Nitrous Oxide–related Postoperative Nausea and Vomiting Depends on Duration of Exposure

Philip J. Peyton, M.D., Ph.D., M.B.B.S., F.A.N.Z.C.A., Christine Yx Wu, M.B.B.S.

BACKGROUND

- Postoperative nausea and vomiting(PONV)is a common and distressing complication of anesthesia

全麻后恶心呕吐（PONV）延长患者滞留时间和出院时间，同时导致一系列的并发症如脱水、电解质紊乱、伤口裂开、误吸等，增加患者痛苦和经济负担，降低手术质量

BACKGROUND

PONV危险因素主要为三方面
一是病人因素，包括女性、非吸烟、有晕动病史、
有PONV史等；
二是麻醉因素，全麻使用的药物如部分吸入麻醉药、阿
片类药物等；
三是手术因素，手术时间>3小时、涉及口颌面部的手术
等

BACKGROUND

- A recent meta-analysis showed that, whereas the risk ratio (RR) for PONV was increased by 20% where nitrous oxide was used

BACKGROUND

- Avoidance of nitrous oxide has been recommended as a strategy to reduce the risk of PONV after general anesthesia
- We conducted an updated literature review and meta-regression analysis to determine whether duration of expo- sure to nitrous oxide in published randomized trials was related to the incidence of PONV.

METHODS

a primary search was performed using an electronic database in the form of PubMed with the search terms "nitrous oxide and nausea," "vomiting," or "PONV"

METHODS

The study protocol restricted the search to published English-language articles in PubMed listed journals reporting trials in adults, which prospectively allocated patients by randomization to groups receiving a nitrous oxide or nitrous oxide−free anesthetic for surgery, where the incidence of PONV within the first 24 postoperative hours was reported in each group, and where the mean or median duration of anesthesia (or duration of surgery if this was not presented) was reported or could be estimated from the data presented

PubMed search: Randomized trials in adults
Intervention: N_2O vs N_2O-free anesthetic
Reporting: Incidence of PONV within 24 postoperative hours
& mean duration of anesthesia (or surgery)

43 papers (47 studies)
$n = 13,685$

Papers excluded

Confounding randomizations: e.g. propofol vs none, opioid vs none, antiemetic vs none:
13 papers (15 studies)
$n = 3,108$

