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Intraoperative Noise Isolation and Postoperative Nausea and Vomiting after Gynecological Laparoscopic Surgery: A Randomized Controlled Trial

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Running head: Earmuffs and Postoperative Nausea and Vomiting

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Key Abbreviations

ASA – American Society of Anesthesiologists

CI – confidence interval

FDR – false discovery rate

GEE – generalized estimating equations

ITT – intention-to-treat

PACU – post-anesthesia care unit

PCIA – patient-controlled intravenous analgesia

PONV – postoperative nausea and vomiting

PP – per-protocol

PTA – pure-tone average

RD – risk difference

SMD – standardized mean difference

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Abstract

Background: Postoperative nausea and vomiting (PONV) remain common after gynecological laparoscopic surgery despite guideline-based prophylaxis. Auditory information is still processed during clinically adequate general anesthesia, and operating rooms are persistently noisy, but whether attenuating intraoperative sound exposure alters PONV is unknown.

Methods: In this single-center, patient- and assessor-blinded randomized trial, women aged 18 to 65 yr undergoing elective gynecological laparoscopic surgery were randomized 1:1 to wear passive noise-attenuating earmuffs from induction until the end of surgery or to usual care. All patients received dexamethasone and palonosetron. The primary outcome was PONV incidence within 48 h, defined as any episode of nausea, retching, or vomiting, assessed across three prespecified windows (post-anesthesia care unit, to 24 h, and 24 to 48 h). Secondary outcomes included PONV severity, its components, rescue antiemetic use, pain, and quality of recovery.

Results: Of 364 patients assessed, 192 were randomized. PONV within 48 h occurred in 34 of 96 patients (35.4%) with noise isolation and 50 of 96 (52.1%) with control (adjusted risk difference, −0.179 [95% CI, −0.318 to −0.040]; $P = 0.012$). Across the three windows the overall adjusted risk difference was −0.134 (95% CI, −0.215 to −0.053; $P = 0.001$), with no treatment-by-window interaction ($P = 0.332$); window-specific values were −0.162, −0.172, and −0.068. PONV severity, retching, and three post hoc endpoints (the vomiting-or-retching composite, complete response 72.9% versus 56.2%, and total response 64.6% versus 47.9%) favored noise isolation after false discovery rate correction. Adverse events, quality of recovery, and opioid exposure (post hoc) showed no evidence of a difference.

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Conclusions: Among women receiving dual antiemetic prophylaxis for gynecological laparoscopic surgery, intraoperative noise isolation was associated with a lower incidence and severity of PONV.

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Introduction

Postoperative nausea and vomiting (PONV) remain among the most common and distressing complications after general anesthesia,[1,2] and the risk is particularly high after gynecological laparoscopic surgery, which current guidelines place among the higher-risk procedures.[1] PONV reduces comfort and satisfaction, delays recovery, and drives unplanned health care use and cost.[3,4] Even with guideline-based multimodal prophylaxis, residual rates approach 40%,[1] and antiemetic agents themselves may cause headache, oversedation, and visual disturbances.[5] Non-pharmacological strategies compatible with existing prophylaxis bundles are therefore of interest.

Operating rooms are persistently noisy, with measured levels commonly reaching 51 to 79 dB and briefly exceeding 85 dB when powered instruments are used.[6,7] Noise of this magnitude is not biologically inert: it elicits autonomic and neuroendocrine stress responses in awake humans,[8,9] and attenuating nighttime noise raises melatonin and lowers cortisol.[10] General anesthesia abolishes awareness but not auditory processing. A meta-analysis of randomized trials found that auditory stimuli are perceived and processed during clinically adequate anesthesia and can produce implicit memory without explicit recall;[11] anesthesia degrades large-scale information integration rather than silencing the brain,[12] and human hippocampal neurons continue to discriminate unexpected sounds and to encode features of speech.[13]

Two randomized trials of intraoperative noise isolation during laparoscopic surgery reported less postoperative pain and opioid requirement,[14,15] but neither was powered for PONV. Whether attenuating intraoperative sound exposure reduces PONV has not been tested in an adequately powered trial. We therefore conducted a randomized clinical trial to determine whether

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intraoperative noise isolation reduces PONV and improves recovery after gynecological laparoscopic surgery.

Materials and Methods

The detailed protocol has been published.[16] This patient- and assessor-blinded randomized controlled trial was conducted at The First Affiliated Hospital of Soochow University (Suzhou, Jiangsu, China), approved by the institutional ethics committee (No. 2024-259; July 9, 2024), and registered before enrollment (ChiCTR2400087460; https://www.chictr.org.cn/showproj.html?proj=236635, principal investigator, Huayue Liu; July 29, 2024). It followed the Declaration of Helsinki, all participants gave written informed consent, and reporting followed the Consolidated Standards of Reporting Trials guidelines.[17] An independent data and safety monitoring committee provided oversight.

Participants

Eligible participants were women aged 18 to 65 yr, American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective laparoscopic gynecological surgery expected to exceed 30 min. Exclusions were hearing impairment (pure-tone average [PTA] above 40 dB at 500 to 4,000 Hz) or ear malformation, pregnancy or lactation, prior chemotherapy, gastrointestinal motility or vestibular disorders, severe hepatic or renal failure, substance misuse, neurological or psychiatric disease, antiemetics or corticosteroids within 24 h, and allergy to a study drug; full criteria are in the protocol.

Randomization and Blinding

Participants were randomized 1:1 by stratified block randomization (block sizes 2 and 4) stratified by age (18 to 35, 36 to 50, 51 to 65 yr). The sequence was generated before enrollment by an independent biostatistician with no further contact with participants or staff and concealed

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in sequentially numbered, opaque, sealed envelopes, opened after the patient entered the operating room by a researcher uninvolved in recruitment, care, or outcome assessment, who was not blinded to allocation. Intraoperative management was fully protocolized, titrated to objective bispectral index (BIS) and surgical pleth index (SPI) targets, and documented in real time. The head and ears of every participant in both groups were covered with a surgical towel after induction, and patients and outcome assessors remained blinded until the final analysis.

Interventions

Patients fasted for 6 to 8 h and received no premedication. Anesthesia was induced with intravenous sufentanil 0.2 to 0.4 µg/kg and propofol 1.5 to 2.5 mg/kg, followed by rocuronium 0.6 mg/kg, and maintained with sevoflurane, remifentanil 0.1 to 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$, and supplemental sufentanil titrated to BIS 40 to 60 and SPI below 50. All patients received dexamethasone 5 mg and palonosetron 0.25 mg and, at the end of surgery, oxycodone 10 mg and sugammadex 200 mg; fluid volumes were at the anesthesiologist's discretion and were recorded. Rescue thresholds were identical in both groups: an additional dose of palonosetron 0.25 mg for any vomiting or persistent moderate-to-severe nausea beyond 10 min, and sufentanil 5 µg in the post-anesthesia care unit (PACU) or flurbiprofen axetil 50 mg on the ward for a pain score of 4 or higher. Patients receiving postoperative patient-controlled intravenous analgesia (PCIA) had sufentanil 1 µg/mL at 2 mL/h from the PACU.

