Dataset Integrity Check for the Nortriptyline for Idiopathic Gastroparesis (NORIG) Clinical Trial Complete Data Files

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Contents

1 Standard Disclaimer

The intent of this DSIC is to provide confidence that the data distributed by the NIDDK repository is a true copy of the study data. Our intent is not to assess the integrity of the statistical analyses reported by study investigators. As with all statistical analyses of complex datasets, complete replication of a set of statistical results should not be expected in secondary analysis. This occurs for a number of reasons including differences in the handling of missing data, restrictions on cases included in samples for a particular analysis, software coding used to define complex variables, etc. Experience suggests that most discrepancies can ordinarily be resolved by consultation with the study data coordinating center (DCC), however this process is labor-intensive for both DCC and Repository staff. It is thus not our policy to resolve every discrepancy that is observed in an integrity check. Specifically, we do not attempt to resolve minor or inconsequential discrepancies with published results or discrepancies that involve complex analyses, unless NIDDK Repository staff suspect that the observed discrepancy suggests that the dataset may have been corrupted in storage, transmission, or processing by repository staff. We do, however, document in footnotes to the integrity check those instances in which our secondary analyses produced results that were not fully consistent with those reported in the target publication.

2 Study Background

Gastroparesis, a syndrome in which patients experience delayed gastric emptying, is characterized by symptoms such as nausea, vomiting, bloating, abdominal pain, and early satiety. Management of gastroparesis is limited by few effective treatments, many of which function by accelerating gastric emptying. Based on the hypothesis that some symptoms of gastroparesis arise because of neuropathic changes in enteric and sensory nerves, tricyclic antidepressants (TCAs) in low doses have been used as neuromodulators to treat refractory symptoms of nausea, vomiting, and abdominal pain, but there is little evidence to support this use. The Nortriptyline for Idiopathic Gastroparesis (NORIG) study is a multicenter, randomized, clinical trial that was designed by the Gastroparesis Clinical Research Consortium (GpCRC) to test whether treatment with nortriptyline, a TCA with reduced anticholinergic side effects, results in symptomatic improvement in patients with idiopathic gastroparesis.

Individuals between the ages of 21 and 68 years old with moderate to severe symptoms of idiopathic gastroparesis for at least 6 months were enrolled. Participants were randomized to treatment with either nortiptyline or placebo. In both groups, dosing was escalated at 3-week intervals (10, 25, 50, 75 mg) up to 75 mg at 12 weeks. At follow-up study visits, which occurred every 3 weeks, symptom questionnaires were administered to assess gastrointestinal and psychological symptoms, quality of life, and TCA side effects. Electrogastrography (EGG) satiety tests and electrocardiography tests were also performed. Treatment was continued for 15 weeks, at which time study medication dose was tapered to zero with a final assessment at 18 weeks. The primary outcome measure was a decrease from the patient's baseline Gastroparesis Cardinal Symptom Index (GCSI) score of at least 50% on two consecutive 3 week GCSI assessments over 15 weeks of treatment. Secondary outcome measures included physiological assessments during satiety testing, clinical and psychological symptom scores, and adverse event rates.

Overall symptomatic improvement, as defined by the primary outcome measure, did not differ between the treatment groups: 23% on nortriptyline versus 21% on placebo. Additionally, treatment with nortriptyline showed no improvement in nausea, fullness/satiety, bloating, or quality of life measures. These findings suggest that TCAs may not be effective in the treatment of idiopathic gastroparesis.

3 Archived Datasets

All SAS data files, as provided by the Data Coordinating Center (DCC), are located in the NORIG data package. For this replication, variables were taken from the various form datasets.

4 Statistical Methods

Analyses were performed to duplicate results for the data published by Parkman et al. [1] in JAMA in 2013.

To verify the integrity of the SAS datasets, descriptive statistics were computed.

5 Results

Table 1 in the publication [1], Baseline patient characteristics by treatment group, reports on baseline characteristics by treatment group. Table A lists the variables that were used in the replication and Table B compares the results calculated from the archived data files to the results published in Table 1. The results of the replication are almost an exact match.

Table 2 in the publication [1], Baseline gastric diagnostic test results by treatment group, reports on baseline gastric diagnostic test results by treatment group. Table C lists the variables that were used in the replication and Table D compares the results calculated from the archived data files to the results published in Table 2.

For Table 3 in the publication [1], Comparison of primary and secondary outcomes by treatment group, Table E lists the variables that were used in the replication and Table F compares the results calculated from the archived data files to the results published in Table 3.

6 Conclusion

The NIDDK repository is confident that the NORIG data files to be distributed are a true copy of the study data.

7 References

[1] Parkman HP, Van Natta ML, Abell TL, McCallum RW, Sarosiek I, Nguyen L, Snape WJ, Koch KL, Hasler WL, Farrugia G, Lee L, Unalp-Arida A, Tonascia J, Hamilton F, Pasricha PJ. Effect of Nortriptyline on Symptoms of Idiopathic Gastroparesis: The NORIG Randomized Clinical Trial. JAMA. 2013;310(24):2640-2649. PMCID: PMC4099968.

Table A: Variables used to replicate Table 1: Baseline Patient Characteristics by Treatment Group

Characteristic	**dataset.variable**
Age, y	rg2.RG211
Women, No. (%)	rg2.RG213
Hispanic	rg2.RG214
Black	rg2.RG215C
White	rg2.RG215E
Other	rg2.RG215A, rg2.RG215B rg2.RG215D
Body mass index	pe2.PE213A, pe2.PE212A where visit in ('s1', 's2')
Proton pump inhibitor	bh2.BH214
Benzodiazepine	bh2.BH215
Prokinetic	bh2.BH217
Antiemetic	bh2.BH218
Selective serotonin reuptake inhibitor	bh2.BH219
GCSI total score	gd1.GD111 where visit in ('s1', 's2')
Nausea subscore	gd1.GD115, gd1.GD116, gd1.GD117 where visit in ('s1', 's2')
Fullness or early satiety subscore	gd1.GD118, gd1.GD119, gd1.GD120, gd1.GD121 where visit in ('s1', 's2')
Bloating subscore	gd1.GD122, gd1.GD123 where visit in ('s1', 's2')
Upper abdominal pain subscore	gd1.GD124, gd1.GD125 where visit in ('s1', 's2')
Lower abdominal pain subscore	gd1.GD126, gd1.GD127 where visit in ('s1', 's2')
GERD subscore	gd1.GD128, gd1.GD129, gd1.GD130, gd1.GD131, gd1.GD132, gd1.GD133, gd1.GD134 where visit in ('s1', 's2')
Constipation score	gd1.GD135 where visit in ('s1', 's2')
Diarrhea score	gd1.GD136 where visit in ('s1', 's2')
Nausea/vomiting predominant symptom, No. (%)	gd1.GD137 where visit in ('s1', 's2')
Clinical Global Patient Impression score	bh2.BH232
GSRS, mean score	gs1.GS111, gs1.GS112, gs1.GS113, gs1.GS114, gs1.GS115, gs1.GS116, gs1.GS117, gs1.GS118, gs1.GS119, gs1.GS120, gs1.GS121, gs1.GS122, gs1.GS123, gs1.GS124, gs1.GS125 where visit in ('s1', 's2')
Physical component summary, score*	N/A

