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Effectiveness and cost-effectiveness of a stepped care intervention for alcohol use disorders in primary care: pilot study

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Background
Screening for alcohol use disorders identifies a wide range of needs, varying from hazardous and harmful drinking to alcohol dependence. Stepped care offers a potentially resource-efficient way of meeting these needs, but requires evaluation in a randomised controlled trial.

Aims
To evaluate the feasibility, effectiveness and cost-effectiveness of opportunistic screening and a stepped care intervention in primary care.

Method
A total of 1794 male primary care attendees at six practices in South Wales were screened using the Alcohol Use Disorders Identification Test (AUDIT). Of these, 112 participants who scored 8 or more on the AUDIT and who consented to enter the study were randomised to receive either 5 minutes of minimal intervention delivered by a practice nurse (control group) or stepped care intervention consisting of three successive steps (intervention group): a single session of behaviour change counselling delivered by a practice nurse; four 50-minute sessions of motivational enhancement therapy delivered by a trained alcohol counsellor; and referral to a community alcohol treatment agency.

Results
Both groups reduced alcohol consumption 6 months after randomisation with a greater, although not significant, improvement for the stepped care intervention. Motivation to change was greater following the stepped care intervention. The stepped care intervention resulted in greater cost savings compared with the minimal intervention.

Conclusions
Stepped care was feasible to implement in the primary care setting and resulted in greater cost savings compared with minimal intervention.

Declaration of interest
None.

Alcohol use disorders generate considerable cost to society and the health system in particular. In the UK it is estimated that alcohol use disorders are linked to 22 000 premature deaths and cost the economy £20 billion annually.[1] A recent national alcohol needs assessment found that over 7 million adults in England are hazardous or harmful drinkers and a further 1.1 million are alcohol dependent.[2] Alcohol is a leading cause of morbidity and mortality, and reducing alcohol-related harm is a key priority of the UK government with publication of the *National Alcohol Harm Reduction Strategy*[3] and the *Choosing Health* White Paper.[4]

There are now 13 meta-analyses and/or systematic reviews of brief alcohol interventions, including five specifically focused on primary care.[5–9] The greatest evidence of efficacy is in populations identified in primary care settings. Overall, there is a 20–30% reduction in alcohol consumption following brief intervention compared with control conditions, and several studies have found significant reductions in healthcare utilisation in the brief intervention group. One review of 34 brief intervention studies indicates that brief interventions are only more effective than control conditions in people who drink excessively identified by opportunistic screening rather than in those seeking alcohol treatment.[10]

Among this wealth of positive evidence regarding efficacy there is also some ambivalence towards the effectiveness of brief interventions. Heather[11,12] suggests that brief interventions delivered in naturalistic settings would probably have smaller effects than efficacy studies tend to suggest. Edwards & Rollnick[13] suggest we should exercise some caution in generalising from efficacy studies to effectiveness. Studies of efficacy often have systematic biases associated with the population under study and tend to be an evaluation of an intervention delivered by motivated practitioners. An appropriate methodology for evaluating effectiveness should involve a pragmatic balance between internal and external validity providing a better indication of 'naturalistic effectiveness'. Howard[14] also noted the limitations in rigorous economic evaluations in the area of brief interventions – there is a clear need for pragmatic randomised clinical trials of brief interventions that address effectiveness and cost-effectiveness aspects of brief interventions.

A further problem with the research literature on brief interventions stems from the varying definitions of interventions used in different studies.[11,15] What is considered a brief intervention in one study is considered an extended intervention in another. A number of reviews and meta-analyses fail to take this intervention heterogeneity into account.[11,16]

Screening for alcohol use disorders identifies a wide range of needs, varying from hazardous and harmful drinking to severe alcohol dependence, that are likely to require a range of types and intensities of treatment. Stepped care interventions offer a potentially resource-efficient means of meeting the needs of individuals in more severe cases. Stepped care provides a means of delivering high-intensity and more costly interventions only to those who fail to benefit from less intensive interventions, more in keeping with the way clinical care is typically delivered than the application of blanket brief interventions. Further, evidence from surveys of primary care practitioners highlights a reluctance to implement brief interventions, in part because they lack the skills to deal with the more severe cases identified.[17] Stepped care

approaches have gained acceptance in the smoking cessation field,[18,19] as well as other areas of medicine such as hypertension treatment, but they also represent an important development in the alcohol treatment field.[20,21]

Stepped care provides a pragmatic clinical algorithm that addresses the needs of a spectrum of alcohol use disorders and provides appropriate interventions for those who fail to benefit from brief interventions. This is a pragmatic pilot study to assess the feasibility, effectiveness and cost-effectiveness of a stepped care alcohol intervention in primary care comparing stepped care with brief interventions alone.

Method

Study design

A prospective pragmatic randomised controlled trial in which eligible consenting participants where randomised with equal probability to either stepped care or minimal intervention. Randomisation was conducted remote from the research centres by the trial randomisation service at the University of York. Block randomisation with seeded random elements was used to minimise the possibility of subversion. Follow-up was conducted at 6 months post-randomisation by a researcher masked to the allocated group.

Sample size

The closest study of opportunistic screening and intervention in a UK primary care population is that of Wallace *et al*.[22] In this study the standardised effect size between intervention and control was 0.36 for males. To replicate this effect requires 177 participants to gain 80% power to detect a difference at the 5% significance level. Assuming that only 75% will be followed up at 6 months inflates this figure to 236, 118 in each randomised group. However, we managed to recruit 112 individuals in total in the time available. So this is best regarded as a pilot study to establish feasibility and to determine the effect size on which to power a larger study.

Participants

Participants were consecutive male attendees at six primary care practices in South Wales. Females were excluded since at the time of designing the trial meta-analyses suggested smaller effect sizes of brief alcohol interventions in women than in men, which would have required a much larger sample size than the funding for the study would allow. However, subsequent research suggests equivalence of outcomes in males and females, and our ongoing research (see below) includes both genders.

