Out with the Old and In with the New? A critical appraisal of Opiate Free TIVA in Bariatric Anaesthesia

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CONFLICT OF INTEREST DISCLOSURE

If you don't have any conflict, please delete the conflict of interest report points:

I have no potential conflict of interest to report

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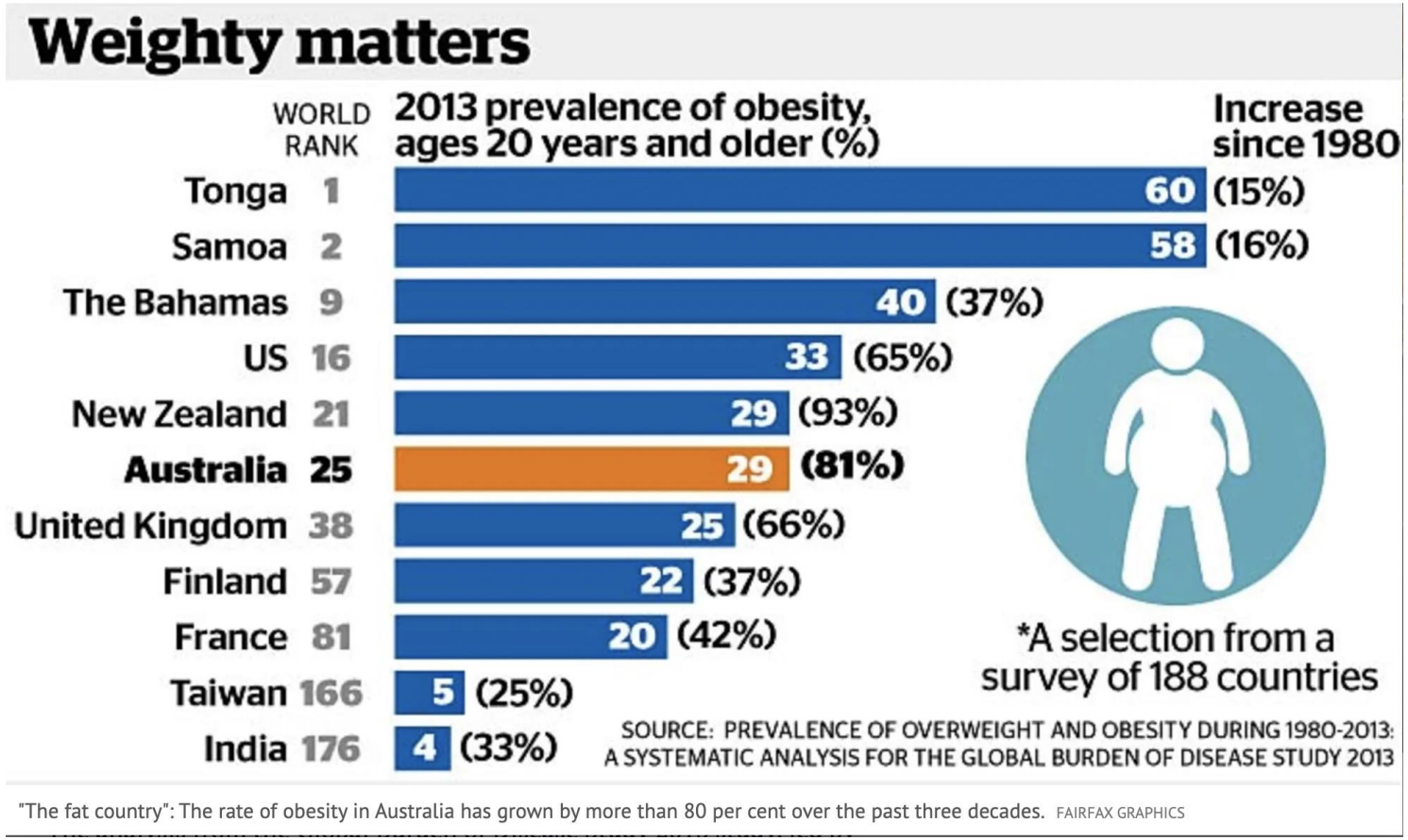
International Incidence of Obesity



https://www.smh.com.au/lifestyle/obesity-rates-soar-in-australia-a-global-survey-reveals-20140528-394s4.html

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Incidence of Obesity over time

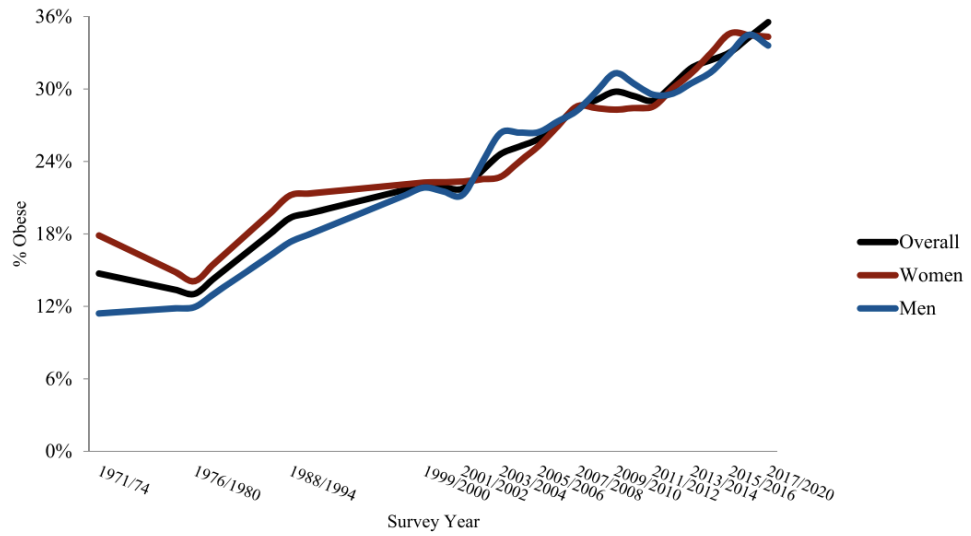

Fig. 2. Historical trends in obesity for adults age 20+ years, 1971–2020: NHANES

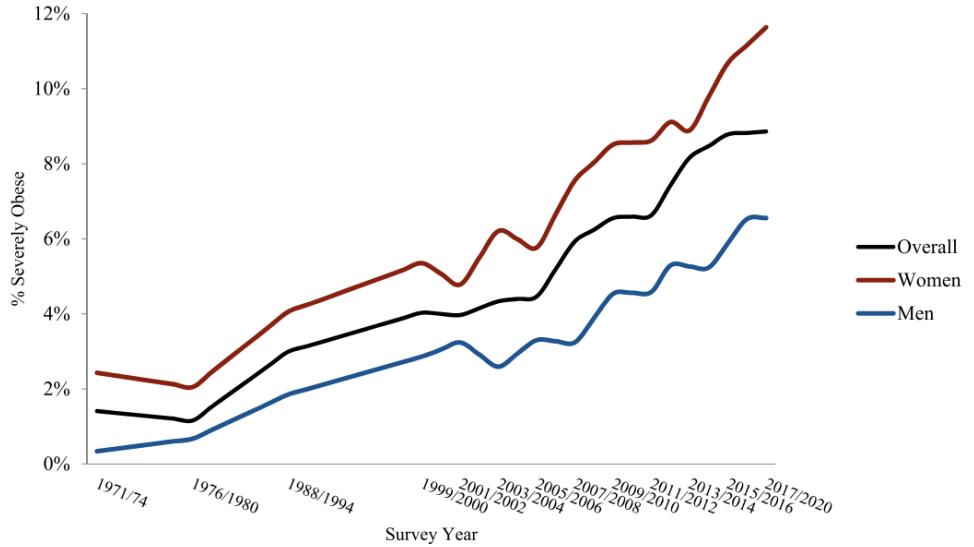

Fig. 3. Historical trends in severe obesity for adults age 20+ years, 1971–2020: NHANES

Ashley W. Kranjac Explaining adult obesity, severe obesity, and BMI: Five decades of change Heliyon 9 (2023) e16210

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Incidence Obesity in Australia 2022 by region

Figure 2: Proportion of adults aged 18 and over with a waist circumference indicating increased risk of metabolic complications, by age group and sex, 2022

