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Severe Nausea and Vomiting in the Evaluation of Nitrous Oxide in the Gas Mixture for Anesthesia II Trial

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Appendix Table 1. Risk factors for severe postoperative nausea and vomiting-adjusted for all listed covariables. Interaction terms between nitrous oxide and Asian included in both models. P value for interaction in the PONV prophylaxis group was 0.38, for the No PONV prophylaxis group 0.16.

	PONV Prophylaxis (n=3,970)				No PONV Prophylaxis (n=3,041)			
	Severe PONV n	%	OR (95% CI)	P value	Severe PONV n	%	OR (95% CI)	P value
Nitrous oxide	270	13.1	1.07 (0.87-1.32)	0.51	234	16.7	1.74 (1.27-2.37)	<0.001
If no nitrous oxide								
Non-Asian	203	11.4	1.00 (ref)		83	8.3	1.00 (ref)	
Asian	22	18.2	0.76 (0.44-1.31)	0.32	70	12.1	1.03 (0.67-1.58)	0.90
If nitrous oxide								
Non-Asia	229	12.1	1.07 (0.87-1.32)	0.51	109	12.4	1.74 (1.27-2.37)	<0.001
Asia	41	24.8	1.08 (0.69-1.69)	0.74	125	23.7	2.47 (1.64-3.72)	<0.001

PONV = postoperative nausea and vomiting.

Appendix Table 2: Univariate risk factors for severe PONV.

	PONV Prophylaxis (n=3,970)				No PONV Prophylaxis (n=3,041)			
	n	%	OR (95% CI)	P value	n	%	OR (95% CI)	P value
Age categories (years)								
<60	106	14.0	1.00 (ref)		44	9.5	1.00 (ref)	
60-69	126	11.2	0.77 (0.58, 1.01)	0.062	111	13.7	1.51 (1.04, 2.18)	0.029
70-79	200	12.9	0.91 (0.71, 1.17)	0.47	166	13.2	1.45 (1.02, 2.06)	0.037
≥80	63	11.8	0.82 (0.59, 1.14)	0.24	68	13.8	1.53 (1.02, 2.29)	0.038
Female	287	17.8	2.24 (1.85, 2.71)	<0.001	177	19.1	2.09 (1.69, 2.60)	<0.001
Asian	63	22.0	2.12 (1.58, 2.85)	<0.001	196	17.7	1.90 (1.53, 2.35)	<0.001
ASA Physical status								
1 or 2	163	15.8	1.00 (ref)		166	14.2	1.00 (ref)	
3	302	11.5	0.69 (0.56, 0.85)	<0.001	199	11.9	0.82 (0.65, 1.02)	0.072
4 or 5	30	9.8	0.58 (0.38, 0.88)	0.010	24	13.0	0.90 (0.57, 1.43)	0.67
BMI categories (kg/m ²)								
< 18.5	12	17.6	1.00 (ref)		22	19.0	1.00 (ref)	
18.5-24.9	155	14.3	0.78 (0.41, 1.48)	0.44	164	13.9	0.69 (0.42, 1.13)	0.14
25-29.9	172	12.2	0.65 (0.34, 1.24)	0.19	131	12.7	0.62 (0.38, 1.03)	0.064
≥30	156	11.1	0.58 (0.31, 1.11)	0.10	72	10.4	0.50 (0.29, 0.84)	0.009
Folate/multivitamin	104	12.9	1.05 (0.83, 1.32)	0.71	63	13.6	1.07 (0.80, 1.44)	0.63
Vitamin B ₁₂ injections	13	11.0	0.86 (0.48, 1.55)	0.63	6	7.1	0.51 (0.22, 1.18)	0.12
Non-smoker	440	13.5	1.87 (1.39, 2.50)	<0.001	346	14.2	2.10 (1.51, 2.92)	<0.001
Diabetes	189	13.9	1.21 (0.99, 1.47)	0.059	156	13.0	1.01 (0.81, 1.26)	0.92
Coronary artery disease	174	11.3	0.83 (0.68, 1.01)	0.067	113	11.2	0.79 (0.62, 1.00)	0.046

Nitrous oxide	270	13.1	1.13 (0.93, 1.36)	0.21	236	16.6	1.89 (1.52, 2.34)	<0.001
Propofol maintenance	22	17.6	1.52 (0.95, 2.43)	0.081	9	9.4	0.69 (0.35, 1.39)	0.30
Regional LA block	173	15.8	1.48 (1.22, 1.81)	<0.001	110	13.6	1.10 (0.86, 1.39)	0.45
BIS monitoring	183	10.6	0.73 (0.60, 0.89)	0.002	106	9.9	0.65 (0.52, 0.83)	<0.001
Morphine	210	12.4	0.98 (0.81, 1.19)	0.83	221	14.2	1.28 (1.03, 1.58)	0.026
Surgery type								
Gastrointestinal*	160	24.7	1.00 (ref)		164	22.1	1.00 (ref)	
Renal/bladder	39	11.2	0.38 (0.26, 0.56)	<0.001	42	16.7	0.71 (0.49, 1.03)	0.068
Neurology/spine	28	6.7	0.22 (0.14, 0.34)	<0.001	16	11.4	0.46 (0.26, 0.79)	0.005
Ear, nose, throat	14	10.4	0.35 (0.20, 0.63)	<0.001	7	10.3	0.41 (0.18, 0.90)	0.027
Orthopedic	56	10.4	0.35 (0.25, 0.49)	<0.001	37	8.8	0.34 (0.23, 0.50)	<0.001
Plastics	10	14.9	0.53 (0.27, 1.07)	0.077	1	3.6	0.13 (0.02, 0.97)	0.047
Gynecology	52	24.3	0.98 (0.68, 1.40)	0.90	23	22.5	1.03 (0.63, 1.69)	0.91
Vascular	121	8.1	0.27 (0.21, 0.35)	<0.001	94	7.7	0.30 (0.23, 0.39)	<0.001
Other	15	15.2	0.54 (0.31, 0.97)	0.039	5	10.0	0.39 (0.15, 1.00)	0.051
Anesthesia duration								
< 2 hours	44	8.5	1.0 (ref)		24	7.7	1.00 (ref)	
2-3 hours	142	10.8	1.31 (0.92, 1.87)	0.14	113	13.4	1.86 (1.17, 2.95)	0.008
3-4 hours	131	12.9	1.60 (1.12, 2.29)	0.010	93	12.4	1.69 (1.06, 2.70)	0.028
4-5 hours	79	14.5	1.83 (1.24, 2.70)	0.002	75	14.4	2.02 (1.25, 3.28)	0.004
≥ 5 hours	99	17.0	2.21 (1.51, 3.22)	<0.001	84	14.3	2.00 (1.24, 3.21)	0.004

*includes hepatobiliary, pancreatic, and colorectal surgery

PONV=postoperative nausea and vomiting; ASA=American Society of Anesthesiologists; LA=local anesthetic, BIS=bispectral index.

