Position Statement on the formulary listing of desflurane

Key points

- Desflurane use has been declining in Australia, owing to increased awareness of its environmental impacts, higher costs, and policy decisions by health service organisations and formularies to restrict its use.
- Desflurane is largely comparable to sevoflurane in its efficacy and safety profile, with desflurane demonstrating modest improvements in extubation times that do not translate to reduced length of stay or a reduction in complications.
- Health Service Organisations and Medicines and Therapeutics Committees should consider not listing desflurane on hospital or state-based formularies.
- CATAG recommends consultation and planning prior to removal of desflurane from formularies and operating theatres.
- Medicines and Therapeutics Committees may consider establishing limited provisions for exceptional use of desflurane based on clinical need.

BACKGROUND

Desflurane is a volatile anaesthetic gas that is one of several medicines that may be given to patients during general anaesthesia. Typically, it is used after general anaesthesia has already commenced, as a maintenance agent.

First manufactured in the early 1990s, there has been considerable debate among anaesthetists about desflurane's merits over the three decades since. With a fast rate of action, low blood solubility and rapid awakening after operations, in 2017 desflurane was general anaesthetic of choice for around 12% of anaesthetists in Australia and New Zealand (McGain et al 2019).

In recent years, desflurane use has been declining in Australia, owing to increased awareness of its environmental impacts, high costs, effective comparator agents and policy decisions by hospitals and formularies to restrict its use (NSW Health 2024, WA Health 2023a). Concerns about climate change and its consequences for health worldwide are motivating efforts to curtail the routine use of clinical procedures and technologies that emit outsized amounts of greenhouse gases, where equally effective or superior clinical alternatives are available. CATAG acknowledges that any decision to change anaesthetic agents should not occur in isolation, with the impact of alternative agents also considered.

Also in recent years, Total Intravenous Anaesthesia (TIVA), generally using propofol, has become more commonplace, with maintenance anaesthesia delivered intravenously, without

the use of inhalational agents. However, for the purposes of this review, the primary focus will be the comparison between desflurane and sevoflurane, desflurane's most direct volatile anaesthetic gas comparator.

PURPOSE

This evidence review has been conducted by the Council of Australian Therapeutic Advisory Groups (CATAG), with the assistance of an Expert Advisory Group (EAG). It reviews the quality of evidence around the safety, efficacy, cost-effectiveness, therapeutic necessity, and environmental impact of desflurane.

This consensus statement aims to facilitate and support the translation of best available evidence into practice and will assist good governance and decision-making for the use of desflurane by Australian health service organisations, Medicines and Therapeutics Committees (MTCs)[1], and health professionals in their evaluation, approval and use of this medicine.

Evidence regarding the responsible clinical use of desflurane is summarised in relation to:

- the availability of safe and clinically equivalent alternatives.
- the cost of desflurane compared to clinically equivalent alternatives.
- desflurane's environmental impact.
- current policies and best practices on desflurane, in Australia and internationally.

MTCs make formulary decisions based on the highest quality of evidence available. These decisions require consideration of the efficacy, safety, cost-effectiveness, place in therapy, affordability of a medicine. These decisions are essential to ensure equity and sustainability of healthcare is maintained.

Where a medicine is not listed on formulary, case-by-case approval through an individual patient use (IPU) / individual patient approval (IPA) process is available within most Australian health care facilities.

Health Service Organisations additionally decide whether to stock or hold a medicine depending on predicted frequency and urgency of use, as well as environmental sustainability factors.

This evidence review will be updated when new evidence becomes available that is likely to affect the direction or strength of the consensus statement.

[1] Examples of Medicines and Therapeutics Committees include Drug and Therapeutics Committees, Medicines Advisory Committees or equivalent, Medication Safety Committees.

RECOMMENDATIONS

1. **Health Service Organisations and Medicines and Therapeutics Committees should consider not listing desflurane on hospital or state-based formularies**

Since the available evidence shows desflurane is unlikely to have any significant clinical advantages over comparable alternatives, whilst causing potential harm to the environment and being much more expensive per clinical use than its comparators, CATAG does not support the listing of desflurane on hospital or statewide formularies.

2. **Health Service Organisations and Medicines and Therapeutics Committees should undertake consultation and planning prior to removal of desflurane from theatres**

When considering the removal of desflurane from formulary, it is essential that MTCs undertake consultation with key stakeholders within their local organisations. Such consultation aims to understand any potential impacts on alternative anaesthetic options and logistical challenges in transitioning away from desflurane. A collaborative approach will assist in developing a comprehensive strategy for a smooth and effective transition.

Implementation of a communication and education strategy along with adequate time and system planning for phasing out desflurane and purchasing alternatives (including any necessary equipment) to desflurane, will assist a smooth transition in clinical practices.

