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Effect of a 1-year short message service in detoxified alcohol-dependent patients: a multi-center, open-label randomized controlled trial

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ABSTRACT

Background and Aims Existing evidence suggests that text message interventions can help people to reduce their alcohol consumption. However, studies with alcohol-dependent patients are lacking. In this study a 1-year automatic mobile phone-based short messaging service (SMS) intervention on alcohol consumption in patients after alcohol detoxification in hospital was compared with treatment as usual. **Design** Multi-center, randomized, controlled, two parallel-group, observer-blinded trial. **Setting and Participants** Primary and secondary care: four hospitals and community (1 million residents, 7600 km^2 area in Germany). A total of 462 patients with alcohol dependence (ICD-10) were included during inpatient detoxification treatment. Patients were randomly assigned (1 : 1) to an SMS intervention and treatment as usual (SMS + TAU; n = 230; mean age: 45.4 years; 22.6% women) or TAU alone (n = 232 mean age: 44.5 years; 22.8% women). Planned, automated messages were sent to patients over 1 year to record assistance needs. A 'yes' or missing response triggered a telephone call from a hospital therapist. Outcome was assessed by an independent survey center. **Measurements** The primary end-point was a three-category alcohol consumption measure covering months 10–12 after discharge: abstinence, non-heavy drinking, heavy drinking [men > 60 g/day; women > 40 g/day equal to World Health Organization (WHO) criteria: high risk and very high risk, mean consumption]. Secondary end-points were number of abstinent days over 12 months and frequency of abstinence. **Results** The arms differed primarily in the heavy drinking category (intervention group 22.2%, TAU-only group 32.3%) in months 9–12. This is reflected by an odds ratio (OR) = 1.68, 95% confidence interval (CI) = 1.11–2.54, P = 0.015 for heavy drinking versus non-heavy drinking/abstinence. No difference between treatments was found with respect to any drinking versus abstinence (OR = 1.13). These results were confirmed by models adjusting for randomization strata. **Conclusions** In Germany, a 12-month mobile phone short messaging service-based intervention enhanced the reduction in heavy drinking for 1 year in routine care among adults with alcohol dependence discharged from inpatient alcohol detoxification.

Keywords Alcohol dependence, alcohol detoxification, continuous care, mHealth, short message service (SMS), telemedicine.

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INTRODUCTION

More than 77% of the net mortality burden caused by alcohol consumption in the European Union is attributable to heavy drinking (> 60 g/day for men, > 40 g/day for women) [1]. Using continuing care to manage alcohol dependence as a chronic condition might generate long-lasting benefits [2]. Mobile phone messaging services such as short message service (SMS) seem promising because of their broad adoption in the general population and the effect of allowing continuous contact at low cost [3]. Even small effects might be cost-effective. SMS in medical care has several advantages, including independence of time and location for patient replies and high use in at-risk populations [3,4]. Socially isolated and hard-to-reach people do not have to take the hurdle of a personal telephone call. We assume that a low-contact threshold helps this group of people.

Earlier, McKay and colleagues found positive effects in patients with alcohol dependence and/or cocaine dependence in a conventional telephone after-care study over 2 years [5]. In this study, a combination of telephone-based weekly contacts with supportive group sessions resulted in higher abstinence rates than standard group counseling. In another study, a stepped-care approach using telephone contacts revealed small to medium effect sizes in reducing the drinking amounts among at-risk drinkers in general practice [6], but telephone contacts up to 2 years yielded no improved drinking outcomes among 622 patients in Croatia [7].

Advantages of SMS for substance abuse treatment/intervention have been reported in various settings and with various end-points [8–13]. Among them were clinical outcomes, relapse prevention, medication adherence and psychological or social issues [13–16]. However, evidence is limited.

One of the largest studies in this field showed that a 12-week automated interactive text-message intervention led to greater reductions in the number of binge drinking days compared with controls at 9 months in 765 young adults with harmful alcohol use after reporting to emergency departments. Also, lower binge drinking prevalence, fewer drinks per drinking day and lower injury prevalence was reported [17].

A-CHESS, a smartphone application providing monitoring, information, communication and support services reported significantly fewer risky drinking days in the intervention group in an unmasked randomized clinical trial involving three residential programs with 349 participants. The intervention period lasted 8 months and the follow-up period 4 months. Four, 8 and 12 months after discharge the patients of the intervention group reported fewer risky drinking days compared with controls (1.39 versus 2.75 days) in the previous 30 days [18].

In 47 patients with alcohol use disorder and depression, units per drinking day, depression and stress scores were reduced after receiving supportive text messages twice daily after 6 months. No differences were found after 1 year between the intervention group and 48 control participants who had received treatment as usual. Patients had previously completed a 30-day inpatient rehabilitation program [19].

One study revealed no intervention effects [20]. In this multi-center, parallel-group randomized study, 825 socially disadvantaged men aged between 25 to 44 years with at least two episodes of binge drinking in the preceding 28 days received 112 text messages during 12 weeks. Interventions were designed using the Health Action Process Approach. The control group received 89 text messages concerning general health. No differences regarding binge drinking were found at 12 months post-intervention.

