Freeborn et al,<sup>34</sup> using an administrative database from a health maintenance organization, found no significant differences in health care utilization during the 2 years after BAI. Fleming et al<sup>32,33</sup> performed a cost-benefit analysis, where the benefits of reduced hospitalizations, reduced emergency department visits, and reduced motor vehicle or criminal events were put in monetary terms and then compared with the overall cost of the screening, assessment, and inter-

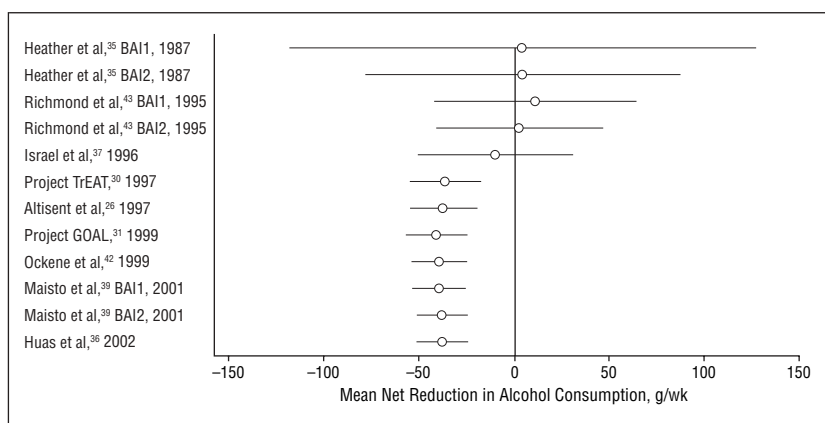
vention. Project TrEAT showed a benefit-cost ratio for brief alcohol intervention of 4.3:1 from a medical perspective and 39:1 from a societal perspective. The net benefits per intervention patient are \$546 from a medical perspective and \$7780 from a societal perspective (US dollars, 1993).

Nine studies<sup>23-27,35,37,38,43,46</sup> reported data related to mental or physical health perception status, well-being, and alcohol-related problems. There were significant differences among 9 of the 21 measures reported, showing an improved or better quality of life in the BAI group than the control group. Group differences in the other 12 measures were not significant. One study<sup>33</sup> examined mortality and found a significant reduction in the number of deaths at 36 months ( $P < .05$ ) in the BAI vs the control group. This effect disappeared by 48 months.

## COMMENT

We selected 19 trials for this systematic review of the effects of BAI on at-risk drinkers in primary care. The important feature of this review was the selective inclusion of patients who came actively to receive usual primary health care. Except for alcohol consumption, we chose not to pool data. Laboratory results, health care utilization outcomes, and mortality results were reported in only a few studies. The definitions and measures of outcomes such as binge drinking, well-being, and problems related to alcohol drinking were too heterogeneous to allow results to be pooled.

Our systematic review and meta-analysis indicated that BAI is effective for both men and women in reducing alcohol consumption at 6 and 12 months. This is supported by the homogeneity of selected studies and by the clear effect shown in studies of high quality. In the study with the longest follow-up period, this effect was also reported 36 and 48 months after BAI when a cumulative analysis was performed.<sup>33</sup> This is consistent with the results of previously conducted systematic reviews that examined the efficacy of BAI conducted in various settings<sup>5,7-9,11,50</sup> and reported compa-



**Figure 3.** Cumulative meta-analysis according to date of publication, using intention-to-treat results (see "Methods" section). BAI indicates brief alcohol intervention; GOAL, Guiding Older Adult Lifestyles; and TrEAT, Trial for Early Alcohol Treatment.