3. **Medicines and Therapeutics Committees may consider establishing limited provisions for exceptional use of desflurane based on clinical need.**

Although this review did not identify strong evidence that desflurane is superior to other agents, in exceptional circumstances some hospitals may decide to hold stock. In these circumstances it is recommended desflurane be accessed via an established protocol approved by the Medicines and Therapeutics Committee or assessed and approved on an individual basis.

EVIDENCE FOR RECOMMENDATIONS

Clinical evidence

There is evidence to demonstrate that desflurane produces up to four minutes faster extubation times compared to other general anaesthetic agents (Macario et al 2005, Stevanovic et al 2015, Lim et al 2016, Guo et al 2017). However, the faster recovery time for patients receiving desflurane did not translate into clinically relevant outcomes such as shorter times spent in the post-anaesthetic care unit (PACU), shorter hospital stays or reduced likelihood of complications.

NICE Review

A recent evidence review by the UK National Institute for Health and Care Excellence (NICE 2024) evaluates the best available evidence comparing desflurane with other general anaesthetic agents, with a focus on clinical and cost benefits (discussed in 'Economic Considerations' section) for two patient groups with higher risk profiles: 1) people having neurological procedures, and 2) people with a body mass index (BMI) of at least 30 kg/m2 having any procedure. The review finds that there is limited evidence to indicate that desflurane is preferable for these patient groups. The review uses Boney et al 2022's core outcome measures for perioperative and anaesthetic care:

(i) mortality/survival (postoperative mortality, long-term survival);
(ii) perioperative complications (major postoperative complications/adverse events; complications/adverse events causing permanent harm);
(iii) resource use (length of hospital stay, unplanned readmission within 30 days);
(iv) short-term recovery (discharge destination, level of dependence, or both); and
(v) longer-term recovery (overall health-related quality of life).

The review summarised studies that focused on patients undergoing neurological procedures (five randomised controlled trials included), finding no statistically significant differences between desflurane and other general anaesthetic agents for all but one of the outcome measures, short term recovery. Sharma et al. (2020), one of the included RCTs reported significantly worse mean cognitive impairment (MCAS) scores for desflurane compared with propofol at discharge or two weeks after surgery (19.09 compared with 22.81 respectively, p=0.013), however it was unclear whether this difference was clinically significant.

For patients with obesity, the NICE review summarised studies focusing on patients with a BMI of at least 30kg/m2 (three studies including a randomised controlled trial, a sub-study of a randomised controlled trial and a retrospective cohort study). The review found no statistically significant differences between desflurane and propofol or sevoflurane for the outcome measures listed above.

Following the NICE review findings of limited evidence to support exceptional use, a consensus statement was agreed upon by anaesthetists and other clinical experts across the UK, defining specific clinical exceptions where use of desflurane may be warranted. In recognition of concerns expressed by neuro-anaesthetists, the Neuro-Anaesthesia and

Critical Care Society (NACCS) agreed to define specific exceptions and keep them updated on its website. The one exception that NACCS currently identifies is for intracranial surgery where the duration of anaesthesia is anticipated to be long (for example, greater than 10 hours) and the intention is to wake the patient at end of surgery (NACCS 2024).

While there is a vast amount of evidence examining comparative short-term recovery for desflurane and sevoflurane, there are fewer studies that analyse other outcomes such as the incidence of post-operative complications for the two agents. The large retrospective cohort study by Zucco et al. (2021) examines post-operative complications and can be considered a robust representation of these impacts. They found that patients exposed to desflurane did not demonstrate a reduced risk of postoperative respiratory complications when compared with sevoflurane. Subgroup analysis by Zucco et al. (2021) in of high BMI, elderly and high-risk patients, found no differences between the two volatile anaesthetic agents.

For more detail regarding the clinical evidence examined for this national statement, refer to Table 1 in Appendix 1.

Environmental considerations and critiques

Desflurane's environmental harm is an important reason to curtail its use. Its effect as a greenhouse gas is 40-50 times the CO_2-equivalent (CO_2e) clinical use of sevoflurane, considering clinical potency and climate impact per unit mass (Andersen et al 2023). Desflurane's high global warming potential over 100 years (GWP_{100}), a key measure of desflurane's relative contribution to global warming, primarily reflects its longer atmospheric lifetime (14 years) than sevoflurane (1.4 years) and isoflurane (3.5 years).

Desflurane is a hydrofluorocarbon (HFC), which alters atmosphere function by preventing heat (as infrared radiation) from escaping into space, as it absorbs wavelengths strongly in the 8-14μm range or 'atmospheric window' (Sulbaek Andersen et al 2010, Sulbaek Anderson et al 2023). It is estimated that HFCs and other halogenated compounds (chlorofluorocarbons and halons) have contributed around 11% of the observed historical warming of the climate, despite being present in tiny concentrations, between 20 parts per quadrillion and 516 parts per trillion (Sherman et al 2021).