Eligible male patients were aged 18 years or more, had a self-completion Alcohol Use Disorders Identification Test (AUDIT)[23] score $\geqslant 8$ and/or a diagnosis of an alcohol use disorder assessed using ICD–10 criteria at baseline assessment (using the CIDI Alcohol Use Disorders interview[24] conducted by the research assessor) and/or were drinking above Department of Health guidelines for hazardous drinking as assessed by the Time Line Follow Back[25] measure of alcohol consumption (see below) (>21 units/week or >8 units/day), lived within commuting distance of the primary care practice, had not received treatment for an alcohol use disorder in the previous 180 days and were willing to consent to receive either treatment and take part in follow-up assessments.

Patients were not eligible if they had a primary drug dependence other than alcohol, suffered from a severe mental or physical illness, severe cognitive impairment or had legal issues that might have interfered with follow-up.

Procedure

Patients attending primary care practices were asked by a practice nurse to complete an AUDIT questionnaire embedded within a general lifestyle questionnaire, which was scored by the practice nurse. Any patient who scored 8 or more was then provided with an information sheet about the study and asked if they would consider taking part. Those willing to participate were offered an appointment with the research assessor within 1 week of screening.

At the initial research assessment, eligibility criteria were established and those eligible invited to consent to participation in the study. Those who were eligible and consented were randomised using the remote randomisation service at the University of York and allocated to either stepped care (intervention group) or minimal intervention (control group).

Six months after randomisation, patients were contacted by the research assessor, who made an appointment for a follow-up interview. The research assessor was masked to the patients' allocation.

Interventions

Control group

Patients received a 5-minute directive advice session from a practice nurse addressing the need for them to reduce their alcohol consumption. Patients also received a short self-help booklet outlining the consequences of excessive alcohol consumption and including details on where to seek help locally for alcohol problems.

Intervention group

Patients received a sequential series of interventions according to need and response after each successive step.

Step 1. All patients randomised to this group were offered a 40-minute session of behaviour change counselling[26] from a trained practice nurse. Each patient was invited for follow-up with the same nurse 28 days after the initial session. Patients who had consumed >21 units of alcohol in any one week or >10 units in any one day during the 28-day period were referred to step 2.

Step 2. All patients referred to step 2 were offered a maximum of four 50-minute sessions of motivational enhancement therapy[27] conducted by a trained alcohol counsellor. Sessions were held at the primary care practice and scheduled for one per week over a 4-week period. Each patient was invited for a follow-up with the practice nurse 28 days after the final session. Patients who had consumed >21 units in any one week or >10 units in any one day in the 28-day period were referred to step 3.

Step 3. Patients were referred to the local community alcohol team for specialist intervention. There was no limit on duration or intensity of treatment, which could encompass, where necessary, detoxification, in-patient treatment, out-patient counselling, relapse prevention and drug therapy. The clinical protocol included a caveat that any patient in the intervention group who needed urgent referral to step 3 at any stage could be referred without going through intermediate care steps.

Study measures

Primary outcome

The primary outcome measure was alcohol consumption as measured over 180 days using the Time Line Follow Back method.[25] This method generates three outcomes: total alcohol consumed in the period, mean number of drinks per drinking day and percentage of days abstinent.

Secondary outcomes

Motivation was measured using the Readiness to Change Questionnaire (RTCQ),[28] specifically designed to assess stages of change in opportunistic brief interventions for people who drink excessively. The 12-item RTCQ allocates scores for each of three stages of change: pre-contemplation, contemplation and action. Scores range from –10 (pre-contemplation) to +10 (action).

Alcohol dependence was measured using the Severity of Alcohol Dependence Questionnaire,[29] which addresses five components of alcohol dependence: physical withdrawal, affective withdrawal, withdrawal relief, alcohol consumption and rapidity of reinstatement. The instrument is self-completed and provides a severity score ranging from 0 (no dependence) to 60 (very severe dependence).

Alcohol-related problems were measured using the Alcohol Problems Questionnaire (APQ).[30] The APQ contains 44 items across eight problem domains (friends, money, police, physical, affective, marital, children and work). The first 23 items are applicable to all individuals and are referred to as the 'common' subscale. This subscale ranges from 0 (no problems) to 23 (many problems).

Self-efficacy was measured using the Situational Confidence Questionnaire.[31] This questionnaire assesses an individual's confidence to resist the urge to drink in a variety of situations. The overall score provides a range from 0 (not at all confident) to 100 (very confident).

Quality of life was measured using an established generic quality-of-life measure, the Short Form–12 (SF–12).[32] The SF–12 generates two component scores relating to physical and mental health. The scores are standardised and norm-based on UK populations. The scores range from 0 to 100 with a standardised population mean of 50.

Economic evaluation

The economic evaluation involved four different components: the costs of training; the costs of the interventions; changes in social costs; and changes in quality-adjusted life-years (QALYs). The costs of training and interventions were derived from therapist and participant take-up recorded at the time of the trial. Local costs of salaries, overheads and premises were used with the take-up data to estimate costs. We calculated participant social costs from a specifically designed questionnaire to ascertain healthcare, social care and accident-related service utilisation along with criminal offences committed 6 months prior to and 6 months after randomisation. Unit costs were derived from national references for service utilisation[33,34] and government sources for the cost of crime.[35] Health outcomes were assessed using QALYs using the EQ–5D at baseline and 6 months with population values.[36–38] The EQ–5D is a generic instrument that measures health on five scales (mobility, self-care, usual activities, pain and discomfort, anxiety and depression).

Analysis

Owing to the pragmatic design of the trial, analysis was conducted as an intention-to-treat analysis whereby participants were analysed according to the group they were allocated to rather than the treatment they received. Comparison between groups at 6 months was adjusted using analysis of covariance (ANCOVA) to take into account variability in corresponding baseline scores.

