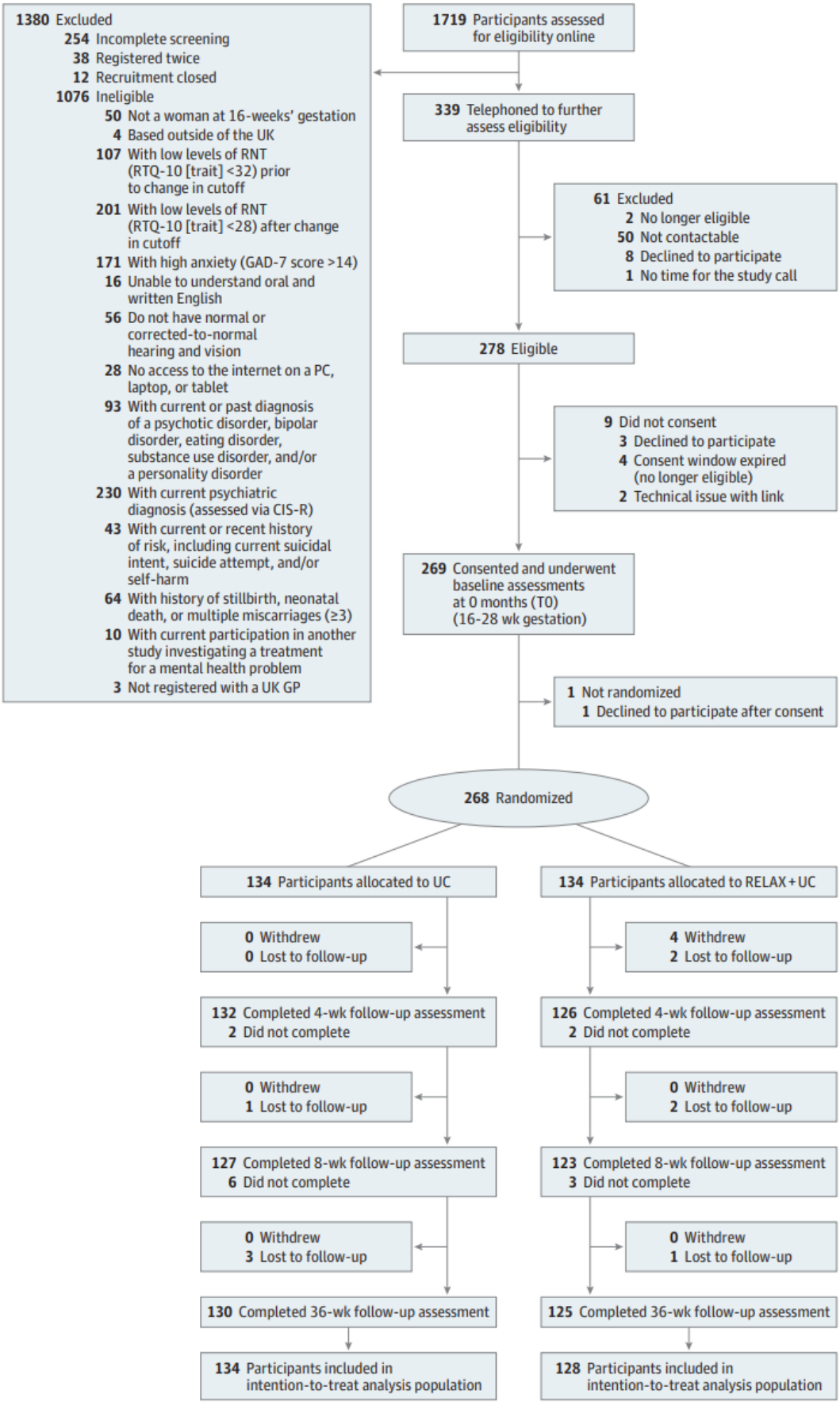
Participant Flow



The primary outcome was anxiety, as assessed by the 7-item Generalized Anxiety Disorder Scale (GAD-7) score at 8 weeks. The primary mechanistic outcome was interpretation bias (Recognition Test) at 4 weeks. CIS-R indicates Clinical Interview Schedule Revised; CONSORT, Consolidated Standards of Reporting Trials; GP, general practitioner; PC, personal computer; RNT, repetitive negative thinking; RTQ-10, 10-item trait version of the Repetitive Thinking Questionnaire; UC, usual care.