Recent contributions to anaesthesia journals have questioned the science supporting concerns about desflurane's impact on global warming (e.g. Slingo and Slingo 2024). These include claims that using GWP_{100} as a comparator is distortionary. There are many debates amongst climate scientists about metric conventions (Blain et al 2019). All attempts at measuring climate impact have limitations. Overall, the science of GWP_{100} as an indicator of relative climate impact to describe desflurane's outsized contribution is valid (Sulbaek Anderson et al 2023).

Slingo and Slingo have also argued that it is more important to address long-lived pollutants such as carbon dioxide rather than short-lived pollutants such as desflurane. Finding the appropriate metrics to compare short-lived pollutants and long-lived pollutants remains a challenge, as identified by the Intergovernmental Panel on Climate Change (IPCC 2018). Yet

there is no reason why both long- and short-lived pollutants cannot be addressed simultaneously – for example action to reduce emissions from anaesthetic gases can occur in parallel to actions to reduce long-lived pollutants, such as switching to renewable energy. Carbon dioxide remains the focus of greenhouse gas pollution mitigation efforts in the health sector with desflurane a small but important component of health sector mitigation efforts worldwide.

Finally, it is crucially important to reduce short-lived climate pollutants (SLCPs), such as desflurane and methane, because such efforts will yield results sooner rather than later, ameliorating some of the worst effects of the climate change that are 'locked in' by longer-lasting pollutants. A policy brief by the World Health Organization states that, "Globally, comprehensive mitigation measures targeting SLCPs could cut the rate of global warming in half (a 0.6°C reduction) … by 2030" (WHO 2022). As the compressed timeframe available to achieve the goals of the Paris Agreement (keeping well below 2°C this century) has become more evident, the importance of addressing SLCPs as part of mitigation efforts has become magnified (Ross et al 2018).

Reassuringly, data from the Healthy Environment and Lives Network demonstrates that CO_2e emissions from desflurane use in Australia have been steadily declining since 2015, while also highlighting that 87% of desflurane CO_2e emissions in 2022 originated from private hospitals (Kazda et al. 2024).

Economic considerations

Desflurane costs around $420 per bottle compared with $95 for a bottle of sevoflurane, and due to the differing potencies, the cost per anaesthetic hour (1 MAC at 1L/min of fresh gas flow) is approximately $33.58 for desflurane and $2.23 for sevoflurane (SWAPNet Queensland 2021). Health services that have ceased the use of desflurane reported significant savings. Figure 1 shows a reduction over time in the monthly cost of volatile anaesthetics and propofol between July 2017 and September 2022 in Western Australia. WA Health reduced its monthly purchase of desflurane from over 120 bottles to zero between July 2018 and November 2022, reducing monthly costs by tens of thousands of dollars (WA Health 2023b).