Characteristic	dataset.variable
Mental component summary, score*	N/A
Beck Depression Inventory Total Score	bd1.BD108 where visit in ('s1', 's2')
Severe depression, No. (%)	bd1.BD109, bd1.BD110, bd1.BD111 where visit in ('s1', 's2')
Brief Pain Inventory Severity score	pi1.PI111, pi1.PI112, pi1.PI113, pi1.PI114 where visit in ('s1', 's2')
Brief Pain Inventory Interference score	pi1.PI118A, pi1.PI118B, pi1.PI118C, pi1.pi118D, pi1.pi118E, pi1.pi118F, pi1.pi118G where visit in ('s1', 's2')
State anxiety score	se1.SE108A where visit in ('s1', 's2')
Trait anxiety score	se1.SE108B where visit in ('s1', 's2')
PHQ-15 score	pq1.PQ110A, pq1.PQ110B, pq1.PQ110C, pq1.PQ110D, pq1.PQ110E, pq1.PQ110F, pq1.PQ110G, pq1.PQ110H, pq1.PQ110I, pq1.PQ110J, pq1.PQ110K, pq1.PQ110L, pq1.PQ110M, pq1.PQ110N, pq1.PQ110O where visit in ('s1', 's2')

Table B: Comparison of values computed in integrity check to reference article Table 1 values

Characteristic	Nortriptyline (n=65) Mean (SD) [Manuscript]	Nortriptyline (n=65) Mean (SD) [DSIC]	Nortriptyline (n=0) Mean (SD) [Diff.]
Demographic/anthropometric			
Age, y	42 (12)	42 (12)	0 (0)
Women, No. (%)	60 (92.3)	60 (92.3)	0 (0.0)
Race/ethnicity, No. (%)			
Hispanic	7 (10.8)	7 (10.8)	0 (0.0)
Black	10 (15.4)	10 (15.4)	0 (0.0)
White	54 (83.1)	54 (83.1)	0 (0.0)
Other	1 (1.5)	1 (1.5)	0 (0.0)
Body mass index	27 (5)	27 (5)	0 (0)
Medications taken in past mo, No. (%)			
Proton pump inhibitor	48 (73.8)	48 (73.9)	0 (0.1)
Benzodiazepine	26 (40.0)	26 (40.0)	0 (0.0)
Prokinetic	23 (35.4)	23 (35.4)	0 (0.0)
Antiemetic	39 (60.0)	39 (60.0)	0 (0.0)
Selective serotonin reuptake inhibitor	7 (10.8)	7 (10.8)	0 (0.0)
Patient-reported outcomes			
PAGI-SYM Severity Index			
GCSI total score	30.9 (6.1)	30.9 (6.1)	0.0 (0.0)
Nausea subscore	8.2 (3.6)	8.2 (3.7)	0.0 (0.1)
Fullness or early satiety subscore	15.4 (3.4)	15.4 (3.4)	0.0 (0.0)
Bloating subscore	7.2 (2.9)	7.2 (2.9)	0.0 (0.0)
Upper abdominal pain subscore	6.8 (2.9)	6.7 (2.9)	0.1 (0.0)
Lower abdominal pain subscore	4.7 (3.3)	4.7 (3.3)	0.0 (0.0)
GERD subscore	15.4 (9.4)	15.4 (9.4)	0.0 (0.0)
Constipation score	2.8 (1.9)	2.8 (1.9)	0.0 (0.0)
Diarrhea score	1.8 (1.7)	1.8 (1.7)	0.0 (0.0)
Nausea/vomiting predominant symptom, No. (%)	27 (41.6)	27 (41.5)	0 (0.1)
Gastroparesis symptoms inventory			
Clinical Global Patient Impression score	-0.7 (0.9)	-0.7 (0.9)	0.0 (0.0)
GSRS, mean score	3.6 (1.1)	3.6 (1.1)	0.0 (0.0)
SF-36 Quality of Life			
Physical component summary, score*	35 (10)	N/A	N/A
Mental component summary, score*	41 (13)	N/A	N/A
Beck Depression Inventory			
Total score	17 (11)	17 (11)	0 (0)
Severe depression, No. (%)	12 (18.5)	12 (18.5)	0 (0.0)

Characteristic	Nortriptyline (n=65) Mean (SD) [Manuscript]	Nortriptyline (n=65) Mean (SD) [DSIC]	Nortriptyline (n=0) Mean (SD) [Diff.]
Brief Pain Inventory			
Severity score	4.0 (2.5)	4.0 (2.5)	0.0 (0.0)
Interference score	4.2 (3.0)	4.2 (3.0)	0.0 (0.0)
State-Trait Anxiety Inventory			
State anxiety score	42 (13)	42 (13)	0 (0)
Trait anxiety score	43 (12)	43 (12)	0 (0)
PHQ-15 score	14 (5)	14 (5)	0 (0)

Characteristic	Placebo (n=65) Mean (SD) [Manuscript]	Placebo (n=65) Mean (SD) [DSIC]	Placebo (n=0) Mean (SD) [Diff.]
Demographic/anthropometric			
Age, y	40 (12)	40 (12)	0 (0)
Women, No. (%)	56 (86.2)	56 (86.2)	0 (0.0)
Race/ethnicity, No. (%)			
Hispanic	8 (12.3)	8 (12.3)	0 (0.0)
Black	9 (13.8)	9 (13.9)	0 (0.1)
White	54 (83.1)	55 (84.6)	1 (1.5)
Other	2 (3.0)	2 (3.1)	0 (0.1)
Body mass index	28 (7)	28 (7)	0 (0)
Medications taken in past mo, No. (%)			
Proton pump inhibitor	49 (75.4)	49 (75.4)	0 (0.0)
Benzodiazepine	14 (21.5)	14 (21.5)	0 (0.0)
Prokinetic	25 (38.5)	25 (38.5)	0 (0.0)
Antiemetic	33 (50.8)	33 (50.8)	0 (0.0)
Selective serotonin reuptake inhibitor	11 (16.9)	11 (16.9)	0 (0.0)
Patient-reported outcomes			
PAGI-SYM Severity Index			
GCSI total score	30.3 (6.5)	30.3 (6.5)	0.0 (0.0)
Nausea subscore	8.2 (4.2)	8.2 (4.2)	0.0 (0.0)
Fullness or early satiety subscore	15.1 (4.1)	15.1 (4.1)	0.0 (0.0)
Bloating subscore	7.0 (2.7)	7.0 (2.7)	0.0 (0.0)
Upper abdominal pain subscore	6.5 (2.9)	6.5 (2.9)	0.0 (0.0)
Lower abdominal pain subscore	4.3 (3.3)	4.3 (3.3)	0.0 (0.0)
GERD subscore	17.9 (10.5)	17.9 (10.5)	0.0 (0.0)
Constipation score	2.4 (1.7)	2.4 (1.7)	0.0 (0.0)
Diarrhea score	2.0 (1.8)	2.0 (1.8)	0.0 (0.0)
Nausea/vomiting predominant symptom, No. (%)	22 (33.9)	22 (33.9)	0 (0.0)

Characteristic	Placebo (n=65) Mean (SD) [Manuscript]	Placebo (n=65) Mean (SD) [DSIC]	Placebo (n=0) Mean (SD) [Diff.]
Gastroparesis symptoms inventory			
Clinical Global Patient Impression score	-0.7 (1.2)	-0.7 (1.2)	0.0 (0.0)
GSRS, mean score	3.7 (1.2)	3.7 (1.2)	0.0 (0.0)
SF-36 Quality of Life			
Physical component summary, score*	36 (10)	N/A	N/A
Mental component summary, score*	40 (13)	N/A	N/A
Beck Depression Inventory			
Total score	18 (12)	18 (12)	0 (0)
Severe depression, No. (%)	15 (23.2)	15 (23.1)	0 (0.1)
Brief Pain Inventory			
Severity score	4.1 (2.7)	4.1 (2.7)	0.0 (0.0)
Interference score	4.1 (3.3)	4.1 (3.3)	0.0 (0.0)
State-Trait Anxiety Inventory			
State anxiety score	41 (12)	41 (12)	0 (0)
Trait anxiety score	43 (13)	43 (13)	0 (0)
PHQ-15 score	14 (5)	14 (5)	0 (0)

