

Postoperativ smärta hos äldre

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2024-05-24

Att tänka på rent allmänt

- Suboptimal preoperativ smärtlindring

och/eller

- Suboptimal intraoperativ smärtlindring

och/eller

- Opioid-inducerad hyperalgesi (OIH)

→ postoperativ smärta ↑

Suboptimal pre-, intraoperativ analgesi, OIH → postoperativ smärta↑

Opioid-inducerad hyperalgesi (OIH) - Remifentanil

Review > Local Reg Anesth. 2018 Apr 9;11:15-23. doi: 10.2147/LRA.S143618. eCollection 2018.

Remifentanil-induced postoperative hyperalgesia: current perspectives on mechanisms and therapeutic strategies

Cristina Santonocito¹, Alberto Noto², Claudia Crimi³, Filippo Sanfilippo¹

Affiliations + expand

PMID: 29670398 PMCID: PMC5898588 DOI: 10.2147/LRA.S143618

The use of remifentanil in clinical practice offers several advantages and it is used for a wide range of procedures, ranging from day-surgery anesthesia to more complex procedures. Nonetheless, remifentanil has been consistently linked with development of opioid-induced hyperalgesia (OIH), which is described as a paradoxical increase in sensitivity to painful stimuli that develops after exposure to opioid treatment. The development of OIH may cause several issues, delaying recovery after surgery and preventing timely patient's discharge. Moreover, it causes patient's discomfort with higher pain scores, greater use of analgesics, and associated side effects. Remifentanil is the opioid most convincingly associated with OIH, and hereby we provide a review of remifentanil-induced hyperalgesia, describing both the underlying mechanisms involved and the available studies investigating experimental and clinical pharmacologic approaches aiming at reducing its incidence and degree.

Tänk på att:

Undvik Remifentanil vid väldigt smärtsamma ingrepp, samt för patienter som är opioidtoleranta! Välj då annan intraoperativ opioid.

Suboptimal pre-, intraoperativ analgesi, OIH → postoperativ smärta↑

Preoperativ nervblockad ger
bättre postoperativ
smärtlindring
än postoperativ nervblockad!

➤ [J Foot Ankle Surg.](#) 2020 Jul-Aug;59(4):788-791. doi: 10.1053/j.jfas.2019.05.012. Epub 2020 May 10.

Comparison of Regional Anesthesia Timing on Pain, Opioid Use, and Postanesthesia Care Unit Length of Stay in Patients Undergoing Open Reduction and Internal Fixation of Ankle Fractures

John C Alexander ¹, Mary Sunna ², Abu Minhajuddin ³, George Liu ⁴, Drew Sanders ⁵, Adam Starr ⁶, Irina Gasanova ⁷, Girish P Joshi ⁷

Regional nerve blocks are an effective method of managing acute pain associated with surgery. The relative benefit of preoperative versus postoperative peripheral nerve blocks is not entirely clear. The primary aim of this study was to determine differences in pain scores in patients undergoing preoperative block versus postoperative block versus no block. We hypothesized that patients receiving preoperative blocks would have reduced pain scores and decreased opioid use in the immediate postoperative period. We conducted a retrospective cohort analysis of 302 consecutive patients undergoing unilateral open reduction and internal fixation of ankle fracture under general anesthesia. We identified 3 groups: preoperative block, postoperative block, or no block. Data obtained from our electronic medical records included demographic information, postanesthesia care unit length of stay, pain scores obtained preoperatively, upon arrival to the postanesthesia care unit, and upon discharge from the postanesthesia care unit as well as intraoperative and postanesthesia care unit opioid utilization. Patients receiving preoperative block had significantly lower pain scores, less intraoperative or postanesthesia care unit opioid use, and shorter postanesthesia care unit dwell time compared with patients receiving postoperative block or no block. **Preoperative popliteal sciatic and adductor canal blocks in patients undergoing ankle fracture surgery appears to be more effective than either postoperative block or no block.**

Postoperativ smärta hos äldre

Fysiologiska förändringar

- gastrointestinal transittid ↓
- muskelmassa ↓
- fettvävnad ↑
- total kroppsvatten (TBW) ↓
- leverns blodflöde (hepatic BF) ↓
- njurar, GFR ↓
- förändringar på receptornivå i CNS



→ Läkemedel som används hos äldre blir mer potenta och får längre verkningsstid!