In the noise-isolation group, passive noise-attenuating earmuffs (Peltor X5A; 3M Company, Saint Paul, Minnesota, United States) were fitted after induction and worn until the end of surgery; the control group wore none. These are industrial hearing protectors providing passive attenuation only; the manufacturer reports a single number rating of 37 dB (EN 352-1:2002) and a noise reduction rating of 31 dB (ANSI S3.19-1974). Sound was measured continuously for

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every patient with a digital sound-level meter (DSM-D1; DELIXI Electric, Yueqing, Zhejiang, China) fixed approximately 5 cm from the head, outside the earmuff, and the time-averaged A-weighted level was recorded for each case. This records the sound arriving at the head rather than the level reaching the ear canal, which the earmuff attenuates by an unmeasured amount; short acoustic peaks were not retained.

Outcomes

The primary outcome was PONV within 48 h, defined as any episode of nausea, retching, or vomiting, assessed in three sequential prespecified windows: in the PACU, from PACU discharge to 24 h (PACU–24 h), and from 24 to 48 h. In the PACU, blinded nurses asked about nausea and recorded retching or vomiting every 15 min until discharge; on the ward, blinded assessors interviewed patients at approximately 24 h and 48 h about the preceding interval, supplemented by nursing records.

Secondary outcomes were PONV severity on a 4-level ordinal scale (none; mild, not affecting daily activities; moderate, intermittently affecting them; severe, preventing them or involving three or more vomiting episodes),[18] the components of PONV, rescue antiemetic use, pain at rest and on coughing on a numerical rating scale,[19,20] rescue analgesic use, Quality of Recovery-15 at 24 h, 48 h, and 30 d,[21] the Richards-Campbell Sleep Questionnaire on the first two nights,[22] time to extubation, length of PACU and hospital stay, intervention for a hemodynamic event, adverse events, satisfaction on a 5-point Likert scale[23] (dichotomized as highly satisfied versus all other scores), and the Postoperative Morbidity Survey at 24 h, 48 h, and 30 d.[24-26]

Four endpoints were analyzed post hoc: the vomiting-or-retching composite, complete response, total response,[27,28] and PACU opioid exposure. Vomiting and retching are the same

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physiologic response, differing only in whether gastric contents are expelled, and were combined into a single composite to which a patient contributed one event whether retching, vomiting, or both were recorded. Complete response was defined as no vomiting or retching and no rescue antiemetic, and total response as no nausea, no vomiting or retching, and no rescue antiemetic. PACU opioid exposure was the total sufentanil received in the PACU from either of the two routes by which it could be given: the PCIA background infusion, calculated as the stay in minutes divided by 60 and multiplied by the 2 mL/h rate of a 1 μg/mL solution, and any 5 μg rescue bolus given for a pain score of 4 or higher. No patient received a rescue bolus in the PACU, so exposure reduces to the PCIA infusion, and patients not receiving PCIA received no opioid in the PACU at all.

Sample Size

The sample size was informed by our own preliminary trial (46 patients, 23 per group), reported in the published protocol,[16] in which 48-h PONV was 21.74% with noise isolation and 47.83% with usual care, and by reported incidences of 42% to 60% after gynecological laparoscopic surgery.[20,29,30] Because that estimate came from a small preliminary sample and was expected to be optimistic, we assumed a 45% control incidence and a 20-percentage-point absolute reduction. With a two-sided α of 0.05 and 80% power (PASS 21.0.3; NCSS, Kaysville, Utah, United States), 86 patients per group were required; allowing 10% attrition, 96 per group (192 total) were enrolled. This figure fixed the sample size and was not a minimal clinically important difference, none of which was prespecified. The calculation was for the primary outcome alone. No power calculation was performed for subgroup or interaction effects, so all subgroup analyses are exploratory and are interpreted by the direction and precision of their estimates rather than by hypothesis testing.

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Statistical Analysis

The prespecified primary approach was intention-to-treat (ITT): all randomized patients analyzed as assigned. The per-protocol (PP) population defined in the protocol[16] excluded patients who received non-protocol antiemetics or postoperative PCIA, deviated from the medication regimen, or were converted to laparotomy. A third, less restrictive PP population retained the recipients of a non-protocol postoperative rescue antiemetic and excluded only the remaining violations.

Categorical data are frequencies (percentages); continuous data are means (standard deviation [SD]) or medians (interquartile range [IQR]) according to the Shapiro-Wilk test. Baseline balance was assessed by standardized mean differences (SMDs) without hypothesis testing, an SMD above 0.10 indicating meaningful imbalance.

Outcomes measured in more than one window are correlated within patient and were analyzed jointly by generalized estimating equations (GEE) clustering on patient, with an exchangeable working correlation and robust variance.[31] Binary outcomes were fitted with an identity link, giving absolute risk differences (RDs), which are the effect measure reported throughout. Ordinal severity used a cumulative-logit model fitted by independence estimating equations with cluster-robust variance, and repeated continuous outcomes linear GEE. Models included treatment, window, and the covariates below, with interaction terms added for window-specific estimates. The overall treatment effect came from the main-effects model, and a 3-degree-of-freedom Wald test on the interaction model tested for an effect in any window; window-specific contrasts and the treatment-by-window interaction are descriptive components of the same model rather than independent tests. Single-observation outcomes used the corresponding regression models with robust variance.

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All models were adjusted for every baseline covariate with an unrounded SMD above 0.10, as the analysis plan specifies[16]: body mass index, history of comorbidities, tumor pathology, type of surgery, the Apfel score, ASA physical status, Surgical Outcome Risk Tool score, and history of PONV or motion sickness. Unadjusted estimates are reported alongside. Sensitivity analyses varied the covariate set, including the fuller set named in the protocol, and replaced the exchangeable working correlation with an independence structure.

Prespecified subgroup analyses of the primary outcome examined age stratum, Amsterdam Preoperative Anxiety and Information Scale score, smoking, history of PONV or motion sickness, Apfel score, and PTA, using adjusted relative risks from modified Poisson regression with robust standard errors[32] and interaction terms; each subgroup model omitted the variable defining that subgroup. The Apfel score is the simplified risk score recorded prospectively on the baseline case report form and is analyzed as 1 to 2 versus 3 to 4. The trial was not powered to detect interaction, so all subgroup analyses are exploratory and their interaction tests are reported for completeness rather than as a basis for inference.