Characteristic	Total (n=130) Mean (SD) [Manuscript]	Total (n=130) Mean (SD) [DSIC]	Total (n=0) Mean (SD) [Diff.]
Demographic/anthropometric			
Age, y	41 (12)	41 (12)	0 (0)
Women, No. (%)	116 (89.2)	116 (89.2)	0 (0.0)
Race/ethnicity, No. (%)			
Hispanic	15 (11.5)	15 (11.5)	0 (0.0)
Black	19 (14.6)	19 (14.6)	0 (0.0)
White	108 (83.1)	109 (83.9)	1 (0.8)
Other	3 (2.4)	3 (2.3)	0 (0.1)
Body mass index	27 (6)	27 (6)	0 (0)
Medications taken in past mo, No. (%)			
Proton pump inhibitor	97 (74.6)	97 (74.6)	0 (0.0)
Benzodiazepine	40 (30.8)	40 (30.8)	0 (0.0)
Prokinetic	48 (36.9)	48 (36.9)	0 (0.0)
Antiemetic	72 (55.4)	72 (55.4)	0 (0.0)
Selective serotonin reuptake inhibitor	18 (13.8)	18 (13.9)	0 (0.1)
Patient-reported outcomes			
PAGI-SYM Severity Index			
GCSI total score	30.6 (6.3)	30.6 (6.3)	0.0 (0.0)

Characteristic	Total (n=130) Mean (SD) [Manuscript]	Total (n=130) Mean (SD) [DSIC]	Total (n=0) Mean (SD) [Diff.]
Nausea subscore	8.1 (3.9)	8.2 (3.9)	0.1 (0.0)
Fullness or early satiety subscore	15.3 (3.7)	15.3 (3.7)	0.0 (0.0)
Bloating subscore	7.1 (2.8)	7.1 (2.8)	0.0 (0.0)
Upper abdominal pain subscore	6.6 (2.9)	6.6 (2.9)	0.0 (0.0)
Lower abdominal pain subscore	4.5 (3.3)	4.5 (3.3)	0.0 (0.0)
GERD subscore	16.7 (10.0)	16.7 (10.0)	0.0 (0.0)
Constipation score	2.6 (1.8)	2.6 (1.8)	0.0 (0.0)
Diarrhea score	1.9 (1.8)	1.9 (1.8)	0.0 (0.0)
Nausea/vomiting predominant symptom, No. (%)	49 (37.7)	49 (37.7)	0 (0.0)
Gastroparesis symptoms inventory			
Clinical Global Patient Impression score	-0.7 (1.0)	-0.7 (1.0)	0.0 (0.0)
GSRS, mean score	3.6 (1.2)	3.6 (1.2)	0.0 (0.0)
SF-36 Quality of Life			
Physical component summary, score*	35 (10)	N/A	N/A
Mental component summary, score*	40 (13)	N/A	N/A
Beck Depression Inventory			
Total score	17 (12)	17 (12)	0 (0)
Severe depression, No. (%)	27 (20.8)	27 (20.8)	0 (0.0)
Brief Pain Inventory			
Severity score	4.0 (2.6)	4.0 (2.6)	0.0 (0.0)
Interference score	4.1 (3.1)	4.1 (3.1)	0.0 (0.0)
State-Trait Anxiety Inventory			
State anxiety score	42 (12)	42 (12)	0 (0)
Trait anxiety score	43 (12)	43 (12)	0 (0)
PHQ-15 score	14 (5)	14 (5)	0 (0)

Table C: Variables used to replicate Table 2: Baseline Gastric Diagnostic Test Results by Treatment Group

Test	**dataset.variable**
1 h Gastric retention, %	ge1.GE113C
2 h Gastric retention, %	ge1.GE113D
4 h Gastric retention, %	ge1.GE113F
Satiety test, volume consumed, median (IQR), mL	st3.ST313 where visit in ('s1', 's2')
Average power in bradygastria region (1.0-2.5 cpm)	
Baseline**	N/A
0-30 min post satiety test**	N/A
Average power in normal region (2.5-3.7 cpm)	
Baseline**	N/A
0-30 min post satiety test**	N/A
Average power in tachygastria region (3.7-10.0 cpm)	
Baseline**	N/A
0-30 min post satiety test**	N/A
Average power in duodenal region (10.0-15.0 cpm)	
Baseline**	N/A
0-30 min post satiety test**	N/A

Table D: Comparison of values computed in integrity check to reference article Table 2 values

Test	Nortriptyline (n=65) Mean (SD) [Manuscript]	Nortriptyline (n=65) Mean (SD) [DSIC]	Nortriptyline (n=0) Mean (SD) [Diff.]
Gastric emptying scintigraphy			
1 h			
No. of evaluable patients	63	63	0
Gastric retention, %	80 (14)	80 (14)	0 (0)
2 h			
No. of evaluable patients	58	58	0
Gastric retention, %	61 (17)	61 (17)	0 (0)
4 h			
No. of evaluable patients	56	56	0
Gastric retention, %	26 (16)	26 (16)	0 (0)
Satiety test, volume consumed, median (IQR), mL	269 (225-424)	269 (225-424)	0 (0-0)
Electrogastrography, %			
No. of evaluable patients**	54	N/A	N/A
Average power in bradygastria region (1.0-2.5 cpm)			
Baseline**	50 (20)	N/A	N/A
0-30 min post satiety test**	40 (13)	N/A	N/A
Average power in normal region (2.5-3.7 cpm)			
Baseline**	20 (15)	N/A	N/A
0-30 min post satiety test**	24 (14)	N/A	N/A
Average power in tachygastria region (3.7-10.0 cpm)			
Baseline**	21 (10)	N/A	N/A
0-30 min post satiety test**	27 (7)	N/A	N/A
Average power in duodenal region (10.0-15.0 cpm)			
Baseline**	10 (13)	N/A	N/A
0-30 min post satiety test**	9 (8)	N/A	N/A

Test	Placebo (n=65) Mean (SD) [Manuscript]	Placebo (n=65) Mean (SD) [DSIC]	Placebo (n=0) Mean (SD) [Diff.]
Gastric emptying scintigraphy			
1 h			
No. of evaluable patients	62	62	0
Gastric retention, %	80 (12)	80 (12)	0 (0)

Test	Placebo (n=65) Mean (SD) [Manuscript]	Placebo (n=65) Mean (SD) [DSIC]	Placebo (n=0) Mean (SD) [Diff.]
2 h			
No. of evaluable patients	61	61	0
Gastric retention, %	59 (17)	59 (17)	0 (0)
4 h			
No. of evaluable patients	61	61	0
Gastric retention, %	25 (17)	25 (17)	0 (0)
Satiety test, volume consumed, median (IQR), mL	240 (177-382)	240 (177-382)	0 (0-0)
Electrogastrography, %			
No. of evaluable patients**	50	N/A	N/A
Average power in bradygastria region (1.0-2.5 cpm)			
Baseline**	43 (18)	N/A	N/A
0-30 min post satiety test**	41 (15)	N/A	N/A
Average power in normal region (2.5-3.7 cpm)			
Baseline**	19 (10)	N/A	N/A
0-30 min post satiety test**	23 (11)	N/A	N/A
Average power in tachygastria region (3.7-10.0 cpm)			
Baseline**	26 (10)	N/A	N/A
0-30 min post satiety test**	28 (10)	N/A	N/A
Average power in duodenal region (10.0-15.0 cpm)			
Baseline**	12 (10)	N/A	N/A
0-30 min post satiety test**	8 (7)	N/A	N/A

Test	Total (n=130) Mean (SD) [Manuscript]	Total (n=130) Mean (SD) [DSIC]	Total (n=0) Mean (SD) [Diff.]
Gastric emptying scintigraphy			
1 h			
No. of evaluable patients			
Gastric retention, %	80 (13)	80 (13)	0 (0)
2 h			
No. of evaluable patients			
Gastric retention, %	60 (17)	60 (17)	0 (0)
4 h			
No. of evaluable patients			
Gastric retention, %	26 (16)	26 (16)	0 (0)

