Svensk förening för Postoperativ Vård (SPOV)

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A review of Enhanced Recovery Care

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Disclosures

- Committee member and website editor ERAS® Society
- UK National Clinical Adviser for ER
- Others
  - Editor of *British Journal of Anaesthesia Education*
  - AAGBI Council/Board member
  - Paid honoraria lecturing/book chapters/educational resources
    - Grunethal
    - Baxter
- No shares in medical companies

Overview

- What is Enhanced Recovery

- Key areas
  - Pathophysiology
  - Avoidance of complications
  - Adherence to pathway

- Preoperative care
  - Carbohydrate loading

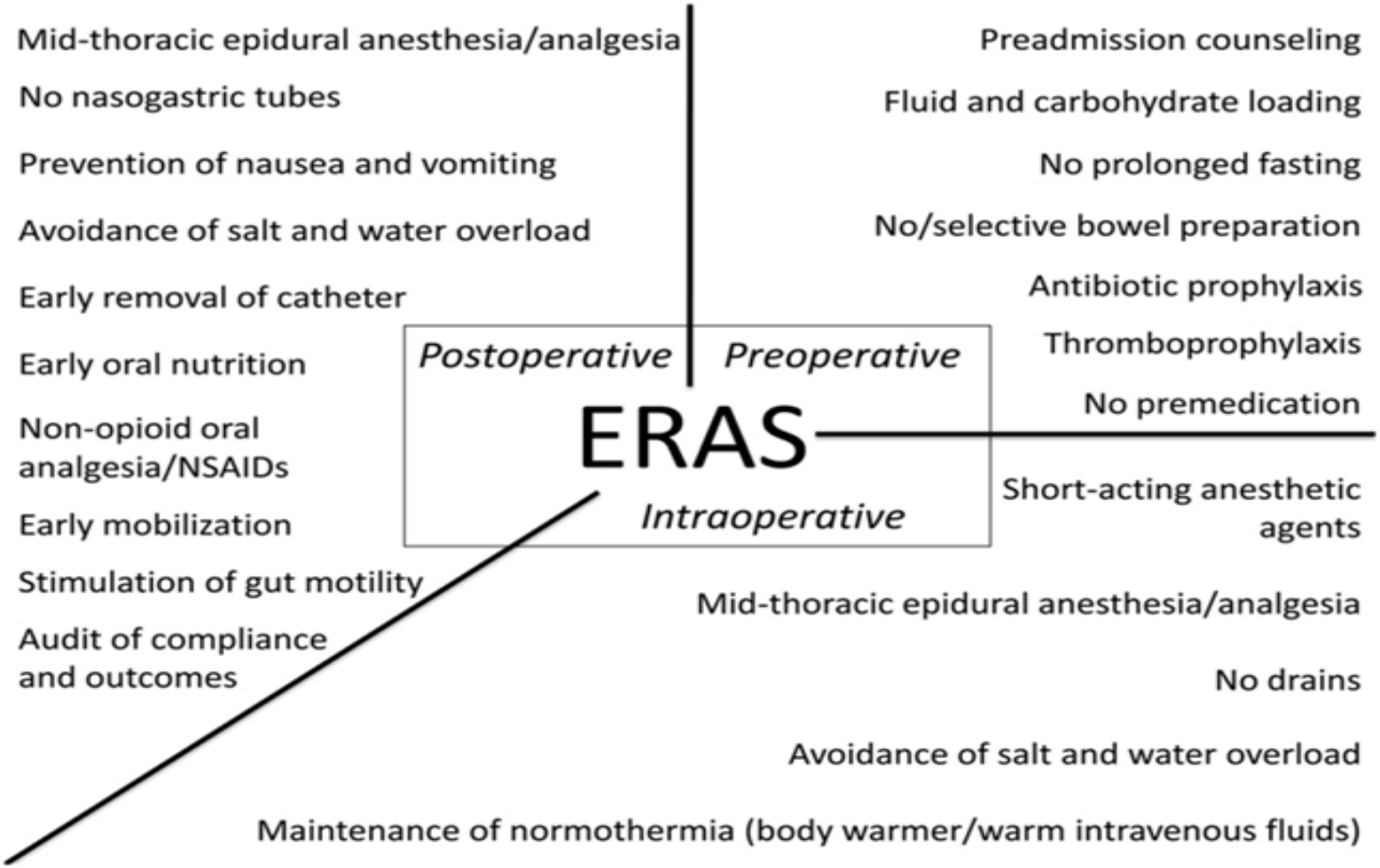
- Intraoperative care
  - Fluid management
  - Analgesia

- Postoperative care
  - Early resumption of normal activities
  - Data collection and audit

What is Enhanced Recovery

- Multistep, evidenced based pathway
- Challenges the dogma concerning the management of elective surgical patients

ERAS Elements

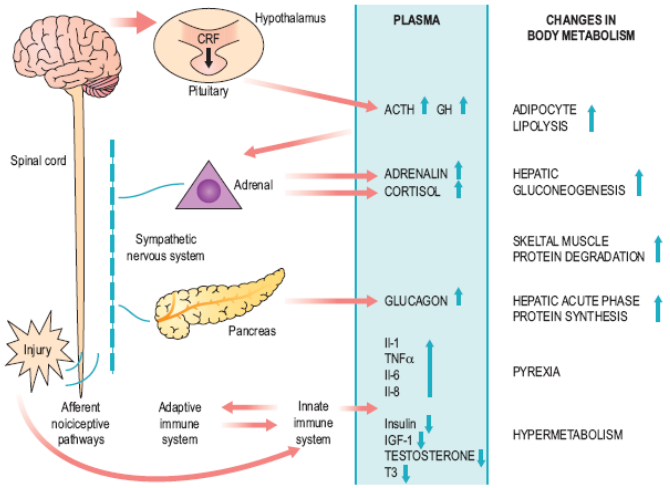


Pathophysiology

Major surgery elicits characteristic and predictable physiological changes:

- Neuroendocrine
  - sympathetic nervous system activation
  - pituitary activation
- Metabolic (catabolism, hyperglycaemia)
- Inflammatory (cytokines, SIRS)
- Immunosuppression (CARS)
- Malaise
- Fatigue

Stress response



- Carbohydrate metabolism
  - hyperglycemia
  - insulin resistance
- Protein metabolism
  - catabolism, especially skeletal muscle
- Lipid metabolism
  - lipolysis
- Salt/water retention and potassium loss

Stress response: Friend or Foe?

Disadvantages	Advantages
Catecholamine excess	??
Protein loss (weakness, immobility and deconditioning)	
?Gut function	
?Immunological changes (infection, cancer outcome)	
?Cognitive changes	

Stress response: Friend or Foe?

Disadvantages	Advantages
Catecholamine excess	Evolutionary survival
Protein loss (weakness, immobility and deconditioning)	
?Gut function	
?Immunological changes (infection, cancer outcome)	
?Cognitive changes	

Stress response modification

- Surgical factors
  - minimally invasive, bowel preparation, tubes, drains etc
- High dose opioids
- Regional blockade
- Fluids management (GDFT)
- Intraoperative warming
- Nutrition
  - carbohydrate loading, early oral nutrition, immunonutrition
- Drugs
  - NSAIDS, glucocorticoids, anabolic steroids, insulin infusion, statins,

Kehlet H, Mythen M. BJA 2011;289-291

Stress response modification

- Surgical factors ✔
  - minimally invasive, bowel preparation, tubes, drains etc
- High dose opioids ✘
- Regional blockade ✔ / ✘
- Fluids management (GDFT) ✔
- Intraoperative warming ✔
- Nutrition ✔
  - carbohydrate loading, early oral nutrition, immunonutrition
- Drugs ✔ / ✘
  - NSAIDS, glucocorticoids, anabolic steroids, insulin infusion, statins,

Kehlet H, Mythen M. BJA 2011;289-291

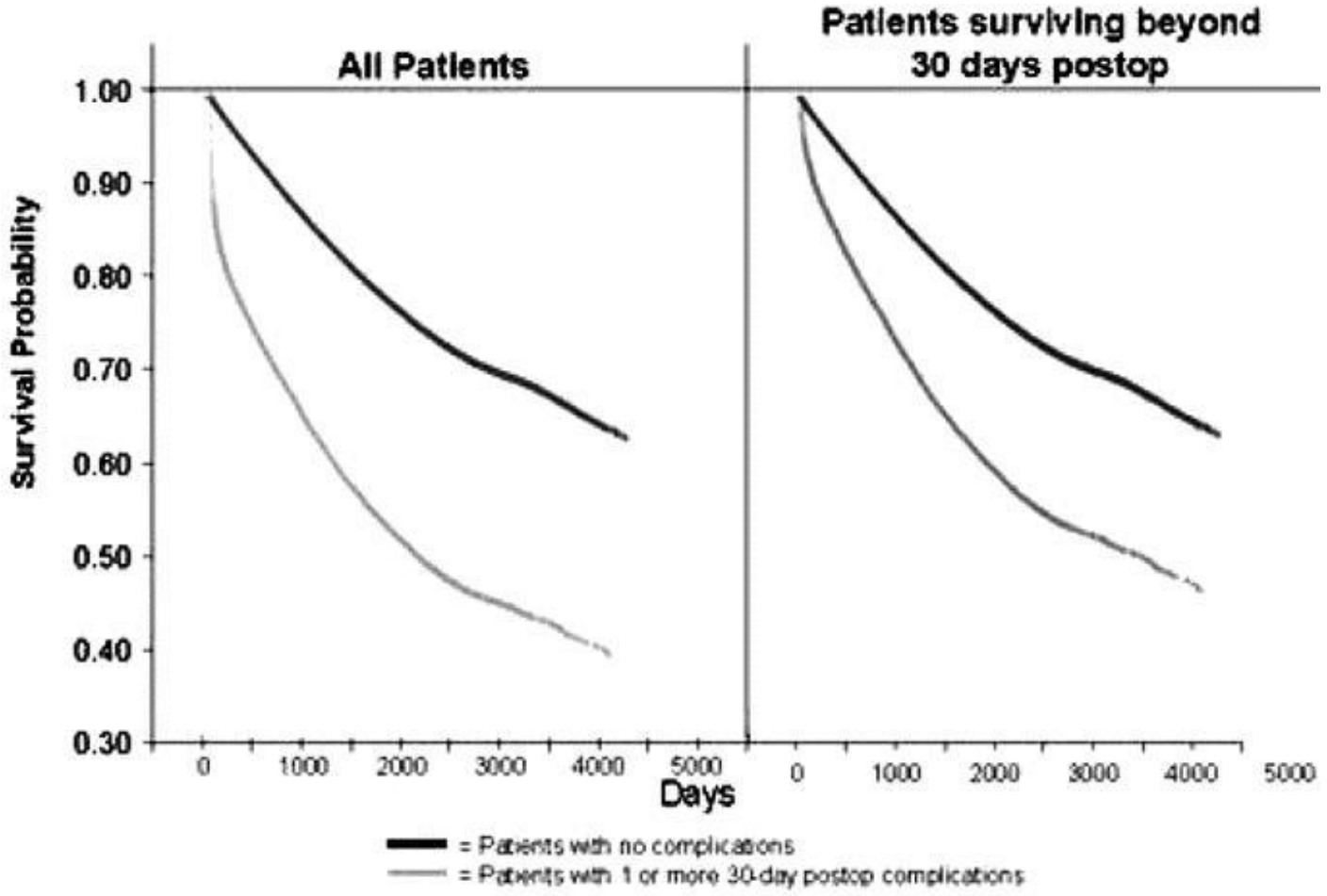
Enhanced Recovery reduces complications

- Reduction in complications are key area of ERAS philosophy
- Not only affects short term morbidity and mortality, but also impacts on long term outcomes
- Complications within 30 days are more important than both preoperative risk and intraoperative factors in determining survival after major surgery
- Complications reduced survival by 69% - from 18.4 years to 5.6 years

Khuri SF et al. Ann Surg 2005

Determinants of Long-Term Survival After Major Surgery and the Adverse Effect of Postoperative Complications

Shukri F. Khuri, MD,†‡ William G. Henderson, PhD,§ Ralph G. DePalma, MD,¶ Cecilia Mosca, MSPH,§ Nancy A. Healey, BS,* Dharam J. Kumbhani, MD, SM,* and the Participants in the VA National Surgical Quality Improvement Program*



Adherence to pathways matters

"Variation is the enemy of quality"

ORIGINAL ARTICLE

Adherence to the Enhanced Recovery After Surgery Protocol and Outcomes After Colorectal Cancer

Ulf O. Gustafsson, MD, PhD; Jonatan Hausel, MD; Anders Thorell, MD, PhD; Olle Ljungqvist, MD, PhD; Mattias Soop, MD, PhD; Jonas Nygren, MD, PhD; for the Enhanced Recovery After Surgery Study Group