In an own-controlled pilot study with a similar design to the study presented in this publication, text messaging was associated with low-risk alcohol consumption and later relapse after 8 weeks in 80 detoxified alcohol-dependent inpatients [21].

Other studies using SMS in alcohol dependence had smaller samples and shorter follow-up periods. Sample sizes usually comprised fewer than 100 people [13]. No study has investigated a group of hospital inpatients after discharge, as summarized in reviews of this topic [8–13].

Evidence for severely affected alcohol-dependent inpatients in treatment populations is lacking. We hypothesized that the use of a simple interactive mobile phone helpline system with a regular assessment of help–need (SMS) and replies by the hospital therapists added to treatment as usual (TAU) would reduce the proportion of patients who report heavy drinking during 1 year after discharge from inpatient detoxification compared with TAU alone.

METHODS

Study design and participants

Participants

The continuity of care among alcohol-dependent patients via mobile phone SMS Study (CAPS) was a multi-center, randomized, controlled, parallel-group, observer-blinded trial conducted in the inpatient units for addiction disorders at four psychiatric hospitals in northern Germany (Greifswald, Rostock, Schwerin and Stralsund) from 30 May 2012 to 26 April 2015. The service area of the four study hospitals covers approximately 1 million residents of a 7600-km^2 area in Germany.

Procedures

Study therapists were members of the hospital therapist team and known to the patients. All patients received a

2-week inpatient treatment by physicians, psychologists, nurses, social workers and occupational therapists and physiotherapists. After inclusion into the study TAU consisted of all usual health-care services, such as general practitioners and psychiatrists, emergency services, addiction counselling, outpatient psychotherapy, day clinic and inpatient treatment and 3 months inpatient rehabilitation programs, paid by the pension fund [21].

Study therapists in the four centers were psychiatrists, psychologists, nurses or medical assistants: $n = 11$; four (36.4%) were men. They were recruited by the heads of the four participating study hospitals. Interested therapists took part in the study. No specific training was provided, except for an introduction to the interactive system. The hospitals were refunded for study-specific extra work.

Inclusion and exclusion criteria

The following inclusion criteria were used: alcohol dependence (ICD-10), ongoing inpatient alcohol detoxification, age ≥ 18 years, ability to send and receive SMS messages (patient statement) and written informed consent. Exclusion criteria were acute withdrawal from illegal drugs within the last 6 months, participation in a drug substitution program for opioid use disorders, expected non-adherence to the planned assessments (e.g. refusal to take part in the telephone follow-up), dementia or acute psychosis, life expectancy < 12 months (therapist judgment) and participation in other clinical trials.

All investigators adhered to the Declaration of Helsinki and the International Council for Harmonization guidelines for good clinical practice. The study protocol was approved by the Ethics Committee of the Medical Faculty of the University of Greifswald (reg. no. BB 79/11; 28 July 2011) and the Ethics Committee of the University of Rostock (reg. no. A 2011 99; 18 August 2011). The study was monitored by the Clinical Trial Center Leipzig (www.zks.uni-leipzig.de) and by a data safety and monitoring committee.

Randomization and masking

Randomization was conducted centrally at the baseline visit at month 0 by the Clinical Trial Center Leipzig using a modified minimization procedure with a stochastic component [22], intervention : control ratio = 1 : 1, stratified by sex and pre-study alcohol consumption as well as trial site. Pre-study alcohol consumption was used to stratify patients into a high- and low-consumption group, based on the results of the pilot study [21]. Neither participants nor investigators were masked to group assignment, but participants were asked not to disclose their assignment (observer-blinded trial).

Interventions

Patients with alcohol dependence usually receive treatment from general practitioners and addiction counseling initially followed by a 2-week inpatient detoxification, including psychosocial treatment. Patients were asked to participate at the end of the detoxification treatment in the hospitals.

SMS messages were sent automatically to the patients' mobile phones (all networks) [21]. Patients received up to 40 SMS messages during the first 12 months after inpatient discharge (two per week—Monday and Thursday—in months 1 and 2; one per week—Monday—in month 3; two per month in months 4–12). The message consisted of a single question: 'Dear Mr/Ms… Did you drink alcohol or do you need help? Please answer with (A) for yes and (B) for no' (Fig. 1). Patients were informed that this question referred to alcohol consumption since discharge or the last SMS prompt. The 'Do you need help?' element could refer to any problem. All SMS were automatically sent and received by an electronic fully automatized system. It allocated incoming SMS from the patients according to content (yes or no) and time (within 24 hours or not). The system automatically generated e-mails to inform the study therapists about patient responses. Receiving an 'A' within 24 hours after the question having been sent triggered a automatically generated call-for-help e-mail to the therapist. The study therapist called back within 24 hours. Receiving a 'B' triggered an automatically generated supportive feedback SMS to the patient. These SMS messages were randomly chosen from 40 prepared answers by the system. Replies with small discrepancies from A or B, such as 'b' or 'B', or other letters or texts (e.g. 'Thank you, I am very well!') were categorized as 'unexpected'. Unexpected SMS messages were also transmitted via e-mail to the therapist who read these messages to decide whether they indicated a need for intervention. If a patient did not answer the automatically generated question via SMS within 24 hours, a 'no-reply e-mail' was automatically sent to the therapist, which also triggered a personal telephone call from the study therapist to the patient. The study therapists called the patients back on working days.

