Figure 1: Participant Flow

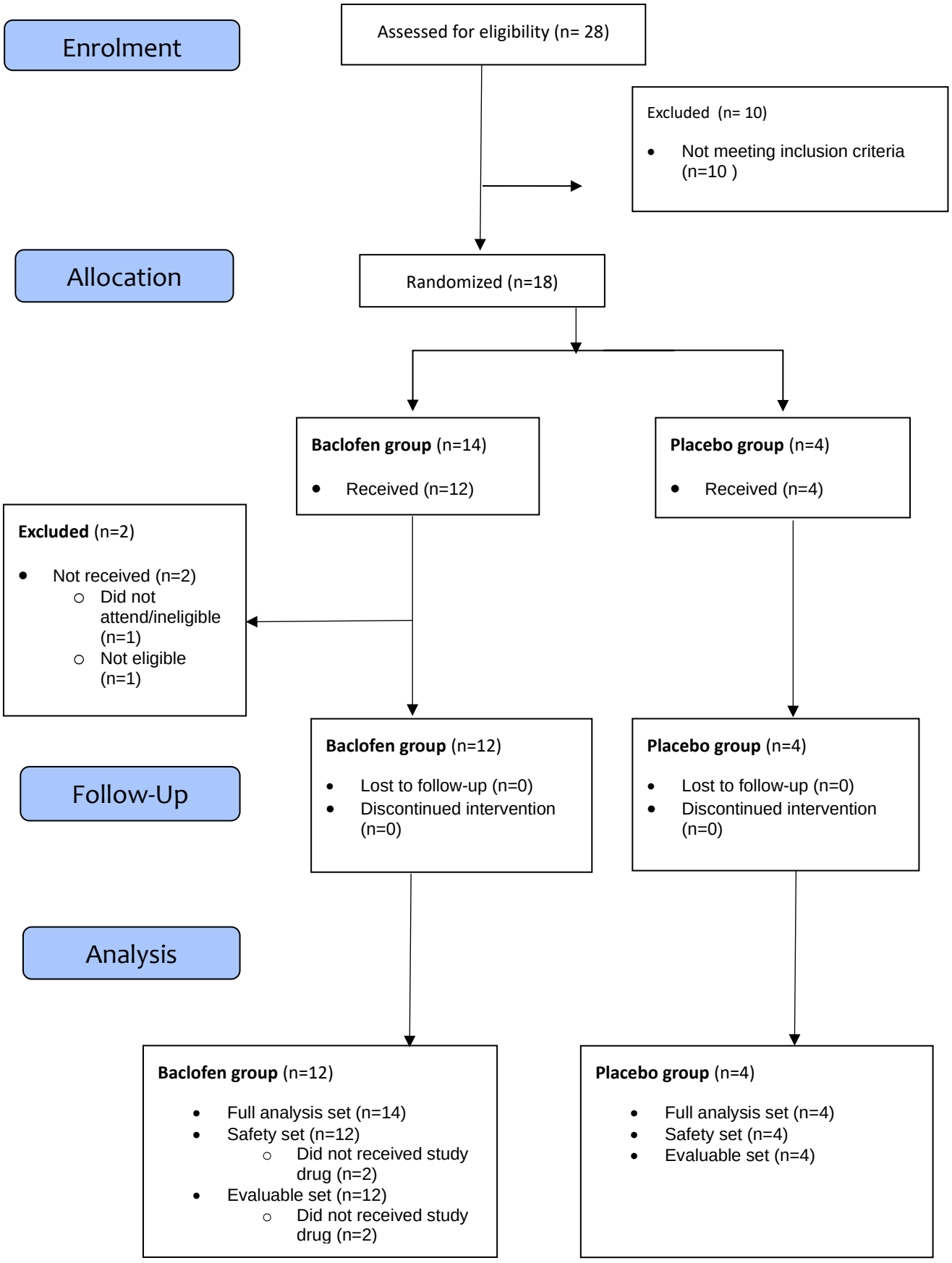

Table 1: Baseline characteristics by treatment arm

Characteristic		Baclofen	Placebo	Total
		N=12	N=4	N=16
Demographics				
Age (years)				
	N (N missing)	12 (0)	4 (0)	16 (0)
	Mean (SD)	47.1 (8.5)	46.0 (7.4)	46.8 (8.0)
	Median (IQR)	49 (44, 53)	45 (42, 51)	47 (44, 53)
Sex, n (%)				
	N (N missing)	12 (0)	4 (0)	16 (0)
	Male	10 (83.3)	4 (100.0)	14 (87.5)
	Female	2 (16.7)	0 (0.0)	2 (12.5)
Ethnicity, n (%)				
	N (N missing)	12 (0)	4 (0)	16 (0)
	White	7 (58.3)	3 (75.0)	10 (62.5)
	Black, African, Caribbean or Black British	2 (16.7)	0 (0.0)	2 (12.5)
	Asian or Asian British	1 (8.3)	1 (25.0)	2 (12.5)
	Other	2 (16.7)	0 (0.0)	2 (12.5)

Primary outcome

No patients in the baclofen arm or the placebo arm experienced a DLT (0 versus 0).

Based on the tested doses of methadone and baclofen, methadone doses of up to 70mg per day and baclofen doses of up to 60mg (acute) are safe, that is the probability of DLT being above the target interval of 15-25% is less than 0.25.

Adverse events

Table 2. Summary of adverse event type by treatment arm

Event type		Baclofen		Placebo		Total	
		Number of events	Number of participants with events (Total N=12)	Number of events	Number of participants with events (Total N=4)	Number of events	Number of participants with events (Total N=16)
		n	n (%)	n	n (%)	n	n (%)
All AE		11	4 (33.3)	1	1 (25.0)	12	5 (31.3)
Non-serious AE	Total	11	4 (33.3)	1	1 (25.0)	12	5 (31.3)
Serious AE	Total	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
	Serious adverse reactions (SAR)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
	Unexpected SAR (USAR)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)

Acronyms: AE – adverse event; SAE – serious adverse event; SAR – serious adverse reaction; USAR – unexpected serious adverse reaction

Table 3. Adverse events by preferred term and treatment arm

System Organ Class	Preferred term	**Baclofen**		**Placebo**		**Total**	
		Number of events	Number of participants with events (Total N=12)	Number of events	Number of participants with events (Total N=4)	Number of events	Number of participants with events (Total N=16)
		n	n (%)	n	n (%)	n	n (%)
Cardiac disorders	Bradycardia	0	0 (0.0)	1	1 (25.0)	1	1 (6.3)
Gastrointestinal disorders	Nausea	1	1 (8.3)	0	0 (0.0)	1	1 (6.3)
	Vomiting	2	2 (16.7)	0	0 (0.0)	2	2 (12.5)
General disorders and administration site conditions	Chills	1	1 (8.3)	0	0 (0.0)	1	1 (6.3)
Nervous system disorders	Dizziness	1	1 (8.3)	0	0 (0.0)	1	1 (6.3)
	Sedation	4	4 (33.3)	0	0 (0.0)	4	4 (25.0)
Respiratory, thoracic and mediastinal disorders	Wheezing	1	1 (8.3)	0	0 (0.0)	1	1 (6.3)
Skin and subcutaneous tissue disorders	Hyperhidrosis	1	1 (8.3)	0	0 (0.0)	1	1 (6.3)