Gustafsson UO et al. Arch Surg 2011; 46: 571–7

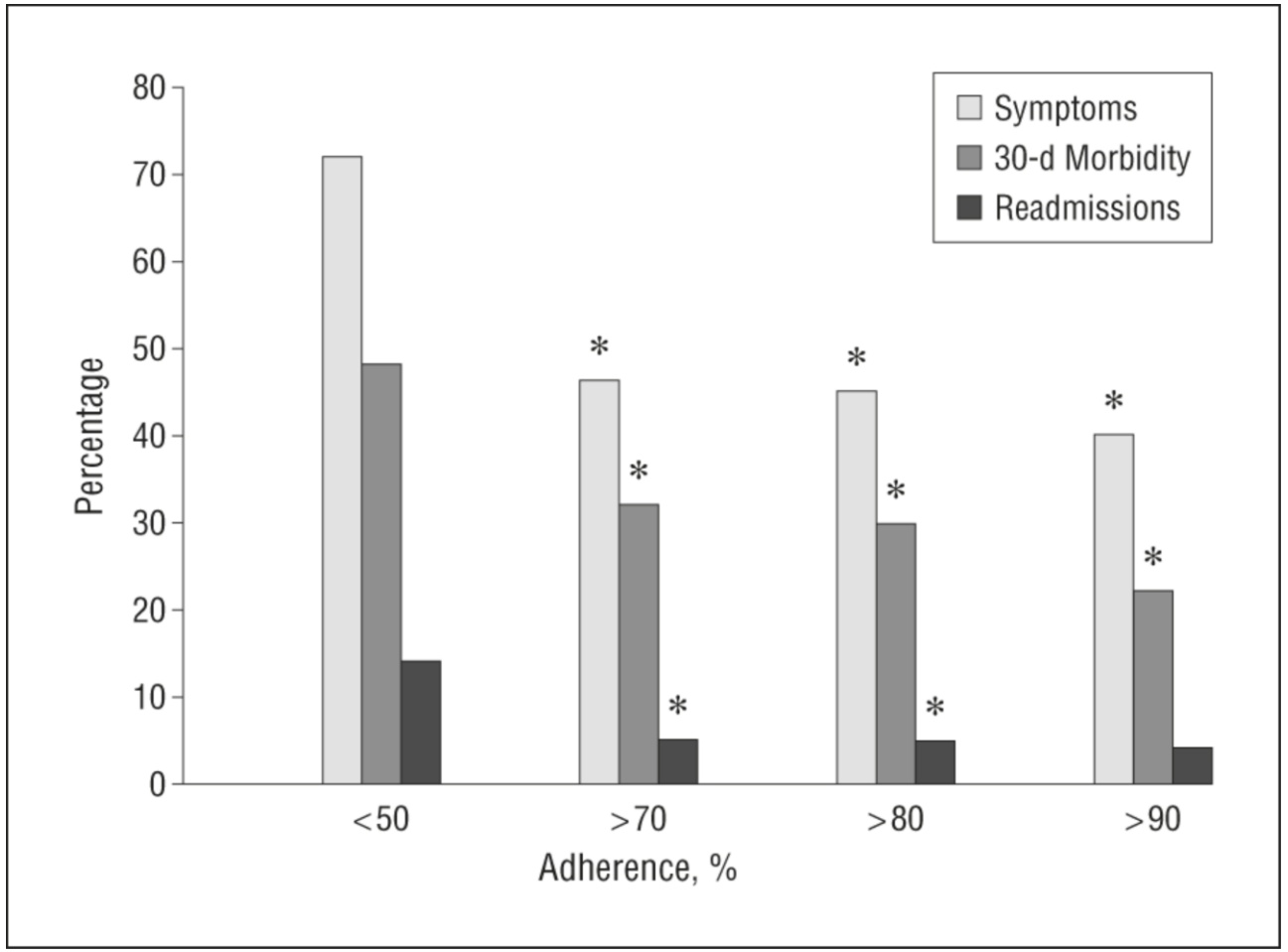
Adherence to ER protocols

- 950 patients
- 2002-2004 and 2005-2007
- 114 variables measured

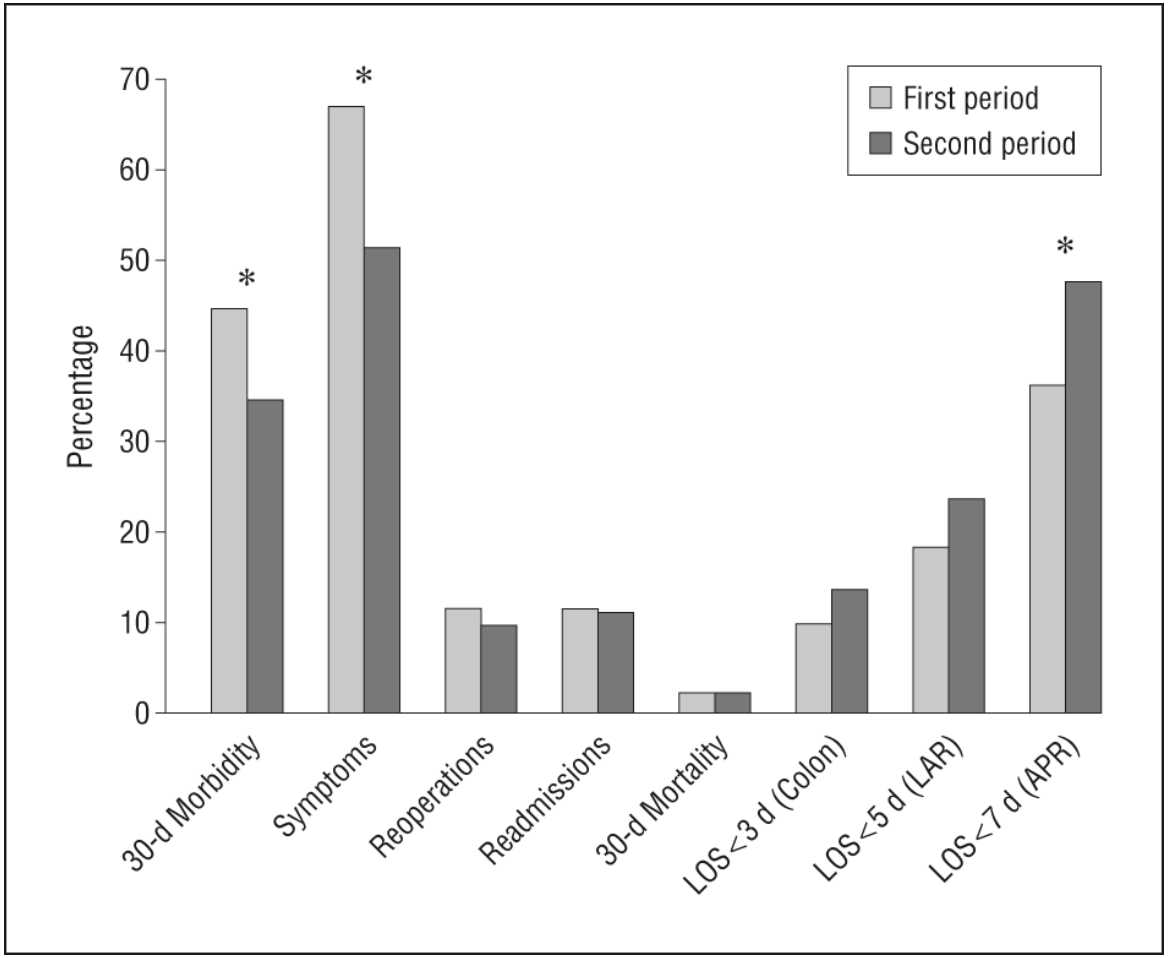
- Increase in ERAS adherence increased from 43% to 71%
- Complications, symptoms and readmissions reduced significantly

Gustafsson UO et al. Arch Surg 2011; 46: 571–7

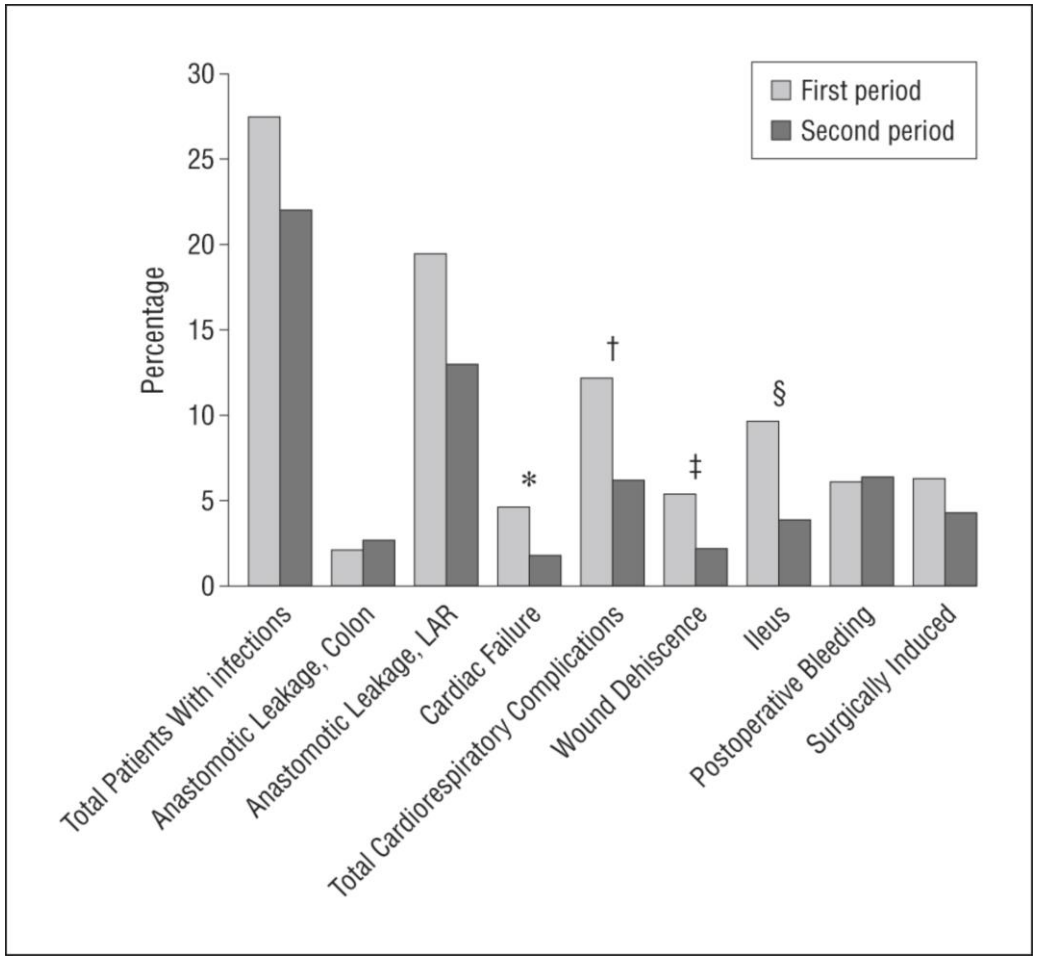
Pathway adherence and postoperative outcomes



Postoperative outcomes



Postoperative complications



Adherence to ER protocols matters

Major independent predictors:

- iv fluid restriction (prevention of fluid overload)
- Preoperative carbohydrate drink

- ‘Dose response curve’ between adherence and outcomes

Gustafsson UO et al. Arch Surg 2011; 46: 571–7

Adherence to ER protocols matters

World J Surg
DOI 10.1007/s00268-016-3460-y

World Journal of Surgery

ORIGINAL SCIENTIFIC REPORT

Adherence to the ERAS protocol is Associated with 5-Year Survival After Colorectal Cancer Surgery: A Retrospective Cohort Study

Ulf O. Gustafsson[1,2] · Henrik Oppelstrup[2,3] · Anders Thorell[2,3] · Jonas Nygren[2,3] · Olle Ljungqvist[4]

ERAS® Society

Royal Surrey County Hospital NHS
NHS Foundation Trust

UCL UNIVERSITY OF SURREY

Adherence to ER protocols matters

- 911 consecutive colorectal cancer patients
- Patients with >70 % adherence to ERAS interventions (N = 273) risk of 5-year cancer-specific death was lowered by 42%
- Significant independent perioperative predictors of increased 5-year survival were
  - avoiding overload of intravenous fluids
  - oral intake on the day of operation
  - low CRP levels on day one

