



RESEARCH ARTICLE

Neuraxial opioids as analgesia in labour and postoperative after caesarean section and hysterectomy: A questionnaire survey in Sweden [version 1; referees: 1 approved, 1 approved with reservations]

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Abstract

Background: Neuraxial opioids improve labour analgesia and analgesia after caesarean section (CS) and hysterectomy. Undesirable side effects and difficulties in arranging postoperative monitoring might influence the use of these opioids. The aim of the present survey was to assess the use of intrathecal and epidural morphine in gynaecology and obstetrics in Sweden. **Methods:** A questionnaire was sent to 47 anaesthesiologists at obstetric units in Sweden concerning the use and postoperative monitoring of morphine, sufentanil and fentanyl in spinal/epidural anaesthesia. **Results:** A total of 32 units responded representing 83% of annual CS in Sweden. In CS spinal anaesthesia, 20/32 units use intrathecal morphine, the most common dose of which was 100 µg (17/21). Intrathecal fentanyl (10-20 µg) was used by 21 units and sufentanil (2.5 -10 µg) by 9/32 of the responding units. In CS epidural anaesthesia, epidural fentanyl (50-100 µg) or sufentanil (5-25 µg) were commonly used (25/32), and 12/32 clinics used epidural morphine, the majority of units used a 2 mg dose. Intrathecal morphine for hysterectomy was used by 20/30 units, with 200 µg as the most common dose (9/32). Postoperative monitoring was organized in adherence to the National Guidelines; the patient is in postoperative care or an obstetrical ward over 2-6 hours and up-to 12 hours in an ordinary surgical ward. Risk of respiratory depression/difficult to monitor was a reason for not using intrathecal opioids. **Conclusions:** Neuraxial morphine is used widely in Sweden in CS and hysterectomy, but is still restricted in some units because of the concern for respiratory depression and difficulties in monitoring.

Open Peer Review

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1 Jakob Walldén , Umeå University Sweden, Johan Styrke , Umeå University Sweden		
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Introduction

Intrathecal and epidural morphine improve postoperative analgesia after caesarean section (CS) and hysterectomy and intrathecal labour analgesia^{1–3}. In 1981, the Swedish Society of Anaesthetists conducted a nationwide survey of experience with intrathecal and extradural opiates⁴. They found intrathecal morphine was administered to only 90–150 patients and ventilatory depression requiring treatment with naloxone was needed in six of these patients. Since then, the use of intrathecal and epidural morphine has expanded, with a decrease in the doses used⁵. Still, the use of intrathecal and epidural morphine in these patient categories vary and the general use in Sweden at present is unknown. Spinal morphine may have undesirable side effects, such as nausea and vomiting, with the most feared side effect being respiratory depression, which is why extended postoperative monitoring is required⁶. Extended postoperative monitoring demands personal resources and is sometimes difficult to arrange, which may influence the use of spinal morphine.

The aim of the present questionnaire survey was to assess the use of intrathecal and epidural opioids in obstetric and gynaecological patients, factors that limit/holdback its use and monitoring routines implemented for patients treated with opioids.

Methods

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical committee approval was not applied for the present study, since the survey concerns only clinical practice and routines and not patient data in accordance to Swedish ethical board guidelines. The permission to carry out the research was obtained from the head of department of each hospital.

Survey participants

A questionnaire survey was sent to anaesthesiologists in charge of Swedish obstetric anaesthesia. In all, 47 obstetric units were identified by the Swedish Medical Birth Register from National Board of Health and Welfare (Sweden).

We identified the anaesthesiologist in charge of the obstetric and gynaecological anaesthesia for each unit by address lists used by Swedish Association of Obstetric Anaesthesia and Intensive Care, and if these were not present the hospital was phoned to get hold of the anaesthesiologist in charge.

Survey questionnaire

The survey consisted of 26 questions sent by mail to the anaesthesiologists identified in December 2014, and this was repeated in April 2015 to those clinics that had not answered the first questionnaire. The second time the same questionnaire was sent by email and by post, including a return envelope. The email included a letter to the anaesthesiologist and the survey in two versions. The first version was a Word document, possible to fill in by the computer, save and return by email to a special email address for the study purpose only. The second version was a PDF-file that could be printed and filled in by hand and send by post to our hospital address.

The questionnaire ([Supplementary File 1](#) and [Supplementary File 2](#)) was produced to reflect how common the use of intrathecal

and epidural morphine, fentanyl and sufentanil as adjunct to local anaesthetics for perioperative care of CS and hysterectomy is, and also the routine use of intrathecal morphine for labour analgesia. The anaesthesiologists were asked to approximate the numbers of CS and hysterectomies performed in spinal and epidural anaesthesia, respectively, and specify the numbers of patients administered with opioids, including neuraxial morphine, for the operations performed. We also asked for doses when spinal/epidural opioids are used. When spinal/epidural morphine is marked “not used” we asked for the reasons behind withholding it. Both multiple choice and written answers were collected. Questions about the organisation of monitoring after neuroaxial morphine administration, and known serious adverse events that had occurred in their units were also included.

We calculated the size of the different units by using annual total number of performed CS in the units, in order to put our findings, with regards to the routine use of opioids, into perspective. The annual numbers are collected from The Swedish Medical Birth Register from National Board of Health and Welfare (Sweden).

Statistical analysis

Data is presented as number and percentage, and range as applicable. No formal statistical tests are used.

Results

Responding clinics

In total, 32 units of 47 mailed returned questionnaires (68% response rate). Units with a large number of births and CS were more willing to respond.

Caesarean sections (CS)

The routine use of intrathecal opioids in CS is shown in [Table 1](#). All responding units use at least one opioid as adjunct to local anaesthesia in CS.

Intrathecal morphine. A total of 20 out of 32 units reported the use of intrathecal morphine as routine in CS spinal analgesia. Three units that did not use intrathecal morphine for CS patients commented that they intended to start using intrathecal morphine within the next year.

For CS the most common intrathecal morphine dose is 100 µg, which is used in 17/20 units and three units use 125 µg. All, except for two units, use morphine in combination with either fentanyl or sufentanil. One of these units reported that they plan to start the addition of fentanyl.