Appendix Table 3: Antiemetic count baseline characteristics (n=4754). *Except for age, weight, body mass index, preinduction heart rate, systolic blood pressure, surgery duration, hemoglobin and creatinine which are presented as mean (SD).

Characteristic	Unweighted						Propensity score weighted					
	No anti-emetic (n=1480) % (n)*	1 anti-emetic (n=2135) % (n)*	≥2 anti-emetics (n=1139) % (n)*	Std. diff. (1 anti-emetic vs. none)	Std. diff. (≥2 anti-emetics vs. none)	P value	No anti-emetic (n=1480) %*	1 anti-emetic (n=2135) %*	≥2 anti-emetics (n=1139) %*	Std. diff. (1 anti-emetic vs. none)	Std. diff. (≥2 anti-emetics vs. none)	P value
Male	75.0 (1110)	63.6 (1357)	51.9 (591)	25.0	49.4	<0.001	63.7	64.3	64.3	-1.2	-1.2	0.95
Age (years)	70.7 (9.4)	69.1 (9.9)	68.3 (9.6)	15.9	24.5	<0.001	69.7 (9.4)	69.4 (11.0)	69.0 (8.3)	2.5	7.1	0.24
Weight (kg)	81.2 (18.0)	82.2 (19.0)	82.7 (20.3)	-5.6	-7.9	0.037	82.0 (18.0)	82.0 (20.9)	82.6 (17.5)	-0.2	-3.4	0.67
Body mass index (kg/m ²)	28.2 (5.9)	28.9 (6.2)	29.5 (6.8)	-12.5	-21.5	<0.001	28.6 (5.8)	28.8 (6.9)	29.2 (5.7)	-3.8	-8.8	0.10
Preinduction heart rate	71.0 (13.9)	72.7 (13.9)	72.8 (14.0)	-11.9	-12.7	0.001	71.7 (13.5)	72.2 (15.2)	72.2 (12.4)	-3.5	-3.3	0.60
Preinduction systolic blood pressure	148.1 (25.6)	148.8 (26.6)	152.8 (26.9)	-2.9	-17.8	<0.001	149.0 (24.4)	149.4 (29.9)	151.5 (23.9)	-1.5	-9.7	0.057
Hemoglobin	13.2 (1.9)	13.3 (1.8)	13.4 (1.6)	-5.0	-14.8	<0.001	13.3 (1.8)	13.3 (2.1)	13.4 (1.4)	-0.8	-8.6	0.071
Creatinine	111.0 (107.0)	103.3 (95.7)	96.2 (94.1)	7.6	14.7	<0.001	107.6 (102.7)	104.4 (111.3)	99.0 (88.7)	3.2	8.5	0.18
Hypertension	85.4 (1264)	82.8 (1768)	85.6 (975)	7.1	-0.6	0.041	83.9	84.2	84.5	-0.6	-1.5	0.93
Coronary artery disease	45.5 (674)	41.4 (884)	37.9 (432)	8.3	15.5	<0.001	42.3	42.0	41.7	0.6	1.2	0.95
Heart failure	9.7 (143)	6.2 (132)	7.4 (84)	12.9	8.2	<0.001	7.7	7.7	7.5	-0.2	0.4	0.99
Previous myocardial infarction	28.4 (421)	25.7 (548)	21.2 (242)	6.3	16.7	<0.001	25.4	25.3	26.1	0.3	-1.5	0.88
Previous CABG/PCI	28.8 (426)	25.9 (553)	25.9 (295)	6.5	6.5	0.12	27.1	26.7	27.4	1.0	-0.5	0.93
Peripheral vascular disease	45.7 (677)	36.7 (784)	27.2 (310)	18.4	39.2	<0.001	37.4	37.7	38.1	-0.6	-1.5	0.93
Previous stroke/TIA	20.5 (304)	17.9 (383)	18.6 (212)	6.6	4.9	0.14	19.2	19.2	19.7	-0.1	-1.3	0.93
High cholesterol	59.6 (882)	59.7 (1275)	60.7 (691)	-0.3	-2.2	0.83	59.2	60.1	60.7	-1.9	-3.0	0.76
Current smoker	24.9 (368)	19.3 (411)	16.3 (186)	13.6	21.2	<0.001	20.9	20.4	20.1	1.1	2.0	0.89
Asthma/COPD	22.2 (328)	19.4 (415)	20.8 (237)	6.7	3.3	0.14	21.8	20.9	20.6	2.1	2.9	0.77

