

GUIDELINES

Remifentanil patient-controlled analgesia for labour analgesia: guidance from the obstetric anaesthetists' association

Recommendations for well tolerated provision of remifentanil PCA for labour analgesia

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BACKGROUND Remifentanil patient-controlled analgesia (PCA) has emerged as an important option for labour analgesia, particularly for women who are unable to receive neuraxial analgesia. Concerns about maternal safety and staffing requirements suggest that in many maternity units, it is only infrequently used, leading to variation in practice. In 2023, the UK National Institute for Health and Care Excellence recommended that all labouring women be informed about the full range of analgesia options, including remifentanil PCA, highlighting the need for a standardised management approach.

METHODS To address these challenges, the Obstetric Anaesthetists' Association convened an expert working group to develop evidence-based guidance. The group undertook a review of the literature, and used a modified Delphi approach to create consensus statements and recommendations. Recommendations were developed based on the evidence. Where evidence was insufficient to support recommendations, statements were provided with an associated level of certainty. These recommendations aim to support clinicians in providing well tolerated, effective and patient-centred care when using remifentanil PCA for labour analgesia. Statements and recommendations are graded according to the US Preventive Services Task Force grading methodology, ensuring transparency and robustness in the development process.

RESULTS A total of 757 articles were identified in the initial literature search. Further screening identified 83 full text articles of relevance. A structured narrative review was produced which covered patient suitability for remifentanil PCA (maternal and foetal factors), practical use of remifentanil PCA, standards of care for women receiving remifentanil PCA and quality assurance and monitoring. The working party agreed on 19 recommendations and six statements. These were generally assigned a low or moderate level of certainty. The safety of mother and baby were the key priorities in producing these guidelines.

CONCLUSIONS Remifentanil PCA can provide effective labour analgesia, particularly when neuraxial techniques are contraindicated or declined. Despite some inherent risks, when managed within defined parameters, there is now an established record of efficacy and safety. It is essential that labour wards have clear protocols for administration and monitoring, and for staff to be trained in recognising and managing complications. There is a lack of data for remifentanil PCA use in higher-risk maternal and foetal groups; this is an area of research priority. These first evidence-based guidelines aim to standardise care and support the well tolerated and effective use of remifentanil PCA in labour.

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Why were these guidelines developed?

Remifentanil PCA has become an increasingly popular choice for labour analgesia, particularly in cases where regional techniques are contraindicated. Despite its growing use over the past two decades, there remains a notable lack of standardised guidance on best practice management. Variation exists in protocols for dosing, monitoring, patient selection and strategies to minimise maternal and neonatal side effects. The absence of evidence-based recommendations underscores the need for further research and consensus to support its well tolerated and effective use in labour.

What guidelines currently exist?

Currently, there are no evidence-based national or international guidelines specifically addressing the use of remifentanil PCA for labour analgesia. Although remifentanil PCA is used in clinical practice, existing protocols are largely institution specific, informed by local expertise, retrospective audits and observational studies.

How do these guidelines differ from existing guidelines?

This specialist society narrative review, with associated recommendations and statements, provides formal, evidence-based guidelines on the use of remifentanil PCA for labour analgesia. These include detailed discussions on dosing protocols, monitoring requirements, safety considerations and the management of potential complications. In addition, they offer practical recommendations to ensure effective analgesia while minimising risks for both mother and foetus.

Introduction

Remifentanil patient-controlled analgesia (PCA) has become increasingly recognised as a useful option for labour analgesia, particularly when neuraxial techniques are contraindicated or declined. Remifentanil is a short-acting synthetic opioid with favourable pharmacokinetic properties, including rapid onset and offset, making it suitable for patient-controlled use during labour. Although its use is supported by an emerging body of evidence and positive patient experience, and it is recommended for labour analgesia in the most recent NICE guidance in the UK,¹ concerns remain around maternal safety, particularly in relation to respiratory depression, and the resource requirements for safe administration.

Despite over two decades of clinical experience, remifentanil PCA remains variably used in UK obstetric units, with significant differences in eligibility criteria, dosing regimens, monitoring standards and staff training. These variations reflect the absence of formal guidance and the challenges of implementation in busy maternity settings, where staffing and infrastructure constraints may limit uptake.

Although some local protocols exist, no national evidence-based guidelines had previously been developed.

In response, the Obstetric Anaesthetists' Association (OAA) convened an international multidisciplinary working group to undertake a review of the evidence and generate best-practice recommendations. This document represents the first guidance to support clinicians in the well tolerated and effective use of remifentanil PCA for labour analgesia. These guidelines have been developed with an awareness that women's experiences of labour analgesia are not uniform. Social, cultural and ethnic factors can shape both access to, and perceptions of, remifentanil PCA. Our aim has been to provide guidance that promotes equity, informed choice and safety for all women and birthing people, and to ensure that implementation does not inadvertently widen existing disparities in maternity care.

Materials and methods

All working party members were selected for their expertise in obstetric anaesthesia and their specific interest in using remifentanil PCA for labour analgesia. In April 2024, a comprehensive literature search was conducted using MEDLINE, Embase and Cochrane CENTRAL. The search, facilitated by a public health librarian at NHS Scotland, included terms such as 'remifentanil PCA', 'labour analgesia', 'maternal outcomes', 'neonatal outcomes', 'opioid analgesia' and 'respiratory depression'. The search was limited to English-language articles published from 1 January 1993 onwards.

Two members of the working party independently screened the search results to determine inclusion or exclusion of each article. In cases of disagreement, a third member resolved conflicts. The selected references were imported into Covidence (www.covidence.org), where further screening was conducted to eliminate irrelevant publications and ensure no important papers were overlooked. Structured narrative reviews on various aspects of remifentanil PCA were then prepared by individual members of the working party, in keeping with the SANRA guidelines for quality assessment.²

Recommendations were developed based on the evidence, graded according to the US Preventive Services Task Force guidance (Table 1). Where evidence was insufficient to support recommendations, statements were provided with an associated level of certainty (Table 2). An interim draft guidance document was prepared by two editors and distributed to the working party for review. A modified Delphi process was used to achieve consensus on the content, wording and grading of each statement and recommendation, requiring more than 75% agreement. Revisions were made iteratively until consensus was achieved.

The final draft was shared with the working party for approval and peer reviewed by the OAA Executive Committee, additional experienced obstetric anaesthetists and with a lay representative.

