Figure SF1. Study Flow-Chart

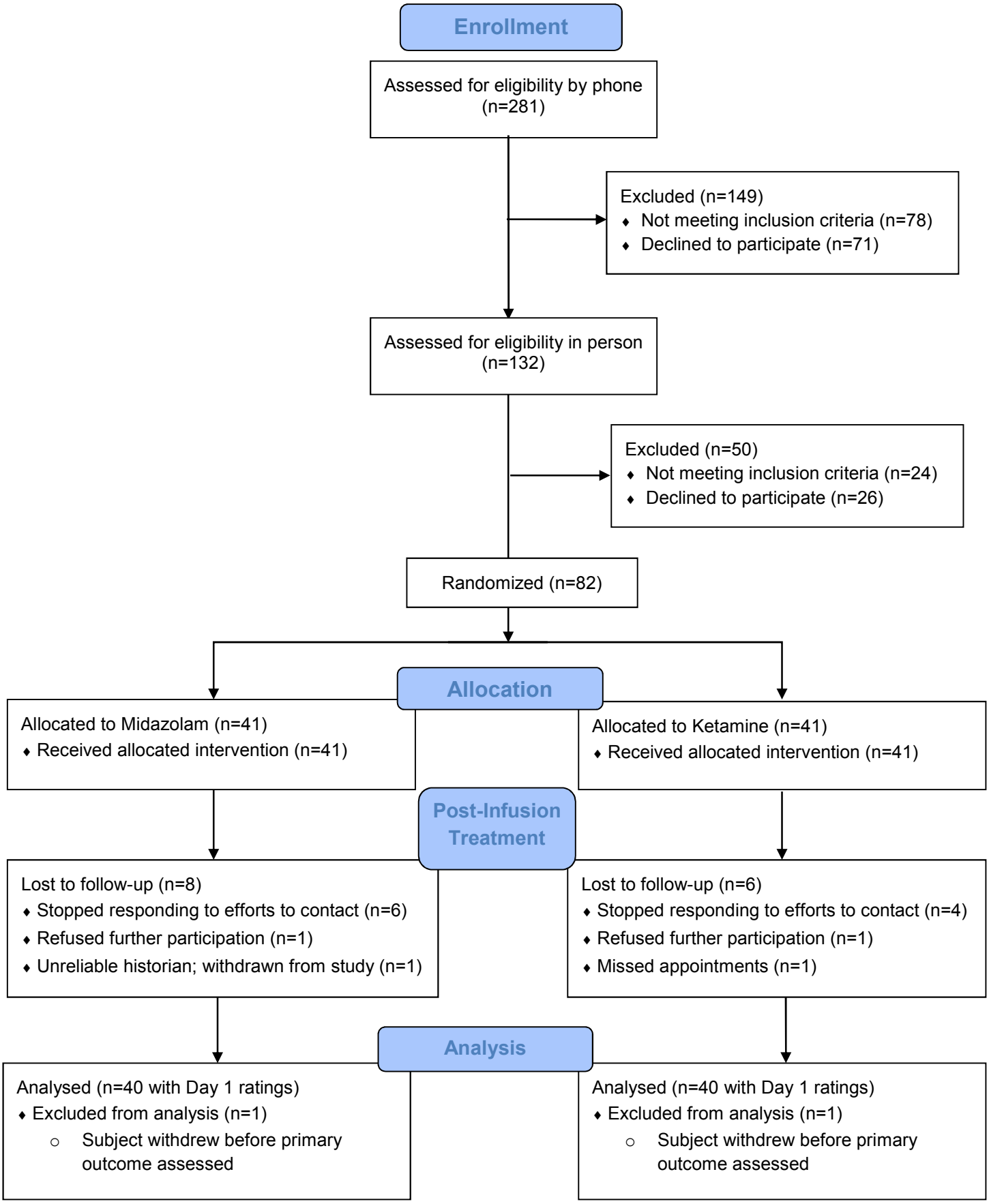


Table SF1. Medication Classes at Baseline for Both Treatment Groups Combined (N=80)

Medication	N	%
Antidepressant	43	53.75
SSRI	14	17.5
SNRI	15	18.75
Tricyclic	6	7.5
MAOI	1	1.25
Other[a]	25	31.25
Anticonvulsant	21	26.25
Antipsychotic	14	17.5
Benzodiazepine	27	33.75
Lithium	2	2.5

[a]Other antidepressants: bupropion, trazodone, mirtazapine, vortioxetine, vilazodone.