From the economic data we calculated the net costs of stepped care and minimal intervention (treatment costs less any difference in social costs at 6 months compared with baseline social costs). Quality-adjusted life-years were calculated for both interventions measuring the area under the curve joining the points at baseline and 6 months.[37] As economic data tend to be skewed, we used bootstrapping techniques to obtain more reliable confidence interval estimates. As the assumptions required to use analysis of covariance are not assumed to hold with these economic data, we followed the advice of Vickers,[39] who suggests that comparing baseline less follow-up values for both intervention groups is an acceptable alternative. We divided the differences in the net costs of interventions by the difference in QALY gains to yield the incremental cost-effectiveness ratio. We estimated the sampling distribution of this ratio from 1000 bootstrapped samples and derived cost-effectiveness acceptability curves.[40] These curves plot the resulting probability that one intervention is better than the other against the maximum decision makers might pay for an additional QALY.

Analysis was conducted using SPSS version 13 for Windows and STATA version 10 for Windows.

Results

Sample characteristics

A total of 1794 male primary care attenders were screened at six primary care practices in South Wales. All patients approached by the practice nurse completed the screening questionnaire. Of these, 447 (25%) scored positive for an alcohol use disorder (AUDIT $\geqslant 8$), all of whom met the eligibility criteria to take part in the study. Overall, 112 (25%) gave consent and were randomised: 54 to the intervention group and 58 to the control group. Those consenting to take part were older (mean 42.7 years *v.* 37.7 years) and had higher AUDIT scores (mean 13.7 *v.* 11.9). All participants randomised to the control group received minimal intervention and 96% (52/54) of those randomised to the intervention group received step 1. A further 31% (17/54) of the intervention group were referred on for step 2 and only one participant was referred on to step 3 for detoxification. In the latter case this occurred on presentation for step 1 because of symptoms of severe alcohol withdrawal.

Of those who were randomised, 81% were followed up at 6 months, 90% in the control group and 72% in the intervention group; Fig. 1 shows the full CONSORT diagram for the study. A total of 81% follow-up is acceptable for alcohol research studies.

The average age of participants was 43 years and they had drunk alcohol on average 62% of the previous 180 days, consuming on average 14 units of alcohol per drinking day (1 unit = 8 g ethanol). Both groups were evenly matched on demographics, primary and secondary outcomes at randomisation (Table 1).

Primary outcomes

At 6 months both groups had reduced their consumption considerably from baseline (Table 2). Greater reduction was observed in the intervention group in terms of total alcohol consumed

(−408.6 g *v.* −238.8 g) and drinks per drinking day (−2.4 *v.* −1.0) with an adjusted mean difference of 145.6 (95% CI −101.7 to 392.9) and 1.1 (−0.9 to 3.1) (Table 3) respectively. This difference was not significant at the 0.05 level, but the standardised effect sizes for drinks per drinking day and total alcohol consumed were comparable with previous studies of brief intervention (0.27 and 0.23 respectively).

Secondary outcomes

At 6 months both groups had a slight increase in attributes associated with precontemplation (intervention group 0.5 *v.* control group 0.5), contemplation (0.1 *v.* 0.1) and action (2.7 *v.* 0.8) stages of change. Adjusted analysis indicates that the mean difference between the groups showed that the control group had a greater level of precontemplation (–0.2; 95% CI –1.7 to 1.1) and contemplation (–0.3; 95% CI –1.7 to 1.1) but that the intervention group scored higher on action (1.8; 95% CI 0.2–3.3), which was significant at the 0.05 level.

Alcohol-related problems and dependence decreased and self-efficacy increased in both groups, but none of these was significantly different between groups. No significant differences in quality of life or mental health were seen between groups at follow-up.

Economic outcomes

The cost assumptions are shown in Table 4. In the control group participants received 5 minutes of brief advice and a self-help booklet. Using 2001 prices[33] the cost per minute of practice nurse time is £0.22; this includes salary, employer's National Insurance, superannuation and an 8% management overhead. We also add premises costs, at £0.54/m^2 per hour, assuming a room of 8 m^2, and the cost of the booklet at £0.13. Thus, the total cost for the minimal intervention is £1.59.

In step 1 of the stepped care intervention participants received 40 minutes of motivational interviewing delivered by a practice nurse, at a cost of £12.74 including salary and premises costs. This was followed by a telephone call 2 weeks later, estimated to last 1.5 minutes at a cost of £0.68. A month after the motivational interview the practice nurse conducted an interview with the participant to assess their current alcohol consumption – this was estimated to take 10 minutes at a cost of £3.18 including staff and premises costs. The total cost of step 1 was estimated at £16.60 per participant.

Step 2 consisted of four 50-minute sessions of motivational enhancement therapy delivered by a trained alcohol counsellor. Sessions attended were costed using full salary costs, including overheads and a management cost of 8% of salary. The cost of the 8 m^2 room was added together with a 10-minute administration time cost. Two weeks after step 2, a 5-minute telephone call was made to the participant at a cost of £1.30. Costs associated with extra telephone calls and letters were recorded and included in the analysis. For sessions where the participant failed to attend a scheduled session, a 5-minute cost was included on the basis that therapists use the time to engage in other tasks.[34]

Step 3 costs are associated with only one participant and no specific data were available on treatments received within the specialist agency: a standard cost of £735 is assumed.[33]