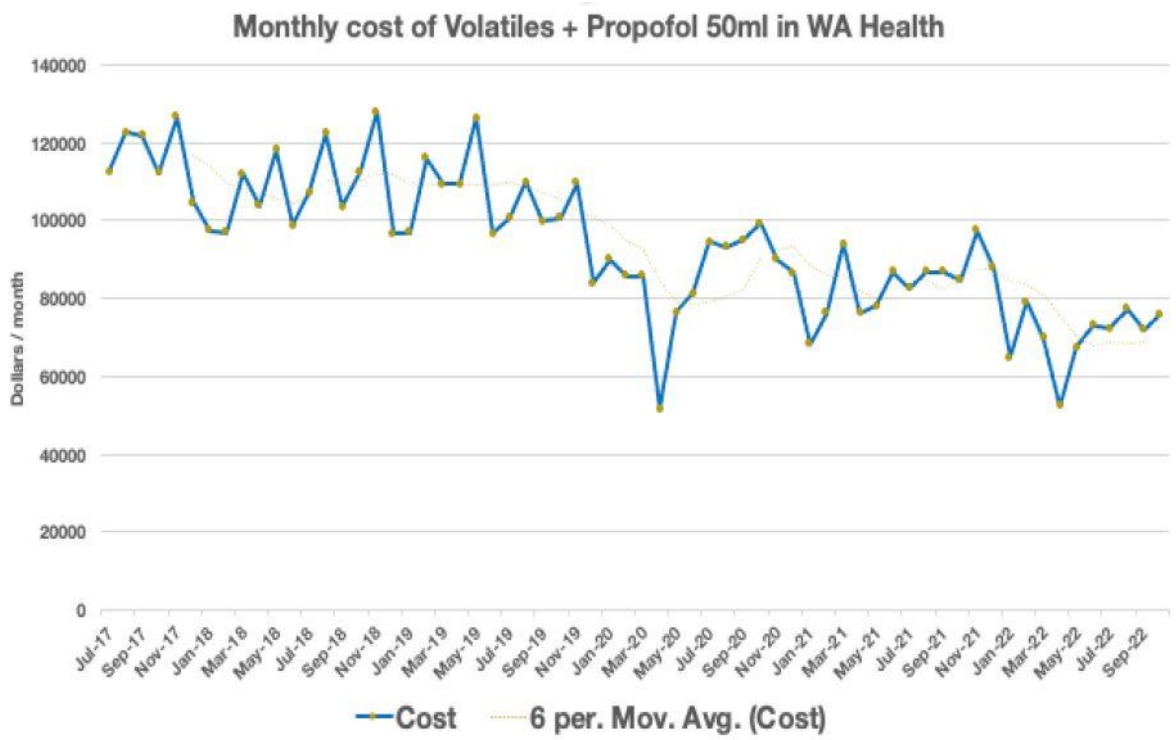

Figure 1: WA Desflurane data on monthly cost of volatile anaesthetics and propofol purchases (Chris Mitchell, Consultant Anaesthetist, in WA Health 2023b).

Hospitals in other jurisdictions have also reported cost savings associated with a reduction in desflurane use. Expenditure for desflurane at the Royal Brisbane and Women's Hospital decreased from $182,992 in 2016 to $15,086 in 2021, with spending for both desflurane and sevoflurane reducing by 58% over this period (Wyssusek et al 2022). A recent study at Austin Health, Melbourne, found that if the anaesthesia minutes of desflurane and isoflurane were delivered by sevoflurane instead, the cost savings would be $89,383 across all operating theatres for the year 2019 (Davies et al 2023). From 2012-2015, Western Health Hospitals were able to reduce the use of desflurane by over 50%, and nitrous oxide use by 15%, saving $22,500 per year (Climate Interactive, 2022).

National and jurisdictional examples of reducing or eliminating use and/or purchasing of desflurane

In December 2023, the Australian Government launched the first National Health and Climate Strategy. Action 4.12 in the Strategy states:

> *The Australian Government will work with the Australian and New Zealand College of Anaesthetists, the Australian Society of Anaesthetists and states and territories to significantly reduce use of desflurane, including by agreeing on a date by which its use will be phased out (Australian Government 2023 p.69).*

Since then, the Australian and New Zealand College of Anaesthetists has released a public statement on desflurane (ANZCA 2024a) advocating for its reduced use.

New South Wales

NSW Medicines Formulary Committee made the decision to remove desflurane from the formulary, effective 1 March 2024 (NSW Health 2024). The Committee cited three main reasons for the decision: the availability of safe and clinically equivalent alternatives to desflurane, the high cost of desflurane, and concerns about desflurane's environmental impact.

South Australia

The Women's and Children's Hospital was the first SA hospital to remove desflurane from use (City of Adelaide 2024). Multiple local health networks have also removed desflurane use from their formularies and a number of private hospitals in SA have implemented actions to reduce its use (ANZCA 2024b), including the removal of desflurane vaporisers from anaesthesia machines.

Victoria

Alfred Health stated in its 2021-22 annual report that medical gases isoflurane and desflurane have been phased out (Alfred Health 2022). Monash Health banned desflurane, as of 1 April 2023, and sent remaining inventory back to the supplier (Monash Health 2022). St Vincent's Hospital, Western Health as well as Albury Wodonga Health have also removed desflurane from their formularies (TRA2SH 2024).

Northern Territory

Top End Health Service has ceased ordering desflurane, meaning hospitals will no longer use desflurane once supplies run out (NT Health 2023).

Queensland

Royal Brisbane and Women's Hospital reduced their use of desflurane from 800 bottles to 35 per year from 2016 to 2021 (Wyssusek et al. 2022). In April 2023, Cairns and Hinterland Hospital and Health Service announced that it will cease use of desflurane in its operating theatres (Whitehead 2023).

Western Australia

Between July 2018 and November 2022, the monthly purchase of desflurane by WA Health reduced from over 120 bottles to zero (WA Health 2023b).

By 2023 there was enough evidence and clinician support for the removal of desflurane from the state medicines formulary in October 2023. The decision was supported by the Western Australian (WA) Therapeutics Advisory Group and endorsed by the WA Medicine Evaluation Panel.

Tasmania

The Royal Hobart Hospital was the first Tasmanian hospital to remove desflurane from use in December 2021. Other public and private hospitals across Tasmania continue to see a decline in use year on year (S. Macdonald, Personal Communication, 16 December 2024).

Private hospitals in Australia

Ramsay, the largest private provider of hospitals in Australia, has reduced desflurane use across its national network, recording a 38% reduction in greenhouse gas emissions from desflurane use in 2023 compared to 2022 (Ramsay Health, 2023). In March 2024, St John of God Health Care became the first Australian private health care organisation to stop purchasing desflurane across its network of 17 hospitals, mostly located in Western Australia (St John of God Health Care 2024).

International case examples

European Union

In January 2024, EU lawmakers agreed to new rules to reduce emissions from fluorinated gases and other ozone-depleting substances. With the new rules, the use of desflurane as an inhalation anaesthetic is prohibited as of 1 January 2026 and will only be permitted when it is strictly required and no other anaesthetic can be used on medical grounds (Iraola 2024).