able effect sizes. Among the published systematic reviews of BAI, 1 focused partially on primary care but did not conclude that BAI was effective because statistical heterogeneity existed among studies.<sup>10</sup> Several trials conducted in primary care have been published after its completion. Our review focused strictly on primary care, and this restriction might explain why we did not find statistical heterogeneity among studies. A cumulative meta-analysis according to date of publication demonstrated that the BAI effects have shown significance since 1997, which could explain the uncertain results reported in the meta-analysis conducted by Poikolainen.<sup>10</sup> Beich et al.<sup>14</sup> recently published a systematic review and meta-analysis of the effectiveness of screening in brief intervention trials conducted in general practice. Most of the focus was on the effectiveness of screening, but they assessed some effects of intervention as well. They reported that only 2 or 3 patients per 1000 screened benefited from BAI, but it seems important to point out that their research was not designed primarily to evaluate the efficacy of BAI but rather to assess the screening process; thus, their conclusions about BAI should be interpreted with caution. All of the studies selected by these authors were also evaluated for suitability in the present work; some were excluded mainly because of the recruitment method.

In April 2004, the US Preventive Services Task Force recommended screening and behavioral counseling interventions to reduce alcohol misuse by adults in primary care settings<sup>51</sup> (grade B recommendation).

The present work is consistent with their recommendations. Our meta-analytic approach adds to the extended systematic review presented by the Preventive Services Task Force.

Despite these recommendations, questions remain about the effectiveness of such interventions in daily practice. In addition to difficulties related to motivating and training physicians to perform BAI, another major challenge for BAI implementation is to find an optimal and practical way to screen. Many validated screening tools have been used for research purposes (AUDIT [Alcohol Use Disorder Identification Test], CAGE [see Table 1 for the CAGE questions], and quantity-frequency questions, as well as specific questionnaires for pregnant women), but these tools are difficult to use in a primary care practice.<sup>13,14</sup> The Preventive Services Task Force did not recommend a specific approach for screening.<sup>51</sup> Routine implementation of screening and BAI requires specific strategies (eg, promoting understanding of and adherence to the BAI concept, interactive sessions to improve practice skills, computer-based decisions aids, interventions conducted in the waiting room or by physician assistants). The difficulties of tailoring and disseminating such strategies are being addressed by ongoing initiatives.<sup>52-54</sup>

Among the 7 studies that reported significant improvement in BAI groups compared with control groups, all but 1 reported an intervention lasting between 5 and 15 minutes. Similarly, all but 1 reported the use of written material and proposed a repeated intervention,

either routinely or after a decision by the patient. Thus, it appears that BAI lasting from 5 to 15 minutes, accompanied by written material and the opportunity for the patient to schedule a follow-up visit, has the potential to significantly reduce alcohol consumption compared with either no intervention, usual care, or less than 5 minutes of intervention.

No evidence of the influence of BAI on laboratory values was observed. The low sensitivity of these tests in a sample of principally non-alcohol-dependent primary care patients and the low response of these tests to moderate reductions in alcohol consumption<sup>55-57</sup> are consistent with our results. Indeed, the use of laboratory values as markers of alcohol consumption was progressively abandoned in more recent trials. The use of BAI seems to reduce health care utilization, but these results were obtained only for health maintenance organization-affiliated patients and thus are not to be generalized to the whole primary care population.<sup>32-34,37</sup> In terms of economic analysis, a favorable benefit-cost ratio for BAI was observed. However, this finding comes from 1 study only, although the largest in our selection. Further research is then needed to evaluate this question more precisely and in various environments. There is scant evidence of the efficacy of brief interventions on morbidity, mortality, and quality-of-life measures. Most studies were not aimed at measuring outcomes by using large sample sizes with longer follow-up intervals; an exception was Project TrEAT, which demonstrated a significant reduction in mortality in its BAI groups.<sup>33</sup> The postulate of BAI reducing morbidity and mortality is suggested by the success of BAI in reducing alcohol consumption coupled with actual knowledge of morbidity and mortality associated with alcohol consumption.<sup>2</sup>

