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

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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 "Datasets" folder in the data package. For this replication, variables were taken from the "table1", "table2", and the "table3" datasets. These datasets were analysis datasets created by the DCC from the forms datasets, which are also included.

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 "Table1", "Table2", and "Table3" SAS datasets, descriptive statistics of baseline characteristics, frequencies, and means were computed, by treatment group (Table B, D, and F).

5 Results

Table 1 in the publication [1], <u>Baseline patient characteristics by treatment group</u>, 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 file to the results published in Table 1. The results of the replication are similar to published results, within rounding error.

Table 2 in the publication [1], <u>Baseline gastric diagnostic test results by treatment group</u>, 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 file to the results published in Table 2. The results of the replication are similar to published results, within rounding error.

Table 3 in the publication [1], <u>Comparison of primary and secondary outcomes by treatment group</u>. Table E lists the variables that were used in the replication and Table F compares the results calculated from the archived data file to the results published in Table 3. The results of the replication are similar to published results, within rounding error.

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

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: <u>Baseline Patient Characteristics by Treatment Group</u>

Table Variable	Variables Used in Replication from the "Table1" Dataset
Age, y	age
Women, No. (%)	female
Hispanic	hisp
RACE	RACE
Body mass indexa	bmi
Proton pump inhibitor	ppi
Benzodiazepine	benz
Prokinetic	prokin
Antiemetic	antiem
Selective serotonin reuptake inhibitor	ssri
GCSI total scoreb	gcsi
Nausea subscoreb	BSUB1
Fullness or early satiety subscoreb	full
Bloating subscoreb	bloat
Upper abdominal pain subscoreb	upain
Lower abdominal pain subscoreb	lpain
GERD subscoreb	BREGURG
Constipation scoreb	constipa
Diarrhea scoreb	diarrhea
Nausea/vomiting predominant symptom, No. (%)	NAUSVOMI
Clinical Global Patient Impression scorec	cgpi
GSRS, mean scored	totgsrs
Physical component summary, score	BPCS
Mental component summary, score	BMCS

Table Variable	Variables Used in Replication from the "Table1" Dataset
Total score[f]	bdi
Severe depression, No. (%)	depress
Brief Pain InventorySeverity score[g]	severity
Brief Pain InventoryInterference score[h]	interfer
State anxiety score[i]	state
Trait anxiety score[j]	trait
PHQ-15 score[k]	phq15

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=65) Mean(SD) [Difference]	Placebo(n=65) Mean(SD) [Manuscript]	Placebo(n=65) Mean(SD) [DSIC]	Placebo(n=65) Mean(SD) [Difference]	Total(n=130) Mean(SD) [Manuscript]	Total(n=130) Mean(SD) [DSIC]	Total(n=130) Mean(SD) [Difference]
Age, y	42 (12)	42(12)	0(0)	40 (12)	40(12)	0(0)	41 (12)	41(12)	0(0)
Women, No. (%)	60 (92.3)	60(92.3)	0(0)	56 (86.2)	56(86.2)	0(0)	116 (89.2)	116(89.2)	0(0)
Hispanic	7 (10.8)	7(10.8)	0(0)	8 (12.3)	8(12.3)	0(0)	15 (11.5)	15(11.5)	0(0)
Black	10 (15.4)	10(15.4)	0(0)	9 (13.8)	9(13.8)	0(0)	19 (14.6)	19(14.6)	0(0)
White	54 (83.1)	54(83.1)	0(0)	54 (83.1)	54(83.1)	0(0)	108 (83.1)	108(83.1)	0(0)
Other	1 (1.5)	1(1.5)	0(0)	2 (3.0)	2(3.1)	0(-0.1)	3 (2.4)	3(2.3)	0(0.1)
Body mass indexa	27 (5)	27(5)	0(0)	28 (7)	28(7)	0(0)	27 (6)	28(6)	-1(0)
Proton pump inhibitor	48 (73.8)	48(73.8)	0(0)	49 (75.4)	49(75.4)	0(0)	97 (74.6)	97(74.6)	0(0)
Benzodiazepine	26 (40)	26(40)	0(0)	14 (21.5)	14(21.5)	0(0)	40 (30.8)	40(30.8)	0(0)
Prokinetic	23 (35.4)	23(35.4)	0(0)	25 (38.5)	25(38.5)	0(0)	48 (36.9)	48(36.9)	0(0)
Antiemetic	39 (60)	39(60)	0(0)	33 (50.8)	33(50.8)	0(0)	72 (55.4)	72(55.4)	0(0)
Selective serotonin reuptake inhibitor	7 (10.8)	7(10.8)	0(0)	11 (16.9)	11(16.9)	0(0)	18 (13.8)	18(13.8)	0(0)
GCSI total scoreb	30.9 (6.1)	30.9(6.1)	0(0)	30.3 (6.5)	30.3(6.5)	0(0)	30.6 (6.3)	30.6(6.3)	0(0)
Nausea subscoreb	8.2 (3.6)	8.2(3.7)	0(-0.1)	8.2 (4.2)	8.2(4.2)	0(0)	8.1 (3.9)	8.2(3.9)	-0.1(0)
Fullness or early satiety subscoreb	15.4 (3.4)	15.4(3.4)	0(0)	15.1 (4.1)	15.1(4.1)	0(0)	15.3 (3.7)	15.3(3.7)	0(0)
Bloating subscoreb	7.2 (2.9)	7.2(2.9)	0(0)	7.0 (2.7)	7.0(2.7)	0(0)	7.1 (2.8)	7.1(2.8)	0(0)

characteristic	Nortriptyline(n=65) Mean(SD) [Manuscript]	Nortriptyline(n=65) Mean(SD) [DSIC]	Nortriptyline(n=65) Mean(SD) [Difference]	Placebo(n=65) Mean(SD) [Manuscript]	Placebo(n=65) Mean(SD) [DSIC]	Placebo(n=65) Mean(SD) [Difference]	Total(n=130) Mean(SD) [Manuscript]	Total(n=130) Mean(SD) [DSIC]	Total(n=130) Mean(SD) [Difference]
Upper abdominal pain subscoreb	6.8 (2.9)	6.7(2.9)	0.1(0)	6.5 (2.9)	6.5(2.9)	0(0)	6.6 (2.9)	6.6(2.9)	0(0)
Lower abdominal pain subscoreb	4.7 (3.3)	4.7(3.3)	0(0)	4.3 (3.3)	4.3(3.3)	0(0)	4.5 (3.3)	4.5(3.3)	0(0)
GERD subscoreb	15.4 (9.4)	15.4(9.4)	0(0)	17.9 (10.5)	17.9(10.5)	0(0)	16.7 (10)	16.7(10)	0(0)
Constipation scoreb	2.8 (1.9)	2.8(1.9)	0(0)	2.4 (1.7)	2.4(1.7)	0(0)	2.6 (1.8)	2.6(1.8)	0(0)
Diarrhea scoreb	1.8 (1.7)	1.8(1.7)	0(0)	2.0 (1.8)	2.0(1.8)	0(0)	1.9 (1.8)	1.9(1.8)	0(0)
Nausea/vomiting predominant symptom, No. (%)	27 (41.6)	27.0(41.5)	0(0.1)	22 (33.9)	22.0(33.8)	0(0.1)	49 (37.7)	49.0(37.7)	0(0)
Clinical Global Patient Impression scorec	-0.7 (0.9)	-0.7(0.9)	0(0)	-0.7 (1.2)	-0.7(1.2)	0(0)	-0.7 (1.0)	-0.7(1.0)	0(0)
GSRS, mean scored	3.6 (1.1)	3.6(1.1)	0(0)	3.7 (1.2)	3.7(1.2)	0(0)	3.6 (1.2)	3.6(1.2)	0(0)
Physical component summary, score	35 (10)	35(10)	0(0)	36 (10)	36(10)	0(0)	35 (10)	35(10)	0(0)
Mental component summary, score	41 (13)	41(13)	0(0)	40 (13)	40(13)	0(0)	40 (13)	40(13)	0(0)
Total scoref	17 (11)	17(11)	0(0)	18 (12)	18(12)	0(0)	17 (12)	17(12)	0(0)
Severe depression, No. (%)	12 (18.5)	12(18.5)	0(0)	15 (23.2)	15(23.1)	0(0.1)	27 (20.8)	27(20.8)	0(0)
Brief Pain InventorySeverity scoreg	4.0 (2.5)	4.0(2.5)	0(0)	4.1 (2.7)	4.1(2.7)	0(0)	4.0 (2.6)	4.0(2.6)	0(0)
Brief Pain InventoryInterference scoreh	4.2 (3.0)	4.2(3.0)	0(0)	4.1 (3.3)	4.1(3.3)	0(0)	4.1 (3.1)	4.1(3.1)	0(0)
State anxiety scorei	42 (13)	42(13)	0(0)	41 (12)	41(12)	0(0)	42 (12)	42(12)	0(0)
Trait anxiety scorej	43 (12)	43(12)	0(0)	43 (13)	43(13)	0(0)	43 (12)	43(12)	0(0)
PHQ-15 scorek	14 (5)	14(5)	0(0)	14 (5)	14(5)	0(0)	14 (5)	14(5)	0(0)

