Opioidfri per- och postoperativ smärtlindring?

- Vad är:
  - → Önskvärt
  - → Möjligt
  - → Rimligt

..kanske viktigare vad är
nyttan och riskerna med opiatfri anestesi
- perioperativt omhändertagande

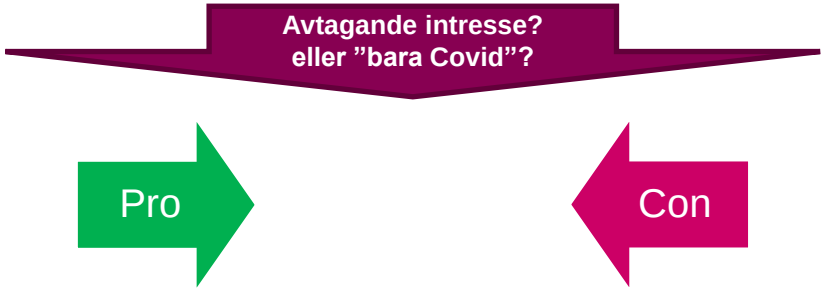
Opiatfri anestesi OFA, *något bättre eller bara något nytt?*

OFA

- Vad innebär det
  - → Genomföra anestesi (och postoperativ smärtlindring) **utan** tillförsel av morfinpreparat
- Varför
  - → ”*opioid crisis*”
  - → PONV
  - → OSAS
- Vinster
  - → *PONV*
  - → *Cancer, cancer reocurence - metastaser*
  - → *Kognitiva effekter, delirium, POCD ….*
- Intresset
  - *Avtagande?!*
- Mer/ytterligare fokus på ***”Opiatsparande multimodal anestesi & analgesi”***

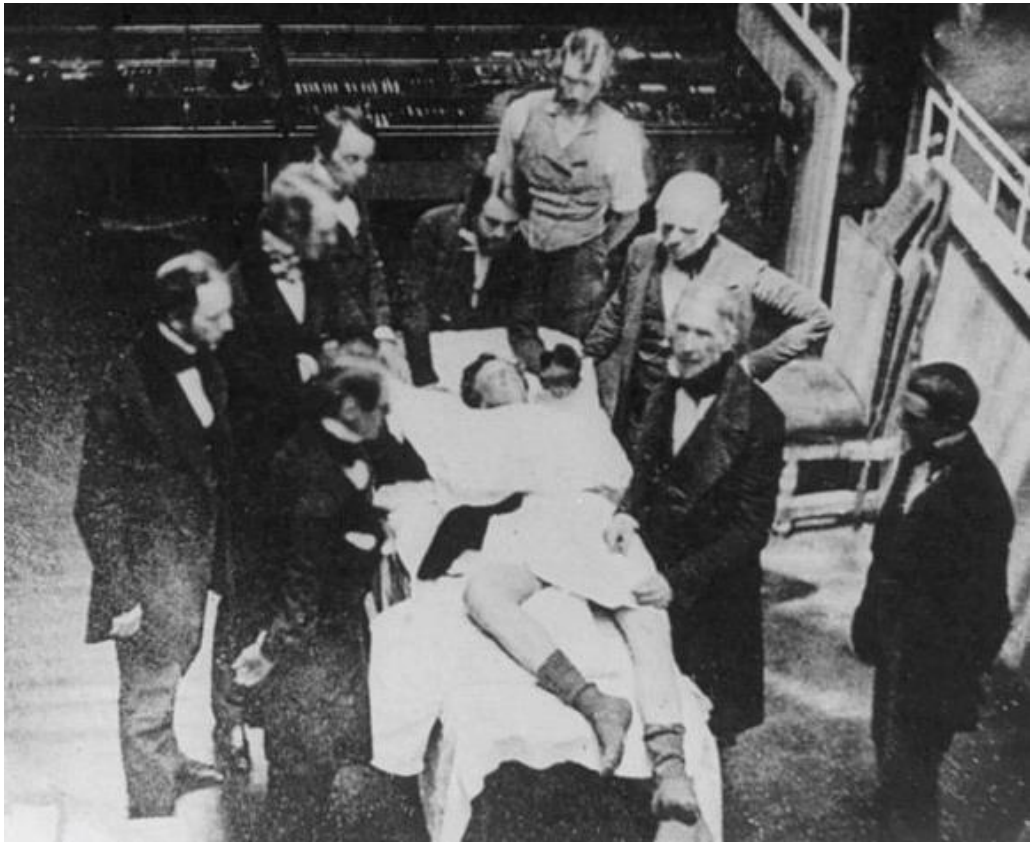
OFA

OFA

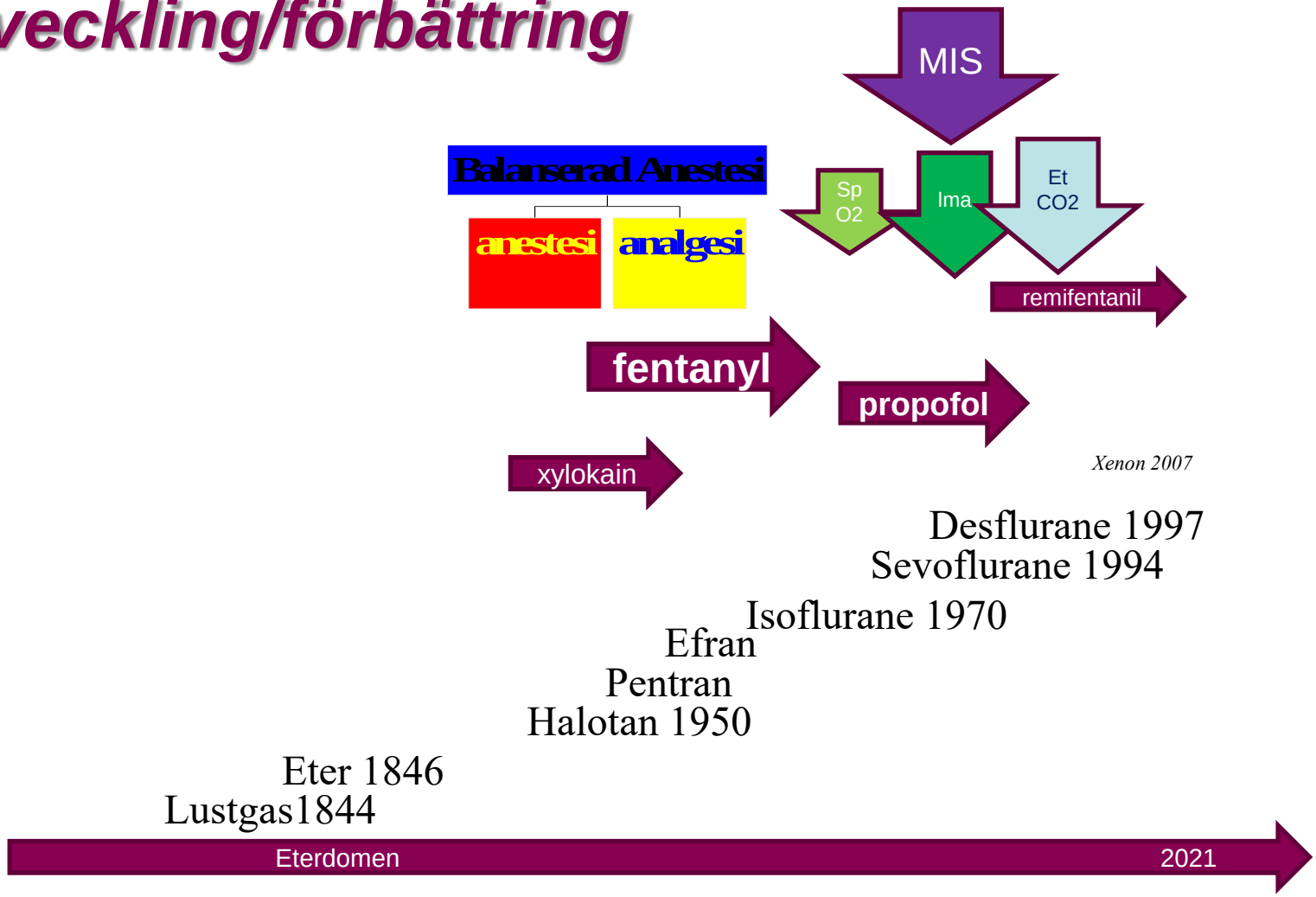


Kommer inte beröra explicita patientgrupper,
speciella behandlingsrekommendationer,
mer försöka ge en översikt av kunskapsläget
evidens för och emot

Utevklingen av anestesi



Anestesi
utveckling/förbättring



Balanced Anaesthesia

- Combining multiple drugs in smaller quantities
- **Maximising benefits**
- *Minimising adverse effects*
- “proving anaesthetist greater control”

Additivity Versus Synergy: A Theoretical Analysis of Implications for Anesthetic Mechanisms

Steven L. Shafer, MD*†‡

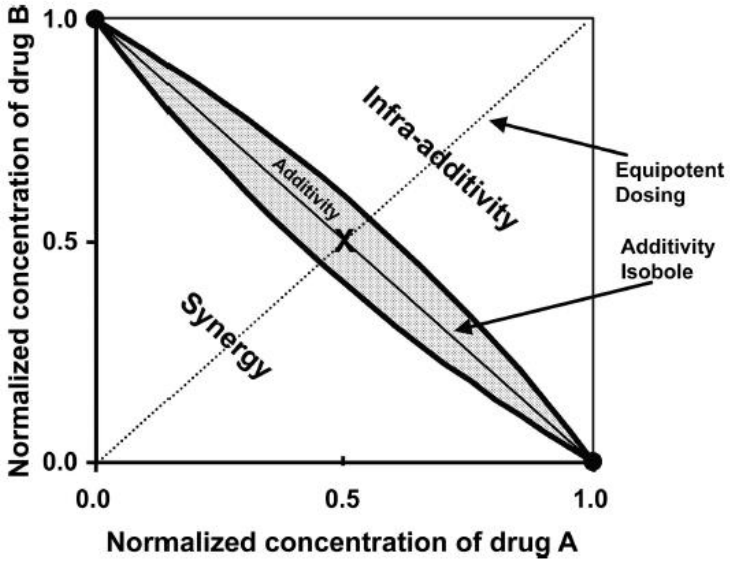
Jan F. A. Hendrickx, MD, PhD†¶

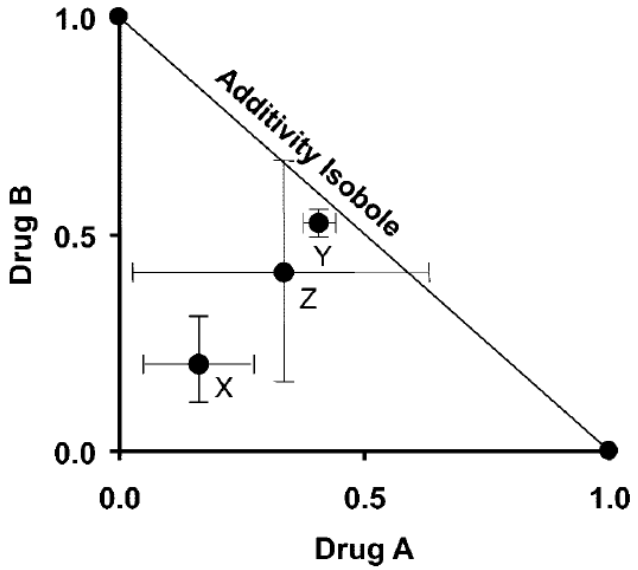
Pamela Flood, MD*

James Sonner, MD§

Edmond I Eger II, MD§

BACKGROUND: Inhaled anesthetics have been postulated to act at multiple receptors, with modest action at each site summing to produce immobility to noxious stimulation. Recent experimental results affirm prior findings that inhaled anesthetics interact additively. Synergy implies multiple sites of action by definition. In this essay, we explore the converse: does additivity imply a single site of action?
METHODS: The interaction of one versus two ligands competing for the same binding site at a receptor was explored using the law of mass action. Circuits were then constructed to investigate how the potency of drugs and the steepness of the concentration versus response relationship is amplified by the arrangement of suppressors into serial circuits, and enhancers into parallel circuits. Assemblies of suppressor and enhancer circuits into signal processing units were then explored to investigate the constraints signal processing units impose on additive interactions. Lastly, the relationship between synergy, additivity, and fractional receptor occupancy was explored to understand the constraints imposed by additivity.





