The Results of Investigation into Dr.Yoshitaka Fujii's papers

Toho University Faculty of Medicine announced on March 8, 2012 that 8 manuscripts of Dr.Yoshitaka Fujii had been retracted because of execution of these clinical studies without proper ethical approval. In addition, an article [Appendix 1] entitled "The analysis of 169 randomised controlled trials to test data integrity." was published on-line as a Special Article in Anaesthesia, the Journal of the Association of Anaesthetists of Great Britain and Ireland, on March 8, 2012. Three Editorials [Appendix 2] have simultaneously been published in Anaesthesia. Accordingly, the Japanese Society of Anesthesiologists set up a Special Investigation Committee to investigate this issue on March 10. On April 6, a group of editors representing 23 medical journals sent an inquiry to seven Japanese institutions about 193 papers published by Dr. Fujii [Appendix 3] .

Appendix 4 lists 249 papers based on a reconciliation of Appendix 3 in the Joint Editors –in-Chief Request for Determination and a comprehensive online research. Appendix 5 lists 212 original papers which the JSA Special Investigation Committee looked into.

The JSA Special Investigation Committee:

1. Investigated original research data, lab note books and the relevant records at institutions.
2. Interviewed with Dr. Fujii and with co-authors of Dr. Fujii's papers

1)The Results of Investigation

All papers were evaluated based on submitted original research data, the record of animal uses, the number of subjects, the record of medication and the reliability of randomized controlled trials (RCTs).

A : NOT Fabricated

Papers which the original data and the number of subjects in papers have been verified authentic and Dr. Fujii had not related to any data collection and processing:

3 papers (No.101,112,150 [Appendix 5])

B : Fabricated

Papers which have any discrepancy in numbers of subjects, medication, capability of the methohd :

171 papers (included 125 papers in RCT, double- blind mammer) [Appendix 5]

154 papers out of 193 papers [Appendix 3]

C : Others

Papers with no evidence to prove them fabricated or not fabricated :

38 papers

(No.1,2,3,4,5,6,7,8,13,15,17,18,23,24,25,26,32,33,34,44,45,46,68,70,71,75,92,93,94,96,97,113,122,123,139,141,152 [Appendix 5])

2) Conclusions

The number of fabricated papers is 171. Only 3 papers are verified authentic and 38 papers have not been proven either fabricated or not fabricated. Both the number of animals and patients are totally different from the institutional records, although some of his early studies might have been done properly. As he stated in his interviewing that he enjoyed the communication with EICs when submitting papers, he seemed to have justified all fabrications if papers were accepted.

In order to be easily accepted by journals, he fabricated in most his papers that he studied large number of cases in a randomized controlled trial in double - blind manner.

The name of the institution and the period of the study have not been specified in his papers so that he could excuse that "the data were obtained at a previously worked hospital or in a place where he took a part-time job. " The institutions of the research ethical committees also have not been specified. Additionally, he made papers as if they were multi-hospital studies, by placing the names of other institutions as his coauthors. He has used these methods effectively to escape from doubts of fabrications.

All fabrications have been done by Dr. Fujii alone. None of coauthors have recognized Dr. Fujii's papers as fabrications. The reason for his putting coauthors in his papers was to escape from suspicions of the fraud. In a recently published letter

(Anaesthesia 2012: 67: 669–670), he states that “I did not write these articles alone, and some of data were collected by others as well.”

Many of coauthors did not sign cover letters by themselves. Although journals recently require signatures of all authors, Dr. Fujii stated that he submitted his papers without coauthors’ signatures, because he had not been required so by EICs. The JSA Investigation Committee has obtained a cover letter signed by 2 authors other than Dr. Fujii. These 2 signatures have been proven to be fabricated.

Out of Dr. Fujii's coauthors, Professor Hidenori Toyooka cannot be excused. He had been supervising Dr. Fujii for a long period, since he was at Tokyo Medical and Dental University until the University of Tsukuba. Professor Toyooka published dozens of papers with Dr. Fujii and signed submitted papers as The Achievements of the University of Tsukuba including 85 papers of Dr. Fujii. In 2000, he recognized the suspicion on Dr. Fujii by Dr. Kranke’s Letter to the Editor (Anesthesia and Analgesia 2009; 90 : 1000-8), however, he did not take any action. Other coauthors had no complicity in the fabrication. Some used these papers as their achievements and others did not even know the papers were published with their names. Actually many of Dr. Fujii’s papers were submitted without coauthors’ approval and they did not receive re-prints of accepted papers. Accordingly, they did not notice that the papers existed.

Dr. Fujii used his papers for several purposes:

- Papers were inevitable to be employed as Assistant Professor of University of Tsukuba and Associate professor of Toho University.
- He received public funds for his studies.
- He applied to the Academic Prize of Japanese Society of Anesthesiologists 5 times but not selected.
- He received some grants by speaking at 2 sponsored seminars.

Koji Sumikawa, M.D.
Vice President, Japanese Society of Anesthesiologists
Chief, Special Investigation Committee on Papers by Fujii

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Special Article

The analysis of 169 randomised controlled trials to test data integrity

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Summary

The purpose of this study was to use some statistical methods to assess if randomised controlled trials (RCTs) published by one particular author (Fujii) contained data of unusual consistency. I searched seven electronic databases, retrieving 169 RCTs published by this author between 1991 and July 2011. I extracted rates for categorical variables and means (SDs) for continuous variables, and compared these published distributions with distributions that would be expected by chance. The published distributions of 28/33 variables (85%) were inconsistent with the expected distributions, such that the likelihood of their occurring ranged from 1 in 25 to less than 1 in 1 000 000 000 000 000 000 000 000 000 000 000 (1 in 10^{33}), equivalent to p values of 0.04 to $< 1 \times 10^{-33}$, respectively. In 142 human studies, 13/13 published continuous variable distributions were inconsistent with expected, their likelihoods being: weight < 1 in 10^{33}; age < 1 in 10^{33}; height < 1 in 10^{33}; last menstrual period 1 in 4.5×10^{15}; baseline blood pressure 1 in 4.2×10^{5}; gestational age 1 in 28; operation time < 1 in 10^{33}; anaesthetic time < 1 in 10^{33}; fentanyl dose 1 in 6.3×10^{8}; operative blood loss 1 in 5.6×10^{9}; propofol dose 1 in 7.7×10^{7}; paracetamol dose 1 in 4.4×10^{2}; uterus extrusion time 1 in 33. The published distributions of 7/11 categorical variables in these 142 studies were inconsistent with the expected, their likelihoods being: previous postoperative nausea and vomiting 1 in 2.5×10^{6}; motion sickness 1 in 1.0×10^{4}; male or female 1 in 140; antihypertensive drug 1 in 25; postoperative headache 1 in 7.1×10^{10}; postoperative dizziness 1 in 1.6×10^{6}; postoperative drowsiness 1 in 3.8×10^{4}. Distributions for individual RCTs were inconsistent with the expected in 97/135 human studies by Fujii et al. that reported more than two continuous variables, their likelihood ranging from 1 in 22 to 1 in 140 000 000 000 (1 in 1.4×10^{11}), compared with 12/139 RCTs by other authors. In 26 canine studies, the distributions of 8/9 continuous variables were inconsistent with the expected, their likelihoods being: right atrial pressure < 1 in 10^{33}; diaphragmatic stimulation (100 Hz) < 1 in 10^{33}; pulmonary artery occlusion pressure < 1 in 10^{33}; diaphragmatic stimulation (20 Hz) < 1 in 10^{33}; heart rate 1 in 6.3×10^{10}; mean pulmonary artery pressure 1 in 2.2×10^{14}; mean arterial pressure 1 in 6.3×10^{7}; cardiac output 1 in 110. Distributions were inconsistent with the expected in 21/24 individual canine studies that reported more than two continuous variables, their likelihood ranging from 1 in 345 to 1 in 51 000 000 000 000 (1 in 5.1×10^{13}).

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Patterns are useful because they tell us something about the processes that create them. When patterns deviate from the expected, we know that something unusual has happened. Random allocation of individuals from a population into different groups distributes both categorical and continuous variables in predictable patterns, the centre, spread and shape of which are necessary consequences of the interaction between the sampled population and the sampling method.

For example, the variation in the means of continuous variables, such as age, depends upon: (i) the mean age of the sampled population; (ii) the population's age distribution; and (iii) the size of the sample. The distribution of mean values for each continuous variable is normal (Gaussian), unless the population variable is both very asymmetric ('skewed') and the samples have been small (often quoted as < 30 individuals). The distribution of means in such cases will be slightly skewed and may cluster more or less tightly around the population mean.

Similarly, the variation in the proportions of binomial characteristics, such as sex, depends upon: (i) the proportions of each sex in the sampled population; and (ii) the size of the sample. The shape and asymmetry of binomial distributions change with these two variables.

Significant deviation from the expected occurrences of one binomial characteristic in the outcomes reported by one particular anaesthetic researcher was publicised by Kranke et al., commenting that: 'Reported data on granisetron and postoperative nausea and vomiting by Fujii et al. are incredibly *nice*!' [1]. Kranke et al. concluded by observing: '…we have to conclude that there must be an underlying influence causing such incredibly nice data reported by Fujii et al.'

Kranke et al. had looked at 47 randomised controlled trials (RCTs) of antiemetics to prevent postoperative nausea and vomiting (PONV), published between 1994 and 1999 by Dr Yoshitaka Fujii and colleagues (references 1–47; Appendix S1; available online, please see details at the end of the paper). Eighteen of these RCTs had reported postoperative rates of headache. Ten had reported the same rate of headache in every group; for instance, in one paper, Fujii et al. reported that they had randomly allocated 270 women to one of six groups (reference 1; Appendix S1). Eighteen of the 270 women had postoperative headaches: 3/45 in each of the six groups. Table 1 shows the reported and expected (i.e. by chance) rates of headache in such patients.

Table 1 Example of the methods used in my analysis. Number of women with headache in groups of 45 women, as reported in a single study (reference 1; Appendix S1) and as would be expected by chance.

Women with a headache in a group of 45	Groups reported with this incidence of headache in this study	Groups expected with this incidence if headaches were distributed randomly across groups
0	0	0.3
1	0	0.9
2	0	1.4
3	6	1.4
4	0	1.0
5	0	0.6
6	0	0.3
7	0	0.1

Kranke et al. proceeded to reject the null hypothesis that 10/18 RCTs would report homogenous rates of headache by chance, calculating a probability of 6.8×10^{9}, or 1 in 147 million. My slight concern is that this indirect calculation confused the probability of a particular incidence's occurring, with the probability that this incidence is consistent with the expected binomial distribution. Kranke et al. calculated the first probability, but it is the second that I am more interested in. This turns out to be ~1 in 5600 for the distribution of headache reported in all 18 RCTs that Kranke et al. analysed: more than Kranke's estimate, but still 280 times smaller than the $p < 0.05$ threshold conventionally regarded as statistically significant.

Kranke et al. had concluded that it was more likely that an 'unnatural mechanism' had obliterated the expected binomial distribution. Moore et al. mention these 'suspect' data in their editorial on scientific fraud [2].

My purpose in this study was to extend the statistical analysis of papers, begun by Kranke et al., to all RCTs published by Fujii. Identification of unnatural patterns of categorical and continuous variables would support the conclusion that these data depart from those that would be expected from random sampling to a sufficient degree that they should not contribute to the evidence base.

Methods

I searched the following databases (author 'Fujii') between 1991 and July 2011: the Cochrane Central

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Register of Controlled Trials (CENTRAL); MEDLINE; EMBASE; CINAHL; ISI WOS; LILAC; and INGENTA. I included RCTs authored by Dr Yoshitaka Fujii, identified as working at the University of Tsukuba Institute of Clinical Medicine, the Tokyo University Medical and Dental School, the Toride Kyodo General Hospital or the Toho University School of Medicine (with Fujii in any position in the list of authors). I analysed the integrity of the data in these RCTs and compared them with 366 RCTs by other authors (Appendices S2–S6; available online) [3].

From the retrieved studies, I extracted the following data: the number of participants or animals in each group; all continuous variables reported as mean (SD), for example age; and all categorical variables, such as the number of women. I included variables measured before or after exposure to the allocated intervention, as long as they had been unaffected by the exposure.

Appendix A details the generation of expected categorical and continuous distributions and their subsequent statistical analysis, whilst an example illustrates the method at the beginning of the Results section, below. Broadly, the analysis is based on two principles focused on the spread of values around the most common value (rather than simply comparing two averages). The first principle is for categorical distributions, which can best be understood by considering the results of tossing two coins: the most likely outcome (50%) is head and tail while two heads or two tails is less likely (25% each). The probability of departures from these frequencies (e.g. finding that two tails occur 75% of the time in a dataset) can be calculated. In this example, one knows that for a single coin, there is an equal chance a head and a tail will be tossed, so one knows the expected shape of the binomial distribution for two coins. For the categorical variables analysed in this paper, one does not know the expected rate for each outcome – for instance, how many men or women one might expect in a sample of patients having cholecystectomy. Fortunately, the answer is given for each study by each study itself – if in total 80/100 patients randomly allocated to five groups are women, then one would expect a binomial distribution that peaks at a female distribution of 16/20 women per group. In this important way, my analysis also looks at the spread of proportions in each group, not just the peak value.

The second principle of analysis, for continuous variables, is known as the 'central limit theorem'. If we calculated the mean height of people in a sample, performed repeated sampling of other groups of people, and then plotted a series of these means, we would obtain a normal curve, even if the distribution of heights within the sampled population was not normal. The standard deviation of this curve can be estimated from the sample standard deviation and is called the standard error of the mean (SEM). The SEM is a measure of the extent to which the sampled means vary from the (true) population mean. The SEM is rather like a standard deviation of the sample means, illustrating their variation. Just as for binomial characteristics, the focus of the analysis in this paper is the spread of means, not the peak value. Authors occasionally mislabel standard deviations (SDs) as standard errors of the mean (SEMs), so I checked whether substitution of one by the other resolved apparently abnormal distributions.

In this paper, each RCT is its own standard: the expected distributions of categorical rates and continuous means for each RCT were generated from within the same RCT. For categorical variables, this mathematical coupling of expected-to-reported measurement actually reduces the power of my analysis to identify aberrant distributions, because the expected result is dependent upon the observed result. In other words, my method is 'conservative' and any finding of aberrant distributions using this technique suggests extremely aberrant data distribution. In contrast, my method of analysis of continuous variables can overestimate clustering of means in small samples due to imprecision of the reported means and SDs or a population distribution that might be skewed. I therefore applied a somewhat arbitrary (but again intentionally conservative) adjustment to reduce any clustering (Appendix A). Any finding of clustering after adjustment indicated that the data were strikingly clustered. Furthermore, I subjected to the same analysis 366 RCTs by authors other than Fujii et al.

Results

I identified and retrieved 169 RCTs published by Fujii and colleagues between 1991 and July 2011: 142 in humans (13 734 participants); 26 in dogs (688 mongrels); and one in guinea pigs (14 animals) (references 1–169; Appendix S1). This alone is a remarkable research output

– over 600 patients per year – and offers much useful material for analysis (Fig. 1). The focus of the human RCTs was prevention of PONV in 92 (54%), pain on injection of propofol in 14 (8%), treatment of PONV in 13 (8%), neuromuscular blockade in 11 (7%), the cardiovascular response to airway manipulation in 9 (5%), and epidural analgesia, middle cerebral artery perfusion and postoperative hypoxaemia in one each (1%). Drug effects on diaphragmatic contractility were the focus of the guinea pig study and 23 canine RCTs (24%), whereas the remaining 3 (2%) canine studies focussed on haemodynamic effects of drugs.

In addition, I analysed 366 other RCTs: 126 RCTs by other authors that reported postoperative rates of headache following prophylactic antiemesis (Appendix S2; available online); 31 RCTs by other authors of PONV prophylaxis with granisetron (Appendix S3; available online); 100 RCTs by other authors of rescue rates for droperidol and metoclopramide (Appendix S4; available online); 65 additional RCTs by other authors that reported rates of side effects after PONV prophylaxis (Appendix S5; available online); 145 RCTs by other authors of PONV prophylaxis reporting age, height or weight of participants (Appendices S2–S6). Some RCTs contributed to more than one analysis.

An example

The following single study serves as an example to illustrate the analyses of categorical and continuous variables. In one paper, Fujii et al. reported the response of 100 adults with PONV (20 per group) to placebo or one of four intravenous doses of granisetron (10, 20, 40 or 80 $\mu g.kg^{-1}$) (reference 90; Appendix S1). Table 2 lists the seven reported continuous variables and Table 3 lists the standardised differences between the mean of each group and the estimated population mean for these variables (see Appendix A for how to obtain the data in Table 3 from the original data in Table 2). Figure 2 presents histograms of the 35 standardised differences from Table 3. Each bar is 0.25 standardised differences wide with a height determined by the number of differences within each bar. The superimposed red curve (left graph) represents the expected distribution of standardised differences, the 'standard curve', with a mean of zero, a standard difference of one and a peak probability density at the mean of 0.40. The superimposed black curve (middle and right graphs) is the probability density curve generated by the data: the statistical test is between the variances of red and black curves. The result was that there was a significantly greater clustering of the actual data around zero than would be expected by chance

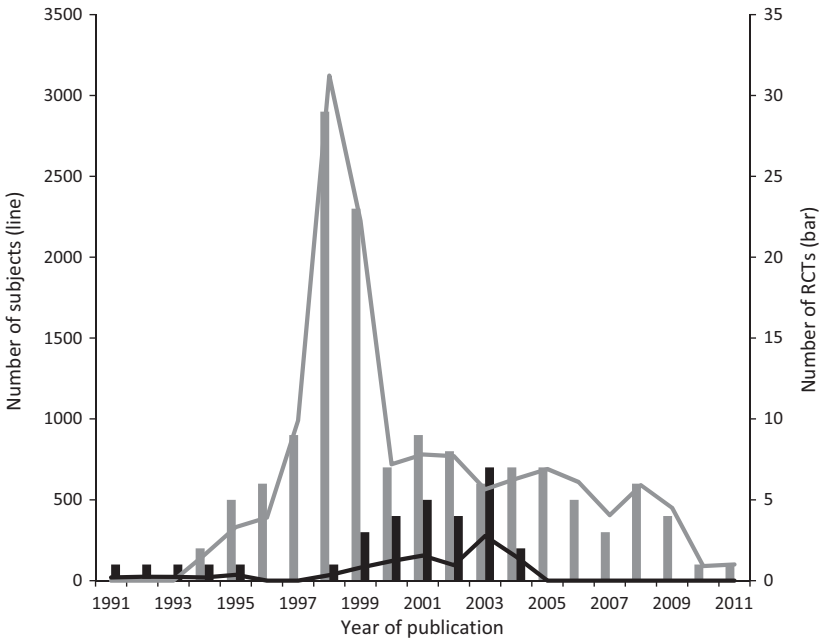

Figure 1 Histogram showing the number of RCTs published per year by Fujii et al. (vertical bars, human RCTs ▩, animal RCTs ■) and the number of subjects these RCTs reported (human grey line, animals black line).

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Table 2 Means ($\bar{m}$) for continuous variables reported for the five groups of a study of granisetron by Fujii et al. (reference 90; Appendix S1). Values are mean (SD).