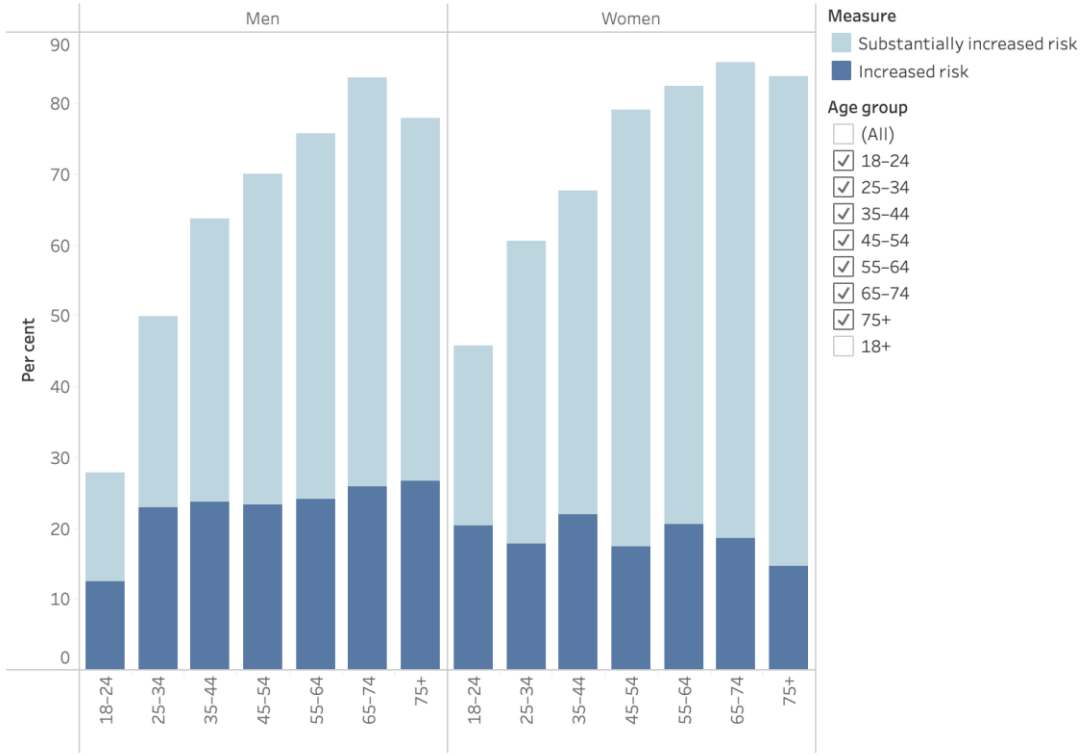
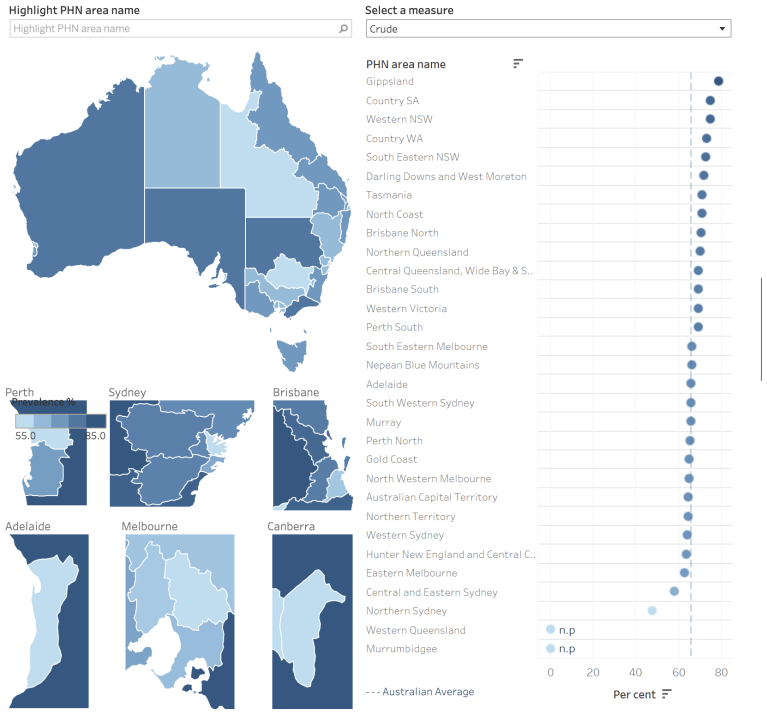


Figure 7: Age-standardised proportion of adults living with overweight and obesity, by remoteness area, 2017–18



† Interpret with caution — The 2022 National Health Survey excluded very remote areas.

https://www.aihw.gov.au/reports/overweight-obesity/overweight-and-obesity/contents/overweight-and-obesity

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Consequences of Obesity: Multi-system disorder

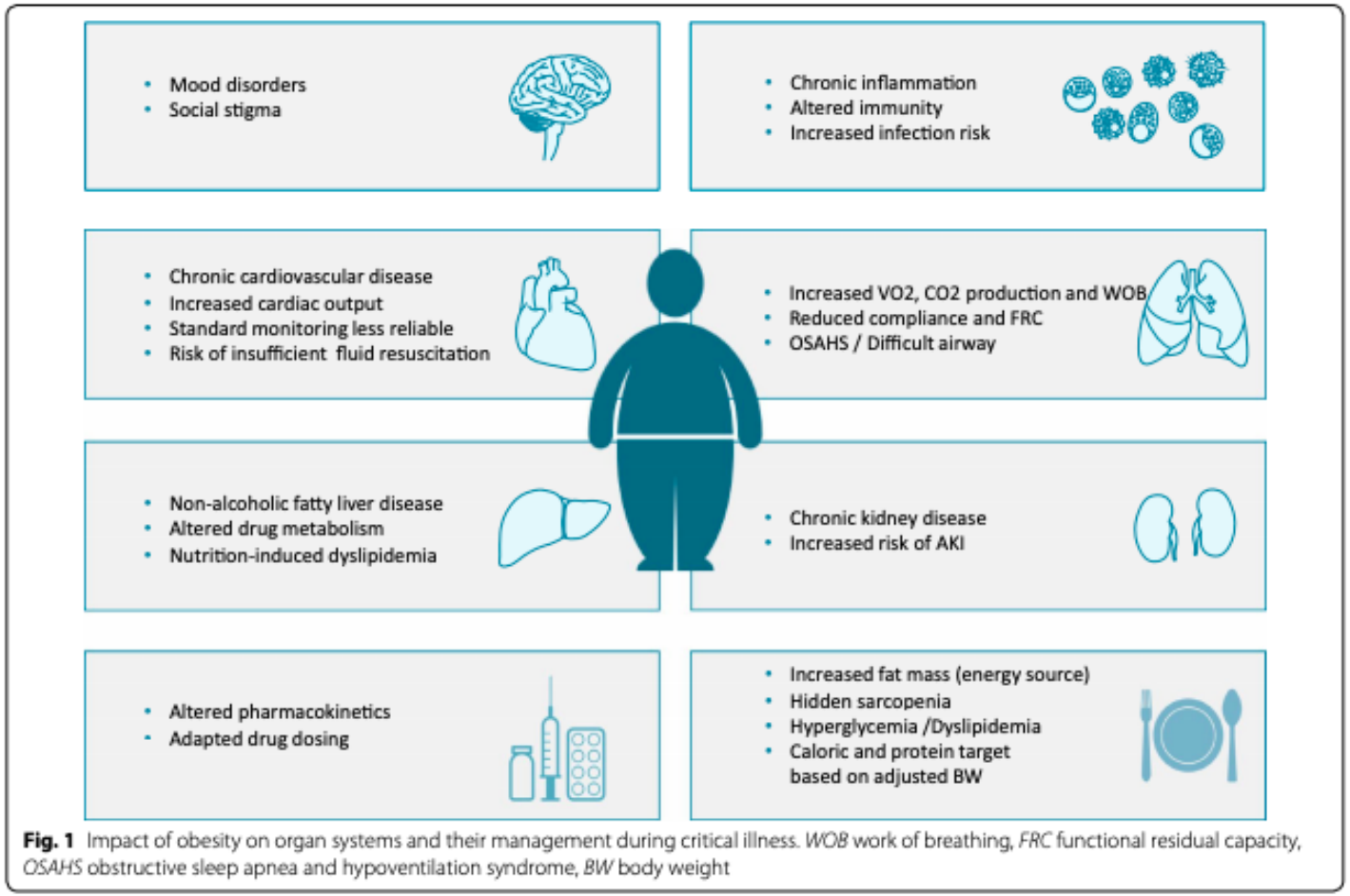
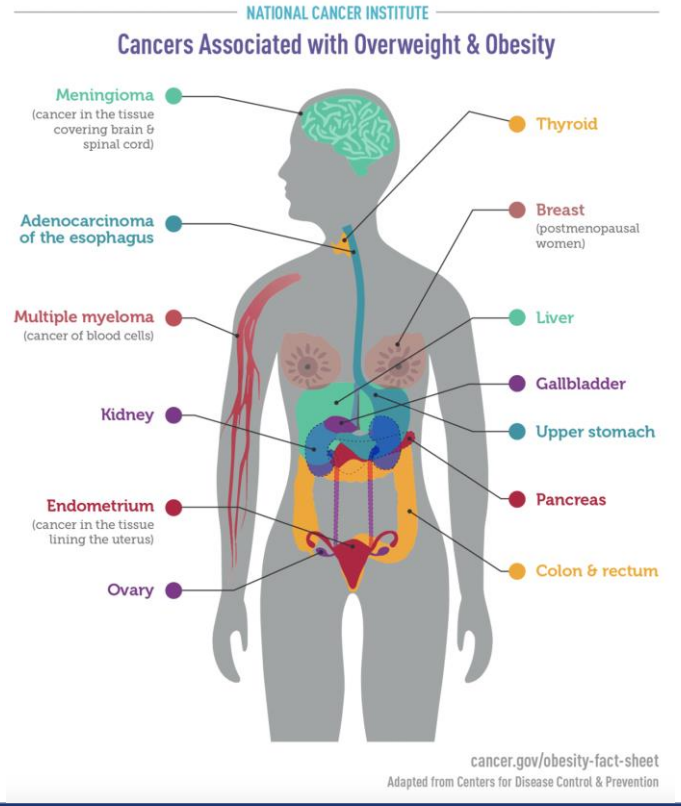