Baseline characteristics

Characteristic	Participants, No. (%)		
	UC (n=134)	RELAX + UC (n=134)	Overall (N=268)
Age, y			
Mean (SD)	34.1 (3.8)	33.4 (4.0)	33.7 (3.9)
Median (IQR)	34.0 (32.0-36.0)	33.5 (31.0-36.0)	34.0 (31.0-36.0)
Missing	0	0	0
Ethnicity[a,b]			
African	2 (1.5)	0	2 (0.7)
Any other Asian background	4 (3.0)	3 (2.2)	7 (2.6)
Any other Black, Black British, or Caribbean background	1 (0.7)	3 (2.2)	4 (1.5)
Any other mixed or multiple ethnic background	4 (3.0)	2 (1.5)	6 (2.2)
Any other White background	19 (14.2)	18 (13.4)	37 (13.8)
Arab	0	0	0
Bangladeshi	0	0	0
Caribbean	1 (0.7)	1 (0.7)	2 (0.7)
Chinese	3 (2.2)	4 (3.0)	7 (2.6)
English, Welsh, Scottish, Northern Irish, or British	88 (65.7)	89 (66.4)	177 (66.0)
Gypsy or Irish Traveller	0	0	0
Indian	4 (3.0)	4 (3.0)	8 (3.0)
Irish	2 (1.5)	2 (1.5)	4 (1.5)
Pakistani	0	1 (0.7)	1 (0.4)
Roma	0	0	0
White and Asian	1 (0.7)	5 (3.7)	6 (2.2)
White and Black African	1 (0.7)	0	1 (0.4)
White and Black Caribbean	2 (1.5)	2 (1.5)	4 (1.5)
Other[c]	2 (1.5)	0	2 (0.7)

Missing	0	0	0
Religion			
No religion	77 (57.5)	76 (56.7)	153 (57.1)
Christian	43 (32.1)	43 (32.1)	86 (32.1)
Buddhist	1 (0.7)	0	1 (0.4)
Hindu	4 (3.0)	5 (3.7)	9 (3.4)
Jewish	2 (1.5)	1 (0.7)	3 (1.1)
Muslim	2 (1.5)	2 (1.5)	4 (1.5)
Sikh	1 (0.7)	0	1 (0.4)
Other	2 (1.5)	1 (0.7)	3 (1.1)
Prefer not to say	2 (1.5)	6 (4.5)	8 (3.0)
Missing	0	0	0
Relationship status			
Single, never married, and never registered in a civil partnership	5 (3.7)	5 (3.7)	10 (3.7)
Married	88 (65.7)	86 (64.2)	174 (64.9)
In a registered civil partnership	0	1 (0.7)	1 (0.4)
In a relationship or cohabiting	38 (28.4)	41 (30.6)	79 (29.5)
Separated, but still legally married	0	0	0
Separated, but still legally in a civil partnership	0	1 (0.7)	1 (0.4)
Divorced	3 (2.2)	0	3 (1.1)
Formerly in a civil partnership that is now legally dissolved	0	0	0
Widowed	0	0	0
Surviving partner from a registered civil partnership	0	0	0
Missing	0	0	0
Employment status			
Full-time student	4 (3.0)	2 (1.5)	6 (2.2)
Employed full-time	99 (73.9)	99 (73.9)	198 (73.9)
Employed part-time	17 (12.7)	19 (14.2)	36 (13.4)