	Granisetron dose; μg.kg^{-1}					
	Placebo (n = 20)	10 (n = 20)	20 (n = 20)	40 (n = 20)	80 (n = 20)	Population mean (μ)
Age; years	46 (8)	47 (7)	45 (11)	47 (10)	50 (11)	47 (9)
Height; cm	159 (10)	158 (9)	155 (11)	157 (10)	159 (9)	158 (10)
Weight; kg	57 (7)	57 (9)	54 (7)	54 (8)	58 (8)	56 (8)
Surgical time; min	86 (35)	92 (31)	83 (34)	87 (36)	92 (27)	88 (33)
Anaesthetic time; min	106 (35)	117 (33)	106 (36)	112 (37)	118 (29)	112 (34)
Fentanyl dose; μg	103 (79)	98 (73)	93 (73)	98 (79)	105 (86)	99 (78)
LMP; days	16 (3)	16 (3)	16 (3)	16 (3)	16 (3)	16 (3)

LMP, last menstrual period.

Table 3 Calculated standardised mean differences (($\bar{m}-\mu$)/SEM where SEM = SD/$\sqrt{20}$; see Appendix A) for the continuous variables presented in Table 2.

		Granisetron dose; μg.kg^{-1}				
	SEM	Placebo (n = 20)	10 (n = 20)	20 (n = 20)	40 (n = 20)	80 (n = 20)
Age; years	2.10	−0.48	0.00	−0.95	0.00	1.43
Height; cm	2.19	0.64	0.18	−1.19	−0.27	0.64
Weight; kg	1.74	0.57	0.57	−1.15	−1.15	1.15
Surgical time; min	7.29	−0.27	0.55	−0.69	−0.14	0.55
Anaesthetic time; min	7.60	−0.76	0.68	−0.76	0.03	0.82
Fentanyl dose; μg	17.44	0.21	−0.08	−0.37	−0.08	0.32
LMP; days	0.67	0.00	0.00	0.00	0.00	0.00

LMP, last menstrual period.

(p = 0.0017), as demonstrated by comparison with the standard curve. This was the case even with the variable 'last menstrual period' (LMP) removed (p = 0.016; please see the Discussion section, below, concerning the invariance of LMP). However, in this example, adjustment of the variance (see Methods, Appendix A) made the distribution consistent with the expected (p = 0.06). Subsequent figures are illustrated with the comparative red standard normal curve.

Table 4 lists the number of participants in each group for the six reported binomial variables in the same study, and Fig. 3 presents histograms of reported and expected rates for these binomial variables. For instance, 40/100 participants were women, which is the best estimate of the proportion (0.40) of women in the population from which 100 participants were drawn. The expected binomial distribution of this variable is therefore determined by the rate of 0.40 and the sample size. Summation of the binomial distributions for the 6 variables in Table 4 results in the expected distribution depicted by white bars in Fig. 3. The reported distribution was no different from that expected (p = 0.13). For this published study taken in isolation, therefore, my conclusion was that it did not contain data of unusual consistency.

Summary of human studies

The approach explained above was applied to perioperative continuous and categorical variables reported in 142 human RCTs (studies specified in the Tables 5–9). Figures 4–7 show the histograms of standardised mean difference for some of the reported continuous variables, illustrating that the reported clustering around zero was more extreme than expected by chance. Recall that for continuous variables, the SDs should be ~1.0 and the p values in Tables 5 and 7 indicate the significance of departures from this expected value. Figures 8 and 9 show the histograms

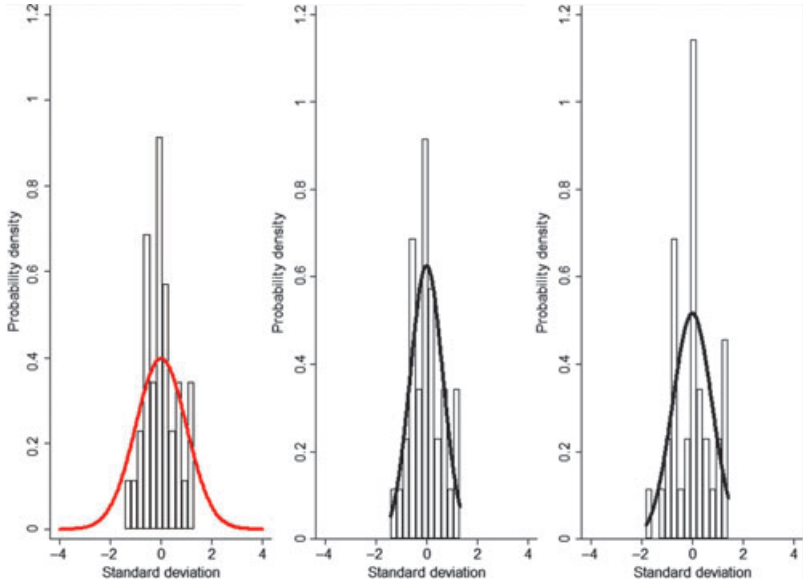

Figure 2 Histograms of reported distributions of the 35 standardised mean differences from Table 3 for seven continuous variables reported in one study of granisetron (reference 90; Appendix S1). The width of each bar is 0.25 SD. The red curve (left graph) is the expected standard normal distribution. The curve generated by the reported distribution (middle graph) was different from the expected, p = 0.0017. After adjustment (right graph), the distribution was not different from the expected, p = 0.06. The point of interest is the abundance of standardised mean differences around zero (above the red curve) and their paucity to either side (i.e. the bars on either side do not extend along the *x*-axis to meet the limits of the curve).

Table 4 Overall rates of six binomial variables and their distribution for the five groups of a representative study of granisetron by Fujii et al. (reference 90; Appendix S1). Values are number.

			Granisetron dose; μg.kg^{-1}			
	Rate	Placebo (n = 20)	10 (n = 20)	20 (n = 20)	40 (n = 20)	80 (n = 20)
Women	0.4	8	7	8	9	8
Motion sickness	0.09	2	1	2	2	2
Previous PONV	0.02	0	1	0	1	0
Operation two*	0.12	2	3	2	2	3
Operation three*	0.11	2	2	3	2	2
No analgesia	0.37	7	8	7	7	8

*Referring to different operations.
PONV, postoperative nausea and vomiting.

of two categorical variables. Tables 6, 8 and 9 list the p values for the distributions of these and nine other categorical variables.

Figure 10 shows the expected and reported rates of headache in RCT groups authored by Fujii et al. and by others. The former studies had a distribution of headache that was strikingly different from the expected binomial distribution ($p = 1.4 \times 10^{-11}$), whereas the distribution of headache in studies by authors other than Fujii et al. was not different from the expected (p = 0.81). The distributions of weight, age and height in RCTs by other authors were consistent with the expected, in contrast to the distributions in RCTs authored by Fujii et al. (Table 10).

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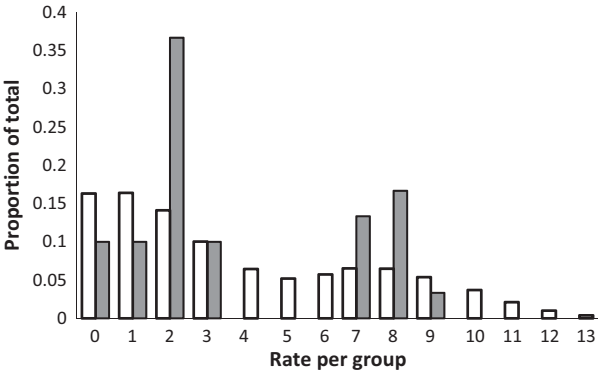

Figure 3 Histograms of reported (■) and expected (by chance; □) distributions of 30 rates (Table 4), summed for six binomial variables reported in a representative study of granisetron (reference 90; Appendix S1). For instance, in Table 4, 11/30 groups reported a rate of 2, which is a proportion of 0.37 on the vertical scale. The reported distribution was not different from the expected distribution, p = 0.13.

Summary of animal studies

Table 11 lists nine continuous variables reported in 26 canine RCTs. The adjusted p values indicate that the distributions are significantly different from that expected for all but one variable, pulmonary capillary wedge pressure; the histograms of the expected and reported distributions for the latter and a representative significantly different variable, transdiaphragmatic pressure at 100 Hz, are shown in Fig. 11.

Individual studies

The preceding analyses combined results from RCTs. I also assessed in isolation each RCT, combining the standardised mean differences for different variables within a study, for instance age, height and weight. Of 142 human RCTs by Fujii et al., 135 (95%) reported mean and SD for at least two continuous variables. Figure 12a shows the p values that the reported

Table 5 Number of reported means for six pre-operative continuous variables in 142 human studies by Fujii et al. (study numbers refer to Appendix S1). The adjusted p value quantifies the chance that the reported distribution was consistent with the expected distribution.

	Groups reporting means with SDs	Standardised SD of means	p value	Studies
Weight	438	0.551	$< 10^{-33}$	1–59, 61–66, 68–73, 75–97, 101–23, 151–69
Age	414	0.567	$< 10^{-33}$	1–17, 19, 21, 24–5, 27–36, 38, 40–6, 48–59, 61–6, 68–73, 75–8, 80–97, 99, 101–3, 105–23, 151–69
Height	447	0.620	$< 10^{-33}$	1–59, 61–66, 68–73, 75–8, 80–97, 99, 101–23, 151–69
LMP	56	0.261	2.22×10^{-16}	37, 42, 47, 50–1, 55–7, 68, 72–3, 81–3, 86, 88, 90, 165
Baseline BP	27	0.363	2.4×10^{-6}	44, 95–7, 105, 107, 115, 151, 153
Gestation	26	0.707	0.036	25, 35, 44, 65, 75, 95–7, 153

BP, blood pressure; LMP, last menstrual period.

Table 6 Number of reported rates for five pre-operative categorical variables in 142 human studies by Fujii et al. (study numbers refer to Appendix S1). The p value quantifies the chance that the reported distribution was consistent with the expected distribution.

	Groups reporting rates	p value	Studies
Previous PONV	83	4.0×10^{-7}	13, 15–8, 22, 27–9, 33, 38–9, 50, 54–5, 57–8, 63, 67–8, 70–1, 80, 90, 92, 95
Motion sickness	88	1.0×10^{-4}	13–8, 22, 27–9, 32–3, 38–9, 50, 54–5, 57–8, 60, 67–8, 70–1, 80, 90, 92, 95
Sex	217	7.1×10^{-3}	1–2, 8, 10–1, 17–9, 21–2, 31, 34, 40–3, 45–6, 49, 52–4, 57–9, 61–4, 66–70, 72–3, 77–8, 80, 82, 85, 87–8, 90–1, 99, 101–12, 114–21, 123, 169
Antihypertensive drugs	73	0.04	105–7, 109, 115, 119
Previous caesarean section	18	0.08	25, 35, 46, 95–7

PONV, postoperative nausea and vomiting.

Table 7 Number of reported means for seven intra-operative continuous variables in 142 human studies by Fujii et al. (study numbers refer to Appendix S1). The adjusted p value quantifies the chance that the reported distribution was consistent with the expected distribution.

	Groups reporting means with SDs	Standardised SD of means	p value	Studies
Operation time	320	0.447	$< 10^{-33}$	1–30, 32–3, 35–45, 47, 49–59, 61–5, 68–73, 75–8, 80–97, 101, 105–6, 108, 111, 113–4, 119, 152–3, 158, 161–2, 165, 167–8
Anaesthetic time	293	0.466	$< 10^{-33}$	1–19, 21–4, 26–30, 32–3, 36–43, 45, 47, 49–59, 61–5, 68–72, 75–8, 80–94, 105–6, 108, 111, 113–4, 119, 152, 158, 161–2, 165, 167–8
Fentanyl	62	0.398	1.6×10^{-9}	57, 65, 71, 73, 75, 80–5, 90, 96–7, 153, 158, 161–2, 165, 167–8
Operative blood loss	32	0.252	1.8×10^{-10}	12, 16, 20, 29, 36, 69, 76, 92, 105, 119
Propofol	63	0.511	1.3×10^{-8}	64–5, 95, 120–1, 123, 154–7, 159–60, 163–4, 166, 169
Paracetamol	19	0.392	2.3×10^{-3}	2, 8, 10–2, 19, 31
Time uterus out	18	0.875	0.03	25, 35, 44, 95–7, 153

Table 8 Number of reported rates for two intra-operative categorical variables in 142 human studies by Fujii et al. (study numbers refer to Appendix S1). The p value quantifies the chance that the reported distribution was consistent with the expected distribution.

	Groups reporting rates	p value	Studies
Uterus exteriorised	18	0.23	25, 35, 44, 95–7
Tubal ligation	18	0.79	25, 35, 44, 95–7

distributions of group means were consistent with the expected distributions in human and animal studies by Fujii et al. The results for other authors are shown in Fig 12b. In the studies by Fujii et al., the distributions were abnormal in 97/135 human RCTs and 22/24 animal RCTs, while distributions were abnormal in 12/139 human RCTs by other authors. A summary of the distribution of adjusted p values for RCTs by Fujii et al. is shown in Table 12. There were insufficient binomial data in any study, human or animal, to generate expected distributions reliably and compare them with reported binomial distributions.

All the continuous variables reported above are combined in Fig. 13, with Fig. 13a displaying 2556 values from RCTs by Fujii et al. (graphs on the left) and 2015 values from other RCTs (graphs on the right). The striking feature is the greater clustering of the data from Fujii, which applies to some extent even to Fujii's trials that do not themselves show distributions different from the expected (Fig. 13b) as well as to those that do show distributions different from expected (Fig. 13c).

The random sampling of eight values from studies by Fujii et al. generates a statistically abnormal distribution whilst an abnormal distribution is only generated after 500 values have been sampled from other RCTs. If these data are combined sequentially, from least to most different from the expected distributions, values from Fujii et al. generate an abnormal distribution after 50 values are analysed and other RCTs generate an abnormal distribution after 333 values are analysed

Table 9 Number of reported rates for four postoperative categorical variables in 142 human studies by Fujii et al. (study numbers refer to Appendix S1). The p value quantifies the chance that the reported distribution was consistent with the expected distribution.

	Groups reporting rates	p value	Studies
Headache	170	1.4×10^{-11}	1–2, 6–16, 21, 24–9, 32, 36, 40–6, 48, 51–2, 54–5, 58–9, 68, 70, 73, 88, 91
Dizziness	117	6.2×10^{-7}	1, 6–7, 9, 12–6, 24–9, 32, 36, 42, 44, 48, 51, 54–5, 58, 68, 70, 76
Drowsiness	201	2.6×10^{-5}	1–2, 6–12, 16, 21, 25, 29, 36, 40–3, 46, 48, 51, 58, 64, 70, 76
Constipation	26	0.08	40–1, 43, 47, 52, 59, 76

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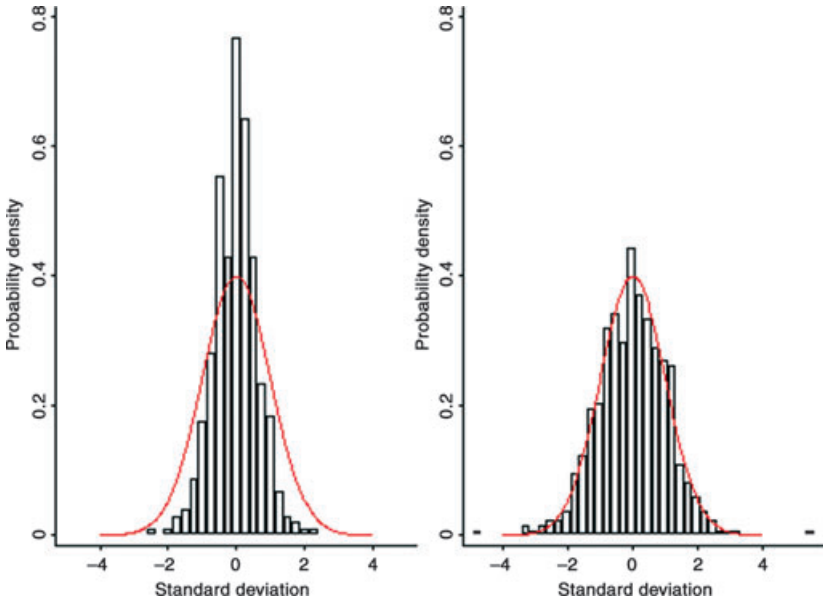

Figure 4 Histograms of mean age distributions reported by Fujii et al. (left) and by others (right). The distribution reported by Fujii et al. was different from the expected, $p < 10^{-33}$, whilst that reported by others was not, $p = 0.132$. The width of each bar is 0.25 SD. The red lines are the respective expected standard normal distribution. The point of interest in the Fujii studies is the abundance of standardised mean differences around zero (above the red curve) and their paucity to either side (i.e. the bars on either side do not extend along the *x*-axis to meet the limits of the red curve).

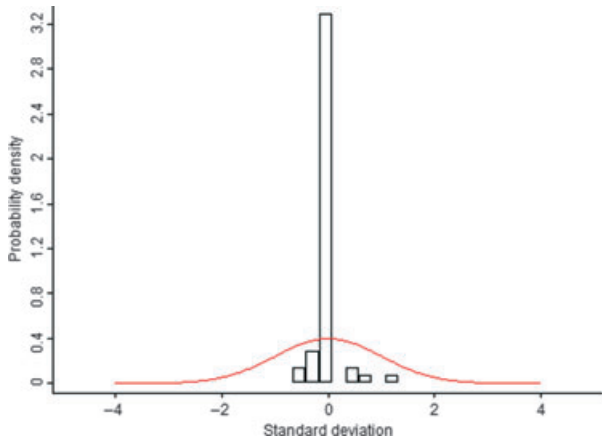

Figure 5 Histogram of 56 standardised mean differences for last menstrual period from 18 human trials by Fujii et al. (Appendix S1; references from the same studies as in Table 5). The reported distribution was different from the expected, $p = 2.22 \times 10^{-16}$. The width of each bar is 0.25 SD. The red line is the expected standard normal distribution. The point of interest in the Fujii studies is the abundance of standardised mean differences around zero (above the red curve) and their paucity to either side (i.e. the bars on either side do not extend along the *x*-axis to meet the limits of the red curve).

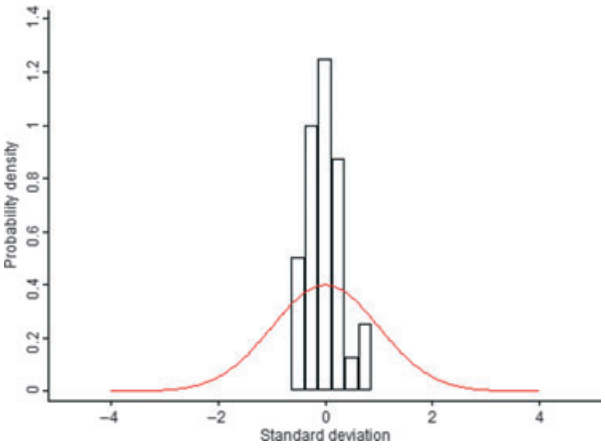

Figure 6 Histogram of 32 standardised mean differences for blood loss from 10 human trials (Appendix S1; references from same studies as in Table 7). The reported distribution was different from the expected, $p = 1.8 \times 10^{-10}$. The width of each bar is 0.25 SD. The red line is the expected standard normal distribution. The point of interest in the Fujii studies is the abundance of standardised mean differences around zero (above the red curve) and their paucity to either side (i.e. the bars on either side do not extend along the *x*-axis to meet the limits of the red curve).