Fig. 1 Impact of obesity on organ systems and their management during critical illness. *WOB* work of breathing, *FRC* functional residual capacity, *OSAHS* obstructive sleep apnea and hypoventilation syndrome, *BW* body weight

Obesity in the critically ill: a narrative review
Intensive Care Med (2019) 45:757–769



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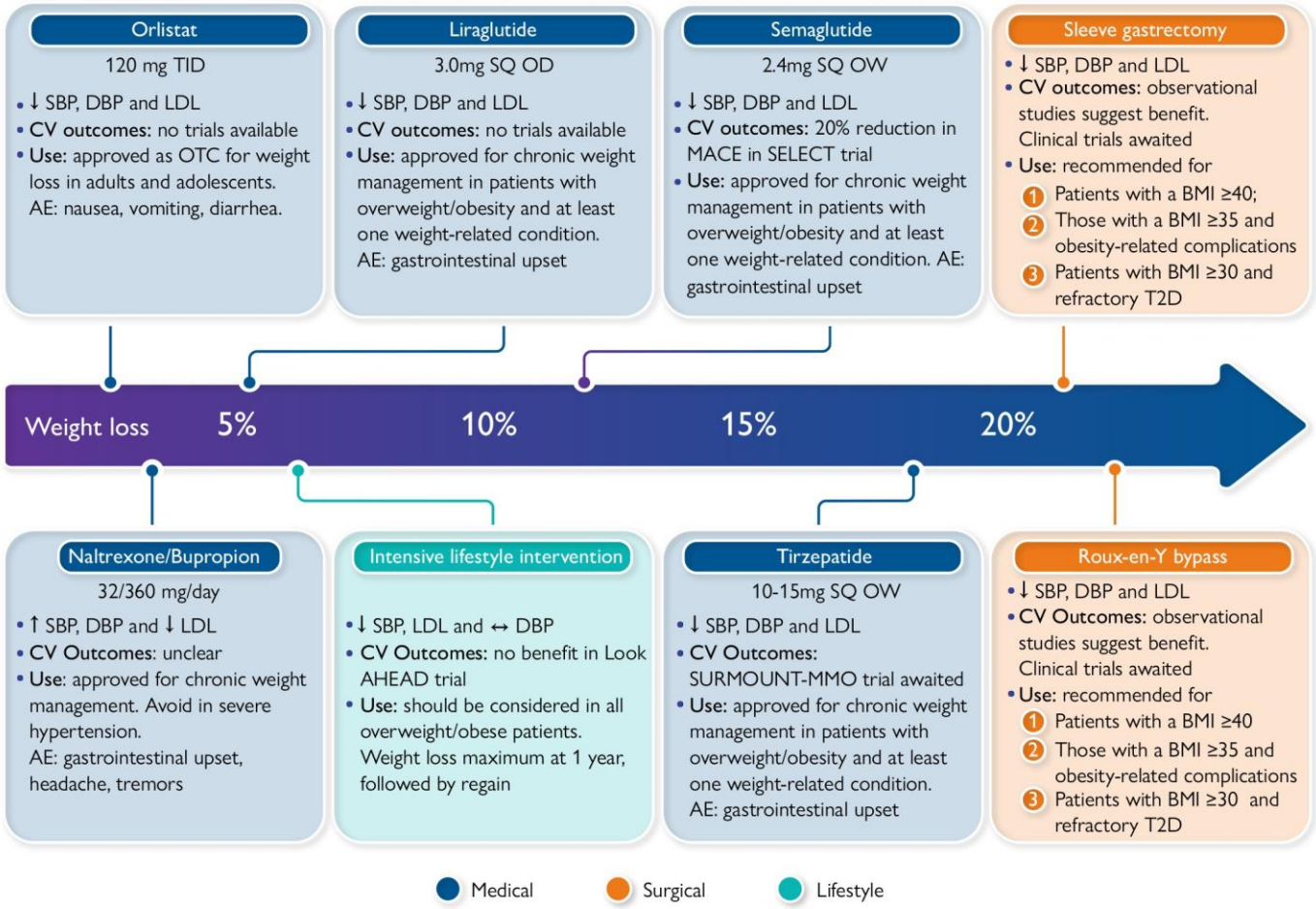
Medical and Surgical Management of Obesity



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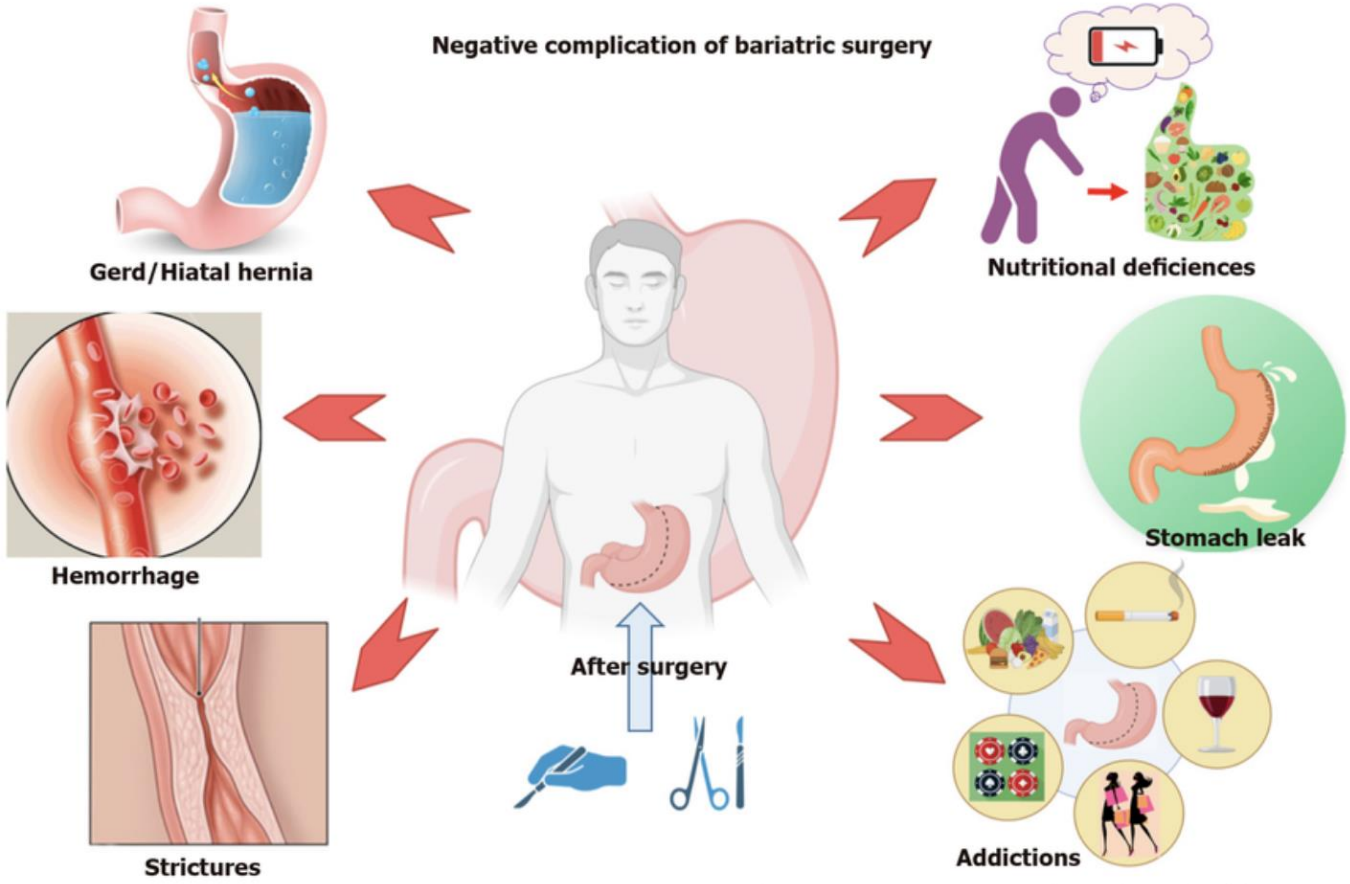
Bariatric Surgical Complications