Intrathecal fentanyl. Addition of fentanyl in intrathecal CS anaesthesia is used in 21/32 units; five units use fentanyl, but no morphine. In total, 18 units use 10–12.5 microgram dose and three units use a 15–20 µg dose.

Intrathecal sufentanil. The addition of sufentanil in intrathecal CS anaesthesia was less commonly used; 9/32 units, where seven units use sufentanil as the sole opioid added. Four units use a 2.5 µg dose, four units use a 5 µg dose and one unit use a 5–10 µg dose of sufentanil.

Table 1. Neuroaxial opioids in caesarean section. IT, intrathecal; EDA, epidural; Mo, morphine; F, fentanyl; S, sufentanil.

		IT Mo					IT F			IT S		EDA Mo		EDA F	EDA S	
	Response rate	Intrathecal Morphine	Intrathecal Morphine dose 100/125microgram	Intrathecal Morphine + fentanyl	Intrathecal Morphine + sufentanil	Intrathecal morphine but no IT fentanyl/sufentanil	Intrathecal fentanyl	Intrathecal fentanyl dose 10–14/15–20 microgram	Intrathecal fentanyl but no IT morphine	Intrathecal sufentanil	Intrathecal sufentanil dose 2.5/5/5–10 microgram	Intrathecal sufentanil but no IT morphine	Epidural morphine	Epidural morphine dose 1/2/4 mg	Epidural fentanyl 50–100 microgram	Epidural sufentanil
Units N	32/47	20	17/3	16	2	2	21	18/3	5	9	4/4/1	7	12	1/10/1	10	15

Thus, 16 units use the combination morphine/fentanyl, two used the combination morphine/sufentanil and two solely use morphine, five solely use fentanyl and seven solely use sufentanil.

Epidural morphine. Addition of epidural morphine to CS performed in epidural anaesthesia was less common than intrathecal morphine in spinal anaesthesia: 12/32 units add morphine to the epidural local anaesthesia. The majority, 10 units, administer 2 mg dose of morphine, one unit 1 mg and one unit use a 4 mg dose of morphine.

Epidural fentanyl. Ten units add fentanyl (50–100 µg) in the epidural for CS anaesthesia.

Epidural sufentanil. In total, 15 units use sufentanil as the fast opioid in the epidural anaesthesia for CS anaesthesia, where 11 use doses up to 10 µg, three administer doses up to 25 µg, and one use a 25–50 µg dose.

Labour analgesia. None of the units use morphine in spinal labour analgesia.

Hysterectomy

Intrathecal morphine. Spinal anaesthesia with morphine added is used in 20 of the 32 answering units in hysterectomy. The most common dose is 200 µg administered by nine clinics, five clinics use 120–140 µg, five use 100 µg and one unit administers 80 µg.

In other types of gynaecological operations, like perineoraphies, malign robot surgery, all gynaecological abdominal surgery seven of 32 clinics use intrathecal morphine. One of 32 clinics used epidural morphine, for malign gynaecological surgery.

Postoperative monitoring. Postoperative monitoring is generally organised within the initial 2–6 hours in the postoperative ward and the following hours, up to 12 hours, in the regular surgical ward, according to the guidelines of SFAI – Swedish Association of Anaesthesia and Intensive Care. In case of CS the initial 2–6 hours of postoperative monitoring are located to either the postoperative ward or obstetrical ward (as it was in eight hospitals as routine

and in some hospitals occasionally) and the following hours, up to 12 hours, in the regular ward.

Seven of the eleven units that chose not to use spinal/epidural morphine describe risk of respiratory depression and difficulties to monitor as the main reasons for withholding its use.

Dataset 1. Raw data for IT and EDA opioid survey

<http://dx.doi.org/10.5256/f1000research.10705.d151418>

IT, intrathecal; EDA, epidural; MO, morphine.

Discussion

We found that all units used opioid supplementation and two thirds of responding units of Swedish obstetric anaesthesia used spinal/epidural morphine as adjunct to local anaesthesia for perioperative care of CS and hysterectomies. Spinal use was rather uniform with 100 µg for CS and up to 200 µg for hysterectomies of intrathecal morphine combined with a low dose of fentanyl or sufentanil. Epidural morphine was used to a lesser extent. Opioids were also commonly added to labour analgesia as sufentanil, but no unit uses morphine as an adjunct in labour analgesia. The common reason for withholding spinal/epidural opioid was the risk for respiratory depression, and thus the demands for post procedural monitoring.

There were some obvious differences in practice in the different units. Winther *et al.* found likewise inconsistencies in clinical guidelines for obstetric anaesthesia for CS⁷. The most effective method for providing pain relief during labour is epidural analgesia and there are good opportunities to get a beneficial epidural in Sweden⁸. In countries with limited resources, a single shot spinal anaesthesia may be a feasible option. Combination of low dose morphine, fentanyl and bupivacaine or morphine, sufentanil and bupivacaine are suggested to achieve effective analgesia with a prolonged effect⁹. However, we were previously unable to find a major advantage of the addition of morphine, when comparing 0, 50 or 100 µg morphine added to 1.25 mg bupivacaine and 5 µg sufentanil during established labour, as this did not show a significant

increased duration of analgesia¹⁰. Morphine is not a preferred drug for labour epidural analgesia and questions about the addition of opioids other than morphine to labour epidurals were not included in this survey. Adding sufentanil or fentanyl is common practice, and may be seen more or less as the gold standard^{11,12}. Sufentanil is the most common opioid added in labour anaesthesia in Sweden, which was reported in a national obstetric anaesthesia meeting from a survey in 2009 (not published).