Is Synergy the Rule? A Review of Anesthetic Interactions Producing Hypnosis and Immobility

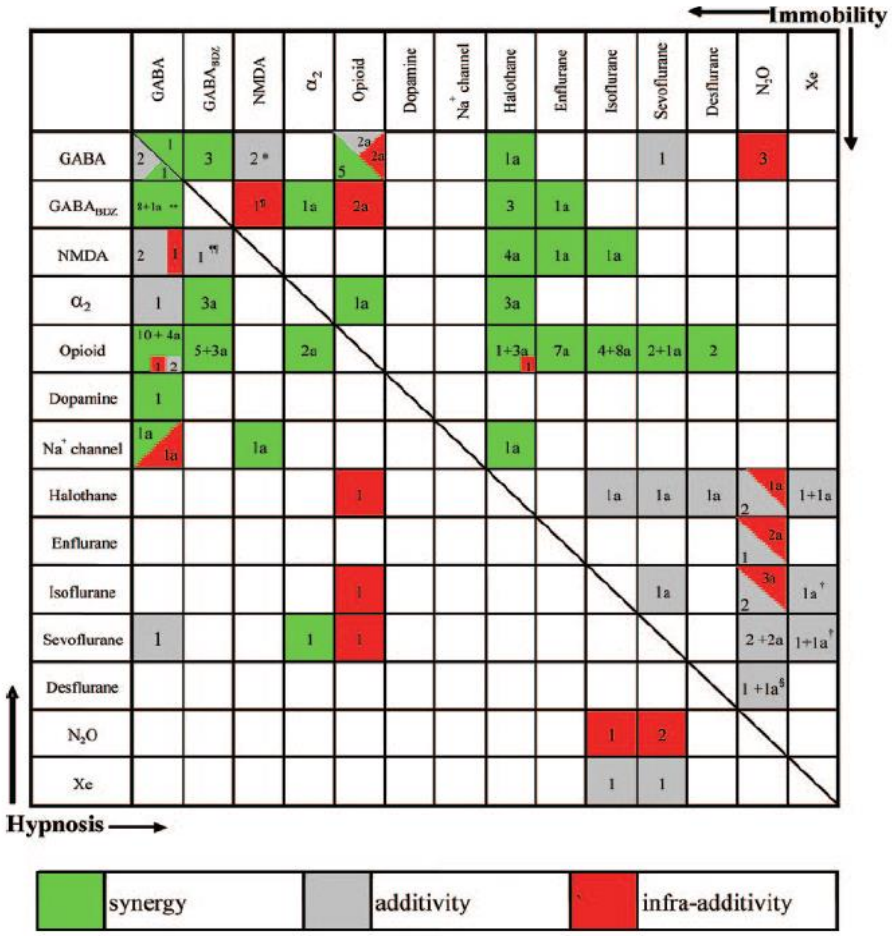
Jan F. A. Hendrickx, MD, PhD*

Edmond I Eger II, MD†

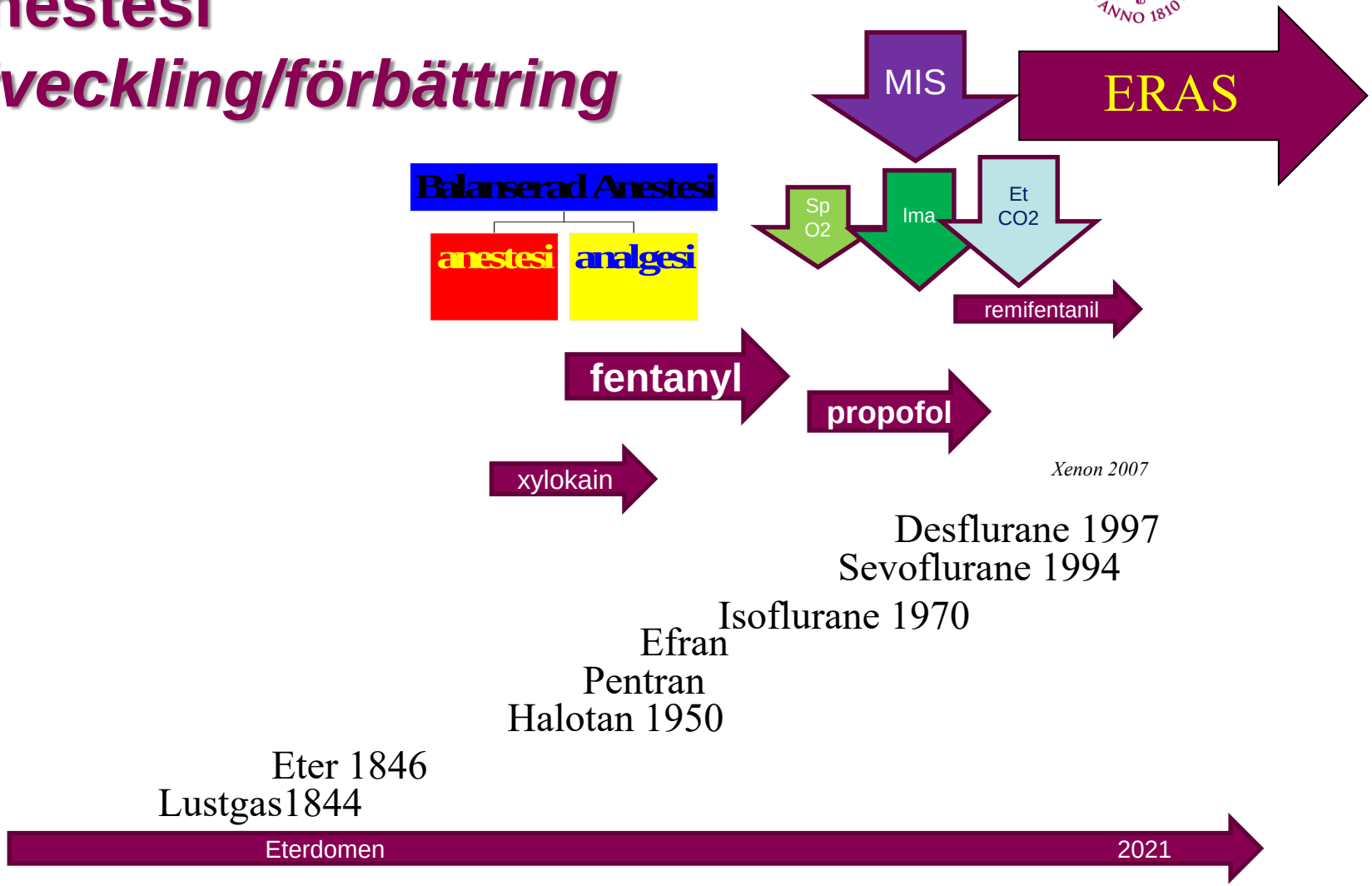
James M. Sonner, MD†

Steven L. Shafer, MD‡

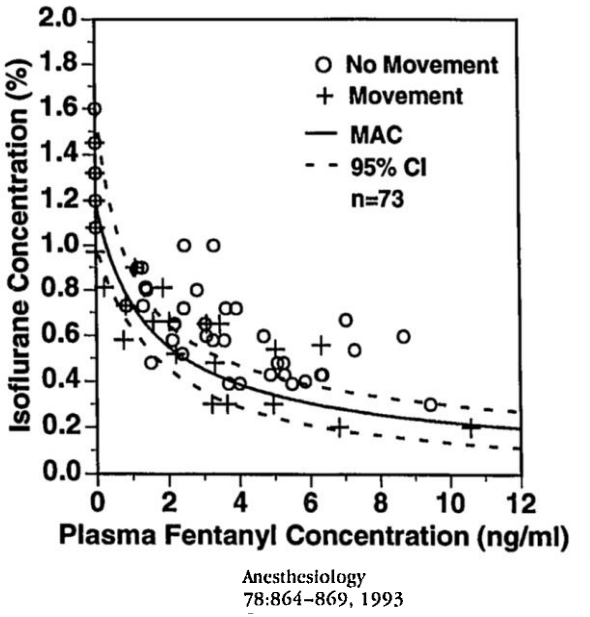
BACKGROUND: Drug interactions may reveal mechanisms of drug action: additive interactions suggest a common site of action, and synergistic interactions suggest different sites of action. We applied this reasoning in a review of published data on anesthetic drug interactions for the end-points of hypnosis and immobility.



Anestesi
utveckling/förbättring

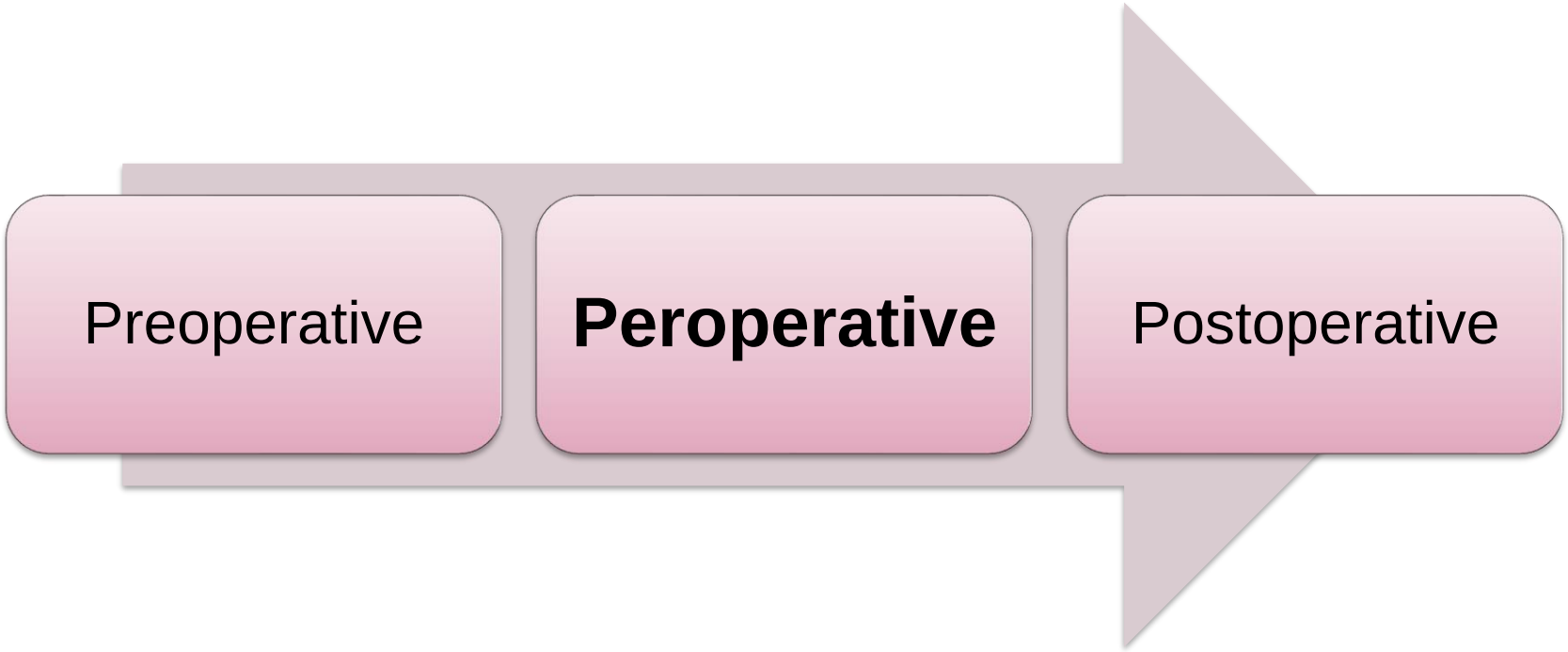


Tillägg till ”***basanestesin***” för att nå hemodynamisk kontroll och blockera smärtupplevelsen

