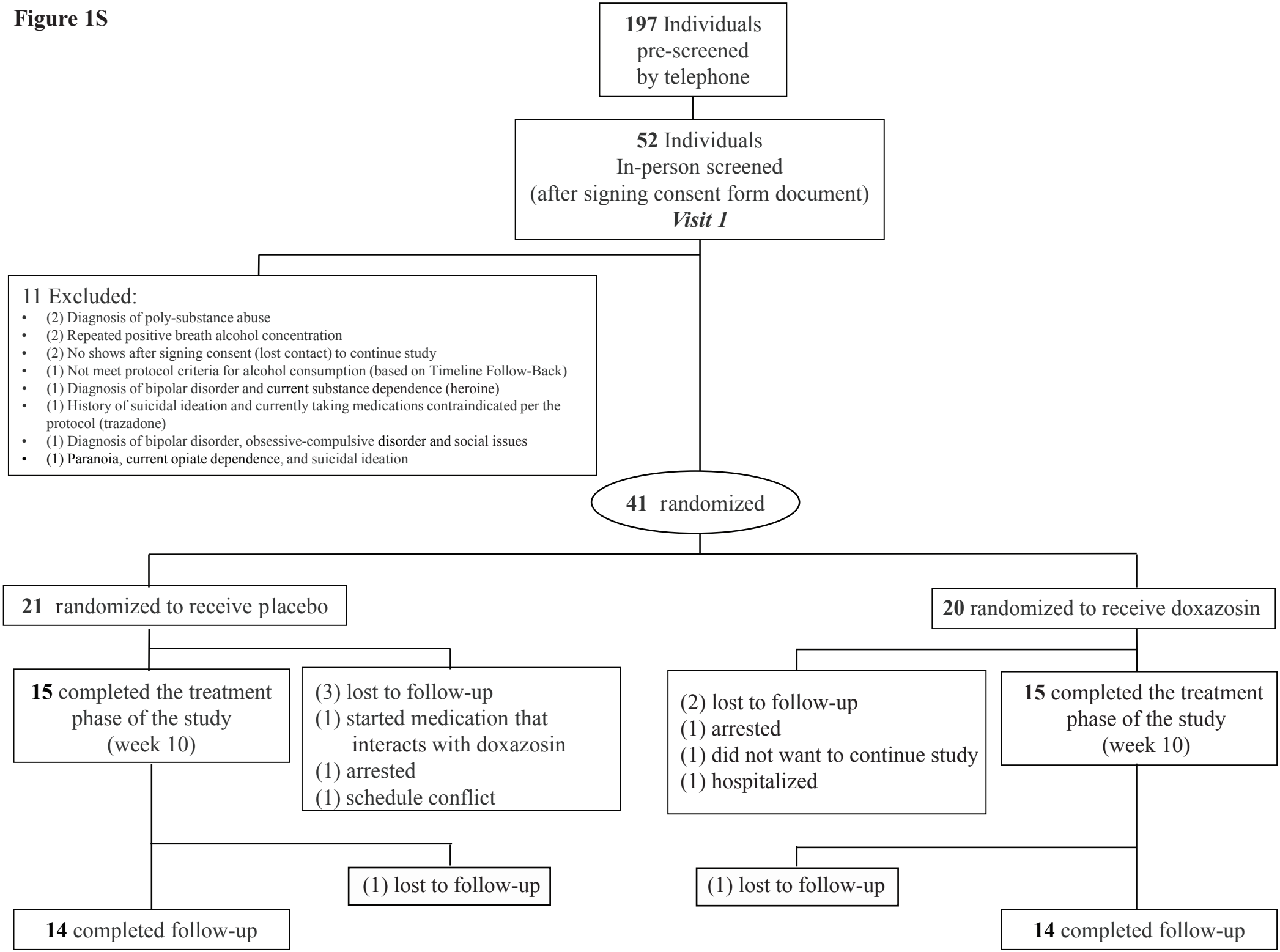
Figure 1S


197 Individuals pre-screened by telephone
52 Individuals In-person screened (after signing consent form document) *Visit 1*
11 Excluded:
• (2) Diagnosis of poly-substance abuse
• (2) Repeated positive breath alcohol concentration
• (2) No shows after signing consent (lost contact) to continue study
• (1) Not meet protocol criteria for alcohol consumption (based on Timeline Follow-Back)
• (1) Diagnosis of bipolar disorder and current substance dependence (heroine)
• (1) History of suicidal ideation and currently taking medications contraindicated per the protocol (trazadone)
• (1) Diagnosis of bipolar disorder, obsessive-compulsive disorder and social issues
• (1) Paranoia, current opiate dependence, and suicidal ideation
41 randomized
21 randomized to receive placebo
20 randomized to receive doxazosin
15 completed the treatment phase of the study (week 10)
(3) lost to follow-up
(1) started medication that interacts with doxazosin
(1) arrested
(1) schedule conflict
(2) lost to follow-up
(1) arrested
(1) did not want to continue study
(1) hospitalized
15 completed the treatment phase of the study (week 10)
(1) lost to follow-up
(1) lost to follow-up
14 completed follow-up
14 completed follow-up

