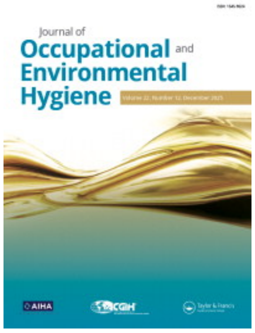

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REVIEW ARTICLE

Occupational exposures to halogenated waste anesthetic gases in healthcare professionals

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ABSTRACT

Waste anesthetic gases (WAGs) are anesthetic gases and vapors that are released or leaked into the surrounding environment during the delivery of anesthesia to patients and anesthesia recovery. In the last few decades, considerable efforts have been made to reduce WAG exposure for healthcare professionals who work in operating rooms (ORs) by using control measures such as scavenging systems and enhanced ventilation. Limited information is available regarding exposure assessment for healthcare workers in postanesthetic care units (PACUs) in hospitals. WAGs are associated with several adverse health effects, including reproductive-related health outcomes. However, previous studies have reported conflicting findings regarding the association between reproductive outcomes and WAG exposure. Before researching the associations between WAG exposures among PACU workers and health risks, it is essential to assess the current levels of exposure to WAGs in PACUs. This review paper describes the existing status of healthcare workers' exposure to WAGs in PACUs, discusses knowledge gaps, and provides recommendations on future research priorities.

KEYWORDS

Adverse reproductive outcomes; halogenated anesthetic gases; healthcare workers; postanesthetic care units (PACUs); waste anesthetic gases (WAGs)

Introduction

Anesthetic gases and vapors that are released or leaked into the surrounding environment during the delivery of anesthesia to patients and anesthesia recovery are considered waste anesthetic gases (WAGs). WAGs are emitted in operating rooms (ORs), during recovery from anesthesia in postanesthetic care units (PACUs), intensive care units in hospitals, and dental clinics. Factors increasing the risk of WAG exposure include loose components in anesthesia systems (Oliveira 2009), incorrect sizes of endotracheal tubes or laryngeal masks, improperly inflated cuffs (CCOHS 2007), inadequately fitting anesthesia masks (Byhahn et al. 2001; Herzog-Niescery et al. 2017; Hoerauf et al. 1997, 1999; Lucio et al. 2018; Saber and Hougaard 2009), and breakdowns of WAG scavenging systems (Borm et al. 1990; Gaya da Costa et al. 2021; Kanmura et al. 1999; Krajewski et al. 2007). Additionally, poor work practices, such as activating anesthetic gas before the scavenging system and filling vaporizers in poorly ventilated areas (Lucio et al. 2018; Oliveira 2009), increase healthcare workers' exposure to WAGs.

Inhaled anesthetics include nitrous oxide (N_2O) and halogenated agents like isoflurane ($C_3H_2ClF_5O$; CAS 26675-47-7), desflurane ($C_3H_2F_6O$; CAS 57041-67-5), and sevoflurane ($C_4H_3F_7O$; CAS 28523-86-6). The choice of anesthetic gases is highly influenced by environmental and financial factors. Survey results from the United States (U.S.) and other countries showed that sevoflurane was the most preferred anesthetic gas, followed by desflurane and isoflurane, because of its lower patient risk and faster induction times (Ard et al. 2016; Keller et al. 2022; McGain et al. 2019).

In the last five decades, considerable efforts were made to minimize occupational exposure to WAGs in healthcare through improved scavenging systems, ventilation, and work practices. An active scavenging system removes excess anesthetic gases by utilizing a vacuum or negative pressure connected to the scavenging interface to contain (e.g., using adsorbents) waste gases or discharge them outdoors (Lahvic and Liu 2023). In contrast, a passive system collects gases by relying on the patient exhaling into ports (i.e., positive pressure) and an absorbent canister (e.g., activated charcoal canisters) to remove WAGs from exhaled breath. The implementation of scavenging systems in ORs considerably reduced gas concentrations compared to their

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absence (Braz et al. 2017; Hoerauf et al. 1997; Imberti et al. 1995; Wiesner et al. 2000). As a result, installation of scavenging systems and improved ventilation systems are almost universal in ORs (Boiano and Steege 2016; Deng et al. 2018). However, these efforts have been primarily limited to ORs in medical settings (Braz et al. 2017; Hoerauf et al. 1997; Imberti et al. 1995; Wiesner et al. 2000). Limited information regarding exposure assessment for WAGs is available for healthcare staff working outside of ORs. Keller et al. (2022) found that of the 101 reviewed technical papers published between 1970 and 2021 that focused on WAG exposure levels, 79% (80/101 papers) characterized WAG exposures in ORs, followed by PACUs (15%), intensive care units (4%), and anesthesia rooms (2%). PACUs rarely employ control measures for WAG emissions from post-surgical patients (AIHA 2021). Due to the limited exposure data, the justification for implementing control strategies within PACUs to minimize healthcare workers' exposure to WAGs is challenging.