Gustafsson UO et al.
World Journal of Surgery;2016 25:1-7

Adherence to ER protocols matters

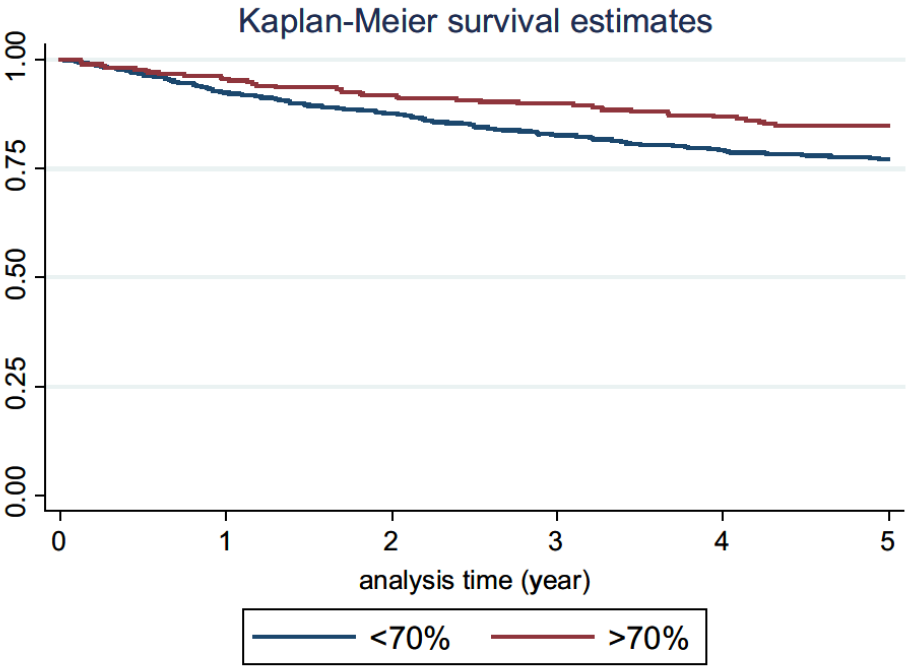


Fig. 1 5-year survival. Patients with ≥70 % rate of compliance with the ERAS protocol showed significantly improved survival rates compared with patients with less than 70 % compliance, $p = 0.0095$ (Log-rank test for equality of survival functions)

But still advantages to ER pathways without MIS…

LAFA trial:

Laparoscopy and/or Fast Track Multimodal care in 9 Dutch hospitals, 427 patients:

- Laparoscopic with fast track
- Laparoscopic with standard care
- Open with fast track
- Open with standard care

Vlug K et al. Ann Surg 2011;254:868-875

LAFA trial – LOS results

Lap + fast track: 5 (4-8 days)

Lap + standard care: 6 (4.5-9.5 days)

Open + fast track 7 (5-11 days)

Open + standard care 7 (6-13 days)

- Optimal treatment is laparoscopy embedded in fast track programme
- Laparoscopic surgery only independent factor to reduces LOS and morbidity
- If open surgery then best with FT programme

LAFA trial – Immune function

79 patients analysed

Immunocompetence assessed by monocyte HLA-DR expression. (Also IL-6, CRP and GH)

Veenhof AAFA et al. Ann Surg 2012;255:216-2212

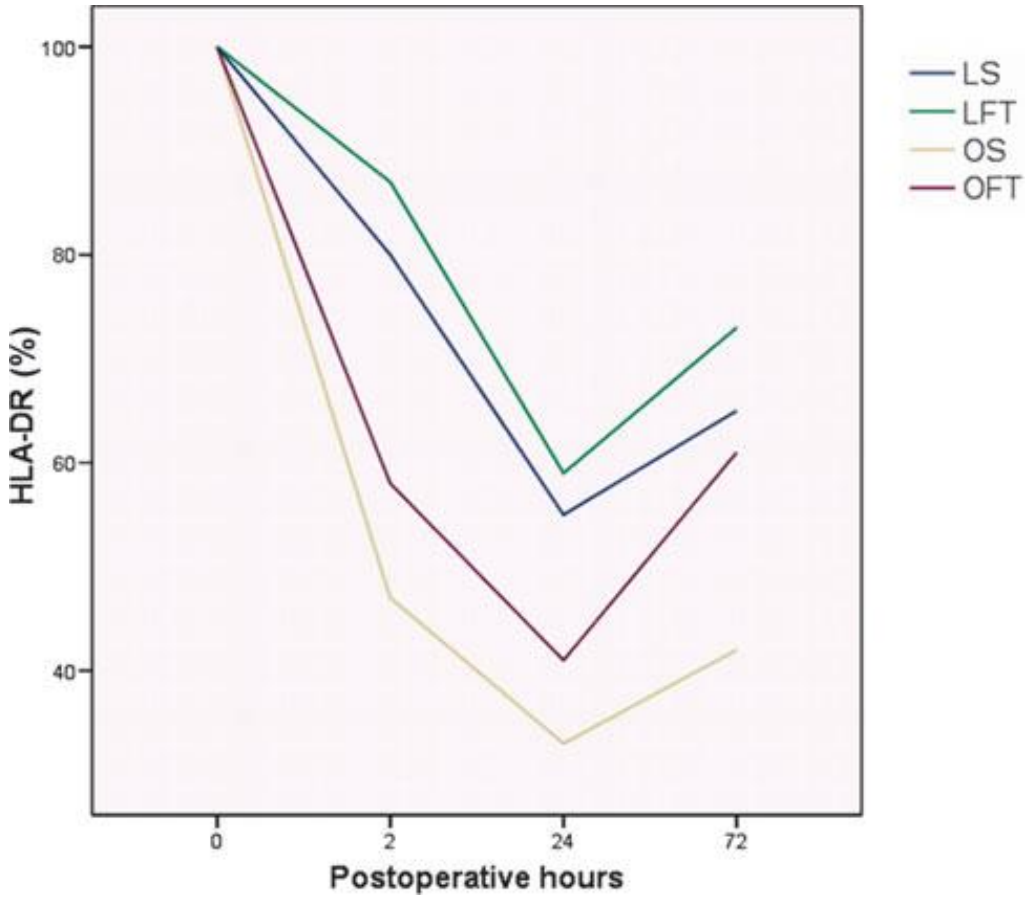
Lap + fast track: 74.8

Lap + standard care: 67.1

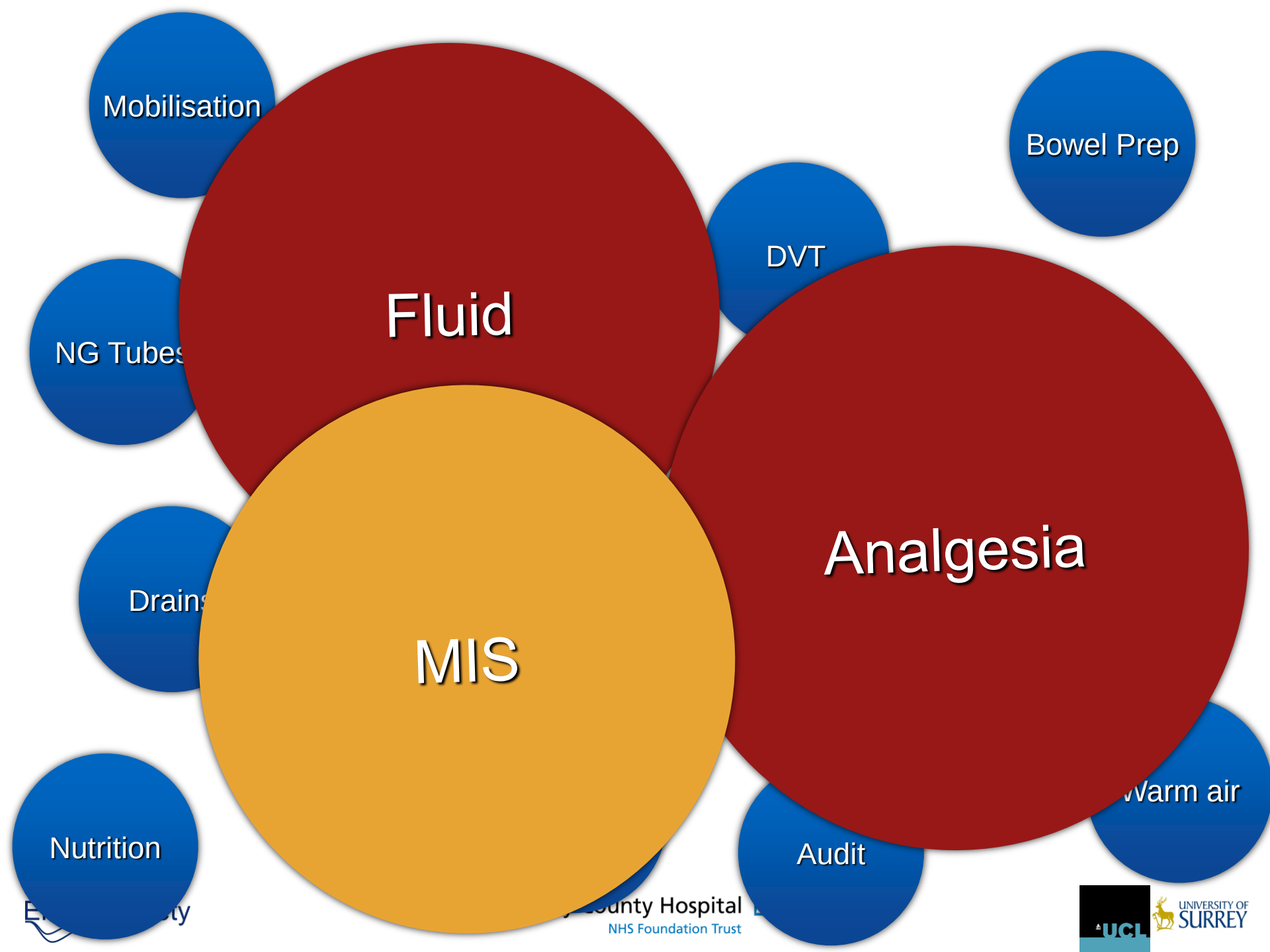
Open + fast track: 52.8

Open + standard care: 40.7

Preservation of immune competence may protect against seeding of tumour cells


100
80
60
40
HLA-DR (%)
0
2
24
72
Postoperative hours
LS
LFT
OS
OFT

Perioperative Care


Mobilisation
Fluid
Bowel Prep
DVT
NG Tubes
Analgesia
Drains
MIS
Nutrition
Audit
Warm air
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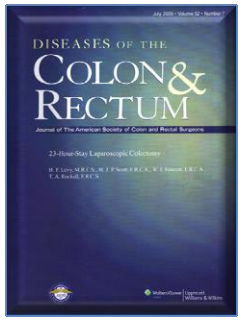
Minimally Invasive Surgery

- Reduction in primary injury
  - Mobilisation
  - Organ handling
  - Collateral damage
- Dramatic reduction in stress response
- Shaped but did not start Enhanced Recovery
- Has permitted some dramatic changes eg 23 hour stay colectomy



Levy BF, Scott MJ, Fawcett WJ, Rockall TA.
23-hour stay laparoscopic colectomy.
Diseases of the Colon and Rectum 2009;**52:**1239-43

Minimally Invasive Surgery

- Requires expenditure for equipment and training:
  - Laparoscopic

  - Robotic

Minimally Invasive Surgery versus open surgery

- Poses very different challenges for the anaesthetist too:

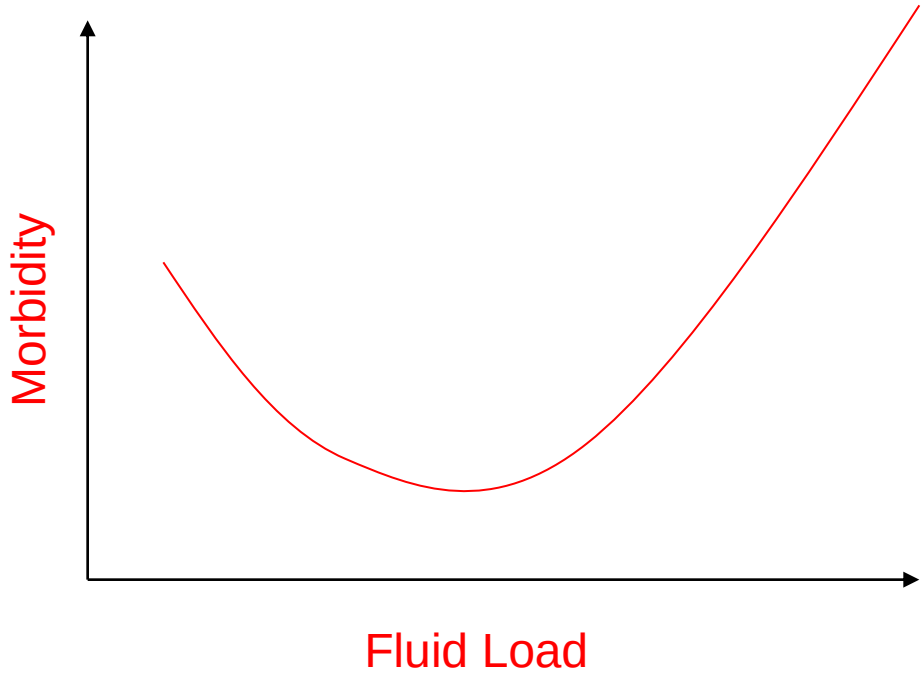
	Laparoscopic	Open surgery
CVS Risk	Probably equal	Probably equal
Intraoperative oxygen delivery	Reduced	Increased (epidural)
Oxygen Consumption	Minimized	Variable
Fluid shifts	Usually minimal after 6 hours	Usually persists for 24 hours or more
Postoperative iv fluid requirements	< 24 hours	Duration of epidural
SIRS	Small	Large
Ileus	Reduced	Prolonged
Mobility	Good	Reduced (pain/pumps)
Lung function	Usually good	Reduced FRC (pain/distension)

Minimally Invasive Surgery versus open surgery

Laparoscopic/robotic surgery, with pneumoperitoneum extremes of positioning may induce marked intraoperative challenges.