United Kingdom

In 2022, NHS Scotland announced it was working to end use of desflurane. After a consultation period with Health Boards, NHS Scotland National Procurement removed desflurane from the national contract in 2023 (Scottish Government 2023).

In 2023, NHS England commissioned the NICE evidence review, consulting with anaesthetists and professional bodies before announcing that desflurane would no longer be used in routine practice by early 2024 (NHS England 2024). At a consensus-building workshop following the NICE review, members of several professional associations in England agreed on a specific clinical exception to the phase out of desflurane (NHS England, 2024): desflurane can still be used in intracranial surgery of long duration where the intention is to wake the patient at the end of surgery (NACCS 2024).

United States of America

In 2022, the US Department of Health and Human Services released a primer to help health care organisations reduce greenhouse gas emissions, including reducing the use of desflurane. Also in 2022, the American Society of Anaesthesiologists released guidance on avoiding desflurane and nitrous oxide as anaesthetics, with further guidance in 2023 on using low flow systems of delivery to reduce emissions (Sax 2023).

Canada

In British Columbia, there were significant reductions in desflurane use between 2013 and 2019, with a 60% reduction in use across three health authorities (de Vos, Alexander 2021). In Ontario, at least 26 hospitals and health networks have removed desflurane from their operating rooms as of 2024 (Mathur et al, 2024). In July 2024, the Quebec Institut National d'Excellence en Santé et en Services Sociaux (INESSS) released recommendations on the best clinical practices to reduce the carbon footprint of general inhalation anaesthesia without

compromising the safety of care. It recommended eliminating use of desflurane “except in very exceptional situations” (Desautels 2024). The number of bottles of desflurane supplied to operating rooms across Quebec has decreased by around 80% between 2019 and 2023.

Conclusion

Clinical evidence indicates that the differences between desflurane and its main comparator, sevoflurane, are minimal, amounting to a marginally faster recovery time, which has no bearing on clinical or operational outcomes (Shelton et al 2020). Desflurane is also not associated with any reduced risk of postoperative respiratory complications when compared with sevoflurane (Zucco et al 2021).

The financial cost per anaesthetic hour for desflurane is fifteen-fold that of sevoflurane. Substantial cost savings have accompanied policies to curtail the use of desflurane in health services, with Australian health services reporting saving up to tens of thousands of dollars per month.

Desflurane is a much more impactful greenhouse gas than clinically equivalent alternatives (Andersen et al 2023). Local and international efforts to minimise the harmful effects of anaesthetic agents whilst maintaining quality patient outcomes are important. Reducing emissions from desflurane is a single but important part of the overall work to decarbonise health systems, to achieve “sustainable, resilient, high-quality net zero health systems” (Australian Government 2023).

Appendix 1: Clinical evidence reviewed

Table 1: Evidence showing outcomes of studies evaluating desflurane for short term recovery and post-operative complications.

Outcome	Study	Focus	Study results and measures	Study limitations	Plain language summary of findings for this outcome
Short-term recovery	Gupta et al 2004	Systematic review and meta-analysis of day surgery cases, comparing propofol, isoflurane, sevoflurane and desflurane n=58 articles	No differences were found between propofol and isoflurane in early recovery. However, early recovery was faster with desflurane compared with propofol and isoflurane and with sevoflurane compared with isoflurane.	• Study is 20 years old, includes a significant period before desflurane was widely used. • Day surgery only. • Potential confounding factors - patient and surgery demographics not defined – lack of data re length of OT, BMI, age, concomitant drug administration including nitrous, prophylactic antiemetics, analgesic requirements. • Acknowledges system factors in discharge times – but inconsistent data on 'home ready' vs 'discharge.' • Limited depth of anaesthesia monitoring.	Desflurane produces up to four minutes faster recovery times compared to other general anaesthetic agents. This does not translate into clinically relevant outcomes such as shorter duration of time in the Post-Anaesthesia Care Unit (PACU) or reduced likelihood of complications. (Shelton et al 2020). There are comparable rates of adverse events between agents.
	Macario et al 2005	Meta-analysis of day surgery cases, n=22 studies, covering 1498 patients.	Patients receiving desflurane recovered 1–2 minutes quicker than patients receiving sevoflurane. They were extubated 1.3 minutes sooner (p = 0.003; 95% CI, 0.4–2.2 minutes). No significant differences were detected in the phase I or II PACU recovery times or in the rate of postoperative nausea and vomiting (PONV).	• Study is 19 years old. • Day surgery only. • Heterogeneity in studies- e.g., each study reported PONV differently, different locations with different patient populations, non-standardisation about other factors e.g. anaesthetic technique.	