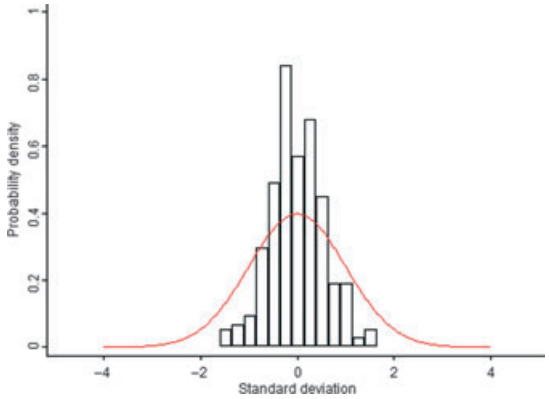

Figure 7 Histogram of 293 standardised mean differences for anaesthetic time from 94 human trials (Appendix S1; references from same studies as in Table 7). The reported distribution was different from the expected, $p < 10^{-33}$. The width of each bar is 0.25 SD. The red line is the expected standard normal distribution. The point of interest in the Fujii studies is the abundance of standardised mean differences around zero (above the red curve) and their paucity to either side (i.e. the bars on either side do not extend along the *x*-axis to meet the limits of the red curve).

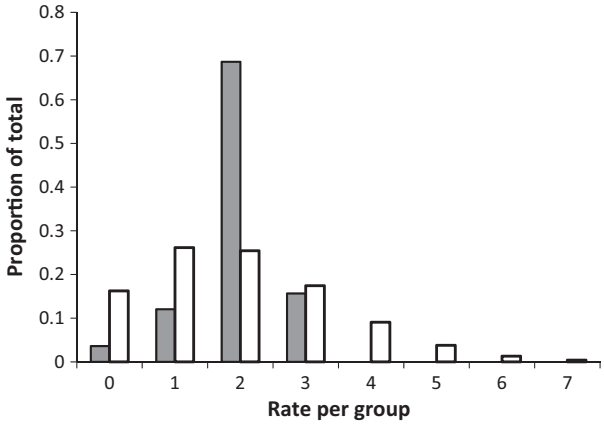

Figure 8 Histograms of the reported (■) and expected (by chance; □) distributions for 83 rates of previous postoperative nausea and vomiting from 26 human trials (Appendix S1; references the same as the studies in Table 6). The reported distribution was different from the expected, $p = 4.0 \times 10^{-7}$. The point of interest is the narrower width of the distribution of reported data and the height of the bars in the centre of the distribution (that suggests clustering) of the reported data vs the expected.

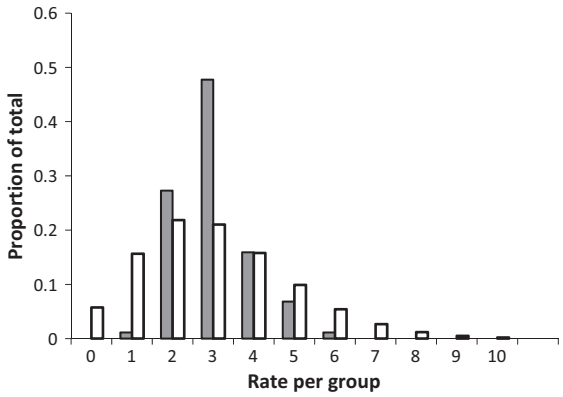

Figure 9 Histograms of the reported (■) and expected (by chance; □) distributions for 88 rates of motion sickness from 28 human trials (Appendix S1; references the same as the studies in Table 6). The reported distribution was different from the expected, $p = 1.0 \times 10^{-4}$. The point of interest is the narrower width of the distribution of reported data and the height of the bars at the centre of the distribution (that suggests clustering) of the reported data vs expected.

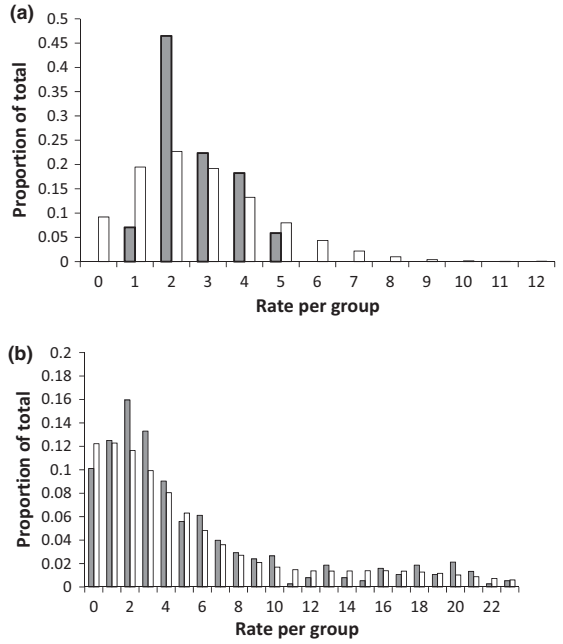

Figure 10 Histograms of the reported (■) and expected (by chance; □) distributions for headache in studies of postoperative nausea and vomiting by (a) Fujii et al. (Appendix S1; available online; references the same as the studies in Table 9) and (b) other authors (Appendix S1; references 1–126). The reported distribution was different from the expected for studies by Fujii et al. ($p = 1.4 \times 10^{-11}$), but was not different for those by other authors, $p = 0.81$.

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Table 10 Number of reported rates for three postoperative categorical variables in 142 human studies by Fujii et al. and 145 other RCTs. The adjusted p value quantifies the chance that the reported distribution was consistent with the expected distribution, which was unlikely for weight, age and height in RCTs by Fujii et al. Appendix S6 is available online.

Variable	Authors	Groups reporting rates	Standardised SD of means	p value	Studies
Weight	Fujii et al.	438	0.551	$< 10^{-33}$	See Table 5
Weight	Other authors	359	1.06	0.13	See Appendix S6
Age	Fujii et al.	414	0.567	$< 10^{-33}$	See Table 5
Age	Other authors	556	1.04	0.14	See Appendix S6
Height	Fujii et al.	447	0.620	$< 10^{-33}$	See Table 5
Height	Other authors	146	0.93	0.24	See Appendix S6

Table 11 Number of reported means for nine continuous variables in 26 canine studies by Fujii et al. (study numbers refer to Appendix S1). The adjusted p value quantifies the chance that the reported distribution was consistent with the expected distribution.

	Groups reporting means with SDs	Standardised SD of means (expected 1)	p value	Studies
Right atrial pressure	87	0	$< 10^{-33}$	124, 126–8, 130–2, 140–1, 147–6
Transdiaphragmatic pressure at 100 Hz stimulation	118	0.203	$< 10^{-33}$	124–137, 140–1, 144–6, 148–9
Pulmonary artery occlusion pressure	56	0.351	$< 10^{-33}$	127–9, 131–2, 143, 145–6
Heart rate	108	0.330	1.6×10^{-11}	124–137, 140–1, 143–8
Transdiaphragmatic pressure at 20 Hz stimulation	77	0.178	$< 10^{-33}$	124–137, 140–1, 144–6, 148–9
Mean pulmonary arterial pressure	69	0.389	4.6×10^{-15}	126–8, 130–2, 140–1, 143, 145–7
Mean arterial pressure	107	0.482	1.6×10^{-8}	124–141, 143–8
Cardiac output	62	0.511	9.5×10^{-3}	126–8, 130–2, 138, 143, 145–6
Pulmonary capillary wedge pressure	18	0.775	0.42	126, 140–1

(thick black and red lines, respectively, in Fig. 14). Artificially increasing the variance by 9% of the 1520 values from RCTs of authors other than Fujii resulted in a cumulative distribution that was as expected (making the line in Fig. 14 horizontal; not shown). This suggested that a degree of clustering was likely when combining different trials (see Discussion); however, adjustment little affected Fujii's data.

Discussion

There is no 'correct' or singular statistical method to detect if data follow highly unusual distributions. Using the methods I have employed, my main conclusion is that the distribution of variables reported by Fujii et al. in the trials analysed varied less than expected by chance. Scientific notation might not convey how unlikely it is that natural processes could account for these distributions. In Table 7, for example, a p value of $< 10^{-33}$ is a probability of fewer than one in a decillion (or 1 in 1 000 000 000 000 000 000 000 000 000 000 000), the chance of selecting one particular atom from all the human bodies on earth. It is also striking that when the results of several trials are combined, the reported distributions for Fujii increasingly depart from the expected, whereas those for other authors do so relatively little (and can be corrected by modest adjustment; Fig. 14).

In my analysis, I did not impose any external theoretical distribution upon the data that was not already a necessary consequence of the data embedded within these RCTs. The single assumption common to calculating the expected variation, for both continuous and categorical variables, was that the study groups represented subjects sampled randomly from the same population. A well-designed RCT should ensure random distribution of variables measured before intervention, including age, weight, height, sex, chronic medications, a history of PONV or motion sickness, LMP and

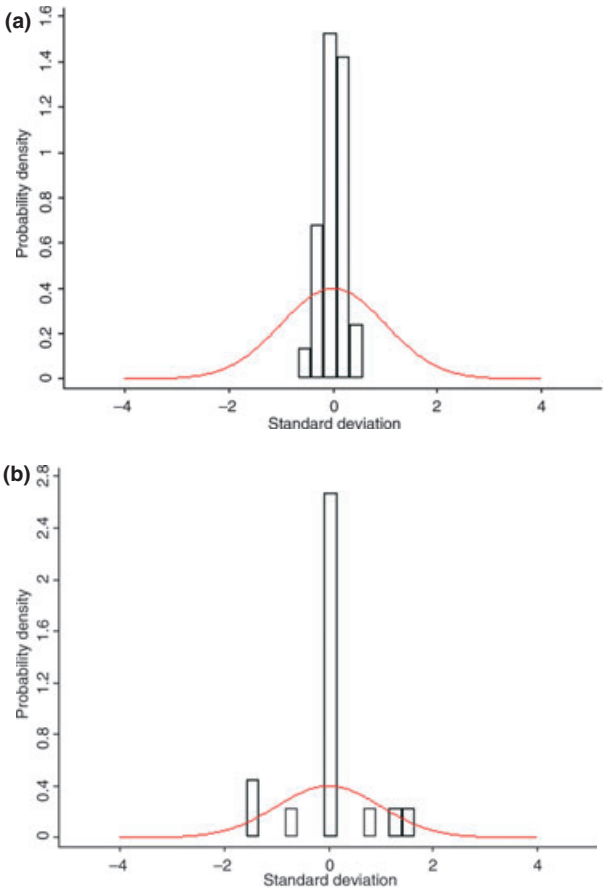

Figure 11 Histograms of the distributions of standardised mean differences for two continuous variables in canine studies by Fujii et al.: (a) transdiaphragmatic pressure at 100 Hz stimulation, $p < 10^{-33}$ (Appendix S1; references 124–137, 140–1, 144–6 and 148–9); and (b) pulmonary capillary wedge pressure, p = 0.42 (Appendix S1; references 126 and 140–1). The width of each bar is 0.25 SD. The red line is the expected standard normal distribution. The point of interest in the Fujii studies is the abundance of standardised mean differences around zero (above the red curve) and their paucity to either side (i.e. the bars on either side do not extend along the *x*-axis to meet the limits of the red curve).

gestation. However, *after* the groups have been exposed to allocated interventions – placebo, drugs and so on – one cannot assume that the distribution of the data from the groups will be the same. One might therefore conclude that comparison of reported vs theoretical distributions is invalid for some of the variables reported here, including side effects such as drowsiness, dizziness and headache, the last of which aroused Kranke et al.'s suspicion [1]. For instance, a group given granisetron might report more headaches than a group given saline. One does not know whether these different rates represent chance variation (sampling from a single population rate) or an effect of granisetron (sampling from two different population rates). One therefore does not know what distribution to expect. However, not only were the rates of these side effects reported by Fujii et al. consistent with sampling from a single population, they were so invariant that they were inconsistent with the variation one would expect to arise by chance.

There are two types of probabilities that one can calculate for the distributions of binomial characteristics: (i) the probability of observing a particular rate of occurrence of an event; and (ii) the probability that a particular rate is consistent with the expected rate. Kranke et al. calculated the first type of probability, whereas I have calculated the second type. The problem with calculating the first, the probability of a specific rate, is interpreting what it means – because any single rate is very unlikely. For example, when rolling two dice, the chance of throwing a 5 and a 2 is exactly the same as the chance of throwing any other combination of two numbers; but the chance of throwing a total of 7 is higher (18%) than for other sums (because it can be attained by more combinations than for other totals), hence the need to study 'distributions' (which, in this analogy, would be the respective incidences of the sum of two dice-throws from 2 to 12) rather than just 'chance of occurrence'. As with rolling dice, the single most likely distribution of 18/270 headaches in one group of 45 women is 3/45, a probability of 0.23, or 1 in 4. Fujii et al. reported this rate in 6/6 groups (reference 1; Appendix S1); the probability of obtaining this precise distribution in this study is 0.23^6, or 1 in 6800. Kranke et al. combined such probabilities across 18 RCTs to estimate a 1 in 147 million chance that 10 of them would report the same headache rate in all groups. However, the starting point for this calculation was that there is something special about equal rates of headache in all groups. A homogenous distribution (such as 3/45 people having headache in all six groups) is not the most likely distribution but it is also not the least likely, which would be all 18 headaches in one group. Indeed, six groups each with 3/45 headaches is a distribution that has borderline probability, given the expected

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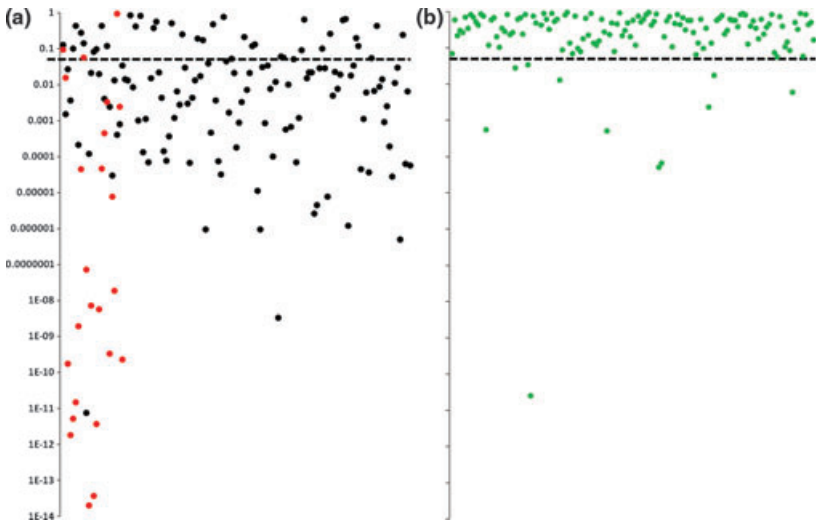

Figure 12 Plot of p values that the reported distribution was consistent with the expected distribution (adjusted). The p values (*y*-axis, log scale) are for (a): Fujii's human RCTs (●) and animal RCTs (●) and (b): the RCTs of other authors (●). The horizontal grey dotted line represents p = 0.05. The point of interest is that whereas only 12 trials from other authors have p values strikingly less than p < 0.05 (panel (b), below the horizontal dotted line), a very large number of Fujii studies do so (including the majority of animal studies).

Table 12 Distributions of adjusted p values arising from testing the null hypothesis that the variance of continuous variable means in individual randomised controlled trials by Fujii et al. (that reported mean and SD for at least two continuous variables) was as expected (sdtest; see Appendix A). Values are number (proportion).

	p < 0.00001	p < 0.001	p < 0.01	p < 0.05	p > 0.049
Human studies (n = 135)	9 (7%)	30 (22%)	27 (20%)	31 (23%)	38 (28%)
Animal studies (n = 24)	15 (62%)	3 (13%)	2 (8%)	1 (4%)	3 (13%)

p values from individual studies are shown in Fig. 12a.

distribution for this study (p is around 0.05, or 1 in 20). A likelihood of 1 in 147 million probably underestimates the chance of 10/18 RCTs' reporting the same rates in all groups, whereas the value I calculated for all the distributions in these 18 RCTs, of 1 in 5650, might well overestimate the chance of this distribution. I calculated the expected rate of a binomial variable from the observed rate. This mathematically couples the expected distribution to the observed distribution, making the comparison less likely to identify differences. In such a conservative analysis, any significant result therefore more robustly implies substantial disparity between the expected and reported distributions. Fujii et al. continued to publish RCTs that included headache rates after Kranke et al.'s letter was published [1]. In addition, I calculated the probability of any reported distribution occurring, rather than limiting the analysis to homogenous distributions. The final probability that the difference between the reported and expected distributions arose by chance was 1 in 71 billion (Table 9).

I have previously mentioned that a graph of sample means will cluster around the population mean, shaped in a normal curve. Two characteristics of the samples determine the width or spread of this curve: the sample size and the variability of the measurements. Less variable measurements (smaller standard deviation) and more measurements will result in less variable means that, in turn, populate a narrower graph of means. The standard deviation in a sample and the sample size should make the calculated width of this

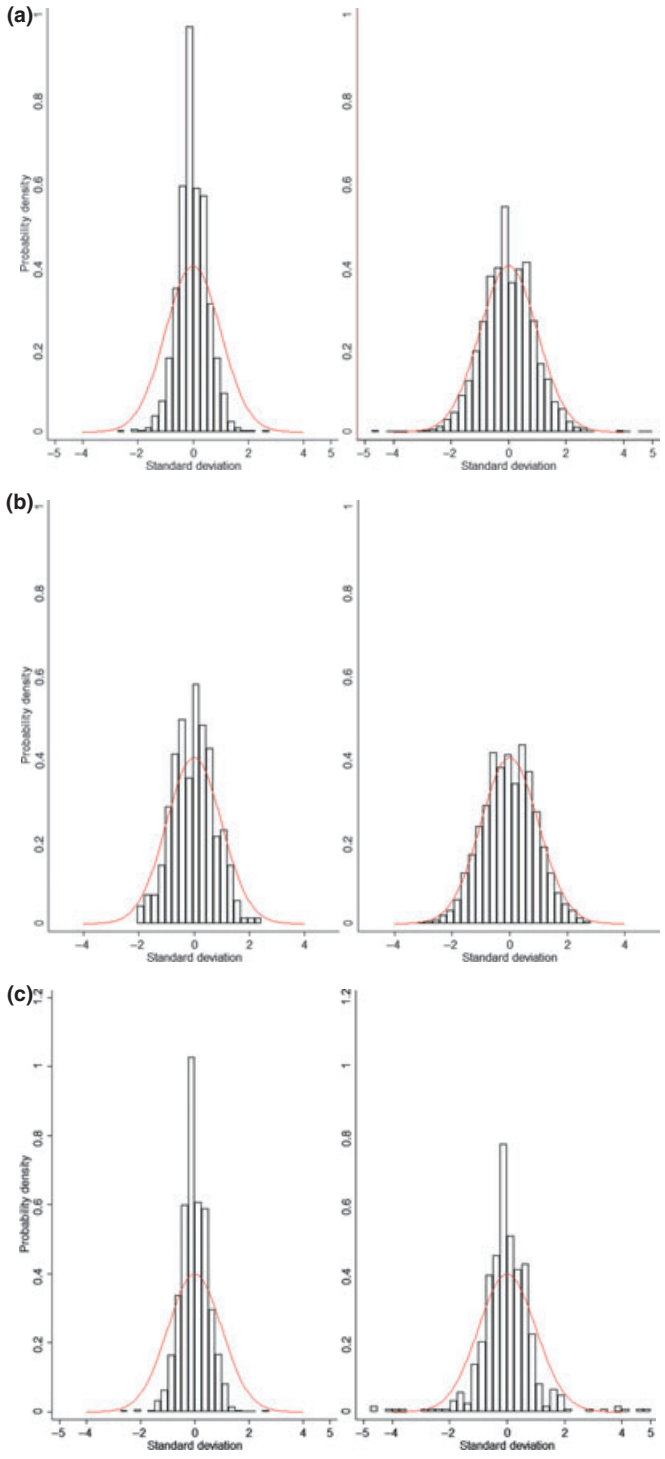

Figure 13 Histograms of the distributions of standardised mean differences for RCTs by Fujii et al. (left) and by others (right): (a) including values from all RCTs (2556 by Fujii et al., 2015 by others); (b) including values from only those RCTs that demonstrated the least aberrant distributions (284 by Fujii et al., 1520 by others); (c) including values only from those RCTs with the most aberrant distributions (2272 by Fujii et al., 495 by others). The width of each bar is 0.25 SD. The red line is the expected standard normal distribution. The point of interest in all the Fujii studies is the abundance of standardised mean differences around zero (above the red curve) and their paucity to either side (i.e. the bars on either side do not extend along the *x*-axis to meet the limits of the red curve).