"minimal access surgery, maximum cardiopulmonary stress"

Fluid therapy

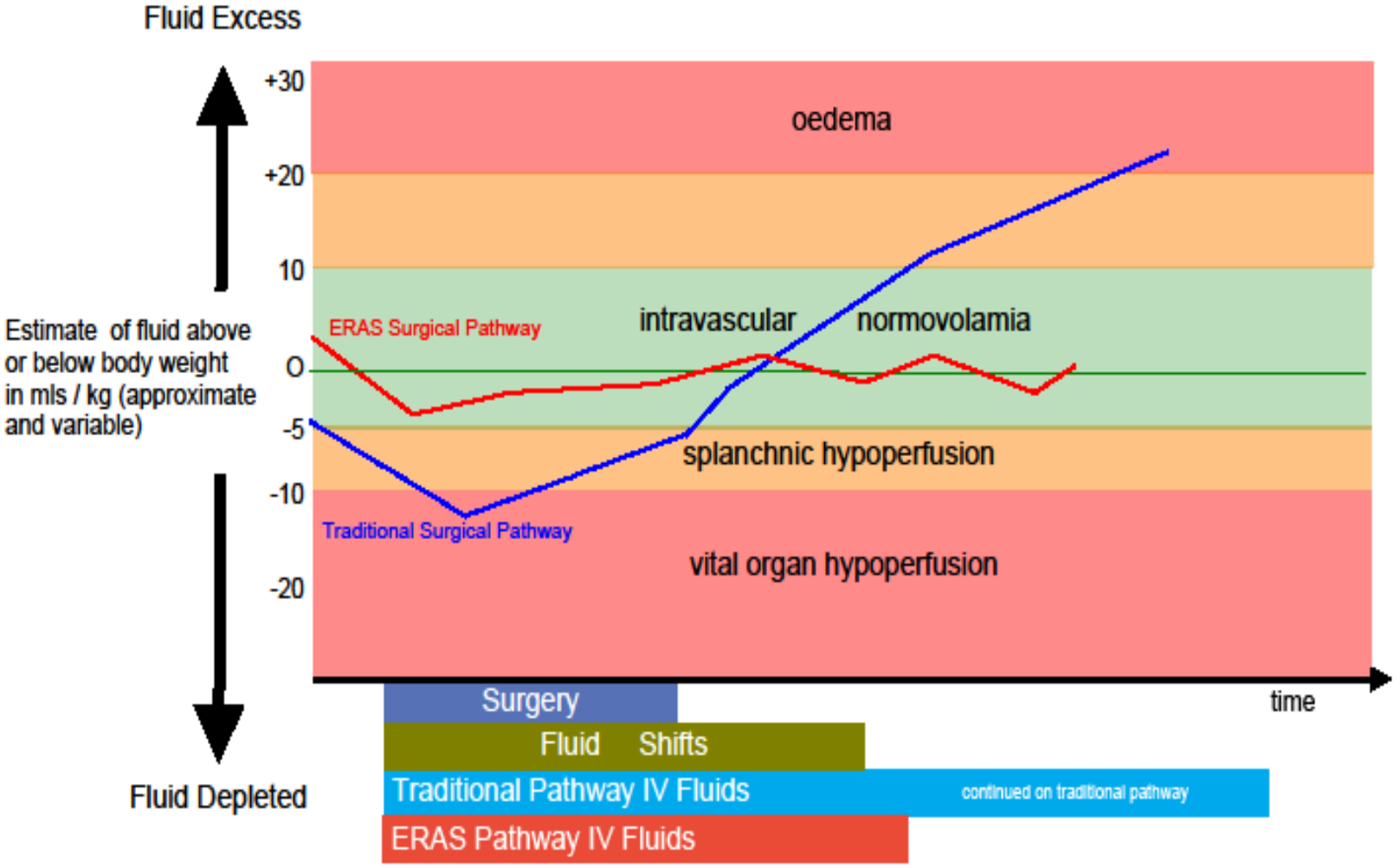


Bellamy MC. BJA 2006;97:755-7

Fluids have changed

- Patient
  - Carbohydrate loading
  - Early resumption of oral fluids (so iv not required)
- Surgery
  - Minimal access/small incision
- Anaesthesia
  - Fluid therapy individualized
  - Permissive oliguria accepted

Perioperative fluid shifts



Perioperative fluids in the real world

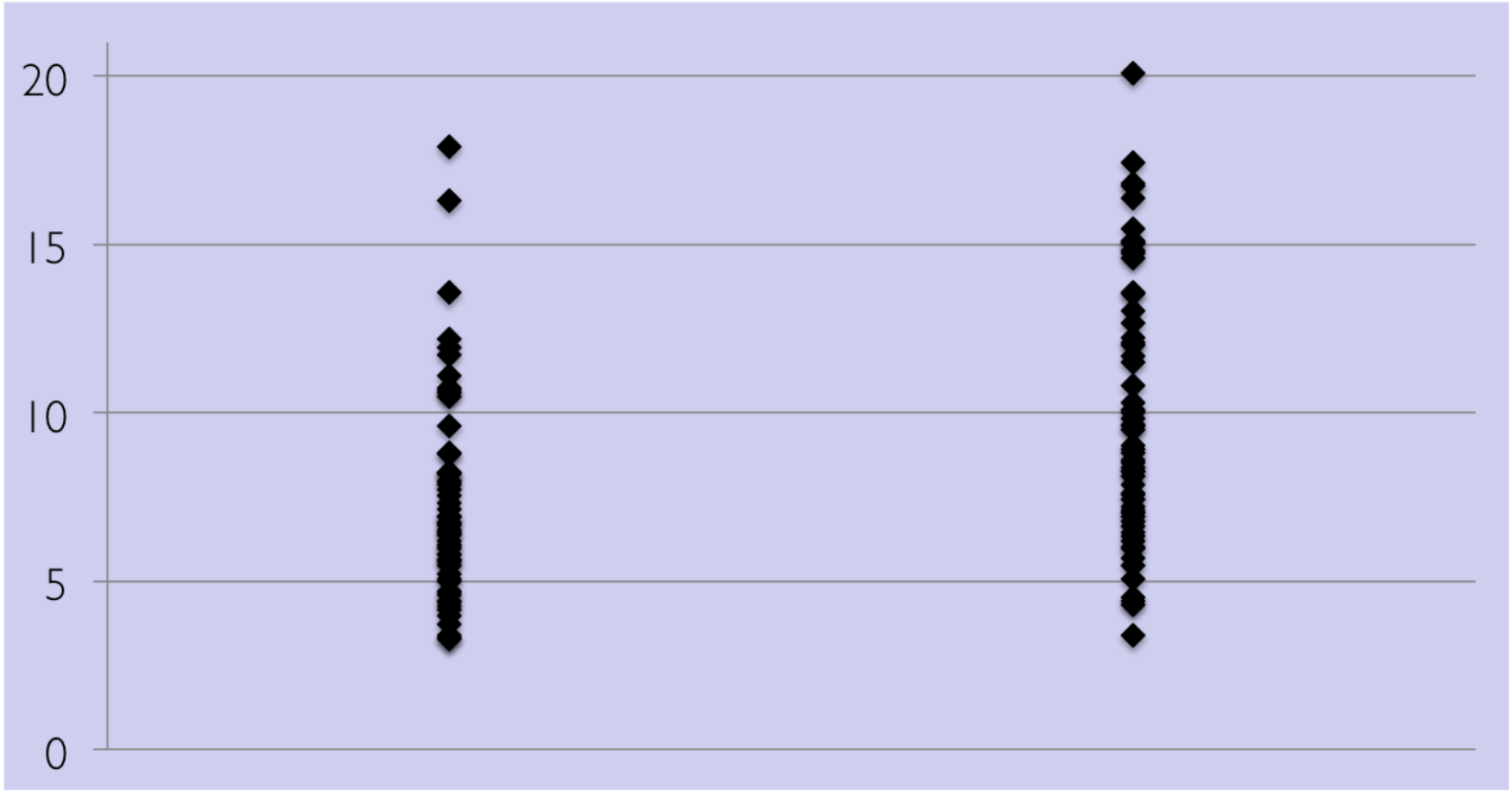
Editorial

Perioperative fluid management: science, art or random chaos?

- Huge variation in fluids administered
- 75kg patient, 4 hr procedure, 400 mls blood loss
- 0.7-5.4 L crystalloid given
- Personnel strongest predictor

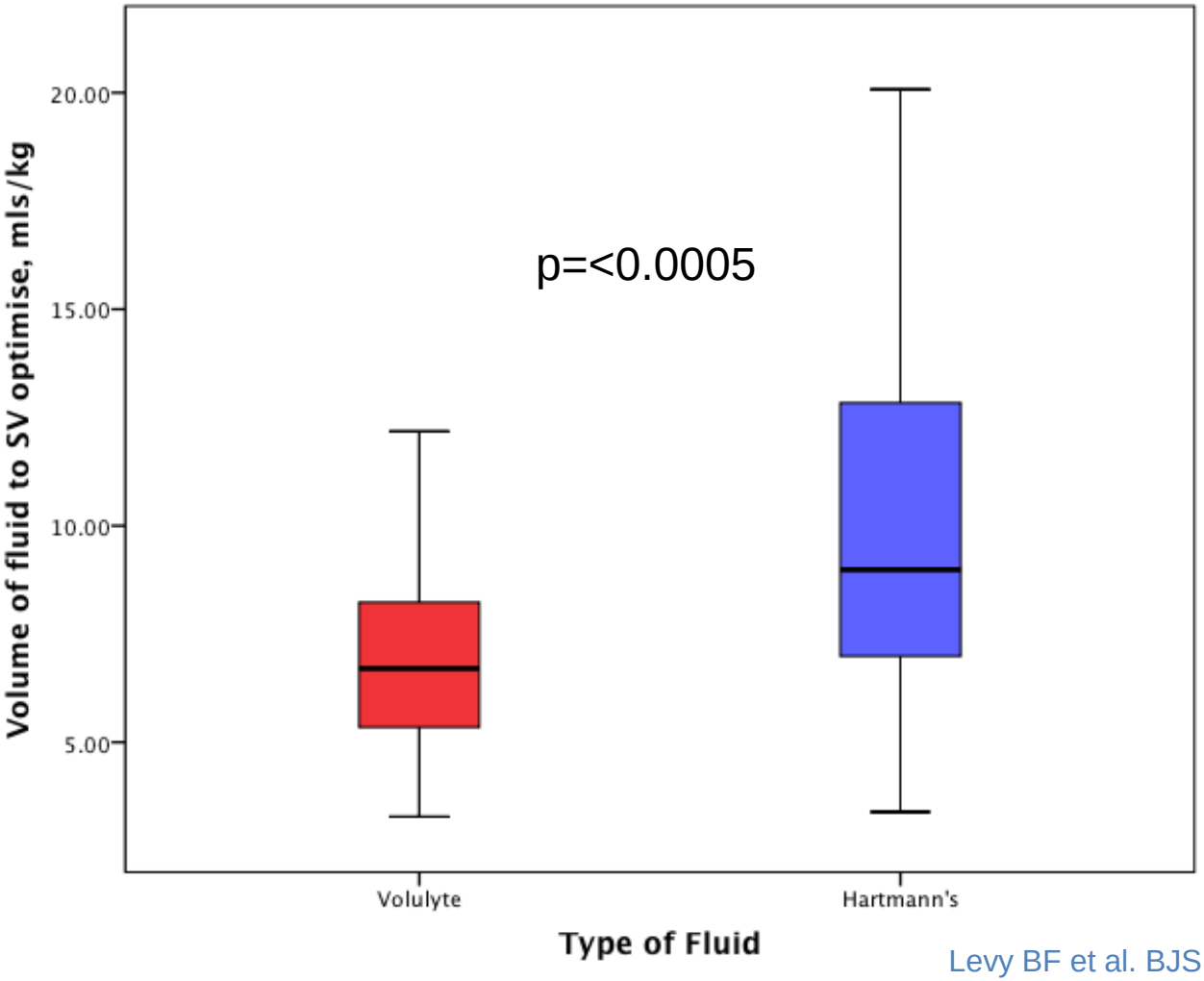
Lilot et al . *Brit J Anaesth* 2015
Minto G, Mythen MG *Brit J Anaesth* 2015

Range of fluid administered, mls/kg



Levy BF et al. BJS 2011;98:1068-1078

Fluid to achieve SV optimisation



Levy BF et al. BJS 2011;98:1068-1078

Fluid therapy – knowns

- Getting fluid therapy wrong increases complications, cost and LOS
- Formulaic treatments (liberal/restrictive) no longer supported
- Fluid responsiveness is key:
  - Individualised (goal directed) therapy using flow (stroke volume or DO2) measurements widely accepted
- Good evidence base for
  - colorectal surgery
  - ODM
- Getting fluids right:
  - Reduces stress response

Noblett SE et al.. Br J Surg 2006;93:1069-76

  - Independent predictor (with CBH drink) of reduced symptoms and complications

Gustafsson UO et al. Arch Surg 2011;46:571-577

Fluid therapy - unknowns

- Optimal fluid management for laparoscopic surgery
  - DO_2 I > 400 mls.min^{-1}.m^{-2} threshold for reducing complications during laparoscopic colorectal surgery

    Levy BF, Fawcett WJ. Colorectal Dis 2012; 14: 887–92
- Optimal fluid type
  - Colloids/crystalloids (latter balanced eg plasmalyte)
- Optimal monitors/goals
  - ODM, arterial waveform analysis, transthoracic bioimpedance
- Optimal duration of therapy
- Optimal technique: Bolus or infusion
  - Probably bolus
- Optimal markers:– lactate, $ScvO_2$?