Spinal anaesthesia is the preferred analgesia in CS when a working epidural is not in place for conversion and top-up. Long acting spinal opioids as a component of the CS spinal anaesthesia has been proven superior as the post-caesarean analgesia over systemic counterparts, and made them a commonly used part of multimodal analgesic regimes¹³. In Sweden, the long acting opioid most commonly used in CS is morphine, and we found that 63% of units used intrathecal morphine as routine in CS spinal analgesia. Since larger units with higher numbers of CS more commonly use intrathecal morphine, the impact of the routine is even more pronounced. The units using intrathecal morphine as routine adjunct to local anaesthesia in CS, covered an estimated 73% of all CS annually performed in responding units. All responding units used intrathecal morphine doses of 100–125 µg. Palmer *et al.* found in a dose response study that morphine at 100 µg added to hyperbaric bupivacaine (12.75 mg) provided analgesia comparable to that provided by doses as high as 500 µg¹. The optimal effective dose for CS is not well defined. The balance between analgesia and side effects must be taken into account. The occurrence of pruritus, has been found to be dose related^{1,6,14}. For nausea and vomiting the relationship is not that clear but nausea and vomiting is seen in a higher frequency in higher doses than in lower dose groups¹⁴.

Intrathecal morphine is suggested to provide better pain control after CS than opioid-free epidural analgesia¹⁵. Intrathecal morphine has also been shown superior regarding postoperative pain relief, as compared to abdominal wall block (TAP)¹³. The more lipophilic diamorphine was the most commonly used opioid in a survey conducted in the UK in 2008⁵. Diamorphine has a more rapid onset of action than morphine because of a high lipophilicity (octanol-water coefficient =280)¹⁶. Diamorphine is metabolised to morphine with long-acting activity; however, diamorphine is not registered/available as pharmaceutical drug in Sweden¹⁶. Fentanyl and sufentanil are the available lipid-soluble opioids used, which have a quick onset for improved perioperative spinal and epidural analgesia¹⁷. A combination of one lipid-soluble opioid and the long-acting water-soluble morphine is added to hyperbaric bupivacaine, which is found to be commonly used in Sweden. It is an attractive combination providing a quick onset with improved perioperative quality and a long-acting postoperative analgesia¹⁶. Yet currently, the present study found that twelve units use solely fast opioid adjuncts to local anaesthesia and two of the units add morphine to local anaesthetics with no addition of fentanyl or sufentanil, but one of the units stated they plan to start adding fentanyl shortly.

When a functional labour epidural is in place, it's recommended to convert this to a full epidural anaesthesia if an emergency CS becomes necessary¹⁸. Twelve of the 32 units add morphine to the epidural local anaesthesia, the most common dose is 2 mg. Singh *et al.* found epidural morphine at 1.5 mg provided none-inferior

post caesarean analgesia and caused fewer adverse effects compared with 3 mg epidural morphine¹⁹. Still the majority of responding units chose not to add morphine in epidural analgesia for CS postoperative analgesia. The addition of sufentanil (15 units) or fentanyl (9 units) was more common, together covering 74% of CS performed annually in responding clinics. Malhotra *et al.* found no support for adding 75 µg fentanyl in top-up epidural for CS regarding time to onset nor quality of analgesia in women already receiving epidural fentanyl during labour²⁰. Yet, the addition of epidural opioids has been proven to enhance postoperative analgesia after CS with earlier onset^{21,22}.

The addition of morphine intrathecal or epidural as adjunct for intra as well as postoperative pain relief is also regarded by many as the 'gold-standard', due to its positive analgesic interaction with local anaesthetics and prolonged duration of action⁶. Spinal anaesthesia with added morphine was used in 63% of responding units for hysterectomy perioperative analgesia. The most common dose used was 200 µg, which is the well in line with the optimal dose found in a study of the three doses (100 µg, 200 µg and 300 µg) versus placebo in abdominal hysterectomy². Intrathecal morphine use in hysterectomy varied regarding type of surgical technique: five units chose to use intrathecal morphine in abdominal, vaginal and laparoscopic hysterectomies, while seven units use intrathecal morphine in abdominal and vaginal, but not in laparoscopic, hysterectomy.

All responding units had guidelines regarding postoperative monitoring after neuroaxial opioids. The routine of dividing the postoperative monitoring between a more monitoring intensive postoperative ward for the first 2–6 hours and a regular surgical ward for the following hours, up to 12 hours, according to the guidelines of SFAI, was common, and was found to be already routine in a European survey in 1996 by Rawal *et al.*²³. In eight units, CS were initially monitored for 2–6 hours in the obstetrical ward. Two units using intrathecal morphine for CS monitored post-operatively only in a regular maternity ward for the whole period. Seven of the eleven units that chose not to use spinal/epidural morphine describe a risk of respiratory depression and difficulties to monitor postoperatively as the main reason for withholding its use. In these units, which do not use morphine because of risk for respiratory depression and difficulties in postoperative monitoring, approximately 15% of CS reported are performed.

Respiratory depression is the most serious side effect associated with neuroaxial morphine; however, its occurrence is rare⁶. In 2010, the subject "All patients receiving neuraxial morphine should be monitored with continuous pulse oximetry" was debated during Controversies in Obstetric Anesthesia²⁴. It was commented that a requirement for pulse oximetry might decrease the use of neuroaxial morphine as post caesarean analgesia and risk more pain in patients with more parenteral morphine consumed with the risk of increased risk of respiratory depression⁶. We have in our institution some 15 years' experience of approximately 2000 annual CS performed, the majority in spinal anaesthesia using a combination of fentanyl (10 µg), morphine (100 µg) and hyperbaric bupivacaine (10–12 mg). Our routine is an initial 2–3 postoperative hours monitoring in a postoperative ward, and the following hours up to 12 hours in the maternity regular ward with midwife hourly

supervision of level of consciousness and in case of sedated (sleeping) patient monitoring of respiratory rate. In the case of an unstable patient, morbid obesity or known sleep apnoea, the patient stays in the postoperative department for a longer time, determined on an individual basis. In line with responding units in this survey, we have no known experience from severe respiratory depression.

The return rate of the questionnaire was 32/47 units (68%), a figure in line with previous questionnaire survey around anaesthesia practice in conjunction to obstetrics^{25,26}. Taking into account the size of the different units, the response routines cover approximately 82% out of 111,364 annual deliveries, as seen in The Swedish Medical Birth Register (2013), and 83% of CS are performed in responding units. All units performing more than 400 annual CS returned the questionnaire. Our main interest was to find the routine use of morphine in CS, since we learned from anaesthesia meetings with colleges that this routine, regarded as “gold standard” was not in use in several units, due to fear of respiratory depression⁶. We included questions regarding spinal/epidural addition of fentanyl and sufentanil as well, but did not in detail ask for monitoring after these adjuvants when morphine was not included. We asked for numbers of performed CS and hysterectomies, including morphine, for each unit. However, those numbers were not possible to extract from the questionnaire because of few answers. When the majority of anaesthesia units are reporting anaesthesia to the Swedish PeriOperative Register (SPOR), hopefully in the coming years there will be better opportunities to answer questions about common routines and outcomes.