This rigorous process ensured the guidelines are evidence-based, clinically relevant and widely supported. The safety of mother and baby were the key priorities in producing these guidelines.

Results

A total of 757 articles were identified in the initial literature search. Further screening identified 153 full text articles of relevance, of which 70 were excluded after full-text screening, leaving 83 articles which were finally included. A structured narrative review was produced which covered patient suitability for remifentanyl PCA (maternal and foetal factors), practical use of remifentanyl PCA, standards of care for women receiving remifentanyl PCA and quality assurance and monitoring. The working party agreed on the content, wording and grading of 19 recommendations and six statements.

Patient suitability for remifentanyl patient-controlled analgesia: maternal and foetal factors

Changing maternal demographics, an increase in patient comorbidity and concerns about lack of data on foetal safety raise questions of whether remifentanyl analgesia in labour can be broadly offered as an option for all patients or whether there are additional concerns or contraindications among certain patient groups.

Maternal comorbidities of interest include extremes of BMI, cardiorespiratory disease, obstructive sleep apnoea, chronic opioid use and severe pre-eclampsia. Concerns relating to foetal status include intrauterine death, intra-uterine growth restriction or small for gestational age, early gestations (below 36 weeks) and multiple pregnancies.

Evidence of the safety of remifentanyl analgesia for labouring women and their offspring who present with these specific conditions, alongside any other serious maternal pathology reported around the use of remifentanyl, were extracted from literature search results. The most notable general finding was the relative lack of literature about any high-risk maternal or foetal groups using remifentanyl analgesia during labour. In general, published studies, reviews and meta-analyses tended to focus on the quality of analgesia, maternal satisfaction and global safety among a relatively healthy population, rather than include a focus on higher-risk groups. Similarly, from a foetal perspective, studies tended to include full-term, singleton babies with no anomalies. These relatively narrow parameters may be explained by the fact that remifentanyl remains a contentious and relatively new drug for labour analgesia, particularly in circumstances where investigators are seeking ethical approval for prospective studies.

Maternal factors

In their recent meta-analysis and systematic review of remifentanyl versus epidural analgesia during labour, Lei *et al.*³ included only studies of healthy patients. They

concluded the need for future studies with larger sample sizes and including different populations.³ In their earlier systematic review of remifentanyl versus meperidine for labour analgesia, Leong *et al.*⁴ similarly comment on excluding high-risk patients from studies, cautioning the generalisability of results for such patient groups.

The 2017 Cochrane Review of remifentanyl versus alternative parenteral methods for pain management in labour,⁵ notes the homogeneity of investigated groups and the almost universal exclusion of high-risk patients, such that outcomes cannot be applied to our increasingly comorbid parturient population.

Among the few studies whose criteria included a population of potential interest in their methodology, published data lacks granularity, with no comment or analysis specific to high-risk groups. D'Onofrio *et al.*⁶ did not consider chronic opioid use as an exclusion criterion, but there is no indication that anyone in their study fell into this group. In their large retrospective study of remifentanyl analgesia during labour, Murray *et al.*⁷ potentially included some high-risk groups of interest. Severe pre-eclampsia, significant medical comorbidities and excessively high or low BMI were all listed as only relative contraindications to remifentanyl. However, there were no granular data on any of these groups, and it is not clear how many, if any, were included.⁷ To date, the RESPITE trial is the most influential randomised controlled trial studying remifentanyl as a labour analgesic. Although eight pre-eclamptic women were included in the remifentanyl group and the upper weight range was 147 kg, no further subgroup information is provided, which is likely to reflect the small numbers of comorbid patients, precluding meaningful data analysis.⁸

Cardiac disease

One study by Knapp *et al.*⁹ reports explicitly on remifentanyl analgesia during labour in patients with heart disease. Nineteen patients with valvular disease, mechanical valves, congenital disease, arrhythmias or aortopathy were given an escalating regimen of remifentanyl, beginning at 20 µg and increasing up to 40 µg, with a 3-min lockout. Indications for remifentanyl were patient preference, refusal of epidural analgesia or therapeutic anticoagulation. There was only one PCA to epidural conversion, and 74% were reported to have managed on the lowest dose of 20 µg. There were no adverse cardiac events or significant changes in maternal haemodynamics compared to baseline. While acknowledging the limitations of their small study, the authors endorse remifentanyl as a potentially beneficial labour analgesic in patients with cardiac disease, and call for further studies in this specific patient group.

Weight and BMI

Most studies that mention weight or BMI as an exclusion criterion, state an arbitrary cut-off of around 100 kg and