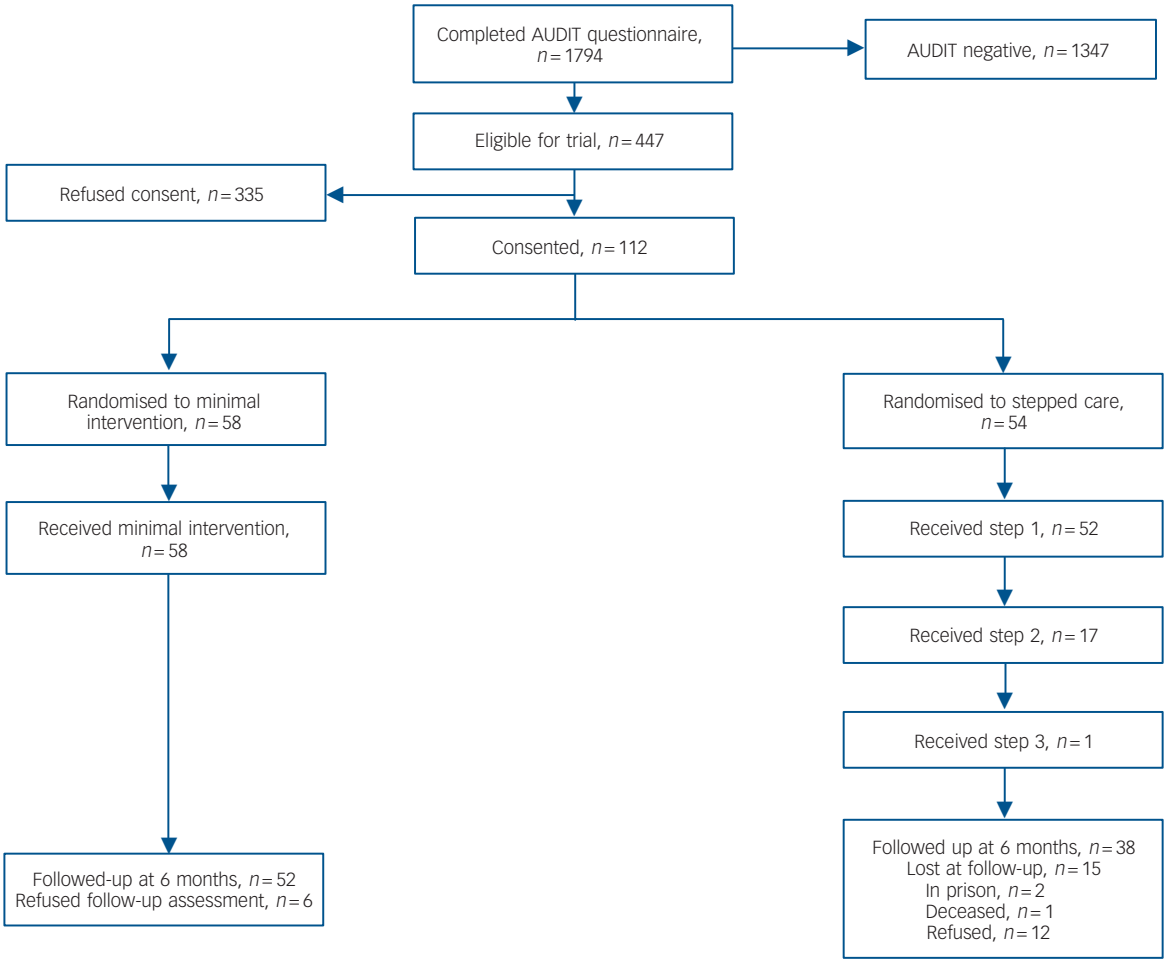

Fig. 1 CONSORT diagram for the study. AUDIT, Alcohol Use Disorders Identification Test.

Table 1 Mean (s.e.) participant demographics, and primary and secondary outcomes at baseline

	Intervention group ($n = 54$), mean (s.e.)	Control group ($n = 58$), mean (s.e.)
Age, years	41.4 (2.3)	42.1 (1.9)
AUDIT score[a]	13.6 (0.8)	13.3 (0.7)
Alcohol consumption (previous 180 days)		
Total number of drinks consumed in period[b]	1699.6 (194.8)	1423.0 (113.3)
Drinks per drinking day[b]	15.2 (1.1)	12.9 (0.8)
Percentage of days abstinent	37.9 (3.8)	36.6 (3.4)
Readiness to Change Questionnaire[c]		
Precontemplation	0.4 (0.6)	−0.5 (0.5)
Contemplation	0.6 (0.6)	1.0 (0.5)
Action	0.1 (0.7)	0.6 (0.6)
Alcohol Problems Questionnaire[d]	5.6 (0.6)	4.7 (0.4)
Severity of Alcohol Dependence Questionnaire[e]	8.2 (0.9)	8.8 (1.2)
Situational Confidence Questionnaire[f]	72.8 (18.0)	74.9 (17.8)
Quality of Life (SF–12)[g]		
Physical health	40.5 (1.0)	40.6 (1.0)
Mental health	45.6 (1.8)	49.2 (1.4)

AUDIT, Alcohol Use Disorders Identification Test; SF–12, Short Form–12.
a. Scores from 0 (low) to 40 (high).
b. One standard drink = 1 unit = 8 g of ethanol.
c. Scores from −10 (low) to +10 (high).
d. Alcohol Problems Questionnaire, common scale; scores from 0 (low) to 23 (high).
e. Scores from 0 (low) to 60 (high).
f. Scores from 0 (low) to 100 (high).
g. Scores from 0 (low) to 100 (high).

Table 2 Mean (s.e.) participant primary and secondary outcomes change at 6 months from baseline

	Intervention group ($n = 39$), mean (s.e.)	Control group ($n = 52$), mean (s.e.)
Alcohol consumption (previous 180 days)		
Total number of drinks consumed in period[a]	−408.6 (128.2)	−236.8 (95.9)
Drinks per drinking day[a]	−2.4 (0.8)	−1.0 (0.8)
Percentage of days abstinent	4.0 (2.9)	6.21 (2.9)
Readiness to Change Questionnaire[b]		
Precontemplation	0.5 (0.7)	0.5 (0.4)
Contemplation	0.1 (0.6)	0.1 (0.5)
Action	2.7 (0.7)	0.8 (0.7)
Alcohol Problems Questionnaire[c]	−1.5 (0.3)	−1.1 (0.4)
Severity of Alcohol Dependence Questionnaire[d]	−1.5 (0.6)	−1.2 (0.8)
Situational Confidence Questionnaire[e]	3.0 (1.6)	2.3 (1.5)
Quality of Life (SF–12)[f]		
Physical health	−0.1 (0.6)	0.1 (0.6)
Mental health	3.2 (1.5)	1.2 (1.0)
Health utility (EQ–5D)[g]	<0.1 (0.1)	<0.1 (0.1)

a. One standard drink = 1 unit = 8 g of ethanol.
b. Scores from −10 (low) to +10 (high).
c. Alcohol Problems Questionnaire, common scale; scores from 0 (low) to 23 (high).
d. Scores from 0 (low) to 60 (high).
e. Scores from 0 (low) to 100 (high).
f. Scores from 0 (low) to 100 (high).
g. Scores from 0 (low) to 1 (high).