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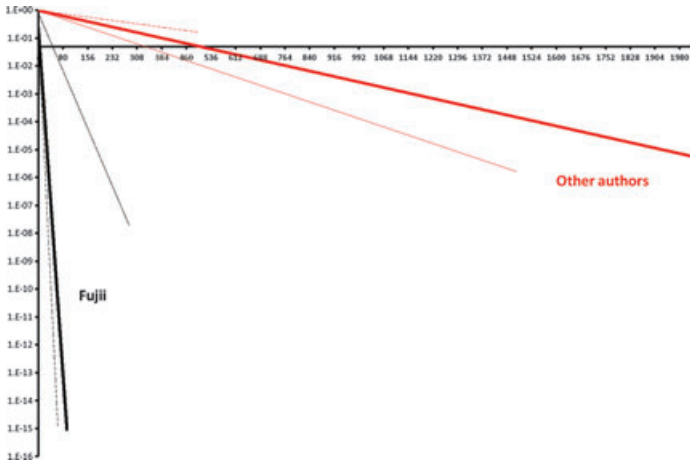

Figure 14 Decreasing probabilities of the reported distributions occurring by chance as more continuous data are analysed. The horizontal axis is the number of standardised mean differences analysed. The vertical axis (exponential scale) is the probability that the analysed distribution is consistent with the expected, where 1.E-02 is 1×10^{-2} or 1 in 100. Black lines are generated from RCTs reported by Fujii et al., red lines are for other RCTs. Thick lines are from all human RCTs (corresponding to Fig. 13a), thin lines are using values from RCTs with the least aberrant distributions (corresponding to Fig. 13b) and broken lines are using values from RCTs with the most aberrant distributions (corresponding to Fig. 13c). The thick and dotted black lines for Fujii et al. have been curtailed and actually extend to a value of $< 1 \times 10^{-600}$.

graph, or SEM, inextricably linked with the spread of the reported means. Just as Fujii et al.'s group rates for binomial variables clustered around the population rate, so too did their group means cluster abnormally tightly around the population mean. However, it is important to recognise that if the mean values are reported insufficiently precisely, artefact may be introduced, itself causing the reported distribution of means to cluster more tightly around the population mean than expected. This is most clearly demonstrated when the SEM calculated for each group is smaller than the precision to which the mean is reported, for instance, if mean height is reported to the nearest centimetre and the SEM is reported as 0.3 cm. In Fujii et al.'s data, the only human continuous variable reported for which this problem increased clustering during analysis was last LMP (Fig. 5). This problem was of particular concern for 46 of 56 groups in which the mean LMP was reported to the nearest day (mean (SEM) 16 (0.52) days in all groups). If means between 15.1 and 16.9 in these 46 groups were rounded up and reported as 16, one would have expected 2/46 means to have been $\leq$ 15 days and 2/46 to have been $\geq$ 17 days; if mean LMPs > 16.5 were rounded up to 17 and those < 15.5 were rounded down to 15, one would have expected about 8/46 means to have been $\leq$ 15 days and 8/46 to have been $\geq$ 17 days. In the first scenario, reporting 46 out of 46 means as 16 days has a probability of 0.17 of occurring by chance and in the second scenario, a probability of 2.5×10^{-6}, 1 in 400 000.

Reported LMP might also cluster because of women's preference to report particular values. However, this cannot explain the results in the animal studies. In RCTs of dog diaphragmatic function, the mean value for right atrial pressure (RAP) in all 87 groups was 5 mmHg. With an average SEM of 0.56 mmHg, one would have expected some RAPs to be 4 or 6. If any RAP mean between 4.1 and 5.9 mmHg was reported as 5 mmHg, one would have expected 9/87 means to have been either 4 or 6 mmHg. If mean RAPs > 5.5 mmHg were rounded up to 6 mmHg, and those < 4.5 mmHg were rounded down to 4 mmHg, one would have expected 32/87 means to have been 4 or 6 mmHg. The probabilities that 87 of 87 means would be 5 mmHg are 1 in 300 in the first scenario and 1 in 72 billion in the second scenario.

The combination of values from RCTs that individually had distributions close to the expected led to abnormal clustering after 50 Fujii values and after 333 values from other RCTs (Fig. 14). This finding might be

because there was something wrong with the values or something wrong with the analysis, or both. Multiplication by 1.09 of the 1520 values from 117 other RCTs with the least aberrant distributions increased their variance and prevented this clustering, whilst multiplication by 1.30 was needed to normalise the 285 values from the 19 Fujii RCTs with the least aberrant distributions. Summation of values (both from Fujii's and other authors' trials) might be revealing aberrant distributions that remain undetected when RCTs are analysed individually, in much the same way that a meta-analysis can identify an effect that is undetected by single underpowered RCTs. By far the majority of RCTs by Fujii et al. remain aberrant despite attempts to correct them and the overall steepness of the lines in Fig. 14 provide a statistical index of suspicion that the data are aberrant.

It is usual to modify or correct analyses of means, medians or rates when tests are not independent. In this paper, there are two sources of correlated variables: those that are biologically associated, such as age, sex, height and weight; and those that are constrained by another analysed variable, such as surgical times being necessarily less than anaesthetic time. I have adjusted the analyses for continuous variables in this paper, but not as a consequence of this concern. The analyses of categorical data were conservative for the reasons I have stated, therefore I did not adjust these further.

In conclusion, I have shown that the distributions of continuous and categorical variables reported in Fujii's papers, both human and animal, are extremely unlikely to have arisen by chance and if so, in many cases with likelihoods that are infinitesimally small. Whether the raw data from any of these studies can be analysed, and whether this might provide an innocent explanation of such results [4], is beyond the scope of this paper. Until such a time that these results can be explained, it is essential that all Fujii et al.'s data are excluded from meta-analyses or reviews of the relevant fields. The techniques explored in this paper offer a method of assessing data integrity in RCTs published by other authors, for instance within systematic reviews by the Cochrane Collaboration.

Competing interests

No external funding and no competing interests declared.

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Appendix A
Method of generation of expected categorical and continuous distributions and their subsequent statistical analysis

I have generalised the analysis of binomial variables, from the specific assessment of equal incidences in study groups to a general comparison of the expected incidences with reported incidences. I have also analysed the distribution of continuous variables, such as height. The central limit theorem applies to the mean values of samples taken repeatedly from the same population. The mean sample values ($\bar{m}$) consequently follow a normal distribution around the mean of the population μ from which the samples were taken. Subtraction of the sample means from the population mean will produce a normal curve of values with a mean of zero. The standard deviation (SD) of this curve is estimated by the SEM of the samples used to construct the curve. The SEM is calculated from the SD of any of the sample SDs and the size of the sample (n):

$$\mathrm{SEM} = \mathrm{SD}/\sqrt{\mathrm{n}}$$

Division of $(\bar{m} - \mu)$ by the SEM will standardise the normal curve so that the distribution of reported mean differences will remain centred on zero, but the SD of the curve should equal one. For example,

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Table 13 Method of calculation.

Variable	Group 1 (n = 24)	Group 2 (n = 23)	Group 3 (n = 23)	Mean
Mean $\bar{m}$	121.1	119.9	117.8	119.6 (μ)
SD	11.5	11.1	10.1	10.9
SEM	2.35	2.31	2.11	2.26
$\bar{m}-\mu$	1.5	0.3	−1.8	0
$(\bar{m}-\mu)/SEM$	0.66	0.13	−0.79	0
Adjusted*	0.72	0.14	−0.86	0

*For the analysis of means in individual RCTs, I increased the variance of the standardised mean differences by an arbitrary factor determined by the standard deviation of the calculated SEMs (SD_{SEM}), divided by the square root of the mean SEM; $(\bar{m}-\mu)/SEM \times (1 + (SD_{SEM}/\sqrt{SEM}))$. In the Table, the standard deviation of the three SEMs (2.35, 2.31, 2.11) is 0.129. The square root of the mean SEM (2.26) is 1.5. Therefore, the adjustment factor is 1 + (0.129/1.5), or 1.086.

Table 13 shows mean (SD) height (in cm) reported in three groups (Appendix 1, reference 2), with calculations of the SEM and standardised mean differences, $(\bar{m} - \mu)/SEM$.

I generated expected binomial distributions in Excel® (v 2007, Microsoft Corp., Redmond, WA, USA).

$$= IF(a > n, 0, BINOMDIST(a, n, p, FALSE)),$$

where a is an integer; n is the number of successes in each group; p is the probability of success (the proportion of participants allocated to the different groups that had a success); FALSE instructs the program not to generate the cumulative probability distribution.

Unlike Kranke et al., I calculated a separate population rate probability 'p' for each RCT rather than assuming that there was a common underlying rate across RCTs. I combined the expected distributions from different studies and compared the summed distribution with that reported.

I used Intercooled STATA® 12 (StataCorp LP, College Station, TX, USA) to test whether the reported-to-expected categorical distributions (Fisher's exact test), and the variances of reported-to-expected standardised distributions, significantly departed from those which would arise from chance (sdtest).

Supporting information

Additional Supporting information may be found with the online version of this article:

Appendix S1 Randomised controlled trials authored by Fujii and colleagues, identified from a literature search between 1991 and July 2011.

Appendix S2 Randomised controlled trials of postoperative nausea and vomiting prophylaxis reporting headache, not authored by Fujii, identified from a literature search between 1991 and July 2011.

Appendix S3 Thirty-one references for RCTs of granisetron, authors other than Fujii.

Appendix S4 One hundred references for RCTs by authors other than Fujii reporting rates of nausea and vomiting with rescue for droperidol, granisetron and metoclopramide.

Appendix S5 Sixty-five references for RCTs by authors other than Fujii reporting rates of side effects in studies of PONV prevention.

Appendix S6 References for weight, age and height in RCTs by authors other than Fujii et al.

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Editorial

Appedix2

On statistical methods to test if sampling in trials is genuinely random

"Man is an orderly animal. He finds it very hard to imitate the disorder of nature." [1].

Humans are not good at identifying randomness: our minds naturally look for patterns, even when there are none. Furthermore, we are poor at creating random data. Famously, as a result of listener complaints, the first iPod 'shuffle function' had to be changed to make it less random, but appear more random to the human ear (see http://electronics.howstuffworks.com/ipod-shuffle2.htm).

Random sampling in research (e.g. by computer- rather than human-generated random numbers) importantly reduces the potential for bias. In this issue of *Anaesthesia*, Carlisle offers persuasive evidence that the sampling upon which the results of Fujii's many published trials are based are so unlikely to arise from chance, that it is appropriate to disregard them from further scientific consideration [2]. The purpose of this commentary is to try to simplify Carlisle's rigorous analysis so that readers might more easily follow his arguments.

Is a coin or set of dice fair?

"…it raises in a sharp and concrete way the question of what is meant by randomness, a question which, I believe, has not been fully worked out." [1].

Carlisle was fundamentally interested in the 'fairness' of the sampling used in Fujii's data. The mathematics evolved from the 16th century, from an interest in gambling where the fundamental question was: are the dice/coins/cards fair? Cardano formally investigated the statistics of gambling in his book *Liber de Ludo Aleae*, and the analysis was continued by Pascal and Fermat, in a famous correspondence that began when advising a mutual gambling friend [3].

Anaesthetists are quite used to statistical testing where, say, two groups are subjected to two different interventions (one of which may be control), and an outcome (e.g. blood pressure (BP)) is assessed using a t-test or nonparametric equivalent to generate a p value. Simply, this indicates the likelihood that the observed BP differences could have arisen from chance; i.e. $p < 0.05$ implies that the observed difference has a 5% probability or less of arising by chance (conventionally regarded as 'significant').

However, Carlisle was *not* interested in this sort of comparison. Rather than assess differences between Fujii's test and control data, or between Fujii's data and the results of other workers, Carlisle instead asked a more subtle question: if we confine our analysis solely to data within Fujii's samples (and particularly the control samples), how likely is it that their reported distributions could have arisen by chance? (Separately within the paper he also asked this of other authors). For example, were the relative proportions of males and females, the incidence of nausea/vomiting, etc, those that would be expected? To answer this entirely different question, Carlisle did not perform a statistical comparison of one experimental dataset versus another but rather, a comparison of the experimental results (in absence of any intervention) with those that *would be expected by chance*.

But how can we predict what chance can produce? We may be tempted to think that any pattern is possible but in fact, chance produces remarkably predictable outcomes in the long run. Carlisle used methods that parallel those described long ago by the biologist JBS Haldane (son of the Oxford physiologist JS Haldane) in two letters to *Nature*, describing his analysis of suspicious data [1, 4, 5]. Haldane, like Carlisle, drew back from an accusation of fraud, but likened the chance to a monkey

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typing out Hamlet by sheer luck. The p values found by Carlisle and Haldane are similar.

There are broadly two types of data in question: categorical, grouped into distinct types (e.g. male/female or headache/no headache); and continuous, having any value within a scale (e.g. BP, in mmHg).

We can try to understand the expected-by-chance distributions of categorical data by using much simpler analogies of tossing coins or throwing dice. For both, the results can only have fixed values of heads/tails or the numbers on the dice, but no value in between. Unsurprisingly, the probability of obtaining a certain value when throwing a single six-sided die is ~16% (Fig. 1) but this is only the *average* expectation. The variance (V), i.e. the degree of departure from expected (or SD, which is $\sqrt{V}$), becomes smaller as the number of throws increases (Fig. 1). This is described by a mathematical function known as the binomial probability distribution (which applies to any case of independent events where there are only two possible outcomes; here, throwing a six on a die vs not throwing a six). If the number of throws is n and the probability of the event is p, then the mean rate (μ) of the event (in this case throwing a six) happening is given by:

$$\mu = n.p \qquad (1)$$

In this case, μ is 16/100 throws, 32/200 throws, etc. The SD of this (which can be proved mathematically for the binomial distribution) is given by:

$$\mathrm{SD} = \sqrt{n\,p(1-p)} \qquad (2)$$

Therefore for 60 throws, the mean (SD) number of sixes should be ~10 (3), for 100 throws it is ~16 (4), for 1000 throws, it will be ~160 (12), and so on. Readers should see that, because we now have a *variance* (or SD), we can use this to assess statistically the departures of any actual data from what is expected (I will not detail the calculations here). Thus if a friend offers a die that results in 30 sixes in 100 throws, we can use statistical testing (using the principles of variation above) to assess its fairness (the actual chance of this is $p < 0.005$; Fig. 1). Incidentally, another approach that can be applied to all the numbers thrown is to use the chi-squared test; this yields the same result.

When throwing *two* dice, the plot of possible totals now resembles something readily recognisable

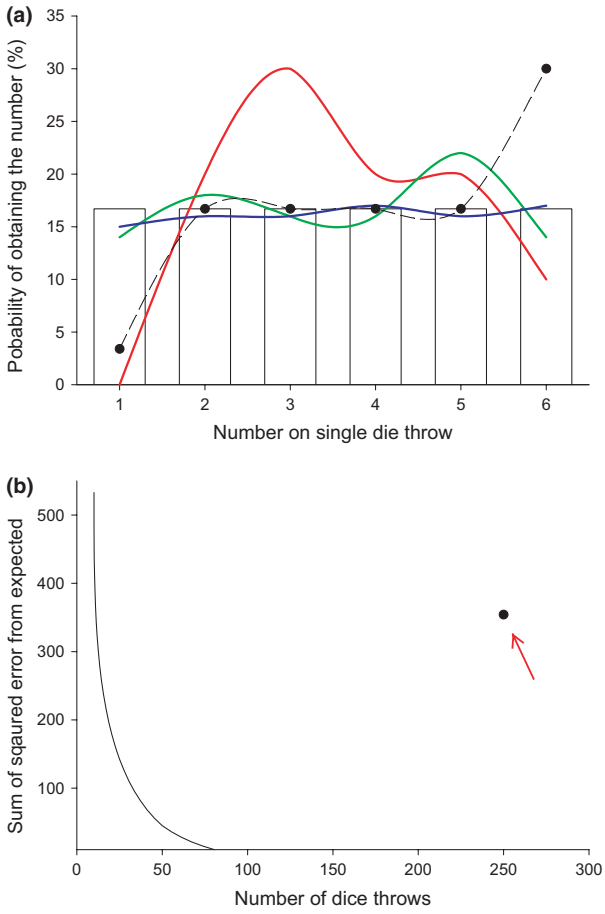

Figure 1 (a) Representation of the average expected probability (bars) of throwing the number (on x-axis) with a single die. The results of simulations throwing a single die 10 (—), 50 (—) and 250 (—) times are plotted (for clarity) as lines, with the dots (– –) representing a slightly loaded die thrown 250 times. (b) Plot of the sum of squared errors for the number of dice throws, showing that with increasing throws, the result gets closer to the expected, becoming a trivial difference after ~50 throws. The single dot (with arrow) shows the sum of squared error for the loaded die (which has a similar sum of squared error as the red line in panel A, but after 250 throws rather than just 10).

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as a normal (Gaussian) distribution for continuous data, with 7 being the most likely total as it arises from most combinations (Fig. 2). If our friend's dice deviate from this overall pattern (Fig. 2), we know exactly how to calculate the probability of that result (this is the basis of the t-test or other tests using variances to compare datasets). Readers might compare the general forms in Fig. 2 with figures 2–10 and 13 in Carlisle's paper [2].

Similar considerations apply with coin throwing. With one coin, the probability of a head (H) or tail (T) is 1:1. With two coins, the ratio of HH, HT, TT is 1:2:1. With three coins, the ratio of 3H, 2HT, 2TH, 3T is 1:3:3:1, and so on. These ratios can be arranged to the pattern commonly known as Pascal's triangle (Fig. 3), which is also obtained by a mathematical function known as the binomial expansion (a term used in Carlisle's paper [2]). This is mathematically related to the binomial probability distribution described above. It is possible to expand any power of $x + y$, denoted $(x + y)^n$, into an expression with a general form (Box 1).

Box 1

$$(x+y)^2 = x^2 + \mathbf{2}xy + y^2 \quad (3)$$

$$(x+y)^3 = {}^3 + \mathbf{3}x^2y + \mathbf{3}xy^2 + y^3 \quad (4)$$

$$(x+y)^4 = x^4 + \mathbf{4}x^3y + \mathbf{6}x^2y^2 + \mathbf{4}xy^3 + y^4 \quad (5)$$

and so on. The coefficients (the bold numbers) form the numbers in Pascal's triangle and are useful as shortcuts in probability calculations. For example, the answer to: 'what is the chance of getting exactly 2 heads with 3 coin tosses?' is obtained by looking at the 3rd row of the triangle, 2nd position along. The sum of numbers (indicating the total possible results (Fig. 3 and Equation 4) is 8, so that chance is 3/8, or ~37.5%. To summarise: binomial probabilities can be described mathematically, in a manner linked to Pascal's triangle, which is in turn a useful shortcut to the calculation of those probabilities.