Postoperativ smärta hos äldre

Opioidnaiva patienter

Anpassad multimodal analgesi

Paracetamol

– Ja!

COX2 – hämmare / NSAID

– OBS! njurfunktion, kontraindikationer

Opioider

– vilken opioid?

Lokalbedövning

– ”Single shot ?” Perifer nervkateter med pump ?

Postoperativ smärta hos äldre

Opioidnaiva patienter

Anpassad multimodal analgesi

Opioider

– vilken opioid ?

Buprenorfin

Passar bra till gamlingar



Buprenorfin: en unik opioid

- **Verkar på 4 olika receptorer:**

1. μ (MOP) receptor partiell agonist,

2. κ (KOP) receptor antagonist

3. δ (DOP) receptor antagonist

4. opioid receptor like (ORL1) (=NOP)-receptor agonist

bindningsaffinitet till MOP, KOP, DOP ↑ ↑ ↑

bindningsaffinitet till (ORL1) NOP ↑

- **aktiv metabolit: norbuprenorfin**
- **utsöndras via lever - galla**

Partiell agonist ? Vad är det ?

J Gudin, J Fudin: A Narrative Pharmacological Review of Buprenorphine. Pain Ther 9:41-54,2020

μ (MOP) receptor agonist	μ (MOP) receptor <u>partial</u> agonist
t.ex. Fentanyl, Morfin, Oxykodon.	Buprenorfin
μ (MOP) receptorerna är "överstimulerade"	μ (MOP) receptorerna är <u>inte</u> "överstimulerade"

Buprenorfin:
Minskad risk för andningspåverkan och/eller rus/euphori och/eller tillvänjning/missbruk

Therefore, despite buprenorphine's partial agonism at the μ -opioid receptor, analgesic efficacy is maintained while the likelihood of respiratory depression and euphoria is decreased and abuse potential is limited by preventing the overstimulation of or excessive signaling from the μ -opioid receptor [6, 11, 13, 14, 23, 39–45].

Partiell agonist ? Vad är det ?

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Buprenorfin:

Lika effektiv postop smärtlindring som andra opioider.

Buprenorphine has shown analgesic efficacy comparable to that of full μ -opioid receptor agonists in moderate to severe post-operative pain and cancer pain, with no demonstrated ceiling effect for analgesia in humans [8]. In fact, the analgesic efficacy observed in clinical trials of two different buprenorphine products FDA approved for the treatment of chronic pain was similar to that of commonly utilized full μ -opioid receptor agonists [51–53].