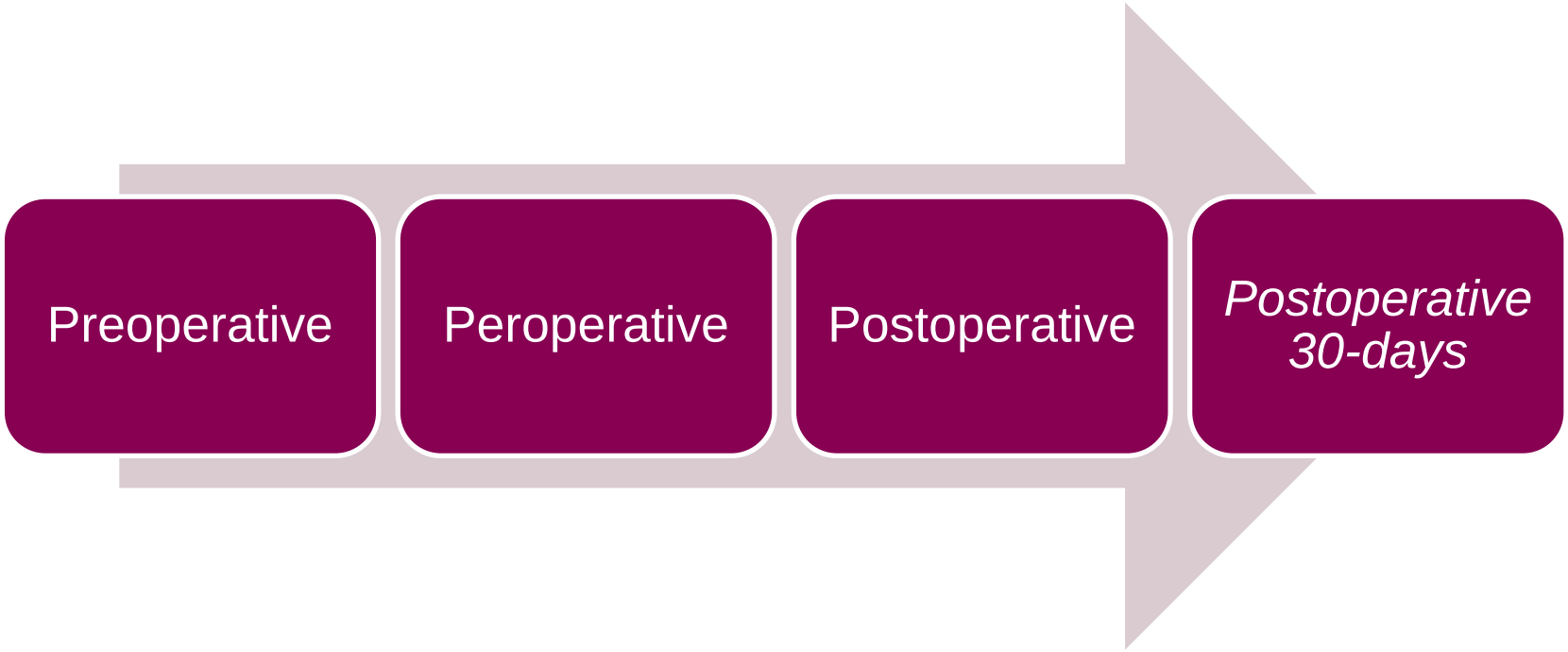


Routine Clinical Anaesthesia

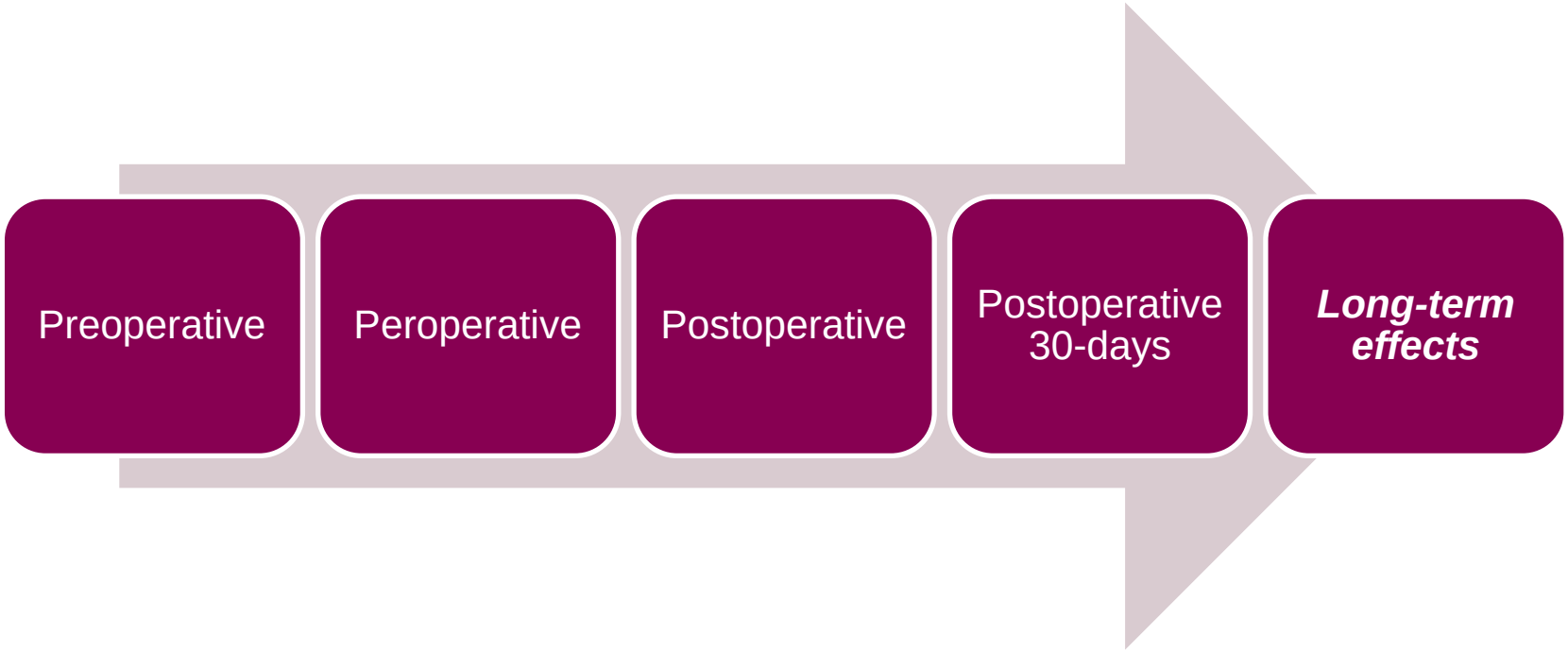
Routine Clinical Anaesthesia



Routine Clinical Anaesthesia



Routine Clinical Anaesthesia



Long term outcome

- Complications
  - Pain
  - PONV
  - Prolonged recovery

  → Infectious complicatins

  → Renal impairment

  → Cardiovascular events

  → Pulmonary complications

  → Thrombo-embolic complications
- ***Postoperative Cognitive Side Effects – POCD - postoperative neurocognitive disorder***
- ***Cancer; metastasis and reoccurence***
- ***Addiction***
- ***...***