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

Table Variable	Variables Used in Replication from the "Table2" Dataset
Gastric retention, % 1h	t1
Gastric retention, % 2h	t2
Gastric retention, % 4h	t4
Satiety test, volume consumed, median (IQR), mL	ensure
No. of evaluable patients Electrogastrography,	bblbrad_c
Average power in bradygastria region (1.0-2.5 cpm) Baseline	bblbrad
Average power in bradygastria region (1.0-2.5 cpm)0-30?min post satiety test	bpstbrad
Average power in normal region (2.5-3.7 cpm) Baseline	bblnorm
Average power in normal region (2.5-3.7 cpm) 0-30?min post satiety test	bpstnorm
Average power in tachygastria region (3.7-10 cpm) Baseline	bbltach
Average power in tachygastria region (3.7-10 cpm) 0-30?min post satiety test	bpsttach
Average power in duodenal region (10-15.0 cpm) Baseline	bblduod
Average power in duodenal region (10-15.0 cpm) 0-30?min post satiety test	bpstduod

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

characteristic	Nortriptyline(n=65) Mean(SD) [Manuscript]	Nortriptyline(n=65) Mean(SD) [DSIC]	Nortriptyline(n=65) Mean(SD) [Difference]	Placebo(n=65) Mean(SD) [Manuscript]	Placebo(n=65) Mean(SD) [DSIC]	Placebo(n=65) Mean(SD) [Difference]	Total(n=130) Mean(SD) [Manuscript]	Total(n=130) Mean(SD) [DSIC]	Total(n=130) Mean(SD) [Difference]
No. of evaluable patients 1h	63	63	0	62	62	0			
Gastric retention, % 1h	80 (14)	80(14)	0(0)	80 (12)	80(12)	0(0)	80 (13)	80(13)	0(0)
No. of evaluable patients2h	58	58	0	61	61	0			
Gastric retention, % 2h	61 (17)	61(17)	0(0)	59 (17)	59(17)	0(0)	60 (17)	60(17)	0(0)
No. of evaluable patients 4h	56	56	0	61	61	0			
Gastric retention, % 4h	26 (16)	26(16)	0(0)	25 (17)	25(17)	0(0)	26 (16)	26(16)	0(0)
Satiety test, volume consumed, median (IQR), mL	269 (225-424)	269(225-424)	0(0-0)	240 (177-382)	240(240-382)	0(0-0)	240 (207-400)	240(207-400)	0(0-0)
No. of evaluable patients Electrogastrography,	54	54	0	50	50	0			
Average power in bradygastria region (1.0-2.5 cpm) Baseline	50 (20)	50(20)	0(0)	43 (18)	43(18)	0(0)	46 (19)	46(19)	0(0)
Average power in bradygastria region (1.0-2.5 cpm)0-30?min post satiety test	40 (13)	40(13)	0(0)	41 (15)	41(15)	0(0)	41 (14)	41(14)	0(0)
Average power in normal region (2.5-3.7 cpm) Baseline	20 (15)	20(15)	0(0)	19 (10)	19(10)	0(0)	20 (13)	20(13)	0(0)
Average power in normal region (2.5-3.7 cpm) 0-30?min post satiety test	24 (14)	24(14)	0(0)	23 (11)	23(11)	0(0)	23 (13)	23(13)	0(0)

characteristic	Nortriptyline(n=65) Mean(SD) [Manuscript]	Nortriptyline(n=65) Mean(SD) [DSIC]	Nortriptyline(n=65) Mean(SD) [Difference]	Placebo(n=65) Mean(SD) [Manuscript]	Placebo(n=65) Mean(SD) [DSIC]	Placebo(n=65) Mean(SD) [Difference]	Total(n=130) Mean(SD) [Manuscript]	Total(n=130) Mean(SD) [DSIC]	Total(n=130) Mean(SD) [Difference]
Average power in tachygastria region (3.7-10 cpm) Baseline	21 (10)	21(10)	0(0)	26 (10)	26(10)	0(0)	23 (10)	23(10)	0(0)
Average power in tachygastria region (3.7-10 cpm) 0-30?min post satiety test	27 (7)	27(7)	0(0)	28 (10)	28(10)	0(0)	27 (8)	27(8)	0(0)
Average power in duodenal region (10-15.0 cpm) Baseline	10 (13)	10(13)	0(0)	12 (10)	12(10)	0(0)	11 (10)	11(12)	0(-2)
Average power in duodenal region (10-15.0 cpm) 0-30?min post satiety test	9 (8)	9(8)	0(0)	8 (7)	8(7)	0(0)	9 (7)	9(7)	0(0)

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

Table Variable	Variables Used in Replication from the "Table3" Dataset
Patient assessment of upper gastro- intestinal symptom severity no. of patient	ctot
Total GCSI score	ctot
Nausea subscore	CSUB1
Fullness or early satiety subscore	CSUB2
Bloating, subscore	CSUB3
Lower abdominal pain score	CLPAIN
GERD subscore	CREGURG
Constipation score	CCONSTIP
Diarrhea score	CDIARRHE
Clinical Global Patient Impression score	CCGPI
Gastrointestinal symptom rating scale, mean score	CTOTGSRS
Physical component summary	CPCS
Mental component summary	CMCS
Beck Depression Inventory Total score	CBDI
Brief Pain Inventory Severity score	CSEVER
Brief Pain Inventory Interference score	CINTER
State anxiety	CSTATE
Trait anxiety	CTRAIT
PHQ-15 score	CPHQ15
BMI Value	cbmi
Satiety test Volume consumed, mL	CENSURE
electrogastrography%	CBLBRAD
Average power in bradygastria region (1.0-2.5 cpm) Baseline	CBLBRAD
Average power in bradygastria region (1.0-2.5 cpm) 0-30?min post satiety test	CPSTBRAD
Average power in normal region (2.5-3.7 cpm) Baseline, %	CBLNORM

Table Variable	Variables Used in Replication from the "Table3" Dataset
Average power in normal region (2.5-3.7 cpm)0-30?min post satiety test	CPSTNORM
Average power in tachygastria region (3.7-10 cpm)Baseline, %	CBLTACH
Average power in tachygastria region (3.7-10 cpm)0-30?min post satiety test	CPSTTACH
Average power in duodenal region (10-15.0 cpm)Baseline, %	CBLDUOD
Average power in duodenal region (10-15.0 cpm) 0-30?min post satiety test, %	CPSTDUOD