Outcome	Study	Focus	Study results and measures	Study limitations	Plain language summary of findings for this outcome
	Liu et al 2015	Meta-analysis of recovery for morbidly obese patients, 11 RCTs.	Patients given desflurane took less time for several measures including being prepared for tracheal extubation (weighted mean difference -3.88 min; 95% CI: -7.42 to -0.34), No significant differences in PACU discharge times, PONV, or the PACU analgesic requirement.	• Heterogeneity in studies: patient characteristics, anaesthetic techniques, doses of medications such as opioids, use of nitrous oxide, surgical procedures. • Methodological quality of studies varied (several studies did not report details of sequence generation or concealment). Several studies did not report details of outcome measurements, limiting the validity of any inferences from this study. • Some RCTs had small sample sizes, thus limiting statistical power of results. • Discharge time vs ready for discharge not defined – nonmedical factors acknowledged • BMI defined as > 30. There may be a case for a more direct focus on higher BMI >40 patients to test desflurane effectiveness for obese patients. • Age of patients (predominantly 30's & 40's) • All studies (except for one) focused on elective bariatric cases.	
	Stevanovic et al 2015	Systematic review and meta-analysis of 13 RCTs comparing recovery time and upper airway events for desflurane, sevoflurane, isoflurane and propofol	Unable to identify a significant difference in the occurrence of upper airway adverse events (cough overall, cough at emergence and laryngospasm total) between desflurane and the other three anaesthetics. Times of all emergence variables were significantly faster in the desflurane group	• There was considerable heterogeneity in studies, making generalisation problematic. Five protocols did not predefine administration of midazolam and opioids. Three trials had a high risk of other potential biases. • Smoking history varied between the desflurane and the sevoflurane group in one study. • In another trial, significantly more patients receiving sevoflurane had	

Outcome	Study	Focus	Study results and measures	Study limitations	Plain language summary of findings for this outcome
			than in all other groups, however trials were all small therefore large-scale studies required.	regional anaesthesia and orthopaedic surgery than the desflurane group. • Outcomes weren't primary endpoints in some trials therefore lacked power in all included RCTs. • Lack of consistent randomisation and blinding.	
	Bansal et al 2021	RCT of 60 obese patients who received either BIS guided desflurane or sevoflurane.	Desflurane and sevoflurane have similar recovery profile in obese patients when anaesthetic concentration is carefully titrated. Reversal of cognitive function is significantly earlier in obese patients anesthetized with sevoflurane.	• Lack of detail on potential confounders. • No discussion of potential study weaknesses in discussion section. Sample size is quite small.	
	White et al 2009	Randomised controlled trial of patients undergoing superficial day surgery procedures, comparing recovery and perioperative coughing for desflurane and sevoflurane N=130	Emergence from anaesthesia was more rapid after desflurane; however, all patients achieved fast-track recovery criteria (fast-track score >=12) before leaving the operating room. (Time to discharge home was 90+ - 31 min in sevoflurane and 98 + - 35 min in desflurane, respectively)	• While the anaesthetist was not blinded, investigator evaluating patients during perioperative period was blinded. • Sample sizes were not large enough to produce statistically significant differences between patient groups.	
	Dexter and Hindman 2023	Systematic review with meta-analysis of relative risk of prolonged times to tracheal extubation ≥15 min with desflurane versus sevoflurane or	Desflurane achieved 65% relative reduction in the incidences of prolonged times to tracheal extubation compared with sevoflurane (95% confidence interval 49% to 76%, P < .0001	• Study funded by Baxter, one of the main suppliers of desflurane worldwide, which was not involved in the conduct of the study. • Reducing extubation time to a binary variable (prolonged yes/no) may	Use of desflurane is less likely to lead to a prolonged time to extubation than sevoflurane.

Outcome	Study	Focus	Study results and measures	Study limitations	Plain language summary of findings for this outcome
		isoflurane N=67 studies with 5167 patients		exaggerate the significance of the difference.	
	Ryu et al 2020	RCT, n=69, Arthroscopic knee surgery patients received either desflurane or sevoflurane general anaesthesia after target-controlled induction of anaesthesia with propofol.	The perfusion index (PI) remained higher under desflurane compared with sevoflurane, both before (mean difference (MD): 3.3; 95% confidence intervals (CIs): 2.0-4.7; P<0.001) and after tetanic stimulation (MD: 2.8; 95% CI: 2.0-3.7; P<0.001). Higher PI paralleled lower mean arterial pressure (MAP) in participants assigned to desflurane anaesthesia (P<0.001), both before (MD: 8 mm Hg; 95% CI: 4-12) and after nociceptive stimulation (MD: 14 mm Hg; 95% CI: 7-22). HR was similar throughout.	• Relatively small sample size, specific patient characteristics, may not be widely generalisable. • PI should be considered a relative rather than an absolute number, and thus it cannot provide precise values. It also can be affected by blood viscosity and intravascular volume.	There is some evidence to suggest that desflurane is likely to elevate the perfusion index above levels caused by sevoflurane, however there is debate regarding the clinical significance of this.
	Oh et al 2023	Retrospective cohort study. Results of a previous clinical trial were analysed, with patients matched in pairs according to propensity, who received either desflurane or sevoflurane. N=460 (230 pairs)	Intraoperative perfusion index (PI) was significantly higher in patients administered desflurane than sevoflurane. However, the impact of the choice between desflurane and sevoflurane on intraoperative PI in this clinical setting was minimal.	• As mentioned above, there are issues with assuming that PI is an indicator of vasodilation. It should be seen as a parameter dependent on various local and systemic factors thus is not a direct indicator of vasodilation.	
	Choi et al 2015	Randomized controlled double-blind study of	Desflurane reduced the incidence of emergence	• Anaesthetist who administered anaesthetics was not blinded to the	It is unclear whether desflurane or sevoflurane is more likely to