Unemployed (looking for work)	3 (2.2)	0	3 (1.1)
Unemployed (not looking for work)	2 (1.5)	3 (2.2)	5 (1.9)
Unable to work	0	0	0
Self-employed	9 (6.7)	11 (8.2)	20 (7.5)
Retired	0	0	0
Other	0	0	0
Missing	0	0	0
Educational attainment			
GCSE or Level 2 NVQ	2 (1.5)	5 (3.7)	7 (2.6)
A level or Level 3 NVQ	6 (4.5)	7 (5.2)	13 (4.9)
Certificate of higher education, higher apprenticeship, or Level 4 NVQ	2 (1.5)	6 (4.5)	8 (3.0)
Foundation degree or NVQ Level 5	1 (0.7)	2 (1.5)	3 (1.1)
Bachelor's degree or NVQ Level 6	57 (42.5)	62 (46.3)	119 (44.4)
Master's degree, postgraduate certificate, postgraduate diploma, or NVQ Level 7	58 (43.3)	45 (33.6)	103 (38.4)
Doctorate or NVQ Level 8	5 (3.7)	7 (5.2)	12 (4.5)
Other	3 (2.2)	0	3 (1.1)
Missing	0	0	0
Preexisting health condition			
Yes	31 (23.1)	37 (27.6)	68 (25.4)
No	103 (76.9)	97 (72.4)	200 (74.6)
Missing	0	0	0
No. of children[d]			
0	94 (70.1)	97 (72.4)	191 (71.3)
1	35 (26.1)	33 (24.6)	68 (25.4)
2	3 (2.2)	3 (2.2)	6 (2.2)
3	2 (1.5)	1 (0.7)	3 (1.1)
Missing	0	0	0

Social support: is there someone (eg, your family or friends) you can count on to listen to you when you need to talk?			
Yes	132 (98.5)	132 (98.5)	264 (98.5)
No	1 (0.7)	0	1 (0.4)
Not sure	1 (0.7)	2 (1.5)	3 (1.1)
Missing	0	0	0
Gestation, wk			
Mean (SD) [e]	21.1 (4.1)	21.0 (3.8)	21.0 (3.9)
Median (IQR)	21.0 (17.0-25.0)	21.0 (18.0-24.0)	21.0 (18.0-24.0)
Missing	0	0	0
Received a diagnosis of a mental health condition in the past			
Yes	45 (33.6)	48 (35.8)	93 (34.7)
No	89 (66.4)	86 (64.2)	175 (65.3)
Missing	0	0	0
Receiving psychological treatment			
Yes	34 (25.4)	14 (10.4)	48 (17.9)
No	100 (74.6)	120 (89.6)	220 (82.1)
Missing	0	0	0
Taking medication for mental health			
Yes	7 (5.2)	15 (11.2)	22 (8.2)
No	127 (94.8)	119 (88.8)	246 (91.8)
Missing	0	0	0
Stratification factors			
Site			
GSTT	23 (17.2)	23 (17.2)	46 (17.2)
KCH	21 (15.7)	23 (17.2)	44 (16.4)
KCL[f]	76 (56.7)	74 (55.2)	150 (56.0)
ESTH[g]	8 (6.0)	8 (6.0)	16 (6.0)
MCHT[g,h]	6 (4.5)	6 (4.5)	12 (4.5)
Missing	0	0	0
Parity			
No previous birth at ≥24 wk	95 (70.9)	97 (72.4)	192 (71.6)
≥1 (had previous birth at ≥24 wk)	39 (29.1)	37 (27.6)	76 (28.4)

Missing	0	0	0
Pregnancy complications[i]			
None	72 (53.7)	68 (50.7)	140 (52.2)
Some (current or past)	62 (46.3)	66 (49.3)	128 (47.8)
Missing	0	0	0

Abbreviations: ESTH, Epsom and St Helier University Hospitals National Health Service (NHS) Trust; GCSE, General Certificate of Secondary Education; GSTT, Guy's and St Thomas' NHS Foundation Trust; KCH, King's College Hospital NHS Foundation Trust; KCL, King's College London; MCHT, Mid Cheshire Hospitals NHS Foundation Trust; NVQ, National Vocational Qualification; RELAX, Reducing Levels of Anxiety; UC, usual care.