Table 1 Recommendations for clinical practice

	Recommendation	Grading/level of certainty
Information for women	1. Women should be informed about the relative benefits of remifentanil PCA compared to other analgesic modalities, as well as the potential side effects, including nausea, pruritus, sedation, and respiratory depression requiring oxygen therapy	Grade A, high level of certainty
Direct Clinical Guidance	2. Whilst remifentanil PCA is generally safe for babies, women should be aware of the small chance that the neonate may require brief respiratory support after birth	Grade A, low level of certainty
	3. Where oral, parenteral or epidural opioids have been given in the preceding 4 h, careful consideration of risks and benefits must be taken prior to starting remifentanil PCA	Grade B, moderate level of certainty
	4. Remifentanil for labour analgesia should be delivered as a patient-controlled analgesia (PCA) demand bolus dose, and not as a continuous infusion	Grade B, moderate level of certainty
	5. All units offering remifentanil PCA should have an adequate number of pumps to accommodate workload demand, and pumps must be capable of delivering a rapid bolus dose	Grade A, high level of certainty
	6. Remifentanil PCA should be delivered via a dedicated cannula where possible. If not using a dedicated cannula, remifentanil must be the infusion nearest the cannula and there must be an antireflux valve between the remifentanil outlet and all other intravenous infusions	Grade C, low level of certainty
	7. A remifentanil PCA lockout time of two minutes should be programmed between boluses	Grade B, moderate level of certainty
	8. Offering an incremental dosing regimen provides flexibility to tailor dosage towards optimal analgesia, with minimal side effects: an initial bolus of 20 to 30 µg is recommended, which may be reduced to 10 to 20 µg or increased to 30 to 40 µg as needed	Grade B, low level of certainty
	9. All women using remifentanil PCA should have continuous oxygen saturation monitoring, with immediate availability of supplemental oxygen, naloxone and ventilation equipment. Supplemental oxygen should be applied when oxygen saturation drops below 94%	Grade A, high level of certainty
	10. All women using remifentanil PCA should have uninterrupted one-to-one care by an appropriately trained healthcare professional to monitor for excessive sedation, oxygen desaturation and apnoea. If continuous healthcare professional presence cannot be maintained, the remifentanil PCA must be discontinued during this period	Grade A, high level of certainty
	11. Each unit should have clear criteria to establish when an anaesthetist should review patients, and when a remifentanil PCA should be discontinued due to excessive sedation and/or respiratory depression	Grade A, low level of certainty
	12. Nitrous oxide may be used in conjunction with remifentanil PCA, using the same standards of monitoring	Grade C, low level of certainty
	13. In a stable parturient, continuous CTG monitoring is not necessary during remifentanil PCA use, in the absence of other CTG indications	Grade C, low level of certainty
	14. Remifentanil PCA may be used for the perineal infiltration of local anaesthetic, but should not be used as analgesia for postnatal interventions per se. If remifentanil has already been discontinued, it should not be re-started. Monitoring and 1 : 1 supervision must be continued. The operator cannot also supervise the patient	Grade I, low level of certainty
Staff Training	15. Women choosing to use remifentanil PCA for labour analgesia must birth in obstetric units with 24-h access to medical staff, oxygen therapy and resuscitation equipment	Grade A, moderate level of certainty
	16. All healthcare professionals providing care for patients using remifentanil PCA in labour should be competent in basic life support and formally trained to understand, monitor and manage common serious side effects, including sedation, respiratory depression, oxygen desaturation and apnoea. In addition, they should undergo regular updates in training, and each department should keep a compliance log to ensure adherence to these protocols	Grade A, low level of certainty
Audit and Research	17. Patient follow-up and regular local audit should be conducted to ensure analgesic quality, patient satisfaction and adherence to safety standards, with improvements implemented where necessary	Grade A, low level of certainty
	18. Work exploring the safety and efficacy of existing remifentanil analgesia protocols and/or alternative 'high-risk' protocols in specific co-morbid parturient and foetal groups is urgently needed	Grade I, low level of certainty
	19. Further research is needed to clarify the optimal remifentanil bolus dose during labour	Grade I, low level of certainty

Table 2 Statements

	Statement	Level of certainty
A	Remifentanil PCA provides better pain relief than other opioids administered parenterally and better pain relief than Entonox alone. Remifentanil PCA is an inferior analgesic option when compared with epidurals	high level of certainty
B	Patient satisfaction has been shown to be comparable between epidural and remifentanil PCA for labour analgesia	moderate level of certainty
C	The initial analgesic effect of remifentanil may be transient and diminish within 2 to 3 h	low level of certainty
D	Small data sets suggest that remifentanil may be a suitable labour analgesic in selected women with heart disease, pre-eclampsia (excluding the most severe complications) and late pregnancy BMI up to 40 kg m ⁻² . An individualised approach, with consideration of comorbidities is recommended if BMI is >40 kg m ⁻² .	low level of certainty
E	Remifentanil may be well tolerated to use in cases of intrauterine death, but in all cases, maternal monitoring, avoiding concomitant use of other opioids and, in particular, continuous healthcare professional presence is mandatory	low level of certainty
F	There is no strong evidence to suggest that remifentanil PCA should be contraindicated due to early gestations, multiple pregnancy or intrauterine growth retardation/small for gestational age foetuses. However, robust safety data is lacking, and parameters beyond which adverse events may be more likely, are absent	low level of certainty

40 kg m⁻², respectively. This includes the RemiPCA SAFE Network six-year audit, reporting on 31 European hospitals.¹⁰ One study reported a weight cut-off of 110 kg and another 120 kg, but the heaviest recruited patients in each study were 82 and 90 kg, respectively.^{11,12} Lower weight and BMI cut-offs were far less frequently stated, and there was no analysis of lower BMI subgroups in any remifentanyl literature reviewed. The RESPITE trial⁸ had a weight range of 45 to 147 kg, with an average weight of 73 kg, but no further data specific to underweight or overweight parturients, presumably reflecting small numbers. One study included a parturient of 133 kg (BMI 48 kg m⁻²) in their 12-person remifentanyl group without further mention.¹³

Pre-eclampsia

El-Kerdawy and Farouk¹⁴ investigated the use of remifentanyl PCA compared with epidural analgesia in a cohort of women with pre-eclampsia. Women with eclampsia, pulmonary oedema, neurological deficits or a platelet count less than $80 \times 10^9 \text{ l}^{-1}$ were excluded, but those with less severe disease were included. All participants were at least 32 weeks' gestation. The authors reported that remifentanyl PCA was effective and well tolerated in this population. However, the study was small ($n = 30$; 15 per group), limiting the generalisability of the findings. Robust data on the safety and efficacy of remifentanyl PCA in women with pre-eclampsia remain limited, and further research is needed to inform clinical practice.

Foetal factors

Gestational age

Freeman *et al.*¹⁵ studied remifentanyl versus epidural analgesia during labour in a large randomised multicentre equivalence trial. Healthy women beyond 32 weeks' gestation were included. However, approximate median [IQR] gestations in the remifentanyl group were 38 [36 to 39] weeks, and the authors state that subgroup analysis for the 32 to 34-week group was not carried out due to only a single remifentanyl data point at this gestational age range. A systematic review of remifentanyl efficacy and safety on term and preterm neonates was published by Maroni *et al.*¹⁶ Remifentanyl use for labour analgesia was one of three areas studied (others were remifentanyl for procedural analgesia and remifentanyl for longer-term sedation). The authors report chest wall rigidity as an adverse effect. However, this appears to be in the context of remifentanyl use for procedural analgesia during the postnatal period and is particularly associated with the rapid administration of the drug. The authors concluded that short-term remifentanyl use is well tolerated in preterm and full-term neonates. Marwah *et al.*¹⁷ conducted a retrospective cohort study of remifentanyl versus fentanyl for intravenous patient-controlled labour analgesia and included pregnancies beyond 24 week's gestation. However, gestations in the remifentanyl group

averaged nearly 39 weeks (standard deviation 3 weeks), and no granular data were presented for gestations less than 36 weeks. A study by El-Kerdawy and Farouk¹⁴ was explicitly concerned with remifentanyl versus epidural analgesia in a population with pre-eclampsia and included gestations at least 32 weeks. However, the remifentanyl group contained just 15 parturients, only some of whom were less than 36 weeks' gestation. No specific comment is made on gestational age effects, and the authors conclude that PCA remifentanyl is a well tolerated analgesic option in labour for patients with pre-eclampsia.