Zero incidence PONV:
3 papers (3 studies)
$n = 117$

27 papers (29 studies)
$n = 10,460$

PUBMED中检索关键字，共检索到43篇相关文章
对于使用静脉而不是笑气吸入及PONV发生率为0的文章予以排除，剩下27篇文章

Fig. 1. The flow diagram indicating the exclusion and inclusion of studies in the meta-regression and meta-analysis. N₂O = nitrous oxide; PONV = postoperative nausea and voming.
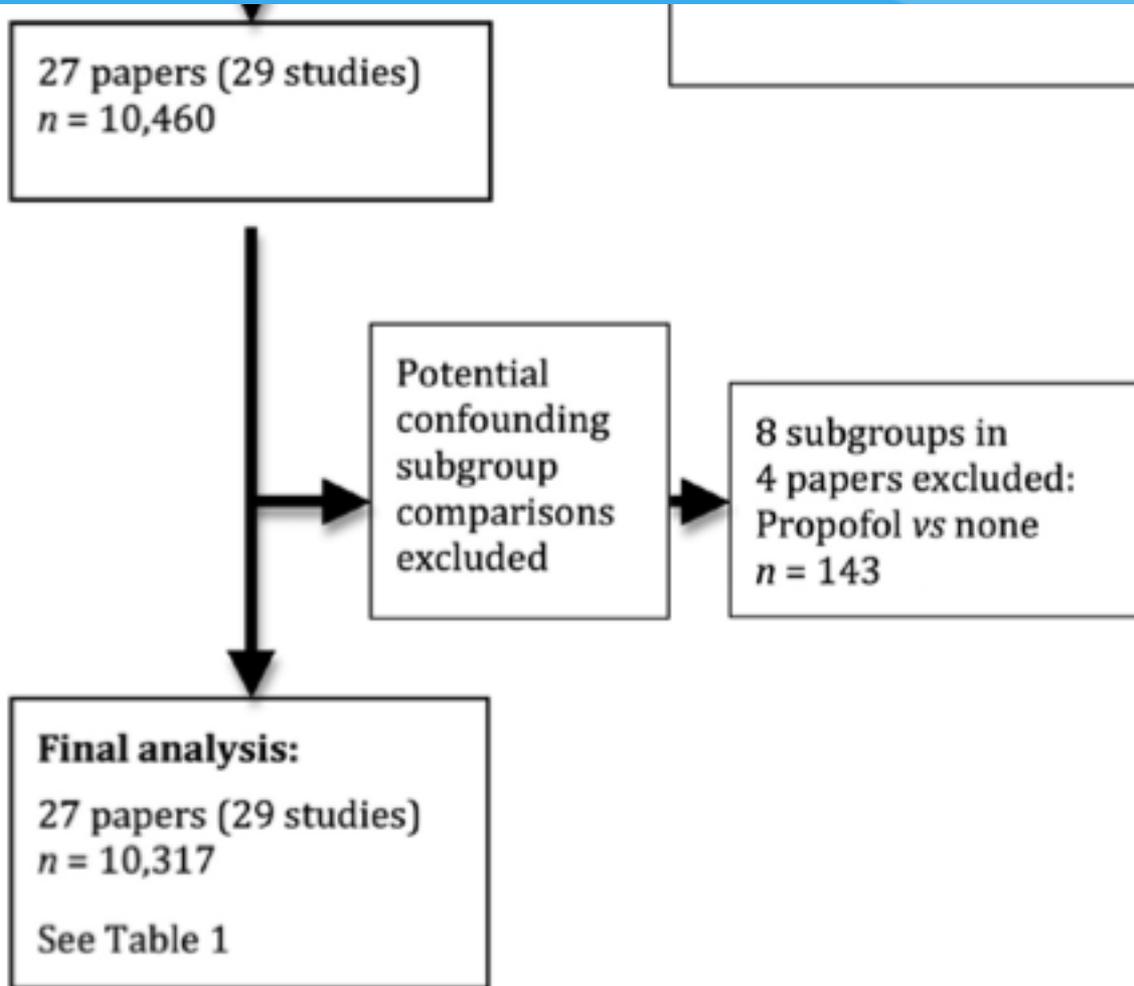
27篇文章中，4篇文章再次分组中存在丙泊酚与空白对照组比较，将再次分组中共143例排除
最后纳入27篇文章共29个临床研究试验对象10317例