The primary endpoint was tested at a two-sided α of 0.05 without multiplicity correction. Because the secondary and post hoc analyses were exploratory, the Benjamini-Hochberg procedure was used to control the false discovery rate (FDR) at q below 0.05 rather than the family-wise error rate.[33] The prespecified secondary outcomes formed one family and the four post hoc endpoints a second, separately corrected family; all were interpreted as hypothesis-generating.

Safety outcomes and Postoperative Morbidity Survey subdomains were descriptive and excluded from the FDR families, with Fisher exact tests and adjusted RDs as exploratory

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estimates; where a window contained a zero cell, inference rests on the risk difference and the exact test.

No interim analyses were planned, primary outcome data were complete and were not imputed, and all tests were two-sided. The analysis plan in the published protocol specified mixed-effects models; marginal models with cluster-robust variance were used instead, to estimate population-averaged effects. Analyses used Python 3.11 (Python Software Foundation, Wilmington, Delaware, United States) with NumPy, SciPy, pandas, and Matplotlib.

Results

Patient Characteristics

Patients were enrolled from September 14, 2024, to November 30, 2025, and 30-day follow-up ended December 30, 2025. Of 364 patients assessed, 172 were excluded before randomization (24 for a PTA above 40 dB); 192 were randomized (96 per group) and all analyzed in the ITT population. The protocol-defined PP population comprised 74 and 75 patients and the less restrictive PP population 83 and 83 (**figure 1**). On the wards metoclopramide 10 mg was given in place of palonosetron in 17 of the 18 patients who required rescue. One patient in the noise-isolation group received droperidol during surgery in addition to the protocol prophylaxis and is excluded from both PP populations.

Baseline characteristics are summarized in **table 1**. Eight had an SMD above 0.10 and were adjusted for in every model: body mass index (0.36), history of comorbidities (0.29), tumor pathology (0.19), type of surgery (0.13), the Apfel score (0.13), ASA physical status (0.13), Surgical Outcome Risk Tool score (0.12), and history of PONV or motion sickness (0.10). Intraoperative characteristics are summarized in **Supplemental table S1 (https://links.lww.com/ALN/E760)**. None differed between the groups except rocuronium

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(median 90.0 [IQR, 70.0 to 120.0] versus 72.5 [57.5 to 100.0] mg; $P = 0.015$, uncorrected for multiplicity), and the time-averaged A-weighted level recorded at the head was similar (median 66.65 [IQR, 64.38 to 67.40] versus 65.85 [64.60 to 67.30] dB; $P = 0.485$).

Primary Outcome

PONV within 48 h occurred in 34 of 96 patients (35.4%) with noise isolation and 50 of 96 (52.1%) with control (unadjusted RD, −0.167 [95% CI, −0.305 to −0.028]; $P = 0.019$; adjusted RD, −0.179 [95% CI, −0.318 to −0.040]; $P = 0.012$) (**figure 2A**; **table 2**). This corresponds to an absolute risk reduction of 16.7 percentage points, a relative risk reduction of 32.0%, a number needed to treat of 6, and an adjusted relative risk of 0.66 (95% CI, 0.48 to 0.93).

When the three windows were analyzed jointly by GEE, the overall adjusted risk difference was −0.134 (95% CI, −0.215 to −0.053; $P = 0.001$), and the 3-degree-of-freedom Wald test was consistent with an effect in at least one window ($\chi^2 = 11.69$; $P = 0.009$). No variation across windows was detected (interaction $\chi^2 = 2.20$, df = 2; $P = 0.332$). Window-specific risk differences were −0.162, −0.172, and −0.068 (**figure 2A**; **table 2**).

Sensitivity analyses did not change the effect. In the protocol-defined PP population, PONV occurred in 21 of 74 (28.4%) versus 35 of 75 (46.7%) (unadjusted RD, −0.183 [95% CI, −0.336 to −0.030]; $P = 0.019$; adjusted RD, −0.198 [95% CI, −0.349 to −0.047]; $P = 0.010$), and in the less restrictive PP population in 30 of 83 (36.1%) versus 43 of 83 (51.8%) (unadjusted RD, −0.157 [95% CI, −0.306 to −0.007]; $P = 0.040$; adjusted RD, −0.174 [95% CI, −0.321 to −0.027]; $P = 0.020$), with overall GEE effects of −0.135 and −0.136 (both $P \leq 0.002$) (**table S2, https://links.lww.com/ALN/E760**). In the ITT population the risk difference ranged from −0.167 (unadjusted) to −0.179 (the adjustment set of the primary model), all $P \leq 0.019$, and an independence working correlation left the across-window effect unchanged.

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Secondary Outcomes

PONV severity was lower with noise isolation (overall adjusted odds ratio, 0.41 [95% CI, 0.23 to 0.72]; $q = 0.014$), with no evidence of a treatment-by-window interaction ($P = 0.695$) (**figure 2B**; **Supplemental table S3, https://links.lww.com/ALN/E760**). Retching occurred in 9 of 96 (9.4%) versus 23 of 96 (24.0%) (overall adjusted RD, −0.087 [95% CI, −0.140 to −0.033]; $q = 0.014$). Vomiting showed no evidence of a difference ($q = 0.593$) and nausea a smaller effect that did not survive FDR correction (−0.075 [95% CI, −0.147 to −0.003]; $q = 0.204$) (**table 3**; **Supplemental figure S1, https://links.lww.com/ALN/E760**).

There was no evidence of a between-group difference in rescue antiemetic or analgesic use, pain, Quality of Recovery-15 or Richards-Campbell Sleep Questionnaire scores, time to extubation, length of PACU or hospital stay, hemodynamic interventions, satisfaction, or postoperative morbidity, for none of which the trial was powered (**table 2**; **Supplemental table S4, https://links.lww.com/ALN/E760**).

Post Hoc Analyses

Over 0 to 48 h, vomiting or retching occurred in 25 of 96 patients (26.0%) versus 42 of 96 (43.8%); across the three windows, the adjusted RD was −0.122 (95% CI, −0.190 to −0.053; $q = 0.002$) (**table 3**). Complete response was achieved by 70 of 96 patients (72.9%) versus 54 of 96 (56.2%); its across-window adjusted RD was 0.113 (95% CI, 0.044 to 0.183; $q = 0.002$). Total response was achieved by 62 of 96 patients (64.6%) versus 46 of 96 (47.9%); its across-window adjusted RD was 0.134 (95% CI, 0.053 to 0.215; $q = 0.002$) (**Supplemental table S5, https://links.lww.com/ALN/E760**).

PACU opioid exposure was similar between groups: postoperative PCIA was used by 10 of 96 (10.4%) versus 11 of 96 (11.5%) (adjusted RD, −0.023 [95% CI, −0.100 to 0.054]; $P = 0.563$;

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q = 0.563), mean PACU sufentanil among those patients was 1.41 versus 1.19 μg (P = 0.360), and across the cohort the adjusted mean difference was −0.015 μg (95% CI, −0.135 to 0.105; P = 0.809).