Three intervention models appeared to have inspired most of the selected interventions. All of them included feedback and advice components, which is consistent with analyses conducted by Bien et al,<sup>5</sup> but they differed in other components and in the style of relationship between patient and provider. Further research is needed to investigate which com-

ponents of brief interventions present evidence of efficacy in the primary care setting.<sup>58</sup>

This study had certain limitations. Although our purpose was to focus on BAI applied to patients actively seeking primary health care, we still found heterogeneity between trials. The heterogeneity of BAI and the lack of detailed description reported limited the ability to identify key elements of efficacy. The lack of standardized control groups also limited comparison between studies. Furthermore, the concept of usual care used in many studies as the control group is probably highly variable between and within studies. Only a few authors have described the training of providers or tried to enhance the homogeneity of interventions by practicing role playing and by video recording the interventions. Whether the therapeutic procedures were carried out as intended was not assessed; thus, it is difficult to ascertain whether any of the described interventions were delivered effectively. The greater homogeneity found in the US studies might be explained by more homogeneous drinking habits and greater consensus about risk levels related to alcohol use and similar inclusion criteria. Methodologic quality was a significant determinant of success after correction for baseline alcohol consumption. Most studies reported a 10% to 30% reduction in alcohol consumption in the control group. This could be due to regression to the mean, to a minimal or quasi-intervention given to control groups, to the proper effect of an assessment centered on alcohol consumption, to a Hawthorn effect, or to the natural course of changes in alcohol use. Contamination could have occurred if providers changed their approach to at-risk drinkers and delivered a quasi-intervention to patients included in the control group. Project GOAL (Guiding Older Adult Lifestyles) is the only trial in which there was no reduction in alcohol use in the control group,<sup>31</sup> but the reason is unclear.

Our results are also restricted by the limitations of the selected studies themselves. In such preventive interventions, double-blind studies are very difficult to implement. The nonvalidated quality scores used to rank the study quality were significantly related to more positive re-

sults of intervention. This finding is dissimilar to those of studies in other areas of research that demonstrated that studies of lower quality were more likely to report positive results.<sup>22</sup> Our findings might be explained by larger effects of contamination within the studies of lower quality. However, collinearity between several different factors (baseline alcohol consumption, study quality, and studies conducted in the United States) precluded us from verifying this hypothesis.

We tried to reduce selection bias as much as possible by reviewing all articles independently and in duplicate. We did not constrain the literature search to any specific language and thus were less prone to language bias; however, no searches in Grey Literature databases could be performed. We may have overlooked some potentially eligible studies during the selection process.

We conclude that BAI aimed at reducing alcohol consumption is effective in primary care settings on the basis of studies that approximate usual practice and are similar in terms of patient context and statistical homogeneity. The typical effective BAI takes no more than 15 minutes, is accompanied by written material, and offers an opportunity for the patient to schedule a follow-up. Positive effects seem to be sustained beyond a year and can last for as long as 48 months. This finding should encourage further research aimed at determining more precisely the components of efficacy and the relationship of BAI to morbidity, mortality, and quality-of-life-related outcomes. Efforts should be sustained to continue the implementation and evaluation of BAI programs.

**Accepted for Publication:** September 22, 2004.

**Correspondence:** Bernard Burnand, MD, MPH, Rue du Bugnon 17, CH-1011 Lausanne, Switzerland (Bernard.Burnand@chuv.ch).

**Funding/Support:** This study was supported by the Clinical Epidemiology Center and the Alcohol Treatment Center, University Hospital, Lausanne, Switzerland.

**Acknowledgment:** We thank Muriel Gaulis and Alexis Rohrbach, MD, for their help in data extraction and Spanish translation, and the au-

thors of the examined studies who provided additional information related to their studies.