Therapist telephone calls were intended to be supportive. No specific therapeutic approach or training was used. A variety of supportive interventions was administered immediately, such as telephone counseling, referral to an outpatient service or re-admission to the hospital. Therapists were free to recommend an intervention of their choice. Patients had been instructed beforehand that telephone calls would be brief. Time limitations were considered important to keep the additional burden to the study therapists tolerable. Patients were informed that the therapist would stay in touch by watching the answers, even when no phone calls occurred.

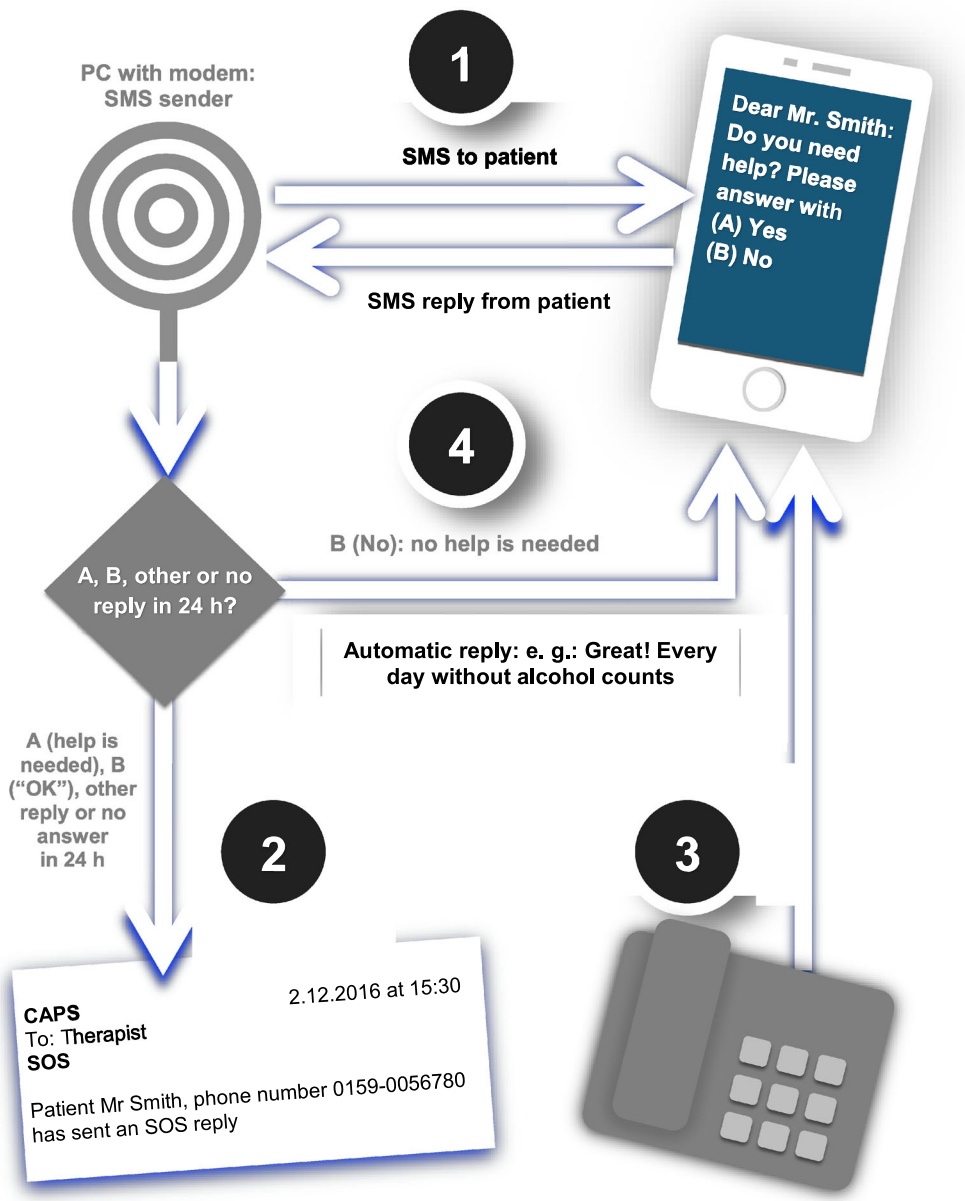

Figure 1 Continuity of care among alcohol-dependent patients (CAPS) system: short messaging service (SMS) messages were sent from the CAPS system to the patients' mobile phones (all networks) (1). The messages (up to 40 SMS per year) to the patients consisted of a single question: 'Dear Mr/Ms… Did you drink alcohol or do you need help? Please answer with (A) for yes or (B) for no'. The CAPS system allocated incoming SMS from the patients according to content (yes or no) and time (no answer in 24 hours; grey rhombus). E-mails to inform the therapists about patient responses were sent from the CAPS system to the therapist's e-mail account (2). Receiving an 'A' ('SOS') within 24 hours of the question triggered a call-for-help e-mail to the therapist, who called back (3). Receiving a 'B' within 24 hours triggered an automatic supportive feedback SMS to the patient, such as 'Well done!' (4). Unexpected SMS messages (not 'A' or 'B' were also evaluated by the therapists to determine whether they indicated a need for intervention. In case of no reply by the patient within 24 hours, a 'no-reply e-mail' was sent to the therapist, which also triggered an intervention