Intrauterine foetal death

Delivery analgesia for patients who have experienced intrauterine foetal death presents unique challenges due to the risk of coagulation abnormalities, differences in the gestational age of foetuses and the additional emotional burden for parents and staff. A 2019 survey reports that 17% of responding UK units would offer remifentanyl in cases of intrauterine death.¹⁸ Two case reports^{19,20} describe cardiorespiratory and respiratory arrest in women receiving remifentanyl for labour analgesia following intrauterine death at 26 and 31 weeks, respectively. Both case reports include multiple contributory factors, and the role of remifentanyl as the primary causative factor is unclear. However, the common theme of ensuring well tolerated maternal monitoring, continuous midwife presence and avoiding concomitant use of other opioids is emphasised.²¹ In particular, the tendency for a compassionate 'light-touch' approach in such circumstances has previously resulted in a noncontinuous midwife presence in women labouring with remifentanyl following intrauterine death. This has been highlighted as a significant contributing factor to adverse events.

Multiple pregnancy

Lucovnik *et al.*²² included multiple pregnancies in their 9-year retrospective study of national data, which included 244 twins. Results suggest that the use of remifentanyl is well tolerated for providing pain relief in twin births. However, the authors state that their study was underpowered to detect slight differences between the epidural and remifentanyl groups. They suggest a larger sample size is required to corroborate their results. The study by Freeman *et al.*¹⁵ included 24 (5% of the total cases) multiple pregnancies in the remifentanyl arm of their randomised multicentre equivalence trial versus epidural analgesia. There was no difference in subgroup analysis between multiple and singleton pregnancy outcomes studied, and no reference is made to adverse events or safety concerns within the multiples group.

Intrauterine growth restriction and the small for gestational age foetus

In a post hoc analysis of the RAVEL trial, Tabernee Heijtmeyer *et al.*²³ looked at the risk of unplanned caesarean birth due to foetal compromise in those receiving

remifentanil versus epidural analgesia. Epidural analgesia was associated with a higher rate of unplanned caesarean birth compared with remifentanil analgesia. However, regardless of the mode of analgesia, the lowest birth weight quintile was the most strongly predictive factor. The authors discuss the greater incidence of placental dysfunction in smaller foetuses, increasing their susceptibility to hypoxia, which may be related to subclinical maternal hypotension following epidural analgesia. However, they do not discuss presumably similar risks, such as maternal desaturation due to remifentanil analgesia, which has been clearly demonstrated. Further research is urgently needed to address the significant gaps in evidence regarding the safety and efficacy of remifentanil PCA for labour in high-risk maternal and foetal populations.

Safety considerations and monitoring with remifentanil patient-controlled analgesia

Although remifentanil PCA has been used routinely for labour analgesia in many units for several years,^{7,24,25} concerns remain regarding the potential for significant adverse events, both for labouring women and for neonates. The optimal level of monitoring to ensure safety remains an area of debate and research, but there is an emerging consensus, as outlined in recent UK national guidance.¹

Safety comparisons have been made between remifentanil PCA and epidural analgesia^{3,5,7,11,12,15,26–30} and other opioids,^{7,8,28,31} including data on sedation, respiratory depression and incidence of desaturation, as well as an impact on neonatal outcomes.^{3,7,8,15,24,25,27,31,32} Observational data on remifentanil PCA safety outcomes accumulated over longer time scales in units using this technique have been published^{7,24,25,32,33} outlining measures taken to mitigate risk. Although there is some agreement on essential monitoring, the intrinsic safety of remifentanil PCA remains a debated topic.^{12,28–30}

Respiratory depression and desaturation

The risk of respiratory depression and desaturation with remifentanil PCA is undoubtedly the major safety challenge associated with this technique. Hypoxic episodes, which are usually mild and of short duration (less than 16 s), can occur in up to 70% of women when a 20 µg bolus with a 1-min lock out interval is used.³² There have been case reports of significant maternal adverse events, including respiratory and cardiac arrest,^{19,20} although contributory factors other than remifentanil have been highlighted in these cases.²¹ These case reports reinforce the need for robust monitoring for respiratory depression when using remifentanil PCA. Although desaturation can occur with other parenteral opioids in labour, there is evidence that the incidence is greater with remifentanil PCA.⁸

Monitoring for respiratory depression has traditionally included continuous pulse oximetry and data on this are included in almost all studies. Even allowing for varying thresholds defining hypoxia in the published

research, it is generally accepted that remifentanil PCA in labour is associated with an increased incidence of desaturation compared with epidural analgesia^{3,5,11,12,15,26,27} or other opioids^{8,17} with an odds ratio relative to neuraxial analgesia quoted as between 2.8 and 7.0.^{26,27} Simple interventions, such as the application of oxygen, adjusting the remifentanil bolus dose and verbal stimulation, have been shown to be effective in managing and preventing further adverse events.

Despite its limitations, continuous SpO₂ monitoring during remifentanil PCA use is accepted as best practice and is clearly emphasised in recent UK guidance from NICE.³¹ Even with SpO₂ monitoring in place, periods of apnoea can go undetected. Many apnoeic episodes during remifentanil PCA use are not associated with desaturation.^{12,30,32,33} Stocki *et al.*¹² reported that SpO₂ remained more than 94% in 59% of apnoea events and Weiniger *et al.*³⁰ found that SpO₂ alone detected fewer than 15% of apnoea episodes. In one randomised controlled trial, short episodes of apnoea were noted within the first hour of starting the remifentanil PCA in 24% of patients.¹² All apnoeas resolved spontaneously or with simple measures, such as verbal stimuli. No patient required resuscitation.

The addition of capnography to improve apnoea detection has been considered or used in some studies.^{7,12,30,33} However, there are issues with its application in the labour setting, due to tolerability for the women and the practicality of using both oral and nasal sampling.^{12,33} Messmer *et al.*³³ concluded that although it was acceptable to labouring women, ‘nasal capnography alone may be a poor monitor of apnoea in this setting’. Even when capnography is well applied, reliability remains an issue, as almost 25% of apnoea episodes are missed and almost two-thirds of alarms were false positives.³⁰ Direct observation of respiratory rate with an appropriate alert trigger has the highest predictive value for detection of apnoea³⁰ reinforcing one-to-one care as essential for patient safety. Monitoring of respiratory rate by the continuous presence of a health professional trained in the use of remifentanil PCA, and able to apply the simple interventions needed to correct apnoea,²⁶ appears to be an essential safety feature of its use.