Outcome	Study	Focus	Study results and measures	Study limitations	Plain language summary of findings for this outcome
		adult patients with orthognathic surgery N=144	agitation compared to sevoflurane (24% vs. 71%, respectively, P < 0.001)	allocation, however recovery assessments were undertaken by a blinded investigator. • Anaesthesia was not based on age-adjusted MAC but on 40 years of age adjusted MAC as an indicator of anaesthetic depth. Patients were aged from 18-43 years.	trigger emergence agitation (EA). While one RCT of adults (Choi et al 2015) found that desflurane is less likely to trigger EA, a network meta-analysis of children (Lim et al 2016) found the opposite outcome. Another study of children, a systematic review and meta-analysis (Lim et al 2016) found that the two agents are similar.
	Lim et al 2016	Systematic review with meta-analysis N=14 studies, 1196 patients, comparing the incidence or severity of emergence agitation and emergence times in children anesthetized with desflurane or sevoflurane	Incidence and severity of emergence agitation similar in two groups. Extubation and awakening times were shorter in the desflurane group than in the sevoflurane group; the weighted mean differences were −2.21 (95% CI: −3.62 to −0.81; I2 = 93%) and −2.74 (95% CI: −3.80 to −1.69; I2 = 85%), respectively.	• While all studies were RCTs, only 7 used random sequence generation. It is unclear whether most studies adequately concealed their allocations. • There may be several confounding factors affecting results. These could include different kinds of scales for EA, different cutoff values for EA, and methods for reducing pain.	
	Guo et al 2017	Network meta-analysis N=48 studies with 4485 patients evaluating recovery characteristics of desflurane, halothane, isoflurane, propofol, and sevoflurane in paediatric anaesthesia	Desflurane has the highest incidence of emergence agitation and worst recovery characteristics. Cases using sevoflurane reported the highest incidence of analgesic requirement. Propofol was recommended as the most efficient and safe anaesthetic in paediatric anaesthesia with few adverse effects.	• Direct and indirect evidence were both included, and consistency between these was not perfect. • Different protocols were applied by different studies, heterogeneity might be elicited.	
Intra-operative and post-operative complications	Satoh et al 2009	Animal model, n=99. The effects of desflurane and sevoflurane on total lung resistance and dynamic	Desflurane but not sevoflurane increased total lung resistance concomitant with a decrease in dynamic	• The experiments tested a high concentration of desflurane, at 2.0 MAC.	There is limited animal evidence that at high doses desflurane can increase lung resistance.

Outcome	Study	Focus	Study results and measures	Study limitations	Plain language summary of findings for this outcome
		lung compliance were investigated in animals that were either untreated, pretreated with atropine or vagotomy, pretreated with the tachykinin receptor antagonists sendide or MEN-10376, or given chronic pretreatment with capsaicin.	lung compliance in guinea pigs. The increase in lung resistance by desflurane might be due to antidromic tachykinin release from afferent C-fibres but not acetylcholine release from parasympathetic efferent nerves.	• There may also be slightly different lung physiologies between guinea pigs and humans.	
	White et al 2009	Randomised controlled trial of patients undergoing superficial day surgery procedures, comparing recovery and perioperative coughing for desflurane and sevoflurane N=130	Although overall incidence of coughing during perioperative period higher in the desflurane group (60% versus 32% in sevoflurane group, P< 0.05), the incidences of coughing during the actual administration of the volatile anaesthetics (i.e., the maintenance period) did not differ between the two groups.	See limitations for White et al (2009) listed above	While incidence of coughing during perioperative period was higher for desflurane, it did not differ during the maintenance period.
	Stevanovic et al 2015	Systematic review and meta-analysis of 13 RCTs comparing recovery time and upper airway events for desflurane, sevoflurane, isoflurane and propofol	Unable to identify a significant difference in the occurrence of upper airway adverse events (cough overall, cough at emergence and laryngospasm total) between desflurane and the other three anaesthetics.	See limitations for Stevanovic et al (2015) listed above	Desflurane did not cause any more upper airway adverse events than other general anaesthetic agents.