Phone calls and attempts were documented by the counselor on brief standardized protocols. A minimum of three attempts was made to call patients back. Study therapists had the opportunity for temporary replacement, e.g. in case of holidays. A CAPS web page allowed the inclusion of new patients from all study sites. Only the starting date, therapist's password and patient's sex, name and mobile phone number were required. Therapists used their PC work-stations and patients their own mobile phones. The hardware components of the interactive CAPS system included a standard personal computer with an internet connection, a mobile communications modem and an expert

system programmed for a Linux operating system. Patients received financial remuneration of €30.00 for the baseline interview and €10.00 for each of the four follow-up interviews.

Outcomes and measures

The primary outcome was the level of alcohol consumption during months 10–12 after randomization with three ordered categories: heavy drinking (men > 60 g/day, women > 40 g/day) > non-heavy drinking > abstinence before the final follow-up interview (equal to World Health Organization (WHO) criteria: high risk and very high risk, mean consumption of the 4th quarter). For this purpose, alcohol consumption was assessed with the German versions of the FORM-90 quick drinking assessment interview (AQ) and the subject telephone assessment of drinking and related behaviors (AT), a retrospective timeline follow-back instrument [23,24]. Alcohol consumption was calculated as mean grams per day by summing up the total number of standard drinks consumed in the 90 days prior to the final interview and multiplying that value by 10.5 g (standard drink of pure ethanol), then dividing by 90 days.

For patients who could not be reached for outcome assessment at the 12-month follow-up, information from collaterals such as relatives, general practitioners and addiction counselors was sought. Collateral information and available intermediate time-point information were presented to a blinded independent end-point committee. Patients without a final interview at the 12-month follow-up were counted as a failure and included in the 'heavy drinking' category, unless the end-point committee decided that available follow-up information was confirmed by collateral evidence (see details in the Supporting information, Appendix, p. 6).

Secondary outcomes were drinking days, drinks per day and drinks per drinking day (Supporting information, Appendix, pp. 15–18). In addition, socio-demographic and diagnostic data were measured using DSM-5 [25], the Adverse Consequences from Drinking Scale (ACD) [26], the Brief Symptom Inventory (BSI) [27] and the Objective Social Outcomes Index (SIX) [28]. Motivation to stop drinking at baseline was tested with a visual analog scale with the question: 'How important is it for you not to drink alcohol?' (Supporting information, Appendix, pp. 25–26).

Data were assessed by blinded experienced trained interviewers at baseline and at 3, 6, 9 and 12 months after discharge via telephone. Only a brief assessment of consumption was performed face-to-face by study therapists using the Form-90-AQ for stratification at inclusion at the study centers.

Statistical analysis

Sample size calculation was based on the primary end-point with three categories: abstinence < non-heavy drinking < heavy drinking (> 60 g/day for men and > 40 g/day for women). A proportional odds model to detect a 10% increase in abstinence rates through the intervention was assumed. The hypothesis of a 10% increase in abstinence as a result of the intervention compared with the control group was formulated as a consensus of the group members involved on the basis of the pilot study [21]. There are still no data available on the effects of text messaging upon consumption in detoxified inpatients. Effects expected were supposed to be smaller compared to clinical trials using face-to face interventions to all patients of the intervention group. The effect size corresponds to proportional odds of approximately 0.63 and equivalently to a probability of superiority [24] $A = P(TAU > SMS + TAU) + 0.5P(TAU = SMS + TAU) = 0.42$, which indicates that a patient of the SMS + TAU arm has the higher drinking category only in 42% of all pairwise comparisons. At a two-sided significance level of 5% and a statistical power of 90%, a sample of 462 patients was needed.

The primary analysis uses the intent-to-treat population, counting missing information as failure. In addition, we report results restricted to informative patients (for whom any follow-up information exists) and the per-protocol population (patients with complete final interview); compare with Fig. 2. Furthermore, we explored results obtained with multiple imputation.

For the primary end-point, the study protocol delineated an ordinal regression model, including study arm, and the randomization strata on sex and consumption category, assuming proportional odds. However, because this condition was questionable, models without this assumption were calculated. Ordinal regression with the three-level categorical variable without assumption of proportional odds calculates two association measures: (1) heavy drinking versus non-heavy drinking and abstinence and (2) any drinking versus abstinence.

In exploratory analysis, we investigated the interactions arm : strata as well as baseline consumption as a covariate. Continuous data (e.g. abstinence days) were compared by the robust *t*-test (Welch). For longitudinal data, a linear mixed model was fitted including a random intercept for center.

Odds ratios (ORs) with 95% confidence intervals (CIs) as well as probabilities of superiority were calculated as effect measures. The study protocol (SP) did not include scheduling of any formal interim analyses.