The role of supplemental oxygen with remifentanil patient-controlled analgesia

In most studies, supplemental oxygen during remifentanil PCA was administered only when required^{7,8,11,15,24,31,32,34} and, once initiated, was typically maintained until remifentanil PCA was discontinued. A minority of studies applied supplemental oxygen from the start of remifentanil PCA use, even without respiratory depression or hypoxia.^{12,30} However, continuous oxygen use did not prevent hypoxic episodes.¹²

Although supplemental oxygen can reduce the frequency of hypoxic events, it does not significantly alter their

severity or duration.³² Moreover, apnoeic episodes may still occur despite oxygen supplementation.¹² Prompt interventions, such as verbal commands or physical stimulation, are often effective in resolving hypoxia and apnoea or bradypnoea.

The routine continuous administration of supplemental oxygen from the start of remifentanyl PCA, in the absence of hypoxia, carries potential risks, including oxidative stress to both the mother and foetus. Studies have highlighted the potential for maternal and foetal harm due to increased oxidative stress when unnecessarily high oxygen concentrations are used.^{35,36} These studies emphasise the importance of judicious oxygen use, striking a balance between its benefits in treating hypoxia and its potential risks.

The threshold for initiating supplemental oxygen typically lies between SpO₂ less than 92% and less than 95% in the majority of studies. Older studies generally employed lower thresholds, but two large retrospective studies spanning 10 and 6 years, respectively, reported a shift, around 2014, towards higher SpO₂ trigger levels of 94 or 95%.^{7,24} Many protocols published after 2014 reflect this change, specifying thresholds of either 94%^{8,24,31,32} or 95%.^{7,11}

In most published protocols, hypoxia is corrected using nasal oxygen at a flow rate of 2 to 3 l min⁻¹,^{7,8,11,24,32} whilst face masks are used less frequently. Supplemental oxygen effectively restores SpO₂ levels^{7,8} and is considered a standard component of most remifentanyl PCA protocols.

Some protocols also define criteria for addressing severe respiratory depression, including bradypnoea, apnoea or significant hypoxia. In such cases, remifentanyl PCA is immediately stopped and a physician is called. Specific criteria include a respiratory rate less than 8 to 9 breaths min⁻¹ or SpO₂ less than 92% without supplemental oxygen, or SpO₂ less than 94 or 95% despite oxygen supplementation.^{7,8,11,24} Once vital parameters normalise, remifentanyl PCA could be restarted at a reduced bolus dose.^{11,24}

The use of supplementary nitrous oxide in oxygen (Entonox) alongside remifentanyl PCA varies considerably across studies. In cases where nitrous oxide was permitted,^{7,32} the same standards of monitoring were applied, regardless of its use. Where explicit data were reported, there was no significant difference in the frequency or severity of desaturation episodes between those who used nitrous oxide and those who did not.³² A large 10-year study, in which nitrous oxide was routinely available with remifentanyl PCA, reported that excessive sedation and desaturation (when treated with supplemental oxygen, if required) were rare events.⁷

Neonatal outcomes

A wealth of reassuring data supports the safety of remifentanyl PCA for neonatal outcomes. Many studies have

assessed neonatal parameters, including Apgar scores at 5 min, the need for resuscitation and neonatal unit admission rates, comparing remifentanyl PCA with epidural analgesia^{3,5,7,15,27} or other parenteral opioids.^{8,31} These studies consistently show no significant differences in neonatal outcomes across these analgesic methods.

In a large UK study comparing remifentanyl PCA with intramuscular pethidine, Wilson *et al.*⁸ found a significantly lower rate of intervention for foetal distress or cardiotocography (CTG) abnormalities with remifentanyl PCA. Similarly, the most recent Cochrane review by Weibel *et al.*⁵ confirmed that remifentanyl PCA does not increase the risk of foetal heart rate abnormalities compared with epidural analgesia and shows a lower risk compared with other opioids.

Further support for the safety of remifentanyl PCA comes from an extensive retrospective multicentre survey,²⁵ which reported an incidence of adverse neonatal events related to remifentanyl PCA of only 0.3% over 10 years. Prospective data from the international RemiPCA SAFE Network also demonstrated an incidence of neonatal resuscitation or ventilation of 1.4%, with serious neonatal adverse events potentially related to remifentanyl reported in just 0.3% of cases.²⁴

To minimise residual remifentanyl in neonates, stopping remifentanyl PCA approximately 10 min (equivalent to 2 to 3 drug half-lives) before birth has been suggested. A large multicentre audit showed that changing clinical instructions to stop remifentanyl 5 to 10 min before delivery reduced the need for neonatal supplemental oxygen from 11.1 to 5.2%.²⁴ Overall, neonatal effects were uncommon and transient, and must be balanced against the ethics of withholding maternal analgesia around the time of birth. There is also a practical consideration of accurately predicting an interval of 5 to 10 min before birth.

Given this strong evidence base supporting neonatal safety with remifentanyl PCA, many units routinely using the technique do not mandate continuous CTG monitoring without other risk factors. This approach aligns with the most recent UK NICE guidance, published in 2023.¹

Optimal delivery of remifentanyl patient-controlled analgesia for labour analgesia

Several systematic reviews, with or without meta-analyses, have evaluated the efficacy of remifentanyl PCA when compared with epidural analgesia,^{3,12,26,27,37,38} parenteral opioids^{4,39} or alternative analgesia techniques.^{5,40,41} These reviews have not compared the efficacy of different combinations of remifentanyl PCA bolus dose or background infusion. Twenty-four randomised studies, 11 retrospective studies and eight prospective studies, were identified and various regimens were described. There was only one dose-finding study.⁴² Most of these studies had relatively small sample sizes.

As a drug with rapid onset and offset, the bolus dose, drug concentration, bolus duration and lockout period are important in determining the efficacy of remifentanil.