SUPPLEMENTAL INFORMATION

Table 1S. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Age ≥18	Females who were of child bearing potential and not practicing effective birth control
Females had to be post-menopausal for >1 year, surgically sterile, or practicing a birth control before entry and throughout the study; have a negative urine pregnancy test at screening and before randomization	Lifetime DSM-IV diagnosis of schizophrenia, bipolar disorder, or other psychosis
Good health (confirmed by medical history, physical, ECG, blood/urine labs)	Recent (past six months) DSM-IV diagnosis of any anxiety disorder or major depression
Diagnosis of AD based on the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) Patient Version	In the investigators' opinion, risk of suicide (e.g. active plan, or recent attempt in last year)
Average of ≥4 drinks/day for women and ≥5 drinks/day for men during 30 days within the 90 days prior to screening	DSM-IV diagnosis of dependence on any psychoactive substance other than alcohol, nicotine and/or marijuana (given the high comorbidity with alcoholism and our goal to provide a proof-of-concept study in a 'real world' population)
Desire to reduce or quit alcohol drinking	Positive urine screen for any substance other than marijuana
	History of hospitalization for alcohol intoxication delirium, seizure or alcohol withdrawal delirium
	Clinical Institute Withdrawal Assessment for Alcohol score ≥10 Treatment with disulfiram, naltrexone, acamprosate, topiramate within 1 month prior to screening
	Current use of psychotropic medications or drugs that interfere with doxazosin's metabolism
	Use of phosphodiesterase (PDE5) inhibitor erectile dysfunction drugs
	Treatment with any antihypertensive drug and/or any α-blocker for BPH or sleep problems
	Baseline hypotension
	History of allergy to any α-blocker
	Contraindications to taking doxazosin (history of fainting and/or syncopal attacks, heart failure, significant liver diseases)
	Serious illnesses, e.g. kidney failure, epilepsy

Table 2S. Drug Titration Schedule

Week(s)	Day(s)	Daily Dose (mg)
1	1-7	1
2	8-14	2
	15-17	4
3	18-19	6
	20-21	8
	22-24	10
4	25-26	12
	27-28	14
5-10	29-70	16
	71	14
	72	12
	73	10
11	74	8
	75	4
	76	2
	77	1
12	78-84	-

Table 3S. Adverse Events (AEs) as frequency percentage (%)

AE	Doxazosin	Placebo
Dizziness (*)	45	14
Decrease in appetite	10	19
Increase in appetite	25	10
Changes in vision	25	5
Difficulty Sleeping	40	33
Slowness, sleepiness, or fatigue	50	48
Difficulty with coordination or balance	10	5
Difficulty with concentration or attention	30	19
Tingling in fingers or toes	15	19
Word finding difficulties	0	10
Memory difficulties	10	10
Change in taste	0	14
Tremor	55	48
Constipation	5	5
Diarrhea	10	24
Nausea	15	19
Vomiting	10	10
Headache (**)	50	10
Restlessness	35	19
Nervousness or Anxiety, irritability	65	52
Depression or other mood disturbance (*)	35	10
Confusion	0	10
Changes in Libido, impotence	5	19
Slowed breathing	5	5
Hyperventilation	10	0
Trouble waking up	25	5
Trouble breathing	20	14
Stupor	10	5
Skin rash, itching, cellulitis	25	14
Trouble urinating[#] (*)	20	0
Palpitations	20	5
Swelling of face or edema	10	0
Osteomuscular pain	25	24
Eye pain, twitch	5	5
Flu-like symptoms	20	14
Peripheral symptoms	5	5
Other GI symptoms	20	10
Calmness	5	0

Unless otherwise noted, percentages of AEs were not different across groups (p's > .05) (*) p < .05; (**) p < .01 ([#]reported by females as frequent passing urine).

Table 4S. Blood Pressure Changes (BPΔ) [*M* ± (*SE*)]

	Doxazosin	**Placebo**	
	entire 10-week treatment period		
Systolic BPΔ	3.6 (1.3)	3.1 (1.3)	$F_{1,34}$ =.07, p = .80
Diastolic BPΔ	-2.2 (1.2)	-2.8 (1.2)	$F_{1,37}$ =.14, p = .71
	treatment period with the 4-week grace period applied		
Systolic BPΔ	4.8 (1.7)	3.9 (1.7)	$F_{1,32}$ =.16, p = .70
Diastolic BPΔ	-2.4 (1.4)	-2.2 (1.5)	$F_{1,33}$ = .01, p = .93

Table 5S. Full Models for Drinking Outcomes

	DPW	HDD
Medication	F(1,36) = 0.43, p = .52	F(1,35) = 1.03, p = .32
Time	F(5,30) = 1.73, p = .16	F(5,33) = 1.23, p = .32
Medication X Time	F(5,30) = 0.43, p = .82	F(5,33) = 0.76, p = .58

Table 6S. Full Models for Craving

	OCDS	ODS	CDS
Medication	F(1,35) = 2.55, p = .12	F(1,33) = 4.92, p = .034	F(1,36) = 0.87, p = .36
Time	F(2,29) = 0.43, p = .65	F(2,32) = 0.41, p = .67	F(2,30) = 1.40, p = .26
Medication X Time	F(2,29) = 0.28, p = .76	F(2,32) = 0.64, p = .54	F(2,30) = 0.05, p = .95

Table 7S. Full Models for Anxiety and Stress

	HAMA	PSS	POMS-TA
Medication	F(1,36) = 0.46, p = .50	F(1,36) = 0.30, p = .59	F(1,34) = 0.34, p = .56
Time	F(2,32) = 0.98, p = .39	F(2,20) = 0.84, p = .45	F(2,33) = 1.13, p = .34
Medication X Time	F(2,32) = 2.28, p = .12	F(2,20) = 0.81, p = .46	F(2,33) = 2.37, p = .11