Supplementary material

Supplementary File 1: Questionnaire in Swedish.

[Click here to access the data.](#)

Supplementary File 2: Questionnaire in English.

[Click here to access the data.](#)

Conclusion

The use of neuraxial opioids is widely spread in Sweden; however somewhat varying regimes exists, where some units chose to use only lipophilic opioids with a rapid onset and few use only long-acting water-soluble morphine. However, a majority use a combination together with local anaesthesia. Still in some units the use of morphine is restricted because of the concern for respiratory depression and difficulties in monitoring.

Data availability

Dataset 1: Raw data for IT and EDA opioid survey. IT, intrathecal; EDA, epidural; MO, morphine. doi, [10.5256/f1000research.10705.d151418](https://doi.org/10.5256/f1000research.10705.d151418)²⁷

Author contributions

All authors have contributed equal to the preparation of the paper, preparation and study design, AH has done most of collection of data, all authors under the lead of AH/JGJ have contributed to the writing and preparation of the manuscript.

Competing interests

No competing interests were disclosed.

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References

- Palmer CM, Emerson S, Volgoropolous D, *et al.*: **Dose-response relationship of intrathecal morphine for postcesarean analgesia.** *Anesthesiology*. 1999; **90**(2): 437–44.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Hein A, Rösblad P, Gillis-Haegerstrand C, *et al.*: **Low dose intrathecal morphine effects on post-hysterectomy pain: a randomized placebo-controlled study.** *Acta Anaesthesiol Scand*. 2012; **56**(1): 102–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Yeh HM, Chen LK, Shyu MK, *et al.*: **The addition of morphine prolongs fentanyl-bupivacaine spinal analgesia for the relief of labor pain.** *Anesth Analg*. 2001; **92**(3): 665–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Gustafsson L, Schildt B, Jacobsen K: **Adverse effects of extradural and intrathecal opiates: report of a nationwide survey in Sweden. 1982.** *Br J Anaesth*. 1998; **81**(1): 86–93. discussion 85.
[PubMed Abstract](#)
- Giovannelli M, Bedford N, Aitkenhead A: **Survey of intrathecal opioid usage in the UK.** *Eur J Anaesthesiol*. 2008; **25**(2): 118–22.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Sultan P, Gutierrez MC, Carvalho B: **Neuraxial morphine and respiratory depression: finding the right balance.** *Drugs*. 2011; **71**(14): 1807–1819.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Winther LP, Mitchell AU, Møller AM: **Inconsistencies in clinical guidelines for obstetric anaesthesia for Caesarean section: a comparison of the Danish,**

- English, American, and German guidelines with regard to developmental quality and guideline content. *Acta Anaesthesiol Scand*. 2013; 57(2): 141–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
8. Anim-Somuah M, Smyth RM, Jones L: **Epidural versus non-epidural or no analgesia in labour.** *Cochrane Database Syst Rev*. 2011; (12): CD000331.
[PubMed Abstract](#) | [Publisher Full Text](#)
 9. Al-Kazwini H, Sandven I, Dahl Leiv V, *et al.*: **Prolonging the duration of single-shot intrathecal labour analgesia with morphine: A systematic review.** *Scand J Pain*. 2016; 13: 36–42.
[Publisher Full Text](#)
 10. Hein A, Rösblad P, Norman M, *et al.*: **Addition of low-dose morphine to intrathecal bupivacaine/sufentanil labour analgesia: A randomised controlled study.** *Int J Obstet Anesth*. 2010; 19(4): 384–9.
[PubMed Abstract](#) | [Publisher Full Text](#)
 11. Li B, Wang H, Gao C: **Bupivacaine in combination with fentanyl or sufentanil in epidural/intrathecal analgesia for labor: a meta-analysis.** *J Clin Pharmacol*. 2015; 55(5): 584–91.
[PubMed Abstract](#) | [Publisher Full Text](#)
 12. Wong C: **Epidural and spinal analgesia/Anesthesia for Labor and Vaginal delivery.** In Chestnut D, Wong C, Tsen L, Ngan Kee W, Beilin Y, Mhyre J. *Chestnut's obstetric Anesthesia Principles and Practice*. Fifth edition. Elsevier Saunders. 2014; 457–517.
[Reference Source](#)
 13. Abdallah FW, Halpern SH, Margarido CB: **Transversus abdominis plane block for postoperative analgesia after Caesarean delivery performed under spinal anaesthesia? A systematic review and meta-analysis.** *Br J Anaesth*. 2012; 109(5): 679–87.
[PubMed Abstract](#) | [Publisher Full Text](#)
 14. Sultan P, Halpern SH, Pushpanathan E, *et al.*: **The Effect of Intrathecal Morphine Dose on Outcomes After Elective Cesarean Delivery: A Meta-Analysis.** *Anesth Analg*. 2016; 123(1): 154–64.
[PubMed Abstract](#) | [Publisher Full Text](#)
 15. Suzuki H, Kamiya Y, Fujiwara T, *et al.*: **Intrathecal morphine versus epidural ropivacaine infusion for analgesia after Cesarean section: a retrospective study.** *JA Clinical Reports*. 2015; 1: 3.
[Publisher Full Text](#)
 16. Carvalho B, Butwick A: **Postoperative analgesia: Epidural and spinal techniques.** In: Chestnut D, Wong C, Tsen L, Ngan Kee W, Beilin Y, Mhyre J. *Chestnut's obstetric Anesthesia Principles and Practice*. Fifth edition. Elsevier Saunders, 2014; 621–661.
[Reference Source](#)
 17. Dahlgren G, Hultstrand C, Jakobsson J, *et al.*: **Intrathecal sufentanil, fentanyl, or placebo added to bupivacaine for cesarean section.** *Anesth Analg*. 1997; 85(6): 1288–93.
[PubMed Abstract](#) | [Publisher Full Text](#)
 18. Levy DM: **Emergency Caesarean section: best practice.** *Anaesthesia*. 2006; 61(8): 786–791.
[PubMed Abstract](#) | [Publisher Full Text](#)
 19. Singh SI, Rehou S, Marmai KL, *et al.*: **The efficacy of 2 doses of epidural morphine for postcesarean delivery analgesia: a randomized noninferiority trial.** *Anesth Analg*. 2013; 117(3): 677–85.
[PubMed Abstract](#) | [Publisher Full Text](#)
 20. Malhotra S, Yentis SM: **Extending low-dose epidural analgesia in labour for emergency Caesarean section - a comparison of levobupivacaine with or without fentanyl.** *Anaesthesia*. 2007; 62(7): 667–671.
[PubMed Abstract](#) | [Publisher Full Text](#)
 21. Cohen S, Amar D, Pantuck CB, *et al.*: **Postcesarean delivery epidural patient-controlled analgesia. Fentanyl or sufentanil?** *Anesthesiology*. 1993; 78(3): 486–491.
[PubMed Abstract](#)
 22. Vora KS, Shah VR, Patel B, *et al.*: **Postoperative analgesia with epidural opioids after cesarean section: Comparison of sufentanil, morphine and sufentanil-morphine combination.** *J Anaesthesiol Clin Pharmacol*. 2012; 28(4): 491–495.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 23. Rawal N, Allvin R: **Epidural and intrathecal opioids for postoperative pain management in Europe—a 17-nation questionnaire study of selected hospitals.** *Euro Pain Study Group on Acute Pain. Acta Anaesthesiol Scand*. 1996; 40(9): 1119–1126.
[PubMed Abstract](#) | [Publisher Full Text](#)
 24. D' Angelo R: **All parturients receiving neuraxialmorphine should be monitored with continuous pulse oximetry.** *Int J Obstet Anesth*. 2010; 19(2): 202–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
 25. Kinsella SM, Walton B, Sashidharan R, *et al.*: **Category-1 caesarean section: a survey of anaesthetic and peri-operative management in the UK.** *Anaesthesia*. 2010; 65(4): 362–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 26. Gardner IC, Kinsella SM: **Obstetric epidural test doses: a survey of UK practice.** *Int J Obstet Anesth*. 2005; 14(2): 96–103.
[PubMed Abstract](#) | [Publisher Full Text](#)
 27. Hein A, Gillis-Haegerstrand C, Jakobsson JG: **Dataset 1 in: Neuraxial opioids as analgesia in labour and postoperative after caesarean section and hysterectomy: A questionnaire survey in Sweden.** *F1000Research*. 2017.
[Data Source](#)