Lockout period

The shortest lockout period reported was 1 min^{43–45} and the longest, 5 min.¹⁴ In some reported protocols, the lockout period could be adjusted according to patient comfort or side effects.^{12,45,46} The most commonly reported lockout period was 2 min, in 21 publications.^{7,8,11,17,19,20,22,34,45,47–58} This includes the most extensive population reported to date, the RemiPCA SAFE Network.²⁴

Bolus dose

The bolus may be set in a number of different ways: as a single fixed dose for all,^{7,8,13,17,19,20,34,50,51,53,54,59–62} as a single fixed dose adjusted for weight^{14,17,43,46,49,63,64} or as a range of incremental fixed doses, adjusted for weight.^{11,42,44,48,52,55–57,65–69}

The inconsistent expression of the units of bolus delivery, adds complexity when attempting to compare regimes between studies. Common notations include μg , $\mu\text{g h}^{-1}$, $\mu\text{g kg}^{-1}$ and $\mu\text{g kg}^{-1} \text{h}^{-1}$. A universal notation would enhance comparative clarity between different regimens.

Weight-based algorithms rarely specify whether lean or actual body weight was used, or the gestation a patient's weight was recorded. Buehner *et al.*⁴⁷ recommend using the lower value of either ideal body weight or prepregnancy weight when determining bolus dose. Three further studies^{57,69,70} advocate using lean body weight, whilst Frauenfelder *et al.*⁶⁸ suggest using prepregnancy weight.

In the only identified dose-finding study, a bolus dose of $0.2 \mu\text{g kg}^{-1}$ was incrementally increased by $0.2 \mu\text{g kg}^{-1}$ during a 60-min study period. Boluses were administered over 1 min, with a 1-min lockout period.⁴² The reported median effective dose was $0.4 \mu\text{g kg}^{-1}$, although individual variability was substantial, ranging from 0.2 to $0.8 \mu\text{g kg}^{-1}$. In a 70 kg woman, this would equate to between a 14 and 56 μg bolus dose, with a median effective dose of 28 μg . These results should be interpreted in light of the bolus duration, which at 1 min, is longer than is reported in other studies.

Several criteria must be considered when determining the optimal bolus dose of remifentanil PCA, including its effect on maternal satisfaction scores, pain relief and minimising maternal and neonatal side effects. Notably, factors such as patient expectations, caregiver support, the quality of the caregiver-patient relationship and involvement in decision-making have been shown to have a more significant impact on maternal satisfaction during labour than pain scores alone. A simple reduction in pain scores does not necessarily correlate with

improved maternal satisfaction.⁴⁵ Finally, using pain scores as the sole determinant for the ideal bolus dose may also be complicated by confounding factors, including parity, the stage of labour and individual perceptions of labour pain.⁴²

Maternal side effects of remifentanil PCA, including sedation and respiratory depression, tend to increase with larger bolus doses. However, individual variability is significant. Some women may experience side effects at very low doses, while others remain unaffected even at higher doses.^{11,32,44,57,69} Neonatal side effects are also a consideration, as the timing of discontinuing remifentanil PCA in relation to the time of birth affects neonatal exposure. Reported effects include foetal heart rate changes, reductions in Apgar scores, the need for respiratory support and hypotension during the first hour of life.⁶⁴ However, these side effects are predominantly limited and quickly reversible, and studies reporting neonatal outcomes cannot be reliably used to determine the ideal bolus dose.

Personalised regimens

Dosing regimens which are weight specific and offer stepwise increments in bolus dose, based on the analgesic requirement and limited by side effects, seem optimal. Tveit *et al.*⁶⁹ provide one example of such a regimen that uses a combination of assessment of visual analogue scale (VAS), respiratory rate, oxygen saturation, blood pressure, heart rate, sedation score, foetal heart rate and acceptable overall clinical assessment to guide the required bolus dose. However, such regimens are highly demanding, requiring extensive maternal and foetal monitoring as well as close collaboration between midwifery and anaesthetic teams, making them impractical for most labour wards to implement effectively.

Rate of bolus administration

Various remifentanil dilutions have been reported, ranging from 10 to 50 $\mu\text{g ml}^{-1}$. The bolus rates varied from 7 to 560 $\mu\text{g min}^{-1}$. Although the hardware used may limit the rate of bolus delivery, the manufacturer and model of the pumps used were only reported in 26 studies.

Background infusions

Although intermittent bolus dosing of remifentanil does not aim to achieve constant therapeutic plasma concentrations, this can be achieved using continuous background infusions.⁷¹ Ten studies reported use of background infusions.^{6,14,17,52,55,56,68,70,72} Infusion rates were fixed in five studies.^{14,17,56,70,72} In the remaining five, the infusion prescriptions ranged from 0.04 to $0.5 \mu\text{g kg}^{-1} \text{min}^{-1}$ at the upper end⁷⁰ to 0.025 to $0.15 \mu\text{g kg}^{-1} \text{min}^{-1}$ at the lower end.⁶

Only three studies reported direct comparisons of remifentanil protocols rather than comparing remifentanil to alternate analgesics. One study compared an escalating

bolus dose with a constant background infusion versus a constant bolus dose with an escalating background infusion.⁵⁵ The group with the escalating background infusion demonstrated less sedation than the group with escalating bolus doses. Satisfaction and analgesia were similar between the two groups. Two prospective studies compared an escalating bolus dose versus an escalating background infusion.^{56,66} In the study by Shen *et al.*,⁵⁶ an escalating patient-controlled bolus of 0.1 to 0.4 $\mu\text{g kg}^{-1}$ (2-min lockout) resulted in better analgesia and similar placental transfer of the drug, compared with an escalating continuous infusion of 0.05 to 0.2 $\mu\text{g kg}^{-1} \text{ min}^{-1}$. Maternal respiratory depression was similar between groups, as were neonatal Apgar and neurologic and adaptive capacity scores at any time point.^{56,66} In the study by Khooshdeh *et al.*,⁶⁶ an escalating patient-controlled bolus of 0.25 to 0.4 $\mu\text{g kg}^{-1}$ resulted in similar maternal satisfaction and pain scores, with less total remifentanyl infused than in the escalating infusion group who received 0.05 to 0.1 $\mu\text{g kg}^{-1} \text{ min}^{-1}$. There was no difference in maternal sedation or neonatal Apgar scores, but details were incomplete.⁶⁶

Use of remifentanyl patient-controlled analgesia in the second stage of labour

Only five studies specifically reported on the continued use of remifentanyl PCA during second stage of labour.^{6,49,55,56,61} In most studies, the remifentanyl cessation time was either not defined, or remifentanyl was ceased at the end of the first stage of labour. In 2013, the RemiPCA SAFE Network Standard Operating Procedure introduced a recommendation to discontinue the PCA 5 to 10 min before cord clamping (which is arguably difficult to predict).²⁴ The study by Ortiz *et al.*⁶¹ evaluated analgesia in the second stage, comparing remifentanyl PCA, epidural, intravenous pethidine or meptazinol, and controls (receiving paracetamol or scopolamine). They reported that those with epidurals and remifentanyl PCA had prolonged second stages, compared to those using other opioids or nonpharmacological analgesia.⁶¹

Use of remifentanyl patient-controlled analgesia for interventions after birth

A prospective observational study of 215 parturients evaluated the use of remifentanyl PCA, with a continuous infusion, ranging from 0.025 to 0.15 $\mu\text{g kg}^{-1} \text{ min}^{-1}$. One-to-one nursing was maintained throughout and remifentanyl was either discontinued at birth or continued until after perineal repair ($n=11$).⁶ There was no reported requirement for maternal oxygen supplementation.