Table 1. List of Eligible Included Studies

| First Author and Ref	Anesthetic		Type of Surgery	Duration (min)	PONV/n (% Incidence)	
	Non-N$_2$O Group	N$_2$O Group			Non-N$_2$O Group	N$_2$O Group
Lonie[27]	Fent-Enf	N$_2$O-Fent-Enf	Gynecological laparoscopy	39	20/46 (43)	20/41 (49)
Korttila[28]	Fent-Iso	N$_2$O-Fent-Iso	Abdominal hysterectomy	102	25/55 (45)	30/55 (55)
Melnick[29]	Iso	N$_2$O-Iso	Minor gynecology	13	1/28 (3)	8/32 (25)
Muir[30]	Morph-Enf	N$_2$O-Morph-Enf	Nonbody cavity	73	67/181 (37)	67/178 (38)
Muir[30]	Morph-Iso	N$_2$O-Morph-Iso	Nonbody cavity	78	62/186 (33)	65/173 (38)
Bloomfield[31]	Iso ± Sufent	N$_2$O-Iso ± Sufent	Extraabdominal	96	5/31 (16)	11/32 (34)
Sengupta[32]	Fent-Iso	N$_2$O-Fent-Iso	DC laparoscopy	23	10/31 (32)	13/33 (39)
Hovorka[33]	Fent-Iso	N$_2$O-Fent-Iso/Enf	Gynecological laparoscopy	38	26/50 (52)	53/100 (53)
Eger[34]	Iso ± Fent	N$_2$O-Iso ± Fent	Various	178	63/147 (46)	64/133 (48)
Scheinin[35]	Fent-Iso	N$_2$O-Fent-Iso	Colonic	266	5/20 (25)	5/20 (25)
Ranta[36]	Fent-Iso	N$_2$O-Fent-Iso	Upper abdominal	121	12/24 (50)	13/26 (50)
Wrigley[8]	Fent-Des	N$_2$O-Fent-Des	DC orthopedic	29	3/13 (23)	6/14 (43)
Rapp[9]	Fent-Des	N$_2$O-Fent-Des	Orthopedic	53	9/22 (41)	10/24 (42)
Taylor[37]	Fent-Iso	N$_2$O-Fent-Iso	Laparoscopic cholecystectomy	87	13/24 (53)	9/26 (35)
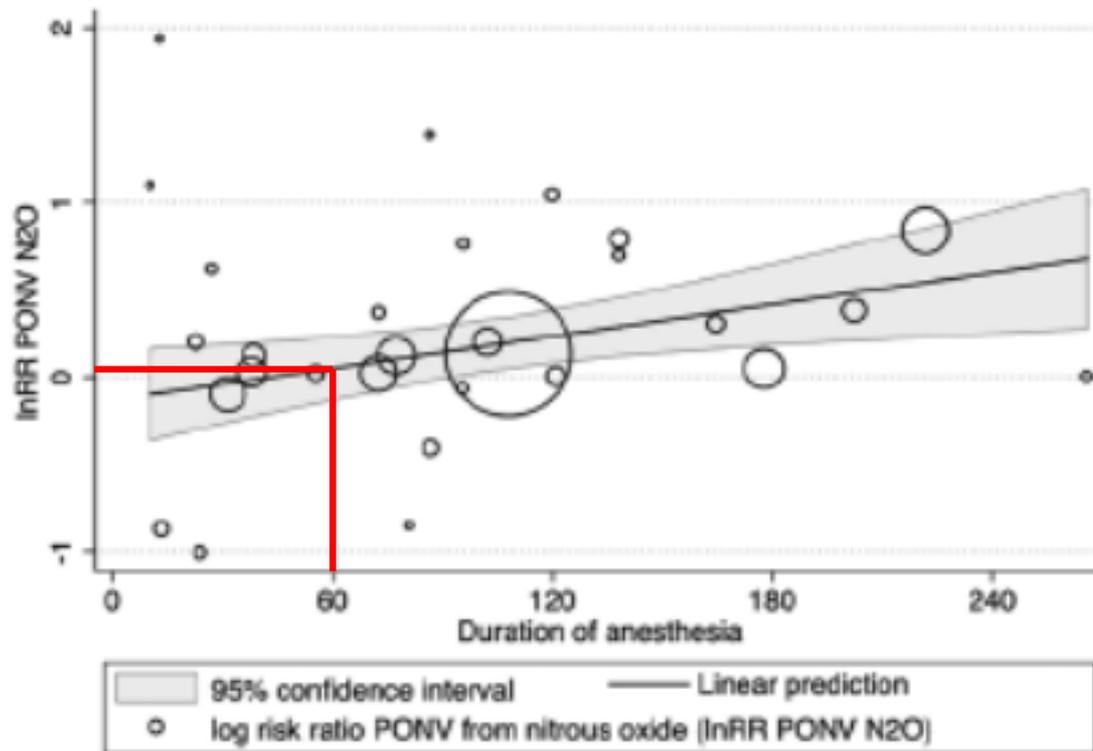
Fig. 2. The relationship between the log risk ratio for postoperative nausea and vomiting from nitrous oxide (lnRR PONV$_{N2O}$) and duration of exposure to nitrous oxide (N$_2$O), as a bubble plot. The meta-regression line of best fit (linear prediction) and upper and lower 95% CIs are shown. Bubble size is inversely proportional to the standard error of the log risk ratio in each study.