Test	Total (n=130) Mean (SD) [Manuscript]	Total (n=130) Mean (SD) [DSIC]	Total (n=0) Mean (SD) [Diff.]
Satiety test, volume consumed, median (IQR), mL	240 (207-400)	240 (207-400)	0 (0-0)
Electrogastrography, %			
No. of evaluable patients**	104	N/A	N/A
Average power in bradygastria region (1.0-2.5 cpm)			
Baseline**	46 (19)	N/A	N/A
0-30 min post satiety test**	41 (14)	N/A	N/A
Average power in normal region (2.5-3.7 cpm)			
Baseline**	20 (13)	N/A	N/A
0-30 min post satiety test**	23 (13)	N/A	N/A
Average power in tachygastria region (3.7-10.0 cpm)			
Baseline**	23 (10)	N/A	N/A
0-30 min post satiety test**	27 (8)	N/A	N/A
Average power in duodenal region (10.0-15.0 cpm)			
Baseline**	11 (10)	N/A	N/A
0-30 min post satiety test**	9 (7)	N/A	N/A

Table E: Variables used to replicate Table 3: Comparison of Primary and Secondary Outcomes by Treatment Group

Outcome	**dataset.variable**
≥ 2 consecutive visits with GCSI score ≤ 50% of baseline, No. (%) [95% CI]	gd1.GD111
Total GCSI score	gd1.GD111 where visit = 'f15'
Nausea subscore	gd1.GD115, gd1.GD116, gd1.GD117 where visit = 'f15'
Fullness or early satiety subscore	gd1.GD118, gd1.GD119, gd1.GD120, gd1.GD121 where visit = 'f15'
Bloating, subscore	gd1.GD122, gd1.GD123 where visit = 'f15'
Upper abdominal pain score	gd1.GD124, gd1.GD125 where visit = 'f15'
Lower abdominal pain score	gd1.GD126, gd1.GD127 where visit = 'f15'
GERD subscore	gd1.GD128, gd1.GD129, gd1.GD130, gd1.GD131, gd1.GD132, gd1.GD133, gd1.GD134 where visit = 'f15'
Constipation score	gd1.GD135 where visit = 'f15'
Diarrhea score	gd1.GD136 where visit = 'f15'
Clinical Global Patient Impression score	Fh1.FH124 where visit = 'f15'
Gastrointestinal symptom rating scale, mean score	gs1.GS111, gs1.GS112, gs1.GS113, gs1.GS114, gs1.GS115, gs1.GS116, gs1.GS117, gs1.GS118, gs1.GS119, gs1.GS120, gs1.GS121, gs1.GS122, gs1.GS123, gs1.GS124, gs1.GS125 where visit = 'f15'
Physical component summary*	N/A
Mental component summary*	N/A
Beck Depression Inventory Total Score	bd1.BD108 where visit = 'f15'
Brief Pain Inventory Severity Score	pi1.PI111, pi1.PI112, pi1.PI113, pi1.PI114 where visit = 'f15'
Brief Pain Inventory Interference score	pi1.PI118A, pi1.PI118B, pi1.PI118C, pi1.pi118D, pi1.pi118E, pi1.pi118F, pi1.pi118G where visit = 'f15'
State anxiety	se1.SE108A where visit = 'f15'
Trait anxiety	se1.SE108B where visit = 'f15'

Outcome	**dataset.variable**
PHQ-15 score	pq1.PQ110A, pq1.PQ110B, pq1.PQ110C, pq1.PQ110D, pq1.PQ110E, pq1.PQ110F, pq1.PQ110G, pq1.PQ110H, pq1.PQ110I, pq1.PQ110J, pq1.PQ110K, pq1.PQ110L, pq1.PQ110M, pq1.PQ110N, pq1.PQ110O where visit = 'f15'
Body mass index	pe2.PE213A, pe2.PE212A where visit = 'f12'
Satiety test Volume consumed, mL	st3.ST313 where visit = 'f12'
Average power in bradygastria region (1.0-2.5 cpm)	
Baseline**	N/A
0-30 min post satiety test**	N/A
Average power in normal region (2.5-3.7 cpm)	
Baseline**	N/A
0-30 min post satiety test**	N/A
Average power in tachygastria region (3.7-10.0 cpm)	
Baseline**	N/A
0-30 min post satiety test**	N/A
Average power in duodenal region (10.0-15.0 cpm)	
Baseline**	N/A
0-30 min post satiety test**	N/A

Table F: Comparison of values computed in integrity check to reference article Table 3 values

Outcome	Nortriptyline (n=65) Mean (95% CI) [Manuscript]	Nortriptyline (n=65) Mean (95% CI) [DSIC]	Nortriptyline (n=65) Mean (95% CI) [Diff.]
Primary outcome			
No. of patients randomized	65	65	0
≥ 2 consecutive visits with GCSI score ≤ 50% of baseline, No. (%) [95% CI]	15 (23.1) [13.5 to 35.2]	15 (23.1) [13.5 to 35.2]	0 (0) [0 to 0]
Secondary outcomes assessed after 15 wk of treatment			
No. of evaluable patients	56	56	0
Patient assessment of upper gastro-intestinal symptom severity			
Total GCSI score	-8.8 (-11.7 to -5.9)	-8.8 (-11.7 to -5.9)	0.0 (0.0 to 0.0)
Nausea subscore	-2.5 (-3.6 to -1.4)	-2.5 (-3.6 to -1.4)	0.0 (0.0 to 0.0)
Fullness or early satiety subscore	-5.0 (-6.5 to -3.5)	-5.0 (-6.5 to -3.5)	0.0 (0.0 to 0.0)
Bloating, subscore	-1.3 (-2.1 to -0.5)	-1.3 (-2.1 to -0.5)	0.0 (0.0 to 0.0)
Upper abdominal pain score	-1.7 (-2.6 to -0.7)	-1.7 (-2.6 to -0.7)	0.0 (0.0 to 0.0)
Lower abdominal pain score	-0.9 (-1.7 to 0.0)	-0.9 (-1.7 to 0.0)	0.0 (0.0 to 0.0)
GERD subscore	-4.3 (-6.8 to -1.9)	-4.3 (-6.8 to -1.9)	0.0 (0.0 to 0.0)
Constipation score	-0.2 (-0.7 to 0.2)	-0.2 (-0.7 to 0.2)	0.0 (0.0 to 0.0)
Diarrhea score	-0.4 (-0.8 to 0.1)	-0.4 (-0.8 to 0.1)	0.0 (0.0 to 0.0)
Gastroparesis symptoms inventory			
Clinical Global Patient Impression score	1.3 (1.0 to 1.6)	1.3 (1.0 to 1.6)	0.0 (0.0 to 0.0)
Gastrointestinal symptom rating scale, mean score	-0.5 (-0.8 to -0.3)	-0.5 (-0.8 to -0.3)	0.0 (0.0 to 0.0)
SF-36 Quality of Life			
Physical component summary*	3.8 (1.3 to 6.4)	N/A	N/A
Mental component summary*	1.8 (-1.4 to 5.1)	N/A	N/A
Beck Depression Inventory			
Total score	-2.6 (-5.0 to -0.2)	-2.6 (-5.0 to -0.2)	0.0 (0.0 to 0.0)