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

characteristic	Nortriptyline(n=65) Mean(95CI) [Manuscript]	Nortriptyline(n=65) Mean(95CI) [DSIC]	Nortriptyline(n=65) Mean(95CI) [Difference]	Placebo(n=65) Mean(95CI) [Manuscript]	Placebo(n=65) Mean(95CI) [DSIC]	Placebo(n=65) Mean(95CI) [Difference]
Patient assessment of upper gastro-intestina	56	56	0	62	62	0
Total GCSI score	-8.8 (-11.7 to -5.9)	-8.8(-11.7 to -5.9)	0(0 to 0)	-7.2 (-9.6 to -4.9)	-7.2(-7.2 to -4.9)	0(0 to 0)
Nausea subscore	-2.5 (-3.6 to -1.4)	-2.5(-3.6 to -1.4)	0(0 to 0)	-2.7 (-3.7 to -1.8)	-2.7(-2.7 to -1.8)	0(0 to 0)
Fullness or early satiety subscore	-5.0 (-6.5 to -3.5)	-5.0(-6.5 to -3.5)	0(0 to 0)	-3.3 (-4.6 to -2.1)	-3.3(-3.3 to -2.1)	0(0 to 0)
Bloating, subscore	-1.3 (-2.1 to -0.5)	-1.3(-2.1 to -0.5)	0(0 to 0)	-1.2 (-1.9 to -0.4)	-1.2(-1.2 to -0.4)	0(0 to 0)
Upper abdominal pain score	-1.7 (-2.6 to -0.7)	-1.7(-2.6 to -0.7)	0(0 to 0)	-1.7 (-2.5 to -1.0)	-1.7(-1.7 to -1.0)	0(0 to 0)
Lower abdominal pain score	-0.9 (-1.7 to 0)	-0.9(-1.7 to 0)	0(0 to 0)	-0.3 (-1.0 to 0.4)	-0.3(-0.3 to 0.4)	0(0 to 0)
GERD subscore	-4.3 (-6.8 to -1.9)	-4.3(-6.8 to -1.9)	0(0 to 0)	-5.6 (-7.7 to -3.5)	-5.6(-5.6 to -3.5)	0(0 to 0)
Constipation score	-0.2 (-0.7 to 0.2)	-0.2(-0.7 to 0.2)	0(0 to 0)	-0.4 (-0.8 to -0.1)	-0.4(-0.4 to -0.1)	0(0 to 0)
Diarrhea score	-0.4 (-0.8 to 0.1)	-0.4(-0.8 to 0.1)	0(0 to 0)	-0.7 (-1.0 to -0.3)	-0.7(-0.7 to -0.3)	0(0 to 0)
Clinical Global Patient Impression score	1.3 (1.0 to 1.6)	1.3(1.0 to 1.6)	0(0 to 0)	0.9 (0.5 to 1.3)	0.9(0.9 to 1.3)	0(0 to 0)
Gastrointestinal symptom rating scale, mean s	-0.5 (-0.8 to -0.3)	-0.5(-0.8 to -0.3)	0(0 to 0)	-0.5 (-0.8 to -0.3)	-0.5(-0.5 to -0.3)	0(0 to 0)
Physical component summary	3.8 (1.3 to 6.4)	3.8(1.3 to 6.4)	0(0 to 0)	1.7 (-0.2 to 3.6)	1.7(1.7 to 3.6)	0(0 to 0)
Mental component summary	1.8 (-1.4 to 5.1)	1.8(-1.4 to 5.1)	0(0 to 0)	0.9 (-1.3 to 3.1)	0.9(0.9 to 3.1)	0(0 to 0)
Beck Depression Inventory Total score	-2.6 (-5.0 to -0.2)	-2.6(-5.0 to -0.2)	0(0 to 0)	-3.1 (-4.9 to -1.3)	-3.1(-3.1 to -1.3)	0(0 to 0)

characteristic	Nortriptyline(n=65) Mean(95CI) [Manuscript]	Nortriptyline(n=65) Mean(95CI) [DSIC]	Nortriptyline(n=65) Mean(95CI) [Difference]	Placebo(n=65) Mean(95CI) [Manuscript]	Placebo(n=65) Mean(95CI) [DSIC]	Placebo(n=65) Mean(95CI) [Difference]
Brief Pain Inventory Severity score	-1.1 (-1.9 to -0.4)	-1.1(-1.9 to -0.4)	0(0 to 0)	-0.5 (-1.1 to 0.1)	-0.5(-0.5 to 0.1)	0(0 to 0)
Brief Pain Inventory Interference score	-1.1 (-1.8 to -0.4)	-1.1(-1.8 to -0.4)	0(0 to 0)	-0.2 (-0.9 to 0.6)	-0.2(-0.2 to 0.6)	0(0 to 0)
State anxiety	0.4 (-2.9 to 3.7)	0.4(-2.9 to 3.7)	0(0 to 0)	-0.1 (-2.6 to 2.4)	-0.1(-0.1 to 2.4)	0(0 to 0)
Trait anxiety	-0.3 (-3.0 to 2.5)	-0.3(-3.0 to 2.5)	0(0 to 0)	-1.7 (-3.5 to 0.1)	-1.7(-1.7 to 0.1)	0(0 to 0)
PHQ-15 score	-2.4 (-3.6 to -1.2)	-2.4(-3.6 to -1.2)	0(0 to 0)	-1.5 (-2.5 to -0.5)	-1.5(-1.5 to -0.5)	0(0 to 0)
Body mass index	55	55	0	59	59	0
BMI Value	0.5 (0.1 to 0.8)	0.5(0.1 to 0.8)	0(0 to 0)	0 (-0.3 to 0.3)	0(0 to 0.3)	0(0 to 0)
Satiety test	49	49	0	55	55	0
Satiety test Volume consumed, mL	7 (-24 to 39)	7(-24 to 39)	0(0 to 0)	1 (-35 to 36)	1(1 to 36)	0(0 to 0)
electrogastrography%	39	39	0	33	33	0
Average power in bradygastria region (1.0-2.5	-1 (-10 to 7)	-1(-10 to 7)	0(0 to 0)	6 (-1 to 13)	6(6 to 13)	0(0 to 0)
Average power in bradygastria region (1.0-2.5	-2 (-7 to 4)	-2(-7 to 4)	0(0 to 0)	-1 (-7 to 4)	-1(-1 to 4)	0(0 to 0)
Average power in normal region (2.5-3.7 cpm)	0 (-5 to 6)	0(-5 to 6)	0(0 to 0)	-2 (-7 to 2)	-2(-2 to 2)	0(0 to 0)

characteristic	Nortriptyline(n=65) Mean(95CI) [Manuscript]	Nortriptyline(n=65) Mean(95CI) [DSIC]	Nortriptyline(n=65) Mean(95CI) [Difference]	Placebo(n=65) Mean(95CI) [Manuscript]	Placebo(n=65) Mean(95CI) [DSIC]	Placebo(n=65) Mean(95CI) [Difference]
Average power in normal region (2.5-3.7 cpm)	-1 (-5 to 3)	-1(-5 to 3)	0(0 to 0)	1 (-4 to 6)	1(1 to 6)	0(0 to 0)
Average power in tachygastria region (3.7-10.	2 (-3 to 6)	2(-3 to 6)	0(0 to 0)	-4 (-8 to 0)	-4(-4 to 0)	0(0 to 0)
Average power in tachygastria region (3.7-10.	2 (-2 to 5)	2(-2 to 5)	0(0 to 0)	0 (-3 to 3)	-0(-0 to 3)	0(0 to 0)
Average power in duodenal region (10-15.0	-1 (-6 to 4)	-1(-6 to 4)	0(0 to 0)	0 (-3 to 4)	0(0 to 4)	0(0 to 0)
Average power in duodenal region (10-15.0	1 (-3 to 6)	1(-3 to 6)	0(0 to 0)	1 (-1 to 3)	1(1 to 3)	0(0 to 0)