First author	Reference	Year	Duration of anesthesia (minutes)		ES (95% CI)	% Weight
Akhtar	38	1993	10.2		3.00 (0.64, 14.11)	0.83
Melnick	29	1987	13		6.94 (0.94, 51.27)	0.52
Arellano	26	2000	13.5		0.42 (0.20, 0.88)	2.65
Sengupta	31	1988	23		1.22 (0.63, 2.38)	3.06
Graham	11	1993	23.8		0.36 (0.15, 0.90)	2.03
Wrigley	8	1991	27.25		1.86 (0.58, 5.90)	1.38
Arellano	26	2000	31.5		0.90 (0.67, 1.21)	5.99
Hovorka	32	1989	38.25		1.02 (0.73, 1.42)	5.62
Lonie	27	1986	38.75		1.12 (0.71, 1.76)	4.56
Rapp	9	1992	55.4		1.02 (0.51, 2.02)	2.95
Muir	30	1987	72.75		1.02 (0.77, 1.34)	6.17
Mraovic	48	2008	72.8		1.44 (0.66, 3.16)	2.48
Muir	30	1987	77.5		1.13 (0.86, 1.49)	6.17
Sukhani	41	1994	80.85		0.42 (0.09, 2.03)	0.81
Taylor	37	1992	87		0.66 (0.35, 1.26)	3.17
Lebenbohm-Mansour	12	1993	87		4.00 (0.99, 16.08)	1.00
Pedersen	40	1993	95.5		0.93 (0.34, 2.53)	1.74
Bloomfield	31	1988	95.75		2.14 (0.83, 5.47)	1.91
Korttila	28	1987	102.5		1.22 (0.84, 1.77)	5.25
Apfel	44	2004	106.3		1.14 (1.05, 1.23)	7.63
Vanacker	43	1999	120		2.83 (1.29, 6.21)	2.48
Raeta	36	1991	121		1.00 (0.58, 1.73)	3.80
El-Galley	47	2007	138.5		2.00 (0.72, 5.54)	1.69
Bloomfield	42	1997	138.55		2.20 (1.22, 3.96)	3.53
Jensen	39	1993	165		1.35 (0.73, 2.48)	3.41
Eger	53	1990	176		1.04 (0.81, 1.35)	6.36
Fleischmann	45	2005	202.5		1.46 (0.93, 2.29)	4.56
Myles	46	2007	222		2.30 (1.85, 2.85)	8.71
Scherin	35	1990	266		1.00 (0.34, 2.94)	1.54
Overall (I-squared = 66.8%, p = 0.000)					1.21 (1.04, 1.40)	100.00

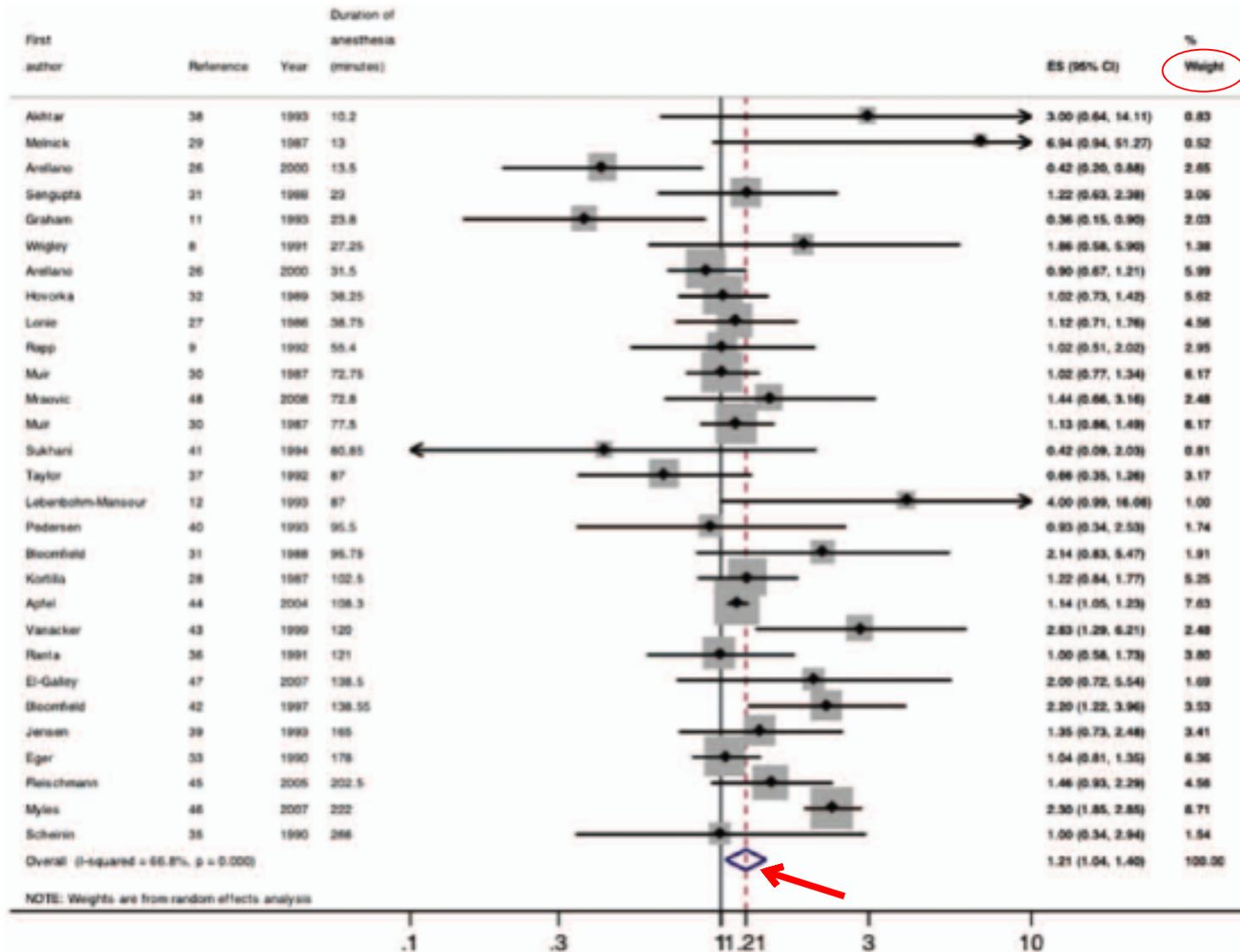NOTE: Weights are from random effects analysis