Fluid therapy within ERAS

META-ANALYSIS

OPEN

Intraoperative Goal-directed Fluid Therapy in Elective Major Abdominal Surgery

A Meta-analysis of Randomized Controlled Trials

Katie E. Rollins, MRCS, and Dileep N. Lobo, DM, FRCS, FACS, FRCPE

Rollins KE, Lobo DN. Annals of Surgery 2016

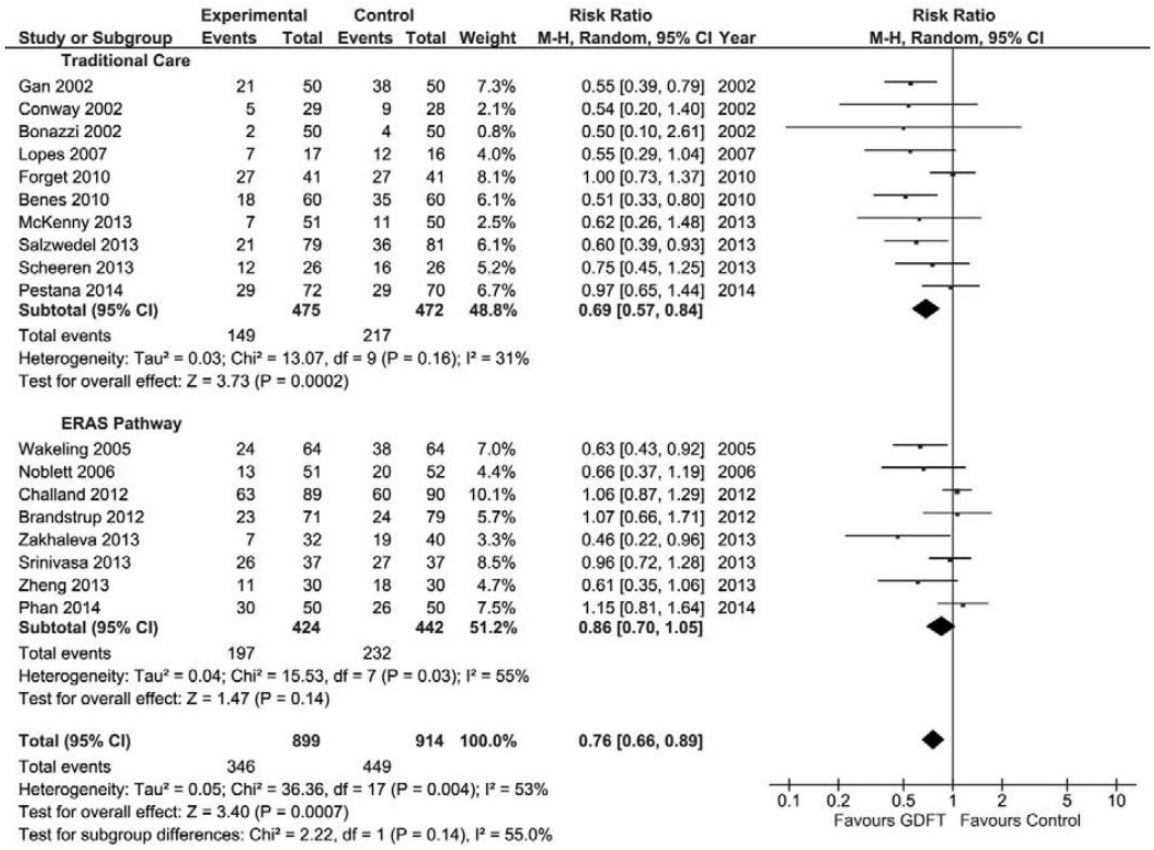
Fluids: Conventional versus ERAS

- 23 studies were included with 2099 patients
  - 1059 received conventional fluid therapy
  - 1040 who underwent GDFT

- Conventional
  - Reduced Morbidity, LOS, bowel function
- ERAS
  - Only ICU LOS reduced

Rollins KE, Lobo DN. Annals of Surgery 2016

Fluids: Conventional versus ERAS - Morbidity



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Traditional Care							
Gan 2002	21	50	38	50	7.3%	0.55 [0.39, 0.79]	2002
Conway 2002	5	29	9	28	2.1%	0.54 [0.20, 1.40]	2002
Bonazzi 2002	2	50	4	50	0.8%	0.50 [0.10, 2.61]	2002
Lopes 2007	7	17	12	16	4.0%	0.55 [0.29, 1.04]	2007
Forget 2010	27	41	27	41	8.1%	1.00 [0.73, 1.37]	2010
Benes 2010	18	60	35	60	6.1%	0.51 [0.33, 0.80]	2010
McKenny 2013	7	51	11	50	2.5%	0.62 [0.26, 1.48]	2013
Salzwedel 2013	21	79	36	81	6.1%	0.60 [0.39, 0.93]	2013
Scheeren 2013	12	26	16	26	5.2%	0.75 [0.45, 1.25]	2013
Pestana 2014	29	72	29	70	6.7%	0.97 [0.65, 1.44]	2014
Subtotal (95% CI)		**475**		**472**	**48.8%**	**0.69 [0.57, 0.84]**	
Total events	149		217				
Heterogeneity: Tau² = 0.03; Chi² = 13.07, df = 9 (P = 0.16); I² = 31%							
Test for overall effect: Z = 3.73 (P = 0.0002)							
ERAS Pathway							
Wakeling 2005	24	64	38	64	7.0%	0.63 [0.43, 0.92]	2005
Noblett 2006	13	51	20	52	4.4%	0.66 [0.37, 1.19]	2006
Challand 2012	63	89	60	90	10.1%	1.06 [0.87, 1.29]	2012
Brandstrup 2012	23	71	24	79	5.7%	1.07 [0.66, 1.71]	2012
Zakhaleva 2013	7	32	19	40	3.3%	0.46 [0.22, 0.96]	2013
Srinivasa 2013	26	37	27	37	8.5%	0.96 [0.72, 1.28]	2013
Zheng 2013	11	30	18	30	4.7%	0.61 [0.35, 1.06]	2013
Phan 2014	30	50	26	50	7.5%	1.15 [0.81, 1.64]	2014
Subtotal (95% CI)		**424**		**442**	**51.2%**	**0.86 [0.70, 1.05]**	
Total events	197		232				
Heterogeneity: Tau² = 0.04; Chi² = 15.53, df = 7 (P = 0.03); I² = 55%							
Test for overall effect: Z = 1.47 (P = 0.14)							
Total (95% CI)		**899**		**914**	**100.0%**	**0.76 [0.66, 0.89]**	
Total events	346		449				
Heterogeneity: Tau² = 0.05; Chi² = 36.36, df = 17 (P = 0.004); I² = 53%							
Test for overall effect: Z = 3.40 (P = 0.0007)							
Test for subgroup differences: Chi² = 2.22, df = 1 (P = 0.14), I² = 55.0%							

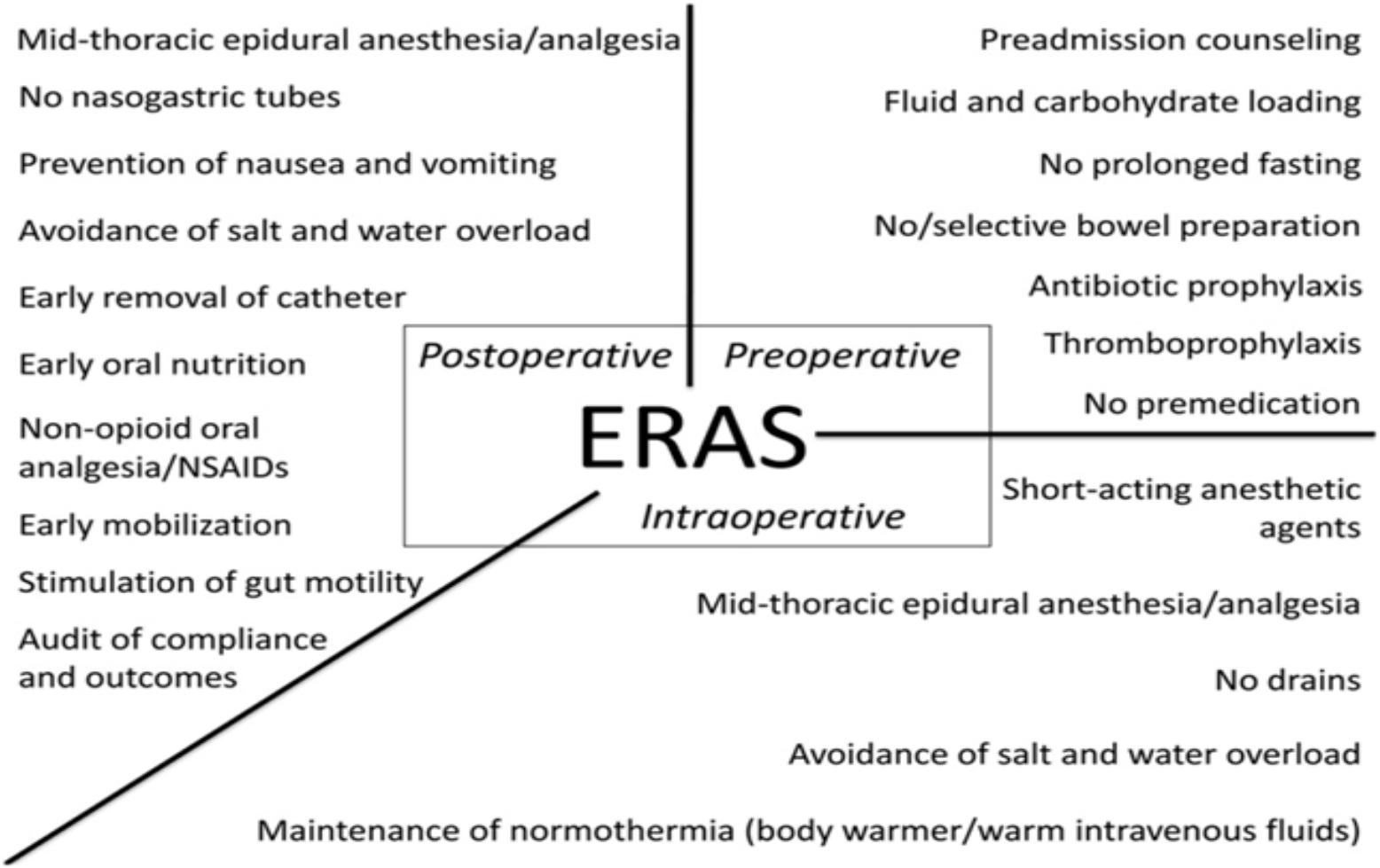
Fluids

- Large ranges of fluids administered described
- Can't all be right!
- Important area, but possibly less so now ERAS has become a standard of care