Outcome	Nortriptyline (n=65) Mean (95% CI) [Manuscript]	Nortriptyline (n=65) Mean (95% CI) [DSIC]	Nortriptyline (n=65) Mean (95% CI) [Diff.]
Brief Pain Inventory			
Severity score	-1.1 (-1.9 to -0.4)	-1.1 (-1.9 to -0.4)	0.0 (0.0 to 0.0)
Interference score	-1.1 (-1.8 to -0.4)	-1.1 (-1.8 to -0.4)	0.0 (0.0 to 0.0)
State-Trait Anxiety Inventory			
State anxiety	0.4 (-2.9 to 3.7)	0.4 (-2.9 to 3.7)	0.0 (0.0 to 0.0)
Trait anxiety	-0.3 (-3.0 to 2.5)	-0.3 (-3.0 to 2.5)	0.0 (0.0 to 0.0)
PHQ-15 score	-2.4 (-3.6 to -1.2)	-2.4 (-3.6 to -1.2)	0.0 (0.0 to 0.0)
Secondary outcomes assessed after 12 wk of treatment			
Body mass index	n=55	n=55	n=0
Value	0.5 (0.1 to 0.8)	0.5 (0.1 to 0.8)	0.0 (0.0 to 0.0)
Satiety test	n=49	n=49	n=0
Volume consumed, mL	7 (-24 to 39)	7 (-24 to 39)	0 (0 to 0)
Electrogastrography, %**	n=39	N/A	N/A
Average power in bradygastria region (1.0-2.5 cpm)			
Baseline**	-1 (-10 to 7)	N/A	N/A
0-30 min post satiety test**	-2 (-7 to 4)	N/A	N/A
Average power in normal region (2.5-3.7 cpm)			
Baseline**	0 (-5 to 6)	N/A	N/A
0-30 min post satiety test**	-1 (-5 to 3)	N/A	N/A
Average power in tachygastria region (3.7-10.0 cpm)			
Baseline**	2 (-3 to 6)	N/A	N/A
0-30 min post satiety test**	2 (-2 to 5)	N/A	N/A
Average power in duodenal region (10.0-15.0 cpm)			
Baseline**	-1 (-6 to 4)	N/A	N/A
0-30 min post satiety test**	1 (-3 to 6)	N/A	N/A

Outcome	Placebo (n=65) Mean (95% CI) [Manuscript]	Placebo (n=65) Mean (95% CI) [DSIC]	Placebo (n=65) Mean (95% CI) [Difference]
Primary outcome			
No. of patients randomized	65	65	0
≥ 2 consecutive visits with GCSI score ≤ 50% of baseline, No. (%) [95% CI]	14 (21.5) [12.3 to 33.5]	14 (21.5) [12.3 to 33.5]	0 (0) [0 to 0]
Secondary outcomes assessed after 15 wk of treatment			
No. of evaluable patients	62	62	0
Patient assessment of upper gastro-intestinal symptom severity			
Total GCSI score	-7.2 (-9.6 to -4.9)	-7.2 (-9.6 to -4.9)	0.0 (0.0 to 0.0)
Nausea subscore	-2.7 (-3.7 to -1.8)	-2.7 (-3.7 to -1.8)	0.0 (0.0 to 0.0)
Fullness or early satiety subscore	-3.3 (-4.6 to -2.1)	-3.3 (-4.6 to -2.1)	0.0 (0.0 to 0.0)
Bloating, subscore	-1.2 (-1.9 to -0.4)	-1.2 (-1.9 to -0.4)	0.0 (0.0 to 0.0)
Upper abdominal pain score	-1.7 (-2.5 to -1.0)	-1.7 (-2.5 to -1.0)	0.0 (0.0 to 0.0)
Lower abdominal pain score	-0.3 (-1.0 to 0.4)	-0.3 (-1.0 to 0.4)	0.0 (0.0 to 0.0)
GERD subscore	-5.6 (-7.7 to -3.5)	-5.6 (-7.7 to -3.5)	0.0 (0.0 to 0.0)
Constipation score	-0.4 (-0.8 to -0.1)	-0.4 (-0.8 to -0.1)	0.0 (0.0 to 0.0)
Diarrhea score	-0.7 (-1.0 to -0.3)	-0.7 (-1.0 to -0.3)	0.0 (0.0 to 0.0)
Gastroparesis symptoms inventory			
Clinical Global Patient Impression score	0.9 (0.5 to 1.3)	0.9 (0.5 to 1.3)	0.0 (0.0 to 0.0)
Gastrointestinal symptom rating scale, mean score	-0.5 (-0.8 to -0.3)	-0.5 (-0.8 to -0.3)	0.0 (0.0 to 0.0)
SF-36 Quality of Life			
Physical component summary*	1.7 (-0.2 to 3.6)	N/A	N/A
Mental component summary*	0.9 (-1.3 to 3.1)	N/A	N/A
Beck Depression Inventory			
Total score	-3.1 (-4.9 to -1.3)	-3.1 (-4.9 to -1.3)	0.0 (0.0 to 0.0)
Brief Pain Inventory			

Outcome	Placebo (n=65) Mean (95% CI) [Manuscript]	Placebo (n=65) Mean (95% CI) [DSIC]	Placebo (n=65) Mean (95% CI) [Difference]
Severity score	-0.5 (-1.1 to 0.1)	-0.5 (-1.1 to 0.1)	0.0 (0.0 to 0.0)
Interference score	-0.2 (-0.9 to 0.6)	-0.2 (-0.9 to 0.6)	0.0 (0.0 to 0.0)
State-Trait Anxiety Inventory			
State anxiety	-0.1 (-2.6 to 2.4)	-0.1 (-2.6 to 2.4)	0.0 (0.0 to 0.0)
Trait anxiety	-1.7 (-3.5 to 0.1)	-1.7 (-3.5 to 0.1)	0.0 (0.0 to 0.0)
PHQ-15 score	-1.5 (-2.5 to -0.5)	-1.5 (-2.5 to -0.5)	0.0 (0.0 to 0.0)
Secondary outcomes assessed after 12 wk of treatment			
Body mass index	n=59	n=59	n=0
Value	0.0 (-0.3 to 0.3)	-0.2 (-0.8 to 0.3)	0.2 (0.5 to 0)
Satiety test	n=55	n=55	n=0
Volume consumed, mL	1 (-35 to 36)	1 (-35 to 36)	0 (0 to 0)
Electrogastrography, %**	n=33	N/A	N/A
Average power in bradygastria region (1.0-2.5 cpm)			
Baseline**	6 (-1 to 13)	N/A	N/A
0-30 min post satiety test**	-1 (-7 to 4)	N/A	N/A
Average power in normal region (2.5-3.7 cpm)			
Baseline**	-2 (-7 to 2)	N/A	N/A
0-30 min post satiety test**	1 (-4 to 6)	N/A	N/A
Average power in tachygastria region (3.7-10.0 cpm)			
Baseline**	-4 (-8 to 0)	N/A	N/A
0-30 min post satiety test**	0 (-3 to 3)	N/A	N/A
Average power in duodenal region (10.0-15.0 cpm)			
Baseline**	0 (-3 to 4)	N/A	N/A
0-30 min post satiety test**	1 (-1 to 3)	N/A	N/A

*Note that the values for SF-36, Physical component summary and Mental component summary were not calculated by the NIDDK Repository due to the copyrighted nature of the form. Note that the analysis datasets contain the summarized SF-36 data. Please see the DSIC for these analysis datasets for calculated results and comparison to the manuscript.

**Note that the values for electrogastrography (ECG) were not calculated because the published results were taken from an expert reading of ECGs by one of the study PIs. The number of ECGs read by this PI was less than the number that completed the Electrogastrogram and Satiety Test (ST) form. The results read by this PI can be found in the NORIG analysis datasets. Please see the DSIC for these analysis datasets for the calculated results and comparison to the manuscript.