DOI: 10.12998/wjcc.v11.i19.4504

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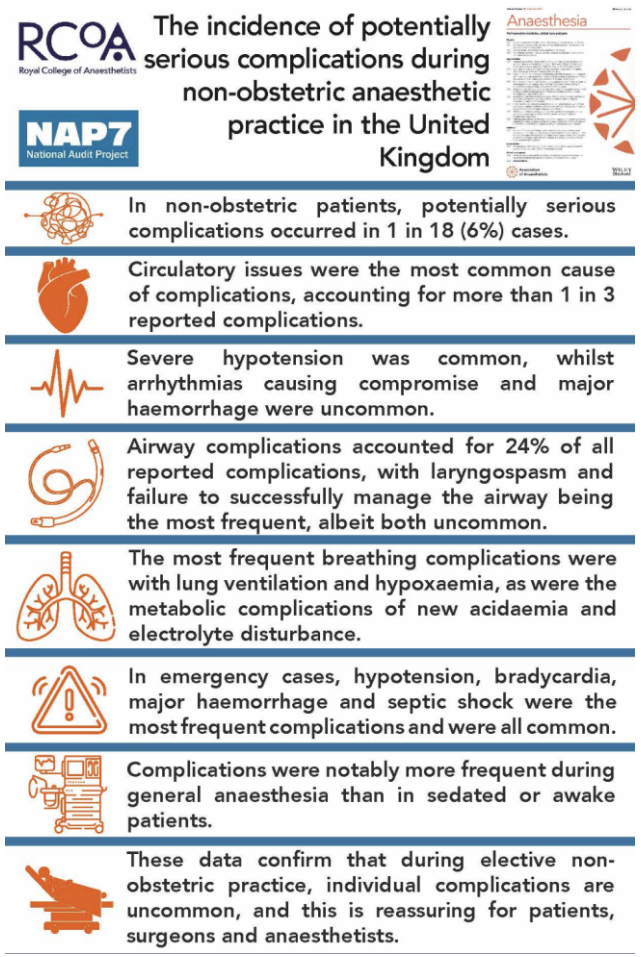
Anaesthetic Complications



Anaesthesia 2024, 79, 43–53 doi:10.1111/anae.16155

Original Article

The incidence of potentially serious complications during non-obstetric anaesthetic practice in the United Kingdom: an analysis from the 7th National Audit Project (NAP7) activity survey

A. D. Kane, T. M. Cook R. A. Armstrong, E. Kursumovic, M. T. Davies, S. Agarwal, J. P. Nolan, J. H. Smith, I. K. Moppett, F. C. Oglesby, L. Cortes, C. Taylor, J. Cordingley, J. Dorey, S. J. Finney, G. Kunst, D. N. Lucas, G. Nickols, R. Mouton, B. Patel, V. J. Pappachan, F. Plaat, B. R. Scholefield, L. Varney, J. Soar,* and **collaborators****

Out with the Old and In with the New? A critical appraisal of Opiate Free TIVA in Bariatric Anaesthesia

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- **Total Intravenous Anaesthesia (TIVA) v's Volatile Anaesthesia**
- **Opiate Free TIVA v's Opiate TIVA**

Out with the Old and In with the New? A critical appraisal of Opiate Free TIVA in Bariatric Anaesthesia

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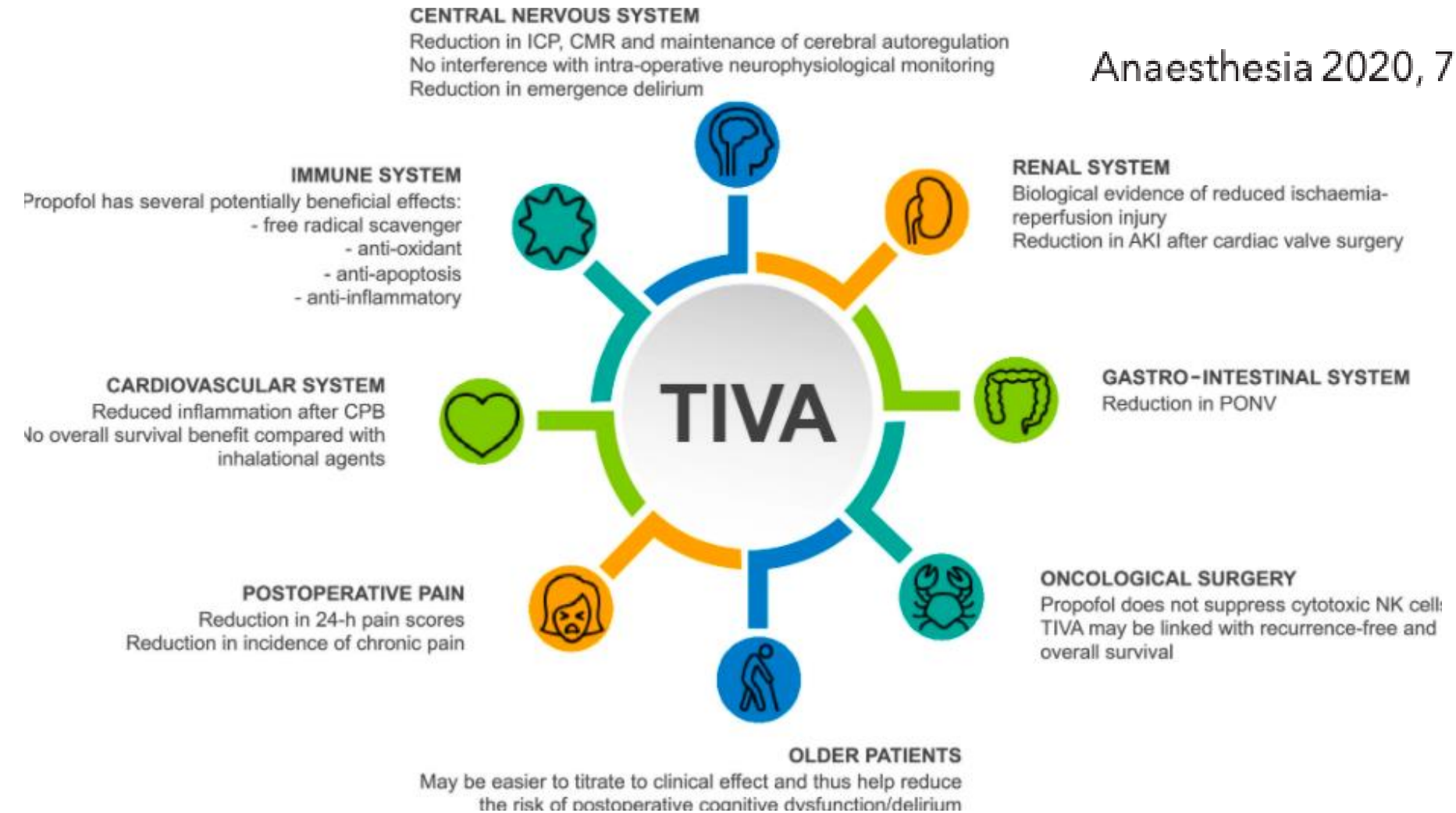