## REFERENCES

1. Reid MC, Fiellin DA, O'Connor PG. Hazardous and harmful alcohol consumption in primary care. *Arch Intern Med*. 1999;159:1681-1689.
2. McGinnis JM, Foege WH. Mortality and morbidity attributable to use of addictive substances in the United States. *Proc Assoc Am Physicians*. 1999;111:109-118.
3. National Institute on Alcohol Abuse and Alcoholism. *Eighth Special Report of the US Congress on Alcohol and Health*. Rockville, Md: National Institutes of Health; 1993.
4. Ashenden R, Silagy C, Weller D. A systematic review of the effectiveness of promoting lifestyle change in general practice. *Fam Pract*. 1997;14:160-176.
5. Bien TH, Miller WR, Tonigan JS. Brief interventions for alcohol problems: a review. *Addiction*. 1993;88:315-335.
6. D'Onofrio G, Degutis LC. Preventive care in the emergency department: screening and brief intervention for alcohol problems in the emergency department: a systematic review. *Acad Emerg Med*. 2002;9:627-638.
7. Dunn C, Deroo L, Rivara FP. The use of brief interventions adapted from motivational interviewing across behavioral domains: a systematic review. *Addiction*. 2001;96:1725-1742.
8. Kahan M, Wilson L, Becker L. Effectiveness of physician-based interventions with problem drinkers: a review. *CMAJ*. 1995;152:851-859.
9. Moyer A, Finney JW, Swearingen CE, Vergun P. Brief interventions for alcohol problems: a meta-analytic review of controlled investigations in treatment-seeking and non-treatment-seeking populations. *Addiction*. 2002;97:279-292.
10. Poikolainen K. Effectiveness of brief interventions to reduce alcohol intake in primary health care populations: a meta-analysis. *Prev Med*. 1999;28:503-509.
11. Wilk AI, Jensen NM, Havighurst TC. Meta-analysis of randomized control trials addressing brief interventions in heavy alcohol drinkers. *J Gen Intern Med*. 1997;12:274-283.
12. The World Health Organization Project in identification and management of alcohol related problems in primary care: phase IV. Available at: <http://www.who-alcohol-phaseiv.net>. Accessed March 9, 2005.
13. Beich A, Gannik D, Malterud K. Screening and brief intervention for excessive alcohol use: qualitative interview study of the experiences of general practitioners. *BMJ*. 2002;325:870.
14. Beich A, Thorsen T, Rollnick S. Screening in brief intervention trials targeting excessive drinkers in general practice: systematic review and meta-analysis. *BMJ*. 2003;327:536-542.
15. Ferri M, Davoli M, Ali R, et al. Cochrane Drugs and Alcohol Group [Cochrane Review on CD-ROM]. Oxford, England: Cochrane Library, Update Software; 2002;issue 3.
16. Altman DG, Schulz KF, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med*. 2001;134:663-694.
17. Jüni P, Altman DG, Egger M. Assessing the quality of randomised controlled trials. In: Egger M, Smith GD, Altman DG, eds. *Systematic Reviews in Health Care: Meta-analysis in Context*. 2nd ed. London, England: BMJ Books; 2001:87-108.
18. Babor TF, Higgins-Biddle JC. *Brief Intervention for Hazardous and Harmful Drinking: A Manual for Use in Primary Care*. Geneva, Switzerland: Department of Mental Health and Substance Dependence, World Health Organization; 2001.
19. Dufour MC. What is moderate drinking? defining "drinks" and drinking levels. *Alcohol Res Health*. 1999;23:5-14.
20. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analysis. *BMJ*. 2003;327:557-560.
21. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics*. 1994;50:1088-1101.
22. Egger M, Smith GD, Altman DB. Systematic reviews in health care: meta-analysis in context. In: *Assessing the Quality of Randomised Controlled Trials*. 2nd ed. London, England: BMJ Books; 2001.