The funder of the study had no role in study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access

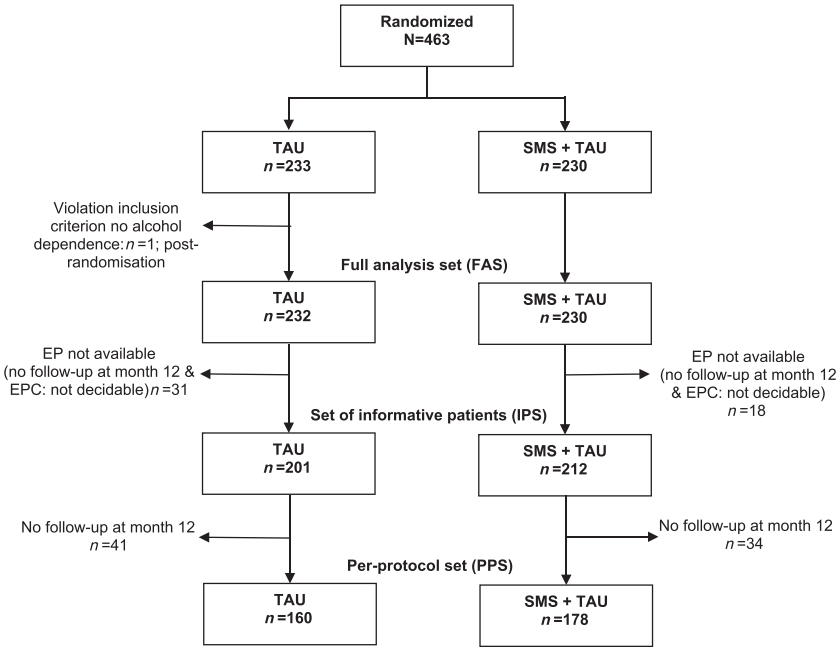

Figure 2 Flow-chart. Full analysis set (FAS): all patients included. Set of informative patients (IPS): patients with information at interview F4 (interview month 12 covering months 10–12) and patients with information of collaterals (e.g. general practitioners) and patients with end-point committee (EPC) decision. Per protocol set (PPS): complete cases regarding interview F4. TAU = treatment as usual; SMS = short messaging service

to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Between 24 May 2012, and 27 November 2013, 463 patients were randomly assigned to SMS + TAU (n = 230) or TAU (n = 233). Of the 463 patients, 230 in the SMS group (SMS + TAU) and 232 in the TAU group started their assigned care, and were included in the full analysis set (Fig. 2). One patient had to be excluded because he was not alcohol-dependent (ICD-10).

The proportion of patients who have been lost during 12 months among those who entered the study (loss to follow-up) was higher in the TAU group than in the SMS + TAU group (72 (31.4%) versus 52 (22.4%), P = 0.031). The study arms differed only marginally in baseline characteristics (Table 1). No serious events relative to the definition in the study protocol were reported.

The primary end-point was assessed by the blinded end-point committee for 47 patients (SMS + TAU: 18, TAU: 29). Conversely, 42 patients were classified as 'heavy drinking' because they were uninformative or had only baseline data (SMS + TAU: 16, TAU: 26).

Primary outcome

In the SMS + TAU group, 22.2% were categorized as heavy drinking (versus non-heavy drinking and abstinence) compared to 32.3% in the TAU group in follow-up months 10–12, an absolute difference of 10.2% (95% CI = 2.1–18.2%; Table 2). For TAU compared to SMS + TAU, the OR for the heavy drinking category (versus non-heavy drinking and abstinence) was 1.68 (95% CI = 1.11–2.54; P = 0.035; Table 3). In addition, after adjustment for sex and pre-study alcohol consumption (primary analysis), the OR for the heavy drinking category was 1.78 (95% CI = 1.17–2.69; P = 0.007) versus non-heavy drinking and abstinence. For the drinking categories (versus abstinent), no effect could be detected (OR = 1.13; 95% CI = 0.78–1.63); adjusted for the strata (OR = 1.11; 95% CI = 0.77–1.61).

All sensitivity analyses agreed qualitatively with the primary analysis (Table 4). For instance, after multiple imputation of missing values, a significant effect was detected for heavy drinking between groups (OR = 2.03; 95% CI = 1.28–3.23; P = 0.006) and after adjustment (OR = 2.17; 95% CI = 1.36–3.45; $P < 0.001$); the absolute risk reduction was 11.5%; 95% CI = 4.2–18.9%.

Secondary end-points

In the SMS + TAU group, more abstinence days were reported during 1 year after randomization than in the TAU group (on average, 267 versus 242; P = 0.037; Table 3).

We found a higher risk for heavy drinking for TAU patients (OR = 1.9; 95% CI = 1.2–2.9) if accounting for low abstinence motivation (visual analog scale < 70, OR = 2.0, n = 433) when using abstinence motivation exploratively as a covariate in the multiple model for the primary outcome (Supporting information, Appendix, pp. 25–26).