Buprenorfin: en unik opioid

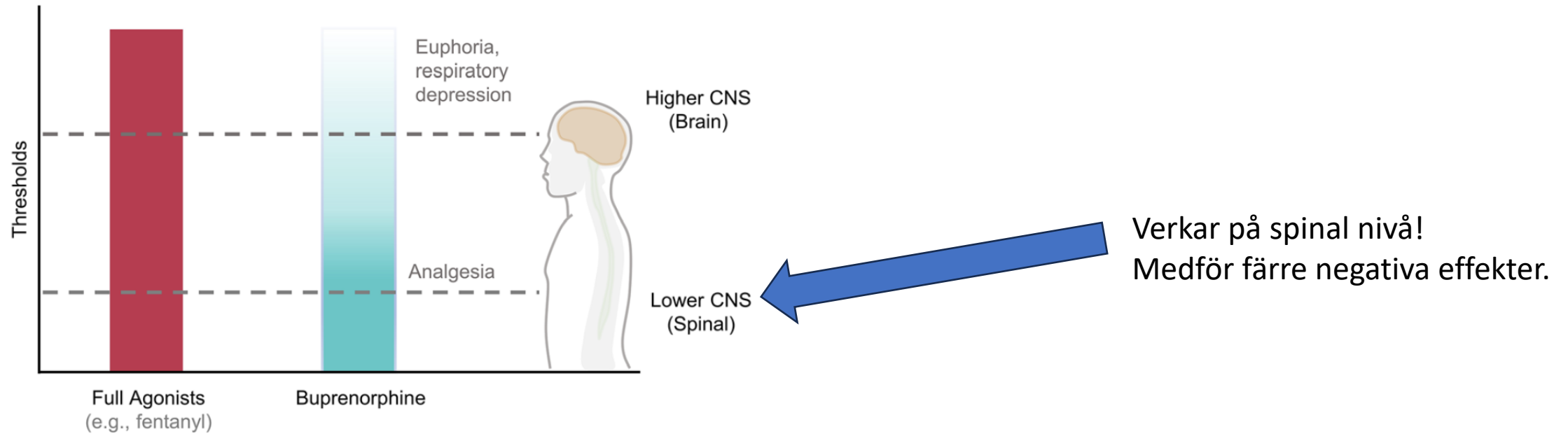


Fig. 3 Buprenorphine activity at spinal μ -opioid receptors provides analgesia while limiting euphoria and respiratory depression. Activation of the μ -opioid receptor results in varying effects depending on the extent of the activation.

J Gudin, J Fudin: A Narrative Pharmacological Review of Buprenorphine. Pain Ther 9:41-54,2020

Buprenorfin

Hur ska det ges?

Table 1 Bioavailability of buprenorphine by formulation

Route of administration	Bioavailability
Intravenous	100%
Buccal	46–65%
Sublingual	28–51%
Transdermal	15%

Percent bioavailability of the intravenous [82], buccal [83], sublingual [84, 85], and transdermal [86] formulations of buprenorphine

J Gudin, J Fudin: A Narrative Pharmacological Review of Buprenorphine. Pain Ther 9:41-54,2020

Buprenorfin

- 1. effektiv mot nociceptiv smärta, neurogen smärta**
- 2. blockerar hyperalgesi och central sensitisering**
- 3. bättre sömn jämfört med andra opioider**
- 4. oförändrad kognitiv förmåga**
- 5. begränsad risk för andningsdepression vid terapeutisk dos**
- 6. mindre risk för falltrauma jämfört med andra opioider**
- 7. kan ges vid njursvikt / dialyskrävande njursvikt**
- 8. inga EKG förändringar (påverkar inte QT –tiden)**

Buprenorfin

9. Passar bra till äldre patienter!
(se punkt 3 – 8 föregående bild)



Buprenorfin

- 10. kan ges vid måttlig – medelsvår leversvikt**
- 11. kan kombineras med andra opioider**
- 12. ingen immunsuppressiv effekt jämfört med andra opioider**
- 13. mildare utsättningssymtom (lindrig abstinens)
jämfört med andra opioider**
- 14. förstoppning - sällan**

Buprenorfin

Review > J Pain Res. 2021 Mar 31;14:871-879. doi: 10.2147/JPR.S280572. eCollection 2021.

