


Efficacy and safety of intrathecal diamorphine: replies

We thank Drs Xu and Rong [1] and Drs Leslie and Stranix [2] for their comments regarding our systematic review and meta-analysis exploring the efficacy and safety of intrathecal diamorphine [3].

Drs Xu and Rong correctly highlighted that the figure we initially presented regarding the risk of bias assessment of the included trials was not derived from the Cochrane Collaboration’s Risk of Bias tool 2 (RoB2) [1], but rather RoB1. Whilst this was an oversight, and represents an educational opportunity for many readers, we fully agree with their observation and are pleased to now present the appropriate figure (Fig. 1) for included studies (online Supporting Information Appendix S1).

Drs. Leslie and Stranix share their experience with intrathecal diamorphine, reporting doses ranging from 0.4 to 1.0 mg with good efficacy and a 10% incidence of postoperative nausea and vomiting [2]. While they acknowledge the need for further trials, they also note the challenge of convincing colleagues to adjust their practices, even in the context of prospective trial results. However, clinical practice should be guided by robust evidence rather than personal experience. We, therefore, encourage Drs. Leslie and Stranix to collect prospective data and publish their results for the benefit of patients across the UK where diamorphine is used commonly. Indeed, as a drug that is used commonly in the UK, it is disappointing that only 12 trials have been published over

the past 35 years. We encourage clinicians and researchers to conduct dose–response studies urgently to better define the efficacy and safety profiles of intrathecal diamorphine.

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References

- Xu N, Rong W. Risk of bias assessment in a meta-analysis investigating the efficacy and safety of intrathecal diamorphine. *Anaesthesia* 2025; **80**: 722. <https://doi.org/10.1111/anae.16431>.
- Leslie D, Stranix N. Do some operations still need more diamorphine. *Anaesthesia* 2025; **80**: 723. <https://doi.org/10.1111/anae.16535>.

Study	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
Abuzaid 1993	Diamorphine	Control	Postoperative pain score	NA	!	!	!	!	!	!
Cowan 2002	Diamorphine	Control	Incidence of intra-operative pain	NA	!	+	+	+	+	+
Graham 1997	Diamorphine	Control	Postoperative pain score	NA	!	+	+	+	+	!
Jacobson 1989	Diamorphine	Control	Postoperative pain score	NA	!	!	!	+	!	!
Kelly 1998	Diamorphine	Control	Postoperative analgesic consumption	NA	!	+	+	+	+	+
King 2004	Diamorphine	Control	Plasma paracetamol concentration	NA	+	+	+	+	+	+
Lane 2005	Diamorphine	Control	Incidence of intra-operative pain	NA	+	+	+	+	+	!
Milligan 1993	Diamorphine	Control	Postoperative pain score	NA	!	!	+	!	!	!
Reay 1989	Diamorphine	Control	Postoperative analgesic consumption	NA	!	!	+	+	!	!
Roulson 1994	Diamorphine	Control	Time to first analgesic request	NA	!	!	!	!	!	!
Skilton 1999	Diamorphine	Control	Postoperative pain score	NA	+	+	+	+	+	+
Wrench 2007	Diamorphine	Control	Postoperative analgesic consumption	NA	!	+	+	+	+	+

Figure 1 Risk of bias 2 of included trials (see details in online Supporting Information Appendix S1). Green, low risk; yellow, some concerns; red, high risk. D1, randomisation process; D2, deviations from the intended interventions; D3, missing outcome data; D4, measurement of the outcome; D5, selection of the reported result.

3. Grape S, El-Boghdadly K, Jaques C, Albrecht E. Efficacy and safety of intrathecal diamorphine: a systematic review and meta-analysis with meta-regression and trial sequential analysis. *Anaesthesia* 2024; **79**: 1081-90. <https://doi.org/10.1111/anae.16359>.

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Supporting Information

Additional supporting information may be found online via the journal website.

Appendix S1. Included studies.