In addition to treatment costs, 1794 participants were screened to identify 112 eligible and consenting participants. The cost of general lifestyle questionnaires and 5 minutes of practice nurse time to interpret the questionnaires is included for all 1794 screened participants divided by 112 consenting participants to arrive at a screening cost of £18.30 per participant. Further, in order to deliver motivational interviewing, practice nurses were trained and supervised at a total cost of £8000 divided by the 54 participants in the intervention group to arrive at a training cost of £148.15 per participant. It is possible that the training costs for stepped care are overestimated in that staff trained to deliver stepped care can continue to apply these skills after the trial is completed. However, as we have no way of knowing how far this would be applied after the trial was completed and all of the staff were redeployed to other posts after the end of the study, we have made a conservative estimate of the training costs in terms of cost-effectiveness.

Social costs for each group at baseline and 6 months are reported in Table 5 along with estimated treatment costs, including training, for patients with follow-up data only. The social costs include healthcare and social care costs, and costs associated with accidents. Crime costs are based on the estimated cost per offence,

Table 3 Adjusted mean (s.e.) participant primary and secondary outcomes at 6 months[a]

	Intervention group (n=39), mean (s.e.)	Control group (n=52), mean (s.e.)	Difference in favour of intervention (95% CI)
Alcohol consumption (previous 180 days)			
Total number of drinks consumed in period[b]	1028.5 (94.1)	1174 (81.4)	145.6 (–101.7 to 392.9)
Drinks per drinking day[b]	10.8 (0.7)	11.9 (0.6)	1.1 (–0.9 to 3.1)
Percentage of days abstinent	11.1 (0.9)	11.8 (0.8)	–0.7 (–1.8 to 3.2)
Readiness to Change Questionnaire[c]			
Precontemplation	0.8 (0.5)	0.6 (0.4)	–0.2 (–1.7 to 1.1)
Contemplation	0.4 (0.5)	0.7 (0.4)	–0.3 (–1.7 to 1.1)
Action	2.0 (0.6)	0.2 (0.5)	1.8 (0.2 to 3.3)*
Alcohol Problems Questionnaire[d]	2.9 (0.3)	3.2 (0.3)	0.3 (-0.6 to 1.8)
Severity of Alcohol Dependence Questionnaire[e]	5.5 (0.7)	6.1 (0.6)	0.6 (–1.4 to 2.5)
Situational Confidence Questionnaire[f]	77.5 (1.5)	77.1 (1.3)	0.4 (–4.3 to 3.5)
Quality of Life (SF–12)[g]			
Physical health	39.5 (0.6)	39.7 (0.5)	–0.2 (–1.6 to 1.8)
Mental health	50.5 (1.4)	49.9 (1.2)	0.6 (–4.2 to 3.0)
Health utility (EQ–5D)[h]	0.7 (0.1)	0.8 (0.1)	–0.1 (–0.1 to 0.1)

a. Adjusted by analysis of covariance for corresponding baseline score.
b. One standard drink = 1 unit = 8 g of ethanol.
c. Scores from −10 (low) to +10 (high).
d. Alcohol Problems Questionnaire, common scale; scores from 0 (low) to 23 (high).
e. Scores from 0 (low) to 60 (high).
f. Scores from 0 (low) to 100 (high).
g. Scores from 0 (low) to 100 (high).
h. Scores from 0 (low) to 1 (high).
*Significant at <0.05 level.

Table 4 Intervention costs per participant (£ sterling) associated with each group

	Intervention group, £ per participant	Control group, £ per participant
Opportunistic screening costs for 1794 screened		
General lifestyle questionnaire	0.80	0.80
5 minutes of practice nurse interpretation[a]	17.50	17.50
Minimal intervention brief advice		
5 minutes of practice nurse time[b]	0.00	1.10
Premises costs[2]	0.00	0.36
Self-help booklet	0.00	0.13
Stepped care		
Step 1: motivational interview		
Training cost for practice nurses	148.15	0.00
40-minute interview, including staff and premises cost[c]	12.74	0.00
Follow-up telephone call	0.68	0.00
Follow-up interview with practice nurse	3.18	0.00
Step 2: motivational enhancement therapy		
Four 50-minute sessions with therapist, including premises	75.67	0.00
Therapist's administration time[d]	12.61	0.00
Practice nurse follow-up telephone call	1.30	0.00
Step 3: specialist alcohol services, specialist intervention[33]	735.00	0.00

a. Includes salary, National Insurance, superannuation and 8% management cost.[33]
b. Premise size of 8m^2 at £0.54/m^2/hour for 5 minutes.[33]
c. Actual training cost £8000 divided by 54 participants.
d. 10 minutes per session.

Table 5 Mean (s.d.) costs in £ sterling for each group at baseline and 6-month follow-up (patients with follow-up data only)

	Intervention group ($n=51$), mean (s.d.)		Control group ($n=39$), mean (s.d.)	
	Baseline	6 months	Baseline	6 months
Service utilisation				
Healthcare	295.48 (597.89)	284.64 (771.94)	383.26 (696.05)	179.70 (316.13)
Social care	46.51 (93.66)	14.21 (45.68)	38.42 (104.88)	47.03 (136.30)
Criminal justice	1725.67 (7284.72)	0.0 (0)	2478.78 (8837.58)	8109.98 (32002.64)
Accidents	3624.36 (6623.54)	2009.49 (5203.22)	3950.78 (8040.47)	4280.39 (15705.63)
Treatment	215.84 (113.08)	NA	20.02	NA

NA, not applicable.

which includes an allowance for the victim's costs of crime. In the intervention group, mean total costs were £5692 at baseline and £2534 at follow-up, compared with £6851 and £12 637 in the control group. At 6 months, the intervention group had a mean 0.3849 QALYs compared with 0.3876 in the control group, a difference of 0.0027 (95% bootstrapped 95% CI –0.0535 to 0.0500). Patients in the control group gained 0.0074 QALYs between baseline and follow-up compared with a decrease of 0.0046 in the intervention group. A cost-effectiveness acceptability curve[40] was constructed, which indicated that stepped care had the greater probability of being the most cost-effective intervention, provided that the value of a QALY was less than £912 000. This result suggests that at an acceptable value of a QALY, between £20 000 to £30 000 in the UK, stepped care would be 98% likely to be the most cost-effective option.