Anaesthesia 2020, 75 (Suppl. 1), e90–e100

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Increasing the utility of target-controlled infusions:one model to rule them all

Table 1 Number and diversity of volunteers and patients included in some target-controlled-infusion models for propofol and remifentanil

Model	Number of patients	Age range (yr)	Weight range (kg)	Number of blood samples	Number of model parameters
Propofol					
Marsh[3,4]	16	25–65	48–84	481	7
Schnider[5]	24	25–81	44–123	1006	11
Eleveld[6]	1033	0.5–82	0.68–160	15 433	18
Remifentanil					
Minto[7]	60	20–85	45–106	1992	11
Eleveld[8]	131	5 days–85	2–106	2634	12
Kim[9]	229	20–85	45–215	4455	9

T. G. Short, D. Campbell and T. D. Egan, British Journal of Anaesthesia, 120 (5): 887e890 (2018)

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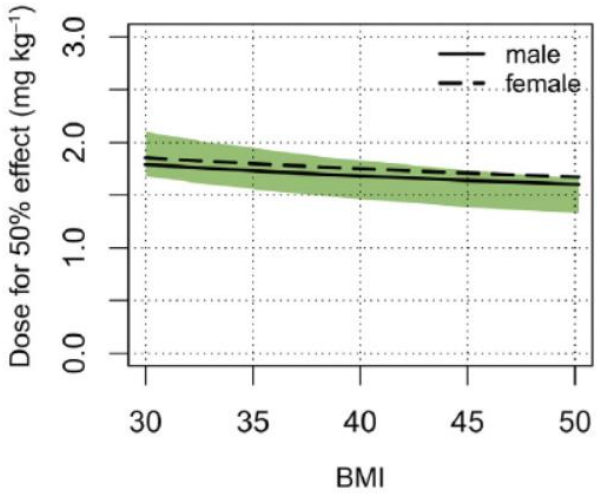
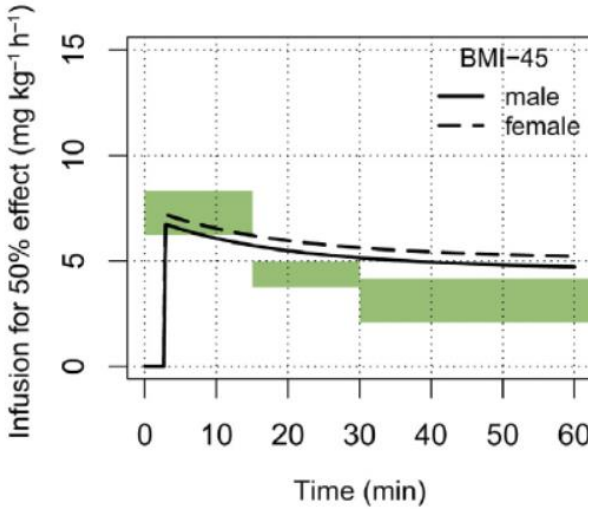
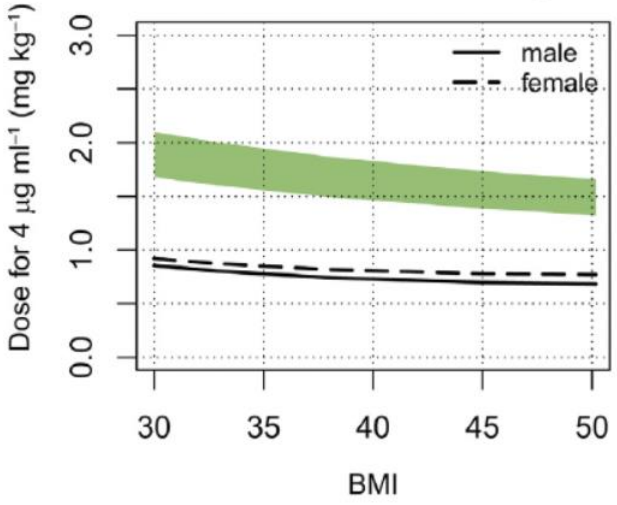
Pharmacokinetic-pharmacodynamic model for Propofol

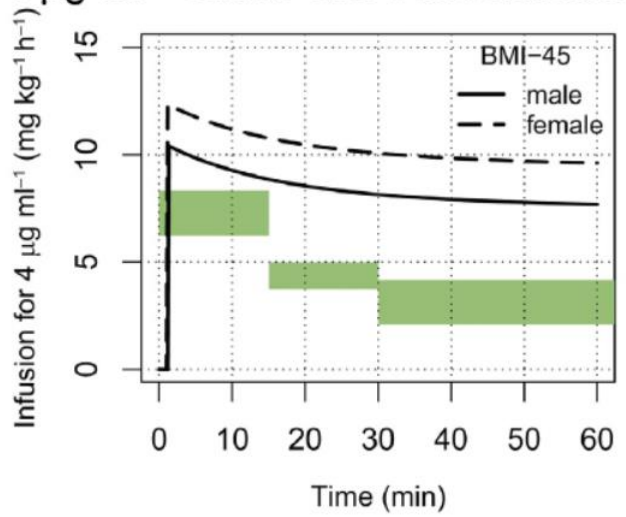
Eleveld PK–PD model targeting 50% drug effect





Schnider PK–PD model targeting 4 μg ml⁻¹ effect–site concentration





D. J. Eleveld, British Journal of Anaesthesia, 120 (5): 942-959 (2018)

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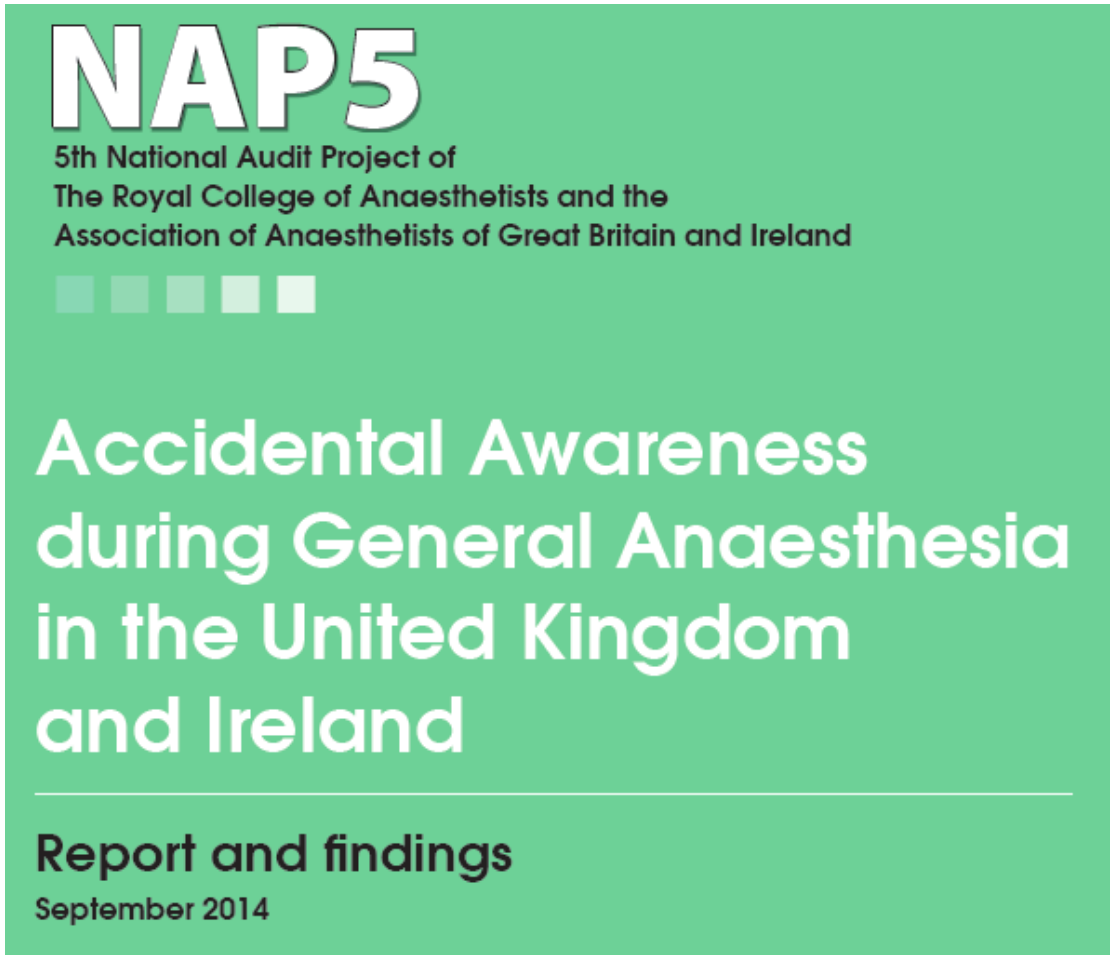