ERAS® Society

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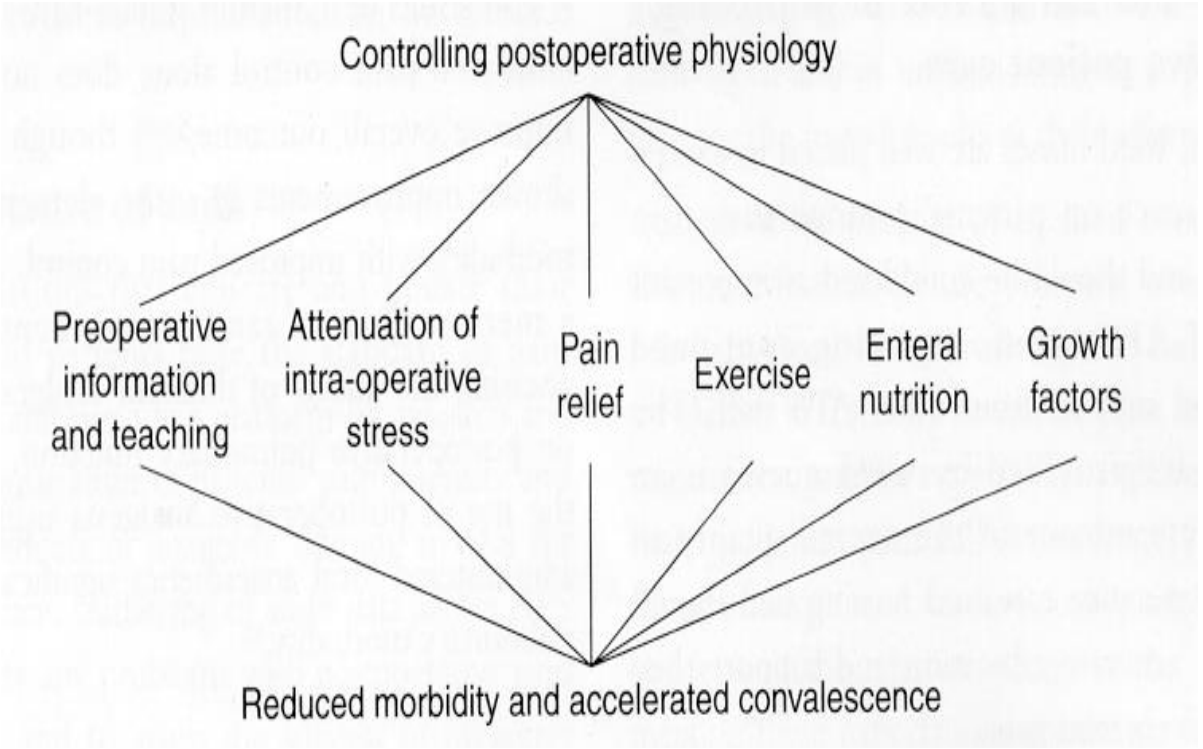
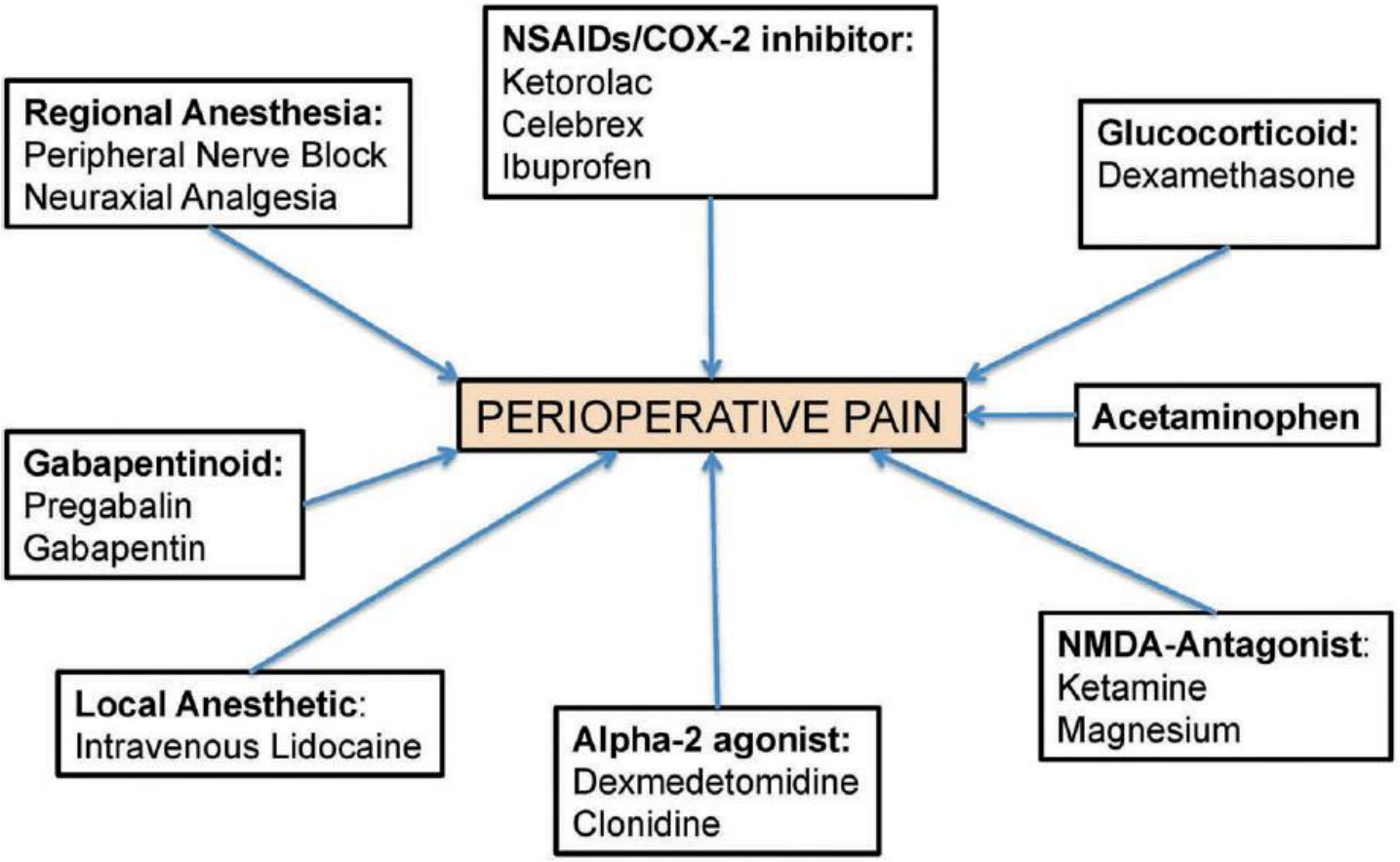
EBPOM
Evidence Based Peri-Operative Medicine

Enhanced recovery:

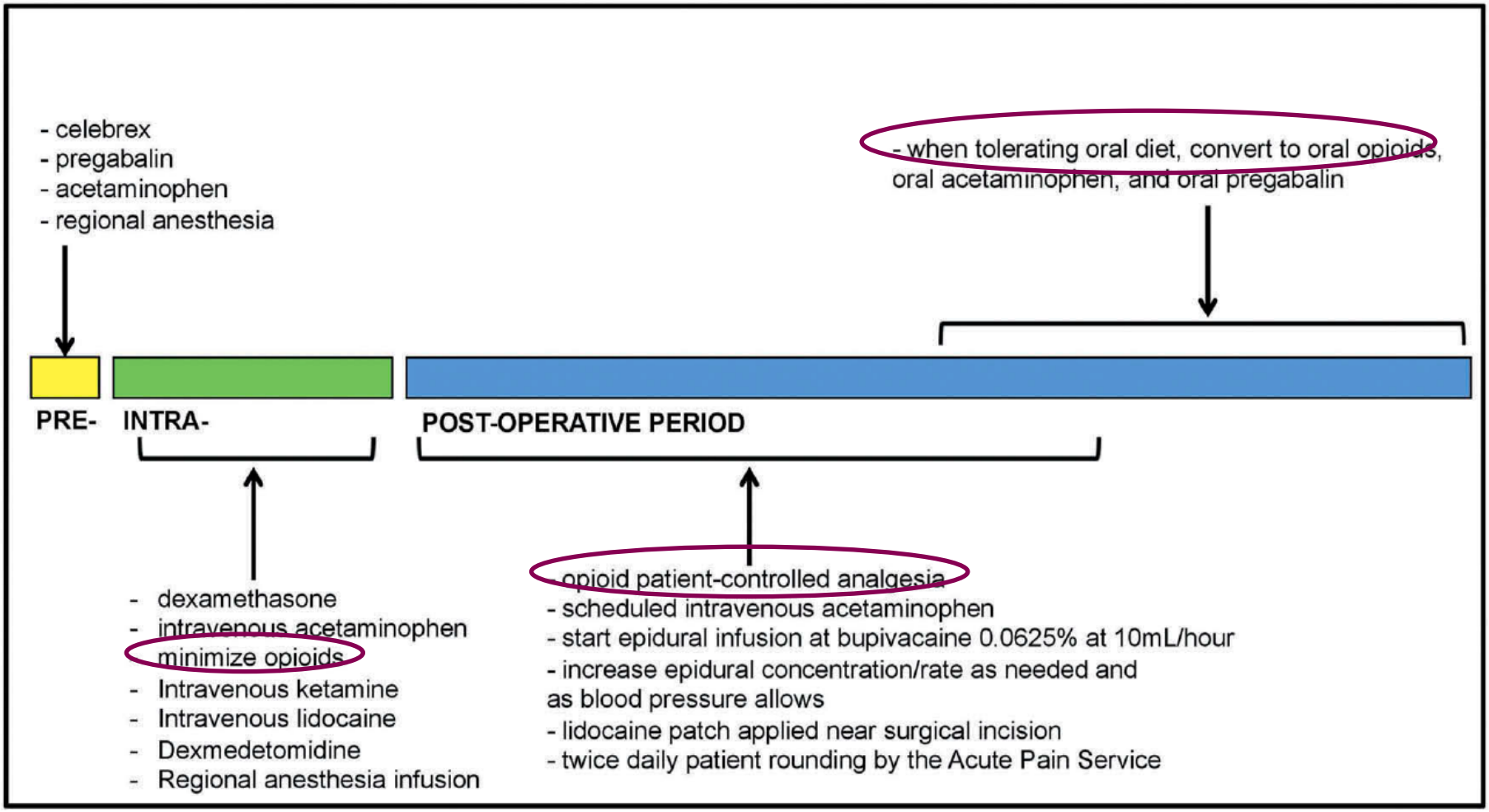
Perioperativ multi-modal / balanserad vård



Multimodal Opioid-Sparing Analgesia

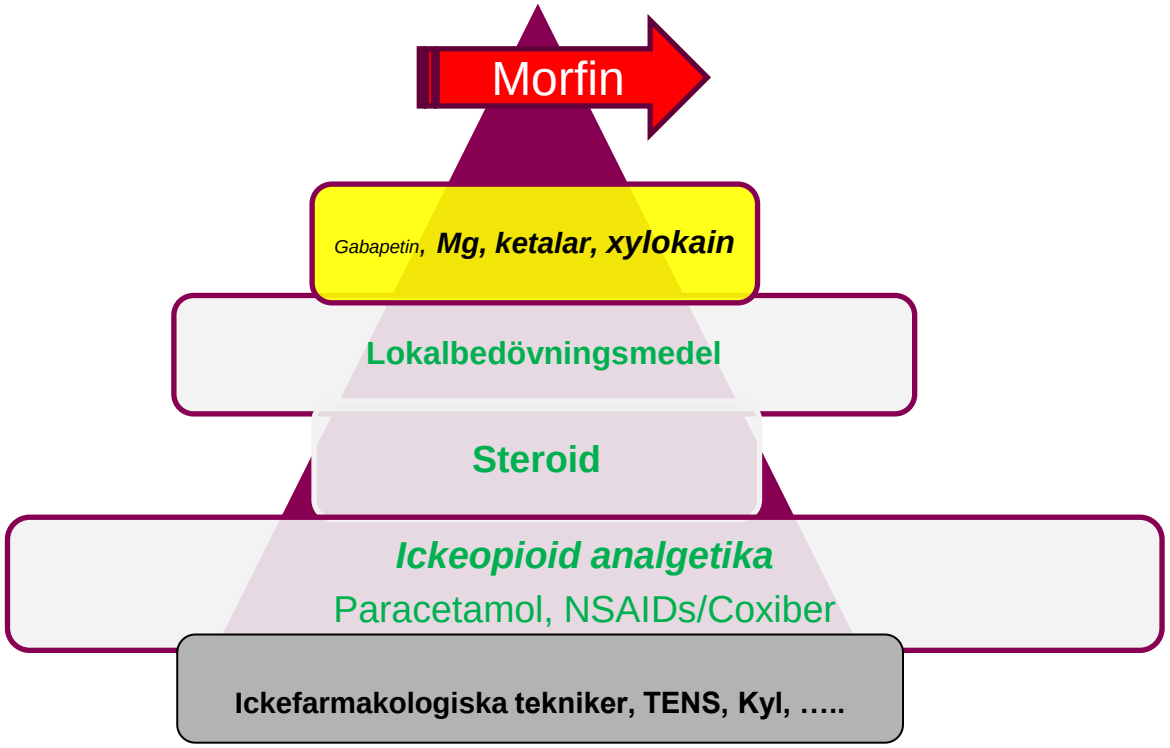


Expert Opin Pharmacother. 2019 Jun;20(8):949-961.