Table SF2. Suicidal Ideation Severity During the Study for Both Treatment Groups Combined

						Test of Change					
	Scale for Suicidal Ideation			Change from Baseline		From Baseline			From Last Time Point		
Time Point	N	Mean	SD	Mean	SD	DF	t	p	DF	t	p
Baseline[a]	80	14.98	6.64	.	.	.	.	.	.	.	.
230 minutes after randomized infusion	80	7.43	6.70	-7.55	7.10	465	-9.57	<.0001	.	.	.
Day 1 after randomized infusion	80	8.84	7.07	-6.14	7.18	465	-7.78	<.0001	465	-2.03	0.0427
Week1	73	6.88	7.40	-7.95	8.49	465	-9.60	<.0001	465	2.26	0.0243
Week2	70	6.60	7.01	-8.11	8.61	465	-9.69	<.0001	465	0.22	0.8252
Week3	67	6.75	7.94	-8.15	9.25	465	-9.27	<.0001	465	-0.35	0.7272
Week4	60	7.40	7.75	-7.93	9.34	465	-8.71	<.0001	465	-0.32	0.7467
Week5	61	6.89	7.47	-7.75	9.02	465	-9.15	<.0001	465	0.42	0.6727
Week6	61	6.72	7.63	-8.52	8.60	465	-9.61	<.0001	465	0.49	0.6255

[a]Baseline is within 24 hours before infusion.

Table SF3. Depression Severity During the Study for Both Treatment Groups Combined

						Test of Change					
	17-Item Hamilton Depression Rating Scale			Change from Baseline		From Baseline			From Last Time Point		
Time Point	N	Mean	SD	Mean	SD	DF	t	p	DF	t	p
Baseline[a]	80	22.43	4.31	.	.	.	.	.	.	.	.
Day 1 after randomized infusion	80	16.76	7.23	-5.66	6.86	382	-7.47	<.0001	.	.	.
Week1	72	15.51	6.98	-6.93	7.03	382	-8.35	<.0001	382	1.17	0.2428
Week2	70	14.63	6.80	-7.86	6.94	382	-9.46	<.0001	382	1.20	0.2320
Week3	66	14.30	6.64	-7.92	6.79	382	-9.42	<.0001	382	0.14	0.8873
Week4	60	14.00	6.76	-8.25	7.52	382	-9.64	<.0001	382	0.49	0.6277
Week5	61	13.74	7.63	-8.64	7.81	382	-10.09	<.0001	382	0.38	0.7008
Week6	59	13.97	7.43	-8.58	7.37	382	-9.94	<.0001	382	-0.05	0.9597

[a]Baseline is within 24 hours before infusion.

Table SF4. Infusion-related Cardio-respiratory Effects in Patients with Major Depressive Disorder and Clinically Significant Suicidal Ideation Given a Single Infusion of Ketamine or Midazolam[a]

Variable	Midazolam N=40 Mean (SD)	Ketamine N=40 Mean (SD)	Open Ketamine N=34 Mean (SD)
Baseline systolic blood pressure (SBP)[b]	120 (9.8)	120 (10.6)	120 (21.5)
Baseline diastolic blood pressure (DBP)	74 (7.0)	74 (9.1)	75 (7.2)
Peak SBP	124 (11.9)	135 (13.7)	140 (16.1)
Peak DBP	78 (7.5)	88 (9.9)	92 (10.1)
Minutes to return to baseline BP[c]	0 (0)	5.3 (9.0)	5.7 (7.7)
Baseline oxygen saturation	98 (1.5)	98 (0.96)	98 (1.2)
Lowest oxygen saturation[d]	96 (2.3)	97 (1.8)	97 (1.5)
Baseline respiratory rate	15 (3.3)	16 (4.0)	15 (3.9)
Lowest respiratory rate[d]	12 (2.9)	11 (1.8)	11 (2.3)