Attachment A: SAS Code

```
**** NORIG Full Dataset DSIC;
**** Programmer: Allyson Mateja;
**** Date: March 4, 2016;

title '/prj/niddk/ims_analysis/NORIG/prog_initial_analysis/norig_full_data_dsic_march2016.sas';
title2 ' ';

libname norigdta '/prj/niddk/ims_analysis/NORIG/private_orig_data/GpCRC_Data_Sharing_NORIG/Datasets_Transport/SASDATA';

proc format;
       value $sexf '1' = 'Male'
                   '2' = 'Female';

       value $ethnicityf '1' = 'Hispanic'
                         '2' = 'Not Hispanic';

       value $yesnof '1'      = 'Yes'
                     '0', '2' = 'No';

       value $predf '15', '17' = 'Yes'
                    '16', '18', '19', '20', '21', '22', '23', '24', '25', '26', '27', '28', '29', '30', '31', '32', '33', '34', '35',
'36' = 'No';

data treatment;
       set norigdta.treatmen;

data rg2;
       set norigdta.rg2;

data pe2;
       set norigdta.pe2;

data bh2;
       set norigdta.bh2;

data gd1;
       set norigdta.gd1;

data gs1;
       set norigdta.gs1;

data qf1;
       set norigdta.qf1;

data bd1;
       set norigdta.bd1;
```

```
data pi1;
       set norigdta.pi1;

data se1;
       set norigdta.se1;

data pq1;
       set norigdta.pq1;

data fh1;
       set norigdta.fh1;

proc contents data = treatment;
proc contents data = rg2;
proc contents data = pe2;
proc contents data = bh2;
proc contents data = gd1;
proc contents data = gs1;
proc contents data = qf1;
proc contents data = bd1;
proc contents data = pi1;
proc contents data = se1;
proc contents data = pq1;
proc contents data = fh1;

proc freq data = pe2;
       tables visit;
       title3 'pe2';

proc freq data = gd1;
       tables visit;
       title3 'gd1';

proc freq data = gs1;
       tables visit;
       title3 'gs1';

proc freq data = qf1;
       tables visit;
       title3 'qf1';

proc freq data = bd1;
       tables visit;
       title3 'bd1';

proc freq data = pi1;
       tables visit;
       title3 'pi1';

proc freq data = se1;
       tables visit;
```

```
        title3 'se1';

proc freq data = pq1;
        tables visit;
        title3 'pq1';

proc freq data = fh1;
        tables visit;
        title3 'fh1';

data pe2_base pe2_followup;
        set pe2;
        if visit in ('s1', 's2') then output pe2_base;
        else if visit = 'f12' then output pe2_followup;

data gd1_base gd1_followup;
        set gd1;
        if visit in ('s1', 's2') then output gd1_base;
        else if visit = 'f15' then output gd1_followup;

data gs1_base gs1_followup;
        set gs1;
        if visit in ('s1', 's2') then output gs1_base;
        else if visit = 'f15' then output gs1_followup;

data qf1_base qf1_followup;
        set qf1;
        if visit in ('s1', 's2') then output qf1_base;
        else if visit = 'f15' then output qf1_followup;

data bd1_base bd1_followup;
        set bd1;
        if visit in ('s1', 's2') then output bd1_base;
        else if visit = 'f15' then output bd1_followup;

data pi1_base pi1_followup;
        set pi1;
        if visit in ('s1', 's2') then output pi1_base;
        else if visit = 'f15' then output pi1_followup;

data se1_base se1_followup;
        set se1;
        if visit in ('s1', 's2') then output se1_base;
        else if visit = 'f15' then output se1_followup;

data pq1_base pq1_followup;
        set pq1;
        if visit in ('s1', 's2') then output pq1_base;
        else if visit = 'f15' then output pq1_followup;

data fh1_followup;
```

```
        set fh1;
        if visit = 'f15' then output fh1_followup;

proc freq data = treatment;
        tables tx_no;
        title3 'Treatment Groups';

proc sort data = rg2;
        by id;

proc sort data = treatment;
        by id;

proc sort data = pe2_base nodupkey;
        by id;

proc sort data = bh2;
        by id;

proc sort data = gd1_base nodupkey;
        by id;

proc sort data = se1_base nodupkey;
        by id;

proc sort data = pq1_base nodupkey;
        by id;

data pq1_base;
        set pq1_base;
        pq110a = pq110a - 1;
        pq110b = pq110b - 1;
        pq110c = pq110c - 1;
        if pq110d ne 'n' then pq110d = pq110d - 1;
        else pq110d = 0;
        pq110e = pq110e - 1;
        pq110f = pq110f - 1;
        pq110g = pq110g - 1;
        pq110h = pq110h - 1;
        pq110i = pq110i - 1;
        pq110j = pq110j - 1;
        pq110k = pq110k - 1;
        pq110l = pq110l - 1;
        pq110m = pq110m - 1;
        pq110n = pq110n - 1;
        pq110o = pq110o - 1;

data subjects;
        merge rg2       (in=val1 drop=visit)
              treatment (in=val2)
              pe2_base  (in=val3 drop = visit)
```

```
              bh2       (in=val4 keep=id bh214 bh215 bh217 bh218 bh219 bh232)
              gd1_base  (in=val5)
              gs1_base  (in=val6)
              qf1_base  (in=val7)
              bd1_base  (in=val8)
              pi1_base  (in=val9)
              se1_base  (in=val10)
              pq1_base  (in=val11);
       by id;
       age = input (RG211, 8.);
       if RG215A = '1' or RG215B = '1' or RG215D = '1' then other_race = '1';
       else other_race = '0';
       if PE212B = 1 then PE212A = PE212A * 2.54;
       if PE213B = 1 then PE213A = PE213A * 0.453592;
       bmi_base = PE213A/((PE212A/100)**2);
       gsci_base = input (gd111, 8.);
       nausea_subscore_base = gd115+gd116+gd117;
       fullness_subscore_base = gd118+gd119+gd120+gd121;
       bloating_subscore_base = gd122+gd123;
       upper_ab_subscore_base = gd124+gd125;
       lower_ab_subscore_base = gd126+gd127;
       gerd_base = gd128+gd129+gd130+gd131+gd132+gd133+gd134;
       constipation_subscore_base = input (gd135, 8.);
       diarrhea_subscore_base = input (gd136, 8.);
       cgpi_base = input (bh232, 8.);
       gsrs_base = (gs111+gs112+gs113+gs114+gs115+gs116+gs117+gs118+gs119+gs120+gs121+gs122+gs123+gs124+gs125)/15;
       bdi_base = input(bd108, 8.);
       if bd109 = 1 or bd110 = 1 or bd111 = 1 then severe_dep = '1';
       else severe_dep = '0';
       bpi_severity_base = (pi111+pi112+pi113+pi114)/4;
       bpi_interference_base = (pi118a+pi118b+pi118c+pi118d+pi118e+pi118f+pi118g)/7;
       if pi110 = '2' then do;
              bpi_severity_base = 0;
              bpi_interference_base = 0;
       end;
       state_anxiety_base = input (se108a, 8.);
       trait_anxiety_base = input (se108b, 8.);
       phq15_base = pq110a+pq110b+pq110c+pq110d+pq110e+pq110f+pq110g+pq110h+pq110i+pq110j+pq110k+pq110l+pq110m+pq110n+pq110o;
       if val1 and val2 and val3 and val4 and val5 and val6 and val7 and val8 and val9 and val10 and val11 then output subjects;

proc means data = subjects;
       var age;
       class tx_no;
       types () tx_no;
       title3 'Table 1 - Age';

proc sort data = subjects;
       by tx_no;

proc freq data = subjects;
       tables RG213;
```

```
        by tx_no;
        format RG213 $sexf.;
        title3 'Table 1 - Gender';

proc freq data = subjects;
        tables RG213;
        format RG213 $sexf.;

proc freq data = subjects;
        tables RG214;
        by tx_no;
        format RG214 $ethnicityf.;
        title3 'Table 1 - Hispanic';

proc freq data = subjects;
        tables RG214;
        format RG214 $ethnicityf.;

proc freq data = subjects;
        tables RG215C /missing;
        by tx_no;
        format RG215C $yesnof.;
        title3 'Table 1 - Black';

proc freq data = subjects;
        tables RG215C /missing;
        format RG215C $yesnof.;

proc freq data = subjects;
        tables RG215E /missing;
        by tx_no;
        format RG215E $yesnof.;
        title3 'Table 1 - White';

proc freq data = subjects;
        tables RG215E /missing;
        format RG215E $yesnof.;

proc freq data = subjects;
        tables other_race;
        format other_race $yesnof.;
        by tx_no;
        title3 'Table 1 - Other Race';

proc freq data = subjects;
        tables other_race;