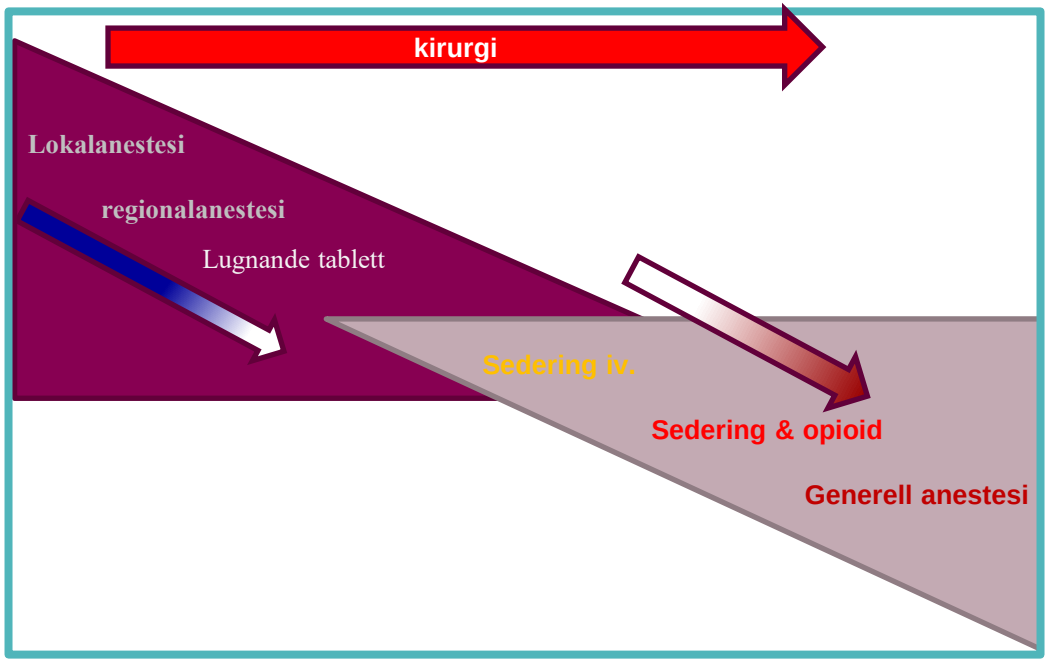


Expert Opin Pharmacother. 2019 Jun;20(8):949-961.

Analgesi

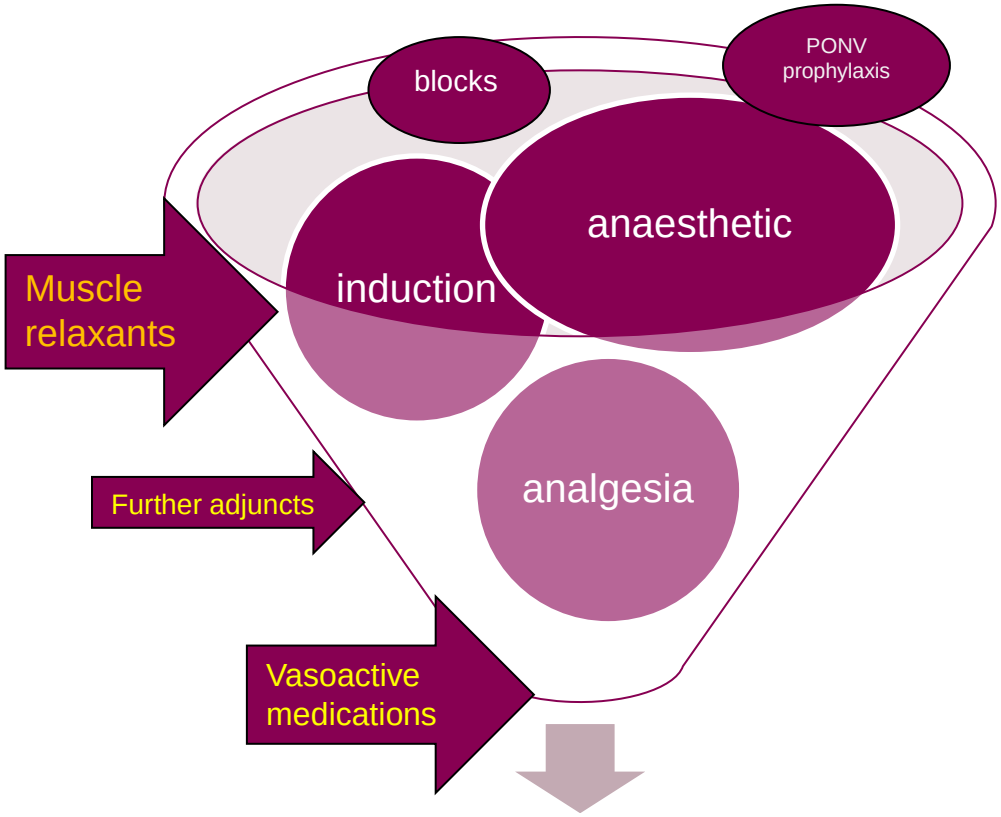

Morfin
Gabapetin, Mg, ketalar, xylokain
Lokalbedövningsmedel
Steroid
Ickeopioid analgetika
Paracetamol, NSAIDs/Coxiber
Ickefarmakologiska tekniker, TENS, Kyl, …..

Anestesi



....alltid lokalbedövning.....

Components in intra-operative care



Balanced anaesthesia

Vad vet vi, evidensen för;

- **TIVA vs inhalation**
  - → Cancer
  - → POCD
  - → Ischemi/reperfusion
- **Opioider**
  - → PONV
  - → *”tillvänjning”*
  - → Cancer
  - → POCD
  - → I/R
- **Xylokain**
  - → Cancer
  - → POCD
  - → Ischemi/reperfusion
- **Dexmedetomidin**
  - → Cancer
  - → POCD
  - → Ischemi/reperfusion
- **Ketalar**
  - → Cancer
  - → POCD
  - → Ischemi/reperfusion

TIVA vs Inhalation

*Opiater effekter, påverkar **tumörceller, cancer/metastaser?***

Karolinska Institutet

TIVA vs Inhalation

- **Recurrence of breast cancer after regional**
  - → Daniel I Sessler 1 , Lijian Pei 2 , Yuguang Hua Tanja A Meyer-Treschan 7 , Martin Grady 6 , Recurrence Collaboration
  - → Lancet. 2019 Nov 16;394(10211):1807-1815
- Abstract
- Background: Three perioperative factor response, use of volatile anaesthetic, a tested the primary hypothesis that brea analgesia using paravertebral blocks a sevoflurane and opioid analgesia. A se
- Methods: We did a randomised control Singapore, and the USA. Women (age computer to either regional anaesthesi opioid analgesia. Pa pain at 6 months and Te ClinicalTrials.gov, NCT0041
- Findings: Between Jan 30, 2007, a surgery. 1043 were assigned to regiona characteristics were well balanced between regional anaesthesia-analgesia, 102 (10%) recu allocated general anaesthesia (hazard ratio 0·97, patients assigned to regional anaesthesia-analges and by 239 (28%) of 854 patients and 232 (27%) 1·00, 95% CI 0·85–1·17; p=0·99). Neuropathic bre 859 patients assigned to regional anaesthesia-ana months, and by 57 (7%) of 857 patients and 57 (7
- Interpretation:
  - → In our study population, regional **not reduce breast cancer recu volatile anaesthesia (sevoflura**
  - → The frequency and severity of pe technique.
  - → **Clinicians can use regional or recurrence and persistent incis**

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PERIOPERATIVE MEDICINE

ANESTHESIOLOGY

Total Intravenous Anesthesia *versus* Inhalation An Breast Cance

A Retrospective Coho

Seokha Yoo, M.D., Han-Byoel L Ph.D., Dong-Young Noh, M.D., Won Ho Kim, M.D., Ph.D., Jin-T

ANESTHESIOLOGY 2019; 130:31–4

Karolinska Institutet

ABSTRACT

Background: The association between type of anesthesia used and recurrence of cancer remains controversial. This retrospective cohort study compared the influence of total IV anesthesia and inhalation anesthesia on the primary outcome of recurrence-free survival after breast cancer surgery.

Methods: The authors reviewed the electronic medical records of patients who had breast cancer surgery at a tertiary care teaching hospital between January 2005 and December 2013. The patients were grouped according to whether IV or inhalation anesthesia was used for surgery. Propensity score matching was used to account for differences in baseline characteristics. Kaplan–Meier

Många retrospektiva studier

atile anesthesia

Riedel 4 5 6 , Global

atic disease
f adrenergic-
ts may translate into
f propofol
rtook a systematic

fect of inhalational

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improve
surgery

→ This is especially evident whe

→ **Nevertheless, given the this meta-analysis these randomized trials to gui**

Men PRCT behövs

Available data thus suggest that to the extent that propofol–total intravenous anesthesia reduces cancer recurrence and improves survival, benefit is most probable in patients having major cancer surgery. Similarly, adjuvant strategies targeting neural and inflammatory signaling (*e.g.*, neuraxial analgesia, β-blockers, nonsteroidal anti-inflammatory drugs, *etc.*), if helpful, are most likely to demonstrate benefit in patients having major rather than minor cancer surgery. Trials comparing cancer recurrence and survival with volatile and intravenous anesthesia for major cancer surgery are already in progress and are well worth doing, because even small reductions in cancer recurrence would save countless lives—and that from an intervention that is essentially cost-free and trivial to implement.

BJA

British Journal of Anaesthesia, 123 (2): 135–150 (2019)

doi: 10.1016/j.bja.2019.04.062

Advance Access Publication Date: 27 June 2019

Review Article

Karolinska Institutet

CLINICAL PRACTICE

Influence of perioperative anaesthetic and analgesic interventions on oncological outcomes: a narrative review

T. Wall[1,2,*], A. Sherwin[1,2], D. Ma[2,3] and D. J. Buggy[1,2,4]

- Despite the hypothesised cancer-stimulating effects of some opioids, it must be borne in mind that evidence exists that poorly controlled pain may drive malignant processes.
- The mechanism is unclear: it may be due to increased activity of both the SNS and the HPA axis, with the subsequent in-crease in circulating catecholamines and glucocorticoids attenuating the activity of immune cells.
- Clinically, poorly controlled pain or increased opioid requirements have retrospectively been associated with poorer survival in patients with advanced NSCLC.
- Therefore, the balance between the immunosuppressive effects of pain, on one hand, and opioids, on the other, may be the key to whether opioid treatment results in greater risk of cancer recurrence.

Br J Anaesth. 2019 Aug;123(2):135-150.