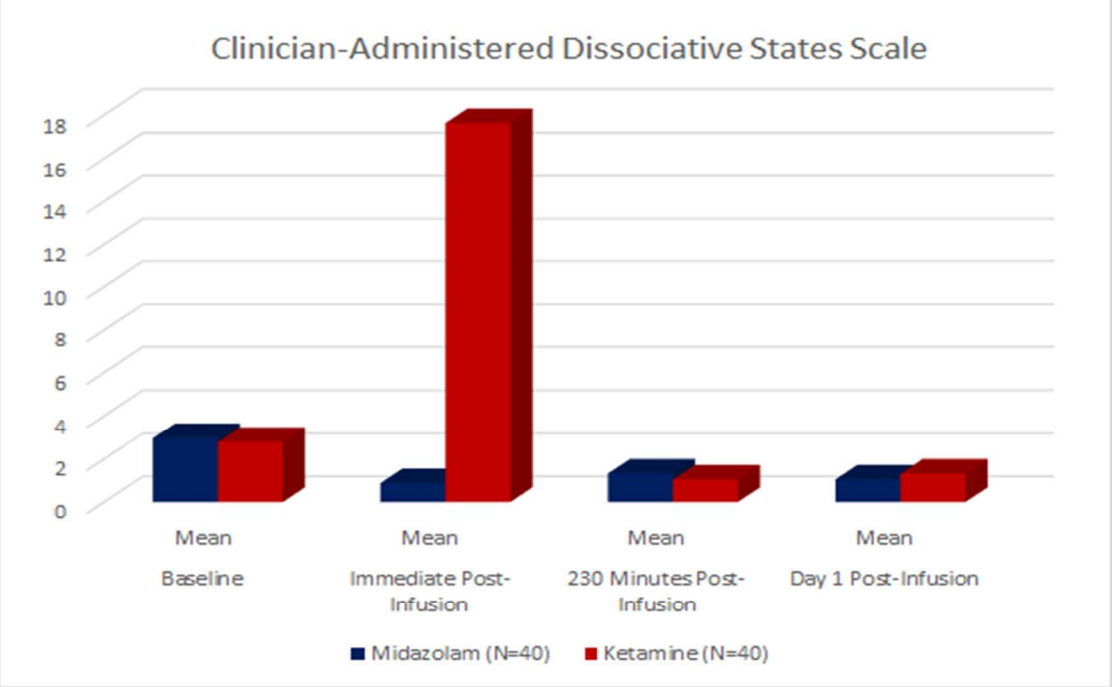
[a]Vital signs were measured every five minutes during treatment with ketamine 0.5 mg/kg or midazolam 0.02 mg/kg in 100 ml normal saline infused over 40 minutes, adjunctive to current, non-benzodiazepine medications.

[b]Blood pressure in millimeters mercury (mm Hg).

[c]Return to baseline blood pressure was operationalized as DBP within 10mm Hg of baseline or DBP<85.

[d]Midazolam was associated with a Mean=1.60 (SD=1.96) point decrease in oxygen saturation from baseline versus a 0.90 (SD=1.22) point decrease with ketamine (t=1.92, df=78, p=0.0584). Ketamine was associated with a decrease in respiratory rate of Mean=4.98 (SD=4.08) breaths per minute compared to 3.25 (SD=3.48) for midazolam (t=-2.04, df=78, p=0.0452).

Figure SF2. Dissociative Effects in Suicidal Patients with Major Depression Randomized to a Sub-anesthetic Infusion of Ketamine or Midazolam[a,b]



[a]Immediate post-infusion rating done by physician supervising infusion.
[b]230 Minute post-infusion rating done by clinical rater who was not present during infusion.

