

Supplementary Appendix 1

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Apfel CC, Korttila K, Abdalla M, et al. A Factorial Trial of Six Interventions for the Prevention of Postoperative Nausea and Vomiting. *N Engl J Med* 2004;350:2441-51.

Table S1: Baseline characteristics of 4086 patients randomized for all six interventions

	Ondansetron/ none	Dexametha- sone/none	Droperidol/ none	Propofol/ Inhalation	Nitrogen/ Nitrous oxide	Remifentanil/ Fentanyl
Patients (N)	2037/2049	2046/2040	2036/2050	2706/1380	2050/2036	2038/2048
Age (years)	47.1/46.6	47/46.7	46.7/47	46.9/46.7	46.7/47.1	47.1/46.7
Females (%)	80.8/79.7	80.6/79.9	80.4/80.1	80.5/79.8	80.8/79.8	80.4/80.2
Non-smoker (%)	79.7/81.3	79.8/81.2	81.1/79.9	80.5/80.5	79.6/81.4	80.2/80.9
History of PONV or MS (%)	53.6/52.5	53.9/52.3	53.2/52.9	53.4/52.4	53.2/52.9	53.8/52.3
Postoperative opioids (%)	80.4/79.6	79.8/80.2	77.8/82.2*	79.4/81.1	80.0/80.0	88.4/71.5*
PONV risk (%)*	58.7/58.5	58.6/58.6	58.4/58.9	58.7/58.6	58.6/58.6	60.4/56.9*
Surgery						
<i>Hernia repair (%)</i>	3/3.6	3.6/2.9	3.7/2.8	3/3.7	3.4/3.1	3.2/3.3
<i>Cholecystectomy (%)</i>	7.1/7.3	7.3/7.1	6.9/7.5	7.2/7.1	7.4/7	7.4/7
<i>Hysterectomy (%)</i>	18/16.5	17.4/17.2	17.5/17.1	17.6/16.7	16.3/18.3	17.6/17
<i>Thyroid surgery (%)</i>	6.5/7.2	6.7/7	6.6/7.1	6.8/6.8	7/6.7	7.5/6.2
<i>Breast surgery (%)</i>	3/2.9	3.1/2.8	2.9/3	3.1/2.7	3/2.9	2.7/3.2
<i>Hip replacement (%)</i>	3.9/4	3.8/4.1	4.1/3.8	4.1/4.6	3.8/4	4.3/3.6
<i>Knee arthroscopy (%)</i>	1.9/1.9	1.8/2	2/1.8	1.8/2.1	1.5/2.3	1.8/2
<i>Upper extremity surgery (%)</i>	2.7/2	2.6/2.1	2.5/2.2	2/2.9	2.8/1.9	2.2/2.5
<i>Ears, nose, throat and eye surgery (%)</i>	9.8/11.1	10.7/10.3	10.3/10.7	10.4/10.6	9.5/11.4	9.8/11.2
<i>Other gynecologic surgery (%)</i>	24.9/26.1	25.4/25.6	25.7/25.3	25.4/25.6	26.1/24.9	25.5/25.6
<i>Other bone surgery (%)</i>	6.2/7	6.7/6.5	5.9/7.3	6.5/6.8	7.3/5.9	7/6.2
<i>Other general surgery (%)</i>	13/10.4	11/12.4	12/11.4	11.9/11.3	11.8/11.5	11.1/12.2
Nasogastric tube (%)	32.7/32	32.2/32.5	32.5/32.2	32.4/32.3	34.1/30.6*	31.9/32.8
Duration of anesthesia (hours)	1.82/1.79	1.81/1.8	1.82/1.79	1.79/1.83	1.82/1.79	1.79/1.82
Muscle relaxant reversal drugs						
<i>None (%)</i>	74.8/75.6	75.5/75.0	75.1/75.4	75.9/73.8	75.2/75.2	77.5/73.0*
<i>Neostigmine (%)</i>	24.3/23.1	23.7/23.6	23.9/23.4	23.1/24.7	23.5/23.8	21.8/25.6*
<i>Pyridostigmine (%)</i>	0.9/1.3	0.8/1.4	1.0/1.2	0.9/1.5	1.3/0.9	0.8/1.4*

*Indicates P≤0.05.

Table S2: Risk factors and outcome variables for the 4086 patients according to all randomized interventions of the factorial design.