Diabetes	34.9 (516)	33.7 (720)	30.5 (347)	2.4	9.4	0.052	32.6	33.6	34.0	-2.1	-3.0	0.76
Infection/fever	6.6 (98)	3.6 (77)	1.8 (21)	13.7	23.9	<0.001	4.2	4.3	5.6	-0.3	-7.0	0.40
Other medical condition	37.5 (555)	42.5 (907)	39.8 (453)	-10.2	-4.7	0.010	42.5	41.2	42.2	2.7	0.6	0.80
Vegan/vegetarian	1.7 (25)	1.9 (40)	1.8 (21)	-1.4	-1.2	0.92	1.6	1.9	1.7	-2.5	-0.7	0.80
Folate/multivitamin	18.0 (266)	22.5 (480)	20.0 (228)	-11.2	-5.2	0.004	20.2	20.4	20.2	-0.6	0.0	0.98
Vitamin B ₁₂ injections	3.6 (53)	3.0 (65)	3.2 (37)	3.0	1.8	0.67	3.8	3.5	3.4	1.5	2.2	0.87
Aspirin last 5 days	49.7 (736)	43.7 (934)	44.8 (510)	12.0	9.9	0.001	46.0	46.0	45.6	0.1	1.0	0.97
Other NSAID last 2 days	4.2 (62)	4.7 (100)	4.0 (45)	-2.4	1.2	0.58	4.6	4.4	6.0	1.1	-7.1	0.35
Clopidogrel last 7 days	6.6 (98)	6.2 (133)	5.5 (63)	1.6	4.6	0.51	6.0	6.3	5.9	-1.4	0.3	0.89
Warfarin last 7 days	5.7 (85)	5.9 (125)	4.7 (54)	-0.5	4.5	0.39	5.6	5.6	5.9	-0.2	-1.6	0.91
Cyclo-oxygenase ₂ inhibitor	2.8 (42)	3.1 (67)	4.2 (48)	-1.8	-7.5	0.13	3.2	3.2	3.2	0.2	0.3	1.00
Nitrates	10.4 (154)	9.6 (206)	8.3 (95)	2.5	7.1	0.20	9.8	10.1	10.6	-1.0	-2.8	0.82
Statins	68.8 (1018)	70.6 (1507)	74.0 (843)	-3.9	-11.6	0.013	71.0	71.2	71.6	-0.5	-1.4	0.93
ACEI/ARB	60.6 (897)	60.9 (1300)	61.0 (695)	-0.6	-0.8	0.98	60.8	61.1	61.0	-0.5	-0.5	0.99
Amiodarone	1.9 (28)	1.3 (27)	1.6 (18)	5.0	2.4	0.32	1.3	1.4	1.3	-0.8	0.3	0.93
Beta blockers	44.0 (651)	36.0 (769)	36.2 (412)	16.3	16.0	<0.001	39.0	38.9	40.4	0.2	-3.0	0.69
Heparin	9.5 (141)	7.7 (164)	7.1 (81)	6.6	8.8	0.049	8.6	8.4	8.7	0.8	-0.3	0.96
Diuretics	25.9 (383)	26.6 (567)	24.1 (275)	-1.5	4.0	0.32	26.0	25.5	25.0	1.0	2.3	0.85
Calcium channel blockers	30.2 (447)	30.0 (641)	29.9 (340)	0.4	0.8	0.98	30.8	30.3	31.2	1.1	-0.8	0.89
Digoxin	4.7 (69)	3.5 (75)	1.9 (22)	5.8	15.3	0.001	3.6	3.5	3.4	0.4	0.9	0.97
Insulin	10.2 (151)	9.6 (205)	7.0 (80)	2.0	11.3	0.013	9.7	9.3	9.2	1.3	1.8	0.91
Oral hypoglycemic	23.0 (341)	24.9 (532)	21.5 (245)	-4.4	3.7	0.079	22.6	23.8	22.6	-2.7	0.0	0.74
Cardiac perfusion scan	16.0 (237)	14.4 (307)	10.9 (124)	4.6	15.1	0.001	13.5	13.7	14.0	-0.6	-1.7	0.91
Clean surgery	92.3 (1366)	90.8 (1938)	91.4 (1041)	5.5	3.3	0.28	89.9	91.0	89.4	-4.0	1.7	0.57
Nitrous oxide	53.9 (798)	50.6 (1081)	43.5 (495)	6.6	21.0	<0.001	50.0	50.2	49.9	-0.4	0.2	0.99
Country						<0.001						0.75
1	26.8 (397)	43.4 (927)	29.1 (331)	-35.3	-5.0		34.3	35.1	36.5	-1.8	-5.0	
61	62.3 (922)	46.5 (993)	51.0 (581)	32.1	22.9		52.4	52.3	51.6	0.2	1.6	
64	10.9 (161)	10.1 (215)	19.9 (227)	2.6	-25.3		13.3	12.6	11.9	2.3	4.0	

Race						0.096							0.81
White	93.2 (1379)	92.5 (1975)	93.2 (1061)	2.6	0.1		94.0	93.1	92.4	3.5	6.3		
Asian	0.9 (14)	0.6 (13)	1.3 (15)	3.8	-3.5		0.6	0.9	0.7	-3.5	-1.1		
Indian/Pakistan	1.6 (24)	1.3 (27)	1.6 (18)	3.0	0.3		1.1	1.3	1.1	-2.1	-0.3		
Hispanic	0.1 (2)	0.7 (14)	0.5 (6)	-8.3	-6.8		0.3	0.5	0.5	-2.5	-2.2		
Black	1.2 (18)	1.8 (38)	1.4 (16)	-4.6	-1.7		1.2	1.5	1.3	-1.7	-0.4		
Other	2.9 (43)	3.2 (68)	2.0 (23)	-1.6	5.7		2.7	2.7	4.0	0.1	-8.2		
ASA Physical status						<0.001							0.88
1 or 2	16.2 (240)	19.2 (410)	27.2 (310)	-7.8	-26.9		19.4	20.1	19.2	-1.8	0.3		
3	73.0 (1080)	70.8 (1512)	67.6 (770)	4.8	11.8		71.7	70.4	70.7	2.8	2.2		
4 or 5	10.8 (160)	10.0 (213)	5.2 (59)	2.7	20.9		9.0	9.6	10.1	-1.9	-4.1		
PONV risk score	0.0 (0)	0.0 (0)	0.0 (0)			<0.001							0.90
0	11.5 (170)	7.9 (168)	5.7 (65)	12.3	20.7		8.5	8.5	7.7	0.0	2.6		
1	45.7 (676)	40.4 (862)	26.7 (304)	10.7	40.3		38.5	39.1	41.1	-1.2	-5.5		
2	36.3 (537)	40.0 (855)	47.1 (537)	-7.8	-22.2		40.4	40.1	39.3	0.6	2.3		
≥3	6.6 (97)	11.7 (250)	20.5 (233)	-18.0	-41.5		12.6	12.3	11.9	1.1	2.2		
Exercise capacity ≥4 METS	71.3 (1055)	73.9 (1577)	76.4 (870)	-5.8	-11.6	0.013	73.8	73.7	73.4	0.4	1.0		0.96
Surgery type						<0.001							1.00
Urology/Kidney	6.5 (96)	8.9 (190)	8.9 (101)	-9.1	-9.0		7.8	7.9	7.8	-0.5	-0.1		
Neurology/spine	3.7 (55)	11.4 (244)	11.4 (130)	-29.5	-29.4		9.7	9.2	9.2	1.9	1.6		
Gastrointestinal	7.1 (105)	6.3 (134)	6.7 (76)	3.3	1.7		6.7	6.7	7.1	-0.2	-1.6		
Liver/pancreas	5.1 (76)	4.9 (104)	5.4 (62)	1.2	-1.4		5.0	4.8	4.9	0.6	0.5		
Ear, nose, throat	2.1 (31)	2.9 (62)	4.7 (54)	-5.2	-14.6		3.0	2.9	2.8	0.4	0.9		
Orthopedic	13.3 (197)	14.1 (300)	15.3 (174)	-2.2	-5.6		14.1	14.0	14.9	0.1	-2.3		
Plastics	1.0 (15)	1.3 (28)	2.5 (28)	-2.8	-11.1		1.4	1.5	1.6	-1.1	-1.5		
Gynecology	1.1 (17)	4.2 (89)	6.8 (77)	-18.9	-29.1		4.5	4.0	4.1	3.4	2.3		
Vascular	55.3 (818)	41.4 (884)	32.1 (366)	28.0	48.0		43.5	44.0	43.0	-1.1	0.9		
Colorectal	2.8 (42)	2.2 (48)	3.6 (41)	3.7	-4.3		2.4	2.5	2.2	-1.1	0.7		
Other	1.9 (28)	2.4 (52)	2.6 (30)	-3.7	-5.0		2.1	2.3	2.3	-1.7	-1.8		
Duration of surgery (hours)	3.0 (1.7)	2.8 (1.5)	2.8 (1.5)	9.4	9.6	0.009	2.9 (1.6)	2.9 (1.7)	2.8 (1.3)	2.0	3.3		0.73

ASA=American Society of Anesthesiologists; BMI, body mass index; CABG/PCI, coronary artery bypass graft/percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; METS, metabolic equivalents; NSAID, non-steroidal anti-inflammatory drug; PONV=postoperative nausea and vomiting; Std diff, standardised difference; TIA, transient ischemic attack.