Superficially, there seems one limitation to applying these examples of coins and dice to real life: we know in advance the precise probability of their average outcomes. How can we know in advance how many headaches there should be in any group of people? The answer is that we don't, but then we don't need to. Instead, we can look for how symptoms like headaches (or other

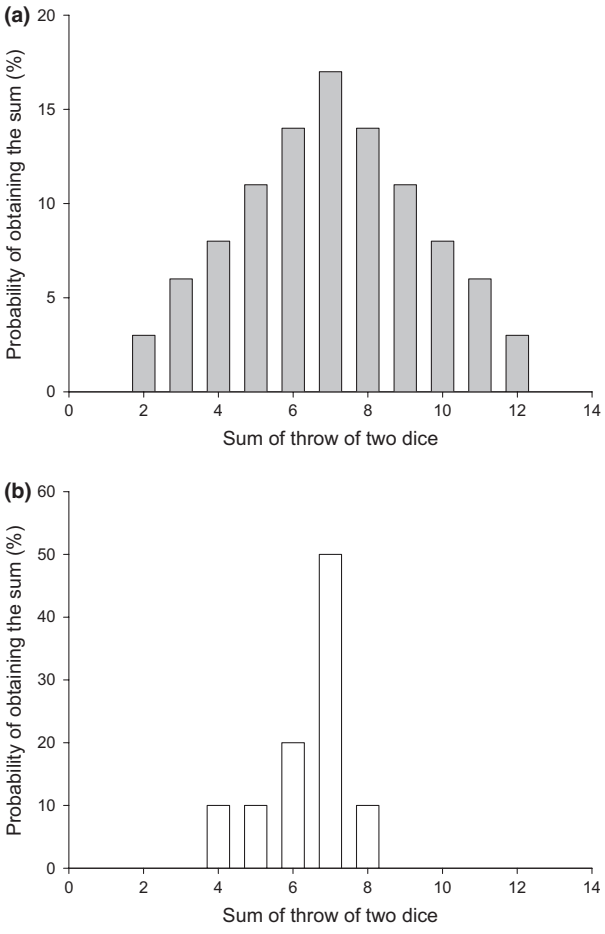

Figure 2 (a) Simulation of the ideal sums of throwing two dice 100 times, resembling a normal (Gaussian) distribution. (b) The simulated sum of throwing a slightly loaded dice 100 times, where only the sums 4–8 appear.

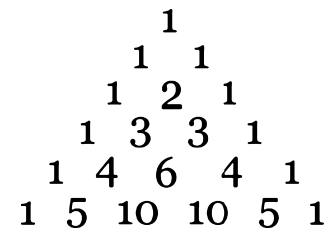

Figure 3 Pascal's triangle. By convention the 1st row (containing only 1) is called row zero.

binomial factors like sex, etc) are *distributed* across randomly selected groups. If 100 women are randomly divided between two groups, we expect there to be 50 women in each group on average (but not precisely; SD = 5 by Equation 2). If the baseline incidence of headache is 10%, then in a group of 100 people there should be 10 headaches on average (but not exactly; SD = 3 by Equation 2). Therefore, the analyses do, in fact, resemble coin tossing. Reported distributions for such things can then be unusual in two ways. First, because they are *more aberrant* than expected (as in our friend's single slightly-loaded die, Fig. 1) or second, because they are *less variable* than expected (as in the friend's two slightly-loaded dice in Fig. 2). Either way, we can calculate (using the mathematics of binomial distribution) a p value for the difference between actual and expected distributions. In short: if we tried to fabricate a dataset, we would find it easy to approximate expected mean values, but very difficult to reproduce the expected variation in values, especially across a range of datasets and especially for binomial data.

Carlisle also uses the notion of 'central limit theorem' in his analysis of continuous data. Variously expressed, this has several important consequences for large datasets. First, the theorem states that when we take multiple samples from a population and measure a characteristic of interest, then a histogram of the sample means resembles ever closer a normal distribution with an increasing number of samples, *even if the histogram of the actual population is not normally distributed*. This is a surprising but very fundamental and robustly proven principle of statistics (Fig. 4). Another aspect of the theorem is that as the number of samples increases, not only does the mean of all the samples ever more closely approximate the population mean, but its variance (known technically as the standard error of the mean) becomes smaller in a precise way. All this is important because while any single random sample may differ greatly from another random sample, combining their means should follow the predictions of central limit theorem. What Carlisle found for Fujii's data is that even when the 'less unusual' data from trials were sequentially combined, the results became *more*, rather than *less*, deviant from expected distributions (see the dotted black line in Fig. 14 of Carlisle's paper [2]).

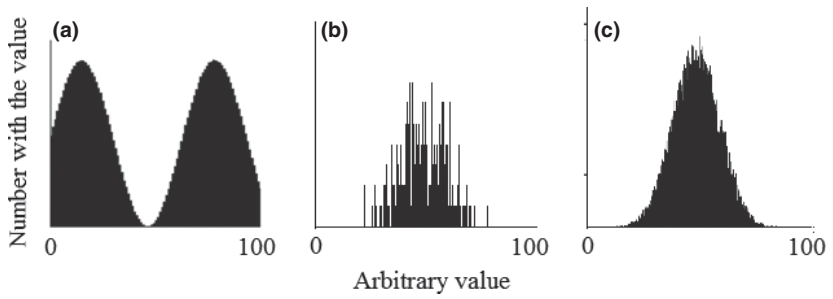

Figure 4 Demonstration of central limit theorem. The underlying distribution of this characteristic (arbitrary units, x-axis) resembles a sine wave (a), where there are a very large number of data points (> 200 000). Repeated random sampling of 100 values 100 times from this population of points (b) and 100 values 10 000 times (c), and plotting the means of these sample values, yields a pattern ever closer to a normal distribution. Readers can check other distributions at: http://elonen.iki.fi/articles/centrallimit/index.en.html#demo.

Does biological variation matter?

> *"In genetical work also, duplicates rarely agree unless they are faked."* [1].

One potential defence of an unusually-distributed dataset is that the vagaries of biology cause it to be so: patients can be odd or respond strangely. Yet even biology shows certain mathematically predictable patterns and statistical analysis can counter this 'biological defence' of unusual data in at least two ways.

The first rests upon an observation developed by GH Hardy. Many traits are strongly determined by genetic factors, and some are determined by 'dominant' alleles. It might be predicted that this would cause the population characteristic to gravitate towards the dominant trait over succeeding generations, resulting in ever narrower variations in human phenotype. But in contrast it is clear that the overall variation in many characteristics (e.g. height, weight) within a population remains constant (and often Gaussian) from one generation to the next. How can the constancy of Gaussian distribution be reconciled with a dominant effect of

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certain alleles? The answer is in part explained by the Hardy-Weinberg Law, which I have discussed before [6]. According to the Law, allele distributions are fixed for all generations (given conditions such as random mating and no breeder selection). For a characteristic governed only by two alleles, the relative proportions of homozygote recessives (*pp*), heterozygotes (*pq*) and homozygote dominants (*qq*) follow the distribution p^2:2*pq*:q^2. These are (as Hardy well knew) the same proportions that describe the outcome of tossing two coins, represented by a binomial distribution (Equation 3, above, whose coefficients also correspond to the 2nd line of Pascal's triangle – 1:2:1). Thus for binary characteristics, distributions should follow the proportions predicted by the Hardy-Weinberg Law, and any other proportions reported by an author must be regarded as unusual. Furthermore, Fisher extended this argument to multi-allele traits [7, 8] to show that where a large number of alleles made a small contribution to a continuous trait (e.g. height), the trait (i.e. phenotype in the population) would be normally distributed but each of the allele pairs would nonetheless follow the Hardy-Weinberg equilibrium (Fig. 5). Therefore, it we wished to fabricate a dataset, we would face the difficult task of ensuring that the phenotype distribution in the population was Gaussian, but that the corresponding allele distributions in our invented data (if later discoverable from the information provided) conformed to the predictions of the Hardy-Weinberg Law (adapted for multiple alleles). This is easy for nature, but not so easy for us. Carlisle

(a)

	h^+	$2h^0$	h^-
h^+	h^+h^+ 72 cm	$2(h^+h^0)$ 70 cm	h^+h^- 68 cm
$2h^0$	$2(h^0h^+)$ 70 cm	$4(h^+h^0)$ 68 cm	$2(h^0h^-)$ 66 cm
h^-	h^-h^+ 68 cm	$2(h^0h^+)$ 66 cm	h^-h^- 64 cm

(b)

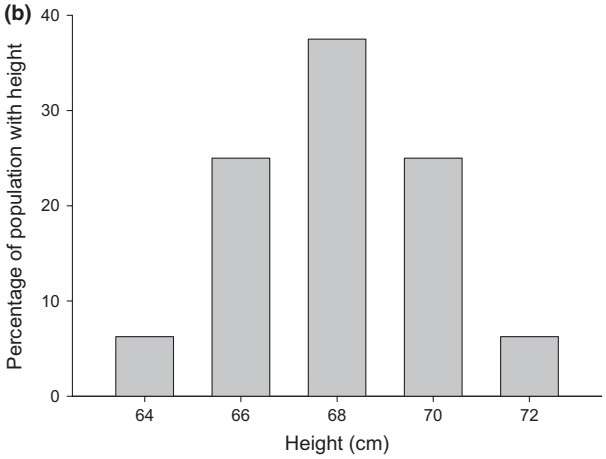

Figure 5 Fisher's argument to demonstrate how a normal distribution in phenotype can arise even when alleles follow the proportions predicted by Hardy-Weinberg equilibrium (for multiple alleles). Suppose three alleles determine height (average 68 cm): h^0 (neutral), h^+ (which adds 2 cm) and h^- (which subtracts 2 cm); h^0 is twice as frequent than the others, which are equally frequent. (a): Punnett square for the population (explained in ref [6], where the characters in bold represent the gametes that combine) with the relative resulting proportions. (b): the histogram of the resulting heights in the population resembling a normal distribution. Adding more loci to the model results in an even smoother histogram.

did not analyse Fujii's data in this way, but the recent discovery of at least one allele associated with postoperative nausea and vomiting (and whose distribution in the population follows Hardy-Weinberg equilibrium) makes possible further analysis of Fujii's voluminous data using these genetic principles [9].

A second reason why it is difficult to invent biology is that many biological traits are themselves inter-related. If we invent one trait then we commit ourselves automatically to inventing several others. Simple examples might be the relationships between height, weight and body mass index, or those between tidal volume, frequency and inspiratory/expiratory time. Other biological traits are exclusive. To adopt the example used by Haldane [1]: suppose three classes of animal have frequencies *p*1, *p*2, *p*3, and the total is 200. If we invent the ratios 50 *p*1 and 40 *p*2 to satisfy the conclusion we wish to reach, in *p*3 (perhaps of no imme-

diate interest) *has* to be 110. Yet, a different value may be needed to satisfy other biological ratios and interactions.

Conclusions

> *"For a successful technology, reality must take precedence over public relations, for nature cannot be fooled."* [11].

Those wishing to invent data have a hard task. They must ensure that all the data satisfy several layers of statistical cross-examination. Haldane referred to these as the 'orders of faking' [1]. In his words, 'first-order faking' is to ensure simply that the mean values match what is expected. For his 'second-order faking', things become more difficult since the variances of these means must also be within those expected, and further consistent with several possibly inter-related variables. His 'third-order faking' is extremely difficult because the results must also match several established laws of nature or mathematics, described by patterns like central limit theorem, the Hardy-Weinberg Law, the law of conservation of energy or mass, and so on. It is therefore always so much easier actually to do the experiment than to invent its results.

It is the very motivation to publish so much that is the undoing of those whose work is questioned or retracted. High publication rates are evident in the retracted work of Reuben and Boldt [12], and the sheer volume of data produced by Fujii is astonishing [2]. Toss a coin just twice and if it gives two heads then nobody notices the loading (the chance of this in a fair coin is anyway 25%). But a 100 heads in 100 tosses is probably more than chance (Fig. 1). These high publication rates leave a rich source of data for us to analyse, so that we can learn aberrant patterns and in time, detect much earlier the warning signs. Carlisle is to be congratulated: his is an astonishing, altruistic piece of work that helps expunge the literature of some (at best) highly unusual data.

The purpose of experimentation is to learn about nature. If the results of experiments are not genuine, then however prolific, influential or politically powerful their author, the results will not withstand statistical scrutiny, cannot be repeated, or will lead to models for our understanding of nature that are so bizarre as to be proven false. For nature cannot be fooled.

Competing interests

No external funding or competing interests declared.

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doi: 10.1111/j.1365-2044.2012.07114.x

April 6, 2012

Professor Kuroda, Dean, Toho University
Professor Takamatsu, Dean, Toho University
Professor Igarashi, Director, Tsukuba University Hospital
Professor Tanaka, Chairman, Department of Anesthesiology, University of Tsukuba
Professor Shintani, Director, JA Toride Medical Center
Professor Makita, Chairman, Department of Anesthesiology, JA Toride Medical Center
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Professor Murakawa, Chairman, Department of Anesthesia, Fukushima Medical University
Professor Kagawa, Chairman, Department of Anesthesiology, Hyogo Prefectural Kobe Children's Hospital
Professor Maekawa, Chairman, Department of Anesthesiology and Perioperative Medicine, Kobe University

Re: Investigation into Research by Yoshitaka Fujii

Dear Professors Kuroda, Takamatsu, Igarashi, Tanaka, Shintani, Makita, Miyasaka, Makita, Murakawa, Kagawa, and Maekawa:

The undersigned Editors-in-Chief are grateful to the University of Toho for investigating the studies of Dr Yoshitaka Fujii, and note the announcement of his dismissal (http://www.toho-u.ac.jp/english/Information/march_6_2012.html).

The journal *Anaesthesia* has published a manuscript that appears to present overwhelming evidence that the distributions of many variables reported by Dr Fujii, in 168 published trials conducted under the auspices of your respective institutions, could not have occurred by chance (Carlisle JB, The analysis of 169 randomised controlled trials to test data integrity. Anaesthesia 2012, Epub 8 Mar 2012; http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2044.2012.07128.x/full). A copy of this manuscript follows this letter. While the title of the paper states 169 papers, there is 1 duplicated reference, so the actual number of papers analyzed in the manuscript is 168.

Appendix 1 lists 193 papers published by Dr. Fujii, based on a reconciliation of Appendix 1 in the Carlisle analysis, a comprehensive Medline search, and correspondence among the undersigned Editors-in-Chief. There are 168 papers from the Carlisle analysis, and 25 not included in the Carlisle analysis. Papers <u>not</u> included in the Carlisle analysis are indicated with an asterisk in Appendix 1.

Appendix 2 lists the papers published by Dr. Fujii sorted by the institution under whose auspices the research was conducted. We are turning to you for a determination of the authenticity of those papers listed in Appendix 2 as representing research <u>attributed by Dr. Fujii to your institution</u>.

The undersigned Editors-in-Chief intend to retract manuscripts from their respective journals based on the evidence of fraud demonstrated in the analysis by Carlisle. However, prior to retraction we wish to offer your institution the opportunity to attest to the integrity of any manuscript conducted under the auspices of your institution, as listed in Appendix 2.

For each study listed in Appendix 2 we ask your institution to state the following:

1. that the study occurred as represented in the paper;
2. that you have examined the original research data and have verified that the data are authentic; and
3. that appropriate research ethical approval for the study was obtained.

Our request follows the guidelines published by the Committee on Publication Ethics. Quoting from Wager E, Kleinert S, on behalf of COPE Council. Cooperation between research institutions and journals on research integrity cases: guidance from the Committee on Publication Ethics (COPE):[1]

"*Research and publication misconduct may not be an isolated incident. In many cases, when serious misconduct comes to light, investigation of the researcher's earlier work reveals further problems. Therefore, when a researcher is found to have committed serious misconduct (such as data fabrication, falsification or plagiarism) the institution should review all the individual's publications, including those published before the proven misconduct took place. In such cases, it may be necessary to alert previous employers to enable them to review work carried out by the discredited researcher when working at their institution, to determine the reliability of publications arising from that work.*"

Fraudulent research must be retracted in a timely manner. If we do not hear from you by June 30 2012 we will assume that you do not intend to respond. If you do intend to respond, please provide a timeline for your assessment.

This is not a confidential communication. To provide transparency to our readers, we intend to post this request letter, and your response, on our journal websites.

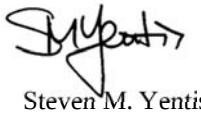
Please direct your response to Dr. Steven Shafer at steven.shafer@stanford.edu.

We appreciate your assistance with this request.