Randomized Interventions [0 = no or comparator, 1 = yes]						Number of Patients	Frequency of Risk Factors [percent]				Duration of Anesthesia [hours]	Risk according to Simplified Score [percent]	Maximum Nausea [average ratings]			Incidence of Nausea [percent of patients]			Average Number of Emesis			Incidence of Vomiting [percent of patients]			Incidence of PONV [percent of patients]		
Ondansetron	Dexamethasone	Droperidol	Propofol	Nitrogen	Remifentanil		Females	History	Nonsmoking	Opioids			Early	Late	Overall	Early	Late	Overall	Early	Late	Overall	Early	Late	Overall	Early	Late	Overall
0	0	0	0	0	0	44	82	64	84	74	1.76	61	1.81	1.91	2.77	36	44	59	0.18	0.16	0.34	11	11	18	36	47	59
0	0	0	0	0	1	44	86	43	89	84	1.75	60	1.00	2.14	2.66	27	39	52	0.11	0.27	0.39	9	23	32	27	41	55
0	0	0	0	1	0	46	85	50	78	76	1.70	58	1.28	1.77	2.51	28	39	52	0.11	0.22	0.33	9	13	20	30	39	52
0	0	0	0	1	1	40	73	50	75	80	1.80	56	1.98	2.28	3.20	40	48	65	0.13	0.23	0.35	10	15	23	40	48	65
0	0	0	1	0	0	88	78	57	83	74	1.77	58	1.67	2.53	2.86	31	46	51	0.11	0.34	0.45	11	24	32	31	51	56
0	0	0	1	0	1	85	72	49	78	89	1.72	57	1.38	2.10	2.75	27	40	52	0.08	0.36	0.45	8	22	28	29	46	56
0	0	0	1	1	0	88	84	49	75	72	1.87	56	1.22	2.41	2.76	20	38	43	0.08	0.20	0.28	6	20	25	20	39	44
0	0	0	1	1	1	84	81	45	86	89	1.66	60	1.08	1.73	2.08	20	38	42	0.05	0.18	0.23	4	15	18	20	39	43
0	0	1	0	0	0	43	72	51	91	81	2.00	59	1.27	1.98	2.97	23	30	44	0.09	0.23	0.33	7	19	26	23	33	47
0	0	1	0	0	1	42	83	60	88	90	1.71	64	1.33	2.33	2.98	17	40	43	0.14	0.26	0.40	10	21	26	17	40	43
0	0	1	0	1	0	40	78	55	85	68	2.33	57	0.70	1.44	1.58	20	28	30	0.03	0.08	0.10	3	8	10	20	28	30
0	0	1	0	1	1	41	83	46	80	80	1.65	58	1.24	1.34	1.71	17	24	29	0.07	0.07	0.15	7	7	12	17	27	32
0	0	1	1	0	0	79	78	49	82	74	1.59	57	0.49	1.23	1.42	13	27	28	0.01	0.22	0.23	1	13	14	13	27	28
0	0	1	1	0	1	87	78	52	86	83	1.67	60	0.53	1.91	2.19	13	37	41	0.02	0.20	0.22	1	14	15	13	37	41
0	0	1	1	1	0	86	84	51	86	62	1.85	57	0.67	1.36	1.70	19	29	38	0.03	0.13	0.16	3	8	9	19	29	38
0	0	1	1	1	1	83	80	54	81	89	1.82	61	0.33	1.35	1.52	7	28	31	0.01	0.17	0.18	1	11	12	7	29	33
0	1	0	0	0	0	42	67	50	83	71	1.93	54	1.26	2.17	2.43	19	40	45	0.14	0.17	0.31	12	12	24	21	43	50