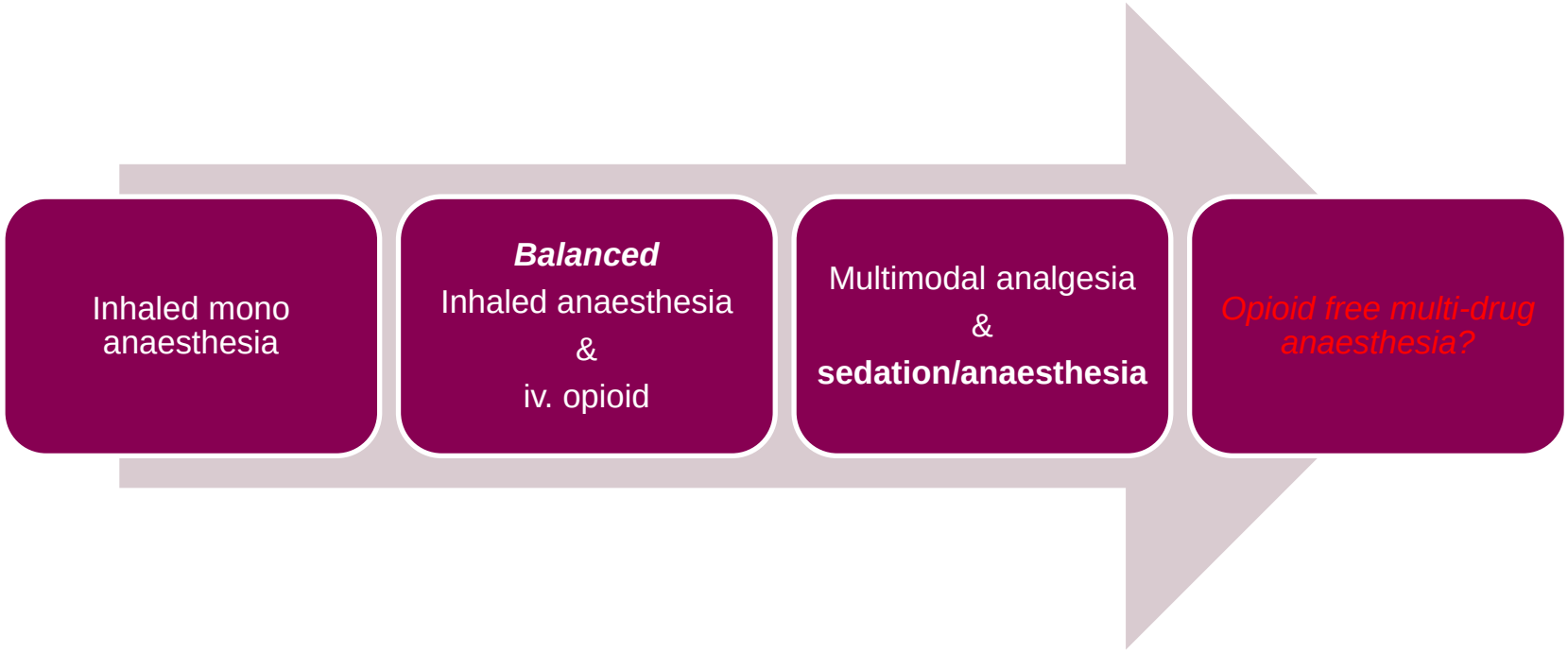
Evidensbaserade kliniska korttidseffekter

	Tidig PONV	Sen PONV	smärta	GI
Opiater	++	+	minskar	Stannar upp
Ketamin	+	0	minskar	0
Dexmeditomedin	0	0	?	?
Xylokain	0	0	+	Minskar ileus?
Mg	0	0	+	?

Evidensbaserade kliniska långtidseffekter

	Ischemi/ reperfusion	POCD	Cancer/ metastaser	Kronisk smärta
Opiater	?	?	-?	?
Ketamin	?	?	?	?
Dexmeditomedin	?	Minskar risk	?	?
Xylokain	?	?	?	?
Mg	?	?	?	?

Ska vi ändra ett paradigm?



Rev Bras Anestesiol. 2015;65(3):191–199

REVISTA BRASILEIRA DE ANESTESIOLOGIA

ELSEVIER

SCIENTIFIC ARTICLE

Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a pro … randomized, double-blinded study☆

Mefkur Bakan[a,*], Tarik Umutoglu[a], Ufuk Topuz[a], Mehmet Bayram[b], Huseyin Kadioglu[c], Ziya Salihc

OFA

Journal of Clinical Anesthesia and Pain Medicine

Scient Open Access

Research Article

A Randomized Controlled, Double-Blind Trial Evaluating the Effect of Opioid-Free Versus Opioid General Anaesthesia on Postoperative Pain and Discomfort Measured by the QoR-40

This article was published in the following Scient Open Access Journal:
Journal of Clinical Anesthesia and Pain Medicine
Received January 31, 2018; Accepted February 07, 2018; Published February 15, 2018

Jan P Mulier[1,2,3*], Ruben Wouters[1,2], Bruno Dillemans[4], Marc Dekock[4]

Abstract

KJA

Korean Journal of Anesthesiology

Letter to the Editor

pISSN 2005-6419 · eISSN 2005-7563

Opioid-free anesthesia using continuous dexmedetomidine and lidocaine infusions in spine surgery

David J. Kim[1], Raheel Bengali[2], and T. Anthony Anderson[1]

British Journal of Anaesthesia 112 (5): 906–11 (2014)
Advance Access publication 18 February 2014 · doi:10.1093/bja/aet551

BJA

Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis

P. Ziemann-Gimmel*, A. A. Goldfarb, J. Koppman and R. T. Marema

Is opioid-free general anesthesia for breast and gynecological surgery a viable option?

- Mulier JP[1,2,3]. Curr Opin Anaesthesiol. 2019 Jun;32(3):257-262.
- **PURPOSE OF REVIEW:** Opioid-free anesthesia (OFA) was introduced to avoid tolerance and hyperalgesia, allowing reduction in postoperative opioids. OFA focused initially on postoperative respiratory safety for patients undergoing ambulatory surgery and for obstructive sleep apnea syndrome patients otherwise requiring intensive care admission. What about using OFA in plastic and oncological breast surgery, in deep inferior epigastric perforators flap surgery, and in gynecological laparoscopy?
- **RECENT FINDINGS:**
- **OFA requires the use of other drugs to block the unwanted reactions from surgical injury.**
- **This can be achieved with a single drug at a high dose or with a combination of different drugs at a lower dose, such as with**
  - → **alpha-2-agonists,**
  - → **ketamine,**
  - → **lidocaine,**
  - → **magnesium,**
- **each working on a different target and therefore described as multitarget anesthesia.**
- ***Three factors can explain OFA success: improved analgesia with less postoperative opioids, the near absence of postoperative nausea and vomiting if no opioid is needed postoperatively, and reduced inflammation enhancing the recovery after surgery.***
- **SUMMARY:** Opioid-free general anesthesia is a viable option for breast and gynecological surgery and its use will only increase when anesthesiologists listen to their patients' experiences after undergoing surgery under general anesthesia.

Best Practice & Research Clinical Anaesthesiology 31 (2017) 533–545

Contents lists available at ScienceDirect

Best Practice & Research Clinical Anaesthesiology

journal homepage: www.elsevier.com/locate/bean

8

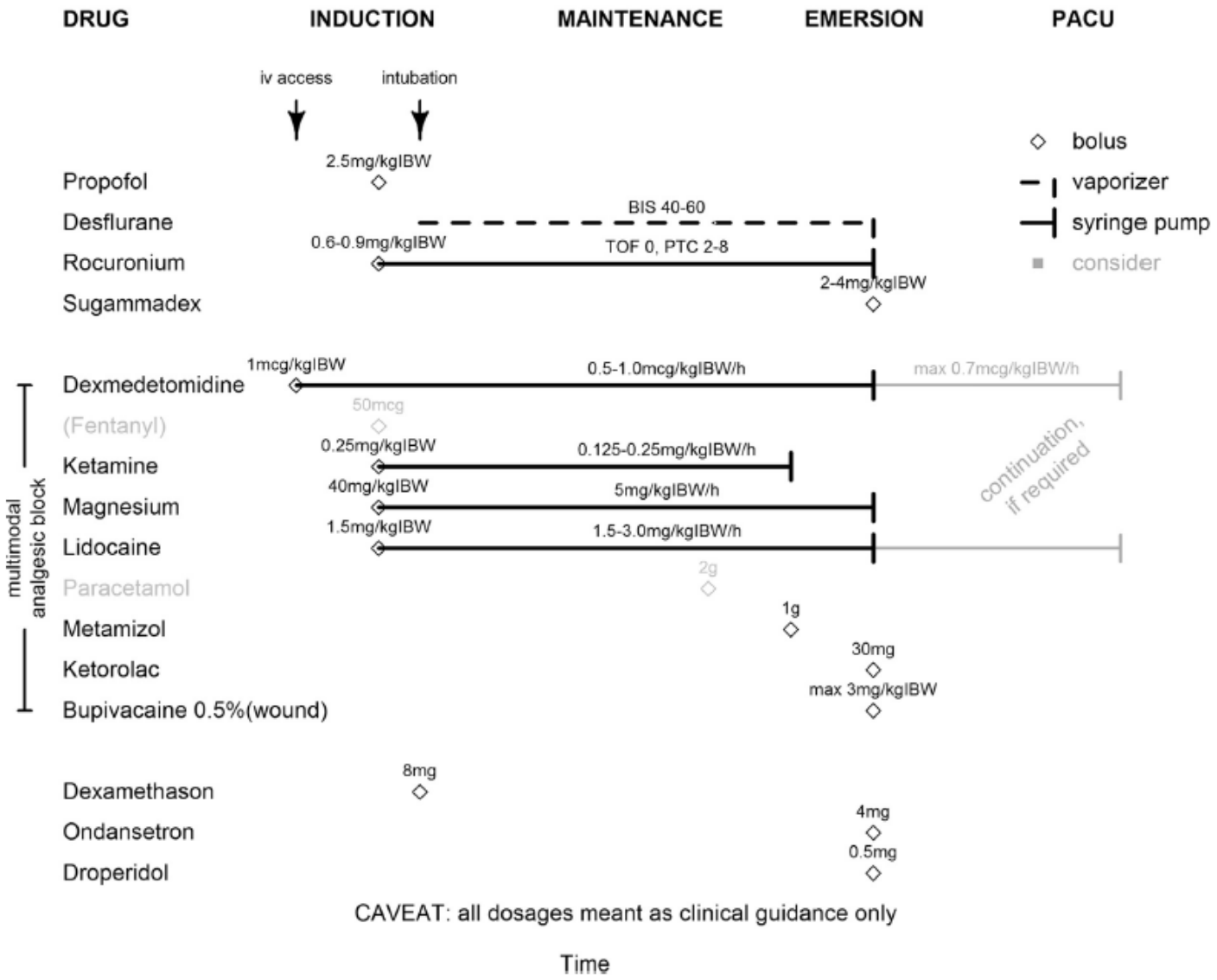
Different protocols used today to achieve total opioid-free general anesthesia without locoregional blocks

Eckhard Mauermann, MD, MSc, Postdoctoral Research Fellow [a, b],
Wilhelm Ruppen, MD, Chair of the Pain Relief Unit [a],
Oliver Bandschapp, MD, Consultant Anaesthetist [a, *]

[a] University Hospital Basel, Department for Anesthesia, Surgical Intensive Care, Prehospital Emergency Medicine and Pain Therapy, Spitalstrasse 21, 4031 Basel, Switzerland
[b] University Hospital Ghent, Department of Anesthesiology and Perioperative Medicine, Building K12-C 2nd Floor, De Pintelaan 185, B-9000, Ghent, Belgium

Best Practice & Research Clinical Anaesthesiology 31 (2017) 533–545

Timing and Dosing of Multimodal Analgesia for Bariatric Surgery



Anaesthesia 2019, 74, 651–662 doi:10.1111/anae.14582

Karolinska Institutet

Review Article

Analgesic impact of intra-operative opioids vs. opioid-free anaesthesia: a systematic review and meta-analysis

J. Frauenknecht,[1] **K. R. Kirkham,**[2] **A. Jacot-Guillarmod**[3] and **E. Albrecht**[4]

1 Resident, 3 Research Assistant, 4 Program Director of Regional Anaesthesia, Department of Anaesthesia, Lausanne University Hospital, Lausanne, Switzerland
2 Consultant, Department of Anaesthesia, Toronto Western Hospital, University of Toronto, Toronto, Canada

Summary

Opioids are administered peri-operatively for pos erative analgesia, and intra-operatively to control the sympathetic response to surgical stimuli, frequentl surrogate for presumed pain. However, opioid use during surgery is a matter of dispute in contemp actice and carries the risk of side-effects such as ated whether opioid-inclusive, compared with t increasing the rate of postoperative nausea ere searched until June 2018. We included of intra-operative opioid administration with nalyses were performed using a random effects model. We rated the quality of evidence for each ome. The primary outcome was pain score at rest (analogue scale, 0–10) at two postoperative hours. C secondary outcomes included the rate of postoperative nausea and vomiting within the first 24 postoperative hours and length of stay in the recovery area. Twenty-three randomised controlled trials, including 1304 patients, were identified. Pain scores at rest at two postoperative hours were equivalent in the opioid-inclusive and opioid-free groups with a mean difference (95%CI) of 0.2 (−0.2 to 0.5), I^2 = 83%, p = 0.38 and a high quality of evidence. Similarly, there was high-quality evidence that the rate of postoperative nausea and vomiting was reduced in the opioid-free group, with a risk ratio (95%CI) of 0.77 (0.61–0.97), I^2 = 16%, p = 0.03 and high-quality evidence for a similar length of stay in the recovery area, the mean difference (95%CI) being 0.6 (−8.2 to 9.3), min, I^2 = 60%, p = 0.90. As there is strong evidence that opioid-inclusive anaesthesia does not reduce postoperative pain, but is associated with more postoperative nausea and vomiting, when compared with opioid-free anaesthesia, we suggest that anaesthetists should reconsider their intra-operative opioid choices on a case-by-case basis.