Exposure to WAGs in the absence of scavenging systems is associated with many known health effects. Acute WAG exposure is associated with nausea, dizziness, headache, fatigue, irritability, drowsiness, and difficulties with judgment and coordination (Izgi et al. 2020; NIOSH 2007; Smith 2010; Tran et al. 1994). Health effects of chronic exposure include DNA damage, genotoxicity, increased oxidative stress, and carcinogenesis (Deng et al. 2018). Additionally, OR staff with long-term exposure to WAGs exhibited significant changes in liver function markers and blood indices, which made them more susceptible to immunotoxicity (e.g., elevated immunomodulatory responses, increased oxidative stress, and higher serum cytokine levels) (Al-Rasheedi et al. 2021; Emara et al. 2020; 2021). However, adverse reproductive outcomes (AROs), including spontaneous abortion, premature delivery, genetic damage, and birth defects, are particularly concerning due to conflicting published results regarding their association with WAG exposure (Molina Aragonés et al. 2016; Scheftel et al. 2017). In the U.S., among 3.5 million registered nurses, 87.4% of all nurses are women, while 12.6% are men (BLS 2023). The National Center for Health Workforce Analysis report indicates that approximately 66% of the nursing workforce is within the reproductive age range (DHHS 2024). Evidence on preterm birth, birth defects, and pregnancy loss in PACU workers is unclear, making the study of associations between WAGs and AROs a priority (Gaya da Costa et al. 2021; Molina Aragonés et al. 2016; Saleh et al. 2020; Scheftel et al. 2017). Studying the risk of AROs epidemiologically could be challenging due to several factors, including the lack of exposure assessment data, the requirements of large population-based studies, the need for longitudinal research, and the complexity of the data involving genetics, lifestyle choices, and environmental exposures (Herzog-Niescery et al. 2018; Kilic et al. 2020; Oliveira et al. 2021). One of the essential components to explore the risk of AROs would be assessing the current levels of exposure to WAGs in PACUs.

Occupational exposure limits

In the U.S., the California Occupational Safety and Health Administration (Cal/OSHA) recommends a full-shift permissible exposure limit (PEL) of 2 parts per million (ppm) for isoflurane, while no PELs have been developed for desflurane and sevoflurane (Cal/OSHA 2018). Additionally, OSHA does not have any PELs regulating halogenated anesthetic agents, including anesthetic gases. In 1977, the National Institute for Occupational Safety and Health (NIOSH) published recommended exposure levels (REL) for halogenated anesthetic agents, setting ceiling concentrations of 2 ppm when used alone or 0.5 ppm when used with nitrous oxide (N_2O) over a sampling period not to exceed one hour (NIOSH 1977). Due to the lack of definitive information on adverse health effects, NIOSH stated that the REL cannot be determined to be safe and advised that the exposure level should be maintained as low as technically feasible. The halogenated agents discussed in this NIOSH document included chloroform, trichloroethylene, halothane, methoxyflurane, enflurane, and fluroxene (NIOSH 1977). Isoflurane, desflurane, and sevoflurane were not included because they were not in clinical use at that time.

However, the NIOSH REL has often been misinterpreted by researchers. Even when assessing a mixture of a halogenated agent with N_2O, most studies have compared WAG exposures to a REL of 2 ppm, not 0.5 ppm for a halogenated agent used in combination with N_2O. Only a few studies (Kim et al. 2016; Özelsel et al. 2018) employed a REL of 0.5 ppm for comparison purposes. Furthermore, the NIOSH REL of 2 ppm is based on sampling periods less than 1 hr, but many studies compared it to full-shift exposures or peak concentrations measured by real-time instruments.

In 2021 and 2023, the American Conference of Governmental Industrial Hygienists (ACGIH) established a threshold limit value (TLV®) time-weighted average (TWA) of 50 ppm for isoflurane and sevoflurane over an 8-hr period in its recommendations on halogenated agents (ACGIH® 2025). These TLVs were recommended with the aim of reducing the risk of adverse health effects, including embryo and fetal damage, maternal body weight effects, central nervous system (CNS) impairment, and cognitive decrements for isoflurane and CNS impairment for sevoflurane (ACGIH 2025). For desflurane, the organization added a TLV-TWA of 100 ppm in the Notice of Intended Changes (NICs) released in 2024 (ACGIH 2024). This recommendation aims to protect workers against CNS impairment and cognitive decrements. Consequently, the proposed TLV of 100 ppm was implemented in 2025 (ACGIH 2025).

While the NIOSH REL of 2 ppm (or 0.5 ppm for halogenated agent and N_2O mixtures) represents a TWA over 1 hr, other U.S. and international agencies issued 8-h full-shift exposure limits and/or 15-minute short-term exposure limits. As shown in Table 1, the full-shift occupational exposure limits (OELs) range from 2 ppm to 50 ppm for isoflurane, 5 ppm to 100 ppm for desflurane, and 5 ppm to 50 ppm for sevoflurane. There is significant variability in OELs for halogenated agents between countries, demonstrating that there is no universal consensus on what is considered a safe level of exposure.

Purpose

This systematic review paper describes the status of healthcare workers' inhalation exposure to WAGs; discusses knowledge gaps in exposure assessments and engineering control measures; and provides recommendations on future research priorities for WAG exposure assessments and control measures. This review is limited to healthcare workers in PACUs, where WAG exposure data is scarce. In addition, the review focuses on three halogenated agents—isoflurane, sevoflurane, and desflurane—that are commonly used as anesthetic gases today.

Methods

For this systematic review, the authors determined keywords to construct the search query, listed in Table 2, and identified relevant articles in PubMed and Scopus. The search query yielded 432 articles, with results limited to English. PubMed contributed 122 articles and Scopus contributed 310 articles (last search conducted on 20 June 2024). The articles were imported into Covidence (Covidence n.d.) to remove duplicates through automatic screening ($n = 96$) and manual review ($n = 10$) of titles and abstracts, resulting in an initial set of 326 articles produced from the query.

Following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, the query results were screened to only include articles involving WAG exposure data in PACUs, with or without engineering controls. Review articles, commentaries, correspondences, case reports, and all articles without

Table 1. Occupational exposure limits (OELs) for isoflurane, desflurane, and sevoflurane.