- Risk Factors for Accidental awareness during general anaesthesia (AAGA):
- **Neuromuscular Blockade**
- Thiopental
- ***Female Gender***
- ***Age (Adults>Children)***
- ***Obesity***
- Previous AAGA
- ***Difficult Airway Management***
- ***Total Intravenous Anaesthesia***
  - Non-Target Controlled Infusion (TCI)
  - Failure to deliver intended dose
    - Disconnection or ***Tissued IV line***
    - Transfer outside Theatre

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Propofol and survival: an updated meta-analysis of randomized trials

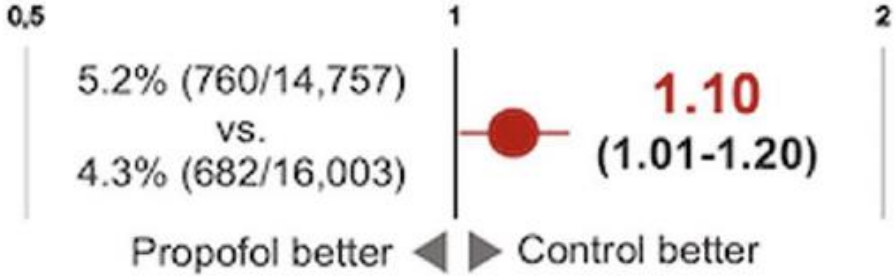
DATA SOURCE 252 RCTs with 30,757 patients

COMPARISON

INTERVENTION	CONTROL
Propofol	Any comparator

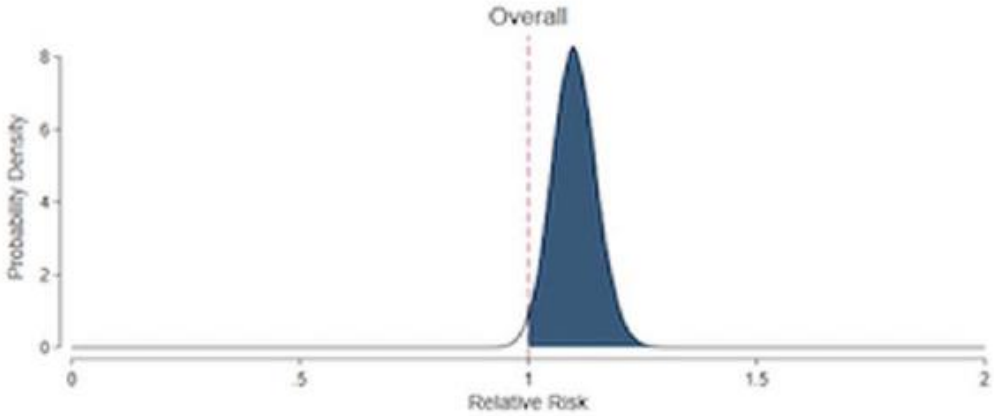
RESULTS

Risk ratio
(95% confidence interval)



Number Needed to Harm = 235

Propofol vs. control
The probability of relative risk of mortality >1.0 = 98.4%



CONCLUSIONS

Propofol likely reduces survival with a number needed to harm of 235.

Yuki Kotani Critical Care (2023) 27:139

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On the horns of a dilemma: TIVA or Volatile

- Rune P. Hasselager British Journal of Anaesthesia, 129 (3): 416e426 (2022)
  - Observational Cohort of 22179 patients Colorectal Surgery from 2004 to 2018
  - Fewer complications with Volatile (22.2% to 25.2%, OR 0.84 CI 0.79-0.91)
  - Wound Breakdown, Anastomotic Leak, Ileus, Wound Abscess. Sepsis
- Explanation
  - More spinal reflexes with TIVA and greater Patient movement
  - Anti-inflammatory and anti-angiogenic TIVA less wound healing
- Balance of late cancer recurrence against wound healing
- Trials in process
  - THRIVE trial (USA), VITALS trial (UK), VAPOR-C Trial (Australia)

Bernhard Riedel British Journal of Anaesthesia, 129 (3): 284e289 (2022)

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Opiate or Opiate Free TIVA

- 8000 year-old hardened Sumerian clay-tablets are the earliest prescriptions of opium (https://www.neurology.org/doi/10.1212/WNL.92.15_supplement.P4.9-055)
- Postoperative respiratory depression and Airway obstruction
- Postoperative ileus (POI) & Postoperative nausea and vomiting (PONV)
- Hyperalgesia
- Inflammation modulation & immune depression especially in oncology surgery
- Poor postoperative analgesia & increased consumption of morphine
- Pruritus
- Urinary retention
- Post operative shivering
- Prolonged length of hospital stay (LOS)

Joel Noutakdie Tochie BMC Anesthesiology (2022) 22:325

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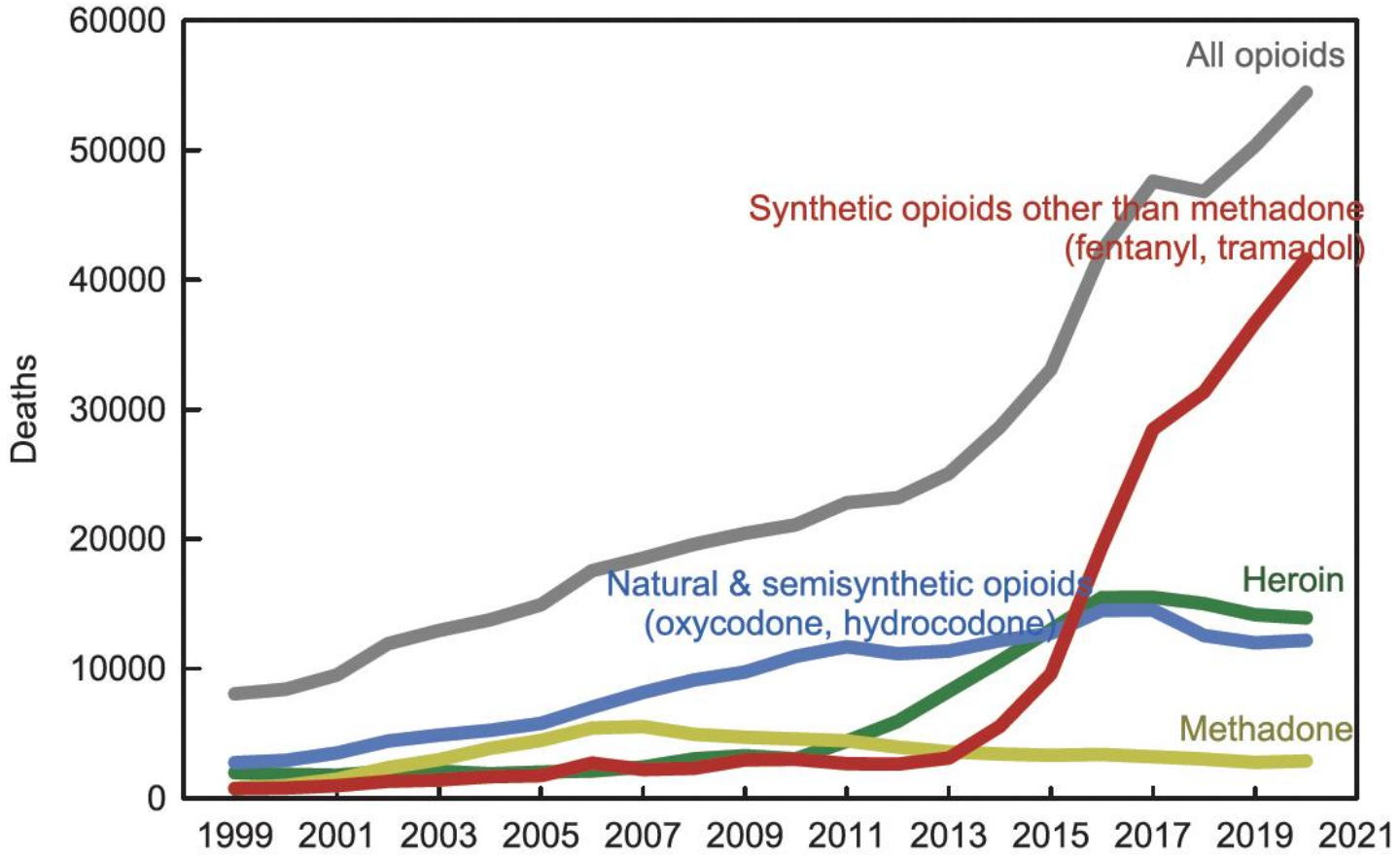

Fig. 1. U.S. drug overdose deaths involving opioids 1999 to 2020 (November), by type of opioid. The data can be accessed at https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm.