.1   .3   1 1.21   3   10

Fig. 3. Forest plot showing the results of meta-analysis of the overall effect of nitrous oxide on the risk of postoperative nausea and vomiting during the first 24 postoperative hours. *Boxes* indicate study weighting on random effects modeling. *Diamonds* and *bars* are mean and 95% confidence limits (CI) for the risk ratio or effect size for each study, and the *large diamond* indicates the overall risk ratio and 95% confidence limits.

Table 2. Stratification of Risk by Duration

Duration of Anesthesia	N Studies	n Total No-N_2O Groups	n Total N_2O Groups	NNT	RR PONV$_{N2O}$	RR PONV$_{N2O}$ 95% CIs
0–1 h	10	963	1,019	128	1.04	0.87–1.25
1–2 h	11	2,674	2,686	23	1.14*	1.05–1.27
>2 h	8	1,501	1,474	9	1.72*	1.48–1.98

The NNT to prevent PONV by avoiding N_2O and the RR and 95% CIs for postoperative nausea or vomiting from using N_2O (RR PONV$_{N2O}$). Studies are stratified into three groups, based on duration of anesthesia.

* Statistically significant, $P < 0.05$.

NNT = number needed to treat; N_2O = nitrous oxide; PONV = postoperative nausea and vomiting; RR = risk ratio.

CONCLUSIONS

- 吸入笑气持续的时间越长，发生**PONV**的可能性越大
- 当吸入笑气时间大于**1**小时，笑气的这种影响会更明显

LIMITATIONS

- Propofol
- High Fio_2
- Other factors

MECHANISMS

- an action on central opioid and dopaminergic

MECHANISMS

- diffusion of nitrous oxide into the middle ear cavity

  rapid increases in middle ear pressures have been demonstrated in animal models and humans after commencement of nitrous oxide, approaching a peak within 20 to 30 min

MECHANISMS

- bowel distension

  Meta-analysis has shown that the degree of bowel distension with nitrous oxide anesthesia is related to duration of anesthesia, with an odds ratio of 2.09 for each additional hour of exposure.

Nitrous oxide−related PONV is clinically insignificant up to at least 1h of exposure and should not be seen as an impediment to nitrous oxide use for limited periods of time, such as in minor or ambulatory surgery.

THANKS!