        format other_race $yesnof.;

proc freq data = subjects;
        tables PE212B PE213B;
        title3 'Units of height and weight measurement';
```

```
proc means data = subjects;
       var bmi_base;
       class tx_no;
       types () tx_no;
       title3 'Table 1 - BMI';

proc freq data = subjects;
       tables bh214;
       format bh214 $yesnof.;
       by tx_no;
       title3 'Table 1 - Proton pump inhibitor';

proc freq data = subjects;
       tables bh214;
       format bh214 $yesnof.;

proc freq data = subjects;
       tables bh215;
       format bh215 $yesnof.;
       by tx_no;
       title3 'Table 1 - Benzodiazepine';

proc freq data = subjects;
       tables bh215;
       format bh215 $yesnof.;

proc freq data = subjects;
       tables bh217;
       format bh217 $yesnof.;
       by tx_no;
       title3 'Table 1 - Prokinetic';

proc freq data = subjects;
       tables bh217;
       format bh217 $yesnof.;

proc freq data = subjects;
       tables bh218;
       format bh218 $yesnof.;
       by tx_no;
       title3 'Table 1 - Antiemetic';

proc freq data = subjects;
       tables bh218;
       format bh218 $yesnof.;

proc freq data = subjects;
       tables bh219;
       format bh219 $yesnof.;
       by tx_no;
```

```
        title3 'Table 1 - Selective serotonin reuptake inhibitor';

proc freq data = subjects;
        tables bh219;
        format bh219 $yesnof.;

proc means data = subjects;
        var gsci_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - GSCI Total Score';

proc means data = subjects;
        var nausea_subscore_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Nausea subscore';

proc means data = subjects;
        var fullness_subscore_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Fullness or early satiety subscore';

proc means data = subjects;
        var bloating_subscore_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Bloating subscore';

proc means data = subjects;
        var upper_ab_subscore_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Upper abdominal pain subscore';

proc means data = subjects;
        var lower_ab_subscore_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Lower abdominal pain subscore';

proc means data = subjects;
        var gerd_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - GERD subscore';

proc means data = subjects;
        var constipation_subscore_base;
        class tx_no;
```

```
        types () tx_no;
        title3 'Table 1 - Constipation score';

proc means data = subjects;
        var diarrhea_subscore_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Diarrhea score';

proc freq data = subjects;
        tables gd137;
        by tx_no;
        format gd137 $predf.;
        title3 'Table 1 - Nausea/vomiting predominant symptom, No. (%)';

proc freq data = subjects;
        tables gd137;
        format gd137 $predf.;

proc means data = subjects;
        var cgpi_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Clinical Global Patient Impression score';

proc means data = subjects;
        var gsrs_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - GSRS';

proc means data = subjects;
        var bdi_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Beck Depression Inventory Total score';

proc freq data = subjects;
        tables severe_dep;
        by tx_no;
        format severe_dep $yesnof.;
        title3 'Table 1 - Severe Depression, No. (%)';

proc freq data = subjects;
        tables severe_dep;
        format severe_dep $yesnof.;

proc means data = subjects;
        var bpi_severity_base;
        class tx_no;
        types () tx_no;
```

```
        title3 'Table 1 - BPI Severity Score';

proc means data = subjects;
        var bpi_interference_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - BPI Interference Score';

proc means data = subjects;
        var state_anxiety_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - State anxiety score';

proc means data = subjects;
        var trait_anxiety_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - Trait anxiety score';

proc means data = subjects;
        var phq15_base;
        class tx_no;
        types () tx_no;
        title3 'Table 1 - PHQ-15 score';

*** Table 2;

data st3;
        set norigdta.st3;

data ge1;
        set norigdta.ge1;

proc contents data = st3;
proc contents data = ge1;

proc freq data = st3;
        tables visit;
        title3 'st3';

data st3_base st3_followup;
        set st3;
        if visit in ('s1', 's2') then output st3_base;
        else if visit = 'f12' then output st3_followup;

proc sort data = st3_base nodupkey;
        by id;

proc sort data = ge1;
        by id;
```

```
data table2;
       merge treatment (in=val1)
             ge1       (in=val2 drop=visit)
             st3_base  (in=val3);
       by id;
       hr1_retention = input (GE113C, 8.);
       hr2_retention = input (GE113D, 8.);
       hr4_retention = input (GE113F, 8.);
       total_volume_base = input (ST313, 8.);
       if val1 and val2 and val3 then output table2;

proc means data = table2;
       var hr1_retention;
       class tx_no;
       types () tx_no;
       title3 'Table 2 - 1 Hr. Gastric Retention, %';

proc means data = table2;
       var hr2_retention;
       class tx_no;
       types () tx_no;
       title3 'Table 2 - 2 Hr. Gastric Retention, %';

proc means data = table2;
       var hr4_retention;
       class tx_no;
       types () tx_no;
       title3 'Table 2 - 4 Hr. Gastric Retention, %';

proc means data = table2 n median p25 p75;
       var total_volume_base;
       class tx_no;
       types () tx_no;
       title3 'Table 2 - Satiety test, volume consumed, median (IQR), mL';

**** Table 3;

data gs1;
       set norigdta.gs1;

data gd1_total_followup;
       set gd1;
       if visit not in ('s1', 's2');

proc freq data=gd1_total_followup;
       tables visit;
       title3 'gs1 total followup visits';

proc sort data = gd1_total_followup;
       by id visit;
```

```
proc sort data = subjects;
       by id;

data gd1_total_followup;
       merge gd1_total_followup (in=val1)
             subjects           (in=val2 keep=id tx_no gsci_base);
       by id;
       gsci_half_base = 0.5*gsci_base;
       if val2 then output gd1_total_followup;

data primary_outcome;
       set gd1_total_followup;
       gsci_score = input (gd111, 8.);
       by id;
       array scores(0:4) score0-score4;
       retain scores 0;
       if first.id then do i=0 to 4;
              scores[i] = 0;
       end;
       if visit = 'f03' then scores[0] = gsci_score;
       if visit = 'f06' then scores[1] = gsci_score;
       if visit = 'f09' then scores[2] = gsci_score;
       if visit = 'f12' then scores[3] = gsci_score;
       if visit = 'f15' then scores[4] = gsci_score;
       if last.id then output primary_outcome;

data primary_outcome;
       set primary_outcome;
       if (0 < score0 <= gsci_half_base and  0 < score1 <= gsci_half_base) or (0 < score1 <= gsci_half_base and  0 < score2 <=
gsci_half_base) or
          (0 < score2 <= gsci_half_base and  0 < score3 <= gsci_half_base) or (0 < score3 <= gsci_half_base and  0 < score4 <=
gsci_half_base)
          then has_primary_outcome = 1;
       else has_primary_outcome = 0;

proc sort data = primary_outcome;
       by tx_no;

proc freq data = primary_outcome;
       tables has_primary_outcome /binomial(level=2);
       by tx_no;

proc sort data = subjects;
       by id;

proc sort data = pe2_followup nodupkey;
       by id;

proc sort data = gd1_followup nodupkey;
       by id;
```

```
proc sort data = se1_followup nodupkey;
       by id;

proc sort data = pq1_followup nodupkey;
       by id;

proc sort data = gs1_followup nodupkey;
       by id;

proc sort data = pi1_followup nodupkey;
       by id;

data pq1_followup;
       set pq1_followup;
       pq110a = pq110a - 1;