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Version 1

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The study of Hein et al. presents results of a nation-wide survey on the use of neuraxial opioids in obstetric and gynecology patients in Sweden. I found especially interesting these parts that were devoted to cesarean section (CS). Multimodal analgesia became a widely used approach to post-CS pain management and the use of intrathecal opioids is one of the important components in this approach. Among intrathecal opioids, low-dose morphine appear to be the most widely recommended¹. However, this hydrophilic opioid has a high frequency of adverse effects² such as nausea and vomiting, pruritus, and potentially serious late respiratory depression³. That's why the question of the current routines related to this topic in Sweden is important in daily life clinical practice.

I think that several things could be corrected to improve quality of the paper.

General comments:

Authors should choose tense in which they present and discuss findings. Personally, I don't like to present tense because, as stated below it can be sometimes misleading. Anyway, consistency is needed. English language could also be improved. There are some awkward expressions such as 'fast opioid' which is not really medical term.

Specific comments:

Title:

The title could be more clear and in better English.

Abstract:

I recommend to maintain consistency regarding the aim of the study, whether it is the use of neuraxial opioids or just morphine.

'the patient is in postoperative care or an obstetrical ward over 2-6 hours and up-to 12 hours in an ordinary surgical ward.' I would add 'is monitored in ...'

Introduction

'Intrathecal and epidural morphine improve postoperative analgesia after caesarean section (CS) and hysterectomy and intrathecal labour analgesia'. Did the authors mean during intrathecal labour

analgesia? This is at least what Yeh et al. had in mind during their study.

Methods:

'A questionnaire survey was sent to anaesthesiologists in charge of Swedish obstetric anaesthesia' I think it sounds a bit strange. Is it not more simple just to write that the questionnaire was sent to the anaesthesiologists in charge of obstetric anaesthesia units in hospitals in Sweden? Furthermore, information about anaesthesiologist is repeated 3 times.

What is 'Swedish Association of Obstetric Anaesthesia and Intensive Care'?

The questionnaire (Supplementary File 1 and Supplementary File 2) was produced to reflect how common the use of intrathecal and epidural morphine, fentanyl and sufentanil as adjunct to local anaesthetics for perioperative care of CS and hysterectomy is, and also the routine use of intrathecal morphine for labour analgesia. I think this sentence could be corrected in underlined parts as it sounds awkward.

'specify the numbers of patients administered with opioids, including neuraxial morphine, for the operations performed' it is not clear if the authors were interested in intrathecal morphine alone or in other intrathecal opioids or, what would be even more interesting what was the combinations of used opioids. It is the same issue what with the aim of the study.

Results

'Epidural sufentanil. In total, 15 units use sufentanil as the fast opioid in the epidural anaesthesia for CS anaesthesia' maybe opioid with rapid onset of action.

50mcg of epidural sufentanil is quite a large dose. I think it should be commented.

It is quite surprising that for hysterectomy and gynecological abdominal surgery opioids are used intrathecally and not with the use of epidural anesthesia. Can the authors comment on that?

'Postoperative monitoring is generally organized within the initial 2–6 hours in the postoperative ward and the following hours, up to 12 hours, in the regular surgical ward, according to the guidelines of SFAI – Swedish Association of Anaesthesia and Intensive Care.' Did you mean this is general routine in Sweden or this was the result of survey? Using present tense in result section is a bit misleading. Also 'in the regular surgical ward, according to the guidelines of SFAI – Swedish Association of Anaesthesia and Intensive Care.' I would change into: ... according to the guidelines of Swedish Association of Anaesthesia and Intensive Care (SFAI).