[a] Ethnicity responses are clustered alphabetically into standard UK ethnic groupings.

[b] Due to an error in the ethnicity question, the overarching ethnicity headings, including "White," were omitted from the demographics form. This may have led to an underestimation of people with Black, Asian, or mixed ethnicity, as some may have selected "English, Welsh, Scottish, Northern Irish, or British."

[c] Other includes Persian (n = 1) and White American (n = 1).

[d] No participants had more than 3 children.

[e] Participants' gestation was calculated by subtracting the difference in weeks between date of randomization and the participants' due date from 40 weeks. This value was rounded down, regardless of the decimal place (eg, 15.9 weeks was rounded to 15 weeks). At 36 weeks, participants submitted their infants' date of birth.

[f] Participants recruited under KCL also included participants recruited via other NHS Trusts via posters, as well as others via social media.

[g] MCHT and ESTH joined the study later, hence lower levels of recruitment.

[h] One participant was incorrectly stratified in MCHT but had actually been recruited via a poster in a different NHS Trust and so should have been stratified in the KCL site. They were analyzed as stratified.

[i] Includes all pregnancy symptoms (ranging from common pregnancy symptoms such as fatigue and low iron to abdominal pain and severe swelling).

Outcome measures

Summary Statistics and Estimated Mean Difference in primary and Secondary Outcomes Between Arms [a]

		UC (n=134)			RELAX+UC (n=134)			Overall (N=268)			Adjusted mean difference	
Scale	**Time**	**No.**	**Mean (SD)**	**Range**	**No.**	**Mean (SD)**	**Range**	**No.**	**Mean (SD)**	**Range**	**Difference (95% CI)**	**P value**
GAD-7 (primary)	T0	134	7.6 (3.5)	0.0 to 16.0	134	7.8 (3.4)	2.0 to 18.0	268	7.7 (3.4)	0.0 to 18.0	NA	NA
	T1	132	6.8 (3.9)	0.0 to 18.0	126	5.0 (3.5)	0.0 to 18.0	258	5.9 (3.8)	0.0 to 18.0	NA	NA
	T2	127	5.7 (3.6)	0.0 to 16.0	123	4.4 (2.8)	0.0 to 14.0	250	5.1 (3.3)	0.0 to 16.0	−1.46 (−2.36 to −0.57)	.001
	T3	130	6.5 (4.9)	0.0 to 21.0	125	5.6 (3.9)	0.0 to 17.0	255	6.1 (4.5)	0.0 to 21.0	−0.99 (−1.88 to −0.10)	.03
PHQ-9	T0	134	5.9 (3.3)	0.0 to 17.0	134	6.4 (3.0)	1.0 to 16.0	268	6.2 (3.2)	0.0 to 17.0	NA	NA
	T1	132	5.3 (3.4)	0.0 to 20.0	126	4.2 (2.7)	0.0 to 14.0	258	4.8 (3.1)	0.0 to 20.0	NA	NA
	T2	127	4.8 (3.5)	0.0 to 18.0	123	4.0 (2.6)	0.0 to 15.0	250	4.4 (3.1)	0.0 to 18.0	−0.79 (−1.52 to −0.06)	.03
	T3	130	4.7 (4.4)	0.0 to 24.0	125	4.6 (3.9)	0.0 to 24.0	255	4.6 (4.1)	0.0 to 24.0	−0.17 (−1.20 to 0.87)	.75
RTQ-10	T0	134	34.4 (6.0)	19.0 to 48.0	134	35.2 (6.0)	16.0 to 49.0	268	34.8 (6.0)	16.0 to 49.0	NA	NA
	T1	132	32.5 (6.7)	16.0 to 49.0	126	29.5 (7.2)	14.0 to 49.0	258	31.0 (7.1)	14.0 to 49.0	NA	NA
	T2	127	29.2 (7.4)	10.0 to 45.0	123	26.7 (8.1)	10.0 to 46.0	250	28.0 (7.8)	10.0 to 46.0	−2.67 (−4.50 to −0.85)	.004
	T3	130	29.9 (9.1)	11.0 to 50.0	125	27.6 (8.2)	10.0 to 44.0	255	28.8 (8.7)	10.0 to 50.0	−2.39 (−4.57 to −0.20)	.03
PSWQ	T0	134	59.7 (8.9)	36.0 to 79.0	134	60.7 (8.9)	32.0 to 79.0	268	60.2 (8.9)	32.0 to 79.0	NA	NA
	T1	132	58.2 (9.6)	34.0 to 76.0	126	54.0 (10.1)	31.0 to 80.0	258	56.2 (10.1)	31.0 to 80.0	NA	NA
	T2	127	57.1 (10.0)	28.0 to 78.0	123	53.9 (9.9)	30.0 to 80.0	250	55.5 (10.0)	28.0 to 80.0	−3.62 (−5.91 to −1.33)	.002