Subgroup Analyses

Point estimates favored noise isolation in every prespecified subgroup and no interaction was significant (all adjusted interaction P greater than 0.05) (**figure 3**, **Supplemental figure S2**, **Supplemental figure S3, https://links.lww.com/ALN/E760**). Only 3 participants smoked, so the smoking stratum is shown with its counts but yields no estimate; in the PACU window the PTA subgroup likewise contained an empty cell (0 of 15 versus 6 of 18), so its relative risk and interaction test are not estimable. Because the trial was powered for the primary outcome only, the absence of significant interaction is uninformative about true effect modification.

Safety Outcomes

Adverse events were infrequent and similar in the two groups (5 of 96 [5.2%] versus 9 of 96 [9.4%]; adjusted RD, −0.039 [95% CI, −0.105 to 0.026]; P = 0.406, Fisher exact test) and predominantly hemodynamic; tachycardia and desaturation after extubation occurred only in the control group. No shivering, emergence agitation, allergic reaction, serious arrhythmia, or cardiac arrest occurred, and no patient reported discomfort attributable to the earmuffs (**Supplemental table S6, https://links.lww.com/ALN/E760**).

Discussion

In 192 women undergoing gynecological laparoscopic surgery, intraoperative noise isolation with passive earmuffs was associated with a lower incidence of PONV within 48 h, with no evidence that the effect varied across the three assessment windows, although the trial was not powered to detect such variation. PONV severity, retching, and three post hoc endpoints also

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favored noise isolation after false discovery rate correction, and the treatment effect was stable across all analysis populations and model specifications. Every patient in both groups received dexamethasone and palonosetron, so the difference was observed on top of guideline-concordant dual prophylaxis, not in place of it.

No previous trial was designed to detect this effect, so the existing evidence neither supports nor contradicts it. Two randomized trials have tested intraoperative noise isolation during laparoscopic surgery; both were powered for postoperative pain, and neither established an effect on PONV.[14,15] The present trial differs in two respects: PONV was the prespecified primary outcome and the trial was powered for it, and the three windows were analyzed in a single correlated-data model. A parallel literature adds sound rather than removing it. Music has been reported to reduce perioperative stress hormones, improve recovery, and ease pain and anxiety.[34-36] The evidence for an effect on PONV, however, is inconsistent.[37] Removing sound and adding structured sound are distinct interventions and have not been compared directly.

The 20-percentage-point reduction assumed for the sample size was a planning figure rather than a clinical threshold. PONV remains common despite guideline-concordant prophylaxis and carries a measurable cost in comfort, recovery, and health care use.[3] Against that background, the observed reduction is potentially meaningful, particularly because the device is inexpensive (listed at approximately RMB 278 on JD.com in China and US$43 to US$53 on Amazon in the United States), adds no drug exposure, and requires no change to anesthetic practice. This reasoning has limits: the confidence interval around the primary risk difference spans effects from modest to large, no minimal clinically important difference was prespecified, and a single trial cannot establish the effect size.

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At the same time, the mechanism remains unproven. Volatile anesthetics, opioids, patient susceptibility, and the procedure dominate PONV risk.[1,38] All were standardized or balanced here, and intraoperative and PACU opioid exposures were similar. We do not suggest that operating room noise outweighs them, only that it may be an additional and incompletely characterized contributor. This hypothesis rests on two observations. First, general anesthesia abolishes awareness but not auditory processing: stimuli presented under clinically adequate anesthesia can generate implicit memory without explicit recall.[11] Anesthesia degrades large-scale information integration rather than silencing the brain.[12] In the anesthetized human hippocampus, neurons continue to discriminate unexpected sounds and to encode speech.[13] Our patients were maintained within the protocol depth-of-anesthesia targets, and none reported explicit recall, so the substrate at issue is auditory processing preserved without awareness. Second, noise activates autonomic and neuroendocrine stress pathways.[8,9] Attenuating nighttime noise alters cortisol and melatonin secretion.[10] Residual auditory processing in an intense acoustic environment may therefore sustain a sympathoadrenal response that lowers the threshold for emesis, but no human study has shown that noise itself causes nausea.

Two aspects of how the trial was run bear on the interpretation of these results. The first is the device. Passive attenuation was chosen because such devices are inexpensive, need no power source or bedside electrical equipment, and isolate the effect of attenuation from that of a superimposed stimulus. How much sound the earmuffs attenuated is uncertain. The manufacturer's ratings of 37 dB and 31 dB come from different test standards, are not directly comparable, and both overestimate field performance.[39,40] Conventional derating of the 31 dB rating leaves roughly 12 dB of real-world attenuation, so the earmuffs are unlikely to have brought the level at the ear down to the 30 dB the World Health Organization recommends for

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ward rooms.[41] The second is rescue. The protocol specified a second dose of palonosetron 0.25 mg, but metoclopramide 10 mg was given instead in almost every patient who required rescue, because the surgical wards stock metoclopramide whereas palonosetron and ondansetron are used in our operating rooms. These patients constitute the non-protocol postoperative rescue antiemetic exclusions from the protocol-defined PP population. Guidelines do not recommend metoclopramide for prophylaxis.[1] At 10 mg it confers only marginal benefit, whereas 25 mg and 50 mg are effective.[42,43] Deviations occurred at a similar rate in the two groups, rescue was infrequent overall, and the complete- and total-response endpoints, which incorporate rescue antiemetic use, were concordant with the primary analysis. Future trials should specify a rescue agent that the receiving wards stock.

In addition, this trial has five principal limitations. First, the acoustic dose reaching the ear was not measured in individual patients, so the exposure contrast underlying the observed difference is unknown; no neural, endocrine, or autonomic mediator was measured, individual noise sensitivity was not assessed, and blinding success was not formally tested. Second, only passive attenuation was studied; the results do not extend to active noise cancellation, earplugs, or structured auditory stimuli such as music. Third, the trial was powered for the primary outcome alone: the absence of differences in pain, recovery, sleep quality, and morbidity is absence of evidence rather than evidence of absence, the subgroup analyses were underpowered to detect interaction, and the secondary and post hoc endpoints remain hypothesis-generating despite false discovery rate control. Fourth, the trial was conducted at a single tertiary hospital in China, in one high-risk procedure that current guidelines group with laparoscopic cholecystectomy and with urological, orthopedic, and bariatric surgery.[1] Anesthesia was maintained with a combined intravenous-inhalational technique, so the effect in other settings,

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procedures, and anesthetic regimens is untested. Fifth, satisfaction was captured only as a coarse dichotomy, neither time to resumption of normal activities nor cost-effectiveness was assessed, follow-up was limited to 48 h for PONV and 30 d for morbidity, and patients and the public were not involved in the design.