Postoperative monitoring: The authors write about 9 units of 32 in case of CS, what happened to patients in the rest of 20 units where morphine was used?

'Seven of the eleven units that chose not to use spinal/epidural morphine' Or was it 12/32 units which did not use morphine as in table 1.

Discussion

I think authors should avoid expressions such as 'Swedish obstetric anaesthesia' because such thing do not exist. Use instead obstetric anaesthesia units in Sweden.

'Opioids were also commonly added to labour analgesia as sufentanil,' please change for clarity into:

'Opioids such as sufentanil were also commonly added to labour analgesia...'

'there are good opportunities to get a beneficial epidural in Sweden' what did you mean by 'beneficial'?

The citation should be placed earlier, as Cochrane's review does not say much how these issues occur in Sweden.

'Sufentanil is the most common opioid added in labour anaesthesia in Sweden, which was reported in a national obstetric anaesthesia meeting from a survey in 2009 (not published).' Oral presentations that were not published should not be mentioned or cited in a good quality paper.

'Spinal anaesthesia is the preferred analgesia in CS when a working epidural is not in place for conversion

and top-up.' What do you mean 'conversion'?

'Yet currently, the present study found that twelve units use solely fast opioid adjuncts to local anaesthesia and two of the units add morphine to local anaesthetics with no addition of fentanyl or sufentanil, but one of the units stated they plan to start adding fentanyl shortly.' Last part of the sentence could be omitted; the authors should filter not important information. On the other hand it could be discussed that even though intrathecal lipophilic opioids in CS are not as effective as intrathecal morphine, they still proved to be beneficial during the period of highest analgesic demand after cesarean section⁴.

'Yet, the addition of epidural opioids has been proven to enhance postoperative analgesia after CS with earlier onset' I don't understand this sentence.

Withdrawing from the use of intrathecal morphine could be discussed in context of other large studies that report usage of intrathecal opioids in obstetrics⁵⁻⁷.

Limitation

Usually, at the end of manuscript, authors should state limitations of the study. Some aspects that could be discussed are:

The postoperative monitoring routines are limited to time perspective. There is nothing about what was actually monitored and how often.

Quality of information obtained from the question regarding complications is very low.

References

1. Goma H, Flores-Carrillo J, Whizar-Lugo V: Spinal Additives in Subarachnoid Anaesthesia for Cesarean Section. 2014. [Publisher Full Text](#)
2. Dahl JB, Jeppesen IS, Jørgensen H, Wetterslev J, Møiniche S: Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in patients undergoing cesarean section with spinal anesthesia: a qualitative and quantitative systematic review of randomized controlled trials. *Anesthesiology*. 1999; **91** (6): 1919-27 [PubMed Abstract](#)
3. Abouleish E, Rawal N, Rashad MN: The addition of 0.2 mg subarachnoid morphine to hyperbaric bupivacaine for cesarean delivery: a prospective study of 856 cases. *Reg Anesth*. **16** (3): 137-40 [PubMed Abstract](#)
4. Weigl W, Bierylo A, Wielgus M, Krzemień-Wiczyńska S, Szymusik I, Kolacz M, Dabrowski MJ: Analgesic efficacy of intrathecal fentanyl during the period of highest analgesic demand after cesarean section: A randomized controlled study. *Medicine (Baltimore)*. 2016; **95** (24): e3827 [PubMed Abstract](#) | [Publisher Full Text](#)
5. Orbach-Zinger S, Ioscovich A, Aviram A, Babytz S, Fein S, Reuveni A, Eidelman LA: National survey of postoperative pain control after cesarean delivery. *Isr Med Assoc J*. 2014; **16** (3): 153-6 [PubMed Abstract](#)
6. Jacques V, Vial F, Lerintiu M, Thilly N, Mc Nelis U, Raft J, Bouaziz H: [Enhanced recovery following uncomplicated elective caesarean section in France: a survey of national practice]. *Ann Fr Anesth Reanim*. 2013; **32** (3): 142-8 [PubMed Abstract](#) | [Publisher Full Text](#)
7. Marcus HE, Behrend A, Schier R, Dagtekin O, Teschendorf P, Böttiger BW, Spöhr F: [Anesthesiological management of Caesarean sections : nationwide survey in Germany]. *Anaesthesist*. 2011; **60** (10): 916-28 [PubMed Abstract](#) | [Publisher Full Text](#)

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Competing Interests: No competing interests were disclosed.

Referee Report 27 February 2017

doi:10.5256/f1000research.11542.r20179



Jakob Walldén¹ , **Johan Styrke²**

¹ Anaesthesia and Intensive Care Section, Umeå University, Umeå, Sweden

² Department of Surgical and Perioperative Sciences, Umeå University, Umeå, Sweden

The present study explores the use of opioids in obstetric and gynaecological surgery in Sweden. The authors have done a nice survey among Swedish hospitals covering a majority of the procedures performed. The study is properly designed, the results reported correctly with adequate clinically relevant conclusions. However, some revisions are needed in the manuscript.

Throughout the manuscript please revise the language according to tenses and report the results in “past time”. Please use a consequent numbering format with numbers and letters.

Consider sending the manuscript for language proof reading to improve the quality.

Abstract:

Change “...47 anaesthesiologists at ob. units...” to “... all anaesthetic obstetric unit..”

Introduction:

Line 5: 90-150 of how many??

Methods:

“..26 questions sent by mail...” Please specify postal mail

“...questionnaire was produced to reflect...” Designed or Formulated might be better than Produced

“...no formal statistical tests WERE used.” Please use past form.

Results

Regarding the responding clinics, was it 32 units that responded with postal mail? Or total response rate? Consider deleting the word “mailed”. The results here are not in accordance with the results in the abstract where you state that the units represented 83% of annual CS.

Better formulation may be: “... 32 of 47 (68%) units responded to the questionnaires representing 83 % of annual CS in Sweden...”

Please provide proof that larger units were more willing to respond. Significant?

Please be consequent with the dosing: now both µg and microgram are used.

Section epidural morphine:

Table 1: The table is difficult to view in the current layout.