Discussion

Summary and relevance of findings

A total of 1794 male attendees at primary care practices were screened using the AUDIT questionnaire. Twenty-five per cent scored positive for hazardous or harmful alcohol consumption, an indication of the prevalence of alcohol use disorders in this population. We have demonstrated the high level of sensitivity and specificity of the AUDIT in this population.[41]

Our study showed that it was feasible to implement a stepped care intervention in this population. Alcohol consumption reduced in both groups following intervention in this non-treatment-seeking population. Differences in terms of actual alcohol consumed were greater, but not significantly, in the intervention group, with an effect size difference in the order of 0.23 and 0.27 for mean daily and total alcohol consumed. These effect sizes are comparable with those found in meta-analyses of brief alcohol interventions.[10] This will be helpful in designing a definitive trial of stepped care intervention and for meta-analysis. Secondary outcomes indicated a similar trend towards better outcomes for the intervention group but none of these was significantly different except for greater motivation to change, which is consistent with the motivational intervention approaches used in the intervention group. However, from this pilot study it is not possible to conclude with confidence that stepped care intervention is superior in terms of clinical effects to minimal intervention because of the possibility of type 2 error.

Other limitations of the study include the relatively small proportion of potential participants who actually gave consent to participate (25%). We also found those who agreed to participate were older and had higher AUDIT scores. This may indicate that those who took part were not truly representative of the population from which they were drawn. It may also be the case that these differences reflect not only differences in willingness to take part in research, but also a difference in willingness to receive alcohol interventions if offered. In common with other trials of brief alcohol interventions in primary care, we excluded patients with severe mental illness on the basis that their needs were unlikely to be met by the control intervention. In typical practice, brief interventions are not intended for this population except in the context of more comprehensive mental healthcare. The pragmatic nature of the study aimed to maximise the generalisability, and the proportion agreeing to take part is similar to that found in meta-analysis of primary care brief intervention studies.[42] However, as we and others have pointed out, as a public health measure, questionnaire screening for alcohol use disorders in primary care is highly cost-effective, as the cost of administering the questionnaire is small and interventions are only offered to those screening positive.[41,43] We will however be exploring the reasons for non-participation, including patient and therapist characteristics, in a subsequent study. Further, based on the experience of this study, our ongoing research includes a considerably reduced baseline research assessment process to maximise willingness to participate as this may have presented a barrier to participation. In line with current methodological research, no collateral measures to verify self-report were included, as collateral reports and blood investigations are not sufficiently reliable or valid compared with self-report obtained by the Time Line Follow-Back interview.[44]

Cost-effectiveness

The cost-effectiveness analysis indicated that the stepped care intervention costs ten times that of the minimal intervention (£216 *v.* £20) as expected. However, social costs in the control group are greater 6 months after randomisation than in the intervention group: the mean social cost per patient in the 6-month period preceding follow-up was £2308 in the intervention group and £12 617 in the control group. These costs are very variable and not statistically significantly different. The analysis of the bootstrapped cost-effectiveness ratios suggest that in 818 (81.8%) of the 1000 cases, stepped care is less costly and more effective, in 165 (16.5%) cases stepped care is less costly and more effective, in 14 (1.4%) cases stepped care is more costly and more effective, and in only 3 (0.3%) cases stepped care is more costly and less effective. The cost-effectiveness applicability curve shows that at accepted values for a QALY, decision makers could have confidence of approximately 98% that the stepped care approach would be more cost-effective than the minimal intervention approach. The net cost saving is almost £9000 ($15 000 USD) in stepped care compared with minimal intervention.

As a result of this study, a large-scale pragmatic randomised controlled trial of stepped care alcohol intervention in primary care has begun.[45] As stepped care is, in research terms, a complex intervention, future research will need to establish the key effective ingredients of stepped care, including the necessary duration, intensity and content of stepped care needed to deliver effective outcomes. This will require more complex trial design and process measurement.

Implementation

On a practical level we found that stepped care offered a new practical clinical approach to the treatment of alcohol use disorders encountered in everyday primary care and a positive inter-agency protocol shared between primary care and specialist alcohol treatment agencies. There is a clear need for the training of primary care staff to implement screening and deliver behaviour change counselling interventions, which include the need for follow-up and reviews of progress. We found that the only way we could implement either of the two interventions was to specifically recruit and train practice nurses rather than seek secondment from existing practice nurse posts. This was due to reported pressures on primary care staff in providing existing care, and was only possible to implement with additional funding to cover the full costs of the screening and interventions. So there are likely to be capacity, financial and workforce issues in implementing an alcohol-screening stepped care intervention in the National Health Service. Stepped care appears to offer a practical clinical methodology suitable for addressing the allocation of limited resources.

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References

1 Prime Minister's Strategy Unit. *Interim Analytical Report.* Prime Minister's Strategy Unit, 2004.

2 Drummond DC, Oyefeso N, Phillips T, Cheeta S, DeLuca P, Perryman K, et al. *Alcohol Needs Assessment Research Project: The 2004 National Alcohol Needs Assessment for England.* Department of Health, 2005.