Most original research on remifentanyl PCA has focused on comparisons with other analgesic techniques and demonstrates substantial variation in bolus doses, lock-out intervals and administration rates. These inconsistencies make it difficult to establish clear evidence-based recommendations; however, valuable insights can be

gained from retrospective studies of large patient populations.

The RemiPCA SAFE Network conducted a retrospective multinational audit involving 5470 patients, assessing safety outcomes related to a standard operating procedure that underwent protocol adjustments during the 6-year reporting period.²⁴ For the latter three years, the recommended bolus dose range was reduced from 20 to 40 μg to 10 to 30 μg , whilst the lock-out interval remained at two minutes. It was also suggested to discontinue the PCA 5 to 10 min before cord clamping. This reduction in bolus dose resulted in reduced analgesic efficacy, but maintained maternal satisfaction, and also a lower incidence of maternal hypoxia. Additionally, discontinuing remifentanyl PCA use before cord clamping was associated with a trend towards fewer neonatal interventions, although the overall incidence of these outcomes remained low. The RemiPCA SAFE Network now reports on outcomes from over 14 000 patients, with contributions from international sites that may employ alternative regimens, which should be considered when interpreting future reports.

Standards of care for women receiving remifentanyl patient-controlled analgesia

Technical and safety requirements for administration of remifentanyl patient-controlled analgesia

It is preferable to run remifentanyl via a dedicated intravenous cannula, with a giving set which includes an antireflux valve to mitigate against inadvertent bolus delivery. This has previously been reported.⁷³ In some circumstances, it may be acceptable to use only a single intravenous cannula. However, in such cases, it is mandatory that the remifentanyl must be the infusion nearest the cannula and there must be an antireflux valve between the remifentanyl outlet and all other infusions

Midwifery care for women receiving remifentanyl patient-controlled analgesia

The NICE guideline on intrapartum care¹ recommends that women in labour should receive one-to-one care, regardless of what pain relief they receive.³¹ However, one-to-one care may not be sufficient as a standard to prevent serious adverse effects. Continuous presence in the room, actively observing the patient who is using remifentanyl PCA, allows early detection of adverse or prodromal symptoms. In case reports, at least one cardiac arrest and one respiratory arrest have been reported whilst the midwife was out of the room.^{19,20}

Information for patients about remifentanyl patient-controlled analgesia for labour analgesia

When discussing pain relief options with women in labour, it is essential to provide clear, balanced and evidence-based information to support informed decision-making. The choice of analgesia is influenced by

factors such as medical and obstetric comorbidities, the stage and progression of labour and, most importantly, the woman's informed preferences.

Remifentanil PCA is an effective analgesic, particularly in the early stages of labour.²⁶ However, its efficacy may diminish during more advanced labour.⁵⁴ Compared with other opioid-based analgesics, such as intramuscular pethidine, remifentanil PCA has been shown to provide superior pain relief.^{4,8,46,62,74} A Cochrane review noted that women using remifentanil PCA reported greater satisfaction with pain relief than those using other opioids, although the overall quality of evidence was limited.³⁹ Studies comparing remifentanil PCA to pethidine PCA and fentanyl PCA found no significant differences in pain scores measured by VAS.^{17,53} Compared with inhalational analgesia using nitrous oxide, remifentanil PCA has demonstrated favourable outcomes.⁴³

Although remifentanil PCA is a valuable option for labour analgesia, neuraxial techniques, particularly epidural analgesia, remain the gold standard for pain relief during labour. Numerous studies and meta-analyses consistently show that epidural analgesia provides superior pain relief across all stages of labour and with various local anaesthetic mixtures.^{15,26,38,39,44,54,67,68,70,75,76} However, one meta-analysis found no significant difference in VAS scores at 2 and 3 h between remifentanil PCA and epidural analgesia.²⁶

When discussing remifentanil PCA, it is important to inform women about its potential side effects, including nausea, vomiting, pruritus, drowsiness, oxygen desaturation and respiratory depression.^{8,12,30,49,56} Serious adverse events due to remifentanil PCA, such as respiratory or cardiac arrest, are exceedingly rare, and early case reports included multiple confounding factors. Nonetheless, this reinforces the importance of close monitoring and clinical vigilance.

Remifentanil readily crosses the placenta and is detectable in umbilical venous blood.^{56,77} Reported neonatal effects are generally minimal and include transient respiratory depression requiring stimulation or supplemental oxygen.^{8,12,25,56}

By providing comprehensive, evidence-based information about remifentanil PCA, healthcare providers can support women in making informed choices about their labour analgesia options while ensuring realistic expectations about its efficacy and potential risks.

Place of birth for women receiving remifentanil patient-controlled analgesia

The well tolerated provision of remifentanil PCA for labour analgesia always requires appropriately trained health professionals and prompt access to medical staff (obstetricians and anaesthetists). Some of the adverse effects of remifentanil PCA use, such as oxygen

desaturation and respiratory depression, may necessitate the administration of supplemental oxygen, naloxone or more advanced measures. These conditions cannot be reliably met in midwifery-led units and are entirely incompatible with use in the home setting. As such, remifentanil PCA should not be offered outside an obstetric unit that has appropriate staffing, monitoring and emergency support.

Follow up after birth for women who received remifentanil patient-controlled analgesia

There is no evidence of significant long-term side effects or consequences after the use of remifentanil PCA for labour. However, good practice would mandate a follow-up process which aims to establish maternal satisfaction with the care received, focusing on effectiveness of pain relief and side effects, such as nausea and vomiting, pruritus and drowsiness. Data will inform and improve departmental policies and protocols.