Appendix Table 4: Antiemetic count baseline characteristics, where at least one anti-emetic has been administered (n=3272). *Except for age, weight, body mass index, preinduction heart rate, systolic blood pressure, surgery duration, hemoglobin and creatinine which are presented as mean (SD).

Characteristic	Unweighted				Propensity score weighted			
	1 anti-emetic (n=2113) % (n)*	≥2 anti-emetics (n=1159) % (n)*	Std. diff	P value	1 anti-emetic (n=2113) %*	≥2 anti-emetics (n=1159) %*	Std. diff	P value
Male	63.4 (1340)	52.6 (610)	22.0	<0.001	59.9	57.4	5.2	0.18
Age (years)	69.1 (9.9)	68.5 (9.6)	6.9	0.061	68.9 (11.1)	68.7 (8.2)	2.4	0.52
Weight (kg)	82.3 (19.0)	82.5 (20.2)	-1.0	0.77	82.4 (21.2)	82.4 (17.3)	0.0	1.00
Body mass index (kg/m ²)	28.9 (6.2)	29.4 (6.8)	-7.9	0.030	29.1 (7.0)	29.2 (5.8)	-1.9	0.62
Preinduction heart rate	72.7 (13.9)	72.7 (14.0)	0.3	0.94	72.7 (15.4)	72.4 (12.1)	2.3	0.56
Preinduction systolic blood pressure	149.0 (26.5)	152.2 (27.0)	-12.3	0.001	150.0 (29.8)	150.7 (23.3)	-2.6	0.51
Hemoglobin	13.3 (1.8)	13.4 (1.6)	-7.4	0.047	13.3 (2.0)	13.4 (1.4)	-3.5	0.36
Creatinine	102.7 (94.9)	96.0 (90.9)	7.2	0.049	102.4 (109.5)	98.2 (85.3)	4.5	0.32
Hypertension	82.8 (1749)	85.6 (992)	-7.7	0.037	83.8	84.9	-3.2	0.40
Coronary artery disease	41.2 (870)	38.1 (442)	6.2	0.090	39.9	38.9	2.0	0.60
Heart failure	6.2 (130)	7.3 (85)	-4.7	0.19	6.7	6.7	0.1	0.98
Previous myocardial infarction	25.5 (538)	22.0 (255)	8.1	0.027	24.1	23.3	1.8	0.64
Previous CABG/PCI	26.0 (549)	26.1 (303)	-0.4	0.92	25.9	26.0	-0.2	0.97
Peripheral vascular disease	36.4 (770)	27.8 (322)	18.6	<0.001	33.7	30.7	6.6	0.093
Previous stroke/TIA	18.1 (383)	18.5 (214)	-0.9	0.81	18.6	18.3	0.6	0.87
High cholesterol	59.7 (1262)	60.5 (701)	-1.5	0.67	60.3	60.7	-0.9	0.81
Current smoker	19.3 (407)	16.7 (193)	6.8	0.065	18.3	17.7	1.5	0.70
Asthma/COPD	19.5 (413)	20.8 (241)	-3.1	0.39	20.1	20.1	-0.1	0.99
Diabetes	33.6 (709)	30.4 (352)	6.8	0.063	32.7	31.4	2.8	0.47
Infection/fever	3.5 (74)	2.2 (26)	7.5	0.045	3.2	2.7	2.8	0.50
Other medical condition	42.4 (895)	39.9 (462)	5.1	0.17	42.1	41.1	2.1	0.59
Vegan/vegetarian	1.9 (40)	1.8 (21)	0.6	0.87	1.9	1.8	0.2	0.96
Folate/multivitamin	22.3 (472)	19.5 (226)	7.0	0.058	21.4	20.1	3.2	0.41

Vitamin B ₁₂ injections	3.0 (63)	3.5 (40)	-2.7	0.46	3.1	3.3	-0.7	0.84
Aspirin last 5 days	43.7 (923)	45.0 (521)	-2.6	0.48	44.3	44.8	-1.1	0.78
Other NSAID last 2 days	4.7 (100)	4.0 (46)	3.7	0.31	4.6	4.2	1.6	0.69
Clopidogrel last 7 days	6.2 (132)	5.7 (66)	2.3	0.53	6.1	6.2	-0.6	0.89
Warfarin last 7 days	5.9 (124)	4.7 (55)	5.0	0.18	5.7	5.0	3.3	0.40
Cyclo-oxygenase ₂ inhibitor	3.2 (67)	4.1 (48)	-5.2	0.15	3.4	3.6	-0.8	0.82
Nitrates	9.6 (203)	8.2 (95)	5.0	0.18	9.6	8.4	4.2	0.28
Statins	70.7 (1493)	73.8 (855)	-7.0	0.059	71.7	73.0	-2.7	0.47
ACEI/ARB	60.6 (1281)	60.4 (700)	0.5	0.90	60.7	60.7	0.0	0.99
Amiodarone	1.3 (27)	1.6 (18)	-2.3	0.52	1.3	1.5	-1.3	0.73
Beta blockers	36.0 (761)	36.8 (427)	-1.7	0.64	36.6	36.5	0.2	0.96
Heparin	7.7 (163)	7.5 (87)	0.8	0.83	7.8	7.9	-0.3	0.95
Diuretics	26.3 (555)	23.9 (277)	5.5	0.14	25.4	24.7	1.7	0.65
Calcium channel blockers	29.9 (631)	29.7 (344)	0.4	0.91	30.0	29.3	1.4	0.71
Digoxin	3.4 (72)	2.2 (25)	7.6	0.044	3.1	2.5	3.3	0.41
Insulin	9.3 (196)	7.3 (85)	7.0	0.058	8.7	8.3	1.6	0.69
Oral hypoglycemic	24.7 (521)	21.2 (246)	8.2	0.027	23.6	22.3	2.9	0.45
Cardiac perfusion scan	14.2 (301)	11.1 (129)	9.4	0.012	13.3	12.7	1.7	0.67
Surgery cleanliness	90.9 (1920)	91.3 (1058)	-1.5	0.69	90.8	91.0	-0.8	0.83
Nitrous oxide	50.4 (1065)	43.6 (505)	13.7	<0.001	48.4	46.0	4.8	0.21
Country				<0.001				0.065
1	42.9 (906)	28.4 (329)	30.6		38.3	34.0	9.1	
61	46.9 (992)	52.1 (604)	-10.3		48.5	51.8	-6.5	
64	10.2 (215)	19.5 (226)	-26.5		13.2	14.2	-3.0	
Race				0.101				0.85
White	92.8 (1960)	93.6 (1085)	-3.4		92.8	93.6	-3.0	
Asian	0.6 (13)	1.3 (15)	-7.0		0.9	1.0	-0.6	
Indian/Pakistan	1.3 (27)	1.5 (17)	-1.6		1.4	1.3	1.2	
Hispanic	0.7 (14)	0.4 (5)	3.1		0.6	0.6	0.0	
Black	1.8 (38)	1.4 (16)	3.3		1.6	1.7	-1.0	
Other	2.9 (61)	1.8 (21)	7.1		2.6	1.8	5.3	