	Isoflurane				Desflurane				Sevoflurane			
	Full-shift		Short-term		Full-shift		Short-term		Full-shift		Short-term	
Country/Agency	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3
U.S. NIOSH	–	–	2[a]	–	–	–	2[a]	–	–	–	2[a]	–
	–	–	0.5[a,b]	–	–	–	0.5[a,b]	–	–	–	0.5[a,b]	–
ACGIH	50	–	–	–	100	–	–	–	50	–	–	–
Cal/ OSHA	2	15	–	–	–	–	–	–	–	–	–	–
Austria	10	80	20	160	–	–	–	–	–	–	–	–
Canada-Ontario	2	15	–	–	–	–	–	–	–	–	–	–
Denmark	5	38	10[c]	76[c]	5	35	10[c]	70[c]	5	42	–	–
Finland	10	77	20[c]	150[c]	10	70	20[c]	140[c]	10	83	20[c]	170[c]
Germany (DFG)	2	15	16[c]	120[c]	–	–	–	–	–	–	–	–
Ireland	50	380	–	–	–	–	–	–	–	–	–	–
Israel	2	15	6[c]	45[c]	–	–	–	–	–	–	2[c]	16[c]
Norway	2	15	–	–	5	35	–	–	5	35	–	–
Poland	–	32	–	–	–	125	–	–		55	–	–
South Africa Mining	50	270	–	–	–	–	–	–	–	–	–	–
Spain	50	383	–	–	–	–	–	–	–	–	–	–
Sweden	10	80	20[c]	150[c]	10	70	20[c]	140[c]	10	80	20[c]	170[c]
Switzerland	10	77	80	616	–	–	–	–	–	–	–	–
United Kingdom	50	383	–	–	–	–	–	–	–	–	–	–

Resource for countries other than the United States (U.S.): IFA GESTIS International Limit Values- https://limitvalue.ifa.dguv.de.

NIOSH = National Institute for Occupational Safety and Health; ACGIH = American Conference of Governmental Industrial Hygienists; Cal/OSHA = California Occupational Safety and Health Administration; DFG = German Research Foundation; ppm = parts per million.

[a]In 1977, NIOSH issued a recommended REL that no employees should be exposed to any halogenated anesthetic agent at ceiling concentrations greater than 2 ppm over a sampling period not to exceed 1 hr (NIOSH 1977). These gases were not included in this document because they were not used at that time.

[b]Exposure limit when used in conjunction with N_2O.

[c]15-min average value.

Table 2. Search queries used (last search: 20 June 2024).

Databases used	Search query
Scopus and PubMed	(("waste anesthetic" OR "anesthetic gases" OR "anesthetic gas") AND ("postanesthetic care unit" OR pacu OR post*)) AND ((sevoflurane OR desflurane OR isoflurane) OR (engine* OR control* OR scaveng* OR ventilation OR active OR passive OR mask) OR (exposure OR occu* OR monitoring OR inhalation OR concentration))

Note that several variations of "postanesthetic care unit," including "post-anesthetic care unit" and "post-anesthetic care unit," yielded the same number of articles and thus, only one term, "postanesthetic care unit," is listed in the table.

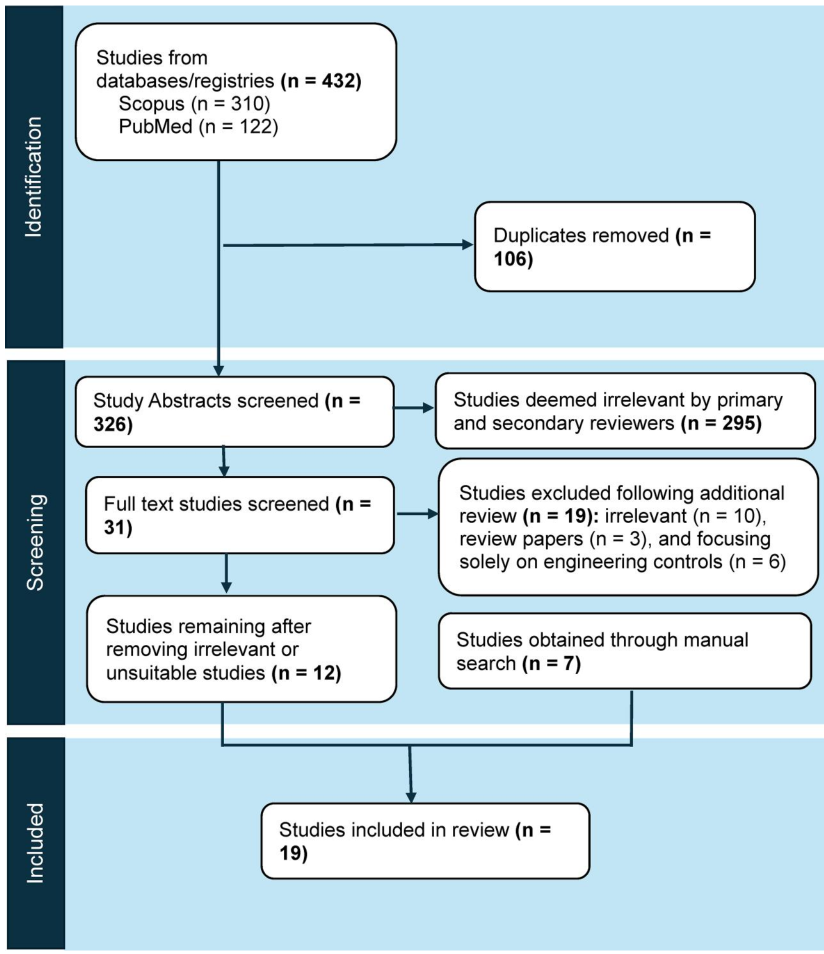

Figure 1. Flow diagram of the literature research and review process.

original datasets were excluded. Articles were also excluded if they were irrelevant or strictly focused on health outcomes, engineering controls with no exposure data, or WAGs other than sevoflurane, desflurane, and isoflurane.