Outcome	Study	Focus	Study results and measures	Study limitations	Plain language summary of findings for this outcome
	Zucco et al 2021	Large cohort, retrospective analysis of adult non-cardiac surgery patients who received sevoflurane (84,608) or desflurane (23,830) for the maintenance of general anaesthesia between 2005 and 2018.	Patients exposed to desflurane did not demonstrate a reduced risk of postoperative respiratory complications when compared with sevoflurane (adjusted odds ratio 0.99, 95%CI 0.94–1.04, p = 0.598).	• Retrospective registry study, which has some shortcomings but reflects real world practice. • Single centre thus may not be applicable to a generalised patient population. However a wide range of demographics access the health network, and the data include a wide range of specialties. • Patients with missing confounding information were excluded. This may affect results; however, a sensitivity analysis was performed to address potential imbalances or residual confounding between study groups. • Included patients who received both desflurane & sevoflurane – allocated via which had the higher age adjusted MAC – effect on results not clear & not discussed.	Following adjustment for confounding variables, there was no difference in the odds of experiencing postoperative respiratory complications between patient groups that received desflurane versus patients receiving sevoflurane.
	Koch et al 2023	Secondary analysis of the SuDoCo trail [ISRCTN 36437985] 1277 patients, older than 60 years undergoing general anaesthesia were included. Study pre-processed and analysed raw EEG files from each patient and evaluated the intraoperative burst suppression duration.	Desflurane is associated with a higher risk to develop post-operative delirium in older patients as compared to propofol or sevoflurane, even though propofol shows prolonged intraoperative burst suppression activity.	• Secondary analysis using endpoints that were not the primary focus of initial study. • The patient groups differed regarding sex, BMI, surgery duration, surgery speciality (however analysis adjusted for risk factors). • Focus on older patients limits generalisability.	The findings of the secondary analysis suggest desflurane may be associated with a higher risk of post operative delirium in older patients, although further studies are required.

Outcome	Study	Focus	Study results and measures	Study limitations	Plain language summary of findings for this outcome
Conditions that permit exceptional use	NICE 2024	Review evaluates the best available evidence comparing desflurane with other general anaesthetic agents, with a focus on clinical and cost benefits for two patient groups with higher risk profiles: 1) people having neurological procedures, and 2) people with a body mass index (BMI) of at least 30 kg/m2 having any procedure.	For neurological cases the studies found no statistically significant differences between desflurane and other anaesthetics for all but 1 of the outcome measures (short term recovery), and even then, it was unclear whether this was of clinical significance. For patients with obesity, the studies found no statistically significant differences between desflurane and propofol or sevoflurane for those outcome measures.	• Analyses of all the outcomes in Sharma et al. (2020) and secondary outcomes in all the studies may lack statistical power to detect differences between the groups, and these results should be interpreted cautiously. • As the patient groups were tightly defined, the number of studies included in the meta-analyses was small (five studies for neurosurgery and three studies for patients with obesity).	The review finds that there is limited evidence to indicate that desflurane is preferable for these patient groups.

Appendix 2: How this guidance was developed

This document is intended to provide short summarised best practice recommendations to hospital and statewide Medicines and Therapeutics Committees (MTCs) using a consensus development model. This will assist good governance and decision-making for health service organisations, MTCs and health professionals.

CATAG has developed this document, based on the review of current literature as of December 2024. A narrative review method was used to gather and summarise evidence. Peer-reviewed journal articles and policy literature were consulted for clinical and environmental evidence, while organisational websites and media articles were also used for up-to-date information on international practice and the cost of desflurane.

On July 31, 2024, CATAG called for expressions of interest for experienced professionals to join an Expert Advisory Group to review the use of desflurane in Australia. An expert advisory group (EAG) was established from across Australia, comprised of individuals reflecting a range of geographies and specialisations, with a focus on representatives from anaesthesia, alongside individuals from pharmacology, pharmacy, nursing, clinical governance and data and analytics. Members of the advisory group reviewed the evidence, agreed on consensus statements, reviewed feedback and drafts of the document and approved the final position statement.

This guidance was developed in consultation with the Australian Society of Anaesthetists (ASA) and the Australian and New Zealand College of Anaesthetists (ANZCA) along with the CATAG member organisations listed below:

- ACT Health
- Clinical Excellence Commission, NSW Health
- NSW Therapeutic Advisory Group (NSW TAG)
- Northern Territory Health Medicines and Therapeutics Committee (NTMTC)
- Queensland Health Medicines Advisory Committee (QHMAC)
- South Australian Medicines Advisory Committee (SAMAC)
- Tasmanian Medicines Access and Advisory Committee (TMACC)
- Victorian Therapeutics Advisory Group (Vic TAG)
- Western Australian Therapeutics Advisory Group (WATAG)

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