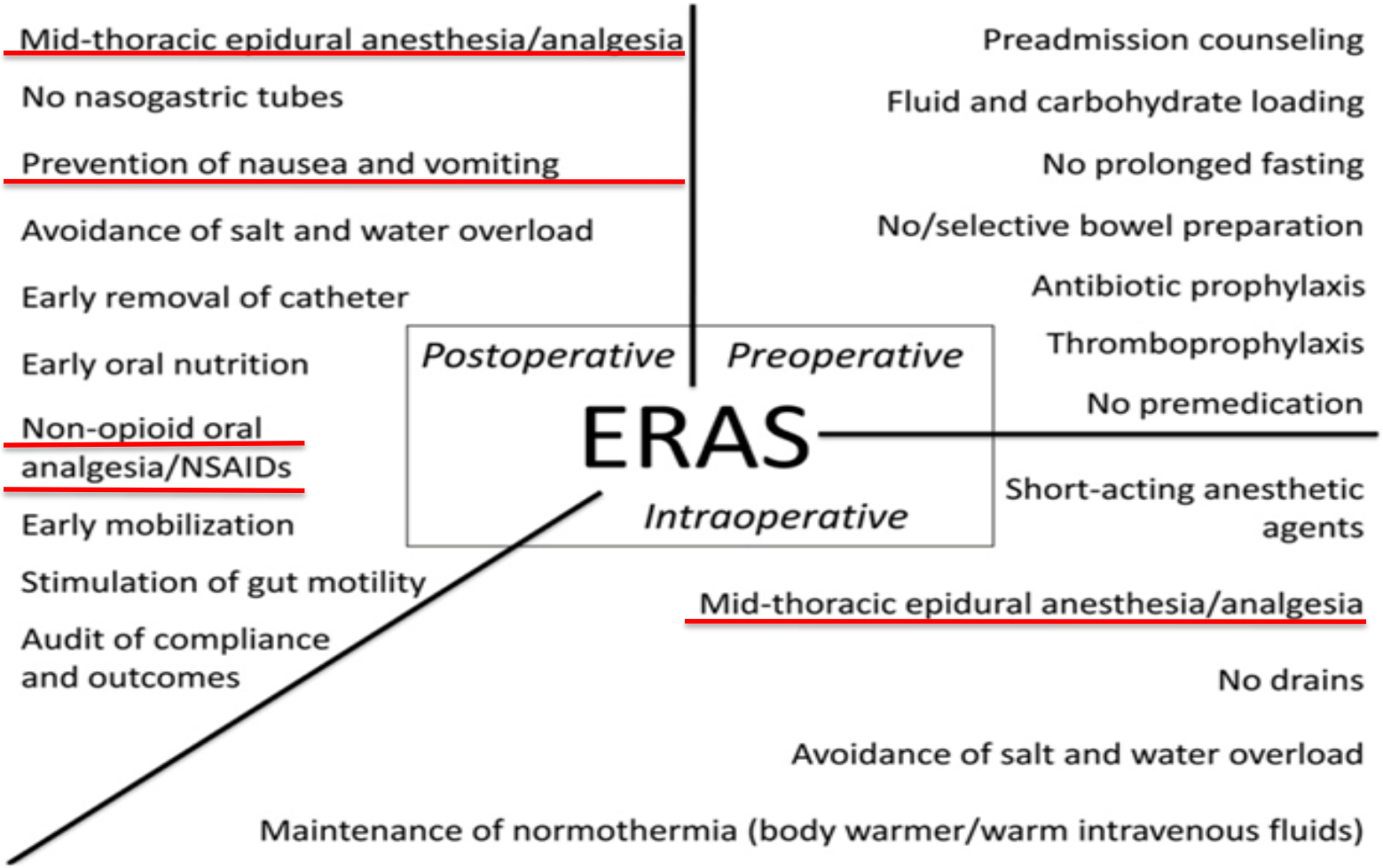
"The benefit conveyed by GDFT is particularly attenuated by its combination with ERAS pathways that are being increasingly implemented internationally. GDFT may be more of use in the intraoperative care of high-risk patients; however, as yet, there are no definitive data to support this belief"

Rollins KE, Lobo DN. Annals of Surgery 2016

Analgesia


Mid-thoracic epidural anesthesia/analgesia
No nasogastric tubes
Prevention of nausea and vomiting
Avoidance of salt and water overload
Early removal of catheter
Early oral nutrition
Non-opioid oral analgesia/NSAIDs
Early mobilization
Stimulation of gut motility
Audit of compliance and outcomes
Postoperative
Preoperative
ERAS
Intraoperative
Preadmission counseling
Fluid and carbohydrate loading
No prolonged fasting
No/selective bowel preparation
Antibiotic prophylaxis
Thromboprophylaxis
No premedication
Short-acting anesthetic agents
Mid-thoracic epidural anesthesia/analgesia
No drains
Avoidance of salt and water overload
Maintenance of normothermia (body warmer/warm intravenous fluids)

Analgesia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Maintenance of normothermia (body warmer/warm intravenous fluids)

Multimodal or balanced analgesia

Multimodal analgesia is achieved by combining different analgesics that act by different mechanisms, resulting in additive or synergistic analgesia with lowered adverse effects of sole administration of individual analgesics

Kehlet H, Dahl JB. *Anesth Analg* 1993

Multimodal or balanced analgesia

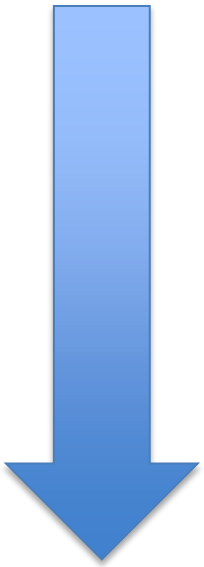
Reduce opioid consumption by using:

- Local anaesthetics
- Systemic analgesics
- Non analgesic methods
  - Acupuncture
  - TENS
  - Hypnosis

Local anaesthetics

Local anesthetics

Central

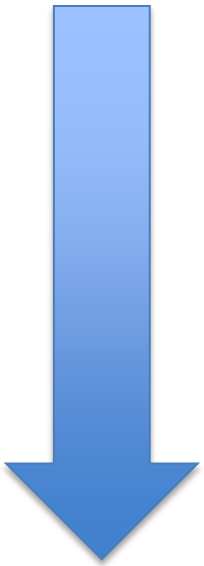


Peripheral

- Neuroaxial blockade (epidural and spinal)
- Paravertebral
- Nerve/plexus blocks
- TAP block
- Rectus sheath catheters
- Intraperitoneal
- Wound catheters/infiltration

Local anesthetics

Central



Peripheral

Less popular

More popular

Neuraxial blockade

- Epidurals viewed as gold standard for open GI surgery:

Advantages	
Superlative analgesia	
Reduction in blood loss	
Reduction in Pulmonary Thromboembolism	
Reduced time for return of GI function	

Neuraxial blockade

- Epidurals viewed as gold standard for open GI surgery:

Advantages	Disadvantages
Superlative analgesia	Failure rare
Reduction in blood loss	Fluid management/hypotension
Reduction in Pulmonary Thromboembolism	Mobility (especially lumbar epidurals)
Reduced time for return of GI function	Risks especially coagulopathy

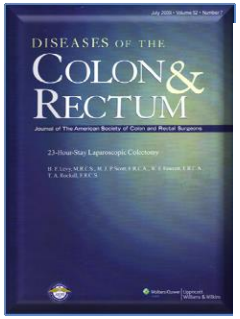
Neuraxial blockade

- Spinal analgesia logical alternative for laparoscopic surgery:

Good analgesia
Simple, quick and safe
Limited duration of action
Still moderate stress response

Epidural vs PCA vs Spinal Randomised Controlled Trial

- Good analgesia (but epidural best early pain relief)
- Rapid mobilisation
- Earlier resumption of GI function
- Earlier removal of urinary catheters
- Early reduction in stress response
  - Glucose
  - Cortisol
- Reduced length of stay (PCA and Spinal vs epidural)
- Able to send spinal patients home in under 24 hours



Randomized clinical trial

British Journal of Surgery 2011; **98**: 1068–1078

Randomized clinical trial of epidural, spinal or patient-controlled analgesia for patients undergoing laparoscopic colorectal surgery

B. F. Levy[1], M. J. Scott[2], W. Fawcett[2], C. Fry[3] and T. A. Rockall[1]

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Levy BF, Scott MJ, Fawcett WJ, Rockall TA. *Diseases of the Colon and Rectum* 2009;**52:**1239-43

Levy BF, Scott MJP, Fawcett WJ, Fry C, Rockall TA. *British Journal of Surgery* 2011;**98:**1068-78

Day AR, Smith RVP, Scott MJP, Fawcett WJ, Rockall TA. *British Journal of Surgery* 2015;**102:**1473-1479

Other use of local anaesthetics

- Paravertebral
- TAP block
- Rectus sheath catheters
- Intraperitoneal
- Wound catheters/infiltration

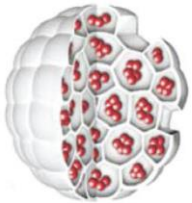
Other use of local anaesthetics

- Paravertebral - oesophageal, breast surgery
- TAP block - GI Surgery
- Rectus sheath catheters - urology
- Intraperitoneal
- Wound catheters/infiltration – emergency surgery

Other use of local anaesthetics

- Paravertebral - pneumothorax
- TAP block - damage to viscera
- Rectus sheath catheters
- Intraperitoneal
- Wound catheters/infiltration

- NB Local Anaesthetic toxicty



Rectus sheath catheters

- Better than wound catheters (qv)
- Opioid sparing
- Avoids mobility/hypotension associated with epidural
- Training of staff
- RCT underway comparing Thoracic Epidural versus Rectus Sheath Catheters (TERSC)
- Early data suggests can be comparable to epidural
- More applicable for open surgery

Crosbie EJ et al Eur J Obstet Gynecol Reprod Biol 2012
Wilkinson KA et al. Trials 2014

TAP blocks

- Reduction in morphine use 31.3 vs. 51.8 mg; (P = 0.03). No other significant effects.

Conhaghan P et al. *Surg Endosc* 2010.

- 353 unselected patients
- TAP > iv paracetamol/oral analgesia > PCA
- Resumption of diet 12,12,36 hours respectively (P<0.001)
- Median LOS 2,3,5 days respectively (P<0.001)

Zafar N et al *Colorectal Disease* 2010

- Metanalysis review supports its use in open surgery (opioid sparing and PONV)
- No complications

Johns N et al. *Colorectal Disease* 2012

TAP blocks – most recently

- Meta analysis in laparoscopic surgery
  - 633 subjects
  - Reduces early and late pain at rest, and opioid consumption
  - Preoperative better than postoperative blocks
  - Dose response: LA with late pain and opioid consumption

De Oliveira GS Jr, et al. *Anesth Analg* 2014

Surgical Site Catheter Analgesia

Practical issues

- Catheter type
  - multiholed
- Catheter placement
  - preperitoneal > subcutaneous
- Bolus or Infusion. Flow rates
  - infusion > bolus.
  - high rates eg 10 mls/hr
- Duration
  - 48 hours
- For use at home ?

Surgical Site Catheter Analgesia

- Varying results:
  - Opioid scores invariably reduced
  - Overall pain scores generally down
  - Some have shown reduced length of stay
  - Some have shown accelerated return of bowel function
  - Infection not increased

Karthikesalingham A et al. *World J Gastroenterol*. 2008

Beaussier M et al. *Anesthesiology* 2007

Surgical Site Catheter Analgesia

- LSCS: better analgesia, less side effects, less need for nursing care, shorter duration of stay compared with epidural morphine

  O'Neill P et al. *Anesth Analg* 2012

- Open colorectal surgery: Comparable pain scores (slightly worse on movement) but less for urinary retention.

  Ventham NT. *Br J Surg* 2013

- Orthopaedics: Also of benefit in following knee > hip surgery

  Kuchalik J et al. *Br J Anaesth* 2013
  Essving P et al. *Anesth Analg* 2011

- Open liver resection. Comapred to epidural,SSCA reduced time to recovery after open liver resection (ns). No advantages for epidurals in terms of attenuation of the inflammatory response or pain scores

  Hughes MJ et al. BJS 2015

- Open thoracic surgery

  Fiorelli A et al. *Eur J Cardiothoracic Surg* 2015

Surgical Site Catheter Analgesia

- Two conflicting reports with SSA vs epidural:
  - good pain control
  - faster recovery of postoperative ileus and bowel function
  - lower incidence of PONV
  - improved sleep

Bertoglio S et al. *Anesth Analg* 2012

  - poorer pain control on the first day
  - worse sleep
  - increased time to both normal gut function and to hospital discharge

Jouve P et al. *Anesthesiology* 2013

Systemic analgesics

Systemic analgesics

- Opioids (strong and weak)
- Paracetamol
- NSAIDs, COX-2

- Anticonvulsants (gabapentin and pregabalin)
- NMDA receptor antagonists (ketamine and magnesium)
- Lidocaine iv infusion
- Glucocorticoids
- Peripheral opioid antagonists
- α-2 agonists (clonidine, dexmedetomidine)
- Beta blockers

Problems with systemic analgesics

- Opioids
- NSAIDs
- Paracetamol
- Local anesthetics
- Steroids
- Clonidine
- Ketamine
- Magnesium

Problems with systemic analgesics

- Opioids: *sedation, dysphoria, constipation, PONV*
- NSAIDs: *renal, bleeding, perforation, healing, CVS risk*
- Paracetamol: *hepatotoxicity*
- Local anaesthetics: *cardiac and CNS toxicity*
- Steroids: *hyperglycemia, poor wound healing*
- Clonidine: *sedation, hypotension*
- Ketamine: *dysphoria*
- Magnesium: *hypotension, weakness*