Of the 326 articles screened, the primary reviewer (ML) and secondary reviewer (EL) deemed 295 articles irrelevant based on the abstract review and excluded them from further consideration. An additional 19 articles were excluded for lack of relevance based on the full text review, leaving 12 articles for the review. Through a manual search of article references, an additional seven studies were retrieved, resulting in a total of 19 articles reviewed (Figure 1).

The review process was conducted by synthesizing WAG exposure data by anesthetic gas type, sampling type and method, sampling time, and ventilation rate, identifying known control measures, and recommending future research priorities based on the findings of previous studies.

Results

Exposure assessment

Few exposure assessment studies are available for PACUs. Table 3 shows a summary of occupational WAG exposures at PACUs, with reported exposures

Table 3. Summary of occupational waste anesthetic gas (WAG) exposures measured at postanesthetic care units (PACUs).

Reference	Sampling Type (N)	Sampling method	Exposure levels	Sampling time	Used as a mixture with N_2O?	Ventilation rate
Sevoflurane						
Krenzischek et al. (2002)	Personal: Nurses (6)	Passive badges	All $<$ 0.14 ppm[a]	4–6 hr for 2 days	Yes	6 ACH
Williams et al. (2014)	Personal: Nurses (N/A)	Tube attached to the nurse's shoulder and analyzed using a MIRAN	All median values: $>$ 3 ppm as high as 6.1 ppm	Up to 15 min following arrival	N/A	N/A
Hiller et al. (2015)	Personal: 20 cm from the mouth of patients (20)	MIRAN	Mean range: 5–8 ppm	60 min	No	10 ACH with 4 fresh air exchange
Cheung et al. (2016)	Personal: 15 cm from the mouth of patients (39)	MIRAN	Median (interquartile range) 1. OR airway removal: 0.5 ppm (0.4–0.7 ppm) 2. PACU airway removal: 0.7 ppm (0.4–1.1 ppm)	N/A	N/A	17 ACH with 10 fresh air exchange
Williams et al. (2019)	Personal: 15 cm from the mouth of patients (108) and nurses' BZ (N/A)	MIRAN	Change of proportion of maximum WAG concentration from traditional mask to ISO-Gard mask[a] 1. Patients' BZ: from 30% to 21% 2. Nurses' BZ: from 4.0% to 2.6%	1 hr with 30 sec interval	No	N/A
Çakmak et al. (2019)	Personal: Nurse (1)	Passive badge	0.43 ppm[a]	8 hr	N/A	N/A
Izgi et al. (2020)	Personal: Nurses (18)	Passive badge	Mean ± SD 0.44 ± 0.2 ppm 35.7% exceeded 0.5 ppm	8 hr	Yes	9 ACH
Herzog-Niescery et al. (2019)	Area: Middle of PACU and PACU corridor (N/A) Personal: 25 cm above the mouth of patients (9-20)	Photoacoustic gas monitor	Mean ± SD (daily maximum ± SD) 1. In the middle of PACU: 0.34 ± 0.07 ppm (4.43 ± 2.37 ppm) 2. Patients' BZ: 0.56 ± 0.17 ppm (1.74 ± 1.54 ppm) 3. PACU corridor: 0.47 ± 0.06 ppm (1.53 ± 0.27 ppm)	Every 35 sec for multiple days	N/A	11.5 ACH without recirculation
McGlothlin et al. (2014)	Personal: 15 cm above the patient's mouth (19) Area: 91 cm away from the patient's BZ (19)	MIRAN	Mean ± SD 1. Nasal cannula or face tent group a. Patient's BZ: 5.04 ± 5.82 ppm b. Area: 0.92 ± 0.33 ppm 2. ISO-Gard group a. Patient's BZ: 1.89 ± 2.01 ppm b. Area: 0.69 ± 0.3 ppm	Every 90 sec for 2.2 hr	Yes	7.54 ACH
Tallent et al. (2018)	Personal: 15 cm from the mouth of patients (120) Area: 91 cm away from the patient's BZ (120)	MIRAN	Mean ± SD 1. ISO-Gard group a. Patient's BZ: 0.41 ± 0.22 ppm b. Area: 0.26 ± 0.13 ppm 2. Standard oxygen mask group a. Patient's BZ: 3.52 ± 2.26 ppm b. Area: 1.12 ± 1.11 ppm	10 and 20 min after arrival	N/A	N/A
Badgwell (1997)	Area: 53 cm from the mouth of patients (22)	MIRAN	1. Nasal prong group ($n = 10$): 58% of the time $>$ 2 ppm[a] 2. Scavenging group ($n = 12$): 0% of the time $>$ 2 ppm[a]	480 min	Yes	N/A
Rieder et al. (2001)	Area: 2 PACUs (N/A)	Proton-transfer reaction mass spectrometry	Mean: 0.0159 ppm (up to ~ 0.3 ppm)	3 working days	N/A	2980 m^3/h

(*Continued*)

Table 3. Continued.