Conclusion

Among women receiving dexamethasone and palonosetron for gynecological laparoscopic surgery, intraoperative noise isolation with passive earmuffs was associated with a lower incidence and severity of PONV within 48 h and with no signal of excess adverse events, though the trial was not powered to detect harm. Whether this justifies adding earmuffs to standard prophylaxis depends on confirmation in multicenter trials that measure the acoustic dose inside the earmuff, examine the physiological mediators this trial could only postulate, and follow patient-centered recovery beyond 48 h.

Reproducible Science

The full trial protocol has been published previously (Fu C, Xia F, Yan Z, et al. BMC Anesthesiol 2025;25:48; doi: 10.1186/s12871-025-02924-3) and is also available from the corresponding author on request. Deidentified individual-patient data underlying the results reported in this article, together with the analytic code used to generate the primary, secondary, and sensitivity analyses, will be made available to qualified investigators on reasonable written request to the corresponding author (docliu.hy@suda.edu.cn), conditional on submission of a methodologically sound proposal, ethics committee approval at the requesting institution, and a signed data-sharing agreement.

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Supplemental Digital Content

Supplemental Material, https://links.lww.com/ALN/E760

Table S1. Intraoperative clinical characteristics

Table S2. Primary outcome in the two per-protocol populations

Table S3. Severity of postoperative nausea and vomiting in the intention-to-treat population

Table S4. Morbidity according to the Postoperative Morbidity Survey (intention-to-treat population)

Table S5. Post hoc analyses in the intention-to-treat population

Table S6. Adverse events in the intention-to-treat population

Figure S1. Component and composite outcomes in the intention-to-treat population

Figure S2. Subgroup analysis of the incidence of PONV in the PACU in the intention-to-treat population

Figure S3. Subgroup analysis of the incidence of PONV from the PACU to 24 h in the intention-to-treat population

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Figure Legends

Figure 1. Flow chart of the trial. The intention-to-treat population comprised all randomized patients. The less restrictive per-protocol population excluded postoperative patient-controlled intravenous analgesia (PCIA), deviation from the medication regimen, conversion to laparotomy, and the one patient given a non-protocol antiemetic during surgery; the protocol-defined per-protocol population additionally excluded recipients of a non-protocol postoperative rescue antiemetic.

Figure 2. Incidence and severity of PONV in the intention-to-treat population. (A) Incidence of PONV within 48 h and in each of the three sequential assessment windows. (B) Distribution of PONV severity in each window. Values above the horizontal bars are risk differences (A) and odds ratios (B) with 95% CIs, adjusted for the eight baseline covariates with a standardized mean difference above 0.10. Window-specific estimates are contrasts within a single model, not independent tests. Abbreviations: PACU, post-anesthesia care unit; PONV, postoperative nausea and vomiting.

Figure 3. Subgroup analysis of the incidence of PONV within 48 h in the intention-to-treat population. Abbreviations: APAIS, Amsterdam Preoperative Anxiety and Information Scale; NA, not estimable; PONV, postoperative nausea and vomiting; PTA, pure-tone average; RR, relative risk.

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Table 1. Baseline and Demographic Characteristics

Characteristic	Patients, No. (%) [a]		SMD [b]
	Noise isolation (n = 96)	Control (n = 96)	
Age, yr			0.06
18–35	32 (33.3)	32 (33.3)	
36–50	33 (34.4)	31 (32.3)	
51–65	31 (32.3)	33 (34.4)	
BMI, kg/m^2, mean (SD)	22.70 (3.53)	23.89 (3.15)	0.36
Type of surgery			0.13
Laparoscopic uterine surgery	35 (36.5)	32 (33.3)	
Laparoscopic ovarian surgery	34 (35.4)	39 (40.6)	
Laparoscopic uterine and ovarian surgery	27 (28.1)	25 (26.0)	
Current smoker			0.08
Yes	1 (1.0)	2 (2.1)	
No	95 (99.0)	94 (97.9)	
History of PONV or motion sickness			0.10
Yes	50 (52.1)	45 (46.9)	
No	46 (47.9)	51 (53.1)	
ASA physical status			0.13
I	44 (45.8)	38 (39.6)	
II	52 (54.2)	58 (60.4)	
History of comorbidities			0.29
None	76 (79.2)	80 (83.3)	

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Cerebrovascular disease	2 (2.1)	2 (2.1)	
Diabetes	5 (5.2)	3 (3.1)	
Hypertension	10 (10.4)	5 (5.2)	
Other	3 (3.1)	6 (6.2)	
Preoperative medication [c]			0.00
Yes	16 (16.7)	16 (16.7)	
No	80 (83.3)	80 (83.3)	
PTA score, dB			0.08
0–25	81 (84.4)	78 (81.2)	
26–40	15 (15.6)	18 (18.8)	
Apfel score			0.13
1–2	36 (37.5)	42 (43.8)	
3–4	60 (62.5)	54 (56.2)	
APAIS score			0.02
≤12	56 (58.3)	55 (57.3)	
>12	40 (41.7)	41 (42.7)	
Tumor pathology			0.19
Benign	89 (92.7)	93 (96.9)	
Malignant	7 (7.3)	3 (3.1)	
SORT score, median [IQR]	0.06 [0.06, 0.06]	0.06 [0.06, 0.09]	0.12

Abbreviations: APAIS, Amsterdam Preoperative Anxiety and Information Scale; ASA, American Society of Anesthesiologists; BMI, body mass index; IQR, interquartile range; PONV, postoperative nausea and vomiting; PTA, pure-tone average; SD, standard deviation; SMD, standardized mean difference; SORT, Surgical Outcome Risk Tool.

[a] Data are No. (%) unless otherwise indicated.

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[b] Covariates were selected on the unrounded standardized mean difference, so history of PONV or motion sickness, shown here as 0.10, is included.

[c] Preoperative medication denotes regular medication taken for a coexisting condition; no patient received sedative premedication before induction.