Opioids

- Aim to avoid/minimise within
- Harm of early opioids?
- Rescue/step down after oesophagectomy
- Sometimes with plain epidural
- Newer opioids/approaches
  - Peripheral opioid antagonists (alvimopan)
  - Tapentadol
  - Transdermal iontophoretic fentanyl (PCA)

Healing and anti-inflammatory drugs

Concerns about anastomotic breakdown

Probably less the smoking, and still widely used but:

- Evidence implicates the non-selective COX inhibitors (p= .006) more than the COX-2 inhibitors (0.741)

  Gorissen KJ et al. *British Journal of Surgery* 2012

- Patients undergoing emergency surgery are more at risk than those undergoing elective colorectal resections

  Hakkarainen TW et al *JAMA surgery* 2015

- No increase in leak but marginal increase in sepsis

  Paulasir S et al. Disease of Colon and Rectum 2015

- COX-2 inhibitors > non-selective COX inhibitors are associated with increase pancreatic fistula in the early postoperative period following pancreaticoduodenectomy

  Behman R et al. Journal of Gastrointestinal Surgery 2015

Lidocaine infusions

- Reduction in analgesic requirements, ileus and PONV
- Opioid consumption reduced by 2/3
- Reduced hospital stay
- Second line therapy

BUT

- May be less relevant in small incision vs classical open surgery

Marrett E et al *Br J Surg* 2008

- Anti-cancer effect

Lirk P. *Br J Anaesth* 2012

Ketamine

When used intraoperatively and via infusion for 48 hours post op (2 mcg/kg/min after a 0.5 mg/kg bolus):

- Morphine consumption halved
- Side effects: sedation, delusions, nightmares, psychiatric disorders not manifest at these doses

Zakine J et al. *Anesth Analg* 2008

- Anti-inflammatory effect as measured by reduced IL-6

Dale O et al. *Anesth Analg* 2012

Ketamine – 2 good reviews

Ketamine both reduces opioid consumption and improves analgesic quality:

- Less PONV, sedation but more nightmares/hallucinations
- Good for thoracic, upper GI and major orthopedics
- Administered at different times
  - preemptively, intraoperatively, postoperatively
- and by different methods
  - bolus, infusion, PCA

Laskowski K et al. *Can J Anaesth* 2011;58:911-23

Adding ketamine to morphine PCA

- mixed drugs were superior to PCA opioid alone in thoracic surgery with significant reduction in
  - pain score
  - total morphine consumption
  - postoperative desaturation.
- ? benefit of adding ketamine for orthopedic or abdominal surgery

Carstensen M et al *Br J Anaesth* 2010;104:401-406

Gabapentinoids

Pregabalin and gabapentin:

- Reduce postoperative pain
- Good opioid sparing effect
- Reduced opioid side effects
- Dose, duration and progression to chronic pain unknown
- BUT: Pregabalin produces visual disturbances

Tiippana E et al. *Anesth Analg* 2007
Zhang J et al *BJA* 2011

- Not used for colorectal surgery but used successfully for laparoscopic cholecystectomy

Agarwal A et al *Br J Anaesth* 2008

- Key area is to prevent Chronic Post Surgical Pain (CPSP) with recent data supporting their use (with TCAs)

Clarke H et al. Anesth Analg 2012;115:428-4
Schmidt PC et al Anesthesiology 2013;119:1215-1221

Glucocorticoids

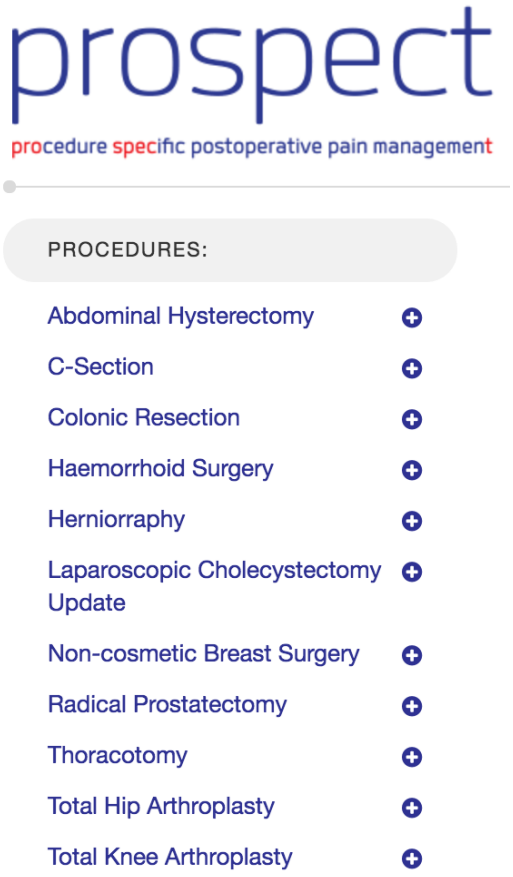
- Which one?
  - Dexamethasone
  - Methylprednisolone
- Analgesic
  - Spinal
  - Anti-inflammatory
- Opioid sparing
- Anti-emetic
- Concerns over
  - Infection
  - Wound healing
  - hyperglycaemia

systemic analgesics summary

- Opioids
- NSAIDs
- Paracetamol
- Local anaesthetics
- Steroids
- Clonidine
- Ketamine
- Magnesium
- Anticonvulsants

- ?early morphine ok
- Anastomotic leakage
- ✔
- Lidocaine iv
- High dose orthopaedics
- ✘
- ?Mix with PCA
- ✘
- Progession to chronic pain

Procedure specific pain management including



http://www.postoppain.org/

ERAS® Society

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NHS Foundation Trust

UCL UNIVERSITY OF SURREY

Carbohydrate loading

"While it is desirable that there should be no solid matter in the stomach when chloroform is administered, it will be found very salutary to give a cup of tea or beef-tea about two hours previously"

Sir Joseph Lister
1827-1912

Carbohydrate loading

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland

Editorial

Oral carbohydrate preload drink for major surgery – the first steps from famine to feast

M. J. Scott Consultant in Anaesthesia and Intensive Care and W. J. Fawcett Consultant in Anaesthesia and Pain Medicine, Senior Fellows

Article first published online: 23 OCT 2014

DOI: 10.1111/anae.12921

Issue

Anaesthesia

Volume 69, Issue 12, pages 1308–1313, December 2014

What is carbohydrate loading?

Preoperative elective surgical patients:

- Mainly maltodextrins (polysaccharide)
- Emptied from stomach reliably after 2 hours
- Commonly used formulation is 50g sachet, diluted to 400 mls
- 12.5% drink, 135 mOsm/kg, approx 200 calories
- 2 sachets (800mls) night prior to surgery
- 1 sachets (400ml) 2-4 hours prior to surgery

Carbohydrate loading

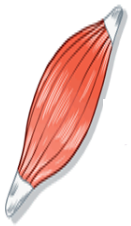
- attenuates insulin resistance
- improves patient comfort and well being
- minimises protein losses
- Improves postoperative muscle function
- reduces complications and LOS
- patient arrives metabolically fed state prior to surgery

With GDFT is a major independent predictor for improved outcome

Gustafsson UO et al. *Arch Surg* 2011

Insulin resistance

- Hyperglycaemia
  - infections
  - renal
  - cardiac
  - neuropathy
- Poor uptake into muscle
  - Reduced glucose uptake
  - Reduced glycogen storage
  - Increased protein catabolism



Insulin resistance

- Hyperglycaemia
  - Infections
  - renal
  - cardiac
  - neuropathy

- Poor uptake into muscle
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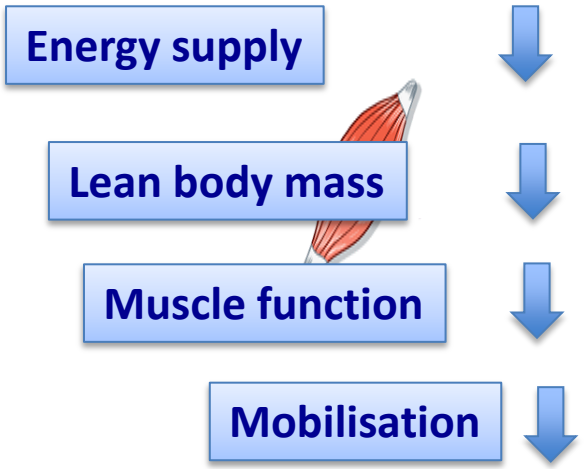
  - Increased protein catabolism



Postoperative insulin resistance increase the risk of complications

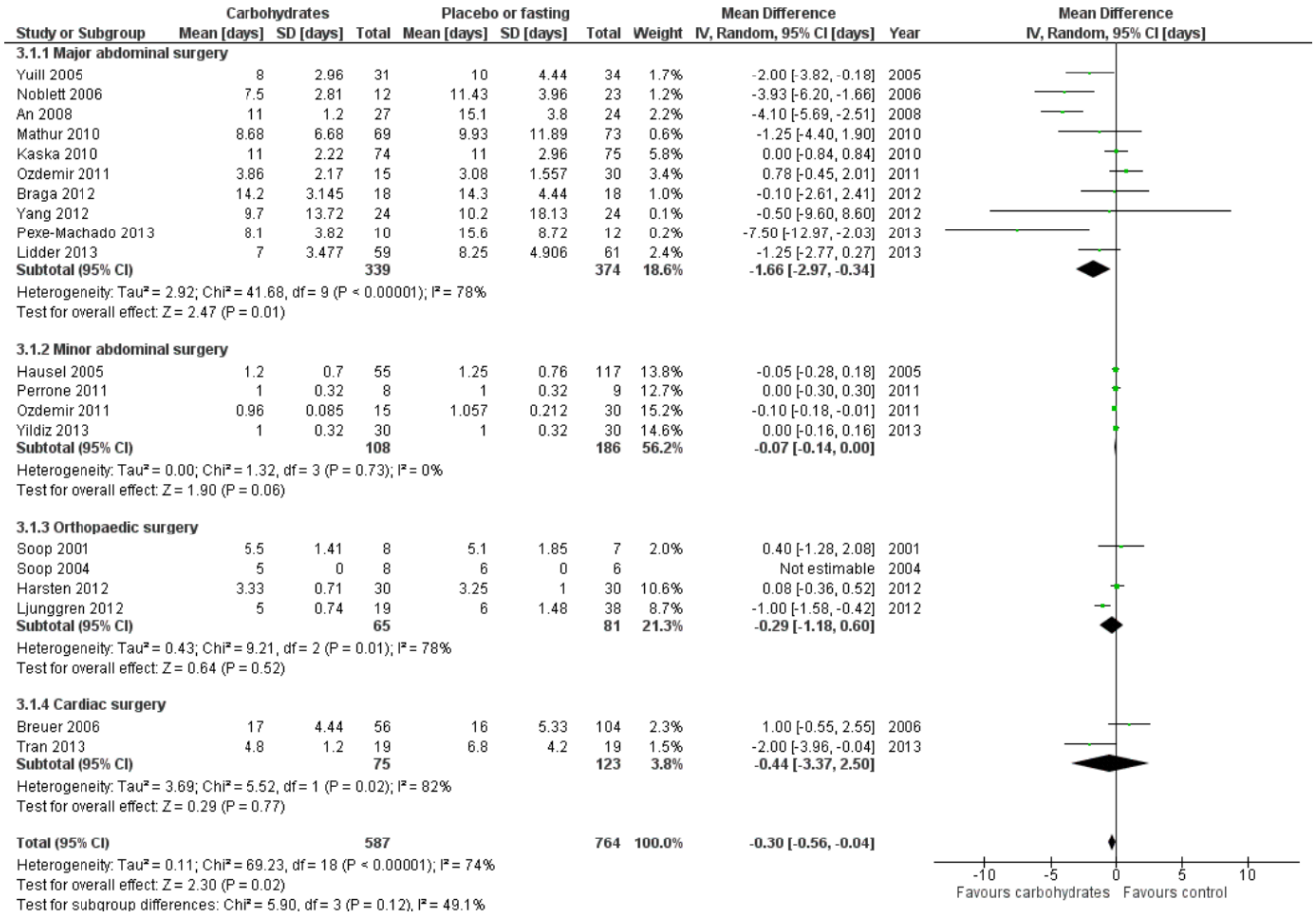
273 patients open cardiac surgery, insulin sensitivity determined at the end of op

Complication	OR for every decrease by 1 mg/kg/min (≈ 25% reduction in Insulin sensitivity)	P value
Death	2.33 (0.94-5.78)	0.067
Major complication	2.23 (1.30-3.85)	0.004
Severe infection	4.98 (1.48-16.8)	0.010
Minor infection	1.97 (1.27-3.06)	0.003