Transdermal Buprenorphine for Acute Pain in the Clinical Setting: A Narrative Review

Joseph V Pergolizzi Jr ¹, Peter Magnusson ^{2 3}, Jo Ann LeQuang ¹, Frank Breve ⁴, Kailyn Mitchell ¹, Maninder Chopra ⁵, Giustino Varrassi ⁶

Transdermal buprenorphine is indicated for chronic pain management, but as its role in the clinical management of acute pain is less clear, this narrative review examines studies of the patch for acute pain, mainly in the postoperative setting. Although perhaps better known for its role in opioid rehabilitation programs, buprenorphine is also an effective analgesic that is a Schedule III controlled substance. Although buprenorphine is a partial agonist at the μ -opioid receptor, it is erroneous to think of the agent as a partial analgesic; it has full analgesic efficacy and unique attributes among opioids, such as a ceiling for respiratory depression and low "drug likeability" among those who take opioids for recreational purposes. Transdermal buprenorphine has been most thoroughly studied for acute pain control in postoperative patients. Postoperative pain follows a distinct and predictable trajectory depending on the type of surgery and patient characteristics. Overall, when the patch is applied prior to surgery and left in place for the prescribed seven days, it was associated with reduced postoperative pain, lower consumption of other analgesics, and patient satisfaction. Transdermal buprenorphine has been evaluated in clinical studies of patients undergoing gynecological surgery, hip fracture surgery, knee or hip arthroscopy/arthroplasty, shoulder surgery, and spinal surgery. Transdermal buprenorphine may also be appropriate pain medication for controlling pain during postsurgical orthopedic rehabilitation programs. Transdermal buprenorphine may result in typical opioid-associated side effects but with less frequency than other opioids. Despite clinical reservations about transdermal buprenorphine and its potential role in acute pain management in the clinical setting, clinical acceptance may be hampered by the fact that it is off-label and buprenorphine is better known as an opioid maintenance agent rather than an analgesic.

Plåster –
fungerar även för
akut smärtlindring

Buprenorfin - administrering

	Smärtlindring	Substitutionsbehandling för opioidberoende
Resoriblett: sublingual	Temgesic 0,2 – 0,4 mg var 6 – 8 h (ges regelbundet eller vb.)	Buprenorphine, Espranor, Suboxone, Bunalict, Zubsolv, Buprenorphine/Naloxone
Depotplåster: transdermal	Buprenorfin, Buprefarm Norspan 5 – 40 µg/h x 1 per vecka	
Injektion: perineural (som adjuvans till LA), im, iv	Buprenorphine 0,3 mg/nerv	
Injektion, depotlösning: sc		Buvidal, Subutex, Sixmo (implantat)

Postoperativ smärta hos äldre

Opioidnaiva patienter

Anpassad multimodal analgesi

Lokalbedövning

– ”Single shot ?” Perifer nervkateter med pump ?

Buprenorfin och nervblockader

Meta-Analysis > Eur J Anaesthesiol. 2017 Sep;34(9):576-586.

doi: 10.1097/EJA.0000000000000628.

Efficacy and safety of buprenorphine in peripheral nerve blocks: A meta-analysis of randomised controlled trials

Alexander Schnabel¹, Sylvia U Reichl, Peter K Zahn, Esther M Pogatzki-Zahn, Christine H Meyer-Frießem