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Table 2. Primary and Secondary Outcomes in the Intention-to-Treat Population

Outcome	Patients, No. (%) [a]		Mean or Risk difference (95% CI) [b]		*P* value [c]	*q* value [d]
	Noise isolation (n = 96)	Control (n = 96)	Unadjusted	Adjusted [e]		
Primary outcome						
PONV within 48 h (primary outcome)	34 (35.4)	50 (52.1)	−0.167 (−0.305 to −0.028)	−0.179 (−0.318 to −0.040)	0.012	NA
Average marginal effect across the three windows (GEE) [f]				−0.134 (−0.215 to −0.053)	0.001	NA
PACU	16 (16.7)	30 (31.2)		−0.162 (−0.279 to −0.044)	0.007	NA
PACU–24 h	33 (34.4)	48 (50.0)		−0.172 (−0.308 to −0.036)	0.013	NA
24–48 h	3 (3.1)	8 (8.3)		−0.068 (−0.138 to 0.002)	0.057	NA
Secondary outcomes						
Rescue antiemetic use, any episode within 48 h	9 (9.4)	9 (9.4)	0.000 (−0.083 to 0.083)	−0.005 (−0.091 to 0.080)	0.903	
Average marginal effect across the three windows (GEE)				0.002 (−0.029 to 0.033)	0.900	0.900
PACU	0 (0.0)	0 (0.0)		−0.001 (−0.010 to 0.007)	0.731	
PACU–24 h	9 (9.4)	8 (8.3)		0.009 (−0.072 to 0.090)	0.830	
24–48 h	1 (1.0)	1 (1.0)		−0.001 (−0.030 to 0.027)	0.919	
Moderate-to-severe pain at rest (NRS ≥ 4), any episode within 48 h	13 (13.5)	9 (9.4)	0.042 (−0.048 to 0.132)	0.047 (−0.048 to 0.143)	0.330	
Average marginal effect across the three windows (GEE)				0.016 (−0.024 to 0.056)	0.428	0.593
PACU	2 (2.1)	3 (3.1)		−0.005 (−0.048 to 0.039)	0.829	
PACU–24 h	11 (11.5)	9 (9.4)		0.026 (−0.060 to 0.113)	0.550	
24–48 h	2 (2.1)	0 (0.0)		0.026 (−0.006 to	0.109	

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				0.059)		
Moderate-to-severe pain on coughing (NRS ≥ 4), any episode within 48 h	46 (47.9)	53 (55.2)	−0.073 (−0.214 to 0.068)	−0.059 (−0.203 to 0.084)	0.418	
Average marginal effect across the three windows (GEE)				−0.038 (−0.115 to 0.039)	0.333	0.593
PACU	7 (7.3)	9 (9.4)		−0.007 (−0.083 to 0.070)	0.863	
PACU–24 h	42 (43.8)	51 (53.1)		−0.080 (−0.221 to 0.061)	0.268	
24–48 h	14 (14.6)	18 (18.8)		−0.028 (−0.135 to 0.080)	0.616	
Quality of Recovery-15 score, median [IQR]				−0.67 (−2.37 to 1.02)	0.435	0.593
24 h	112 [106, 117]	113 [108, 118]		−1.08 (−4.14 to 1.97)	0.488	
48 h	127 [122, 131]	128 [124, 131]		−1.21 (−3.43 to 1.02)	0.288	
30 d	150 [148, 150]	150 [148, 150]		0.26 (−0.49 to 1.02)	0.494	
Richards-Campbell Sleep Questionnaire score, median [IQR]				1.79 (−1.74 to 5.31)	0.321	0.593
First postoperative night	78 [66, 83]	75 [60, 82]		3.25 (−1.38 to 7.88)	0.169	
Second postoperative night	86 [77, 90]	84 [77, 91]		0.32 (−2.90 to 3.55)	0.845	
Rescue analgesic use, 0–48 h	37 (38.5)	36 (37.5)	0.010 (−0.127 to 0.148)	−0.019 (−0.139 to 0.102)	0.764	0.818
Time to extubation, median [IQR], min	5 [2, 7]	5 [2, 7]		0.96 (−0.97 to 2.88)	0.330	0.593
Length of PACU stay, median [IQR], min	44 [29, 59]	45 [30, 60]		−2.84 (−9.64 to 3.96)	0.413	0.593
Length of hospital stay, median [IQR], d	4 [3, 5]	4 [3, 5]		−0.09 (−0.53 to 0.35)	0.676	0.780
Intervention for hemodynamic event	3 (3.1)	6 (6.2)	−0.031 (−0.091 to 0.029)	−0.033 (−0.083 to 0.017)	0.191	0.593

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Highly satisfied (score 5)	92 (95.8)	91 (94.8)	0.010 (−0.050 to 0.070)	0.015 (−0.047 to 0.077)	0.632	0.780
POMS [g]						
0–24 h	12 (12.5)	18 (18.8)	−0.063 (−0.165 to 0.040)	−0.065 (−0.167 to 0.037)	0.212	NA
24–48 h	4 (4.2)	5 (5.2)	−0.010 (−0.070 to 0.050)	−0.026 (−0.089 to 0.036)	0.410	NA
30 d	0 (0.0)	1 (1.0)	−0.010 (−0.031 to 0.010)	−0.008 (−0.024 to 0.008)	0.313	NA

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; GEE, generalized estimating equations; IQR, interquartile range; NRS, numerical rating scale; PACU, post-anesthesia care unit; POMS, Postoperative Morbidity Survey; PONV, postoperative nausea and vomiting.

[a] Data are No. (%) unless otherwise indicated.

[b] From generalized estimating equations clustered on patient (exchangeable correlation, robust variance). Window-specific rows are contrasts within that model, not independent tests.

[c] *P* values are from the adjusted estimate.

[d] Benjamini-Hochberg false discovery rate, applied within two families: fifteen prespecified secondary outcomes (eleven here, three in table 3, PONV severity in table S4) and four post hoc endpoints (table 3 and table S3). NA, outside both families; the primary outcome belonged to neither.

[e] Adjusted for the eight baseline covariates with a standardized mean difference above 0.10: body mass index, history of comorbidities, tumor pathology, type of surgery, the Apfel score, ASA physical status, Surgical Outcome Risk Tool score, and history of PONV or motion sickness.

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[f] Treatment × window interaction, primary outcome, risk-difference model: $\chi^2 = 2.20$, df = 2, $P = 0.332$. The average marginal effect is the mean risk difference across the three windows, not the 48-h risk difference, which counts each patient once.

[g] Recorded separately at each time point; no cumulative 0–48 h measure.