Attachment A: SAS Code

```
/*************************************************************************************************
***Program: /prj/niddk/ims_analysis/NORIG/prog_initial_analysis/norig_integrity_check.sas;
***Programmer: Jane Wang
***Date Created: 10/17/2013
***Purpose: To perform a Dataset Integrity Check (DSIC) between the NORIG data and the primary outcome paper:
Effect of Nortriptyline on Symptoms
of Idiopathic Gastroparesis
The NORIG Randomized Clinical Trial
Henry P. Parkman, MD; Mark L. Van Natta, MHS; Thomas L. Abell, MD; RichardW. McCallum, MD;
Irene Sarosiek, MD; Linda Nguyen, MD; William J. Snape, MD; Kenneth L. Koch, MD; William L. Hasler, MD;
Gianrico Farrugia, MD; Linda Lee, MD; Aynur Unalp-Arida, MD, PhD; James Tonascia, PhD;
Frank Hamilton, MD, MPH; Pankaj J. Pasricha, MDs
***
*************************************************************************************************/;


title1 "%sysfunc(getoption(sysin))";
title2 " ";

options nofmterr;

libname prv_data '/prj/niddk/ims_analysis/NORIG/private_orig_data/NORIG_PrimaryResults_DB/Datasets/SASDATA';



*** Data from the Primary outcome paper that was converted to .csv format so that the DSIC data could be easily compared;
FILENAME table1  '/prj/niddk/ims_analysis/NORIG/private_created_data/table1_data.csv';
FILENAME table2  '/prj/niddk/ims_analysis/NORIG/private_created_data/table2_data.csv';
FILENAME table3  '/prj/niddk/ims_analysis/NORIG/private_created_data/table3_data.csv';


*** Output CSV files that will be converted to .xls before being added to the DSIC document;
FILENAME out_t1  '/prj/niddk/ims_analysis/NORIG/private_created_data/norig_table1_dsic.csv';
FILENAME out_t2  '/prj/niddk/ims_analysis/NORIG/private_created_data/norig_table2_dsic.csv';
FILENAME out_t3  '/prj/niddk/ims_analysis/NORIG/private_created_data/norig_table3_dsic.csv';


*** Reading in the analysis datasets used for the DSIC;
data figure2  ;  set prv_data.figure2  ;
data figure3  ;  set prv_data.figure3  ;
data table1  ;   set prv_data.table1  ;
data table2  ;   set prv_data.table2  ;
data table3  ;   set prv_data.table3  ;

***********************************************************************************;
*************** Check Table 1 *****************************************************;
***********************************************************************************;

%macro baseline_freq(dataset,var_name);
```

```
      *** Creating a frequency table in the format of Table 1 in the primary outcome paper;
  proc freq data = &dataset;
      table (&var_name.)*tx ;
      title3 "Frequency table of the &var_name. variable in the analysis dataset";

      *** Outputting the frequency data to work.&var_name._cross using the ODS output;
  ods output CrossTabFreqs = work.&var_name._cross;

proc freq data = &dataset;
      table &var_name / list missing;
      title3 "Frequency table of the MMF subjects to generate the output to check the Table 2 Frequencies";

      *** Outputing the frequency table data to the level_mmf_freq dataset using ODS;
      ods output OneWayFreqs = &var_name._freq;

  proc print data =&var_name._cross;
      *** Creating two datases (one per arm) so that the data can be in the correct format;
      data &var_name._cross_Nor &var_name._cross_Plb;
        set &var_name._cross ;
    length table_name $ 30.;
    table_name = "&var_name.";
        if TX ne '' and not missing(&var_name);
        if TX = "Nor"  then output &var_name._cross_Nor;
        else if TX = "Plb"   then output &var_name._cross_Plb;

*** Placing the statisitics in the same order as the primary outcome paper using first and second as the placement of the Plb
subjects;
      data &var_name._cross_Nor (keep =  &var_name. first_stat second_stat table_name);
            set &var_name._cross_Nor;
      first_stat = frequency;
            second_stat = round(colpercent,0.1);

*** Placing the statisitics in the same order as the primary outcome paper using third and fourth as the placement of the Nor
subjects;
      data &var_name._cross_Plb (keep =  &var_name. third_stat fourth_stat table_name);
        set &var_name._cross_Plb;
            third_stat = frequency;
            fourth_stat = round(colpercent,0.1);

      data &var_name._freq (keep =  &var_name. fifth_stat sixth_stat table_name);
            set &var_name._freq;
    length table_name $ 30.;
    table_name = "&var_name.";
        fifth_stat = frequency;
            sixth_stat = round(Percent,0.1);
  proc print data =&var_name._freq;


*** Creating a dataset with the merged data with the variables that contain the order of the statisitics;
```

```
        data &var_name._merge;
          merge &var_name._cross_Nor  (in = in1)
                &var_name._cross_Plb  (in = in2)
                &var_name._freq       (in = in3);
          by table_name &var_name.;
                if in1 and in2 and in3 then output &var_name._merge;
          else abort;

  proc print data = &var_name._merge;
%mend;

%macro baseline_mean(dataset,var_name);

  proc sort data = &dataset;
    by tx;

        *** Creating a means table in the format of Table 1 in the primary outcome paper that contain the median 25th percentile and
75th percentile;
  proc means data = &dataset MEAN STD;
    var &var_name.;
    by tx;

        *** Outputting the statisitics to the work.&var_name._summary dataset using the ODS output;
  ods output Summary = work.&var_name._MEAN;
  run;

  data &var_name._MEAN (keep = table_name first_stat second_stat third_stat fourth_stat );
    set &var_name._MEAN end = lastobs;
    length table_name $ 30.;
    table_name = "&var_name.";
    retain first_stat second_stat third_stat fourth_stat fifth_stat sixth_stat .;
    characteristic = "egfr_study_summary";
    if tx = "Nor" then do;
    first_stat  = &var_name._Mean;
    second_stat = &var_name._StdDev;
    end;
    else if tx = "Plb" then do;
    third_stat  = &var_name._Mean;
    fourth_stat  = &var_name._StdDev;
    end;
    else abort;
    if lastobs then output &var_name._MEAN;

  proc print data = &var_name._MEAN;


  proc means data = &dataset MEAN STD n;
    var &var_name.;
  ods output Summary = work.&var_name._MEANall;
  run;
```

```
   data &var_name._MEANall(keep = table_name fifth_stat sixth_stat);
     set &var_name._MEANall;
     length table_name $ 30.;
     table_name = "&var_name.";
     fifth_stat  = &var_name._Mean;
     sixth_stat  = &var_name._StdDev, ;

   proc print data = &var_name._MEANall;

   data &var_name._summary;
     merge &var_name._MEAN &var_name._MEANall;
     by table_name;
   proc print data = &var_name._summary;

%mend;

%macro table2_mean(dataset,var_name);

   proc sort data = &dataset;
     by tx;

       *** Creating a means table in the format of Table 1 in the primary outcome paper that contain the median 25th percentile and
75th percentile;
   proc means data = &dataset n;
     var &var_name.;
     by tx;

       *** Outputting the statisitics to the work.&var_name._summary dataset using the ODS output;
   ods output Summary = work.&var_name._num;
   run;

   data &var_name._num (keep = table_name first_stat second_stat  );
     set &var_name._num end = lastobs;
     length table_name $ 30.;
     table_name = "&var_name.";
     retain first_stat second_stat ;
     if tx = "Nor" then do;
     first_stat  = ROUND(&var_name._N, 1);
     end;
     else if tx = "Plb" then do;
     second_stat  = ROUND(&var_name._N, 1);
     end;