	T3	130	56.6 (11.4)	23.0 to 79.0	125	55.4 (10.5)	35.0 to 80.0	255	56.0 (11.0)	23.0 to 80.0	−1.40 (−4.05 to 1.26)	.30
EPDS	T0	134	10.1 (3.5)	1.0 to 19.0	134	9.6 (3.6)	2.0 to 18.0	268	9.8 (3.6)	1.0 to 19.0	NA	NA
	T1	132	8.9 (3.9)	0.0 to 18.0	126	7.0 (3.6)	0.0 to 22.0	258	8.0 (3.8)	0.0 to 22.0	NA	NA
	T2	127	7.9 (3.9)	0.0 to 19.0	123	6.8 (3.7)	0.0 to 17.0	250	7.3 (3.8)	0.0 to 19.0	−1.06 (−1.95 to −0.16)	.02
	T3	130	8.5 (4.9)	0.0 to 25.0	125	7.2 (3.7)	0.0 to 18.0	255	7.9 (4.4)	0.0 to 25.0	−1.28 (−2.35 to −0.20)	.02
PASS	T0	134	33.7 (12.2)	13.0 to 67.0	134	33.3 (13.2)	6.0 to 75.0	268	33.5 (12.7)	6.0 to 75.0	NA	NA
	T1	132	27.7 (13.3)	4.0 to 64.0	126	19.1 (11.0)	0.0 to 56.0	258	23.5 (13.0)	0.0 to 64.0	NA	NA
	T2	127	24.7 (12.7)	2.0 to 58.0	123	19.3 (11.0)	2.0 to 51.0	250	22.1 (12.2)	2.0 to 58.0	−5.48 (−8.20 to −2.77)	<.001
	T3	130	24.2 (14.8)	2.0 to 90.0	125	22.2 (12.8)	0.0 to 65.0	255	23.2 (13.9)	0.0 to 90.0	−2.08 (−5.52 to 1.36)	.24
WSAS	T0	134	11.4 (6.5)	0.0 to 29.0	134	11.7 (5.6)	0.0 to 24.0	268	11.5 (6.0)	0.0 to 29.0	NA	NA
	T1	132	11.1 (6.7)	0.0 to 28.0	126	8.8 (5.6)	0.0 to 26.0	258	10.0 (6.3)	0.0 to 28.0	NA	NA
	T2	127	9.4 (6.8)	0.0 to 27.0	123	8.6 (6.4)	0.0 to 28.0	250	9.0 (6.6)	0.0 to 28.0	−1.01 (−2.53 to 0.51)	.19
	T3	130	10.7 (8.5)	0.0 to 35.0	125	9.9 (6.8)	0.0 to 30.0	255	10.3 (7.7)	0.0 to 35.0	−0.78 (−2.73 to 1.17)	.43
RT Positive Index	T0	132	−0.1 (0.7)	−2.2 to 2.4	134	−0.1 (0.7)	−2.2 to 2.4	266	−0.1 (0.7)	−2.2 to 2.4	NA	NA
	T1	126	−0.0 (0.7)	−1.8 to 1.7	125	1.4 (0.7)	−0.5 to 3.0	251	0.7 (1.0)	−1.8 to 3.0	NA	NA