Suggestion

Number of units

Response rate 32/47**Intrathecal morphine 20**

Standard dose 100 µg	17
Standard dose 125 µg	3
Combined with fentanyl	16
Combined with sufentanil	2

Intrathecal Fentanyl 21

Standard dose 10-14 µg	18
Etc...	

Discussion

Please add "...all responding units used..." to the first sentence.

"...a survey in 2009 (not published)". I "Data on file" might be a better formulation than "not published"

"The addition of sufentanil (15 units) or fentanyl (9units...)" Please reformulate so that it is clear that you mean number of OB/Gyn units and not units of the drugs.

Last paragraph of the Discussion: Move the results to the first part of the results section.

Please also include limitations of the study in the discussion. Were there any pit-falls? Can the results be generalised outside Sweden? The standard care for the units are reported, but is there a variability at the units that has to be discussed?

Consider reducing the length of the discussion.

References

There is a mixed format of the references with special attention to the page numbering. Please adhere to the Index Medicus/Medline format.

Check page number ref 23.

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

Discuss this Article

Version 1

Author Response (Member of the F1000 Faculty and F1000Research Advisory Board Member) 24 Mar 2017

Jan Jakobsson, Department of Physiology and Pharmacology, Karolinska Institutet, Sweden

To **Jakob Walldén**, Anaesthesia and Intensive Care Section, Umeå University, Umeå, Sweden
and **Johan Styrke**, Department of Surgical and Perioperative Sciences, Umeå University, Umeå, Sweden

I am most grateful for your referee comments and that you find our article interesting, properly designed, correctly reported and with clinically relevant conclusions. I agree with your suggested revisions to improve quality of the paper and hope you will find I have corrected accordingly to your comments.

Tense is changed to "past time".

Numbering format is used in abstract and results and in discussion we use letters apart from doses.

Abstract:

Change "...47 anaesthesiologists at ob. units..." to "... all anaesthetic obstetric unit.." *We have changed according to your suggestion.*

Introduction:

Line 5: 90-150 of how many?. *In the reference survey they found intrathecal morphine was administered in total to only 90-150 patients in 10 of 93 responding units.*

Methods:

"..26 questions sent by mail..." is specified e-mail.

"...questionnaire was produced to reflect...." is changed to "Designed" according to your suggestion.

Results

Regarding the responding clinics, was it 32 units that responded with postal mail? Or total response rate? Consider deleting the word "mailed". The results here are not in accordance with the results in the abstract where you state that the units represented 83% of annual CS.

Better formulation may be: "... 32 of 47 (68%) units responded to the questionnaires representing 83 % of annual CS in Sweden..."

We have changed to according to your suggestion

Please provide proof that larger units were more willing to respond. - *We added "Among the 21 units with more than 2000 births/year 19 units responded (90%) versus 12/25 (48%) units with less than 2000 births/year. In units performing more CS than 300/year, 23/28 units responded (82%) versus 9/19 (47%) units with less than 300/ year. In the 15 units performing more than 400 CS/year we got 100% responding."*

We changed to consequently use μg .

Thank you for your fine suggestion to improve Table 1, the table is changed according to your draft

Discussion

"...all responding units used...." Is added to the first sentence.

"...a survey in 2009 (not published)" We changed to your suggested "Data on file"

The addition of sufentanil (15 units) or fentanyl (9 units...)” *We reformulated to clarify fifteen obstetric units, nine obstetric units.*

We included limitations of the study in the discussion according to your suggestion.

References

We changed page numbering according to Index Medicus/Medline format.

Once again thank you for taking your time to referee our article and your suggestions to clarify and improve the quality of the paper.

Best regards

Anette Hein

*MD Department of Anaesthesia & Intensive Care, Danderyds Hospital, Stockholm, 182 88, Sweden
anette.hein@sll.se*

To W Weigl

I am most grateful for your referee comments and that you find our article interesting. I agree with your suggested corrections to improve quality of the paper and hope you will find I have corrected accordingly to your comments.

VIEWS 5

DOI: [10.5256/f1000research.11542.r20178](https://doi.org/10.5256/f1000research.11542.r20178)

READ ALL

The study of Hein *et al.* presents results of a nation-wide survey on the use of neuraxial opioids in obstetric and gynecology patients in Sweden. I found especially interesting these parts that were devoted to cesarean section (CS). Multimodal analgesia became a widely used approach to post-CS pain management and the use of intrathecal opioids is one of the important components in this approach. Among intrathecal opioids, low-dose morphine appear to be the most widely recommended¹. However, this hydrophilic opioid has a high frequency of adverse effects² such as nausea and vomiting, pruritus, and potentially serious late respiratory depression³. That's why the question of the current routines related to this topic in Sweden is important in daily life clinical practice.

I think that several things could be corrected to improve quality of the paper.

General comments:

Authors should choose tense in which they present and discuss findings. Personally, I don't like to present tense because, as stated below it can be sometimes misleading. Anyway, consistency is needed.

English language could also be improved. There are some awkward expressions such as 'fast opioid' which is not really medical term.

Tense is changed to past tense through the paper.

Fast opioid is changed to opioid with rapid onset and short duration

Specific comments:

Title:

The title could be more clear and in better English.

Title is changed to Neuraxial opioids as analgesia in labour, caesarean section and hysterectomy: A questionnaire survey in Sweden

Abstract:

I recommend to maintain consistency regarding the aim of the study, whether it is the use of neuraxial opioids or just morphine.

The primary aim of the present questionnaire survey was to assess the use of intrathecal and epidural morphine in obstetric and gynaecological patients, factors that limit/holdback its use and monitoring routines implemented. Additional aim was to assess the use of other opioids with more rapid onset and shorter duration for these patients. This is clarified in the paper.

'the patient is in postoperative care or an obstetrical ward over 2-6 hours and up-to 12 hours in an ordinary surgical ward.' I would add 'is monitored in ...'

"is monitored in" is added according to your suggestion.

Introduction

'Intrathecal and epidural morphine improve postoperative analgesia after caesarean section (CS) and hysterectomy and intrathecal labour analgesia'. Did the authors mean during intrathecal labour analgesia?

This is at least what Yeh *et al.* had in mind during their study.

"during" is added in the sentence according to your suggestion.