3 Prime Minister's Strategy Unit. *Alcohol Harm Reduction Strategy for England*. Prime Minister's Strategy Unit, 2004.

4 Department of Health. *Choosing Health: Making Healthy Choices Easier*. Department of Health, 2004.

5 Kaner EF, Beyer F, Dickinson HO, Pienaar E, Campbell F, Schlesinger C, et al. Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database Syst Rev* 2007; (2): CD004148.

6 Poikolainen K. Effectiveness of brief interventions to reduce alcohol intake in primary health care populations: a meta-analysis. *Prev Med* 1999; **28**: 503–9.

7 Ballesteros J, Duffy JC, Querejeta I, Arino J, Gonzalez-Pinto A. Efficacy of brief interventions for hazardous drinkers in primary care: systematic review and meta-analysis. *Alcohol Clin Exp Res* 2004; **28**: 608–18.

8 Whitlock EP, Polen MR, Green CA, Orleans T, Klein J. Behavioral counselling interventions in primary care to reduce risky/harmful alcohol use by adults: a summary of the evidence for the US Preventive Services Task Force. *Ann Intern Med* 2004; **140**: 557–68.

9 Bertholet N, Daeppen JB, Wietlisbach V, Fleming M, Burnand B. Brief alcohol intervention in primary care: systematic review and meta-analysis. *Arch Intern Med* 2005; **165**: 986–95.

10 Moyer A, Finney J, Swearingen C, 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**: 279–92.

11 Heather N. Interpreting the evidence on brief interventions for excessive drinkers: the need for caution. *Alcohol Alcohol* 1995; **30**: 287–96.

12 Heather N. Effectiveness of brief interventions proved beyond reasonable doubt. *Addiction* 2002; **97**: 293–4.

13 Edwards AG, Rollnick S. Outcome studies of brief alcohol intervention in general practice: the problem of lost subjects. *Addiction* 1997; **92**: 1699–704.

14 Howard MO. Assessing the cost-effectiveness of alcoholism treatments: a comment on Holder, Longabaugh, Miller and Rubonis. *J Stud Alcohol* 1993; **54**: 667–74.

15 Jonson H, Hermansson U, Rönnberg S, Gyllenhammar C, Forsberg L. Comments on brief intervention of alcohol problems: a review of a review. *Addiction* 1995; **90**: 1118–9.

16 Drummond DC. Alcohol interventions: do the best things come in small packages? *Addiction* 1997; **92**: 375–9.

17 Deehan A, Templeton L, Taylor C, Drummond DC, Strang J. How do general practitioners manage alcohol misusing patients? Results from a national survey of GPs in England and Wales. *Drug Alcohol Rev* 1998; **17**: 259–66.

18 Orleans TC. Treating nicotine dependence in medical settings: a stepped care approach. In *Nicotine Addiction: Principles and Management* (eds TC Orleans, J Slade): 145–61. Oxford University Press, 1993.

19 Abrams DB, Orleans TC, Niaura RS, Goldstein MG, Prochaska JO, Velcier W. Integrating individual and public health perspectives for treatment of tobacco dependence under managed health care: a combined stepped care and matching model. *Ann Behav Med* 1996; **18**: 290–304.

20 Sobell MB, Sobell LC. Treatment for problem drinkers: a public health priority. In *Addictive Behaviours Across the Lifespan: Prevention, Treatment, and Policy Issues* (eds JS Baer, GA Marlatt, RJ McMahon): 138–57. Sage, 1993.

21 Breslin FC, Sobell MB, Sobell LC, Buchan G, Cunningham JA. Toward a stepped care approach to treating problem drinkers: the predictive utility of within treatment variables and therapist prognostic ratings. *Addiction* 1997; **92**: 1479–89.

22 Wallace P, Cutler S, Haines A. Randomized controlled trial of general practitioner intervention with excessive alcohol consumption. *BMJ* 1988; **297**: 663–8.

23 Saunders JB, Aasland OG, Babor TF, De La Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption. II. *Addiction* 1993; **88**: 791–804.

24 World Health Organization. *Composite International Diagnostic Interview. Version 2.1*. World Health Organization, 1997.

25 Miller WR. *Form 90: A Structured Assessment Interview for Drinking and Related Behaviors. Test Manual. Project MATCH Monograph Series, Vol. 5. DHHS Publication No. 96-4004*. National Institute on Alcohol Abuse and Alcoholism, 1996.

26 Rollnick S, Butler CC, Allison J, Barth T, Rosengren D, Balliostes S, et al. Brief adaptations of motivational interviewing. In *Motivational Interviewing: Preparing People to Change (2nd edn)* (eds W Miller, S Rollnick). Guilford Press, 2002.

27 Miller WR, Zweben A, DiClemente CC, Rychtarik RG. *Motivational Enhancement Therapy Manual: A Clinical Research Guide for Therapists Treating Individuals with Alcohol Abuse and Dependence*. National Institute on Alcohol Abuse and Alcoholism, 1992.

28 Rollnick S, Heather N, Gold R, Hall W. Development of a short Readiness to Change Questionnaire for use in brief, opportunistic interventions among excessive drinkers. *Br J Addict* 1992; **87**: 743–54.

29 Stockwell T, Hodgson R., Edwards G. Taylor C, Rankin H. The development of a questionnaire to measure severity of alcohol dependence. *Br J Addict Alcohol Other Drugs* 1979; **74**: 79–87.

30 Drummond DC. The relationship between alcohol dependence and alcohol-related problems in a clinical population. *Br J Addict* 1990; **85**: 357–66.

31 Annis HM, Graham JM. *Situational Confidence Questionnaire (Users Guide)*. Addiction Research Foundation, 1988.

32 Ware Jr J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; **34**: 220–33.

33 Netten A, Rees T, Harrison H. *Unit Costs of Health and Social Care 2001*. Personal Social Services Research Unit, University of Canterbury, 2001.

34 Coyle D, Godfrey C, Hardman G, Raistrick D. Costing substance misuse services. *Addiction* 1997; **92**: 1007–15.

35 Brand S, Price R. *The Economic and Social Costs of Crime. Home Office Research Study 217*. Home Office, 2000.

36 EuroQol Group. EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* 1990; **16**: 199–208.

37 Brooks R, Rabin RE, de Charro FTH. *The Measurement and Valuation of Health Status using EQ–5D: A European Perspective*. Springer, 2003.