Reference	Sampling Type (N)	Sampling method	Exposure levels	Sampling time	Used as a mixture with N_2O?	Ventilation rate
Kim et al. (2016)	Area: 1 PACU (85)	MIRAN	All measurements < 1 ppm[a]	2 nonconsecutive weeks	Yes	N/A
Heiderich et al. (2018)	Area: 2 PACUs (N/A)	Ion mobility spectrometry with GC pre-separation	Median (highest concentration) 1. PACU #1: 0.12 ppm (0.96 ppm) 2. PACU #2: 0.11 ppm (0.82 ppm)	5 min interval for 1 week	N/A	PACU #1 = 11. 9 ACH and PACU #2 = 8.7 ACH
Özelsel et al. (2018)	Area: 1 PACU (N/A)	MIRAN	Often exceeding 0.5 ppm for the PACU having at least 2 patients[a]	Every 3 min for 3 wk	Yes	9.5 ACH with 6 fresh air exchange
Garcia et al. (2022)	Area: 3 PACUs (N/A)	FTIR	Mean: < 2 ppm Maximum concentration range: 0.3–46.2 ppm	1 h	Varying	5.8–8.0 ACH
Isoflurane						
Sessler and Badgwell (1998)	Personal: Nurses' BZ (19)	Tube attached to the nurse's shoulder and analyzed using a MIRAN	TWA Mean ± SD: 1.1 ± 0.7 ppm; 12% of the time > 2 ppm	~ 60 min	Yes	8–9 ACH
Henderson and Matthews (1999)	Personal: Nurses (6)	Reservoir bag and analyze using a MIRAN	Mean (range): 1 ppm (range: 0–2 ppm)	Every 1 min for 20 min	Yes	N/A
Krenzischek et al. (2002)	Personal: Nurses (6)	Passive badges	All < 0.096 ppm[a]	4 – 6 hr for 2 days	Yes	6 ACH
Rieder et al. (2001)	Area: 2 PACUs (N/A)	Proton-transfer reaction mass spectrometry	Mean: 0.0095 ppm (up to ~0.05 ppm)	3 working days	N/A	2980 m^3/h
Garcia et al. (2022)	Area: 3 PACUs (N/A)	FTIR	Mean: < 2 ppm Maximum concentration range: 0–8 ppm	1 hr	Varying	5.8–8.0 ACH
Desflurane						
Sessler and Badgwell (1998)	Personal: Nurses' BZ (31)	Tube attached to the nurse's shoulder and analyzed using a MIRAN	TWA Mean ± SD: 2.1 ± 1.2 ppm; 49% of the time > 2 ppm	~ 60 min	Yes	8–9 ACH
Cheung et al. (2016)	Personal: 15 cm from the mouth of patients (39)	MIRAN	Median (interquartile range) 1. OR airway removal: 2.1 ppm (1.6–3.3 ppm) 2. PACU airway removal: 4.1 ppm (2.5–5.2 ppm)	N/A	N/A	17 ACH with 10 fresh air exchange
Williams et al. (2019)	Personal: 15 cm from the mouth of patients (108) and nurses' BZ (N/A)	MIRAN	Change of proportion of maximum WAG concentration from traditional mask to ISO-Gard mask[a] 1. Patients' BZ: from 34% to 24% 2. Nurses' BZ: from 5.9% to 1.5%	1 hr with 30 sec interval	No	N/A
Izgi et al. (2020)	Personal: Nurses (18)	Passive badge	Not detected	8 hr	Yes	9 ACH
Tallent et al. (2018)	Personal: 15 cm from the mouth of patients (120) Area: 91 cm away from the patient's BZ (120)	MIRAN	Mean ± SD 1. ISO-Gard group a. Patient's BZ: 0.74 ± 0.41 ppm b. Area: 0.39 ± 0.17 ppm 2. Standard oxygen mask group a. Patient's BZ: 9.06 ± 5.97 ppm b. Area: 1.96 ± 1.24 ppm	10 and 20 min after arrival	N/A	N/A
Kampan (2019)	N/A (N/A)	N/A	0.25 and 0.21 ppm[a]	N/A	Yes	Maximum air flow ranges up to 1,500 m^3/h

[a]These values represent point estimates based on the sampling time, and no measure of central tendency or range was reported by the authors.

Note that while the measured concentrations were reported as personal exposure, even if sampling tubes or media were not directly attached to patients or nurses, provided the distance between the measurement point and the patients or nurses was within a 30-cm radius from their faces (which was defined as the breathing zone).

Abbreviation: PACUs = postanesthetic care units; N = number of patients or nurses participated in the study; BZ = Breathing zone; SD = Standard Deviation; ppm = Parts per million; TWA = Time weighted average; ACH = Air changes per hour; MIRAN = Miniature infrared analyzer, N/A = Not available, FTIR = Fourier transform infrared spectrometer.

summarized by average, median, and point exposure values. Note that in Table 3, the measured concentrations were reported as personal exposures even if the sampling tubes were not directly attached to patients, provided the distance between the measurement point and the patients was within a 30-centimeter (cm) radius from their faces (which was defined as the breathing zone (ISO 2016). Overall, the reported exposures to isoflurane were less than 2 ppm, while the average or median exposures to sevoflurane and desflurane ranged from $<$ 0.01 ppm to 8 ppm in PACUs. Regardless of the anesthetic gas type, none of the samples collected for more than 4 h surpassed the OELs presented in Table 1 (Badgwell 1997; Çakmak et al. 2019; Heiderich et al. 2018; Herzog-Niescery et al. 2019; Kim et al. 2016; Krenzischek et al. 2002; Izgi et al. 2020; Özelsel et al. 2018; Rieder et al. 2001). On the other hand, samples collected for approximately one hour exhibited personal exposures exceeding the NIOSH REL of 2 ppm when using an anesthetic gas alone (Hiller et al. 2015) or 0.5 ppm when using an anesthetic gas with N_2O (Sessler and Badgwell 1998).

Engineering control measures

Only a few studies have examined the effectiveness of scavenging systems by comparing WAG exposures between traditional masks and ISO-Gard (McGlothlin et al. 2014; Tallent et al. 2018; Williams et al. 2019), as well as between a nasal prong group and a scavenging group (Badgwell 1997) (Table 3). For instance, McGlothlin et al. (2014) evaluated the effectiveness of a system called an ISO-Gard mask, which can be worn by patients in PACUs. McGlothlin's study found that average sevoflurane concentrations (± standard deviation), collected at 6 inches above the patient's nose and mouth for 50 min with the ISO-Gard mask, were 1.9 ± 2.0 ppm compared to 5.0 ± 5.8 ppm without the ISO-Gard mask. Another study conducted by Tallent et al. (2018) reported that the group wearing the ISO-Gard mask showed breathing zone concentrations that were 8.6 times lower for sevoflurane and 12.2 times lower for desflurane compared to the group wearing a standard oxygen mask. Badgwell (1997) assessed the capture efficiency of WAGs using a source control system equipped with a closed-system suction port. They found that area air concentrations of sevoflurane, measured with a real-time instrument, did not exceed 2 ppm during the 480-minute measurement period. In contrast, the nasal prong group showed concentrations exceeding 2 ppm for approximately 58% of the monitoring time.