Abbreviations: EPDS, Edinburgh Postnatal Depression Scale; GAD-7, 7-item General Anxiety Disorder Scale; NA, not applicable; PASS, Perinatal Anxiety Screening Scale; PHQ-9, Patient Health Questionnaire-9; PSWQ, Penn State Worry Questionnaire; RELAX, Reducing Levels of Anxiety; RT Positive Index, Recognition Test–Positive Interpretation Bias; RTQ-10, 10-item trait version of the Repetitive Thinking Questionnaire; T0, baseline; T1, 4 weeks after randomization; T2, 8 weeks after randomization; T3, 36 weeks after randomization; UC, Usual Care; WSAS, Work and Social Adjustment Scale.

[a] Total scores are presented for GAD-7, PHQ-9, RTQ-10, PSWQ, EPDS, PASS, WSAS, and RT Positive Index.

Harms/adverse events

Occurrence of adverse events and serious adverse events was comparable in both arms. None were device (RELAX) related or trial related or caused death, most occurred between T2 and T3.

Adverse events by arm and overall

Adverse Events (AEs)[a]		Number of events (Number of people)		
		UC[b] N=134	RELAX+UC[b] N=134	Overall N = 268
Description of AE				
	1=Cardiovascular	3 (3)	2 (2)	5 (5)
	2=Respiratory	11 (10)	11 (11)	22 (21)
	3=Hepatic	3 (2)	3 (3)	6 (5)
	4=Gastro-intestinal	11 (9)	17 (15)	28 (24)
	5=Genito-urinary/renal	13 (11)	5 (4)	18 (15)
	6=Endocrine	9 (7)	10 (10)	19 (17)
	7=Hematological	11 (11)	5 (5)	16 (16)
	8=Musculo-skeletal	19 (17)	18 (18)	37 (35)
	9=Neoplasia	0 (0)	0 (0)	0 (0)
	10=Neurological	2 (2)	1 (1)	3 (3)
	11=Psychological	3 (3)	6 (6)	9 (9)
	12=Immunological	5 (4)	5 (5)	10 (9)
	13=Dermatological	7 (7)	8 (7)	15 (14)
	14=Allergies	3 (3)	3 (3)	6 (6)
	15=Eyes, ear, nose, throat	2 (2)	3 (3)	5 (5)
	16=Other	41 (35)	34 (29)	75 (64)
Timing of AE:				
	After T0, Before T1	26 (24)	11 (8)	37 (32)
	After T1, Before T2	25 (23)	24 (19)	49 (42)
	After T2, Before T3	92 (64)	96 (68)	188 (132)
Related to trial:				
	Unrelated	143 (83)	131 (76)	274 (159)
	Unlikely	0 (0)	0 (0)	0 (0)
	Possibly	0 (0)	0 (0)	0 (0)
	Probably	0 (0)	0 (0)	0 (0)
	Definitely	0 (0)	0 (0)	0 (0)
Expected[a]:				
	Yes	91 (60)	82 (56)	173 (116)
	No	52 (42)	49 (37)	101 (79)
Total AEs (total number of people)		143 (83)	131 (76)	274 (159)

[a]The definition of an unexpected adverse event is as follows: An adverse event which is not consistent with the information about the procedure clearly defined in the protocol.