Table 1 Baseline characteristics of 429 informative patients according to treatment group, short messaging service (SMS) + treatment as usual (TAU) versus TAU

Characteristic	*SMS + TAU*		*TAU*	
Female	52	(22.6)[a]	53	(22.8)
Age (years)	45.4±	9.2[b]	44.5±	9.7
Body mass index (BMI) (kg/m^2)	25.8±	4.0	25.2±	4.2
Obesity (%)	27	(11.7)	36	(15.5)
Marital status (%)				
Married, living together	39	(18.6)	34	(16.0)
Married, separated	15	(7.1)	10	(4.7)
Never married	85	(40.5)	95	(44.6)
Divorced	66	(31.4)	65	(30.5)
Widowed	5	(2.4)	9	(4.2)
Partnership	57	(33.1)	55	(30.2)
Own housing	187	(87.4)	188	(87.4)
Social outcome index (SIX); range 0–6)	3.8±	1.3	3.8±	1.4
Brief symptom inventory (BSI) general distress	3.5±	2.6	3.5±	2.7
Social status: number of days (90 days before inclusion)				
Prison or custody	0.4	(5.6)	0.5	(5.8)
Homeless	1.0	(9.1)	0.8	(8.2)
Employed	37.3	(42.5)	37.2	(42.3)
School or education	2.0	(12.4)	4.3	(17.8)
Treatment 3 months before study				
Inpatient detoxification	36	(16.8)	27	(13.0)
Self-help group	20	(9.3)	22	(10.6)
Alcohol consumption and severity				
Drinks[c] (number/days last 12 months)	12.5±	13.0	11.6±	13.2
Pre-study strata				
Women ≤ 5 drinks/day[c]	21	(9.1)	21	(9.1)
Women > 5 drinks/day	31	(13.5)	32	(13.8)
Men ≤ 12 drinks/day	100	(43.5)	100	(43.1)
Men > 12 drinks/day	78	(33.9)	79	(34.1)
Diagnostic criteria for alcohol use disorder (mean, SD)	5.6±	1.1	5.5±	1.2
2–3 (mild; *n* %)	11	(4.8)	13	(5.6)
4–5 (moderate)	94	(40.9)	105	(45.2)
6 + (severe)	57	(24.8)	55	(23.7)
Adverse consequences from drinking (ACD)				
ACD (9 items)	7.42±	4.98	7.77±	4.57

[a]*n* (%) for categorical data; [b]mean ± standard deviation (SD) for continuous covariates. Data are mean ± SD or *n* (%); [c]1 drink = 10.5 g alcohol

Table 2 Primary outcome: three-level drinking category during months 10–12

	SMS + TAU	*TAU*	*Total (n = 462)*	*OR (95% CI)*	*P*
Abstinent	104 (45.2)[a]	98 (42.2)	202 (43.7)	1.68 (1.11–2.54)	0.035
Non-heavy drinking	75 (32.6)	59 (25.4)	134 (29.0)		
Heavy drinking[b]	51 (22.2)	75 (32.3)	126 (27.3)		

[a]Number (%); [b]heavy drinking: more than 60 g pure alcohol/day for men, more than 40 g alcohol/day for women. SMS = short messaging service; TAU = treatment as usual; SP = study protocol; OR = odds ratio; CI = confidence interval. This is the primary analysis with the end-point definition of the study protocol. Following the SP, ordinal regression assuming proportional odds was performed.

For the continuous consumption variables, 'psychopathology' and 'self-rated health', we found no differences between groups (Table 3; Supporting information, Appendix, pp. 19–23). Service use was not different between groups and will be detailed in another publication.

The SMS system performed 24 375 operations (e.g. sending and receiving SMS or e-mails) automatically during the study period. Altogether, 9019 SMS messages with the question: 'Do you drink alcohol…?' were sent to the 230 patients in the SMS group. Patients responded with

Table 3 Secondary outcomes: alcohol consumption variables for the total 360 days assessed by telephone interviews at months 3, 6, 9 and 12

	SMS + TAU	*TAU*	*95% CI for difference*	*P*
No. of reported abstinence days	267 ± 123	242 ± 140	1.5 to 49.5	0.037
Longest abstinence period (days)	189 ± 126	175 ± 132	−9.2 to 38.0	0.23
No. of reported drinking days	30.8 ± 61.8	31.0 ± 60.1	−11.3 to 11.0	0.98
No. of reported heavy drinking days	25.6 ± 53.4	27.8 ± 58.4	−12.4 to 8.1	0.68
Drinks per day AC	1.8 ± 3.6	2.1 ± 4.8	−1.1 to 0.5	0.49
Drinks per day MIc	2.1 ± 3.7	2.2 ± 4.3	−0.9 to 0.7	0.83
Drinks per drinking day	11.9 ± 12.1	12.1 ± 12.2	−2.8 to 2.2	0.83

SMS = short messaging service; TAU = treatment as usual; CI = confidence interval; AC = adverse consequences; MI = multiple imputed.