38 Richardson G, Manca A. Calculation of Quality-Adjusted Life Years in the published literature: a review of methodology and transparency. *Health Econ* 2004; **13**: 1203–10.

39 Vickers AJ. The use of percentage change from baseline as an outcome in a controlled trial is statistically inefficient: a simulation study. *BMC Med Res Methodol* 2001; **1**: 6.

40 Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of cost-effectiveness acceptability curves. *Health Econ* 2001; **10**: 779–87.

41 Coulton S, Drummond C, James D, Godfrey C, Parrott S, Peters T. Opportunistic screening for alcohol use disorders in primary care: a comparison of screening methods. *BMJ* 2006; **332**: 511–7.

42 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.

43 Saitz R. Alcohol screening as good as other recommended screens (eLetter). *BMJ* 2003; 28 September (http://www.bmj.com/cgi/eletters/327/7414/536#37131).

44 Babor TF, Steinberg K, Anton R, Del Boca F. Talk is cheap: measuring drinking outcomes in clinical trials. *J Stud Alcohol* 2000; **61**: 55–63.

45 Coulton S, Watson J, Bland M, Drummond C, Kaner E, Godfrey C, et al. The effectiveness and cost-effectiveness of opportunistic screening and stepped care interventions for older hazardous alcohol users in primary care (AESOPS) – a randomised control trial protocol. *BMC Health Serv Res* 2008; **8**: 129.

extra

The original 'magic bullet' is 100 years old

Frank Heynick

Today, even long-retired psychiatrists are unlikely to recall having seen more than some occasional cases of syphilis-induced paralytic dementia. But not many generations earlier, 'general paresis of the insane' accounted for some 10% – even as much as a third – of the admissions to mental hospitals in Europe and the USA. All that began to change on the day in August of 1909 when Paul Ehrlich fired the first 'magic bullet'.

Dyes

Born in 1854 to a middle-class Jewish family in Strehlen, Germany, Ehrlich came on the scene at the right time and place, for it was the dawn of the 'heroic age of medicine' and, not coincidentally, an era of rapid advances in the chemical industry. While chemists were revolutionising textile manufacturing through the development of a new spectrum of synthetic dyes such as mauve and indigo, medical microscopists, especially in Germany, were using the new aniline stains to tease out the secrets of sub-visible life, particularly the identification and classification of microbial pathogens.

Already as a young boy, Paul Ehrlich was fascinated by the dyestuffs and colours of the nearby Silesian textile plants. His doctoral dissertation at the University of Leipzig introduced the concept of counterstaining *in vitro* and he soon went on to develop dynamic vital staining *in vivo*.

As professor in Berlin and Frankfurt, the physician/chemist Ehrlich pioneered the fields of haematology, serum therapy, oncology and, most notably, the molecular side-chain theory of immunity that would be honoured with the Nobel prize.

However, the triumph for which Ehrlich would forever be remembered was yet to come. As director of the new Royal Institute of Experimental Therapy in Frankfurt early in the new century, Ehrlich returned to his youthful dream of developing a chemotherapeutic antibiotic or, as he called it, *Zauberkugel* – magic bullet.

Arsenic

Put simply: Ehrlich envisioned a very selective dye-like compound – it could even be colourless – which, when injected into the bloodstream, would home in on specific pathogens and deliver a fatal blow, while leaving the other cells of the body undisturbed.

Arsenic could be found in the *materia medica* since medieval times. French, British and American scientists had recently been experimenting on its use for combating the trypanosomes of sleeping sickness. Ehrlich joined in the hunt for a safe antimicrobial arsenical 'dye'.

But the downside to this approach was obvious. Arsenic was, after all, the favourite poison of murderers and assassins. Ehrlich's critics publicly cartooned him as 'Dr Phantasus' and several of his master chemists quit in frustration. Ehrlich himself began questioning the value of further investment of money, time and effort on sleeping sickness, which was, after all, a tropical disease of peripheral concern to Europeans.

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Then, in 1905, came the news of the discovery by the German microscopist Fritz Schaudinn of the tiny, ghostly pale, corkscrew-shaped causative agent of syphilis *Treponema pallidium*. On the basis of morphological similarity Schaudinn took the dubious liberty of relating it to the trypanosome of sleeping sickness, and therefore perhaps susceptible to similar chemotherapeutic agents.

This gave renewed vigour to Ehrlich's quest for the magic bullet. Having already experienced several hundred failures, he was ready to tolerate several hundred more.

On 31 August 1909 came the breakthrough, as the 606th arsenical compound rapidly cured a rabbit of syphilis and produced no side-effects. There followed tests with a few human patients and subsequently a historically unprecedented clinical trial with 65 000 doses. The overall results were astounding. Only then was Salvarsan (the trade name, meaning 'safe' or 'saving arsenic') put on the market.

Within a decade, the incidence of syphilis in many countries was slashed by three-quarters and more. Most important from the psychiatric standpoint: admissions to mental hospitals of patients with neurosyphilis were beginning to be a thing of the past.

The magic bullet, let it be said, was not free from backfiring: liver and kidney dysfunction and occasional fatal shock. Yet Salvarsan – and Ehrlich's later variant, Neosalvarsan – would remain the treatment of choice for syphilis until the advent of penicillin in the Second World War.

Dream

In today's post-industrialised world, the challenges facing medicine – cardiovascular disease, cancers, genetic defects, and geriatric care – are more complex than the targeting of pathogens in the heyday of the 'microbe-hunters'. This is all the more so with regard to the array of mental and psychosomatic afflictions confronting so many members of our society.

Yet the dream lives on of chemotherapeutic wonder-drugs that may alleviate depression (or reverse senile dementia, or dry up various cancers) in such a specifically targeted way as to have minimal side-effects. This is in the spirit of Paul Ehrlich and the first magic bullet created a century ago.

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