Evan D. Kharasch

Opioid-free Anesthesia:

Time to Regain Our Balance

ANESTHESIOLOGY, V 134

NO 4 April 2021 509

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Opiate or Opiate Free TIVA

- Pubmed Publications on Opiate Free TIVA
  - 2010 to 2015: 100
  - 2015 to 2021: 200
- Agents used
  - Dexmedetomidine
  - Ketamine
  - Lignocaine

Harsha Shanthanna, A Critical Review of Opioid-free versus Opioid-sparing Approaches Anesthesiology 2021; 134:645–59

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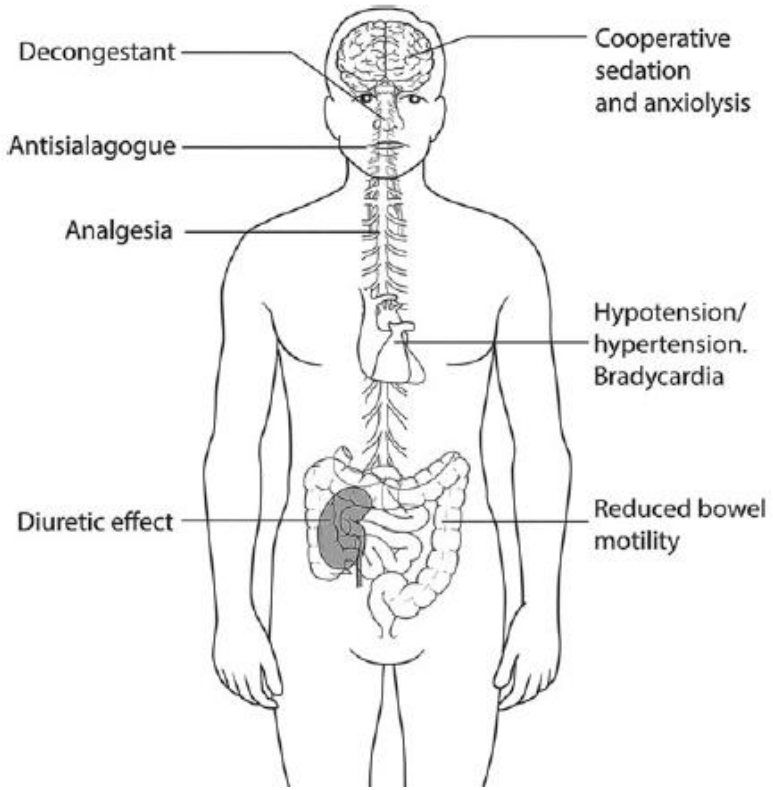
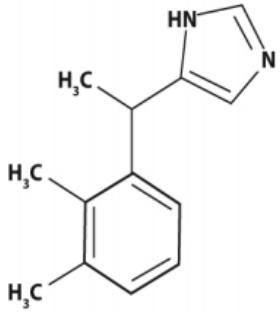
Dexmedetomidine: Selective Alpha II Agonist

Dexmedetomidine: its use in intensive care medicine and anaesthesia

VL Scott-Warren MBChB (Hons) FRCA[1] and J Sebastian BSc MBBS MRCP FRCA[2]



- Opiate substitute with Volatile GA
  - Can J Anesth 2005 52:2 176-180
    - 433kg, 0.7mcg/kg/hour, Isofurane MAC 0.5, Ketamine 60mg for AFOI
  - J Clin Anesth 2006 18(1) 24-8
    - Fentanyl (0.5mcg/kg/hr)
    - Dexmed (0.4mcg/kg/hr)
    - Less Desflurane & Morphine post op
- Bariatric dose 0.2-0.4mcg/kg/hr LBW
  - Anaesthesia, 120 (5): 969e977 (2018)
- Amnesia in 50% of Patients
  - SA Journ. Anaesth. & Analg, 2010 16:1, 101



Dexmedetomidine

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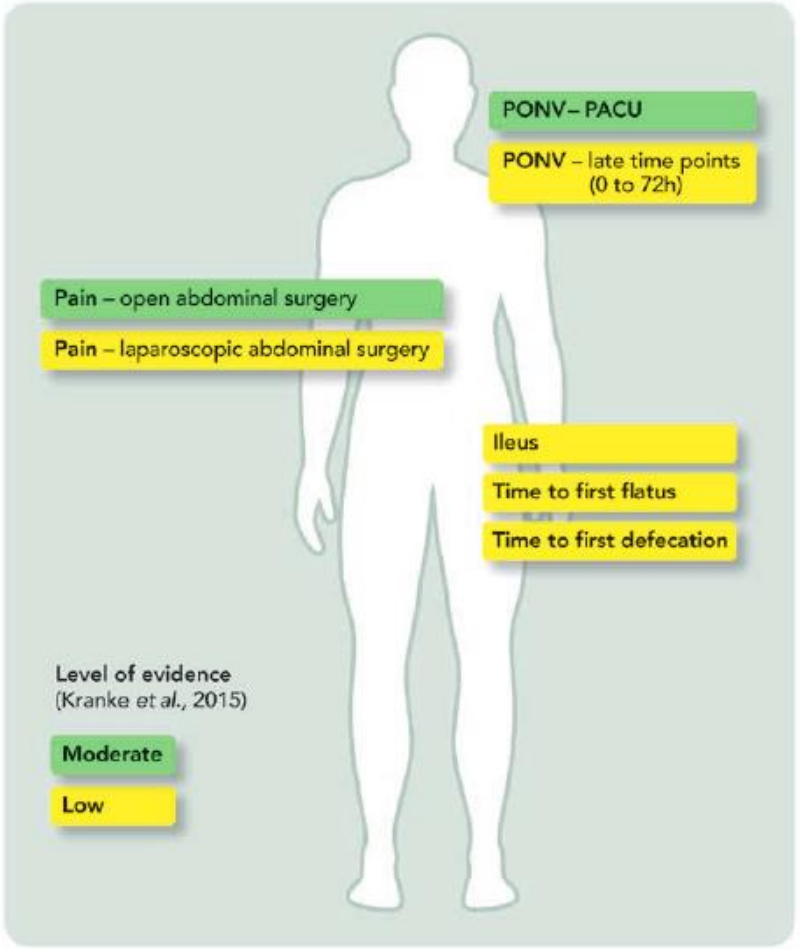
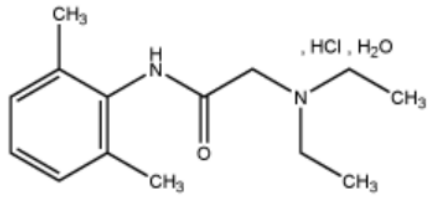


Lignocaine



Lignocaine hydrochloride

Perioperative Use of Intravenous Lidocaine

Lauren K. Dunn, M.D., Ph.D., Marcel E. Durieux, M.D., Ph.D.

Anesthesiology 2017; 126:729-37

Local Anesthetics and the Inflammatory Response

A New Therapeutic Indication?