Table 4 Sensitivity analysis: OR for heavy drinking (versus non-heavy drinking and abstinence) for the TAU versus SMS + TAU groups

	Heavy drinking[a]	*Drinking versus abstinence*	
	OR[a] *(95% CI)*	*OR (95% CI)*	*P*[c]
FAS: primary analysis, non-adjusted	1.68 (1.11, 2.54)	1.13 (0.78, 1.63)	0.035
FAS: primary analysis, adjusted[b]	1.78 (1.17, 2.69)	1.11 (0.77, 1.61)	0.009
FAS: multiple imputed, non-adjusted	2.03 (1.28, 3.23)	1.10 (0.76, 1.59)	0.006
FAS: multiple imputed, adjusted[b]	2.17 (1.36, 3.45)	1.09 (0.56, 2.12)	< 0.001
IPS, non-adjusted	1.55 (0.90, 2.65)	0.99 (0.67, 1.46)	0.21
IPS, adjusted[b]	1.77 (1.03, 3.04)	0.99 (0.49, 1.99)	< 0.001
PPS, non-adjusted	1.58 (0.76, 3.26)	0.89 (0.58, 1.37)	0.25
PPS, adjusted[b]	1.88 (0.91, 3.88)	0.97 (0.45, 2.09)	0.01

FAS = full analysis set; SMS = short messaging service; TAU = treatment as usual; IPS = set of informative patients; PPS = per-protocol set; OR = odds ratio; CI = confidence interval. FAS: SMS + TAU: *n* = 230, TAU: *n* = 232; PPS: SMS + TAU: *n* = 178, TAU: *n* = 160; IPS: SMS + TAU: SMS + TAU: *n* = 212, TAU: *n* = 201. [a]These two columns reflect the ordinal model: OR for heavy drinking versus non-heavy drinking/abstinence and heavy/non-heavy drinking versus abstinence; [b]adjusted for baseline strata, sex, and consumption category [c]*P*-values are from a likelihood-ratio test of a model with versus without the treatment arm.

Table 5 SMS system: SMS sent and received by patients

	N (%)		*n*[a] *SMS at least once*	*Mean (SD) per person*		*Minimum per person*	*Maximum per person*
Automatic SMS system							
SMS prompts to patient	9019	(63.5)	228	39.6	4.5	2	42
Feedback SMS to patient	5176	(36.5)	213	24.3	12.0	1	41
Total	14 195	(100.0)					
Patient SMS responses							
A (SOS)	278	(2.7)	97	2.9	3.2	1	20
B (OK)	5176	(50.8)	213	24.3	12.0	1	41
Unexpected/unclear SMS	1946	(19.1)	206	9.5	11.0	1	68
No answer to SMS prompt	2780	(27.3)	213	13.1	11.1	1	41
Total	10 180	(100.0)					
Total no. of operations (SMS system and responses)	24 375						

[a]Number of patients sending or receiving at least one short messaging service (SMS) of the respective categories, e.g. 97 patients have sent at least one 'A' (SOS).

5454 replies, as follows: A ('I have drunk or need help') or B ('I have not drunk; everything is OK'). A total of 51 of 230 SMS patients (22.2%) responded to 90% or more of the SMS prompts with A or B; 213 (92.6%) of the patients sent at least one 'B', and 97 (42.2%) called for help with an 'A' at least once. Overall, 'A' or 'SOS' responses were chosen in 278 (2.7%) of all responses (Table 5). A total of 1765 phone calls took place between therapists and patients. The most frequent content was telephone counseling, occurring in 1472 (83%) of the phone calls (Table 6).

The total number of SMS indicating need for help ('A') during the total study duration were correlated with drinking amount (R^2 = 0.19) in follow-up months 10–12 (Supporting information, Appendix, p. 29).

The SMS system worked, except for 19 technical failures resulting in messaging delay (Supporting information, Appendix, pp. 3–4). All SMS messages and e-mails to therapists were ultimately delivered.

DISCUSSION

We evaluated a simple interactive text messaging system plus personal telephone emergency brief counseling for the reduction of heavy drinking among detoxified inpatients with alcohol dependence (CAPS). The proportion of heavy drinkers was lower after SMS + TAU than after TAU alone.

The rate of probably informative drop-outs was high (Fig. 2). We performed extensive sensitivity analyses, which all qualitatively agreed that the risk of heavy drinking for the TAU arm was increased (OR = 1.55–2.17; see Table 4), supporting the main result. The effect of our intervention is by no means separate from the detoxification treatment because of confounding of the effects of the SMS system and of the detoxification treatment, especially in patients who remained abstinent.

The working mechanism of SMS + TAU might be an increased likelihood of detecting drinking earlier compared with patient-initiated help-seeking. Spontaneous reporting is compromised by a variety of barriers, such as shame and self-stigmatization [29]. Subsequent timely therapeutic interventions can support patients to stop consumption. Consequently, patients in the SMS + TAU group reported a significantly higher number of abstinence days. Finally, according to patient anecdotal statements, the personal contacts with the therapists were valued highly and might thus have contributed to the effect. TAU patients were not called by the hospital therapists.

Automated SMS messages had no effect on other secondary outcomes, particularly mean consumption. An increase in remission and abstinence days, but not in mean consumption, is consistent with results from a lay counselor-delivered brief intervention (CAP) in males with harmful drinking in India [30]. Furthermore, both CAP and our study similarly showed better effects for patients with low baseline motivation values, despite using different motivation measures. Thus, the SMS approach could provide a particular support for a group of patients who have low motivational resources to change behavior themselves.