Discussions

Exposure assessment

As shown in Table 3, in general, isoflurane exposures were below 2 ppm, whereas the reported exposures for sevoflurane and desflurane in PACUs varied from $<$ 0.01 ppm to 8 ppm. Desflurane exposures were close to or often exceeded 2 ppm and were generally higher than isoflurane exposures (Cheung et al. 2016; Sessler and Badgwell 1998). Similarly, sevoflurane exposure levels were higher than isoflurane because of sevoflurane's faster elimination rate in the patient than isoflurane (Krenzischek et al. 2002; Rieder et al. 2001).

When both personal and area exposure monitoring were conducted in the same environment, personal exposure levels were higher than those measured at more distant fixed locations (McGlothlin et al. 2014; Tallent et al. 2018). For example, the average personal exposure was 9.06 ppm for desflurane, while the area air concentration measured at a distance of 91 cm from the patient's mouth was 1.96 ppm for the patient group wearing standard oxygen masks (Tallent et al. 2018). In addition, NIOSH researchers conducted measurements of area air concentrations at three PACUs every 6 sec using infrared spectrometry for durations ranging from 159 to 755 min and reported one-minute average concentrations (Garcia et al. 2022). While the overall average concentrations measured for both isoflurane and sevoflurane were below 2 ppm, the one-minute averaged maximum concentrations ranged from less than detectable to 8 ppm for isoflurane and 0.3 ppm to 46.2 ppm for sevoflurane. Since the NIOSH study focused on area concentration measurements at fixed locations, they suggested further industrial hygiene evaluations to assess WAG exposures within the PACU workers' breathing zones to better understand personal worker exposures (Garcia et al. 2022).

The sampling strategy used appears to have an impact on the reported exposure level of WAGs. When the WAG exposures were measured with real-time instruments (e.g., infrared ambient analyzer, photoacoustic gas monitor), almost half of studies reported that exposure levels measured in the breathing zones of patients and/or nurses at stationary locations were greater than 2 ppm (Cheung et al. 2016; Hiller et al. 2015; Sessler and Badgwell 1998; Williams et al. 2014, 2019). When exposures were measured with passive badges (i.e., non-real-time instruments), all TWA exposures were less than 2 ppm (Çakmak et al. 2019; Izgi et al. 2020; Krenzischek et al. 2002). The differences in results between real-time instruments and passive badges may be attributed to several factors, including the sampling durations (e.g., 20 min with an infrared ambient analyzer vs. 8-h full-shift using a passive badge), as well as the sampling locations. In addition, all previous studies reported TWA concentrations obtained exclusively through passive monitoring methods, which allowed vapors to enter the sampling medium via diffusion (Table 3). OSHA Method 103 (OSHA 1994) recommends collecting isoflurane samples using an active sampling method, which enables the collection of vapors on the sampling medium (e.g., sorbent tube) through mechanical force (e.g., pump). However, none of the previous studies employed sorbent tubes to assess WAG exposure levels among PACU healthcare workers.

Work practices, such as location of airway device removal after anesthesia (i.e., OR vs. PACU) (Cheung et al. 2016; Keller et al. 2022), use of a scavenging mask (McGlothlin et al. 2014), type of scavenging mask (McGlothlin et al. 2014; Tallent et al. 2018), and time taken to extubate a patient in the PACU (Garcia et al. 2022), are also associated with the nurses' exposures to WAGs. For instance, Cheung et al. (2016) reported that WAG exposures measured at a distance of 15 cm above the patient's mouth were higher in the PACU when their airway devices were removed than in the OR (e.g., desflurane = 4.1 ppm [PACU] vs. 2.1 ppm [OR]). Other factors affecting WAG exposures in PACUs include, but are not limited to, the number of patients admitted to a PACU per hour (Herzog-Niescery et al. 2019; Özelsel et al. 2018), sampling locations (Herzog-Niescery et al. 2019; McGlothlin et al. 2014), distance between patients (Krenzischek et al. 2002), PACU airflow pattern (Hiller et al. 2015) and air exchange rate (15 ACH for OR vs. 6 ACH for PACU), duration of anesthesia, and demographic characteristics of patients (Sessler and Badgwell 1998).

Unfortunately, exposure data reported in previous PACU studies are not sufficiently representative of PACU nurses' exposures. Beyond the aforementioned factors affecting WAG exposure, associations for nurses' WAG exposures were not comprehensively investigated. Additionally, there is a lack of WAG exposure data for PACU nurses. Keller et al. (2022) compared 48 studies of ORs and 10 studies of PACUs and reported that overall WAG concentrations of sevoflurane, isoflurane, and desflurane in ORs were higher than those in PACUs during the years of the 2000s and 2010s. Keller et al. strongly suggested collecting more exposure data in PACUs to obtain WAG exposure measurements that are representative of PACUs. Also, fewer studies were reported for isoflurane and desflurane compared to sevoflurane (Table 3).

Additionally, variability in WAG concentration estimates due to differing measurement methods leads to inconsistencies in understanding exposure risks. For example, McGlothlin et al. (2014) reported considerably higher WAG concentrations in patients' breathing zones during their first 15 min in a PACU, while Krenzischek et al. (2002) showed peak WAG levels occurred one hour after a patient's arrival to the PACU. Although many researchers reported factors affecting exposure levels, these factors were not comprehensively investigated. For instance, information about air exchange rates in PACUs and whether N_2O was used during anesthetic procedures was missing for some studies, as shown in Table 3. A lack of understanding of PACU ventilation and other factors, like the location of airway device removal and sampling locations, makes the generalizability of findings difficult.