     else abort;
     if lastobs then output &var_name._num;

   proc print data = &var_name._num;

%mend;

%macro baseline_mean(dataset,var_name);
```

```sas
   proc sort data = &dataset;
     by tx;

        *** Creating a means table in the format of Table 1 in the primary outcome paper that contain the median 25th percentile and
75th percentile;
   proc means data = &dataset MEAN STD;
     var &var_name.;
     by tx;

        *** Outputting the statisitics to the work.&var_name._summary dataset using the ODS output;
   ods output Summary = work.&var_name._MEAN;
   run;

   data &var_name._MEAN (keep = table_name first_stat second_stat third_stat fourth_stat );
     set &var_name._MEAN end = lastobs;
     length table_name $ 30.;
     table_name = "&var_name.";
     retain first_stat second_stat third_stat fourth_stat fifth_stat sixth_stat .;
     characteristic = "egfr_study_summary";
     if tx = "Nor" then do;
     first_stat  = &var_name._Mean;
     second_stat = &var_name._StdDev;
     end;
     else if tx = "Plb" then do;
     third_stat   = &var_name._Mean;
     fourth_stat  = &var_name._StdDev;
     end;
     else abort;
     if lastobs then output &var_name._MEAN;

   proc print data = &var_name._MEAN;


   proc means data = &dataset MEAN STD n;
     var &var_name.;
   ods output Summary = work.&var_name._MEANall;
   run;

   data &var_name._MEANall(keep = table_name fifth_stat sixth_stat);
     set &var_name._MEANall;
     length table_name $ 30.;
     table_name = "&var_name.";
     fifth_stat  = &var_name._Mean;
     sixth_stat  = &var_name._StdDev;

   proc print data = &var_name._MEANall;

   data &var_name._summary;
     merge &var_name._MEAN &var_name._MEANall;
     by table_name;
   proc print data = &var_name._summary;
```

```
%mend;
%macro table2_median(dataset,var_name);

  proc sort data = &dataset;
    by tx;

        *** Creating a means table in the format of Table 2 in the primary outcome paper that contain the median 25th percentile and
75th percentile;
  proc means data = &dataset Median P25 P75;
    var &var_name.;
    by tx;

        *** Outputting the statisitics to the work.&var_name._summary dataset using the ODS output;
  ods output Summary = work.&var_name._num;
  run;
 proc print data = &var_name._num;
  data &var_name._num (keep = table_name first_stat second_stat third_stat fourth_stat fifth_stat sixth_stat );
    set &var_name._num end = lastobs;
    length table_name $ 30.;
    table_name = "&var_name.";
    retain first_stat second_stat  third_stat fourth_stat fifth_stat sixth_stat;
    if tx = "Nor" then do;
      first_stat    = ROUND(&var_name._Median, 1);
      second_stat   = ROUND(&var_name._P25, 1);
      third_stat    = ROUND(&var_name._P75, 1);
    end;
    else if tx = "Plb" then do;
      fourth_stat   = ROUND(&var_name._Median, 1);
      fifth_stat    = ROUND(&var_name._P25, 1);
      sixth_stat    = ROUND(&var_name._P75, 1);
    end;
    else abort;
    if lastobs then output &var_name._num;

  proc print data = &var_name._num;

  proc means data = &dataset Median P25 P75;
    var &var_name.;

        *** Outputting the statisitics to the work.&var_name._summary dataset using the ODS output;
  ods output Summary = work.&var_name._all;

  data &var_name._all(keep = table_name seventh_stat eightth_stat nineth_stat);
    set &var_name._all;
    length table_name $ 30.;
    table_name = "&var_name.";
      seventh_stat   = ROUND(&var_name._Median, 1);
      eightth_stat   = ROUND(&var_name._P25, 1);
      nineth_stat    = ROUND(&var_name._P75, 1);
```

```
   data &var_name._uni;
     merge &var_name._num  &var_name._all;
     by table_name;

   proc print data = &var_name._uni;

%mend;

%macro table3_mean(dataset,var_name);

   proc sort data = &dataset;
     by tx;

         *** Creating a means table in the format of Table 1 in the primary outcome paper that contain the median 25th percentile and
75th percentile;
   proc means data = &dataset MEAN CLM;
     var &var_name.;
     by tx;

         *** Outputting the statisitics to the work.&var_name._summary dataset using the ODS output;
   ods output Summary = work.&var_name._MEAN;
   run;

   data  &var_name._MEAN;
     set  &var_name._MEAN;
     length table_name $ 30.;
     table_name = "&var_name.";

proc print data = &var_name._MEAN;

         *** Creating two datases (one per arm) so that the data can be in the correct format;
         data &var_name._cross_Nor &var_name._cross_Plb;
           set &var_name._MEAN ;
           if TX = "Nor"  then output &var_name._cross_Nor;
           else if TX = "Plb"   then output &var_name._cross_Plb;




*** Placing the statisitics in the same order as the primary outcome paper using first and second as the placement of the Plb
subjects;
       data &var_name._cross_Nor (keep = TX first_stat second_stat third_stat table_name);
             set &var_name._cross_Nor;
     first_stat  = &var_name._Mean;
     second_stat = &var_name._LCLM;
     third_stat  = &var_name._UCLM;

*** Placing the statisitics in the same order as the primary outcome paper using third and fourth as the placement of the Nor
subjects;
       data &var_name._cross_Plb (keep =  TX  fourth_stat fifth_stat sixth_stat table_name);
         set &var_name._cross_Plb;
     fourth_stat = &var_name._Mean;
```

```
    fifth_stat  = &var_name._LCLM;
    sixth_stat  = &var_name._UCLM;

proc print data = &var_name._cross_Nor;
proc print data = &var_name._cross_Plb;



*** Creating a dataset with the merged data with the variables that contain the order of the statisitics;
      data &var_name._merge(drop=tx);
        merge &var_name._cross_Nor  (in = in1)
              &var_name._cross_Plb  (in = in2)
;
      by table_name;
              if in1 and in2  then output &var_name._merge;
      else abort;

  proc print data = &var_name._merge;


%mend;

*******************************************************************************;
*************** Check Table 1 ************************************************;
*******************************************************************************;

%baseline_mean(table1,age       );
%baseline_mean(table1,gcsi      );
%baseline_mean(table1,naus      );
%baseline_mean(table1,full      );
%baseline_mean(table1,bloat     );
%baseline_mean(table1,upain     );
%baseline_mean(table1,lpain     );
%baseline_mean(table1,indigest  );
%baseline_mean(table1,constipa  );
%baseline_mean(table1,diarrhea  );
%baseline_mean(table1,cgpi      );
%baseline_mean(table1,totgsrs   );
%baseline_mean(table1,bdi       );
%baseline_mean(table1,depress   );
%baseline_mean(table1,severity  );
%baseline_mean(table1,interfer  );
%baseline_mean(table1,state     );
%baseline_mean(table1,trait     );
%baseline_mean(table1,phq15     );
%baseline_mean(table3,BMI       );
%baseline_mean(table3,BSUB1     );
%baseline_mean(table3,BREGURG   );
%baseline_mean(table3,BPCS      );
%baseline_mean(table3,BMCS      );
```

```
*** Running the baseline_freq on the 6 categorical variables in the Table 1 manuscript file;
%baseline_freq(table1,female   );
%baseline_freq(table1,race    );
%baseline_freq(table1,hisp     );
%baseline_freq(table1,ppi      );
%baseline_freq(table1,benz     );
%baseline_freq(table1,prokin   );
%baseline_freq(table1,antiem   );
%baseline_freq(table1,ssri     );
%baseline_freq(table1,NAUSVOMI );
%baseline_freq(table1,depress );



data compare_table1_mean(keep = first_stat second_stat  third_stat fourth_stat fifth_stat sixth_stat table_name );