..intraoperativ opiat påverkar inte postoperativ smärta

Anaesthesia 2019, 74, 651–662 doi:10.1111/anae.14582

Review Article

Analgesic impact of intra-operative opioids vs. opioid-free anaesthesia: a systematic review and meta-analysis

J. Frauenkne

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Karolinska Institutet

Analgesic impact of intra-operative opioids vs. opioid-free anaesthesia: a systematic review and meta-analysis.

- Frauenknecht J[1], Kirkham KR[2], Jacot-Guillarmod A[1], Albrecht E[1]. Anaesthesia. 2019 May;74(5):651-662
- **Abstract**

Opioids are administered peri-operatively for postoperative analgesia, and intra-operatively to control the sympathetic response to surgical stimuli, frequently as a surrogate for presumed pain. However, opioid use during surgery is a matter of dispute in contemporary practice and carries the risk of side-effects such as postoperative nausea and vomiting. This meta-analysis investigated whether opioid-inclusive, compared with opioid-free anaesthesia, would reduce postoperative pain, without increasing the rate of postoperative nausea and vomiting. The electronic databases Medline and PubMed were searched until June 2018. We included trials investigating pain outcomes and comparing any type of intra-operative opioid administration with placebo injection or no intra-operative opioid. Most meta-analyses were performed using a random effects model. We rated the quality of evidence for each outcome. The primary outcome was pain score at rest (analogue scale, 0-10) at two postoperative hours. Our secondary outcomes included the rate of postoperative nausea and vomiting within the first 24 postoperative hours and length of stay in the recovery area. Twenty-three randomised controlled trials, including 1304 patients, were identified. Pain scores at rest at two postoperative hours were equivalent in the opioid-inclusive and opioid-free groups with a mean difference (95%CI) of 0.2 (-0.2 to 0.5), I^2 = 83%, p = 0.38 and a high quality of evidence. Similarly, there was high-quality evidence that the rate of postoperative nausea and vomiting was reduced in the opioid-free group, with a risk ratio (95%CI) of 0.77 (0.61-0.97), I^2 = 16%, p = 0.03 and high-quality evidence for a similar length of stay in the recovery area, the mean difference (95%CI) being 0.6 (-8.2 to 9.3), min, I^2 = 60%, p = 0.90.

- *As there is strong evidence that:*
  - → ***opioid-inclusive anaesthesia does not reduce postoperative pain,***
  - → ***but is associated with more postoperative nausea and vomiting, when compared with opioid-free anaesthesia,***
- *we suggest that anaesthetists should reconsider their intra-operative opioid choices on a case-by-case basis.*

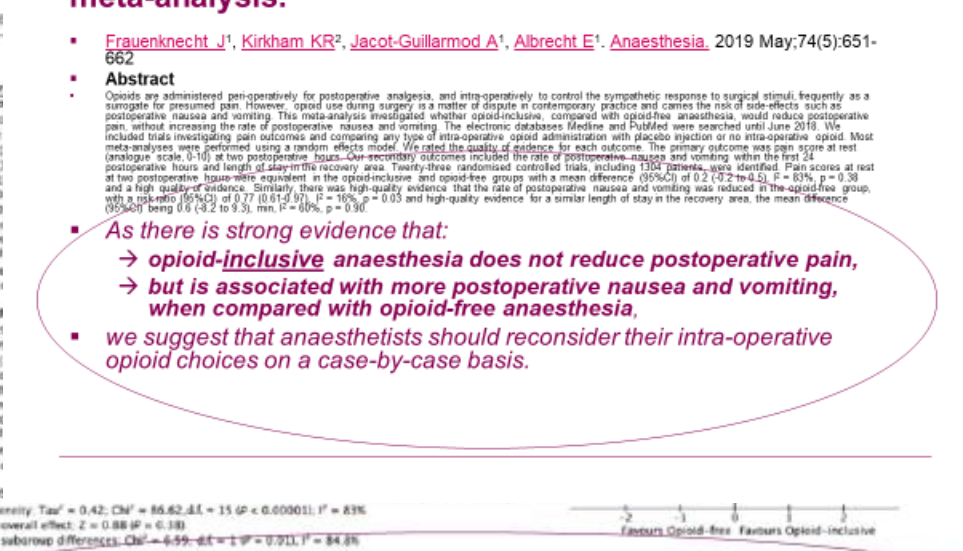

Figure 3 Pain score at rest at two postoperative hours according to the type of intra-operative opioid regimen (remifentanil vs. other opioid).

Anaesthesia 2019, 74, 793–800 doi:10.1111/anae.14657

Review Article

Intra-operative analgesia with remifentanil vs. dexmedetomidine: a systematic review and meta-analysis with trial sequential analysis

S. Grape,[1] **K. R. Kirkham,**[2] **J. Frauenknecht**[3] and **E. Albrecht**[4]

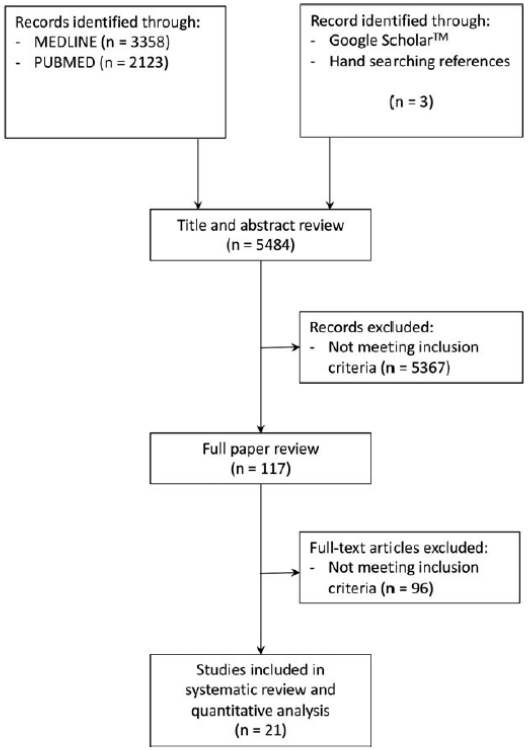

Figure 1 PRISMA flow diagram showing literature search results.

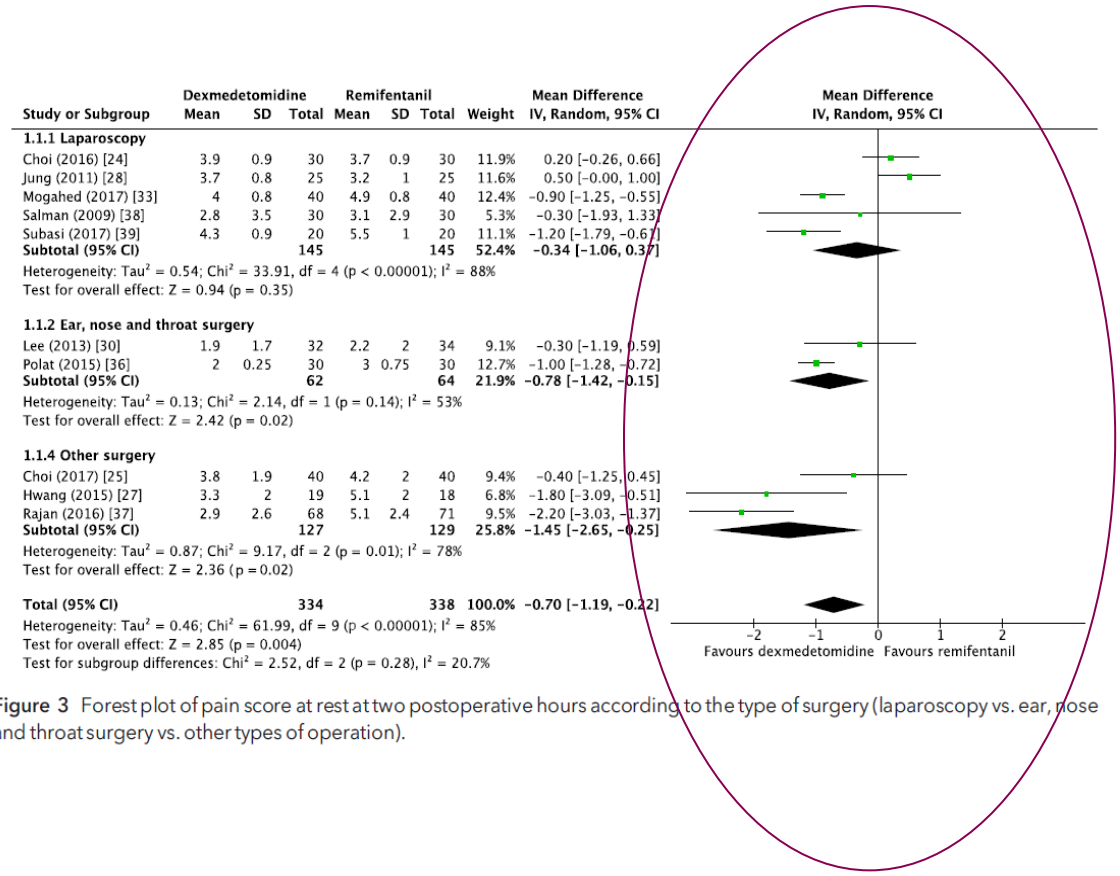

Figure 3 Forest plot of pain score at rest at two postoperative hours according to the type of surgery (laparoscopy vs. ear, nose and throat surgery vs. other types of operation).