[b]UC: Usual Care, RELAX+UC; RELAX intervention in addition to Usual Care

Serious adverse events by arm and overall

Serious Adverse Events (SAE)[a]		Number of events (Number of people)		
		UC[b] N=134	RELAX+UC[b] N=134	Overall N=268
Description of SAE (Body system code)				
	1=Cardiovascular	8 (8)	3 (3)	11 (11)
	2=Respiratory	5 (5)	3 (3)	8 (8)
	3=Hepatic	0 (0)	3 (3)	3 (3)
	4=Gastro-intestinal	6 (5)	3 (3)	9 (8)
	5=Genito-urinary/renal	7 (7)	2 (2)	9 (9)
	6=Endocrine	2 (2)	0 (0)	2 (2)
	7=Hematological	3 (3)	2 (2)	5 (5)
	8=Musculo-skeletal	3 (2)	4 (3)	7 (5)
	9=Neoplasia	0 (0)	0 (0)	0 (0)
	10=Neurological	0 (0)	0 (0)	0 (0)
	11=Psychological	0 (0)	2 (2)	2 (2)
	12=Immunological	2 (2)	5 (5)	7 (7)
	13=Dermatological	0 (0)	0 (0)	0 (0)
	14=Allergies	0 (0)	0 (0)	0 (0)
	15=Eyes, ear, nose, throat	2 (2)	1 (1)	3 (3)
	16=Other	30 (22)	27 (22)	57 (44)
SAE type:				
	Death	0 (0)	0 (0)	0 (0)
	Life threatening	3 (3)	3 (3)	6 (6)
	Hospitalisation or prolongation of existing hospitalization	52 (41)	38 (31)	90 (72)
	Persistent or significant disability or incapacity	1 (1)	0 (0)	1 (1)
	Congenital anomaly or birth defect	12 (10)	14 (13)	26 (23)
Timing of AE:				
	After T0, Before T1	8 (7)	3 (3)	11 (10)
	After T1, Before T2	4 (3)	2 (2)	6 (5)
	After T2, Before T3	56 (49)	50 (36)	106 (85)
Related to trial:				
	Unrelated	68 (51)	55 (40)	123 (91)
	Unlikely	0 (0)	0 (0)	0 (0)
	Possibly	0 (0)	0 (0)	0 (0)
	Probably	0 (0)	0 (0)	0 (0)
	Definitely	0 (0)	0 (0)	0 (0)
Expected:				
	Yes	46 (40)	36 (27)	82 (67)
	No	22 (20)	19 (17)	41 (37)
Total SAEs (total number of people)		68 (51)	55 (40)	123 (91)

[a]The definition of an unexpected serious adverse event is as follows: A serious adverse event which is not consistent with the information about the procedure clearly defined in the protocol.
[b]UC: Usual Care, RELAX+UC; RELAX intervention in addition to Usual Care

Conflicts of interest

Prof Hirsch reported receiving grants from the National Institute of Health and Care Research (NIHR) during the conduct of the study; and grants from Wellcome Trust, MQ Mental Health Research, and the Medical Research Council during the conduct of the study but outside of the submitted work. Ms Towner reported receiving grants from the NIHR during the conduct of the study. Ms Newburn reported receiving personal fees from King's College London during the conduct of the study. Ms Misgalla reported receiving personal fees from King's College London during the conduct of the study. Prof Newby reported receiving grants from the National Health and Medical Research Council during the conduct of the study; and receiving grants from the National Health and Medical Research Council, Wellcome Trust, Medical Research Future Fund, and Koneski outside the submitted work. Prof Goldsmith reported receiving grants from the NIHR during the conduct of the study; and grants from the Medical Research Council, Wellcome Trust, and the National Institutes of Health outside the submitted work. Prof Moulds reported receiving grants from the NIHR during the conduct of the study. No other disclosures were reported.