Methods:

'A questionnaire survey was sent to anaesthesiologists in charge of Swedish obstetric anaesthesia' I think it sounds a bit strange. Is it not more simple just to write that the questionnaire was sent to the anaesthesiologists in charge of obstetric anaesthesia units in hospitals in Sweden? Furthermore, information about anesthesiologist is repeated 3 times.

It is changed to: was sent to the anaesthesiologists in charge of obstetric anaesthesia units in hospitals in Sweden.

What is 'Swedish Association of Obstetric Anaesthesia and Intensive Care'?

'Swedish Association of Obstetric Anaesthesia and Intensive Care' is an association within SFAI – Swedish Association of Anaesthesia and Intensive Care', anaesthesiologists specialized in obstetric anaesthesia, <https://sfai.se/delforeningar/sfoai/om-sfoai/>

The questionnaire (Supplementary File 1 and Supplementary File 2) was produced to reflect how common the use of intrathecal and epidural morphine, fentanyl and sufentanil as adjunct to local anaesthetics for perioperative care of CS and hysterectomy is, and also the routine use of intrathecal morphine for labour analgesia. I think this sentence could be corrected in underlined parts as it sounds awkward.

The sentence is changed to: The questionnaire (Supplementary File 1 and Supplementary File 2) was designed to reflect how common the use of intrathecal and epidural morphine, fentanyl and sufentanil as adjunct to local anaesthetics for perioperative care of CS and hysterectomy is, and included questions about the routine use of intrathecal morphine for labour analgesia.

'specify the numbers of patients administered with opioids, including neuraxial morphine, for the operations performed' it is not clear if the authors were interested in intrathecal morphine alone or in other intrathecal opioids or, what would be even more interesting what was the combinations of used opioids. It

is the same issue what with the aim of the study.

Primary and additional aim is clarified.

Results

'Epidural sufentanil. In total, 15 units use sufentanil as the fast opioid in the epidural anaesthesia for CS anaesthesia' maybe opioid with rapid onset of action.

The sentence is changed according to your suggestion

50mcg of epidural sufentanil is quite a large dose. I think it should be commented.

The anaesthesiologist answered "25-50 microg sufentanil" is added as sole opioid.

It is quite surprising that for hysterectomy and gynecological abdominal surgery opioids are used intrathecally and not with the use of epidural anesthesia. Can the authors comment on that?

A comment is added in the discussion.

'Postoperative monitoring is generally organized within the initial 2–6 hours in the postoperative ward and the following hours, up to 12 hours, in the regular surgical ward, according to the guidelines of SFAI – Swedish Association of Anaesthesia and Intensive Care.' Did you mean this is general routine in Sweden or this was the result of survey? Using present tense in result section is a bit misleading.

We have changed findings in result section to past tense.

Also 'in the regular surgical ward, according to the guidelines of SFAI – Swedish Association of Anaesthesia and Intensive Care.' I would change into: ... according to the guidelines of Swedish Association of Anaesthesia and Intensive Care (SFAI).

We have changed according to your suggestion "the guidelines of Swedish Association of Anaesthesia and Intensive Care (SFAI)."

Postoperative monitoring: The authors write about 9 units of 32 in case of CS, what happened to patients in the rest of 20 units where morphine was used?

9/32 units added sufentanil in CS.

'Seven of the eleven units that chose not to use spinal/epidural morphine' Or was it 12/32 units which did not use morphine as in table 1.

One unit answered they routinely used intrathecal morphine for CS but did not present any dose of intrathecal morphine and is consequently not included in Table 1 and we changed to consider the unit as none user of morphine.

"Seven of the twelve units that did not to use spinal/epidural morphine describe risk of respiratory depression and difficulties to monitor as the main reasons for withholding its use. "

Discussion

I think authors should avoid expressions such as 'Swedish obstetric anaesthesia' because such thing do not exist. Use instead obstetric anaesthesia units in Sweden.

We have changed to your suggested "obstetric anaesthesia units in Sweden."

'Opioids were also commonly added to labour analgesia as sufentanil,' please change for clarity into:

'Opioids such as sufentanil were also commonly added to labour analgesia... '

We have changed according to your suggestion.

'there are good opportunities to get a beneficial epidural in Sweden' what did you mean by 'beneficial'?

The citation should be placed earlier, as Cochrane's review does not say much how these issues occur in

Sweden.

The citation is placed earlier and the sentence clarified.

'Sufentanil is the most common opioid added in labour anaesthesia in Sweden, which was reported in a national obstetric anaesthesia meeting from a survey in 2009 (not published).'

We changed to "data on file" according to referee Wallden and Styrke.

'Spinal anaesthesia is the preferred analgesia in CS when a working epidural is not in place for conversion and top-up.' What do you mean 'conversion'?

The sentence is changed to "Spinal anaesthesia is the preferred analgesia in CS when a labour epidural is not in place to top up for perioperative use".

'Yet currently, the present study found that twelve units use solely fast opioid adjuncts to local anaesthesia and two of the units add morphine to local anaesthetics with no addition of fentanyl or sufentanil, but one of the units stated they plan to start adding fentanyl shortly.' Last part of the sentence could be omitted; the authors should filter not important information.

Last part of the sentence is omitted according to your suggestion.

On the other hand it could be discussed that even though intrathecal lipophilic opioids in CS are not as effective as intrathecal morphine, they still proved to be beneficial during the period of highest analgesic demand after cesarean section.

We added according to your suggestion and are grateful for your reference.

'Yet, the addition of epidural opioids has been proven to enhance postoperative analgesia after CS with earlier onset' I don't understand this sentence.

We changed the sentence.

Limitation

Usually, at the end of manuscript, authors should state limitations of the study. Some aspects that could be discussed are:

The postoperative monitoring routines are limited to time perspective. There is nothing about what was actually monitored and how often.

Quality of information obtained from the question regarding complications is very low.

We added "Limitation" according to your suggestion, including aspects of the postoperative monitoring routines and quality of information obtained from the question regarding complications.

Once again thank you for your time and interest! We are most grateful!

Anette Hein

MD Department of Anaesthesia & Intensive Care, Danderyds Hospital, Stockholm, 182 88, Sweden
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Competing Interests: None