On behalf of our respective journals,

Lars S. Rasmussen
Editor-in-Chief, ***Acta Anaesthesiologica Scandinavica***

[1] http://publicationethics.org/files/Research_institutions_guidelines_final.pdf



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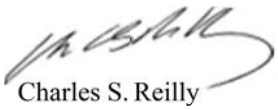
Editor-in-Chief, ***Anaesthesia***

Neville Gibbs
Editor-in-Chief, ***Anaesthesia & Intensive Care***

Masashi Kawamoto
Editor-in-Chief, ***Anesthesia and Resuscitation***

Steven L. Shafer
Editor-in-Chief, ***Anesthesia & Analgesia***



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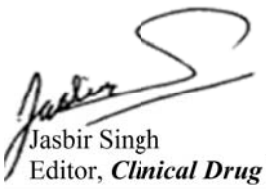
Editor-in-Chief, ***British Journal of Anaesthesia***

Donald R. Miller
Editor-in-Chief, ***Canadian Journal of Anesthesia/Journal canadien d'anesthésie***

Robert Gaiser
Editor-in-Chief, ***Clinical Anesthesia***



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Phil Walson
Editor-in-Chief, ***Clinical Therapeutics***

Martin R. Tramèr
Editor-in-Chief, ***European Journal of Anaesthesiology***

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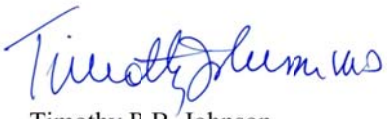
Editor-in-Chief, ***International Journal of Obstetric Anesthesia***



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Editor-in-Chief, ***International Journal of Gynecology and Obstetrics***

Kazuyoshi Hirota
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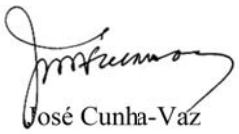

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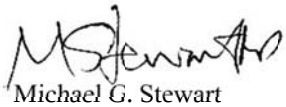

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Appendix5

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
C	1		○	○					麻酔	横隔膜疲労における神経筋伝達不全の関与	大島勉	東京都立広尾病院	藤井善隆	東京医科歯科大学医学部麻酔蘇生学教室	豊岡秀訓	東京医科歯科大学医学部　麻酔蘇生学教室	宇田川友之	東京医科歯科大学医学部　麻酔蘇生学教室	横山訓典	東京医科歯科大学医学部麻酔蘇生学教室	天羽敬祐	東京医科歯科大学医学部麻酔蘇生学教室	1990	犬						
C	2	○		○				○	Journal of Anesthesia	Diaphragmatic fatigue and its recovery are influenced by cardiac output	藤井善隆	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院							1991	犬					20	
C	3		○	○					麻酔	重篤な低心拍出量の横隔膜疲労および回復に及ぼす影響と神経筋伝達不全の関与	藤井善隆	取手協同病院	大島勉	東京医科歯科大学医学部麻酔蘇生学教室	豊岡秀訓	東京医科歯科大学医学部　麻酔蘇生学教室	宇田川友之	東京医科歯科大学医学部　麻酔蘇生学教室	江畑俊哉	東京医科歯科大学医学部麻酔蘇生学教室	天羽敬祐	東京医科歯科大学医学部麻酔蘇生学教室	1991	犬				犬	20	
C	4		○	○					Anesthesia and Resuscitation = 麻酔と蘇生	Prostaglandin E1の横隔膜収縮力に及ぼす影響	藤井善隆	取手協同病院	田中弘彦	取手協同病院									1991	犬	プロスタグランディン				10	
C	5	○		○				○	Canadian Journal of Anesthesia	Dobutamine increases diaphragmatic contractility in dogs	江畑俊哉	東京医科歯科大学医学部附属病院	藤井善隆	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1992	犬					24	
C	6		○	○					Anesthesia and Resuscitation = 麻酔と蘇生	横隔膜収縮力に及ぼすNicardipineの影響	藤井善隆	取手協同病院	田中弘彦	取手協同病院									1992	犬	ニカルジピン				11	
C	7		○	○					Anesthesia and Resuscitation = 麻酔と蘇生	プロスタグランジンE1の呼吸因子−1回換気量,分時換気量−に及ぼす影響	藤井善隆	取手協同病院	田中弘彦	取手協同病院									1992	呼吸	プロスタグランディン			外科 耳科		30
C	8	○		○				○	Canadian Journal of Anesthesia	Contractility of fatigued diaphragm is improved by dobutamine	藤井善隆	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院	江畑俊哉	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院					1993	犬					20	
B	9		○	○					麻酔	ドロペリドールの術後制吐効果に対する検討	藤井善隆	取手協同病院	田中弘彦	取手協同病院									1993	PONV	ドロペリドール	メトクロプラシド		婦人科		60
B	10		○	○					麻酔	小児におけるラリンジアルマスクの循環動態と術後咽頭痛,嗄声に及ぼす影響	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部　麻酔蘇生学教室							1993	咽頭痛				小児		40
B	11	○		○			RCTDB	○	Canadian Journal of Anesthesia	Optimal anti-emetic dose of granisetron for preventing postoperative nausea and vomiting	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1994	PONV	グラニセトロン			婦人科 大手術		100
B	12	○		○			RCT	○	Canadian Journal of Anesthesia	Reduction of postoperative nausea and vomiting with granisetron	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1994	PONV				婦人科 大手術		60
C	13	○		○				○	Canadian Journal of Anesthesia	Nicardipine enhances diaphragmatic fatigue	藤井善隆	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院							1994	犬					20	
B	14	○		○				○	Journal of Anesthesia	Airway occlusion pressure is an indicator of respiratory depression with isoflurane	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院					1994	気道	イソフルラン			婦人科 大手術		10
C	15	○		○				○	Journal of Anesthesia	Effects of dobutamine on the fatigued diaphragm: A comparison with dopamine	藤井善隆	取手協同病院	宇田川友之	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1994	犬	ドブタミン	ドーパミン			26	
B	16	○		○				○	Anesthesia and Analgesia	Middle cerebral arterial blood flow velocity increases during laparoscopic cholecystectomy.	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Tsuruoka Shin	取手協同病院（脳神	豊岡秀訓	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院			1994	中大脳動脈				胆摘		10
C	17		○	○					Anesthesia and Resuscitation = 麻酔と蘇生	実験的横隔膜疲労におけるニカルジピンの横隔膜収縮力に及ぼす影響	藤井善隆	取手協同病院	田中弘彦	取手協同病院									1994	犬	ニカルジピン				15	
C	18		○	○					日本臨床麻酔学会誌	膝関節鏡手術の麻酔方法に対する検討	藤井善隆		田中弘彦										1994	不要						
B	19	○		○			RCTDB	○	Canadian Journal of Anesthesia	Prevention of postoperative nausea and vomiting with granisetron: a randomised, double-blind comparison with droperidol	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1995	PONV	グラニセトロン			婦人科 大手術		100
B	20	○		○			RCTDB	○	Canadian Journal of Anesthesia	Granisetron-dexamethasone combination reduces postoperative nausea and vomiting	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1995	PONV	グラニセトロン	デキサメサゾン		婦人科 大手術		88
B	21	○		○			RCTDB	○	Canadian Journal of Anesthesia	Circulatory responses to laryngeal mask airway insertion or tracheal intubation in normotensive and hypertensive patients	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1995	挿管反応				全科		46
B	22	○		○				○	Canadian Journal of Anesthesia	Effects of calcium blockers on circulatory response to tracheal intubation in hypertensive patients: nicardipine versus diltiazem	藤井善隆	取手協同病院	田中弘彦	取手協同病院	齋藤祐司	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院					1995	挿管反応				全科		37
C	23	○		○				○	Canadian Journal of Anesthesia	Post-tetanic burst count: a stimulating pattern for profound neuromuscular blockade	齋藤祐司	東京医科歯科大学医学部附属病院	藤井善隆	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院					1995	#N/A	#N/A	#N/A	#N/A	#N/A		
C	24	○		○				○	Canadian Journal of Anesthesia	Amrinone improves contractility of fatigued diaphragm in dogs	藤井善隆	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院							1995	犬					36	
C	25	○		○				○	Journal of Anesthesia	The dose-response relationship of amrinone in increasing the contractility of fatigued diaphragm in dogs	藤井善隆	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院									1995	犬	アムリノン				16	
C	26	○		○				○	Journal of Anesthesia	Effects of nicardipine on diaphragmatic fatigue in the dog: The relationship between dosage and fatigability	藤井善隆	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院									1995	犬	ニカルジピン				24	

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
B	**27**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Antiemetic efficacy of granisetron and metoclopramide in children undergoing ophthalmic or ENT surgery	藤井善隆	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院							1996	PONV	グラニセトロン	メトクロプラマイド		小児斜視・扁摘		70
B	**28**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Granisetron and dexamethasone provide more improved prevention of postoperative emesis than granisetron alone in children	藤井善隆	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1996	PONV	グラニセトロン	デキサメサゾン		小児斜視・扁摘		60
B	**29**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Antiemetic effects of granisetron on postoperative nausea and vomiting in patients with and without motion sickness	藤井善隆	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院							1996	PONV	グラニセトロン			婦人科大手術		110
B	**30**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Granisetron reduces vomiting after strabismus surgery and tonsillectomy in children	藤井善隆	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1996	PONV	グラニセトロン			小児斜視・扁摘		50
B	**31**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Effective dose of granisetron for preventing postoperative emesis in children	藤井善隆	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院							1996	PONV	グラニセトロン			小児斜視・扁摘		80
C	**32**	○		○				○	Anaesthesia and Intensive Care	Intraoperative ventilation with air and oxygen during laparoscopic cholecystectomy decreases the degree of postoperative hypoxaemia	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	東京医科歯科大学医学部附属病院							1996	低酸素				胆摘		30
C	**33**	○		○				○	Journal of Anesthesia	Dibutyryl cyclic AMP increases the contractility of fatigued diaphragm in dogs	藤井善隆	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院							1996	犬	DBCAMP				36	
C	**34**	○		○				○	Journal of Anesthesia	Dobutamine increases contractility of fatigued diaphragm in dogs: The relationship between dose and diaphragmatic contractility	藤井善隆	東京医科歯科大学医学部附属病院	豊岡秀訓	東京医科歯科大学医学部附属病院									1996	犬	ドブタミン				16	
B	**35**	○		○			RCTDB	○	Anesthesia and Analgesia	The effects of dexamethasone on antiemetics in female patients undergoing gynecologic surgery	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1997	PONV	デキサメサゾン			婦人科大手術		270
B	**36**	○		○			RCTDB	○	Acta Anaesthesiologica Scandinavica	Granisetron reduces incidence of nausea and vomiting after breast surgery	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1997	PONV	グラニセトロン			乳がん		50
B	**37**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Prevention of PONV with granisetron, droperidol and metoclopramide in female patients with history of motion sickness	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院							1997	PONV	グラニセトロン	ドロペリドール	メトクロプラマイド	婦人科大手術		120
B	**38**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Prophylactic antiemetic efficacy of granisetron in patients with and without previous postoperative emesis	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1997	PONV	グラニセトロン			婦人科大手術		90
B	**39**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Granisetron reduces postoperative nausea and vomiting throughout menstrual cycle	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1997	PONV	グラニセトロン			婦人科大手術		120
B	**40**	○		○			RCTDB	○	Acta Anaesthesiologica Scandinavica	Effective dose of granisetron in the reduction of nausea and vomiting after breast surgery	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1997	PONV	グラニセトロン			乳がん		120
B	**41**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Granisetron reduces the incidence and severity of nausea and vomiting after laparoscopic cholecystectomy	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1997	PONV	グラニセトロン			胆摘		80
B	**42**	○		○			RCTDB	○	British Journal of Anaesthesia	Granisetron reduces the incidence of nausea and vomiting after middle ear surgery	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院							1997	PONV	グラニセトロン			中耳		60
B	**43**	○		○				○	Canadian Journal of Anesthesia	Cardiovascular responses to tracheal extubation or LMA removal in normotensive and hypertensive patients	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院							1997	抜管反応	LMA			整形四肢		80
C	**44**	○		○				○	Journal of Anesthesia	Nicardipine inhibits amrinone-enhanced contractility in fatigued diaphragm	藤井善隆	東京医科歯科大学医学	豊岡秀訓	筑波大学附属病院									1997	犬	ニカルジピン	アムリノン			20	
C	**45**	○		○					Anesthesia and Resuscitation = 麻酔と蘇生	Dopamine enhances contractility of fatigued diaphragm in anestheized dogs: Dose effects on strength of contraction	藤井善隆												1997	犬					20	
C	**46**	○		○					Anesthesia and Resuscitation = 麻酔と蘇生	Dose-response effect of dibutyryl cyclic AMP on contractility in fatigued diaphragm	藤井善隆												1997	犬					16	
B	**47**	○		○			RCTDB	○	British Journal of Anaesthesia	Oral granisetron prevents postoperative vomiting in children	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院							1998	PONV	グラニセトロン			小児扁摘		160
B	**48**	○		○			RCTDB	○	British Journal of Anaesthesia	Granisetron-droperidol combination for the prevention of postoperative nausea and vomiting in female patients undergoing breast surgery	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院							1998	PONV	グラニセトロン	ドロペリドール		乳がん		150
B	**49**	○		○			RCTDB	○	Anesthesia and Analgesia	A granisetron-droperidol combination prevents postoperative vomiting in children	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院							1998	PONV	グラニセトロン	ドロペリドール		小児扁摘		180
B	**50**	○		○			RCTDB	○	British Journal of Anaesthesia	Prophylactic antiemetic therapy with a combination of granisetron and dexamethasone in patients undergoing middle ear surgery	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院							1998	PONV	グラニセトロン	デキサメサゾン		中耳		120
B	**51**	○		○			RCTDB	○	Anaesthesia	Prophylactic anti-emetic therapy with granisetron, droperidol and metoclopramide in female patients undergoing middle ear surgery	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院							1998	PONV	グラニセトロン	ドロペリドール	メトクロプラマイド	中耳		180
B	**52**	○		○			RCTDB	○	Anesthesia and Analgesia	Prophylactic oral antiemetics for preventing postoperative nausea and vomiting: granisetron versus domperidone	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1998	PONV	グラニセトロン	ドンペリドン		婦人科大手術		100

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
B	53	○		○			RCTDB	○	Acta Anaesthesiologica Scandinavica	Prevention of nausea and vomiting with granisetron, droperidol and metoclopramide during and after spinal anaesthesia for caesarean section: a	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1998	PONV	グラニセトロン	ドロペリドール	メトクロプラミド	帝切		120
B	54	○		○			RCTDB	○	British Journal of Anaesthesia	Granisetron in the prevention of nausea and vomiting after middle-ear surgery: a dose-ranging study	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院						1998	PONV	グラニセトロン			中耳		120
B	55	○		○			RCTDB	○	Acta Anaesthesiologica Scandinavica	Preoperative oral granisetron prevents postoperative nausea and vomiting	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院						1998	PONV	グラニセトロン			婦人科大手術		120
B	56	○		○			RCTDB	○	Canadian Journal of Anesthesia	Prophylactic antiemetic therapy with granisetron-droperidol combination in patients undergoing laparoscopic cholecystectomy	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1998	PONV	グラニセトロン	ドロペリドール		女性胆摘		150
B	57	○		○			RCTDB	○	Acta Anaesthesiologica Scandinavica	Prevention of nausea and vomiting in female patients undergoing breast surgery: a comparison with granisetron, droperidol, metoclopramide and placebo	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院						1998	PONV	グラニセトロン	ドロペリドール	メトクロプラミド	乳がん		120
B	58	○		○			RCTDB	○	Anesthesia and Analgesia	Prevention of postoperative nausea and vomiting with a combination of granisetron and droperidol	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院						1998	PONV	グラニセトロン	ドロペリドール		婦人科大手術		150
B	59	○		○			RCTDB	○	Pediatric Anesthesia	Comparison of granisetron and droperidol in the prevention of vomiting after strabismus surgery or tonsillectomy in children	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1998	PONV	グラニセトロン	ドロペリドール		小児扁摘斜視		80
B	60	○		○			RCTDB	○	Canadian Journal of Anesthesia	Prevention of PONV with granisetron, droperidol or metoclopramide in patients with postoperative emesis	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1998	PONV	グラニセトロン	メトクロプラミド	ドロペリドール	婦人科大手術		90
B	61	○		○			RCTDB	○	European Journal of Anaesthesiology	Anti-emetic efficacy of prophylactic granisetron, droperidol and metoclopramide in the prevention of nausea and vomiting after laparoscopic	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1998	PONV	グラニセトロン	ドロペリドール	メトクロプラミド	女性胆摘		120
B	62	○		○			RCTDB	○	Pediatric Anesthesia	Prophylactic therapy with granisetron in the prevention of vomiting after paediatric surgery: a randomised, double-blind comparison with droperidol and	藤井善隆	取手協同病院	田中弘彦	取手協同病院								1998	PONV	グラニセトロン	ドロペリドール	メトクロプラミド	小児体表		100
B	63	○		○			RCTDB	○	Acta Anaesthesiologica Scandinavica	Granisetron prevents nausea and vomiting during spinal anaesthesia for caesarean section	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院						1998	PONV	グラニセトロン			帝切		100
B	64	○		○			RCTDB	○	Acta Anaesthesiologica Scandinavica	Prophylactic antiemetic therapy with granisetron-dexamethasone combination in women undergoing breast surgery	藤井善隆	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院						1998	PONV	グラニセトロン	デキサメサゾン		乳がん		135
B	65	○		○			RCTDB	○	British Journal of Anaesthesia	Prophylactic antiemetic therapy with granisetron in women undergoing thyroidectomy	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1998	PONV	グラニセトロン			甲状腺		100
B	66	○		○			RCTDB	○	European Journal of Anaesthesiology	Effective dose of granisetron for the prevention of post-operative nausea and vomiting in patients undergoing laparoscopic cholecystectomy	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1998	PONV	グラニセトロン			女性胆摘		120
B	67	○		○			RCTDB	○	British Journal of Anaesthesia	Prevention of postoperative nausea and vomiting in female patients during menstruation: comparison of droperidol, metoclopramide and granisetron	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院						1998	PONV	グラニセトロン	ドロペリドール	メトクロプラミド	女性全科		120
C	68	○		○				○	Anaesthesia	Recovery of post-tetanic count and train-of-four responses at the great toe and thumb	齋藤祐司	東京医科歯科大学医学部附属病院	藤井善隆	筑波大学附属病院	Takahashi K	東京医科歯科大学医学部附属病院	槇田浩史	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	天羽敬祐	東京医科歯科大学医学部附属病院	1998	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
B	69	○		○			RCTDB	○	Canadian Journal of Anesthesia	Calcium channel blockers attenuate cardiovascular responses to tracheal extubation in hypertensive patients	藤井善隆	筑波大学附属病院	Kihara Shinichi	筑波大学附属病院	高橋伸二	筑波学園病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院			1998	挿管反応				整形外科		60
C	70	○		○				○	European Journal of Anaesthesiology	Post-tetanic burst count and train-of-four during recovery from vecuronium-induced intense neuromuscular block under different types of anaesthesia	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	藤井善隆	筑波大学附属病院	槇田浩史	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院			1998	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
C	71	○		○				○	Acta Anaesthesiologica Scandinavica	Modified double burst stimulation at varying stimulating currents	齋藤祐司	東京医科歯科大学医学部附属病院	藤井善隆	筑波大学附属病院	槇田浩史	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	天羽敬祐	東京医科歯科大学医学部附属病院			1998	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
B	72	○		○				○	Canadian Journal of Anesthesia	Cardiovascular responses to tracheal extubation or LMA removal in children	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1998	挿管反応				小児LMA		60
B	73	○		○			RCT	○	European Journal of Anaesthesiology	Efficacy of thoracic epidural analgesia following laparoscopic cholecystectomy	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	田中弘彦	取手協同病院						1998	術後痛	硬麻			男女胆摘		44
B	74	○		○			RCTDB	○	Canadian Journal of Anesthesia	Diltiazem-lidocaine combination for the attenuation of cardiovascular responses to tracheal intubation in hypertensive patients	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	高橋伸二	筑波学園病院	豊岡秀訓	筑波大学附属病院				1998	挿管反応	ジルチアゼム	リドカイン		全科高血圧		60
C	75	○		○				○	European Journal of Anaesthesiology	Accelographic and mechanical post-tetanic count and train-of-four ratio assessed at the great toe	齋藤祐司	取手協同病院	藤井善隆	筑波大学附属病院	Ueki M	東京医科歯科大学医学部附属病院	槇田浩史	東京医科歯科大学医学部附属病院	天羽敬祐	東京医科歯科大学医学部附属病院			1998	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
C	76	○		○				○	Anesthesia and Analgesia	The effects of milrinone and its mechanism in the fatigued diaphragm in dogs	藤井善隆	筑波大学附属病院	高橋伸二	筑波大学附属病院	豊岡秀訓	筑波大学附属病院						1998	犬					34	
B	77	○		○			RCTDB	○	Anesthesia and Analgesia	Comparison of ramosetron and granisetron for preventing postoperative nausea and vomiting after gynecologic surgery	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1999	PONV	グラニセトロン	ラモセトロン		婦人科大手術		120
B	78	○		○			RCTDB	○	European Journal of Anaesthesiology	Prophylactic therapy with combined granisetron and dexamethasone for the prevention of post-operative vomiting in children	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院				1999	PONV	グラニセトロン	デキサメサゾン		小児ヘルニア包茎		150