0	1	0	0	0	1	43	88	44	84	93	1.95	61	1.79	2.05	2.65	28	35	42	0.16	0.16	0.33	16	14	28	30	37	44
0	1	0	0	1	0	43	81	60	79	81	2.19	61	0.91	1.33	1.91	21	28	40	0.05	0.12	0.16	5	9	14	21	28	40
0	1	0	0	1	1	44	84	52	77	93	1.82	62	1.02	1.25	1.82	16	27	34	0.09	0.05	0.14	7	5	11	16	27	34
0	1	0	1	0	0	84	82	51	79	70	1.63	56	0.65	1.44	1.78	17	29	36	0.04	0.18	0.21	4	12	14	18	30	37
0	1	0	1	0	1	89	79	60	82	88	1.73	61	1.29	1.22	1.89	25	22	35	0.13	0.16	0.29	11	9	17	26	22	35
0	1	0	1	1	0	82	73	51	77	70	1.84	54	0.49	1.58	1.77	13	27	30	0.00	0.22	0.22	0	13	13	13	27	30
0	1	0	1	1	1	85	84	52	79	93	1.79	61	0.92	1.54	2.04	20	26	34	0.06	0.19	0.25	5	14	15	20	27	35
0	1	1	0	0	0	42	79	60	88	75	1.87	60	0.69	1.45	1.98	19	31	40	0.10	0.19	0.29	10	14	21	21	31	40
0	1	1	0	0	1	44	82	52	91	80	1.64	60	1.56	1.30	1.99	30	27	36	0.16	0.07	0.23	11	7	14	32	27	39
0	1	1	0	1	0	46	76	39	74	70	1.87	52	0.25	1.16	1.27	7	24	24	0.00	0.07	0.07	0	7	7	7	24	24
0	1	1	0	1	1	44	80	66	73	90	1.66	61	0.25	0.61	0.68	9	18	23	0.00	0.02	0.02	0	2	2	9	18	23
0	1	1	1	0	0	86	83	59	84	67	1.74	58	0.47	1.44	1.62	13	27	30	0.02	0.17	0.20	2	10	12	14	27	31
0	1	1	1	0	1	86	79	58	81	93	1.78	62	0.51	0.91	1.14	13	21	24	0.05	0.10	0.15	5	8	13	14	22	26
0	1	1	1	1	0	87	77	48	78	68	1.83	54	0.61	0.82	0.97	13	16	21	0.01	0.07	0.08	1	6	7	14	16	22
0	1	1	1	1	1	82	82	52	76	84	1.82	59	0.55	0.79	1.12	16	20	27	0.02	0.07	0.10	2	5	7	17	20	28
1	0	0	0	0	0	43	86	51	81	74	1.83	58	1.10	1.74	2.10	21	35	40	0.12	0.09	0.21	9	7	14	23	37	42
1	0	0	0	0	1	41	80	63	78	93	2.12	63	1.99	1.95	2.76	37	32	46	0.24	0.20	0.44	17	7	20	37	32	46
1	0	0	0	1	0	45	78	56	82	84	1.95	60	1.22	1.49	2.07	24	36	44	0.09	0.18	0.27	7	11	13	27	38	44
1	0	0	0	1	1	45	76	49	82	98	1.50	61	0.71	0.96	1.27	11	16	22	0.18	0.18	0.36	11	16	22	16	22	31
1	0	0	1	0	0	86	81	59	84	67	1.87	58	0.78	1.24	1.59	17	24	30	0.05	0.17	0.22	3	9	12	19	25	31
1	0	0	1	0	1	83	84	48	77	92	1.83	60	0.80	1.61	2.03	17	28	36	0.07	0.23	0.30	6	16	18	18	29	36
1	0	0	1	1	0	80	76	48	80	76	1.66	56	0.45	1.67	1.78	9	33	34	0.04	0.14	0.18	3	10	13	9	33	34
1	0	0	1	1	1	89	81	57	78	94	1.85	62	0.64	1.59	1.95	18	34	38	0.01	0.20	0.21	1	12	13	18	35	39
1	0	1	0	0	0	47	72	34	79	72	1.59	51	0.66	0.69	1.14	13	15	22	0.11	0.02	0.13	9	2	9	17	17	23