Markus W. Hollmann, M.D., and Marcel E. Durieux, M.D., Ph.D.†*

Anesthesiology, V 93, No 3, Sep 2000

OBES SURG (2014) 24:212–218
DOI 10.1007/s11695-013-1077-x

ORIGINAL CONTRIBUTIONS

Systemic Lidocaine to Improve Quality of Recovery after Laparoscopic Bariatric Surgery: A Randomized Double-Blinded Placebo-Controlled Trial

Gildasio S. De Oliveira Jr. · Kenyon Duncan · Paul Fitzgerald · Antoun Nader · Robert W. Gould · Robert J. McCarthy

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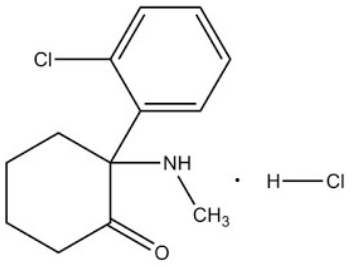
Ketamine in Metabolic Bariatric Anaesthesia

- **Magnesium and Ketamine Reduce Early Morphine (Obesity Surgery 2020, 30, 1452)**
  - Magnesium 8mg/kg/hr and Ketamine 0.15mg/kg/hr
  - Less Morphine in PACU (v's 4.51mg *p=0.045)*
  - Reduction Post Op Morphine first 24 hours (87% v's 21% *p*=0.03)
- **Role and Advantageousness of Ketamine in Obese (J Anesth Clin Res 2018, 9:5)**
  - Awake Fibre-optic intubation with dexmedetomidine or midazolam
- **Improves pain relief and less sedation (Can J Anaesth. 2003, 50 (4):336)**
  - Gastric By Pass Surgery with BMI >50 under Sevoflurane GA
  - Fentanyl or Non-Opiate (Clonidine, Lignocaine, Magnesium, Ketamine)
  - Non-opioid used Morphine PCA 5.2mg in PACU
  - Fentanyl used Morphine PCA 7.8mg (P < 0.05) in PACU
  - No difference in pain score one or 16 hr after surgery



Ketamine Hydrochloride

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Non Metabolic Bariatric Opiate Free TIVA RCT

- **Gynaecology** (77 cases)
  - Less Pain & PONV, Slow wake up (BMC Anesthesiol. (2023) 23: 34 Less Pain, Hypoxia and Paralytic Ileus (BMC Anesthesiology (2022) 22: 325)
- **Cardiac** (80 cases)
  - Less Morphine in 48 hours, AF & NIPPV (BMC Anesthesiology (2021) 21: 166)
- **Orthopedic** (100 cases)
  - Less Pain, Reduced PACU and Hospital stay (BJA (2021) 126: 136)
- **Urology** (80 cases)
  - Less Hypoxia & Pain, Early PACU discharge (J. Anaesth. Clin. Pharm. (2019) 35: 4)
- **General Surgery** (80 cases)
  - Less Pain (Rev Bras Anaesthesiol. 2015 65(3) 191)
  - Less Pain & PONV (Anesth Pain Med 2024;19:109)

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Metabolic Bariatric Opiate Free TIVA RCT

- Jan P. Mulier, Brugge, Belgium
  - Retro: 9246 cases Opiate Free TIVA Safer (Ana. Obes. Surg. (2019) 29: 1841)
  - RCT 50 cases Opiate Free TIVA Less Pain, Hypoxia, Hypertension, Bleeds and PONV (J Clin Anesth Pain Med (2018) 2: 1, 15)
- Opiate Free TIVA: Dexmedetomidine > OFA clonidine > Opiate GA for Pain (257 cases: J Clin Anesth. (2022) 81: 110966)
- Opiate Free TIVA & TAP Block Less Pain, PONV, Paralytic Ileus (103 cases: BMC Anesthesiology (2022) 22: 29)
- Less Pain and PONV (Obesity Surgery (99 cases: 2023) 33: 1687)
- Less PONV (119 cases: British Journal of Anaesthesia (2014) 112: 906)
- Associated with less IL-6 release (40 cases: BMC Anesthesiology (2022) 22: 294)
  - Degree of Obesity and Operative duration also associated with IL-6 levels

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ANZCTR
Australian New Zealand Clinical Trials Registry

Public title	Improving the ways we put patients to sleep (anaesthesia) for weight loss surgery
Scientific title	SOOThe: Study of Obesity-reduction and Opiate-free Total Intravenous Anaesthesia (TIVA). Using TIVA in bariatric surgery improve the analgesia and reduce post operative nausea and vomiting.
Secondary ID [1]	Nil Known
Universal Trial Number (UTN)	U1111-1247-3539
Trial acronym	SOOThe: Study of Obesity-reduction and Opiate-free Total Intravenous Anaesthesia
Linked study record	Not applicable

Prospective Randomised double blind control trial of Patients randomised to Volatile and Opiate anaesthesia v's Propofol (4mcg/ml TCI), Ketamine (6mcg/kg/min), Lignocaine (2mg/kg/hr) and Dexmedetomidine (0.8mcg/kg/hour) in context of universal triple anti-emetic use.

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ANESTHESIOLOGY

Balanced Opioid-free Anesthesia with Dexmedetomidine *versus* Balanced Anesthesia with Remifentanil for Major or Intermediate Noncardiac Surgery

The Postoperative and Opioid-free Anesthesia (POFA) Randomized Clinical Trial

Helene Beloeil, M.D., Ph.D., Matthias Garot, M.D., Gilles Lebuffe, M.D., Ph.D., Alexandre Gerbaud, M.D., Julien Bila, M.D., Philippe Cuvillon, M.D., Ph.D., Elisabeth Dubout, M.D., Sebastien Oger, M.D., Julien Nadaud, M.D., Antoine Becret, M.D., Nicolas Coullier, M.D., Sylvain Lecoeur, M.D., Julie Fayon, M.D., Thomas Godet, M.D., Michel Mazerolles, M.D., Fouad Atallah, M.D., Stephanie Sigaut, M.D., Pierre-Marie Choinier, M.D., Karim Asehnoune, M.D., Ph.D., Antoine Roquilly, M.D., Ph.D., Gerald Chanques, M.D., Ph.D., Maxime Esvan, Ms.C., Emmanuel Futier, M.D., Ph.D., Bruno Laviolle, M.D., Ph.D., for the POFA Study Group* and the SFAR Research Network†

ANESTHESIOLOGY 2021; 134:541–51

When Opiate Free TIVA goes wrong

- Randomised
  - Remifentanil Cet TCI (3 to 5 ng/ml) IBW
  - Dexmedetomidine (0.4 to 1.4 µg/kg/hour) IBW
- Dexmedetomidine group
  - Trail ceased early due to 5 cases of severe bradycardia including 3 cases of asystole
  - Post-operative hypoxemia
  - Delayed extubation Prolonged PACU stay, and intra-operative bradycardia
  - Less morphine consumption
  - Less PONV

Out with the Old and In with the New? A critical appraisal of Opiate Free TIVA in Bariatric Anaesthesia

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"Opioid-free anesthesia may be feasible. Nevertheless, it appears neither logical nor beneficial to patients."

Opioid-free Anesthesia: Time to Regain Our Balance

Evan D. Kharasch, M.D., Ph.D., J. David Clark, M.D., Ph.D.

- Anesthesiology 2021, 134 4 509-514
- No evidence that opioid-free strategies
  - Have benefits above and beyond opioid-sparing strategies,
  - Influence the risk or prevent persistent post-operative opioid use, or
  - Prevent post-operative opioid overprescription

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Metabolic Bariatric Opiate Free TIVA Meta-Analysis

- PONV Universal agreement
  - Obes Surg. (2022) 32: 3113
  - Cureus (2024) 16: e54094
  - Acta Anaesthesiol Scand. (2022) 66:170
  - Healthcare (2024) 2, 1094
  - J. Clin. Med. (2021) 10, 2069
- Incomplete evidence and conflicting data on
  - Pain Scores
  - PACU Opiate use, Post-operative Opiate use, Hyperalgesia and Opiate Tolerance
  - Safety and Sedation
  - Haemo-dynamic stability
  - Length of Stay

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Limitations to Metabolic Bariatric Opiate Free TIVA Studies

- Large Retrospective Cohorts Studies or Small RCT usually of less than 100 cases
- Variety Opiate Free TIVA protocols reported
  - Drug type & doses
- Opiate Free TIVA dose not allow titration of analgesia through the case
- Opiate Free TIVA not consistently compared with multi-modal analgesia including Opiate sparing strategies
- Encouraging data on PACU Pain and PACU discharge could be a function of the half lives Dexmedetomidine, Lignocaine and Ketamine
- Limited Data on Opiate requirements in the Post-operative period and at Discharge

J. Clin. Med. 2021, 10, 2069; Healthcare (2024) 2, 1094; Anesthesiology 2021; 134: 645 ; Anesthesiology 2021, 134: 509

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What to do Now?

- Clear Evidence for OFA in Metabolic Bariatric Anaesthesia for PONV
- Large Double Blind Placebo Randomised Controlled Trials
  - Opiate Free TIVA v's Multimodal Opiate Sparing
  - Pain and Opiate Use Post operatively and after discharge
  - Safety and Sedation
  - Length of Stay

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'And I'm leaving Santa a leaflet on obesity and some blood pressure pills'

Any Questions?