ASA physical status				<0.001					0.059
1 or 2	19.4 (409)	26.5 (307)	-17.0		21.8	22.7	-2.2		
3	71.0 (1500)	68.3 (792)	5.8		69.8	71.3	-3.2		
4 or 5	9.7 (204)	5.2 (60)	17.2		8.4	6.0	9.2		
PONV risk score				<0.001					0.33
0	7.8 (165)	5.7 (66)	8.4		7.1	6.4	2.9		
1	40.2 (850)	27.8 (322)	26.5		36.4	33.6	5.8		
2	40.1 (848)	46.4 (538)	-12.7		41.8	43.9	-4.3		
≥3	11.8 (250)	20.1 (233)	-22.7		14.7	16.1	-3.7		
Exercise capacity ≥4 METS	73.9 (1561)	76.7 (889)	-6.6	0.074	74.6	75.5	-2.0		0.60
Surgery type				<0.001					0.99
Urology/Kidney	8.8 (187)	8.8 (102)	0.2		8.8	8.7	0.1		
Neurology/spine	11.5 (243)	10.7 (124)	2.6		11.3	10.9	1.2		
Gastrointestinal	6.2 (132)	6.9 (80)	-2.6		6.5	6.5	0.1		
Liver/pancreas	4.9 (103)	5.4 (63)	-2.5		4.9	5.4	-2.1		
Ear, nose, throat	2.9 (62)	4.7 (54)	-9.0		3.4	3.7	-1.4		
Orthopedic	14.1 (298)	15.2 (176)	-3.1		14.4	14.9	-1.4		
Plastics	1.3 (28)	2.4 (28)	-8.1		1.8	2.0	-1.5		
Gynecology	4.2 (89)	6.6 (77)	-10.7		5.0	5.6	-2.7		
Vascular	41.3 (872)	33.0 (382)	17.3		38.9	36.8	4.3		
Colorectal	2.2 (47)	3.5 (41)	-7.9		2.4	2.7	-1.6		
Other	2.5 (52)	2.8 (32)	-1.9		2.6	2.8	-1.3		
Duration of surgery (hours)	2.8 (1.5)	2.8 (1.5)	-0.5	0.89	2.8 (1.7)	2.8 (1.3)	-1.1		0.78

ASA=American Society of Anesthesiologists; BMI, body mass index; CABG/PCI, coronary artery bypass graft/percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; METS, metabolic equivalents; NSAID, non-steroidal anti-inflammatory drug; PONV=postoperative nausea and vomiting; Std diff, standardised difference; TIA, transient ischemic attack.

Appendix Table 5: Antiemetic combinations (n= 4497)

	Unweighted								Propensity score weighted							
	No anti-emetic (n=1511) % (n)*	5-HT ₃ only (n=1149) % (n)*	Dex only (n=890) % (n)*	Dex and 5-HT ₃ (n=947) % (n)*	Std. diff (5-HT ₃ vs. none)	Std. diff (Dex vs. none)	Std. diff (5-HT ₃ +Dex vs. None)	P value	No anti-emetic (n=1511) %*	5-HT ₃ only %*	Dex only (n=890) %*	Dex and 5-HT ₃ (n=947) %*	Std. diff (5-HT ₃ vs. none)	Std. diff (Dex vs. none)	Std. diff (5-HT ₃ +Dex vs. None)	P value
Male	73.5 (1111)	62.4 (717)	64.7 (576)	53.6 (508)	24.0	19.2	42.2	<0.001	64.3	65.6	63.1	64.7	-2.8	2.7	-0.9	0.78
Age (years)	70.6 (9.5)	68.8 (10.2)	69.6 (9.5)	68.4 (9.8)	18.2	10.0	22.4	<0.001	69.5 (11.3)	69.7 (10.4)	69.2 (8.4)	69.6 (8.7)	-2.1	3.1	-1.3	0.81
Weight (kg)	81.3 (18.2)	82.6 (19.9)	81.3 (17.9)	82.5 (20.8)	-7.2	-0.1	-6.1	0.30	82.1 (22.2)	81.8 (19.0)	81.8 (16.9)	81.8 (18.0)	1.5	1.6	1.4	0.99
Body mass index (kg/m ²)	28.3 (6.0)	(6.5)	(5.9)	(7.1)	-12.2	-6.5	-18.6	<0.001	28.9 (7.3)	28.8 (6.3)	28.9 (5.8)	28.8 (6.0)	2.1	0.1	1.0	0.98
Preinduction heart rate	71.2 (14.0)	73.1 (13.8)	72.2 (13.9)	72.7 (14.2)	-13.5	-7.2	-10.9	0.017	72.1 (16.4)	72.1 (13.4)	72.5 (12.6)	72.5 (13.3)	0.0	-2.2	-2.2	0.95
Preinduction systolic blood pressure	148.2 (25.7)	147.7 (26.2)	150.3 (26.9)	151.8 (26.2)	1.7	-8.0	-13.9	<0.001	148.9 (29.6)	149.5 (27.7)	150.0 (24.2)	149.1 (23.1)	-2.2	-3.9	-0.8	0.88
Hemoglobin	13.2 (1.9)	(1.9)	(1.8)	(1.7)	5.8	-17.3	-11.9	<0.001	13.3 (2.2)	13.2 (1.9)	13.3 (1.6)	13.2 (1.6)	4.1	0.5	4.1	0.77
Creatinine	110.3 (106.2)	107.7 (104.9)	97.5 (82.0)	96.4 (92.1)	2.5	13.6	14.0	<0.001	104.1 (112.5)	104.7 (97.5)	105.4 (90.5)	107 (110.9)	-0.5	-1.4	-3.1	0.97
Hypertension	85.4 (1290)	83.6 (960)	81.6 (726)	84.8 (803)	5.0	10.2	1.6	0.084	83.7	83.0	83.0	84.2	1.9	1.9	-1.3	0.92
Coronary artery disease	45.3 (685)	41.6 (478)	40.2 (358)	36.3 (344)	7.5	10.3	18.4	<0.001	42.1	40.6	41.9	41.6	3.0	0.5	1.0	0.94
Heart failure	9.4 (142)	7.2 (83)	5.2 (46)	6.5 (62)	7.9	16.3	10.5	0.001	7.4	7.5	8.3	7.4	-0.3	-3.5	0.2	0.90
Previous myocardial infarction	28.2 (426)	25.0 (287)	25.7 (229)	21.6 (205)	7.3	5.6	15.2	0.004	25.5	24.2	26.6	25.2	3.1	-2.3	0.8	0.78
Previous	28.7	25.5	26.1	25.1	7.3	6.0	8.1	0.15	27.4	24.8	26.5	28.3	6.0	2.2	-2.0	0.48