       pq110b = pq110b - 1;
       pq110c = pq110c - 1;
       if pq110d ne 'n' then pq110d = pq110d - 1;
       else pq110d = 0;
       pq110e = pq110e - 1;
       pq110f = pq110f - 1;
       pq110g = pq110g - 1;
       pq110h = pq110h - 1;
       pq110i = pq110i - 1;
       pq110j = pq110j - 1;
       pq110k = pq110k - 1;
       pq110l = pq110l - 1;
       pq110m = pq110m - 1;
       pq110n = pq110n - 1;
       pq110o = pq110o - 1;

data table3;
       merge subjects     (in=val1 keep=id tx_no bmi_base gsci_base nausea_subscore_base fullness_subscore_base bloating_subscore_base
upper_ab_subscore_base lower_ab_subscore_base
                                  gerd_base constipation_subscore_base diarrhea_subscore_base cgpi_base gsrs_base bdi_base
bpi_severity_base bpi_interference_base state_anxiety_base
                                  trait_anxiety_base phq15_base)
        pq1_followup (in=val2)
        gd1_followup (in=val3)
        bd1_followup (in=val4)
        se1_followup (in=val5)
        gs1_followup (in=val6)
        pi1_followup (in=val7)
        fh1_followup (in=val8);
       by id;
       gsci_followup = input (gd111, 8.);
       nausea_subscore_followup = gd115+gd116+gd117;
       fullness_subscore_followup = gd118+gd119+gd120+gd121;
       bloating_subscore_followup = gd122+gd123;
       upper_ab_subscore_followup = gd124+gd125;
```

```
        lower_ab_subscore_followup = gd126+gd127;
        gerd_followup = gd128+gd129+gd130+gd131+gd132+gd133+gd134;
        constipation_subscore_followup = input (gd135, 8.);
        diarrhea_subscore_followup = input (gd136, 8.);
        gsrs_followup = (gs111+gs112+gs113+gs114+gs115+gs116+gs117+gs118+gs119+gs120+gs121+gs122+gs123+gs124+gs125)/15;
        bdi_followup = input(bd108, 8.);
        bpi_severity_followup = (pi111+pi112+pi113+pi114)/4;
        bpi_interference_followup = (pi118a+pi118b+pi118c+pi118d+pi118e+pi118f+pi118g)/7;
        if pi110 = '2' then do;
                bpi_severity_followup = 0;
                bpi_interference_followup = 0;
        end;
        state_anxiety_followup = input (se108a, 8.);
        trait_anxiety_followup = input (se108b, 8.);
        phq15_followup = pq110a+pq110b+pq110c+pq110d+pq110e+pq110f+pq110g+pq110h+pq110i+pq110j+pq110k+pq110l+pq110m+pq110n+pq110o;
        if val1 and (val2 or val3 or val4 or val5 or val6 or val7) then output table3;

data table3;
        set table3;
        gsci_diff = gsci_followup-gsci_base;
        nausea_subscore_diff = nausea_subscore_followup-nausea_subscore_base;
        fullness_subscore_diff = fullness_subscore_followup-fullness_subscore_base;
        bloating_subscore_diff = bloating_subscore_followup-bloating_subscore_base;
        upper_ab_subscore_diff = upper_ab_subscore_followup-upper_ab_subscore_base;
        lower_ab_subscore_diff = lower_ab_subscore_followup-lower_ab_subscore_base;
        gerd_diff = gerd_followup-gerd_base;
        constipation_subscore_diff = constipation_subscore_followup-constipation_subscore_base;
        diarrhea_subscore_diff = diarrhea_subscore_followup-diarrhea_subscore_base;
        cgpi_diff = FH124 - cgpi_base;
        gsrs_diff = gsrs_followup - gsrs_base;
        bdi_diff = bdi_followup - bdi_base;
        bpi_severity_diff = bpi_severity_followup-bpi_severity_base;
        bpi_interference_diff = bpi_interference_followup-bpi_interference_base;
        state_anxiety_diff = state_anxiety_followup-state_anxiety_base;
        trait_anxiety_diff = trait_anxiety_followup-trait_anxiety_base;
        phq15_diff = phq15_followup - phq15_base;

proc freq data = table3;
        tables tx_no;
        title3 'Table 3 - Number of Subjects';

proc means data = table3 n mean alpha=0.05 clm;
        var gsci_diff;
        class tx_no;
        title3 'Table 3 - Mean Change from Baseline - GSCI Total Score';

proc means data = table3 n mean alpha=0.05 clm;
        var nausea_subscore_diff;
        class tx_no;
        title3 'Table 3 - Mean Change from Baseline - Nausea Subscore';
```

```
proc means data = table3 n mean alpha=0.05 clm;
       var fullness_subscore_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Fullness Subscore';

proc means data = table3 n mean alpha=0.05 clm;
       var bloating_subscore_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Bloating Subscore';

proc means data = table3 n mean alpha=0.05 clm;
       var upper_ab_subscore_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Upper abdominal pain score';

proc means data = table3 n mean alpha=0.05 clm;
       var lower_ab_subscore_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Lower abdonimal pain score';

proc means data = table3 n mean alpha=0.05 clm;
       var gerd_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - GERD Subscore';

proc means data = table3 n mean alpha=0.05 clm;
       var constipation_subscore_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Constipation score';

proc means data = table3 n mean alpha=0.05 clm;
       var diarrhea_subscore_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Diarrhea score';

proc means data = table3 n mean alpha=0.05 clm;
       var cgpi_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline -Clinical Global Patient Impression Score';

proc means data = table3 n mean alpha=0.05 clm;
       var gsrs_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Gastrointenstinal symptom rating scale';

proc means data = table3 n mean alpha=0.05 clm;
       var bdi_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Beck Depression Inventory Total score';

proc means data = table3 n mean alpha=0.05 clm;
```

```
        var bpi_severity_diff;
        class tx_no;
        title3 'Table 3 - Mean Change from Baseline - Brief Pain Inventory, Severity score';

proc means data = table3 n mean alpha=0.05 clm;
        var bpi_interference_diff;
        class tx_no;
        title3 'Table 3 - Mean Change from Baseline - Brief Pain Inventory, Interference score';

proc means data = table3 n mean alpha=0.05 clm;
        var state_anxiety_diff;
        class tx_no;
        title3 'Table 3 - Mean Change from Baseline - State anxiety score';

proc means data = table3 n mean alpha=0.05 clm;
        var trait_anxiety_diff;
        class tx_no;
        title3 'Table 3 - Mean Change from Baseline - Trait anxiety score';

proc means data = table3 n mean alpha=0.05 clm;
        var phq15_diff;
        class tx_no;
        title3 'Table 3 - Mean Change from Baseline - PHQ-15 Score';

data table3_bmi;
        merge subjects     (in=val1 keep=id tx_no bmi_base)
              pe2_followup (in=val2);
        by id;
        if PE212B = 1 then PE212A = PE212A * 2.54;
        if PE213B = 1 then PE213A = PE213A * 0.453592;
        bmi_followup = PE213A/((PE212A/100)**2);
        bmi_diff = bmi_followup-bmi_base;
        if val1 and val2 then output table3_bmi;

proc freq data = pe2_followup;
        tables PE212B PE213B;
        title3 'Table 3 Subjects - Height and Weight Measurement Units';

proc means data = table3_bmi n mean alpha=0.05 clm;
        var bmi_diff;
        class tx_no;
        title3 'Table 3 - Mean Change from Baseline - BMI';

proc sort data = table2;
        by id;

proc sort data = st3_followup nodupkey;
        by id;

data table3_12wk;
```

```
       merge table2       (in=val1 keep=id tx_no bl1_base bl2_base bl3_base bl4_base post1_base post2_base post3_base post4_base
total_volume_base)
              st3_followup (in=val2);
       by id;
       total_volume_followup = input (ST313, 8.);
       if val1 then output table3_12wk;

data table3_12wk;
       set table3_12wk;
       volume_diff = total_volume_followup - total_volume_base;

proc means data = table3_12wk n mean alpha=0.05 clm;
       var volume_diff;
       class tx_no;
       title3 'Table 3 - Mean Change from Baseline - Satiety test, Volume consumed, mL';
```