Incomplete Optiflow™ switching and the potential for confusion

As the evidence base supporting the use of peri-intubation high-flow nasal oxygen (HFNO) continues to expand [1], there have been advances in the design of the latest generation of systems for use in operating theatres. We would like to highlight several practice point considerations relating to use of such systems.

A limitation of previous designs is that applying a tight-fitting anaesthetic facemask over the incompressible nasal prongs is contraindicated due to the risks of gastric insufflation and barotrauma. The Fisher and Paykel Optiflow™ Switch (Fisher and Paykel, Auckland, New Zealand) modification [2] incorporates a flow-regulated pressure relief valve and a compressible inflow to the nasal prongs so that there is interruption of the 100% oxygen nasal prong gas flow when a tight-fitting facemask is applied. This allows safe and seamless transitions from anaesthetic mask pre-oxygenation and facemask ventilation to HFNO and vice versa.

The user should be aware that, even when a firmly applied facemask is applied over the nasal prongs, the nasal oxygen flow is not completely 'switched off'. It is likely to be variable but with Optiflow Switch flows above 10 l.min⁻¹ it is apparent that there is ongoing oxygen ingress via the nasal prongs into the facemask during pre-oxygenation and facemask ventilation. The product literature details that the pressure delivered to the patient will be limited to 30 cmH₂O between flows of 30-70 l.min⁻¹ [3].

Figure 1 shows the gas analyser data observed when a firmly applied facemask connected to a circle anaesthetic circuit with flow rates 10 l.min⁻¹ of room air (F_IO₂ 0.21) is applied over the Optiflow Switch nasal prongs and the HFNO flow rate is increased. The analyser measures increasing levels of inspired and end-tidal oxygen consistent with increasing oxygen ingress via the nasal prongs. Additionally, the capnography trace is attenuated, the extent of which is related to the HFNO flow rate. It does

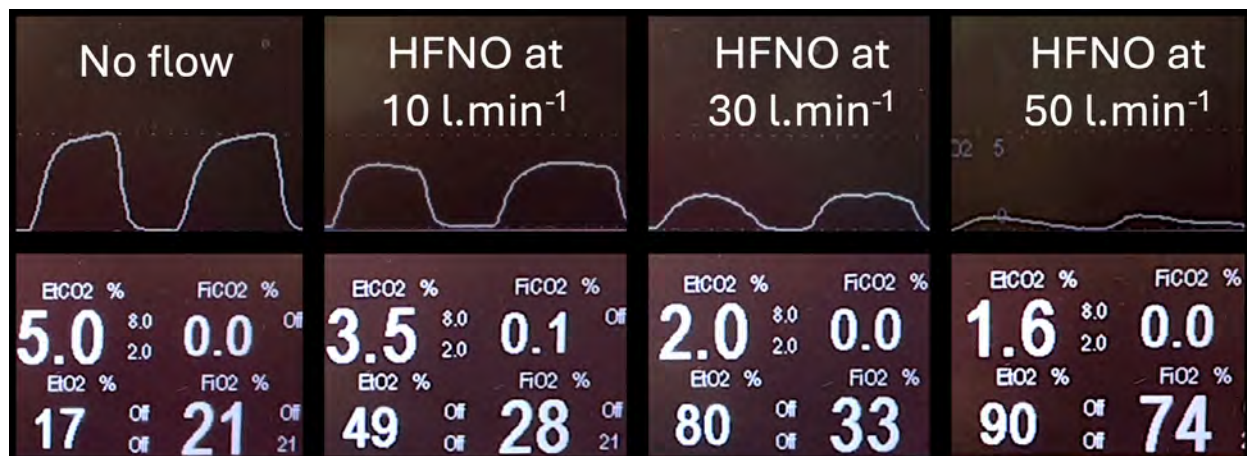


Figure 1 Photos stitched together show representative gas analyser readings and end-tidal carbon dioxide traces when a firmly applied facemask connected to a circle anaesthetic circuit with flow rates 10 l.min⁻¹ of room air (F_IO₂ 0.21) is applied over the Optiflow Switch nasal prongs and the high-flow nasal oxygen (HFNO) flow rate is increased.