Randomized Interventions [0 = no or comparator, 1 = yes]						Number of Patients	Frequency of Risk Factors [percent]				Duration of Anesthesia [hours]	Risk according to Simplified Score [percent]	Maximum Nausea [average ratings]			Incidence of Nausea [percent of patients]			Average Number of Emesis			Incidence of Vomiting [percent of patients]			Incidence of PONV [percent of patients]		
Ondansetron	Dexamethasone	Droperidol	Propofol	Nitrogen	Remifentanyl		Females	History	Nonsmoking	Opioids			Early	Late	Overall	Early	Late	Overall	Early	Late	Overall	Early	Late	Overall	Early	Late	Overall
1	0	1	0	0	1	43	74	51	72	83	1.76	56	0.65	1.65	1.95	12	33	35	0.05	0.19	0.23	2	9	9	12	33	35
1	0	1	0	1	0	43	86	47	81	70	1.90	57	0.09	0.79	0.81	7	19	23	0.02	0.02	0.05	2	2	5	9	19	26
1	0	1	0	1	1	45	80	60	78	87	1.78	61	0.36	0.93	1.16	7	22	24	0.04	0.09	0.13	2	7	9	7	22	24
1	0	1	1	0	0	83	78	53	82	72	1.82	58	0.36	0.86	0.96	12	17	23	0.01	0.12	0.13	1	10	10	12	18	23
1	0	1	1	0	1	81	79	54	81	89	2.02	61	0.49	1.51	1.69	10	32	37	0.06	0.09	0.15	5	9	14	10	32	37
1	0	1	1	1	0	84	85	56	83	64	1.92	57	0.45	1.58	1.83	11	26	31	0.04	0.17	0.20	4	13	14	12	30	33
1	0	1	1	1	1	82	80	57	76	90	1.86	61	0.43	1.15	1.35	10	16	22	0.01	0.07	0.09	1	7	9	10	16	22
1	1	0	0	0	0	43	81	51	79	79	1.94	58	1.28	1.53	2.33	19	28	37	0.16	0.28	0.44	12	14	21	21	30	37
1	1	0	0	0	1	44	73	39	80	89	1.76	56	1.41	0.73	1.68	25	25	34	0.14	0.05	0.18	9	5	11	25	27	34
1	1	0	0	1	0	38	87	58	76	74	1.85	59	1.11	1.68	1.87	32	32	42	0.03	0.13	0.16	3	11	13	32	32	42
1	1	0	0	1	1	46	74	67	72	93	1.86	61	0.72	1.37	1.85	17	28	35	0.07	0.07	0.13	2	7	9	17	28	35
1	1	0	1	0	0	85	79	51	73	71	1.82	54	0.34	0.96	1.09	9	19	21	0.01	0.15	0.16	1	8	9	9	19	21
1	1	0	1	0	1	81	79	51	83	88	1.63	60	0.60	1.01	1.35	11	16	21	0.04	0.15	0.19	2	9	10	11	17	22
1	1	0	1	1	0	85	84	61	87	79	1.67	62	0.08	0.79	0.86	4	14	16	0.00	0.07	0.07	0	7	7	4	15	18
1	1	0	1	1	1	85	86	56	79	91	1.82	62	0.25	0.78	0.91	7	16	22	0.00	0.06	0.06	0	6	6	7	16	22
1	1	1	0	0	0	44	86	52	82	74	2.08	59	0.61	1.20	1.36	14	20	23	0.09	0.09	0.18	5	9	11	14	20	23
1	1	1	0	0	1	39	85	62	79	76	1.56	60	0.99	1.28	2.01	15	26	33	0.00	0.21	0.21	0	15	15	15	26	33
1	1	1	0	1	0	44	75	43	77	72	1.63	53	0.25	0.93	1.09	7	20	25	0.05	0.05	0.09	5	5	9	7	20	25
1	1	1	0	1	1	42	83	55	79	88	2.06	61	0.86	1.07	1.52	19	26	29	0.05	0.07	0.12	5	7	10	21	29	31
1	1	1	1	0	0	82	85	50	79	67	1.86	56	0.53	0.73	0.98	11	12	17	0.04	0.07	0.11	4	4	6	11	12	17
1	1	1	1	0	1	83	81	57	76	89	1.89	60	0.40	0.67	0.89	10	14	18	0.00	0.08	0.08	0	6	6	10	17	19
1	1	1	1	1	0	90	81	53	79	66	1.83	56	0.19	0.70	0.77	6	18	20	0.00	0.03	0.03	0	2	2	6	18	20
1	1	1	1	1	1	86	84	57	88	80	1.85	62	0.10	0.60	0.69	8	12	17	0.00	0.08	0.08	0	5	5	8	12	17

History = History of PONV or motion sickness, Opioids = postoperative use of opioids. Risk according to the simplified score reflects the probability of PONV based on the four most important risk factors.¹⁷

Maximum nausea intensities reflect the average values on a 0 to 10 rating scale. Early reflects the first 2 postoperative hours, late afterwards (>120 postoperative minutes) and overall the 0 to 24 hour interval.