Deng et al. (2018) addressed how WAG exposures in PACUs are overlooked despite higher concentrations of WAGs compared with ORs. The American Society of PeriAnesthesia Nurses (ASPAN) released a position statement on WAGs outside of ORs in 2022 (ASPAN 2022). In the statement, ASPAN addressed the importance of utilizing engineering controls (e.g., source-control scavenging systems), conducting surveillance or measurement of WAG exposures, and implementing regulatory approaches. This statement was endorsed by the American Industrial Hygiene Association Board of Directors to minimize WAG exposure for nurses, patients, and their families (ASPAN 2022). Adequate protection of healthcare workers in the PACUs cannot be achieved until WAG exposure levels and factors influencing exposure levels are determined.

Engineering control measures

There are several ways to minimize healthcare workers' exposure to WAGs in ORs, including adoption of scavenging systems (active or passive), delivery of anesthetics using a double-mask system (Freilich et al. 2007; Kurrek et al. 2013; Westberg et al. 2008), selection of anesthesia airway delivery methods that reduce WAG exposures (e.g., endotracheal tube) (Herzog-Niescery et al. 2015; Hoerauf et al. 1996; Schebesta et al. 2010), and adoption of closed loop and low flow technology during the delivery of anesthesia to patients (Brattwall et al. 2012; Dexter et al. 2011; Feldman 2012; Kennedy and French 2008; Weinberg et al. 2010).

In PACUs, scavenging systems have proven effective (Badgwell 1997; McGlothlin et al. 2014; Tallent et al. 2018). Additionally, although WAG exposure levels were not monitored in the PACUs, Prichard et al. (2021) demonstrated that a negative pressure scavenger kit, which includes a nasal cannula and an oxygen mask specifically designed for use in PACUs, removed 96% of the exhaled particle mass using a computational fluid dynamics model. To minimize healthcare workers' exposure to WAGs, controlling source emissions is essential. For example, although it is not specifically designed for capturing WAGs, the disposable oxygen face tent could potentially be used for this purpose (Tsui 2020). Another effective strategy could be to improve room ventilation. According to the American Society of Heating, Refrigeration and Air Conditioning Engineers Standard 170-2021, the recommended ventilation of PACUs is much lower than that in the ORs; the current recommended room air exchanges per hour (ACH) is 6 ACH in PACUs and 20 ACH in ORs (ASHRAE 2021). To ensure that PACU healthcare workers are protected in a room environment with 6 ACH, collecting workers' exposure data and comparing it to the OELs is necessary.

Future research priorities

Inhalation exposure assessment methods

Most previous studies on WAG exposures collected exposure measurements in ORs using real-time instruments or time-integrated samplers (i.e., passive badges or sorbent tubes). Although real-time exposure assessment methods have advantages over time-integrated methods (e.g., determining peak concentration by task), they are typically less reliable (e.g., accuracy, precision, sensitivity, and specificity) and are often used in conjunction with time-integrated monitoring methods (Keller et al. 2022). Therefore, a sampling strategy that combines real-time instruments with time-integrated sampling would provide the most valuable data for assessing health effects and identifies opportunities to mitigate these exposures. This approach allows for the determination of peak concentrations by tasks along with TWA concentrations, providing insights into full-shift or short-term exposure levels.

Additionally, the real-time instruments (e.g., infrared spectrometry, photoacoustic gas monitor) used in the previous studies pose challenges for adapting them to personal sampling due to their size, particularly over a full shift, and thus are limited to measuring area air concentrations. For instance, a portable infrared spectrophotometer with dimensions of 39 cm wide, 16 cm high, and 40 cm deep, along with a weight of 14 kg, is too cumbersome for a worker to wear. To our knowledge, there are currently no commercially available real-time instruments that can be worn by employees to measure WAG exposures. Development of a portable instrument that can be attached to a worker's breathing zone would enable real-time monitoring of personal exposures.

All previous studies introduced in Table 3 employed either real-time instruments or passive badges to evaluate WAG exposures, despite OSHA's introduction of an active sampling method (OSHA 1994). Passive badges are small, lightweight, and less expensive than active samplers. They are also easy to use, allowing sample collection to be performed without the need for trained personnel. Conversely, environmental factors such as temperature and relative humidity can affect the performance of passive samplers. Bergemalm-Rynell et al. (2008) conducted a laboratory study to determine the uptake rates of a diffusive sampler for halogenated anesthetic compounds, including desflurane, sevoflurane, isoflurane, enflurane, and halothane at concentrations of 1, 5, and 10 ppm. They subsequently performed a field evaluation at a facility during the cleaning of anesthesia equipment and reported a high level of agreement between the passive and active samplers for halothane, sevoflurane, and isoflurane. They concluded that the passive badge can be used for a full-shift sample collection. However, if short-term sample collection (e.g., task-based) is needed and high concentration peaks are anticipated, they recommend using an active sampling method. It should be noted that the concentration levels reported by Bergemalm-Rynell et al. (2008) were considerably higher than those observed in the PACUs listed in Table 3; all WAG exposures measured with passive badges were below 0.5 ppm. Additionally, only one type of passive badge from a company was evaluated, while another badge developed by a different company is also often used to measure WAG exposures. Thus, future research comparing several passive samplers to active samplers at lower concentration levels than those evaluated in a previous study (Bergemalm-Rynell et al. 2008) would assist occupational professionals in selecting the most appropriate sampling method.