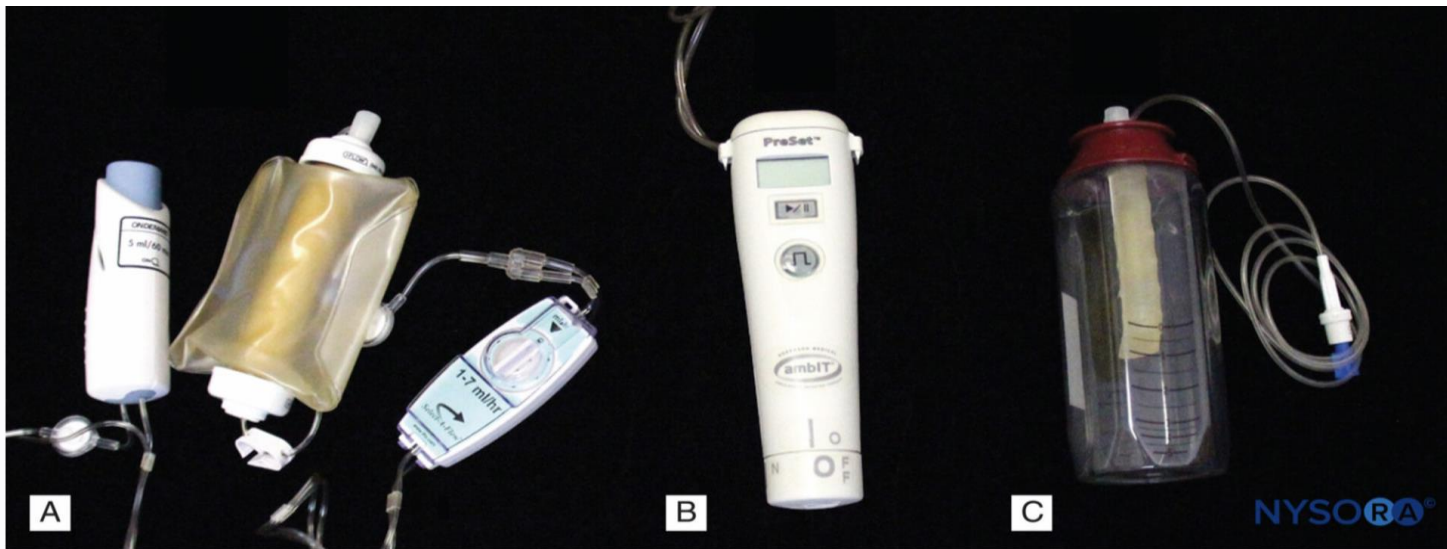
Conclusion: This meta-analysis revealed that the addition of buprenorphine to a local anaesthetic peripheral nerve block prolongs postoperative analgesia for about 8 h but significantly increases the risk for PONV. Perineural administration is more effective than systemic application but is associated with a similar risk of PONV. However, these results were influenced by heterogeneity so that further trials (especially head-to-head comparisons) are needed in the future.

Tillägg av Buprenorfin
till lokalbedövnings-
medel i perifer
nervblockad ➡ 8 tim
förlängd postop
smärtlindring

Framtid – Fler äldre patienter i dagkirurgi

Lokalbedövning – Perifer nervkateter med pump

Infusionspumpar som patienterna kan ha med sig hem,
läkemedel räcker i 2-3 dygn



The ON-Q* pump continuously delivers the medication at a very slow flow rate. It is completely portable and may be clipped to your clothing or placed in a small carrying case.

THE ON-Q* PAIN RELIEF SYSTEM MAY PROVIDE:

- More comfortable recovery after surgery
- Better pain relief without the side effects of narcotics
- Quicker return to normal
- Earlier release from the hospital



Frågor?



Suboptimal pre-, intraoperativ analgesi, OIH → postoperativ smärta↑

➤ [JAMA Surg. 2023 Aug 1;158\(8\):854-864. doi: 10.1001/jamasurg.2023.2009.](#)

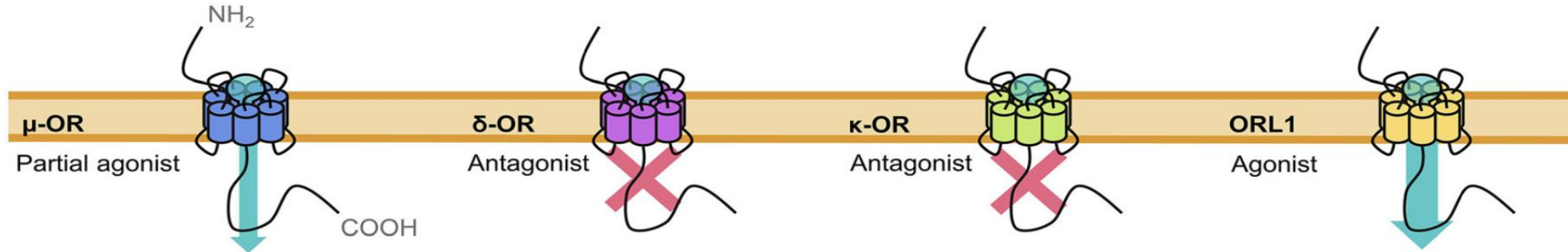
Association of Intraoperative Opioid Administration With Postoperative Pain and Opioid Use