Anaesthesia 2019, 74, 793–800 doi:10.1111/anae.14657

Review Article

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Records ident
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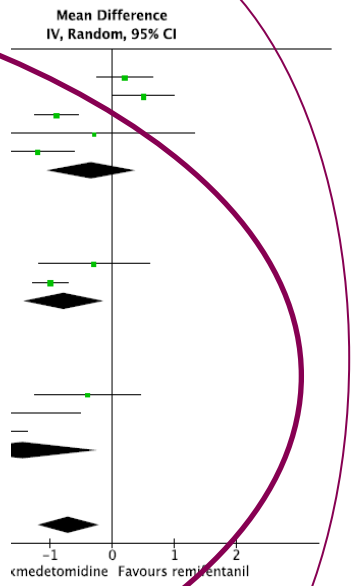
Discussion

This systematic review and meta-analysis investigated the effect of intra-operative dexmedetomidine on postoperative pain when compared with intra-operative remifentanil. Based on 21 randomised controlled trials, which included a total of 1309 patients, we demonstrated that dexmedetomidine was superior to remifentanil with improved pain outcomes in the immediate postoperative period, and for up to 24 postoperative hours. Furthermore, dexmedetomidine was associated with significantly fewer episodes of hypotension, shivering and postoperative nausea and vomiting. Although no difference for pain at rest



of surgery (laparoscopy vs. ear, nose

Figure 1 Pl
results.

REVIEW ARTICLE

ANESTHESIOLOGY

Perioperative Opioid Administration

A Critical Review of Opioid-free *versus* Opioid-sparing Approaches

Harsha Shanthanna, M.D., Ph.D., F.R.C.P.C.,
Karim S. Ladha, M.D., M.Sc., F.R.C.P.C.,
Henrik Kehlet, M.D., Ph.D.,
Girish P. Joshi, M.B.B.S., M.D., F.F.A.R.C.S.I.

ANESTHESIOLOGY 2021; 134:645–59

April 2021

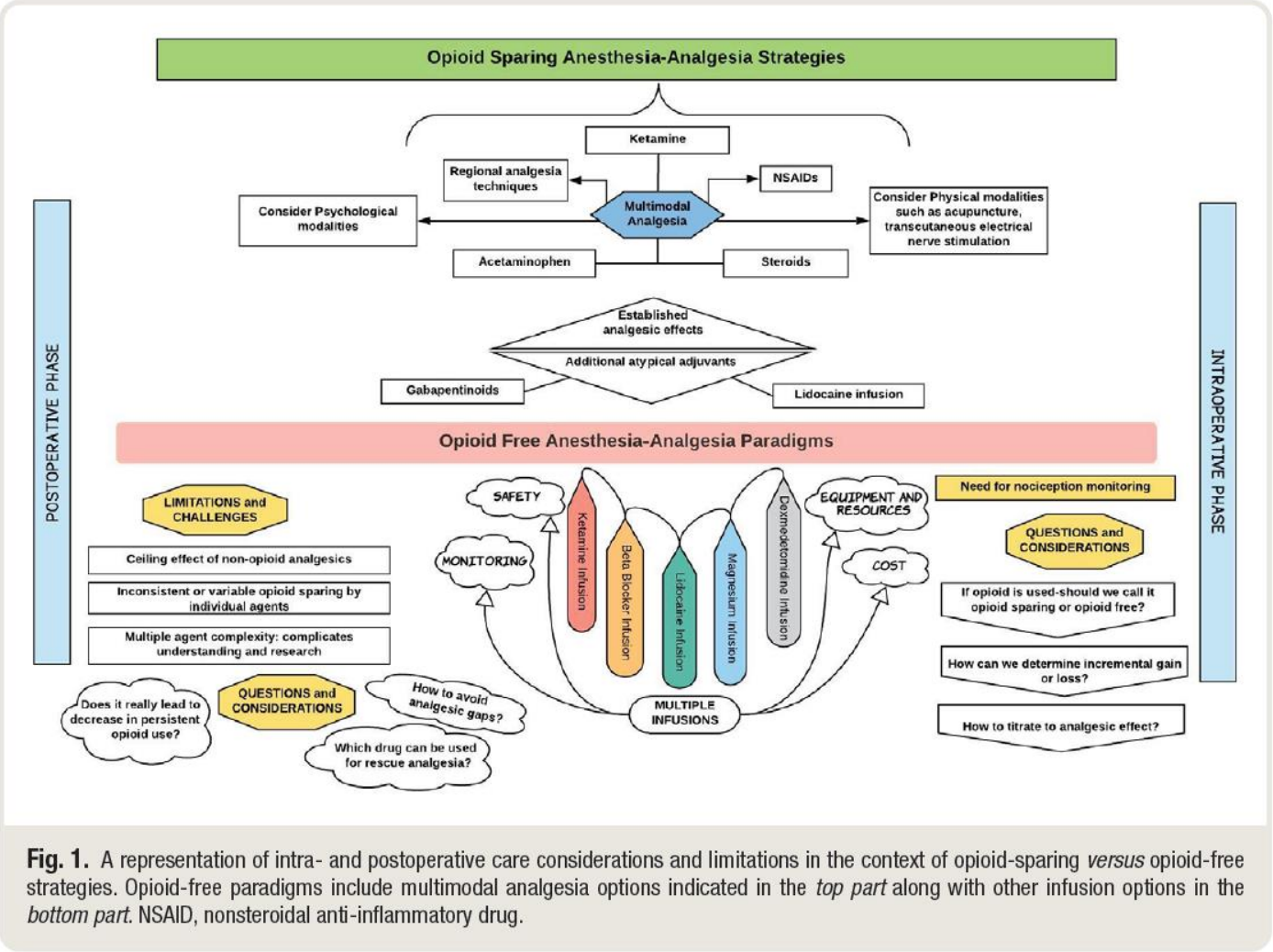


Fig. 1. A representation of intra- and postoperative care considerations and limitations in the context of opioid-sparing *versus* opioid-free strategies. Opioid-free paradigms include multimodal analgesia options indicated in the *top part* along with other infusion options in the *bottom part*. NSAID, nonsteroidal anti-inflammatory drug.

April 2021

Is Complete Opioid Sparing Possible in the Context of Existing Multimodal Opioid-sparing Strategies?

Yes, but only in some contexts and procedures. Opioid use during surgery is not a must; for example, surgeries can be performed under neuraxial anesthesia or effective regional analgesia. Similarly, some outpatient procedures can be opioid-free in their postoperative period and after discharge. However, individual titration of analgesics based on patient needs is important.

Shanthanna H, Ladha KS, Kehlet H, Joshi GP. Perioperative Opioid Administration. Anesthesiology. 2021 Apr 1;134(4):645-659. doi: 10.1097/ALN.0000000000003572. PMID: 32991672.

Conclusions

Do Opioid-free Strategies Have Benefits beyond and above Opioid-sparing Strategies?

April 2021

To date, there is no evidence. Multimodal analgesia can lead to significant opioid sparing. At this time, the clinical benefits of such limited opioid use do not outweigh the challenges and limitations associated with the suggested opioid-free strategies.

Shanthanna H, Ladha KS, Kehlet H, Joshi GP. Perioperative Opioid Administration. Anesthesiology. 2021 Apr 1;134(4):645-659. doi: 10.1097/ALN.0000000000003572. PMID: 32991672.

Anestesiteknik 2021?

	Peroperativt		Postoperativt
Underhåll	Inhalation	Intravenös	
Analgesi	?	?	*Opiat rescue*
Analgesi	Multimodal opiatsparande analgesi	Multimodal opiatsparande analgesi	Multimodal opiatsparande analgesi

Opioidfri per- och postoperativ smärtlindring?

- Vad är:
  - → Önskvärt – fortfarande oklart
  - → Möjligt – *ja men kräver kunskap och troligen flera alternativa läkemedel*
  - → Rimligt – *öppen fråga*

..kanske viktigare vad är
nyttan och riskerna med opiatfri anestesi
- perioperativt omhändertagande

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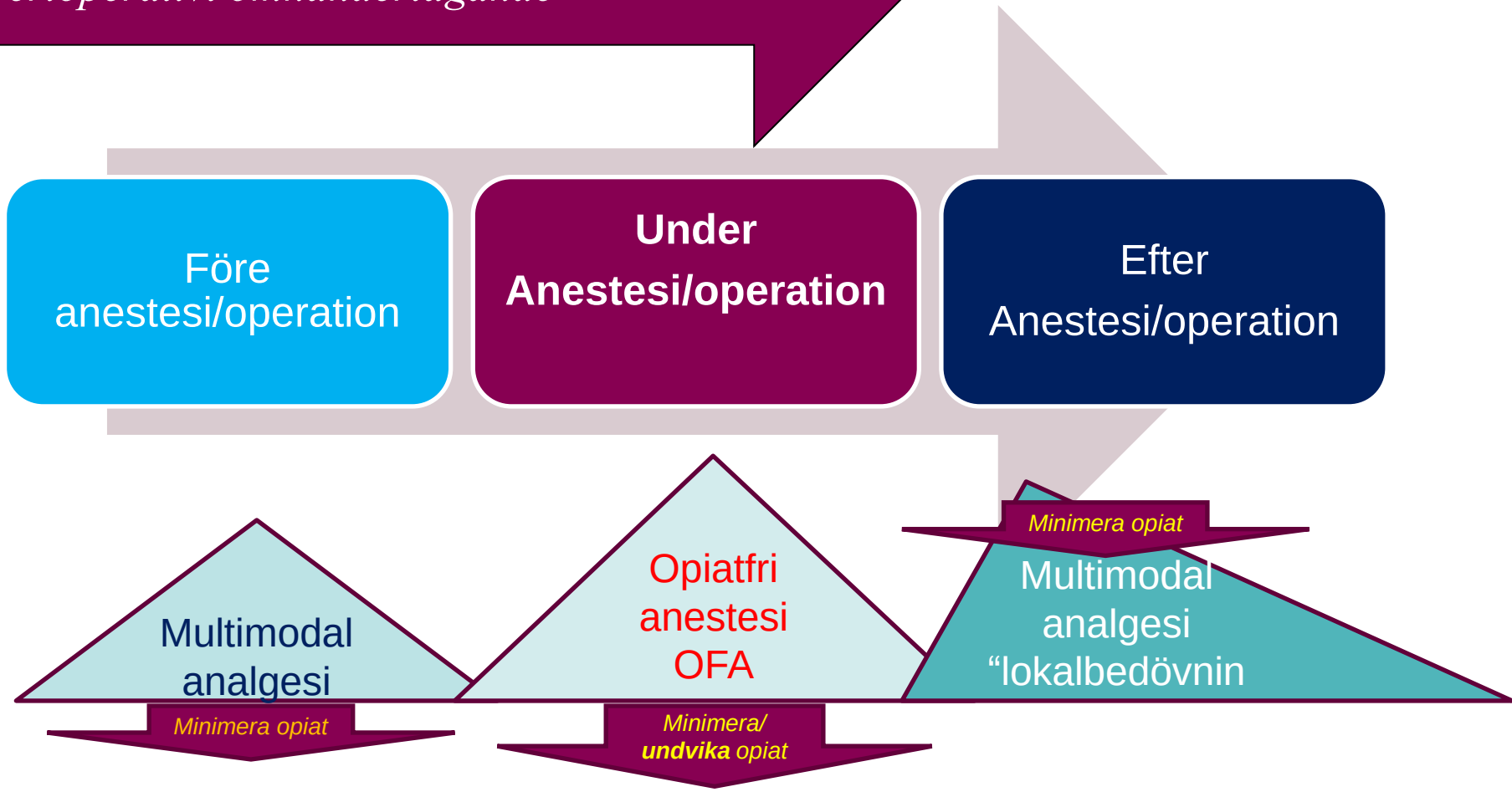

Opportunity for studies

SweERAS or SPOR