23. Aalto M, Saksanen R, Laine P, et al. Brief intervention for female heavy drinkers in routine general practice: a 3-year randomized, controlled study. *Alcohol Clin Exp Res*. 2000;24:1680-1686.
24. Aalto M, Seppa K, Mattila P, et al. Brief intervention for male heavy drinkers in routine general practice: a three-year randomized controlled study. *Alcohol Alcohol*. 2001;36:224-230.
25. Acuda W. Nairobi, Kenya. In: Babor TF, Grant M, eds. *Project on Identification and Management of Alcohol-Related Problems Report on Phase II: A Randomized Clinical Trial of Brief Intervention in Primary Care*. Geneva, Switzerland: World Health Organization; 1992:113-127.
26. Altisent R, Cordoba R, Delgado MT, et al. Multi-center study on the efficacy of advice for the prevention of alcoholism in primary health care [in Spanish]. *Med Clin (Barc)*. 1997;109:121-124.
27. Burge SK, Amodoi N, Elkin B, et al. An evaluation of two primary care interventions for alcohol abuse among Mexican-American patients. *Addiction*. 1997;92:1705-1716.
28. Cordoba R, Delgado MT, Pico V, et al. Effectiveness of brief intervention on non-dependent alcohol drinkers (EBIAL): a Spanish multi-centre study. *Fam Pract*. 1998;15:562-568.
29. Fernandez San Martin MI, Bermejo Caja CJ, Alonso Perez M, et al. Effectiveness of brief medical counseling to reduce drinkers' alcohol consumption [in Spanish]. *Aten Primaria*. 1997;19:127-132.
30. Fleming MF, Barry KL, Manwell LB, Johnson K, London R. Brief physician advice for problem alcohol drinkers: a randomized controlled trial in community-based primary care practices. *JAMA*. 1997;277:1039-1045.
31. Fleming MF, Manwell LB, Barry KL, Adams W, Stauffacher EA. Brief physician advice for alcohol problems in older adults: a randomized community-based trial. *J Fam Pract*. 1999;48:378-384.
32. Fleming MF, Mundt MP, French MT, Manwell LB, Stauffacher EA, Barry KL. Benefit-cost analysis of brief physician advice with problem drinkers in primary care settings. *Med Care*. 2000;38:7-18.
33. Fleming MF, Mundt MP, French MT, Manwell LB, Stauffacher EA, Barry KL. Brief physician advice for problem drinkers: long-term efficacy and benefit-cost analysis. *Alcohol Clin Exp Res*. 2002;26:36-43.
34. Freeborn DK, Polen MR, Hollis JF, Senft RA. Screening and brief intervention for hazardous drinking in an HMO: effects on medical care utilization. *J Behav Health Serv Res*. 2000;27:446-453.
35. Heather N, Campion PD, Neville RG, Maccabe D. Evaluation of a controlled drinking minimal intervention for problem drinkers in general practice (the DRAMS scheme). *J R Coll Gen Pract*. 1987;37:358-363.
36. Huas D, Pessione F, Bouix JC, Demeaux JL, Allemant H, Rueff B. Efficacité à un an d'une intervention brève auprès des consommateurs d'alcool à problèmes. *Rev Prat Med Gen*. 2002;16:1343-1348.
37. Israel Y, Hollander O, Sanchez-Craig M, et al. Screening for problem drinking and counseling by the primary care physician-nurse team. *Alcohol Clin Exp Res*. 1996;20:1443-1450.
38. Machona AM. Harare, Zimbabwe. In: Babor TF, Grant M, eds. *Project on Identification and Management of Alcohol-Related Problems Report on Phase II: A Randomized Clinical Trial of Brief Intervention in Primary Care*. Geneva, Switzerland: World Health Organization; 1992:211-220.
39. Maisto SA, Conigliaro J, McNeil M, Kraemer K, Conigliaro RL, Kelley ME. Effects of two types of brief intervention and readiness to change on alcohol use in hazardous drinkers. *J Stud Alcohol*. 2001;62:605-614.