Minimum training standards for midwives looking after women using remifentanil patient-controlled analgesia

The increasing use of remifentanil PCA for labour analgesia and interdepartmental variations in protocols have highlighted the need for standardised training among midwives or other health professionals caring for labouring women. There are no studies that identify the optimal training package, minimum caseload exposure or the frequency of retraining required.

Comprehensive training should focus on educating midwives and other health professionals caring for labouring women to recognise and manage potential complications, including respiratory depression, sedation and oxygen desaturation. This includes ensuring familiarity with monitoring tools, such as continuous oxygen saturation and respiratory rate, and appropriate responses, including discontinuation of PCA, supplemental oxygen and other interventions. Standardised training protocols and periodic re-training are essential to ensure safe and effective practice.

Remifentanil patient-controlled analgesia in low-income and middle-income settings

All pregnant women should have equitable access to well tolerated and effective analgesia during childbirth. However, the use of remifentanil PCA presents particular challenges in low and middle-income countries (LMIC), where resource constraints, particularly the availability of continuous one-to-one midwifery or nursing care and reliable monitoring, may make its use impractical or unsafe. In most LMIC settings, these limitations effectively preclude the well tolerated use of remifentanil PCA. Where remifentanil PCA is being considered in such contexts, it is essential that all core safety standards outlined in this guideline are strictly adhered to, including continuous monitoring, immediate access to

resuscitation equipment and the presence of trained staff able to provide one-to-one care throughout administration.

Discussion

The use of remifentanyl PCA for labour analgesia is becoming increasingly popular, not only in situations where neuraxial techniques are contraindicated but also as the preferred mode of analgesia by maternal request. Despite this, formal guidance on the optimal use of remifentanyl PCA has been notably absent from the literature. Variability in protocols, including dosing, monitoring and management of side effects, coupled with limited evidence on safety, has contributed to inconsistencies in its application across clinical settings. The 7th National Audit Project,⁷⁸ which found that only 50% of UK obstetric units offered remifentanyl PCA for labour analgesia, highlights the inconsistency in its availability. This lack of standardisation compromises maternal choice and quality of care.

In response to these challenges, the Obstetric Anaesthetists' Association convened a working party to review the evidence and develop practical, evidence-based guidance on the use of remifentanyl PCA for labour analgesia. By incorporating the latest evidence and expert consensus, the working party sought to produce guidelines that are not only clinically relevant but also practical and implementable in real-world settings.

Although the guidance provides a strong foundation for the well tolerated use of remifentanyl PCA, it also highlights significant gaps in the evidence base, particularly regarding safety outcomes. The authors advocate further research, including large-scale observational studies and randomised controlled trials, to address these gaps and refine future guidance. Specific focus for research should be on the application and safety of PCA remifentanyl in parturients with comorbidity, including those living with obesity, cardiac disease or pre-eclampsia. Similar questions around remifentanyl PCA use in cases of intrauterine death, early gestations, intrauterine growth restriction and multiple pregnancies, must be addressed with equal importance. In general, there is under-representation across the available literature in all high-risk maternal and foetal groups.

The evidence supporting this guidance is limited, mainly due to the relatively small number of studies available, many of which rely on retrospective and observational designs. Few well designed randomised controlled trials have been conducted, and the patient populations included in these studies are often limited in size. This paucity of high-quality evidence meant that some of the Recommendations and Statements were inevitably influenced by reaching a consensus of authors' expert opinion.

There were some particular areas of focused discussion in preparing this guideline.

Many hospital guidelines, including the RemiPCA SAFE Network, advocate a minimum period of 4 h between previous opioid administration and initiation of remifentanyl PCA, to mitigate potentially exaggerated adverse effects of remifentanyl, in the presence of other systemic opioids. Our recommendations marginally soften this position, but only where there is careful consideration of individual risks and benefits. Examples may include a parturient with failed epidural analgesia (including low-dose epidural fentanyl), who is in severe pain and distress where it seems counter-intuitive to withhold effective analgesia for a somewhat arbitrary 4-h period. However, the principle of a 4-h opioid-free window remains as a fundamental starting point.

All authors subscribed to the principle of a single dedicated cannula, and several viewed this as an absolute. However, it was recognised that in certain situations, it may be acceptable to use a nondedicated cannula, as long as remifentanyl is the infusion nearest the cannula and there is an antireflux valve between the remifentanyl outlet and all other intravenous infusions. Examples may include a parturient with extremely difficult venous access or severe needle phobia.

A limited amount of evidence has suggested that discontinuation of remifentanyl (e.g. 5 to 10 min before cord clamping) may reduce opioid-related adverse effects in the neonate. This approach was discussed but rejected by a consensus of authors. First, timing of discontinuation would be very difficult to predict, potentially leaving parturients without analgesia for a prolonged period. Second, there is an ethical concern about providing an analgesic modality which will be knowingly withdrawn, arguably, at the moment it is most needed. Such evidence as exists was not deemed robust enough to supersede these concerns.

There is precedent in some units for continuing remifentanyl PCA following birth, for example during perineal repairs. The authors' consensus was that this was an unwarranted extension of the primary indication for labour analgesia, and it was neither an appropriate analgesic, nor a well tolerated use of remifentanyl in this context. It cannot be assumed, following the cessation of labour pain, that the patient's response to remifentanyl will remain within previously well tolerated parameters. Authors did however feel that remifentanyl PCA may be used for the perineal infiltration of local anaesthetic, but must then be discontinued. If remifentanyl has already been discontinued, it should not be re-started for this purpose. Monitoring and one-to-one supervision must be maintained, and the operator cannot also supervise the patient.

The primary aim of this guideline is to provide clear recommendations to improve safety, enhance the quality of care and standardise practice. This guidance offers a comprehensive set of best practices with international relevance.

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AM: Founder and operator of the RemiPCA SAFE Network (nonprofit organisation).

YM: Executive Editor of Anaesthesia Reports and IJOA Editorial Board member.

PA: Involved with Ariste Health in the design of their disposable remifentanyl PCA pump. Has received fees from Ariste Health for lecturing.

MvdV Has received fees for lecturing and advise in the last three years from CSL Behring, CSL Vifor, CAF-CDF, Viatrix, Aquettant, Aspen and BBraun.

NL: President of the OAA and editor for IJOA.

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