The features of CAPS making the difference at the patient level might be the regular personal support and the SMS-based feedback, and at the institutional level, the automatic and economic allocation of treatment resources. Hospital treatment usually ends at discharge. CAPS was developed simply to fill this gap. SMS responses serve as real-time indicators to trigger timely action by the therapist, and CAPS refrains from complex features to keep user barriers to a minimum. In contrast to counseling approaches such as CAP, basically no training for the

Table 6 Telephone calls from the hospital therapists to the patients in response to short messaging service (SMS) indicating help–need or when patients failed to respond to SMS prompts

Telephone calls and call attempts to patients (reasons)						
	N[a] total	*n[b] patients*	*Mean (SD) per person*		*Minimum*	*Maximum*
Telephone call was triggered for the following reason						
No response to SMS prompt	2621	208	12.6	(10.7)	1	39
Reponse to 'A' (SOS)	273	101	2.7	(2.9)	1	14
Unexpected SMS: help–need	149	62	2.4	(2.2)	1	11
Appointed follow-up	184	54	3.4	(4.0)	1	26
Other reasons	215	58	3.7	(4.2)	1	27
Content of completed telephone calls between patients and therapists						
Telephone counseling	1472	184	8.0	(7.6)	1	36
Referral to addiction counseling	79	36	2.2	(2.3)	1	13
Referral to general practitioner	28	14	2.0	(1.6)	1	7
Admission to hospital	186	62	3.0	(2.3)	1	11

[a]*N* (total): total number of telephone calls and call attempts or completed telephone calls, respectively; [b]*n* (patient): number of patients with at least one of the respective types of telephone contacts

therapists was necessary for the study. The method is open for easy implementation in various settings.

Strengths and weaknesses of this study

Strengths of the study include the relatively long study duration of 12 months and the multi-center design. The Clinical Trial Center Leipzig ensured implementation of the ICH good clinical practice standards for maximum safety and quality. Most importantly, the broad eligibility criteria precluded recruitment of an artificial sample, allowing a close reflection of 'the messy, real-world' [31] of routine care.

Among the limitations, we cannot rule out negative side-effects, although we identified none. Secondly, self-report of alcohol consumption might be prone to bias; however, biochemical verification is not a feasible alternative [30]. Interviews are of equal accuracy [32]. Taking blood, urine or hair samples with personal contacts can increase assessment reactivity [33], and would have required higher resources. Finally, because of missing data dependent on the end-point, missing at random may be questionable, although we performed extensive sensitivity analyses to test the robustness of this result. The differential attrition in the arms may also have biased the results. For example, TAU patients with lower consumption might have been more likely to be lost to follow-up, thus biasing the TAU arm towards people with heavier alcohol use;

9019 SMS prompts were sent and 5454 replies were counted, resulting in 1765 phone calls. Other sources of help or ambivalence due to the disorder might be an explanation for missing replies.

Inclusion and exclusion criteria were simple and straightforward. However, it might be possible that study therapists, who knew their patients, only approached patients directly whom they considered to be suitable for the study.

Comparison to other studies

Earlier conventional telephone after-care showed positive effects in patients with alcohol dependence [5]; however, all patients had to be called personally because no SMS-filter function was used. Few studies involving SMS for reducing alcohol consumption have been published [8–13]. One of the largest studies in this field showed that a 12-week automated interactive text-message intervention led to less consumption and lower injury prevalence at 9 months in 765 young adults with harmful alcohol use after reporting to emergency departments [17]. However, attrition was high, and outcome was not assessed by interviewers. The number needed to treat (NNT) of 13 to prevent one young adult from binge drinking was similar to that of CAPS.

A-CHESS, a smartphone application, reported significantly fewer risky drinking days in the intervention group in a study with 349 participants [18]. However, using an application with multiple services requires much more commitment compared to simply answering an SMS. Also, even in cases of not answering the SMS, patients were called by the study therapists in our study. In our opinion, this is the lowest possible contact threshold. The other SMS studies with various alcohol-related end-points were shorter and smaller in number, and no other study has investigated a severely affected hospital population [8–13].

Unanswered questions

Future studies should not use incentives and minimize assessment reactivity [33], which might have accounted for high effects in the TAU group. Implementation in non-research settings, cost-effectiveness and countable benefits of the reduced proportion of patients in the heavy-drinking group in terms of better health (less organ damage, better level of functioning) remain unanswered.

CONCLUSION

In conclusion, the SMS system applied in this study helped to reduce heavy drinking in routine care settings using available technology.

Trial Registration

ClinicalTrials.gov Identifier: International Standard Randomized Controlled Trial Number: ISRCTN78350716.

Declaration of interests

The authors have no conflicts of interest to declare.

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Data sharing

Individual participant data that underlie the results reported in this article, after de-identification (text, tables, figures and appendices), will be available beginning 3 months and ending 5 years after article publication to researchers who provide a methodologically sound proposal. The study protocol and statistical analysis plan will also be available. To gain access, data requestors will need to sign a data access agreement.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1 Calculating quantity drunk.
Figure S2 Procedure for multiple imputation according to van Buuren & Groothuis-Oudshoorn (2009).
Figure S3 Determining quantity drunk (primary EP) for the primary analysis (FAS).
Figure S4 As the treatment of non-informative patients is classified as a failure, the primary EP in the FAS can be analysed for all trial participants.