  set
  age_summary
  BMI_summary
  gcsi_summary
  BSUB1_summary
  full_summary
  bloat_summary
  upain_summary
  lpain_summary
  BREGURG_summary
  constipa_summary
  diarrhea_summary
  cgpi_summary
  totgsrs_summary
  BPCS_summary
  BMCS_summary
  bdi_summary
  severity_summary
  interfer_summary
  state_summary
  trait_summary
  phq15_summary
 ;

proc print data = compare_table1_mean;
  title3 "Printout of the Table 1 Dataset from dataset (mean)";


data race_merge;
  set race_merge;
  table_name = strip(table_name) || '_' || strip(race);

data compare_table1_freq(keep = first_stat second_stat  third_stat fourth_stat fifth_stat sixth_stat table_name );
  set
  female_merge(where = (female = 1))
```

```sas
   hisp_merge   (where = (hisp = 1))
   race_merge
   ppi_merge         (where = (ppi       = 1))
   benz_merge        (where = (benz      = 1))
   prokin_merge      (where = (prokin    = 1))
   antiem_merge      (where = (antiem    = 1))
   ssri_merge        (where = (ssri      = 1))
   NAUSVOMI_merge    (where = (NAUSVOMI = 1))
   depress_merge     (where = (depress   = 1))
   ;

proc print data = compare_table1_freq;
   title3 "Printout of the Table 1 Dataset from dataset(freq)";



*** Importing the Table 1 Data taken from the primary outcome paper;

data table1_data;
   infile table1 delimiter = ',' MISSOVER DSD  firstobs=1 ls=1080;
   length characteristic $45 table_name $30 char_stat1 char_stat2 char_stat3 $12;
   input characteristic $ table_name $ char_stat1 $  char_stat2 $ char_stat3 $ ;
   if lengthn(characteristic) NE 0 then output table1_data;

data table1_data;
   set table1_data;
   char_stat1 = strip(char_stat1);
   char_stat2 = strip(char_stat2);
   char_stat3 = strip(char_stat3);
   stat1_m = input(strip(substr(char_stat1,1,index(char_stat1,'(')-1)),8.);
   stat2_m = input(substr(char_stat1,index(char_stat1,'(')+1, length(char_stat1)-index(char_stat1,'(')-1 ),8.);
   stat3_m = input(strip(substr(char_stat2,1,index(char_stat2,'(')-1)),8.);
   stat4_m = input(substr(char_stat2,index(char_stat2,'(')+1, length(char_stat2)-index(char_stat2,'(')-1 ),8.);
   stat5_m = input(strip(substr(char_stat3,1,index(char_stat3,'(')-1)),8.);
   stat6_m = input(substr(char_stat3,index(char_stat3,'(')+1, length(char_stat3)-index(char_stat3,'(')-1 ),8.);
   sort_order = _n_;
   table_name = upcase(table_name);

proc print data = table1_data;
   title3 "Printout of the Table 1 Dataset from the primary outcome paper";



data compare_table1;
   set compare_table1_mean   compare_table1_freq;
   table_name = upcase(table_name);

proc sort data = compare_table1;
   by table_name;

proc sort data = table1_data;
   by table_name;
```

```
data combined_table1_dataset;
  merge compare_table1
        table1_data    ;
  by table_name;
  if table_name in ('AGE' 'BMI' 'STATE' 'TRAIT' 'PHQ15' 'BPCS' 'BMCS' 'BDI') then do;
    diff_1 = round((round(stat1_m,1)  -  round(first_stat ,1)),  1);
    diff_2 = round((round(stat2_m,1) -   round(second_stat,1)),  1);
    diff_3 = round((round(stat3_m,1)  -  round(third_stat ,1)),  1);
    diff_4 = round((round(stat4_m,1) -   round(fourth_stat,1)),  1);
    diff_5 = round((round(stat5_m,1)  -  round(fifth_stat ,1)),  1);
    diff_6 = round((round(stat6_m,1)  -  round(sixth_stat ,1)),  1);

    char_1 = strip(put(first_stat,8.)) || '(' || strip(put(second_stat,8.)) || ')';
    char_2 = strip(put(third_stat,8.)) || '(' || strip(put(fourth_stat,8.)) || ')';
    char_3 = strip(put(fifth_stat,8.)) || '(' || strip(put(sixth_stat, 8.)) || ')';

    char_diff_1 = strip(put(diff_1,8.)) || '(' || strip(put(diff_2,8.)) || ')';
    char_diff_2 = strip(put(diff_3,8.)) || '(' || strip(put(diff_4,8.)) || ')';
    char_diff_3 = strip(put(diff_5,8.)) || '(' || strip(put(diff_6,8.)) || ')';

  end;
  else if table_name in ('FEMALE' 'HISP' 'RACE_BLACK' 'RACE_WHITE' 'RACE_OTHER' 'BMI' 'PPI' 'BENZ' 'PROKIN' 'ANTIEM' 'SSRI' 'DEPRESS'
) then do;
    diff_1 = round((round(stat1_m,1)  -  round(first_stat ,.1)),  1);
    diff_2 = round((round(stat2_m,.1) -   round(second_stat,.1)),  .1);
    diff_3 = round((round(stat3_m,1)  -  round(third_stat ,.1)),  1);
    diff_4 = round((round(stat4_m,.1) -   round(fourth_stat,.1)),  .1);
    diff_5 = round((round(stat5_m,1)  -  round(fifth_stat ,.1)),  1);
    diff_6 = round((round(stat6_m,.1)  -  round(sixth_stat ,.1)),  .1);

    char_1 = strip(put(first_stat,8.)) || '(' || strip(put(second_stat,8.1)) || ')';
    char_2 = strip(put(third_stat,8.)) || '(' || strip(put(fourth_stat,8.1)) || ')';
    char_3 = strip(put(fifth_stat,8.)) || '(' || strip(put(sixth_stat, 8.1)) || ')';


    char_diff_1 = strip(put(diff_1,8.)) || '(' || strip(put(diff_2,8.1)) || ')';
    char_diff_2 = strip(put(diff_3,8.)) || '(' || strip(put(diff_4,8.1)) || ')';
    char_diff_3 = strip(put(diff_5,8.)) || '(' || strip(put(diff_6,8.1)) || ')';
  end;

  else do;
    diff_1 = round((stat1_m  -  first_stat),  0.1);
    diff_2 = round((stat2_m -   second_stat), 0.1);
    diff_3 = round((stat3_m  -  third_stat),  0.1);
    diff_4 = round((stat4_m -   fourth_stat), 0.1);
    diff_5 = round((stat5_m  -  fifth_stat),  0.1);
    diff_6 = round((stat6_m  -  sixth_stat), 0.1);

    char_1 = strip(put(first_stat,8.1)) || '(' || strip(put(second_stat,8.1)) || ')';
```

```
      char_2 = strip(put(third_stat,8.1)) || '(' || strip(put(fourth_stat,8.1)) || ')';
      char_3 = strip(put(fifth_stat,8.1)) || '(' || strip(put(sixth_stat, 8.1)) || ')';


      char_diff_1 = strip(put(diff_1,8.1)) || '(' || strip(put(diff_2,8.1)) || ')';
      char_diff_2 = strip(put(diff_3,8.1)) || '(' || strip(put(diff_4,8.1)) || ')';
      char_diff_3 = strip(put(diff_5,8.1)) || '(' || strip(put(diff_6,8.1)) || ')';
    end;

    label
      char_stat1          = "Nortriptyline(n=65) Mean(SD)  [Manuscript]"
      char_1              = "Nortriptyline(n=65) Mean(SD)  [DSIC]      "
      char_diff_1         = "Nortriptyline(n=65) Mean(SD)  [Difference]"
      char_stat2          = "Placebo(n=65) Mean(SD)  [Manuscript]"
      char_2              = "Placebo(n=65) Mean(SD)  [DSIC]      "
      char_diff_2         = "Placebo(n=65) Mean(SD)  [Difference]"
      char_stat3          = "Total(n=130) Mean(SD)  [Manuscript]"
      char_3              = "Total(n=130) Mean(SD)  [DSIC]      "
      char_diff_3         = "Total(n=130) Mean(SD)  [Difference]"
      ;


proc sort data = combined_table1_dataset;
  by sort_order;
*proc print data = combined_table1_dataset(keep =char_diff_1-char_diff_3 table_name char_stat1-char_stat3 diff_1-diff_6  first_stat
second_stat  third_stat fourth_stat fifth_stat sixth_stat) ;

*** Outputting the dataset to a csv file to be added to the DSIC;

ods csv file = out_t1;

run;

proc print data = combined_table1_dataset NOOBS label;
       var characteristic char_stat1 char_1 char_diff_1 char_stat2 char_2 char_diff_2 char_stat3 char_3 char_diff_3;
       title3 "DSIC Check of Table 1 | baselin patient characteristics by treatment group";

run;

ods csv close;



***********************************************************************************;
*************** Check Table 2 *****************************************************;
***********************************************************************************;

%table2_mean(table2,t1          );
%table2_mean(table2,t2          );
%table2_mean(table2,t4          );
```

```sas
%table2_mean(table2,bblbrad    );