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
B	**79**	○		○			RCTDB	○	European Journal of Anaesthesiology	Anti-emetic efficacy of prophylactic granisetron compared with perphenazine for the prevention of postoperative vomiting in children	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1999	PONV	グラニセトロン	ベルフェナジン		小児扁摘		90
B	**80**	○		○			RCTDB	○	Journal of Clinical Anesthesia	Combination of granisetron and droperidol in the prevention of nausea and vomiting after middle ear surgery	藤井善隆	取手協同病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1999	PONV	グラニセトロン	ドロペリドール		男女中耳		150
B	**81**	○		○			RCTDB	○	European Journal of Anaesthesiology	Granisetron reduces post-operative vomiting in children: a dose-ranging study	藤井善隆	取手協同病院	田中弘彦	取手協同病院									1999	PONV	グラニセトロン			小児ヘルニア包茎		120
B	**82**	○		○			RCTDB	○	Anesthesia and Analgesia	Granisetron/dexamethasone combination for reducing nausea and vomiting during and after spinal anesthesia for cesarean section	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1999	PONV	グラニセトロン	デキサメサゾン		腰麻帝切		120
B	**83**	○		○			RCTDB	○	Anesthesia and Analgesia	Preoperative oral antiemetics for reducing postoperative vomiting after tonsillectomy in children: granisetron versus perphenazine	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1999	PONV	グラニセトロン	ベルフェナジン		小児扁摘		100
B	**84**	○		○			RCTDB	○	Pediatric Anesthesia	Combination of granisetron and droperidol for the prevention of vomiting after paediatric strabismus surgery	藤井善隆	筑波大学附属病院	齋藤祐司	東京医科歯科大学医学部附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1999	PONV	グラニセトロン	ドロペリドール		小児斜視		120
B	**85**	○		○			RCTDB	○	Laryngoscope	Granisetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting after thyroidectomy	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kobayashi Noriaki	取手協同病院(耳鼻咽喉科)							1999	PONV	グラニセトロン	ドロペリドール	メトクロプラマイド	女性甲状腺		120
B	**86**	○		○			RCTDB	○	European Journal of Anaesthesiology	Prevention of post-operative nausea and vomiting with combined granisetron and droperidol in women undergoing thyroidectomy	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1999	PONV	グラニセトロン	ドロペリドール		女性甲状腺		180
B	**87**	○		○			RCTDB	○	Laryngoscope	Prevention of nausea and vomiting after middle ear surgery: granisetron versus ramosetron	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kobayashi Noriaki	取手協同病院(耳鼻咽喉科)							1999	PONV	グラニセトロン	ラモセトロン		男女中耳		100
B	**88**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Ramosetron vs granisetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1999	PONV	ラモセトロン	グラニセトロン		女性胆摘		80
B	**89**	○		○			RCTDB	○	Pediatric Anesthesia	Prevention of postoperative vomiting with granisetron in paediatric patients with and without a history of motion sickness	藤井善隆	筑波大学附属病院	齋藤祐司	筑波大学附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					1999	PONV	グラニセトロン			小児扁摘		120
B	**90**	○		○			RCTDB	○	Ophthalmology	Preoperative oral granisetron for the prevention of vomiting after strabismus surgery in children	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Ito Mutsuko	取手協同病院(眼科)							1999	PONV	グラニセトロン			小児斜視		120
B	**91**	○		○			RCTDB	○	Journal of Anesthesia	Prophylactic antiemetic therapy with droperidol in patients undergoing laparoscopic cholecystectomy	藤井善隆	筑波大学附属病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院							1999	PONV	ドロペリドール			男女胆摘		60
C	**92**	○		○				○	Anaesthesia	Relationship between stimulating current and accelerographic train-of-four response at the great toe	齋藤祐司	取手協同病院	鳴海豊	取手協同病院	藤井善隆	筑波大学附属病院	Ueki M	東京医科歯科大学医学部附属病院					1999	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
C	**93**	○		○				○	British Journal of Anaesthesia	Tactile evaluation of fade of the train-of-four and double-burst stimulation using the anaesthetist's non-dominant hand	齋藤祐司	取手協同病院	鳴海豊	取手協同病院	藤井善隆	筑波大学附属病院	Ueki M	東京医科歯科大学医学部附属病院					1999	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
C	**94**	○		○				○	British Journal of Anaesthesia	Post-tetanic count and train-of-four responses during neuromuscular block produced by vecuronium and infusion of nicardipine	齋藤祐司	取手協同病院	鳴海豊	取手協同病院	藤井善隆	筑波大学附属病院							1999	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
B	**95**	○		○				○	Anaesthesia and Intensive Care	Blood flow velocity in the middle cerebral artery response to tourniquet release	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	Ishikawa E	筑波大学附属病院(脳神経外科)	Kato N	筑波大学附属病院(脳神経外科)					1999	中大脳動脈				整形四肢		30
C	**96**	○		○				○	British Journal of Anaesthesia	Electromyographic assessment of neuromuscular block at the gastrocnemius muscle	齋藤祐司	取手協同病院	鳴海豊	取手協同病院	藤井善隆	筑波大学附属病院	Ueki M	東京医科歯科大学医学部附属病院	槇田浩史	東京医科歯科大学医学部附属病院			1999	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
C	**97**	○		○				○	Anesthesia and Analgesia	The ulnistatin-induced effect on neuromuscular block caused by vecuronium	齋藤祐司	取手協同病院	藤井善隆	筑波大学附属病院	大島勉	岐阜大学附属病院							1999	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
B	**98**	○		○			RCTDB	○	Canadian Journal of Anesthesia	Combined diltiazem and lidocaine reduces cardiovascular responses to tracheal extubation and anesthesia emergence in hypertensive patients	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	高橋伸二	筑波大学附属病院	豊岡秀訓	筑波大学附属病院					1999	抜管反応	ジルチアゼム			高血圧整形四肢		60
B	**99**	○		○				○	Anesthesia and Analgesia	The effect of olprinone compared with milrinone on diaphragmatic muscle function in dogs	藤井善隆	筑波大学附属病院	高橋伸二	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							1999	犬					40	
B	**100**	○		○				○	Anesthesia and Analgesia	Propofol decreases diaphragmatic contractility in dogs	藤井善隆	筑波大学附属病院	星拓男	筑波大学附属病院	高橋伸二	筑波大学附属病院	豊岡秀訓	筑波大学附属病院					1999	犬					30	
A	**101**	○		○				○	Canadian Journal of Anesthesia	Landiolol decreases a dysrhythmogenic dose of epinephrine in dogs during halothane anesthesia	高橋伸二	筑波大学附属病院	藤井善隆	筑波大学附属病院	Inomata Shin ichi	筑波大学附属病院	宮部雅幸	筑波大学附属病院	豊岡秀訓	筑波大学附属病院			1999	犬	#N/A	#N/A	#N/A	#N/A	10	10
B	**102**	○		○				○	European Journal of Anaesthesiology	Milrinone enhances the contractility of fatigued diaphragm in dogs:a dose-ranging study.	藤井善隆	筑波大学附属病院	高橋伸二	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							1999	犬					24	
B	**103**	○		○				○	Anaesthesia and Intensive Care	Protection from diaphragmatic fatigue by nitric oxide synthase inhibitor in dogs.	藤井善隆	筑波大学附属病院	高橋伸二	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							1999	犬					26	
B	**104**	○		○			RCTDB	○	European Journal of Anaesthesiology	Granisetron/dexamethasone combination for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					2000	PONV	グラニセトロン	デキサメサゾン		男女胆摘		120

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
B	105	○		○			RCTDB	○	Anaesthesia and Intensive Care	Granisetron/dexamethasone combination for the prevention of postoperative nausea and vomiting after thyroidectomy	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kobayashi Noriaki	取手協同病院(耳鼻咽喉科)							2000	PONV	グラニセトロン	デキサメサゾン		女性甲状腺		130
B	106	○		○			RCTDB	○	Anesthesia and Analgesia	Ramosetron for preventing postoperative nausea and vomiting in women undergoing gynecological surgery	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					2000	PONV	ラモセトロン			婦人科大手術		120
B	107	○		○			RCTDB	○	American Journal of Obstetrics and Gynecology	Granisetron, droperidol, and metoclopramide for the treatment of established postoperative nausea and vomiting in women undergoing	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Somekawa Yoshiaki	取手協同病院(産婦人科)							2000	PONV	グラニセトロン	ドロペリドール	メトクロプラミド	婦人科大手術		120
B	108	○		○			RCTDB	○	British Journal of Surgery	Randomised clinical trial of granisetron, droperidol and metoclopramide for the treatment of nausea and vomiting after laparoscopic cholecystectomy	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kawasaki Tsuneo	取手協同病院(外科)							2000	PONV	グラニセトロン	ドロペリドール	メトクロプラミド	男女胆摘		120
B	109	○		○			RCTDB	○	Anaesthesia and Intensive Care	Subhypnotic dose of propofol for the prevention of nausea and vomiting during spinal anaesthesia for caesarean section	沼崎満子	筑波大学附属病院	藤井善隆	筑波大学附属病院									2000	血管痛				腰麻帝切		60
B	110	○		○			RCTDB	○	Pediatric Anesthesia	Pretreatment with oral clonidine attenuates cardiovascular responses to tracheal extubation	藤井善隆	筑波大学附属病院	齋藤祐司	取手協同病院	田中弘彦	取手協同病院	豊岡秀訓	筑波大学附属病院					2000	抜管反応	クロニジン	ジアゼパム		小児ヘルニア包茎		50
B	111	○		○				○	Anesthesia and Analgesia	The effect of sedative drugs on diaphragmatic contractility in dogs: propofol versus midazolam	藤井善隆	筑波大学附属病院	星拓男	筑波大学附属病院	高橋伸二	筑波大学附属病院	豊岡秀訓	筑波大学附属病院					2000	犬					30	
A	112	○		○				○	Canadian Journal of Anesthesia	Modifications of the hemodynamic consequences of theophylline intoxication with landiolol in halothane-anesthetized dogs	高橋伸二	筑波大学附属病院	藤井善隆	筑波大学附属病院	星拓男	筑波大学附属病院	Inomata Shin ichi	筑波大学附属病院	宮部雅幸	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	2000	犬					34	
C	113	○		○				○	Canadian Journal of Anesthesia	Effect of xenon on diaphragmatic contractility in dogs	星拓男	筑波大学附属病院	藤井善隆	筑波大学附属病院	高橋伸二	筑波大学附属病院	豊岡秀訓	筑波大学附属病院					2000	犬					21	
B	114	○		○				○	Canadian Journal of Anesthesia	Different effects of olprinone on contractility in nonfatigued and fatigued diaphragm in dogs	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院									2000	犬					36	
B	115	○		○			RCTDB	○	Archives of Otolaryngology Head and Neck Surgery	Prevention of postoperative nausea and vomiting with antiemetics in patients undergoing middle ear surgery: comparison of a small dose of propofol	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kobayashi Noriaki	取手協同病院(耳鼻咽喉科)							2001	PONV	ドロペリドール	メトクロプラミド		中耳		90
B	116	○		○			RCTDB	○	Otolaryngology - Head and Neck Surgery	Small doses of propofol, droperidol, and metoclopramide for the prevention of postoperative nausea and vomiting after thyroidectomy	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kobayashi Noriaki	取手協同病院(耳鼻咽喉科)							2001	PONV	ドロペリドール	メトクロプラミド		甲状腺		90
B	117	○		○			RCTDB	○	Journal of Pediatric Surgery	Comparison of granisetron, droperidol, and metoclopramide for prevention of postoperative vomiting in children with a history of motion sickness undergoing	藤井善隆	取手協同病院	田中弘彦	取手協同病院									2001	PONV	グラニセトロン	ドロペリドール	メトクロプラミド	小児扁摘		90
B	118	○		○			RCTDB	○	European Journal of Surgery	Preoperative oral granisetron for the prevention of postoperative nausea and vomiting after breast surgery	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kawasaki Tsuneo	取手協同病院(外科)							2001	PONV	グラニセトロン			乳がん		100
B	119	○		○			RCTDB	○	Laryngoscope	Prevention of vomiting after tonsillectomy in children: granisetron versus ramosetron	藤井善隆	取手協同病院	齋藤祐司	取手協同病院	Kobayashi Noriaki	取手協同病院(耳鼻咽喉科)							2001	PONV	グラニセトロン	ラモセトロン		小児扁摘		90
B	120	○		○			RCTDB	○	British Journal of Ophthalmology	Ramosetron compared with granisetron for the prevention of vomiting following strabismus surgery in children	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Ito Mutsuko	取手協同病院(眼科)							2001	PONV	ラモセトロン	グラニセトロン		小児斜視		80
B	121	○		○			RCTDB	○	Archives of Surgery	Prophylaxis with oral granisetron for the prevention of nausea and vomiting after laparoscopic cholecystectomy: a prospective randomised study	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kawasaki Tsuneo	取手協同病院(外科)							2001	PONV	グラニセトロン			男女胆摘		120
C	122	○		○			RCTDB	○	Pediatric Anesthesia	The efficacy of oral clonidine premedication in the prevention of postoperative vomiting in children following strabismus surgery	半田冨美(筒井冨美)	兵庫県立こども病院	藤井善隆	筑波大学附属病院									2001	PONV	クロニジン			斜視		60
C	123	○		○				○	Canadian Journal of Anesthesia	Nicorandil accelerates recovery of neuromuscular block caused by vecuronium	齋藤祐司	福島医科大学病院	Kaneda Koh	取手協同病院	藤井善隆	筑波大学附属病院	大島勉	岐阜大学附属病院					2001	不要						
B	124	○		○				○	Anesthesia and Analgesia	Colforsin daropate improves contractility in fatigued canine diaphragm	藤井善隆	筑波大学附属病院	星拓男	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							2001	犬					32	
B	125	○		○				○	Anesthesia and Analgesia	Dose-response characteristics of midazolam for reducing diaphragmatic contractility	藤井善隆	筑波大学附属病院	星拓男	筑波大学附属病院	上村明	筑波大学附属病院	豊岡秀訓	筑波大学附属病院					2001	犬					24	
B	126	○		○				○	Anesthesia and Analgesia	The dose-range effects of propofol on the contractility of fatigued diaphragm in dogs	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							2001	犬					24	
B	127	○		○				○	British Journal of Anaesthesia	Midazolam versus propofol for reducing contractility of fatigued canine diaphragm	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院									2001	犬					30	
B	128	○		○			RCTDB	○	Anesthesia and Resuscitation = 麻酔と蘇生	Diltiazem or verapamil attenuates cardiovascular responses to tracheal intubation in hypertensive patients	藤井善隆	筑波大学附属病院											2001	挿管反応	ジルチアゼム	ベラパミル		全科高血圧		45
B	129	○		○			RCTDB	○	Obstetrics and Gynecology	Dexamethasone for the prevention of nausea and vomiting after dilatation and curettage: a randomised controlled trial	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院									2002	PONV	デキサメサゾン			中絶		120
B	130	○		○			RCTDB	○	Pediatric Anesthesia	Preoperative oral granisetron for the prevention of vomiting following paediatric surgery	藤井善隆	取手協同病院	田中弘彦	取手協同病院									2002	PONV	グラニセトロン			小児		100

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
B	131	○		○			RCTDB	○	European Journal of Surgery	Prophylaxis of nausea and vomiting after laparoscopic cholecystectomy with ramosetron: Randomised controlled trial	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院	田中弘彦	取手協同病院							2002	PONV	ラモセトロン			胆摘		100
B	132	○		○			RCTDB	○	Clinical Therapeutics	Comparison of granisetron and ramosetron for the prevention of nausea and vomiting after thyroidectomy	藤井善隆	取手協同病院	田中弘彦	取手協同病院									2002	PONV	グラニセトロン	ラモセトロン		甲状腺		80
B	133	○		○			RCTDB	○	Journal of Oral and Maxillofacial Surgery	Small dose of propofol for preventing nausea and vomiting after third molar extraction	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院	Nakano Mayu	筑波大学附属病院(口頭・顎顔面外科)							2002	PONV	プロポフォール			歯科抜歯		90
B	134	○		○			RCTDB	○	Clinical Therapeutics	Double-blind, placebo-controlled, dose-ranging study of ramosetron for the prevention of nausea and vomiting after thyroidectomy	藤井善隆	取手協同病院	田中弘彦	取手協同病院									2002	PONV	ラモセトロン			甲状腺		80
B	135	○		○			RCTDB	○	Ophthalmologica	Treatment of vomiting after paediatric strabismus surgery with granisetron, droperidol, and metoclopramide	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Ito Mutsuko	取手協同病院(眼科)							2002	PONV	グラニセトロン	ドロペリドール	メトクロプラマイド	小児斜視		120
B	136	○		○			RCTDB	○	Obstetrics and Gynecology	Dose-range effects of propofol for reducing emetic symptoms during cesarean delivery	藤井善隆	筑波大学附属病院	沼崎満子	筑波大学附属病院									2002	PONV	プロポフォール			帝切		80
B	137	○		○				○	Anesthesia and Analgesia	The dose-related efficacy of diltiazem for enhancing diaphragmatic fatigability in dogs	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							2002	犬					24	
B	138	○		○				○	Anesthesia and Analgesia	Flumazenil recovers diaphragm muscle dysfunction caused by midazolam in dogs	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							2002	犬					24	
C	139	○		○				○	British Journal of Anaesthesia	Inhaled olprinone improves contractility of fatigued canine diaphragm	上村明	筑波大学附属病院	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							2002	犬					24	
B	140	○		○				○	Canadian Journal of Anesthesia	High-dose colforsin daropate increases diaphragmatic contractility in dogs	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院									2002	犬					24	
C	141	○		○				○	Acta Anaesthesiologica Scandinavica	Comparative effects of xenon and nitrous oxide on diaphragmatic contractility in dogs.	星拓男	筑波大学附属病院	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							2002	犬					21	
B	142	○		○			RCTDB	○	Clinical Drug Investigation	Prevention of nausea and vomiting with ramosetron after total hip replacement	藤井善隆	取手協同病院	田中弘彦	取手協同病院									2003	PONV	ラモセトロン			股関節置換		80
B	143	○		○			RCTDB	○	Clinical Therapeutics	Randomised, double-blind, placebo-controlled, dose-finding study of the antiemetic effects and tolerability of ramosetron in adults undergoing middle	藤井善隆	取手協同病院	田中弘彦	取手協同病院									2003	PONV	ラモセトロン			中耳		100
B	144	○		○			RCTDB	○	Canadian Journal of Anesthesia	Prevention of nausea and vomiting after dental surgery: a comparison of small doses of propofol, droperidol, and metoclopramide	Nakano Mayu	筑波大学附属病院	藤井善隆	筑波大学附属病院									2003	PONV	ドロペリドール	メトクロプラマイド		歯科口腔外科		90
B	145	○		○			RCTDB	○	Current Therapeutic Research	A randomised, double-blind comparison of granisetron alone and combined with dexamethasone for post-laparoscopic cholecystectomy emetic symptoms	藤井善隆	筑波大学附属病院	田中弘彦	取手協同病院	Kawasaki Tsuneo	取手協同病院(外科)							2003	PONV	グラニセトロン	デキサメサゾン		胆摘		100
B	146	○		○			RCTDB	○	Clinical Therapeutics	A comparison of granisetron, droperidol, and metoclopramide in the treatment of established nausea and vomiting after breast surgery: a double-blind,	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Kawasaki Tsuneo	取手協同病院(外科)							2003	PONV	グラニセトロン	ドロペリドール	メトクロプラマイド	乳がん		75
B	147	○		○			RCTDB	○	Clinical Therapeutics	Granisetron versus granisetron/dexamethasone combination for the treatment of nausea, retching, and vomiting after major gynecologic	藤井善隆	取手協同病院	田中弘彦	取手協同病院									2003	PONV	グラニセトロン	デキサメサゾン		婦人科大手術		120
B	148	○		○				○	Anesthesia and Analgesia	Midazolam-induced muscle dysfunction and its recovery in fatigued diaphragm in dogs	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							2003	犬					24	
B	149	○		○				○	Anesthesia and Analgesia	The effect of inhaled colforsin daropate on contractility of fatigued diaphragm in dogs	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院	豊岡秀訓	筑波大学附属病院							2003	犬					24	
A	150	○		○				○	Canadian Journal of Anesthesia	Milrinone attenuates the negative inotropic effects of landiolol in halothane-anesthetized dogs	高橋伸二	筑波大学附属病院	藤井善隆	筑波大学附属病院	星拓男	筑波大学附属病院	上村明	筑波大学附属	宮部雅幸	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	2003	犬					18	
B	151	○		○				○	European Journal of Anaesthesiology	Effects of diltiazem compared with nicardipine on diaphragmatic fatigability in vivo	藤井善隆	筑波大学附属病院											2003	犬					16	
C	152	○		○				○	Anesthesia and Analgesia	Olprinone for the treatment, but not prevention, of fatigue-induced changes in guinea-pig diaphragmatic contractility	上村明	筑波大学附属病院	藤井善隆	筑波大学附属病院	豊岡秀訓	筑波大学附属病院	鈴木ｾﾂｺ	筑波大学附属	Sawada Kohei	筑波大学附属病	Adachi Hideyuki	筑波大学附属病院(研究所)	2003	モルモット					21	
B	153	○		○			RCTDB	○	Clinical Therapeutics	Results of a prospective, randomized, double-blind, placebo-controlled, dose-ranging trial to demonstrate the effective dose of ramosetron for the prevention of	藤井善隆	取手協同病院	田中弘彦	取手協同病院									2003	PONV	ラモセトロン			小児扁摘		80
B	154	○		○			RCTDB	○	Journal of Clinical Anesthesia	Reduction of emetic symptoms during Cesarean delivery with antiemetics: propofol at subhypnotic dose versus traditional antiemetics	沼崎満子	筑波大学附属病院	藤井善隆	筑波大学附属病院									2003	PONV	プロポフォール	ドロペリドール	メトクロプラマイド	帝切		100
B	155		○	○					麻酔	ジルチアゼムの横隔膜収縮力及び横隔膜筋電図に及ぼす影響	藤井善隆	筑波大学 臨床医学系麻酔科											2003	犬	ジルチアゼム				18	
B	156	○		○					Current Therapeutic Research Clinical and Experimental	Treatment of Diaphragmatic Fatigue with Inhaled Aminophylline Therapy in an Experimental Canine Model: An Open-Label, Dose-Ranging, Pharmacologic	藤井善隆												2003	犬					28	