CABG/PCI	(434)	(293)	(232)	(238)												
Peripheral vascular disease	44.7 (675)	37.7 (433)	36.1 (321)	29.4 (278)	14.2	17.6	32.1	<0.001	38.0	38.2	39.7	38.1	-0.3	-3.5	-0.2	0.89
Previous stroke/TIA	20.4 (308)	16.6 (191)	19.9 (177)	18.9 (179)	9.7	1.2	3.7	0.087	18.8	21.0	18.0	18.7	-5.7	1.9	0.2	0.50
High cholesterol	59.8 (903)	61.6 (708)	58.9 (524)	60.4 (572)	-3.8	1.8	-1.3	0.63	60.0	59.7	60.5	59.9	0.7	-1.0	0.2	0.99
Current smoker	24.6 (371)	19.0 (218)	19.2 (171)	17.0 (161)	13.6	12.9	18.7	<0.001	21.3	20.5	22.8	19.6	1.8	-3.7	4.1	0.52
Asthma/COPD	22.2 (335)	17.4 (200)	21.6 (192)	19.7 (187)	12.0	1.4	6.0	0.016	20.9	19.5	21.4	20.0	3.5	-1.3	2.2	0.80
Diabetes	34.5 (521)	40.6 (467)	23.1 (206)	29.5 (279)	-12.8	25.2	10.8	<0.001	31.7	33.3	32.1	32.2	-3.2	-0.9	-1.0	0.92
Infection/fever	6.2 (94)	4.9 (56)	2.0 (18)	2.4 (23)	5.9	21.2	18.7	<0.001	4.2	5.1	4.6	4.6	-3.9	-2.1	-2.0	0.90
Other medical condition	38.4 (580)	46.4 (533)	38.0 (338)	41.2 (390)	-16.2	0.8	-5.7	<0.001	42.8	41.1	39.9	42.6	3.4	5.9	0.3	0.65
Vegan/vegetarian	1.7 (26)	1.7 (20)	2.2 (20)	2.0 (19)	-0.2	-3.8	-2.1	0.79	1.7	2.0	2.1	1.8	-2.0	-2.8	-0.4	0.94
Folate/multivitamin	18.1 (273)	28.3 (325)	14.9 (133)	19.3 (183)	-24.4	8.4	-3.2	<0.001	19.4	20.2	19.0	20.0	-2.0	1.2	-1.6	0.92
Vitamin B ₁₂ injections	3.6 (55)	3.1 (36)	2.8 (25)	3.6 (34)	2.8	4.7	0.3	0.67	3.5	3.4	2.7	3.6	0.2	4.5	-0.7	0.73
Aspirin last 5 days	49.4 (746)	44.0 (506)	43.6 (388)	44.0 (417)	10.7	11.6	10.7	0.007	45.9	46.5	46.9	45.8	-1.3	-2.1	0.2	0.97
Other NSAID last 2 days	4.2 (63)	4.4 (51)	4.9 (44)	3.8 (36)	-1.3	-3.7	1.9	0.66	4.8	4.3	4.6	4.2	2.2	1.0	2.9	0.96
Clopidogrel last 7 days	6.5 (98)	7.0 (81)	5.2 (46)	5.7 (54)	-2.2	5.6	3.3	0.30	6.2	6.0	6.8	6.3	0.7	-2.6	-0.6	0.93
Warfarin last 7 days	5.8 (88)	5.6 (64)	6.3 (56)	4.6 (44)	1.1	-2.0	5.3	0.46	5.8	5.6	5.1	5.9	1.1	3.0	-0.4	0.91
COX2	2.8 (43)	2.8 (32)	3.8 (34)	3.8 (36)	0.4	-5.4	-5.3	0.33	3.3	2.8	3.5	3.1	3.0	-1.1	0.9	0.88
Nitrates	10.4 (157)	9.7 (112)	9.3 (83)	8.3 (79)	2.1	3.6	7.0	0.40	9.5	10.3	8.9	9.2	-2.7	2.0	1.2	0.82

status																
1 or 2	16.5 (249)	15.7 (180)	24.2 (215)	25.3 (240)	2.2	-19.2	-21.9		18.9	20.5	20.0	19.3	-4.3	-3.0	-1.1	
3	72.9 (1102)	71.1 (817)	70.0 (623)	67.8 (642)	4.1	6.5	11.3		72.0	69.8	70.5	71.4	4.8	3.3	1.3	
4 or 5	10.6 (160)	13.2 (152)	5.8 (52)	6.9 (65)	-8.2	17.3	13.2		9.2	9.8	9.5	9.3	-1.8	-1.1	-0.5	
PONV risk score								<0.001								0.76
0	11.3 (170)	9.0 (103)	6.4 (57)	6.3 (60)	7.6	17.1	17.4		8.7	9.4	9.3	7.8	-2.3	-2.0	3.2	
1	44.7 (676)	46.1 (530)	33.6 (299)	29.5 (279)	-2.8	23.0	32.0		39.2	41.2	37.3	41.0	-4.1	3.8	-3.7	
2	36.4 (550)	36.0 (414)	44.7 (398)	45.7 (433)	0.8	-17.0	-19.0		39.6	38.9	42.3	39.7	1.5	-5.4	-0.2	
≥3	7.6 (115)	8.9 (102)	15.3 (136)	18.5 (175)	-4.6	-24.3	-32.7		12.5	10.4	11.1	11.5	7.3	4.3	2.9	
Exercise capacity ≥4 METS	71.6 (1082)	74.0 (850)	73.5 (654)	78.0 (739)	-5.3	-4.2	-14.8	0.006	74.0	72.9	75.0	73.2	2.4	-2.1	1.9	0.81
Surgery type								<0.001								1.000
Urology/Kidney	6.6 (99)	10.5 (121)	6.5 (58)	8.1 (77)	-14.3	0.1	-6.1		7.5	7.9	6.8	7.8	-1.4	3.1	-1.1	
Neurology/spine	4.6 (70)	8.4 (97)	15.6 (139)	10.6 (100)	-15.5	-37.0	-22.5		9.9	8.4	8.4	9.3	6.1	4.8	2.1	
Gastrointestinal	7.2 (109)	6.7 (77)	5.4 (48)	7.0 (66)	2.0	7.5	1.0		6.7	6.5	6.4	7.0	0.7	1.2	-1.4	
Liver/pancreas	5.0 (76)	5.9 (68)	3.8 (34)	5.8 (55)	-3.9	5.9	-3.4		5.2	5.6	5.6	5.7	-1.7	-2.0	-1.9	
Ear, nose, throat	2.1 (32)	3.0 (35)	2.8 (25)	4.3 (41)	-5.9	-4.5	-12.5		2.8	3.0	2.7	3.0	-1.4	0.5	-1.1	
Orthopedic	13.2 (199)	12.8 (147)	14.2 (126)	13.8 (131)	1.1	-2.9	-1.9		13.2	13.7	14.1	13.1	-1.3	-2.5	0.3	
Plastics	1.0 (15)	1.0 (11)	1.8 (16)	2.7 (26)	0.4	-6.9	-13.0		1.4	1.6	1.5	1.6	-1.7	-0.7	-1.7	
Gynecology	1.8 (27)	5.0 (57)	3.6 (32)	7.7 (73)	-17.6	-11.2	-28.1		4.5	4.0	4.1	4.3	2.8	2.3	0.7	