Most WAG exposure studies published to date primarily focused on short-term exposures related to specific tasks, with only a few reporting full-shift or longer-than-full-shift exposures (Table 3). This might be attributed to the fact that most previous studies on WAG exposure monitoring were conducted using real-time instruments instead of attaching passive badges and/or sorbent tubes to the breathing zone of nurses or patients. In the U.S., it was only recently that ACGIH recommended full-shift TLVs for isoflurane, desflurane, and sevoflurane. Additionally, most countries have OELs based on full-shift rather than short-term exposures, which is especially true for isoflurane (Table 1). For future studies, it is crucial that occupational professionals assess full-shift exposures of healthcare workers.

Finally, as shown in Table 3, fewer studies were reported for isoflurane and desflurane compared to sevoflurane in PACUs. More exposure assessment studies would be necessary for isoflurane and desflurane to determine associations between WAG exposures and the risk of adverse health effects. Additional studies on WAG exposure among healthcare workers in PACUs could also distinguish exposures by job type, task, and occupational setting.

Development of job exposure matrices

Job exposure matrices (JEMs) are effective tools for efficiently estimating occupational exposures, particularly in large population-based studies and/or when individual exposure data are unavailable (Descatha et al. 2022). JEMs consolidate available exposure data into a table of exposure levels categorized by job title or standardized job codes, while task exposure matrices consolidate exposure data by task. Developing well-established JEMs requires large sets of exposure data along with detailed information about the characteristics of the work environment and work practices. JEMs also benefit from consensus among researchers.

Most JEMs developed from 1983 to the present were designed to study adverse health outcomes, such as cancers (47%) and respiratory disease (18%) (Descatha et al. 2022). JEMs have also been used to study AROs. One study from the Netherlands linked job titles to chemical exposures for a large cohort of women and found that a JEM was more reliable for determining associations between phthalate and pesticide exposure and delayed pregnancy/low birth weight than self-reported exposures (Burdorf et al. 2011). JEMs are limited in their ability to account for individual exposure variation within the same job, and exposure misclassification is possible. However, a strength of JEMs is removing recall bias inherent in self-reported worker exposures (Descatha et al. 2022).

As far as the authors are aware, currently, no JEMs for PACU workers exposed to WAGs are reported, limiting ARO and other health effect assessments. A JEM for WAG exposure in PACU workers would be immensely helpful and could be applied to assess the risk of AROs associated with occupational WAG exposure, particularly large population-based studies (e.g., $>$ 1,000 participants), since AROs are rare. More high-quality data and consistent investigation of environmental and/or work practice factors affecting WAG exposures in PACUs are needed to generate efficient job and task exposure matrices.

Emission source controls

Source-control scavenging systems for patients have the potential to be one of the most efficient control measures to prevent healthcare workers' exposure in PACUs. Limited efforts introduced commercially available products (e.g., the ISO-Gard scavenging mask, FELIX-1 negative pressure scavenger kit) for use in the PACU environment; however, these products have not gained widespread acceptance in practice. Their limited adoption may be attributed to a lack of awareness among healthcare workers and/or employers regarding issues of overexposure of PACU employees to WAGs (AIHA 2021). Additionally, the absence of regulatory OELs for more recently used anesthetics, as well as cost considerations compared to using an oxygen mask or nose cannula, may contribute to the limited implementation of these products. Only a few studies have investigated the effectiveness of those products, and a comprehensive evaluation of their efficacy may help justify widespread adoption.

Other cost-effective control measures could also be considered. For instance, NIOSH introduced a ventilated headboard to reduce healthcare workers' exposures to airborne infection viruses exhaled from patients in healthcare settings (Mead 2020). While the ventilated headboard was originally developed to protect healthcare workers from airborne infectious diseases, a similar concept could be applied to patients recovering from surgery in the PACU environment.

Limitations

The exposure data in this study is limited to research published in English, although the authors noted that some studies exist in other languages. Consequently, important findings may have been missed due to this limitation. Additionally, the conclusions are based on a small number of studies, which the authors highlighted as a priority for future research. Collecting more comprehensive exposure data could potentially change the findings regarding healthcare workers' exposure in PACUs. Finally, the exposure results were categorized by anesthetic gas type, sampling method (personal or area), sampling time, use of N_2O mixtures, and ventilation rate (Table 3). However, the authors acknowledge that these conclusions are general rather than definitive, primarily because there is a lack of detailed descriptions of the workplaces studied. For example, many studies did not provide information on the ventilation rates in PACUs, which meant the authors could only compare exposure levels without establishing a connection between those levels and ventilation rates.

Conclusions

This study conducted a systematic review to assess healthcare workers' exposure to WAGs in PACUs, focusing specifically on three halogenated agents: isoflurane, sevoflurane, and desflurane. The existing data on WAG exposure for PACU healthcare workers is insufficient, making it challenging to recommend and implement control strategies to minimize WAG exposure. In the last few decades, considerable efforts were made to decrease occupational WAG exposures in ORs, but little is known about WAG exposure prevention in PACUs. While the use of source control options and improved ventilation may help reduce worker exposures to WAGs, some of these methods (e.g., scavenging masks) are not widely accepted in PACUs. Additional worker education and training may help PACU staff adopt these prevention measures, but more information on contributors to WAG exposure is needed to substantiate the implementation of control measures. Work practices and workplace factors determining WAG exposures for PACU workers are also not well understood, nor are health outcomes affected by WAGs. JEMs compile findings from many exposure assessments and offer an efficient tool for estimating occupational exposures, particularly in large epidemiological studies that aid in the assessment of rare health issues like AROs. However, more exposure assessment studies, particularly those investigating workplace factors that contribute to WAG exposure, are important to thoroughly evaluate WAG exposures in PACUs and build a JEM that is robust enough to be applied at the population level.

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Disclaimer

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