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
B	157	○		○			RCTDB		Anesthesia and Re	Small dose of propofol for preventing emetic episodes in women undergoing mastectomy	上村明	筑波大学附属病院											2003	PONV				乳がん		40
B	158	○		○					Anesthesia and Re	Supplemental Oxygen for the Prevention o	上村明		藤井善隆										2003	犬					18	
B	159	○		○			RCTDB	○	International Journal of Obstetric Anesthesia	A randomised, double-blind, placebo-controlled trial of ramosetron for preventing nausea and vomiting during termination of pregnancy	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Somekawa Yoshiaki	取手協同病院(産婦人科)						2004	PONV	ラモセトロン			中絶		80
B	160	○		○			RCTDB	○	American Journal of Therapeutics	Benefits and risks of granisetron versus ramosetron for nausea and vomiting after breast surgery: a randomised, double-blinded, placebo-controlled trial	藤井善隆	筑波大学附属病院	田中弘彦	取手協同病院	Kawasaki Tsuneo	取手協同病院(外科)						2004	PONV	グラニセトロン	ラモセトロン		乳癌		90
B	161	○		○			RCTDB	○	Current Therapeutic Research	Treatment of postoperative emetic symptoms with granisetron in women undergoing abdominal hysterectomy: a randomised, double-blind, placebo-	藤井善隆	筑波大学附属病院	田中弘彦	取手協同病院	Somekawa Yoshiaki	取手協同病院(産婦人科)						2004	PONV	グラニセトロン			子宮摘出		100
B	162	○		○			RCTDB	○	Clinical Therapeutics	Effects of granisetron in the treatment of nausea and vomiting after laparoscopic cholecystectomy: a dose-ranging study	藤井善隆	筑波大学附属病院	田中弘彦	取手協同病院	Kawasaki Tsuneo	取手協同病院(外科)						2004	PONV	グラニセトロン			胆摘		100
B	163	○		○			RCTDB	○	Clinical Therapeutics	Randomised, double-blind comparison of subhypnotic-dose propofol alone and combined with dexamethasone for emesis in parturients undergoing cesarean	藤井善隆	筑波大学附属病院	沼崎満子	筑波大学大学院(人間総合科学研究科)								2004	PONV	デキサメサゾン			帝切		120
B	164	○		○			RCTDB	○	Anaesthesia and Intensive Care	Effect of metoclopramide on pain on injection of propofol	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院								2004	血管痛	メトクロプラマイド			全科		100
B	165	○		○				○	Canadian Journal of Anesthesia	Pretreatment with flurbiprofen axetil and venous occlusion to reduce pain during injection of propofol	藤井善隆	筑波大学附属病院										2004	血管痛	ロピオン			女性円錐切除		40
B	166	○		○				○	Anesthesia and Analgesia	The recovery profile of reduced diaphragmatic contractility induced by propofol in dogs	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院	豊岡秀訓	筑波大学附属病院						2004	犬					28	
B	167	○		○			RCTDB	○	Clinical Drug Investigation	Reduction of propofol-induced pain through pretreatment with lidocaine and/or flurbiprofen	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院								2004	血管痛	ロピオン			形成		120
B	168		○	○					Anesthesia and Resuscitation = 麻酔と蘇生	乳房切除術患者の術後悪心・嘔吐に対する少量のプロポフォールの制吐効果	萩谷圭一	筑波大学附属病院	藤井善隆	筑波大学大学院								2004	PONV	プロポフォール			乳がん		80
B	169	○		○					Pulmonary Pharmacology and Therapeutics	Comparative effects of dopamine and dobutamine on hypercapnic depression of diaphragmatic contractility in dogs	藤井善隆											2004	犬					30	
B	170	○		○					Pulmonary Pharmacology and Therapeutics	Inhaled milrinone for the improvement of contractility of fatigued diaphragm in dogs: A dose-ranging study	藤井善隆											2004	犬					28	
B	171	○		○					Anesthesia and Re	Aerosolized isoproterenol increases contr	沼崎満子		藤井善隆										2004	犬					21	
B	172	○		○			RCTDB	○	Archives of Ophthalmology	A randomised clinical trial of a single dose of ramosetron for the prevention of vomiting after strabismus surgery in children	藤井善隆	取手協同病院	田中弘彦	取手協同病院	Ito Mutsuko	取手協同病院(眼科)						2005	PONV	ラモセトロン			小児斜視		80
B	173	○		○			RCTDB	○	Clinical Therapeutics	Effects of dexamethasone in preventing postoperative emetic symptoms after total knee replacement surgery: a prospective, randomised, double-blind,	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院								2005	PONV	デキサメサゾン			膝関節置換		80
B	174	○		○			RCTDB	○	Canadian Journal of Anesthesia	Antiemetic efficacy of propofol at small doses for reducing nausea and vomiting following thyroidectomy	沼崎満子	筑波大学附属病院	藤井善隆	筑波大学附属病院								2005	PONV	ロピオン	プロポフォール		こうじょうせん		80
B	175	○		○			RCTDB	○	Journal of Clinical Anesthesia	Reduction of postoperative emetic episodes and analgesic requirements with dexamethasone in patients scheduled for dental surgery	沼崎満子	筑波大学附属病院	藤井善隆	筑波大学附属病院								2005	PONV	デキサメサゾン			歯科抜歯		120
B	176	○		○			RCTDB	○	Canadian Journal of Anesthesia	A lidocaine/metoclopramide combination decreases pain on injection of propofol	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院								2005	血管痛	メトクロプラマイド	リドカイン		形成		90
B	177	○		○			RCTDB	○	Clinical Therapeutics	Flurbiprofen axetil preceded by venous occlusion in the prevention of pain on propofol injection in the hand: a prospective, randomized, double-blind,	藤井善隆	筑波大学附属病院	志賀由佳	筑波大学附属病院								2005	血管痛	ロピオン			全科		120
B	178	○		○			RCTDB	○	Clinical Drug Investigation	Efficacy of lignocaine plus ketamine at different doses in the prevention of pain due to propofol injection	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院								2005	血管痛		ケタミン		婦人科ラパロ		120
B	179	○		○			RCTDB	○	Anesthesia and Resuscitation = 麻酔と蘇生	Effective dose of propofol at small dose for preventing postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy	藤井善隆	筑波大学大学院(人間総合科学研究科)										2005	PONV	プロポフォール			胆摘		80
B	180	○		○					Current Therapeutic Research Clinical and Experimental	Effects of diazepam on diaphragmatic functionand recovery in pentobarbital-anesthetized dogs: An open-label, dose-finding, pharmacologic study	藤井善隆											2005	犬					24	
B	181	○		○					Anesthesia and Resuscitation = 麻酔と蘇生	Comparative antiemetic efficacy of small dose of propofol and metoclopramide for preventing nausea and vomiting after laparoscopic cholecystectomy	志賀由香											2005	PONV				胆摘		30
B	182	○		○			RCTDB	○	Clinical Drug Investigation	Efficacy of granisetron for the treatment of postoperative nausea and vomiting in women undergoing breast surgery	藤井善隆	取手協同病院	田中弘彦	取手協同病院								2006	PONV	グラニセトロン			乳がん		100

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
B	183	○		○			RCTDB	○	Clinical Therapeutics	Influence of age on flurbiprofen axetil requirements for preventing pain on injection of propofol in Japanese adult surgical patients: a prospective,	藤井善隆	東邦大学医学部　麻酔科学第1講座	中山 Masahiro	筑波大学附属病院									2006	血管痛	ロピオン			全科		150
B	184	○		○			RCTDB	○	Clinical Drug Investigation	Age-related differences in metoclopramide requirement for pain on injection of propofol	藤井善隆	筑波大学附属病院	志賀由佳	筑波大学附属病院									2006	血管痛	メトクロプラマイド			全科		120
B	185	○		○			RCTDB	○	Journal of Clinical Anesthesia	Influence of aging on lidocaine requirements for pain on injection of propofol	藤井善隆	筑波大学附属病院	志賀由佳	筑波大学附属病院									2006	血管痛	リドカイン			全科		160
B	186	○		○				○	Anesthesia and Resuscitation = 麻酔と蘇生	Jiachiruzemu does not affect the force of contraction of the diaphragm and EMG fatigue.	藤井善隆	筑波大学大学院（人間総合科学研究科）											2006	犬	ジルチアゼム				10	
B	187	○		○				○	Anesthesia and Resuscitation = 麻酔と蘇生	No Beneficial Effect of Neostigmine Pretreatment on Diaphragmatic Fatigue in Pentobarbital-Anesthetized Dogs.	藤井善隆	東邦大学医学部　麻酔科学第1講座	上村明	筑波大学附属病院									2006	犬					21	
B	188	○		○					Current Therapeutic Research Clinical and Experimental	Olprinone/dopamine combination for improving diaphragmatic fatigue in pentobarbital-anesthetized dogs	藤井善隆												2006	犬					28	
B	189	○		○			RCTDB	○	Breast Journal	Reduction of postoperative nausea and vomiting and analgesic requirement with dexamethasone in women undergoing general anesthesia for mastectomy	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院									2007	PONV	デキサメサゾン			乳癌		94
B	190	○		○			RCTDB	○	Otolaryngology - Head and Neck Surgery	Efficacy of dexamethasone for reducing postoperative nausea and vomiting and analgesic requirements after thyroidectomy	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院（耳鼻咽喉科）									2007	PONV	デキサメサゾン			甲状腺		75
B	191	○		○			RCTDB	○	Clinical Therapeutics	Prevention of pain due to injection of propofol with iv administration of lidocaine 40mg + metoclopramide 2.5, 5, or 10mg or saline: a randomised, double-	藤井善隆	東邦大学医学部　麻酔科学第1講座	中山 Masahiro	筑波大学附属病院									2007	血管痛	メトクロプラマイド	リドカイン		全科		240
B	192	○		○			RCTDB	○	British Journal of Oral and Maxillofacial Surgery	Propofol alone and combined with dexamethasone for the prevention of postoperative nausea and vomiting in adult Japanese patients having third	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院	Nakano Mayu	筑波大学附属病院（口頭・顎顔面外科）						2007	PONV	デキサメサゾン	プロポフォール		口外（歯科抜歯？）		120
B	193	○		○				○	Anesthesia and Analgesia	The effects of different dobutamine infusion rates on hypercapnic depression of diaphragmatic contractility in pentobarbital-anesthetized dogs.	藤井善隆	筑波大学附属病院	上村明	筑波大学附属病院									2007	犬					24	雑種
B	194	○		○				○	Anesthesia and Resuscitation = 麻酔と蘇生	Effect of diaphragmatic electromyogram and force of contraction of the diaphragm flumazenil.	藤井善隆	東邦大学医学部　麻酔科学第1講座	上村明	筑波大学大学院（人間総合科学研究科）									2007	犬					8	雑種
B	195	○		○				○	Anesthesia and Resuscitation = 麻酔と蘇生	Low-Dose of Diazepam, but not Midazolam, Delays Recovery from Diaphragm Muscle Dysfunction in Dogs.	藤井善隆	東邦大学医学部　麻酔科学第1講座	上村明	筑波大学附属病院									2007	犬					18	雑種
B	196	○		○					Current Therapeutic Research Clinical and Experimental	Effects of milrinone and olprinone on hypercapnic depression of diaphragmatic contractility in pentobarbital-anesthetized dogs	藤井善隆		上村明										2007	犬					24	
B	197	○		○			RCTDB	○	International Journal of Gynecology and Obstetrics	Dexamethasone for reduction of nausea, vomiting and analgesic use after gynecological laparoscopic surgery	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院									2008	PONV	デキサメサゾン			婦人科		90
B	198	○		○			RCTDB	○	Clinical therapeutics	Comparison of propofol, droperidol, and metoclopramide for prophylaxis of postoperative nausea and vomiting after breast cancer surgery: a prospective,	藤井善隆	東邦大学医学部　麻酔科学第1講座	板倉美千代	牛久愛和総合病院									2008	PONV	ドロペリドール	メトクロプラマイド		乳がん		100
B	199	○		○			RCTDB	○	Surgical Endoscopy	Prevention of postoperative nausea and vomiting with a small dose of propofol alone and combined with dexamethasone in patients undergoing laparoscopic	藤井善隆	筑波大学附属病院	中山 Masahiro	筑波大学附属病院									2008	PONV	プロポフォール	デキサメサゾン		胆摘		120
B	200	○		○			RCTDB	○	Anesthesia and Resuscitation = 麻酔と蘇生	Supplemental oxygen prevents postoperative nausea and vomiting in patients undergoing gynecological laparoscopic surgery	藤井善隆	東邦大学医学部　麻酔科学第1講座	板倉美千代	牛久愛和総合病院									2008	PONV	酸素			婦人科腹腔鏡		60
B	201	○		○			RCTDB	○	Clinical Therapeutics	Comparison of lidocaine, metoclopramide, and flurbiprofen axetil for reducing pain on injection of propofol in Japanese adult surgical patients: a prospective,	藤井善隆	東邦大学医学部　麻酔科学第1講座	板倉美千代	牛久愛和総合病院									2008	血管痛	メトクロプラマイド	ロピオン		全科		100
B	202	○		○					Current Therapeutic Research Clinical and Experimental	Dose-related effects of olprinone on hypercapnia-induced impairment of diaphragmatic contractility in pentobarbital-anesthetized dogs	藤井善隆		上村明										2008	犬					24	
B	203	○		○			RCTDB	○	Clinical Therapeutics	Pretreatment with flurbiprofen axetil, flurbiprofen axetil preceded by venous occlusion, and a mixture of flurbiprofen axetil and propofol in reducing pain on	藤井善隆	東邦大学医学部　麻酔科学第1講座	板倉美千代	牛久愛和総合病院									2009	血管痛	ロピオン			全科		150
B	204	○		○			RCTDB	○	International Journal of Gynecology and Obstetrics	Low-dose propofol propofol to prevent nausea and vomiting after laparoscopic surgery	藤井善隆	牛久愛和総合病院	板倉美千代	牛久愛和総合病院									2009	PONV	プロポフォール			婦人科腹腔鏡		90
B	205	○		○			RCTDB	○	Clinical Therapeutics	A comparison of pretreatment with fentanyl and lidocaine preceded by venous occlusion for reducing pain on injection of propofol: a prospective,	藤井善隆	東邦大学医学部　麻酔科学第1講座	板倉美千代	牛久愛和総合病院									2009	血管痛	フェンタニル	リドカイン		全科		120
B	206	○		○					Methods and Findings in Experimental and Clinical	Dexamethasone for the reduction of postoperative nausea and vomiting and analgesic requirements after middle ear surgery in adult Japanese patients	藤井善隆		Nakayama M										2009	PONV				中耳	93	
B	207	○		○			RCTDB	○	Surgical Endoscopy	Reduction of postoperative nausea, vomiting, and analgesic requirement with dexamethasone for patients undergoing laparoscopic cholecystectomy	藤井善隆	牛久愛和総合病院	板倉美千代	牛久愛和総合病院									2010	PONV	デキサメサゾン			胆摘		90
B	208	○		○			RCTDB	○	Clinical Therapeutics	A prospective, randomized, double-blind, placebo-controlled study to assess the antiemetic effects of midazolam on postoperative nausea and vomiting in	藤井善隆	東邦大学医学部　麻酔科学第1講座	板倉美千代	牛久愛和総合病院									2010	PONV	ミダゾラム			婦人科		90

判定	通番	英文論文	和文論文	原著	総説	症例報告	RCT	JointEIC調査対象	雑誌	タイトル	著者	著者所属	共著者1	共著者1所属	共著者2	共著者2所属	共著者3	共著者3所属	共著者4	共著者4所属	共著者5	共著者5所属	年	研究(テーマ)	薬剤1	薬剤2	薬剤3	対象	犬頭数	症例数
B	209	○		○				○	Anesthesia and Resuscitation = 麻酔と蘇生	Dopamine in a dose-dependent manner to improve the force of contraction of the diaphragm decreased by high CO2 blood.	藤井善隆	東邦大学医学部　麻酔科学第1講座	高橋伸二	筑波大学大学院(人間総合科学研究科)									2010	犬	ドーパミン				8	雑種
B	210	○		○					Current Therapeutic Research - Clinical and	Effects of dibutyryl cyclic adenosine monophosphate on hypercapnic depression of diaphragmatic contractility in pentobarbital-anesthetized dogs	藤井善隆		Uemura A										2010	犬					21	
B	211	○		○			RCTDB	○	Minerva Anestesiologica	Efficacy of the lidocaine / flurbiprofen axetil combination for reducing pain during the injection of propofol	藤井善隆	東邦大学医学部　麻酔科学第1講座	板倉美千代	牛久愛和総合病院									2011	血管痛	ロピオン			全科		100
B	212	○		○			RCTDB	○	Otolaryngology - Head and Neck Surgery	Antiemetic efficacy of low-dose midazolam in patients undergoing thyroidectomy.	藤井善隆	牛久愛和総合病院	板倉美千代	牛久愛和総合病院									2011	PONV	ミダゾラム			甲状腺		90