%baseline_mean(table2,t1          );
%baseline_mean(table2,t2          );
%baseline_mean(table2,t4          );
%baseline_mean(table2,bblbrad    );
%baseline_mean(table2,bpstbrad   );
%baseline_mean(table2,bblnorm    );
%baseline_mean(table2,bpstnorm   );
%baseline_mean(table2,bbltach    );
%baseline_mean(table2,bpsttach   );
%baseline_mean(table2,bblduod    );
%baseline_mean(table2,bpstduod   );

data compare_table2_num(keep = first_stat second_stat table_name );
  set

  t1_num
  t2_num
  t4_num
  bblbrad_num
;
  table_name = strip(table_name) || '_C';

proc print data = compare_table2_num;
  title3 "Printout of the Table 2 Dataset from dataset(count)";


data compare_table2_mean(keep = first_stat second_stat  third_stat fourth_stat fifth_stat sixth_stat table_name );
  set

  t1_summary
  t2_summary
  t4_summary
  bblbrad_summary
  bpstbrad_summary
  bblnorm_summary
  bpstnorm_summary
  bbltach_summary
  bpsttach_summary
  bblduod_summary
  bpstduod_summary
;
proc print data = compare_table2_mean;
  title3 "Printout of the Table 2 Dataset from dataset(mean)";


%table2_median(table2,ensure    );

data compare_table2;
  set compare_table2_mean   compare_table2_num ENSURE_UNI;
```

```sas
   table_name = upcase(table_name);

proc print data = compare_table2;
  title3 "Printout of the Table 2 Dataset from dataset";


data table2_data;
  infile table2 delimiter = ',' MISSOVER DSD  firstobs=1 ls=1080;
  length characteristic $100 table_name $30 char_stat1 char_stat2 char_stat3 $20;
  input characteristic $ table_name $ char_stat1 $  char_stat2 $ char_stat3 $ ;
  if lengthn(characteristic) NE 0 then output table2_data;

data table2_data;
  set table2_data;
  char_stat1 = strip(char_stat1);
  char_stat2 = strip(char_stat2);
  char_stat3 = strip(char_stat3);
  if index(char_stat1,'(') = 0 then do;
   stat1_m = input(char_stat1,8.);
   stat2_m = input(char_stat2,8.);
  end;
  else if index(char_stat1,'-') > 0 then do;
    stat1_m = input(strip(substr(char_stat1,1,index(char_stat1,'(')-1)),8.);
    stat2_m = input(substr(char_stat1,6,3),8.);
    stat3_m = input(substr(char_stat1,10,3),8.) ;
    stat4_m = input(strip(substr(char_stat2,1,index(char_stat2,'(')-1)),8.);
    stat5_m = input(substr(char_stat2,6,3),8.);
    stat6_m = input(substr(char_stat2,10,3),8.) ;
    stat7_m = input(strip(substr(char_stat3,1,index(char_stat3,'(')-1)),8.);
    stat8_m = input(substr(char_stat3,6,3),8.);
    stat9_m = input(substr(char_stat3,10,3),8.) ;
  end;
  else do;
    stat1_m = input(strip(substr(char_stat1,1,index(char_stat1,'(')-1)),8.);
    stat2_m = input(substr(char_stat1,index(char_stat1,'(')+1, length(char_stat1)-index(char_stat1,'(')-1 ),8.);
    stat3_m = input(strip(substr(char_stat2,1,index(char_stat2,'(')-1)),8.);
    stat4_m = input(substr(char_stat2,index(char_stat2,'(')+1, length(char_stat2)-index(char_stat2,'(')-1 ),8.);
    stat5_m = input(strip(substr(char_stat3,1,index(char_stat3,'(')-1)),8.);
    stat6_m = substr(char_stat3,index(char_stat3,'(')+1, length(char_stat3)-index(char_stat3,'(')-2 );
  end;
  sort_order = _n_;

  table_name = upcase(table_name);


proc sort data = compare_table2;
  by table_name;

proc sort data = table2_data;
  by table_name;
```

```
proc print data = table2_data;
   title3 "Printout of the Table 2 Dataset from the primary outcome paper";

data combined_table2_dataset;
   merge compare_table2
         table2_data    ;
   by table_name;

   if table_name in ('ENSURE') then do;
      diff_1 = round((round(stat1_m,1)  -  round(first_stat ,1)),  1);
      diff_2 = round((round(stat2_m,1) -   round(second_stat,1)),  1);
      diff_3 = round((round(stat3_m,1)  -  round(third_stat ,1)),  1);
      diff_4 = round((round(stat4_m,1) -   round(fourth_stat,1)),  1);
      diff_5 = round((round(stat5_m,1)  -  round(fifth_stat ,1)),  1);
      diff_6 = round((round(stat6_m,1)  -  round(sixth_stat ,1)),  1);
      diff_7 = round((round(stat7_m,1) -   round(seventh_stat,1)),  1);
      diff_8 = round((round(stat8_m,1)  -  round(eightth_stat ,1)),  1);
      diff_9 = round((round(stat9_m,1)  -  round(nineth_stat ,1)),  1);

      char_1 = strip(put(first_stat,8.))   || '(' || strip(put(second_stat,8.))   || '-' || strip(put(third_stat,8.))   ||')';
      char_2 = strip(put(fourth_stat,8.))  || '(' || strip(put(fourth_stat,8.))   || '-' || strip(put(sixth_stat,8.))   ||')';
      char_3 = strip(put(seventh_stat,8.)) || '(' || strip(put(eightth_stat, 8.)) || '-' || strip(put(nineth_stat, 8.)) ||')';

      char_diff_1 = strip(put(diff_1,8.)) || '(' || strip(put(diff_2,8.)) || '-' || strip(put(diff_3,8.)) || ')';
      char_diff_2 = strip(put(diff_4,8.)) || '(' || strip(put(diff_5,8.)) || '-' || strip(put(diff_6,8.)) || ')';
      char_diff_3 = strip(put(diff_7,8.)) || '(' || strip(put(diff_8,8.)) || '-' || strip(put(diff_9,8.)) || ')';
   end;
   else if index(table_name, '_') > 0 then do;
      diff_1 = round((round(stat1_m,1)  -  round(first_stat ,1)),  1);
      diff_2 = round((round(stat2_m,1) -   round(second_stat,1)),  1);

      char_1 = strip(put(first_stat,8.));
      char_2 = strip(put(second_stat,8.)) ;

      char_diff_1 = strip(put(diff_1,8.));
      char_diff_2 = strip(put(diff_2,8.));
   end;
   else do;
      diff_1 = round((round(stat1_m,1)  -  round(first_stat ,1)),  1);
      diff_2 = round((round(stat2_m,1) -   round(second_stat,1)),  1);
      diff_3 = round((round(stat3_m,1)  -  round(third_stat ,1)),  1);
      diff_4 = round((round(stat4_m,1) -   round(fourth_stat,1)),  1);
      diff_5 = round((round(stat5_m,1)  -  round(fifth_stat ,1)),  1);
      diff_6 = round((round(stat6_m,1)  -  round(sixth_stat ,1)),  1);

      char_1 = strip(put(first_stat,8.)) || '(' || strip(put(second_stat,8.)) || ')';
      char_2 = strip(put(third_stat,8.)) || '(' || strip(put(fourth_stat,8.)) || ')';
      char_3 = strip(put(fifth_stat,8.)) || '(' || strip(put(sixth_stat, 8.)) || ')';


      char_diff_1 = strip(put(diff_1,8.)) || '(' || strip(put(diff_2,8.)) || ')';
```

```
      char_diff_2 = strip(put(diff_3,8.)) || '(' || strip(put(diff_4,8.)) || ')';
      char_diff_3 = strip(put(diff_5,8.)) || '(' || strip(put(diff_6,8.)) || ')';
  end;
    label
     char_stat1          = "Nortriptyline(n=65) Mean(SD)  [Manuscript]"
     char_1              = "Nortriptyline(n=65) Mean(SD)  [DSIC]       "
     char_diff_1          = "Nortriptyline(n=65) Mean(SD)  [Difference]"
     char_stat2          = "Placebo(n=65) Mean(SD)  [Manuscript]"
     char_2              = "Placebo(n=65) Mean(SD)  [DSIC]       "
     char_diff_2          = "Placebo(n=65) Mean(SD)  [Difference]"
     char_stat3          = "Total(n=130) Mean(SD)  [Manuscript]"
     char_3              = "Total(n=130) Mean(SD)  [DSIC]       "
     char_diff_3          = "Total(n=130) Mean(SD)  [Difference]"
     ;


proc sort data = combined_table2_dataset;
  by sort_order;

*proc print data = combined_table2_dataset(keep =char_diff_1-char_diff_3 table_name char_stat1-char_stat3 diff_1-diff_6  first_stat
second_stat  third_stat fourth_stat fifth_stat sixth_stat) ;

*** Outputting the dataset to a csv file to be added to the DSIC;

ods csv file = out_t2;

run;

proc print data = combined_table2_dataset NOOBS label;
       var characteristic char_stat1 char_1 char_diff_1 char_stat2 char_2 char_diff_2 char_stat3 char_3 char_diff_3;
       title3 "DSIC Check of Table 2 | baseline gastric diagnostic test results by treatment group";

run;

ods csv close;