	54.0	41.3	42.4	34.4													
Vascular	(816)	(475)	(377)	(326)	25.6	23.5	40.2		44.7	44.4	45.8	43.8	0.6	-2.3	1.8		
Colorectal	2.7 (41)	2.5 (29)	2.0 (18)	2.7 (26)	1.2	4.5	-0.2		2.0	2.9	2.2	2.2	-5.8	-1.3	-1.0		
Other	1.8 (27)	2.8 (32)	1.9 (17)	2.7 (26)	-6.7	-0.9	-6.4		2.1	2.0	2.3	2.1	0.5	-1.8	0.1		
Duration of surgery (hours)	2.9 (1.7)	2.8 (1.5)	2.8 (1.5)	2.8 (1.5)	7.3	7.0	7.3	0.064	2.9 (1.9)	2.9 (1.6)	2.9 (1.4)	2.9 (1.4)	-2.6	0.1	-0.3	0.95	

ASA=American Society of Anesthesiologists; CABG/PCI, coronary artery bypass graft/percutaneous coronary intervention; COPD, chronic obstructive pulmonary disease; METS, metabolic equivalents; NSAID, non-steroidal anti-inflammatory drug; PONV=postoperative nausea and vomiting; Std diff, standardised difference; TIA, transient ischemic attack.

Appendix Table 6: Antiemetic combinations, among those patients who received at least one of 5-HT₃ antagonist or dexamethasone (n=2785).

	Unweighted						Propensity score weighted					
	5-HT ₃ only (n=953) % (n)	Dex only (n=889) % (n)	5-HT ₃ + Dex (n=943) % (n)	Std. diff (Dex vs. 5-HT ₃)	Std. diff (5-HT ₃ + Dex vs. 5-HT ₃)	P value	5-HT ₃ only (n=953) % (n)	Dex only (n=889) % (n)	5-HT ₃ + Dex (n=94) % (n)	Std. diff (Dex vs. 5-HT ₃)	Std. diff (5-HT ₃ + Dex vs 5-HT ₃)	P value
Male	59.5 (567)	64.8 (576)	53.8 (507)	-10.9	11.6	<0.001	60.5 68.7	59.6 68.7	60.4 69.0	1.9	0.2	0.93
Age (years)	68.6 (10.4)	69.6 (9.5)	68.4 (9.8)	-10.1	2.3	0.61	(11.0) 82.4	(9.2) 81.4	(9.5) 82.3	-0.5	-2.7	0.85
Weight (kg)	82.3 (19.7)	81.2 (17.8)	82.5 (20.9)	5.8	-0.9	0.84	(20.3) 29.2	(17.9) 28.8	(20.0) 29.1	5.1	0.7	0.63
Body mass index (kg/m ²)	29.1 (6.5)	28.6 (5.8)	29.5 (7.1)	8.0	-5.4	0.22	(6.9) 72.8	(5.9) 73.4	(6.7) 72.7	5.5	1.5	0.62
Preinduction heart rate	73.1 (13.7)	72.3 (13.8)	72.7 (14.2)	6.4	2.9	0.53	(13.9) 151.0	(13.6) 150.7	(14.3) 149.7	-4.5	0.7	0.63
Preinduction systolic blood pressure	148.9 (26.2)	150.3 (26.9)	151.8 (26.3)	-5.1	-10.8	0.020	(28.2) 13.3	(25.8) 13.3	(25.5) 13.3	1.1	4.6	0.65
Hemoglobin	13.2 (1.9)	13.5 (1.8)	13.4 (1.7)	-17.7	-12.8	0.005	(1.9) 99.4	(1.7) 104.1	(1.7) 100.7	2.5	0.3	0.88
Creatinine	102.6 (96.3)	97.5 (82.0)	95.9 (90.8)	5.7	7.2	0.11	(93.4) 81.8	(94.6) 82.5	(102.6) 83.2	-5.2	-1.3	0.73
Hypertension	83.3 (794)	81.6 (725)	84.6 (798)	4.6	-3.6	0.21	81.8	82.5	83.2	-2.0	-3.8	0.81
Coronary artery disease	38.5 (367)	40.3 (358)	36.3 (342)	-3.6	4.6	0.21	36.1	37.7	38.6	-3.3	-5.1	0.63
Heart failure	6.6 (63)	5.2 (46)	6.4 (60)	6.1	1.0	0.39	6.5	6.4	6.0	0.4	1.9	0.94
Previous myocardial infarction	23.4 (223)	25.8 (229)	21.6 (204)	-5.5	4.2	0.11	22.4	23.6	23.5	-2.9	-2.7	0.84
Previous CABG/PCI	24.9 (237)	26.1 (232)	25.0 (236)	-2.8	-0.4	0.81	24.2	24.1	25.4	0.3	-2.8	0.82
Peripheral vascular disease	35.7 (340)	36.1 (321)	29.1 (274)	-0.9	14.2	0.001	34.5	35.1	33.3	-1.3	2.5	0.78
Previous stroke/TIA	17.2 (164)	19.9 (177)	18.9 (178)	-7.0	-4.3	0.32	19.5	17.6	19.1	5.0	1.1	0.62
High cholesterol	60.4 (576)	58.9 (524)	60.4 (570)	3.1	0.0	0.75	59.1	59.5	60.9	-0.8	-3.6	0.78
Current smoker	19.8 (189)	19.1 (170)	17.0 (160)	1.8	7.4	0.25	19.2	18.7	17.8	1.4	3.7	0.79
Asthma/COPD	17.8 (170)	21.5 (191)	19.7 (186)	-9.2	-4.8	0.14	20.0	19.2	19.8	2.0	0.5	0.93
Diabetes	36.1 (344)	23.1 (205)	29.4 (277)	28.9	14.4	<0.001	32.5	34.0	32.9	-3.2	-0.7	0.85