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Table 3. Component Outcomes for Postoperative Nausea and Vomiting in the Intention-to-Treat Population

Outcome	Patients, No. (%) [a]		Mean or Risk difference (95% CI) [b]		*P* value [c]	*q* value [d]
	Noise isolation (n = 96)	Control (n = 96)	Unadjusted	Adjusted [e]		
Nausea, any episode within 48 h	21 (21.9)	32 (33.3)	−0.115 (−0.240 to 0.011)	−0.131 (−0.258 to −0.004)	0.043	
Average marginal effect across the three windows (GEE)				−0.075 (−0.147 to −0.003)	0.041	0.204
PACU	13 (13.5)	19 (19.8)		−0.078 (−0.182 to 0.025)	0.139	
PACU–24 h	19 (19.8)	28 (29.2)		−0.110 (−0.229 to 0.010)	0.073	
24–48 h	2 (2.1)	4 (4.2)		−0.037 (−0.091 to 0.017)	0.182	
Retching, any episode within 48 h	9 (9.4)	23 (24.0)	−0.146 (−0.249 to −0.042)	−0.151 (−0.251 to −0.051)	0.003	
Average marginal effect across the three windows (GEE)				−0.087 (−0.140 to −0.033)	0.002	0.014
PACU	3 (3.1)	12 (12.5)		−0.097 (−0.171 to −0.023)	0.010	
PACU–24 h	9 (9.4)	21 (21.9)		−0.128 (−0.227 to −0.029)	0.011	
24–48 h	0 (0.0)	3 (3.1)		−0.035 (−0.073 to 0.004)	0.076	
Vomiting, any episode within 48 h	19 (19.8)	20 (20.8)	−0.010 (−0.125 to 0.104)	−0.026 (−0.146 to 0.093)	0.668	
Average marginal effect across the three windows (GEE)				−0.030 (−0.087 to 0.027)	0.307	0.593
PACU	3 (3.1)	7 (7.3)		−0.051 (−0.117 to 0.015)	0.133	
PACU–24 h	19 (19.8)	20 (20.8)		−0.019 (−0.135 to 0.096)	0.742	
24–48 h	1 (1.0)	2 (2.1)		−0.019 (−0.057 to 0.019)	0.318	

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Vomiting or retching (composite), any episode within 48 h [f]	25 (26.0)	42 (43.8)	−0.177 (−0.310 to −0.044)	−0.193 (−0.327 to −0.060)	0.004	
Average marginal effect across the three windows (GEE)				−0.122 (−0.190 to −0.053)	<0.001	0.002
PACU	6 (6.2)	19 (19.8)		−0.146 (−0.240 to −0.053)	0.002	
PACU–24 h	25 (26.0)	40 (41.7)		−0.167 (−0.298 to −0.036)	0.012	
24–48 h	1 (1.0)	5 (5.2)		−0.052 (−0.106 to 0.001)	0.053	

Abbreviations: CI, confidence interval; GEE, generalized estimating equations; PACU, post-anesthesia care unit.

[a] Data are No. (%) unless otherwise indicated.

[b] From generalized estimating equations clustered on patient (exchangeable correlation, robust variance). Window-specific rows are contrasts within that model, not independent tests.

[c] *P* values are from the adjusted estimate.

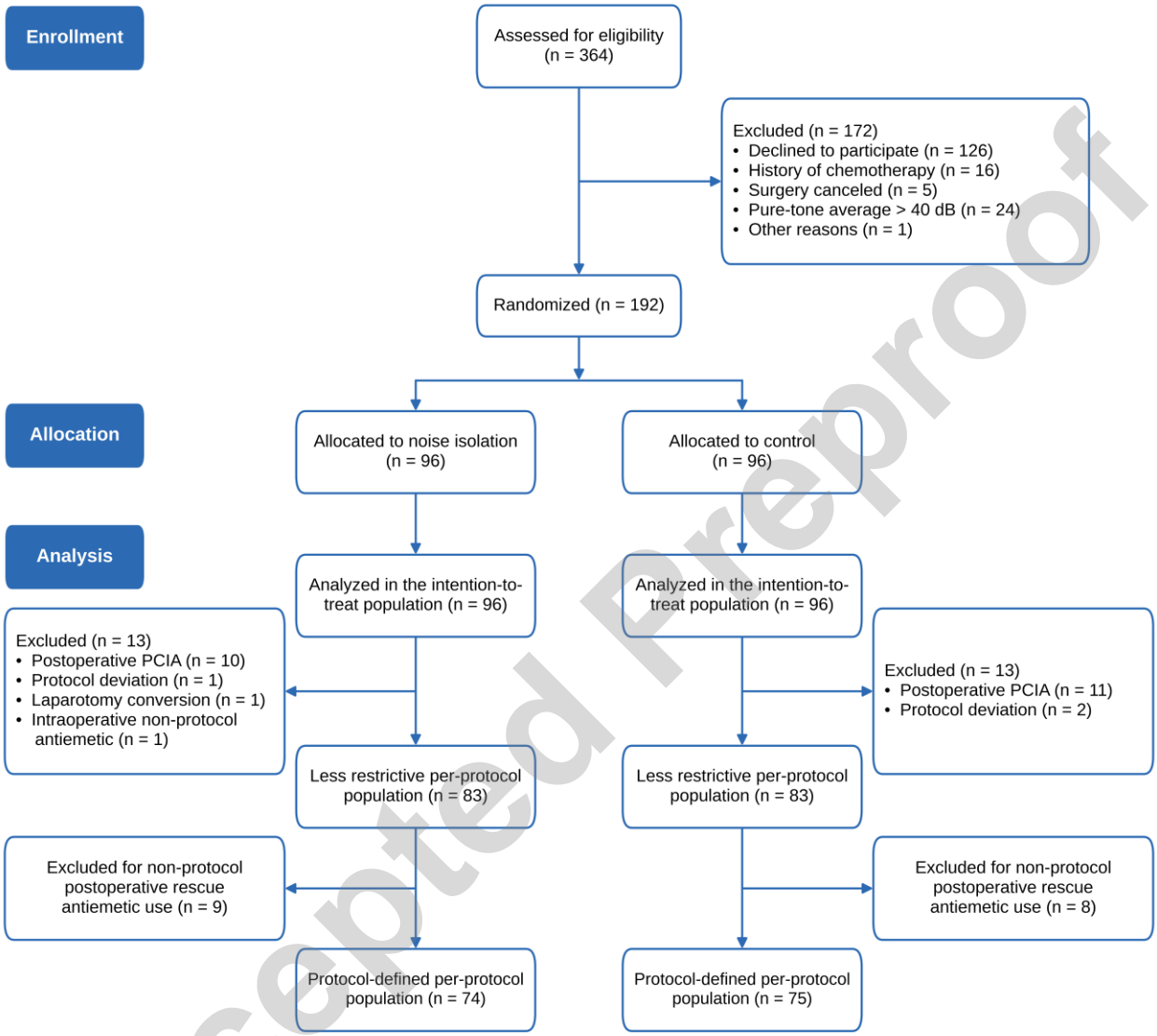
[d] Benjamini-Hochberg false discovery rate. Nausea, retching and vomiting belong to the family of fifteen prespecified secondary outcomes (the rest in table 2 and table S4); the composite belongs to the family of four post hoc endpoints (the rest in table S3).

[e] Adjusted for the eight baseline covariates listed in table 2.

[f] Counts each patient once whether retching, vomiting, or both occurred, so it is smaller than the sum of the two components.