Table SF5. Systematic Assessment for Treatment Emergent Events-General Inquiry (SAFTEE) ratings in a study of ketamine *vs.* midazolam in patients with major depression and clinically significant suicidal ideation[a]

	Ketamine (N=40) N (%)			Midazolam (N=40) N (%)		
SEVERITY OF EVENTS[b]	**Baseline**	**Immediate post-infusion**	**Day 1**	**Baseline**	**Immediate post-infusion**	**Day 1**
Patients with any severe event	2 (5)	3 (8)	0	1 (3)	1 (3)	0
Patients with any moderate event	3 (8)	6 (15)	3 (8)	8 (20)	6 (15)	3 (8)
Patients with any mild event	6 (15)	14 (35)	8 (20)	7 (18)	25 (63)	10 (25)
Patients with any event[c]	11 (28)	21 (53)	10 (25)	15 (38)	32 (80)	12 (30)
	Ketamine (N=40) N (%)			**Midazolam (N=40) N (%)**		
TYPE OF EVENT	**Baseline**	**Immediate post-infusion**	**Day 1**	**Baseline**	**Immediate post-infusion**	**Day 1**
Numbness		6 (15)			1 (3)	
Perceptual problems		5 (13)	2 (5)	1 (3)		1 (3)
Dizziness/ faintness		5 (13)	1 (3)			
Drowsiness		5 (13)			16 (40)	
Headache	3 (8)	2 (5)	1 (3)	8 (20)	5 (13)	3 (8)
Dry Mouth		2 (5)	1 (3)			
Nausea		2 (5)			1 (3)	
Cold sensation		1 (3)			4 (10)	
Vomiting		1 (3)				
Rapid heartbeat		1 (3)				
Difficulty swallowing		1 (3)				
Musculoskeletal pain	4 (10)		3 (8)	2 (5)		2 (5)
Fatigue	3 (8)		2 (5)	2 (5)	11 (28)	2 (5)
Constipation	3 (8)		1 (3)			
Anxiety			1 (3)			
Memory problems			1 (3)			
Loss of consciousness					1 (3)	
Diarrhea	1 (3)			1 (3)		2 (5)
Stomach/abdominal discomfort				2 (5)		1 (3)
Irritability						1 (3)
Interrupted sleep						1 (3)
Tinnitus	1 (3)					
Concentration difficulty	1 (3)					
Sore throat	1 (3)					
Skin irritation				1 (3)		
Appetite increase				1 (3)		
Edema				1 (3)		

[a]Comparisons between treatment groups: frequency of all events immediately post-infusion (U=615.50, p=0.0508) and on Day 1 (U=768.00, p=0.6932); severity of events immediately post-infusion (U=645.00, p=0.1162) and on Day 1 (U=771.00, p=0.7216).
[b]Patients who experienced multiple events with varying severity are counted in more than one severity category.

SF6. Table of Serious Adverse Events Requiring Institutional Review Board (IRB) Report

Randomized Group	Responder[a]	Remitter[b]	Open Infusion	Open infusion response	Timepoint of event	Brief Description
Midazolam	No	No	Yes	Remitter	Month 4	Zolpidem misuse without suicidal intent
Ketamine	Yes	No	No		Week 7 and Month 6	Medical illness unrelated to study
Midazolam	Yes	Yes	No		Month 6	Inpatient admission for increased suicidal ideation
Ketamine	Yes	No	No		Week 6	Inpatient admission for increased suicidal ideation
Ketamine	No	No	No		Month 5	Overdose resulting in inpatient admission
Midazolam	Yes	No	Yes	Remitter	Before study procedures	Overdose, discussed with therapist, did not lead to inpatient admission
Ketamine	Yes	No	No		Month 7	Overdose resulting in inpatient admission
Midazolam	No	No	Yes	Non-responder	Month 4	Inpatient admission for increased suicidal ideation
Ketamine	Yes	Yes	No		Week 2	Overdose

[a]Response = Day 1 Scale for Suicidal Ideation score ≥50% lower than baseline.
[b]Remission = Day 1 Scale for Suicidal Ideation score ≥50% lower than baseline and <4.