Infection/fever	3.9 (37)	1.9 (17)	2.3 (22)	11.8	8.9	0.023	3.2	2.4	3.3	4.6	-0.7	0.58
Other medical condition	45.0 (429)	38.0 (338)	40.9 (386)	14.2	8.3	0.009	41.2	43.1	42.5	-3.8	-2.7	0.78
Vegan/vegetarian	2.0 (19)	2.2 (20)	2.0 (19)	-1.8	-0.2	0.91	2.2	1.9	2.3	1.9	-0.7	0.89
Folate/multivitamin	24.3 (232)	14.8 (132)	19.2 (181)	24.1	12.5	<0.001	19.7	18.9	21.7	2.1	-4.8	0.44
Vitamin B ₁₂ injections	3.4 (32)	2.8 (25)	3.6 (34)	3.2	-1.4	0.62	3.2	2.9	3.1	2.0	0.3	0.91
Aspirin last 5 days	45.1 (430)	43.5 (387)	44.1 (416)	3.2	2.0	0.79	45.0	45.3	44.3	-0.7	1.3	0.93
Other NSAID last 2 days	4.4 (42)	4.8 (43)	3.8 (36)	-2.0	3.0	0.56	4.7	4.2	4.5	2.4	0.9	0.90
Clopidogrel last 7 days	6.9 (66)	5.2 (46)	5.7 (54)	7.4	4.9	0.27	5.9	6.2	6.6	-1.1	-2.7	0.88
Warfarin last 7 days	5.5 (52)	6.3 (56)	4.7 (44)	-3.6	3.6	0.31	5.2	5.7	5.6	-2.2	-2.1	0.90
COX2	3.1 (30)	3.8 (34)	3.8 (36)	-3.7	-3.7	0.66	3.2	3.3	3.5	-0.9	-1.8	0.94
Nitrates	9.0 (86)	9.3 (83)	8.2 (77)	-1.1	3.1	0.66	8.5	8.2	8.5	0.8	0.0	0.98
Statins	69.7 (664)	72.0 (640)	73.2 (690)	-5.1	-7.7	0.23	72.7	69.9	72.2	6.0	1.0	0.48
ACEI/ARB	59.0 (562)	62.1 (552)	60.1 (567)	-6.4	-2.4	0.39	59.0	58.6	60.4	0.7	-2.8	0.78
Amiodarone	1.0 (10)	1.2 (11)	1.4 (13)	-1.8	-3.0	0.81	1.0	1.1	1.3	-0.7	-2.7	0.85
Beta blockers	35.8 (341)	33.1 (294)	35.1 (331)	5.7	1.4	0.45	35.0	33.9	35.6	2.4	-1.2	0.79
Heparin	7.8 (74)	6.3 (56)	7.1 (67)	5.7	2.5	0.47	7.7	7.3	8.3	1.8	-2.1	0.79
Diuretics	26.2 (250)	22.5 (200)	23.3 (220)	8.7	6.7	0.14	23.7	25.0	24.3	-2.9	-1.3	0.87
Calcium channel blockers	30.1 (287)	29.8 (265)	29.1 (274)	0.7	2.3	0.87	30.7	31.1	29.3	-0.7	3.2	0.75
Digoxin	2.9 (28)	3.3 (29)	2.1 (20)	-1.9	5.2	0.30	3.2	2.9	2.3	1.7	5.3	0.63
Insulin	9.4 (90)	5.3 (47)	6.5 (61)	16.0	11.0	0.002	7.7	8.3	9.5	-2.2	-6.4	0.57
Oral hypoglycemic	27.0 (257)	17.2 (153)	21.2 (200)	23.7	13.5	<0.001	23.8	25.0	24.2	-2.9	-0.8	0.88
Cardiac perfusion scan	11.6 (111)	14.4 (128)	10.4 (98)	-8.2	4.0	0.028	11.3	11.3	13.2	-0.1	-6.1	0.45
Clean surgery	89.3 (851)	91.0 (809)	90.1 (850)	-5.7	-2.8	0.47	89.2	88.2	90.6	3.4	-4.8	0.32
Nitrous oxide	49.3 (470)	50.6 (450)	44.6 (421)	-2.6	9.4	0.026	49.3	50.1	49.2	-1.6	0.2	0.94
Country						<0.001						0.52
1	55.1 (525)	19.6 (174)	34.3 (323)	78.9	42.9		36.9	39.7	41.4	-6.3	-9.2	
61	35.7 (340)	67.8 (603)	49.7 (469)	-68.0	-28.7		50.3	47.5	47.0	5.9	6.8	
64	9.2 (88)	12.6 (112)	16.0 (151)	-10.8	-20.5		12.7	12.7	11.6	0.1	3.5	
Non-white	7.7 (73)	4.8 (43)	6.2 (58)	11.7	6.0	0.04	93.3	92.8	92.2	2.2	4.2	0.79

Appendix Table 7. Risk of severe postoperative nausea and vomiting (PONV) up to 24 hours after surgery according to anti-emetics prophylaxis.

	Number of patients with PONV prophylaxis	PONV n(%)	Unadjusted		Propensity-score adjusted	
			RR (95% CI)	P-value	RR (95% CI)	P-value
Number of anti-emetics used						
0	1470	105 (7.1)	1.00 (ref)		1.00 (ref)	
1	2132	181 (8.5)	1.19 (0.94, 1.50)	0.14	1.06 (0.83, 1.35)	0.66
2 or more	1130	110 (9.7)	1.36 (1.06, 1.76)	0.018	1.07 (0.81, 1.41)	0.64
Anti-emetic combinations						
No prophylaxis	1508	110 (7.3)	1.00 (ref)		1.00 (ref)	
Dexamethasone	1146	96 (8.4)	1.15 (0.88, 1.49)	0.30	1.02 (0.75, 1.40)	0.88
5-HT ₃ antagonist	889	75 (8.4)	1.16 (0.87, 1.53)	0.31	1.22 (0.89, 1.68)	0.22
Dexamethasone and 5-HT ₃ antagonist	947	85 (9.0)	1.23 (0.94, 1.61)	0.13	0.93 (0.69, 1.27)	0.66