*************************************************************************************;
*************** Check Table 3 ******************************************************;
*************************************************************************************;

%table3_mean(table3,ctot          );
%table3_mean(table3,CSUB1        );
%table3_mean(table3,CSUB2        );
%table3_mean(table3,CSUB3        );
%table3_mean(table3,CUPAIN       );
%table3_mean(table3,CLPAIN       );
%table3_mean(table3,CREGURG      );
%table3_mean(table3,CCONSTIP     );
%table3_mean(table3,CDIARRHE     );
%table3_mean(table3,CCGPI        );
```

```
%table3_mean(table3,CTOTGSRS     );
%table3_mean(table3,CPCS         );
%table3_mean(table3,CMCS         );
%table3_mean(table3,CBDI         );
%table3_mean(table3,CSEVER       );
%table3_mean(table3,CINTER       );
%table3_mean(table3,CSTATE       );
%table3_mean(table3,CTRAIT       );
%table3_mean(table3,CPHQ15       );
%table3_mean(table3,CBMI         );
%table3_mean(table3,CENSURE      );
%table3_mean(table3,CBLBRAD      );
%table3_mean(table3,CPSTBRAD     );
%table3_mean(table3,CBLNORM      );
%table3_mean(table3,CPSTNORM     );
%table3_mean(table3,CBLTACH      );
%table3_mean(table3,CPSTTACH     );
%table3_mean(table3,CBLDUOD      );
%table3_mean(table3,CPSTDUOD     );


data compare_table3_mean(keep = first_stat second_stat  third_stat fourth_stat fifth_stat sixth_stat table_name );
  set
ctot_merge
CSUB1_merge
CSUB2_merge
CSUB3_merge
CUPAIN_merge
CLPAIN_merge
CREGURG_merge
CCONSTIP_merge
CDIARRHE_merge
CCGPI_merge
CTOTGSRS_merge
CPCS_merge
CMCS_merge
CBDI_merge
CSEVER_merge
CINTER_merge
CSTATE_merge
CTRAIT_merge
CPHQ15_merge
CBMI_merge
CENSURE_merge
CBLBRAD_merge
CPSTBRAD_merge
CBLNORM_merge
CPSTNORM_merge
CBLTACH_merge
CPSTTACH_merge
CBLDUOD_merge
```

```
            CPSTDUOD_merge
             ;

%table2_mean(table3,ctot            );
%table2_mean(table3,cbmi          );
%table2_mean(table3,CENSURE         );
%table2_mean(table3,CBLBRAD     );

data compare_table3_num(keep = first_stat second_stat table_name );
  set

  ctot_num
  cbmi_num
  CENSURE_num
  CBLBRAD_num
;
  table_name = strip(table_name) || '_C';

proc print data = compare_table3_num;
  title3 "Printout of the Table 3 Dataset from dataset(count)";

proc print data = compare_table3_mean;
  title3 "Printout of the Table 3 Dataset from dataset(mean)";

data compare_table3;
  set compare_table3_mean   compare_table3_num ;
  table_name = upcase(table_name);


data table3_data;
  infile table3 delimiter = ',' MISSOVER DSD  firstobs=1 ls=1080;
  length characteristic $45 table_name $30 char_stat1 char_stat2  $32;
  input characteristic $ table_name $ char_stat1 $  char_stat2  $ ;
  if lengthn(characteristic) NE 0 then output table3_data;

data table3_data;
  set table3_data;
  char_stat1 = strip(char_stat1);
  char_stat2 = strip(char_stat2);
  if index(char_stat1,'(') = 0 then do;
   stat1_m = input(char_stat1,8.);
   stat2_m = input(char_stat2,8.);
  end;
else do;
    stat1_m = input(strip(substr(char_stat1,1,index(char_stat1,'(')-1)),8.);
    stat2_m = input(substr(char_stat1,index(char_stat1,'(')+1, index(char_stat1,'t')-index(char_stat1,'(')-1 ),8.);
    stat3_m = input(substr(char_stat1,index(char_stat1,'o')+2, index(char_stat1,')')-index(char_stat1,'o')-2 ),8.);
    stat4_m = input(strip(substr(char_stat2,1,index(char_stat2,'(')-1)),8.);
    stat5_m = input(substr(char_stat2,index(char_stat2,'(')+1, index(char_stat2,'t')-index(char_stat2,'(')-1 ),8.);
    stat6_m = input(substr(char_stat2,index(char_stat2,'o')+2, index(char_stat2,')')-index(char_stat2,'o')-2 ),8.);
end;
```

```
   sort_order = _n_;
   table_name = upcase(table_name);


proc sort data = compare_table3;
  by table_name;

proc sort data = table3_data;
  by table_name;


proc print data = table3_data;
  title3 "Printout of the Table 3 Dataset from the primary outcome paper";

data combined_table3_dataset;
  merge compare_table3
        table3_data     ;
  by table_name;
  length char_diff_1 char_diff_2 char_1 char_2$ 30.;
  if index(table_name, '_') > 0 then do;
    diff_1 = round((round(stat1_m,1)  -  round(first_stat ,1)),  1);
    diff_2 = round((round(stat2_m,1) -   round(second_stat,1)),  1);

    char_1 = strip(put(first_stat,8.));
    char_2 = strip(put(second_stat,8.)) ;

    char_diff_1 = strip(put(diff_1,8.));
    char_diff_2 = strip(put(diff_2,8.));
  end;
  else if table_name in ('CENSURE'  'CBLBRAD'  'CPSTBRAD'  'CBLNORM'  'CPSTNORM' 'CBLTACH'  'CPSTTACH'  'CBLDUOD'  'CPSTDUOD') then
do;
    diff_1 = round((round(stat1_m,1)  -  round(first_stat ,1)),  1);
    diff_2 = round((round(stat2_m,1) -   round(second_stat,1)),  1);
    diff_3 = round((round(stat3_m,1)  -  round(third_stat ,1)),  1);
    diff_4 = round((round(stat4_m,1) -   round(fourth_stat,1)),  1);
    diff_5 = round((round(stat5_m,1)  -  round(fifth_stat ,1)),  1);
    diff_6 = round((round(stat6_m,1)  -  round(sixth_stat ,1)),  1);

    char_1 = strip(put(first_stat,8.))    || '(' || strip(put(second_stat,8.))    || ' to ' || strip(put(third_stat,8.))   ||')';
    char_2 = strip(put(fourth_stat,8.))  || '(' || strip(put(fourth_stat,8.))    || ' to ' || strip(put(sixth_stat,8.))   ||')';

    char_diff_1 = strip(put(diff_1,8.)) || '(' || strip(put(diff_2,8.)) || ' to ' || strip(put(diff_3,8.)) || ')';
    char_diff_2 = strip(put(diff_4,8.)) || '(' || strip(put(diff_5,8.)) || ' to ' || strip(put(diff_6,8.)) || ')';

  end;
  else do;
    diff_1 = round((round(stat1_m,.1)  -  round(first_stat ,.1)),  .1);
    diff_2 = round((round(stat2_m,.1) -   round(second_stat,.1)),  .1);
    diff_3 = round((round(stat3_m,.1)  -  round(third_stat ,.1)),  .1);
    diff_4 = round((round(stat4_m,.1) -   round(fourth_stat,.1)),  .1);
    diff_5 = round((round(stat5_m,.1)  -  round(fifth_stat ,.1)),  .1);
```

```
    diff_6 = round((round(stat6_m,.1)  -  round(sixth_stat ,.1)),  .1);

    char_1 = strip(put(first_stat,8.1))   || '(' || strip(put(second_stat,8.1))   || ' to ' || strip(put(third_stat,8.1))   ||')';
    char_2 = strip(put(fourth_stat,8.1))  || '(' || strip(put(fourth_stat,8.1))   || ' to ' || strip(put(sixth_stat,8.1))   ||')';


    char_diff_1 = strip(put(diff_1,8.1)) || '(' || strip(put(diff_2,8.1)) || ' to ' || strip(put(diff_3,8.1)) || ')';
    char_diff_2 = strip(put(diff_4,8.1)) || '(' || strip(put(diff_5,8.1)) || ' to ' || strip(put(diff_6,8.1)) || ')';


  end;
    label
     char_stat1         = "Nortriptyline(n=65) Mean(95CI)  [Manuscript]"
     char_1             = "Nortriptyline(n=65) Mean(95CI)  [DSIC]       "
     char_diff_1         = "Nortriptyline(n=65) Mean(95CI)  [Difference]"
     char_stat2         = "Placebo(n=65) Mean(95CI)  [Manuscript]"
     char_2             = "Placebo(n=65) Mean(95CI)  [DSIC]       "
     char_diff_2         = "Placebo(n=65) Mean(95CI)  [Difference]"
;
proc sort data = combined_table3_dataset;
  by sort_order;

*proc print data = combined_table3_dataset(keep =char_diff_1-char_diff_2 table_name char_stat1-char_stat2 diff_1-diff_6  first_stat
second_stat  third_stat fourth_stat fifth_stat sixth_stat) ;

*** Outputting the dataset to a csv file to be added to the DSIC;

ods csv file = out_t3;

run;

proc print data = combined_table3_dataset NOOBS label;
      var characteristic char_stat1 char_1 char_diff_1 char_stat2 char_2 char_diff_2 ;
      title3 "DSIC Check of Table 3 | Comparison of primary and secondary outcomes by treatment group";

run;

ods csv close;
```