40. Manwell LB, Fleming MF, Mundt MP, Stauffacher EA, Barry KL. Treatment of problem alcohol use in women of childbearing age: results of a brief intervention trial. *Alcohol Clin Exp Res*. 2000;24:1517-1524.
41. McIntosh MC, Leigh G, Baldwin NJ, Marmulak J. Reducing alcohol consumption: comparing three brief methods in family practice. *Can Fam Physician*. 1997;43:1959-1962, 1965-1967.
42. Ockene JK, Adams A, Hurley TG, Wheeler EV, Hebert JR. Brief physician- and nurse practitioner-delivered counseling for high-risk drinkers: does it work? *Arch Intern Med*. 1999;159:2198-2205.
43. Richmond R, Heather N, Wodak A, Kehoe L, Webster I. Controlled evaluation of a general practice-based brief intervention for excessive drinking. *Addiction*. 1995;90:119-132.
44. Senft RA, Polen MR, Freeborn DK, Hollis JF. Brief intervention in a primary care setting for hazardous drinkers. *Am J Prev Med*. 1997;13:464-470.
45. Seppa K. Intervention in alcohol abuse among macrocytic patients in general practice. *Scand J Prim Health Care*. 1992;10:217-222.
46. Vinson DC, Devera-Sales A. Computer-generated written behavioral contracts with problem drinkers in primary medical care. *Subst Abuse*. 2000;21:215-222.
47. Miller WR, Rollnick S. *Motivational Interviewing: Preparing People to Change Addictive Behavior*. New York, NY: Guilford Press; 1991.
48. Sanchez-Craig M. Brief didactic treatment for alcohol and drug-related problems: an approach based on client choice. *Br J Addict*. 1990;85:169-177.
49. Wallace P, Cutler S, Haines A. Randomised controlled trial of general practitioner intervention in patients with excessive alcohol consumption. *BMJ*. 1988;297:663-668.
50. Ballesteros J, Arino J, Gonzalez-Pinto A, Querejeta I. Effectiveness of medical advice for reducing excessive alcohol consumption: meta-analysis of Spanish studies in primary care [in Spanish]. *Gac Sanit*. 2003;17:116-122.
51. US Preventive Services Task Force. Screening and behavioral counseling interventions in primary care to reduce alcohol misuse: recommendation statement. *Ann Intern Med*. 2004;140:554-556.
52. Kaner EF, Lock CA, McAvoy BR, Heather N, Gilvarry EA. RCT of three training and support strategies to encourage implementation of screening and brief alcohol intervention by general practitioners. *Br J Gen Pract*. 1999;49:699-703.
53. Babor TF, Higgins-Biddle JC. Alcohol screening and brief intervention: dissemination strategies for medical practice and public health. *Addiction*. 2000;95:677-686.
54. Babor TF, Higgins-Biddle JC, Higgins PS, Gassman RA, Gould BE. Training medical providers to conduct alcohol screening and brief interventions. *Subst Abuse*. 2004;25:17-26.
55. Aithal GP, Thornes H, Dwarakanath AD, Tanner AR. Measurement of carbohydrate-deficient transferrin (CDT) in a general medical clinic: is this test useful in assessing alcohol consumption? *Alcohol Alcohol*. 1998;33:304-309.
56. Reynaud M, Schellenberg F, Loiseux-Meurier MN, et al. Objective diagnosis of alcohol abuse: compared values of carbohydrate-deficient transferrin (CDT),  $\gamma$ -glutamyl transferase (GGT), and mean corpuscular volume (MCV). *Alcohol Clin Exp Res*. 2000;24:1414-1419.
57. Sillanaukee P, Aalto M, Seppa K. Carbohydrate-deficient transferrin and conventional alcohol markers as indicators for brief intervention among heavy drinkers in primary health care. *Alcohol Clin Exp Res*. 1998;22:892-896.
58. Heather N. Brief alcohol interventions have expanded in range but how they work is still mysterious. *Addiction*. 2003;98:1025-1026.