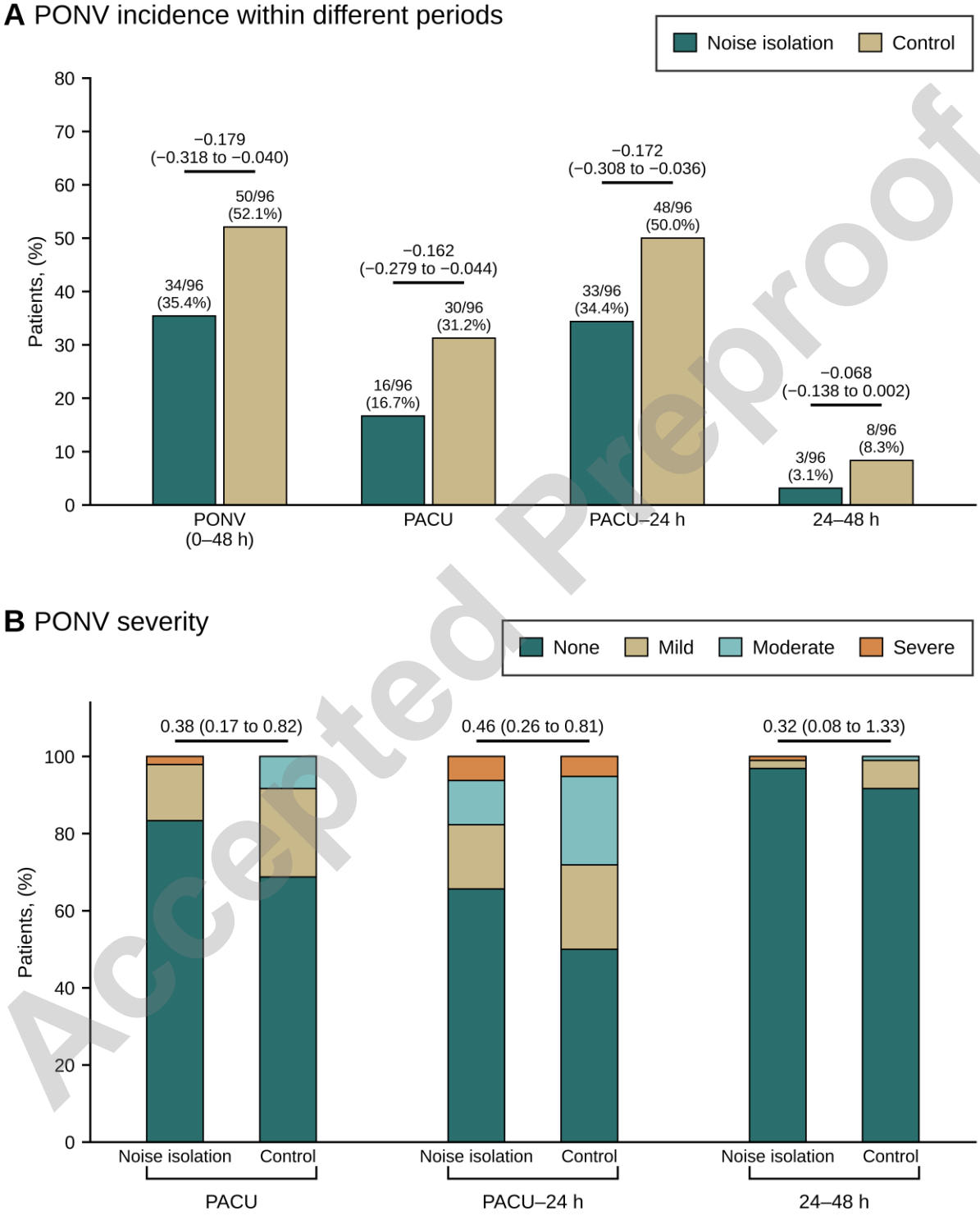
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Figure 1



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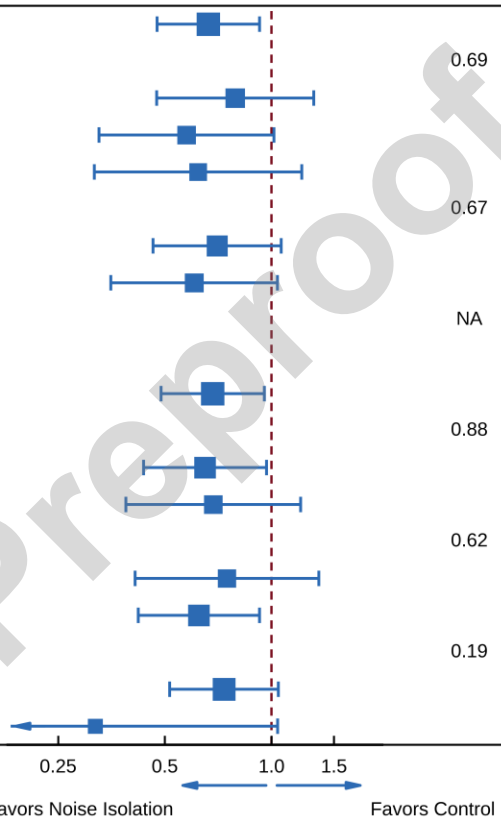
Figure 2



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Figure 3

Subgroup	No. of Events/Total (%)		Adjusted RR (95% CI)	*P* Value for Interaction
	Noise Isolation	Control		
Overall	34/96 (35.4)	50/96 (52.1)	0.66 (0.48-0.93)	
Age, yr				0.69
18–35	14/32 (43.8)	18/32 (56.2)	0.79 (0.47-1.32)	
36–50	11/33 (33.3)	19/31 (61.3)	0.58 (0.33-1.02)	
51–65	9/31 (29.0)	13/33 (39.4)	0.62 (0.32-1.22)	
APAIS score				0.67
≤12	21/56 (37.5)	29/55 (52.7)	0.70 (0.46-1.06)	
>12	13/40 (32.5)	21/41 (51.2)	0.60 (0.35-1.04)	
Current smoker				NA
Yes	0/1 (0.0)	2/2 (100.0)	NA	
No	34/95 (35.8)	48/94 (51.1)	0.68 (0.49-0.95)	
History of PONV or motion sickness				0.88
Yes	21/50 (42.0)	29/45 (64.4)	0.65 (0.44-0.97)	
No	13/46 (28.3)	21/51 (41.2)	0.68 (0.39-1.21)	
Apfel score				0.62
1–2	11/36 (30.6)	18/42 (42.9)	0.75 (0.41-1.36)	
3–4	23/60 (38.3)	32/54 (59.3)	0.62 (0.42-0.93)	
PTA score				0.19
0–25 dB	31/81 (38.3)	41/78 (52.6)	0.73 (0.52-1.05)	
26–40 dB	3/15 (20.0)	9/18 (50.0)	0.32 (0.10-1.04)	



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