Results: The study cohort included a total of 61 249 individuals undergoing surgery (mean [SD] age, 55.44 [17.08] years; 32 778 [53.5%] female). Increased intraoperative fentanyl and intraoperative hydromorphone were both associated with reduced maximum pain scores in the PACU. Both exposures were also associated with a reduced probability and reduced total dosage of opioid administration in the PACU. In particular, increased fentanyl administration was associated with lower frequency of uncontrolled pain; a decrease in new chronic pain diagnoses reported at 3 months; fewer opioid prescriptions at 30, 90, and 180 days; and decreased new persistent opioid use, without significant increases in adverse effects.

Conclusions and relevance: Contrary to prevailing trends, reduced opioid administration during surgery may have the unintended outcome of increasing postoperative pain and opioid consumption. Conversely, improvements in long-term outcomes might be achieved by optimizing opioid administration during surgery.

Buprenorfin: en unik opioid

J Gudin, J Fudin: A Narrative Pharmacological Review of Buprenorphine. Pain Ther 9:41-54,2020



- Potent analgesia
- Ceiling on respiratory depression and euphoria
- Limited impact on GI motility
- Limited physical dependence, abuse potential, and withdrawal symptoms
- Reduced immunosuppression and impact on the HPA axis
- Reduction in suicidal thoughts, anxiety, and depression
- Limited dysphoria

- Anti-opioid effects
- Myocardial protection
- Limited impact on GI motility*
- Limited respiratory depression*

- Reduced depression, dysphoria, suicidal tendencies, anxiety, and hostility
- Limited potential for addiction* and tolerance
- Reduced immunosuppression

- Enhanced spinal analgesia
- Reduced supraspinal analgesia
- Diminished opioid-rewarding effects
- Limited potential for tolerance

Buprenorphine

Review > J Support Oncol. 2012 Nov-Dec;10(6):209-19. doi: 10.1016/j.suonc.2012.05.002.

Epub 2012 Jul 17.

Twelve reasons for considering buprenorphine as a frontline analgesic in the management of pain

Mellar P Davis ¹

Buprenorphine is an opioid that has a complex and unique pharmacology which provides some advantages over other potent mu agonists. We review 12 reasons for considering buprenorphine as a frontline analgesic for moderate to severe pain: (1) Buprenorphine is effective in cancer pain; (2) buprenorphine is effective in treating neuropathic pain; (3) buprenorphine treats a broader array of pain phenotypes than do certain potent mu agonists, is associated with less analgesic tolerance, and can be combined with other mu agonists; (4) buprenorphine produces less constipation than do certain other potent mu agonists, and does not adversely affect the sphincter of Oddi; (5) buprenorphine has a ceiling effect on respiratory depression but not analgesia; (6) buprenorphine causes less cognitive impairment than do certain other opioids; (7) buprenorphine is not immunosuppressive like morphine and fentanyl; (8) buprenorphine does not adversely affect the hypothalamic-pituitary-adrenal axis or cause hypogonadism; (9) buprenorphine does not significantly prolong the QTc interval, and is associated with less sudden death than is methadone; (10) **buprenorphine is a safe and effective analgesic for the elderly**; (11) buprenorphine is one of the safest opioids to use in patients in renal failure and those on dialysis; and (12) withdrawal symptoms are milder and drug dependence is less with buprenorphine. In light of evidence for efficacy, safety, versatility, and cost, buprenorphine should be considered as a first-line analgesic.