The ORs were adjusted for potential confounders

Sato et al, JCEM 2010

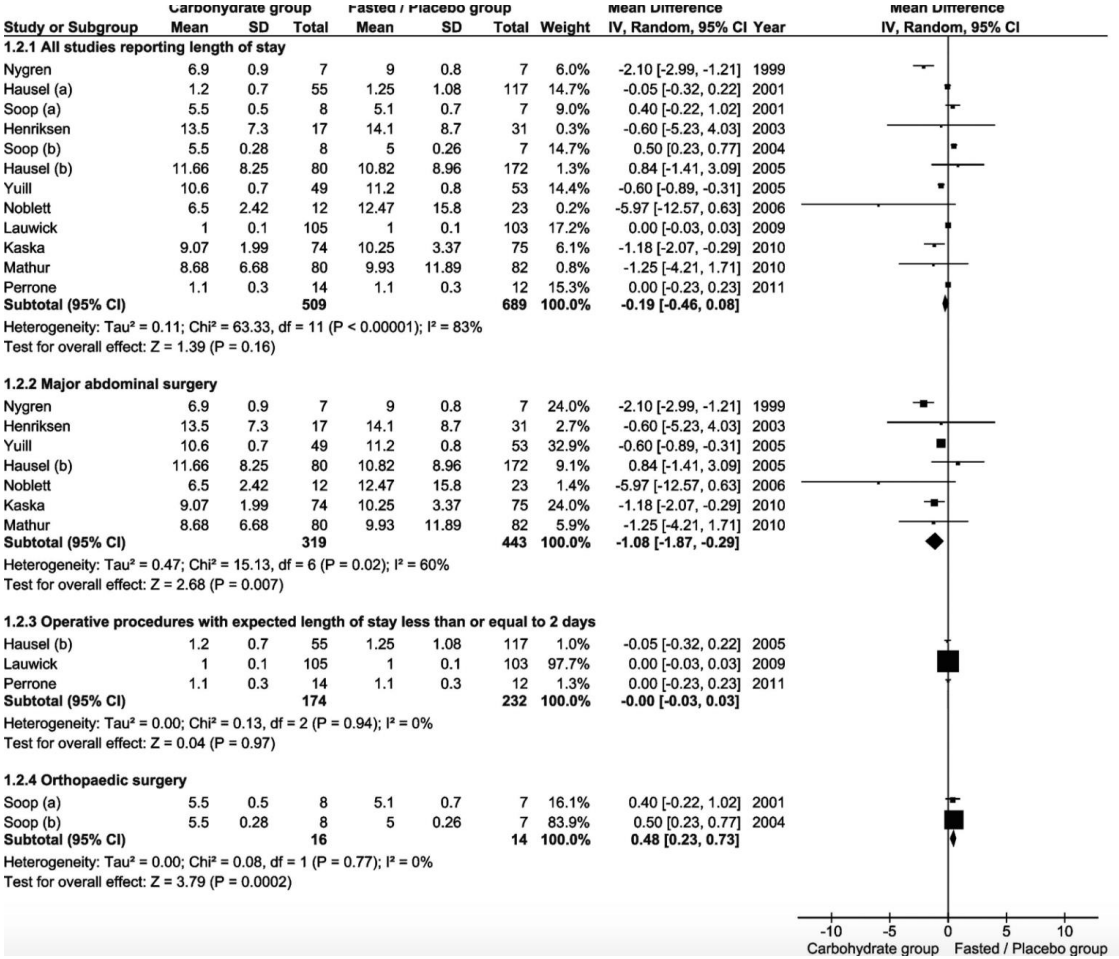
Preoperative carbohydrates reduce length of stay



Study or Subgroup	Carbohydrates Mean [days]	SD [days]	Total	Placebo or fasting Mean [days]	SD [days]	Total	Weight	Mean Difference IV, Random, 95% CI [days]	Year
3.1.1 Major abdominal surgery									
Yuill 2005	8	2.96	31	10	4.44	34	1.7%	-2.00 [-3.82, -0.18]	2005
Noblett 2006	7.5	2.81	12	11.43	3.96	23	1.2%	-3.93 [-6.20, -1.66]	2006
An 2008	11	1.2	27	15.1	3.8	24	2.2%	-4.10 [-5.69, -2.51]	2008
Mathur 2010	8.68	6.68	69	9.93	11.89	73	0.6%	-1.25 [-4.40, 1.90]	2010
Kaska 2010	11	2.22	74	11	2.96	75	5.8%	0.00 [-0.84, 0.84]	2010
Ozdemir 2011	3.86	2.17	15	3.08	1.557	30	3.4%	0.78 [-0.45, 2.01]	2011
Braga 2012	14.2	3.145	18	14.3	4.44	18	1.0%	-0.10 [-2.61, 2.41]	2012
Yang 2012	9.7	13.72	24	10.2	18.13	24	0.1%	-0.50 [-9.60, 8.60]	2012
Pexe-Machado 2013	8.1	3.82	10	15.6	8.72	12	0.2%	-7.50 [-12.97, -2.03]	2013
Lidder 2013	7	3.477	59	8.25	4.906	61	2.4%	-1.25 [-2.77, 0.27]	2013
Subtotal (95% CI)			**339**			**374**	**18.6%**	**-1.66 [-2.97, -0.34]**	
Heterogeneity: Tau² = 2.92; Chi² = 41.68, df = 9 (P < 0.00001); I² = 78%									
Test for overall effect: Z = 2.47 (P = 0.01)									
3.1.2 Minor abdominal surgery									
Hausel 2005	1.2	0.7	55	1.25	0.76	117	13.8%	-0.05 [-0.28, 0.18]	2005
Perrone 2011	1	0.32	8	1	0.32	9	12.7%	0.00 [-0.30, 0.30]	2011
Ozdemir 2011	0.96	0.085	15	1.057	0.212	30	15.2%	-0.10 [-0.18, -0.01]	2011
Yildiz 2013	1	0.32	30	1	0.32	30	14.6%	0.00 [-0.16, 0.16]	2013
Subtotal (95% CI)			**108**			**186**	**56.2%**	**-0.07 [-0.14, 0.00]**	
Heterogeneity: Tau² = 0.00; Chi² = 1.32, df = 3 (P = 0.73); I² = 0%									
Test for overall effect: Z = 1.90 (P = 0.06)									
3.1.3 Orthopaedic surgery									
Soop 2001	5.5	1.41	8	5.1	1.85	7	2.0%	0.40 [-1.28, 2.08]	2001
Soop 2004	5	0	8	6	0	6		Not estimable	2004
Harsten 2012	3.33	0.71	30	3.25	1	30	10.6%	0.08 [-0.36, 0.52]	2012
Ljunggren 2012	5	0.74	19	6	1.48	38	8.7%	-1.00 [-1.58, -0.42]	2012
Subtotal (95% CI)			**65**			**81**	**21.3%**	**-0.29 [-1.18, 0.60]**	
Heterogeneity: Tau² = 0.43; Chi² = 9.21, df = 2 (P = 0.01); I² = 78%									
Test for overall effect: Z = 0.64 (P = 0.52)									
3.1.4 Cardiac surgery									
Breuer 2006	17	4.44	56	16	5.33	104	2.3%	1.00 [-0.55, 2.55]	2006
Tran 2013	4.8	1.2	19	6.8	4.2	19	1.5%	-2.00 [-3.96, -0.04]	2013
Subtotal (95% CI)			**75**			**123**	**3.8%**	**-0.44 [-3.37, 2.50]**	
Heterogeneity: Tau² = 3.69; Chi² = 5.52, df = 1 (P = 0.02); I² = 82%									
Test for overall effect: Z = 0.29 (P = 0.77)									
Total (95% CI)			**587**			**764**	**100.0%**	**-0.30 [-0.56, -0.04]**	
Heterogeneity: Tau² = 0.11; Chi² = 69.23, df = 18 (P < 0.00001); I² = 74%									
Test for overall effect: Z = 2.30 (P = 0.02)									
Test for subgroup differences: Chi² = 5.90, df = 3 (P = 0.12), I² = 49.1%									

Smith MD et al, Cochrane Library 2014

Preoperative carbohydrates reduce length of stay



Study or Subgroup	Carbohydrate group Mean	SD	Total	Fasted / Placebo group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
1.2.1 All studies reporting length of stay									
Nygren	6.9	0.9	7	9	0.8	7	6.0%	-2.10 [-2.99, -1.21]	1999
Hausel (a)	1.2	0.7	55	1.25	1.08	117	14.7%	-0.05 [-0.32, 0.22]	2001
Soop (a)	5.5	0.5	8	5.1	0.7	7	9.0%	0.40 [-0.22, 1.02]	2001
Henriksen	13.5	7.3	17	14.1	8.7	31	0.3%	-0.60 [-5.23, 4.03]	2003
Soop (b)	5.5	0.28	8	5	0.26	7	14.7%	0.50 [0.23, 0.77]	2004
Hausel (b)	11.66	8.25	80	10.82	8.96	172	1.3%	0.84 [-1.41, 3.09]	2005
Yuill	10.6	0.7	49	11.2	0.8	53	14.4%	-0.60 [-0.89, -0.31]	2005
Noblett	6.5	2.42	12	12.47	15.8	23	0.2%	-5.97 [-12.57, 0.63]	2006
Lauwick	1	0.1	105	1	0.1	103	17.2%	0.00 [-0.03, 0.03]	2009
Kaska	9.07	1.99	74	10.25	3.37	75	6.1%	-1.18 [-2.07, -0.29]	2010
Mathur	8.68	6.68	80	9.93	11.89	82	0.8%	-1.25 [-4.21, 1.71]	2010
Perrone	1.1	0.3	14	1.1	0.3	12	15.3%	0.00 [-0.23, 0.23]	2011
Subtotal (95% CI)			**509**			**689**	**100.0%**	**-0.19 [-0.46, 0.08]**	
Heterogeneity: Tau² = 0.11; Chi² = 63.33, df = 11 (P < 0.00001); I² = 83%									
Test for overall effect: Z = 1.39 (P = 0.16)									
1.2.2 Major abdominal surgery									
Nygren	6.9	0.9	7	9	0.8	7	24.0%	-2.10 [-2.99, -1.21]	1999
Henriksen	13.5	7.3	17	14.1	8.7	31	2.7%	-0.60 [-5.23, 4.03]	2003
Yuill	10.6	0.7	49	11.2	0.8	53	32.9%	-0.60 [-0.89, -0.31]	2005
Hausel (b)	11.66	8.25	80	10.82	8.96	172	9.1%	0.84 [-1.41, 3.09]	2005
Noblett	6.5	2.42	12	12.47	15.8	23	1.4%	-5.97 [-12.57, 0.63]	2006
Kaska	9.07	1.99	74	10.25	3.37	75	24.0%	-1.18 [-2.07, -0.29]	2010
Mathur	8.68	6.68	80	9.93	11.89	82	5.9%	-1.25 [-4.21, 1.71]	2010
Subtotal (95% CI)			**319**			**443**	**100.0%**	**-1.08 [-1.87, -0.29]**	
Heterogeneity: Tau² = 0.47; Chi² = 15.13, df = 6 (P = 0.02); I² = 60%									
Test for overall effect: Z = 2.68 (P = 0.007)									
1.2.3 Operative procedures with expected length of stay less than or equal to 2 days									
Hausel (b)	1.2	0.7	55	1.25	1.08	117	1.0%	-0.05 [-0.32, 0.22]	2005
Lauwick	1	0.1	105	1	0.1	103	97.7%	0.00 [-0.03, 0.03]	2009
Perrone	1.1	0.3	14	1.1	0.3	12	1.3%	0.00 [-0.23, 0.23]	2011
Subtotal (95% CI)			**174**			**232**	**100.0%**	**-0.00 [-0.03, 0.03]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 2 (P = 0.94); I² = 0%									
Test for overall effect: Z = 0.04 (P = 0.97)									
1.2.4 Orthopaedic surgery									
Soop (a)	5.5	0.5	8	5.1	0.7	7	16.1%	0.40 [-0.22, 1.02]	2001
Soop (b)	5.5	0.28	8	5	0.26	7	83.9%	0.50 [0.23, 0.77]	2004
Subtotal (95% CI)			**16**			**14**	**100.0%**	**0.48 [0.23, 0.73]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.77); I² = 0%									
Test for overall effect: Z = 3.79 (P = 0.0002)									

Awad S et al Clin Nutr 2013

Carbohydrate loading - controversies

- Gastric emptying and aspiration risk
  - Ultrasound/ Co-administration of paracetamol studies
  - Maltodextrins empty readily and predictably from the stomach (unlike glucose or milk)
- Diabetics
  - risk of hyperglycaemia and pulmonary aspiration (autonomic neuropathy)
  - T2DM

Gustafsson UO et al
***Acta Anaesthesiologica Scandinavica* 2008**

  - Give with usual medication

Scott MJ, Fawcett WJ Anaesthesia 2014

  - Glycaemic Endothelial Drink (GED) with less maltodextrin and citrulline

Fawcett WJ , Levy N . RCOA Bulletin 2016

Other areas

- Ventilation strategies
  - Bespoke ventilation
- Neuromuscular blockade monitoring
  - Reduce awareness and POPC
  - Deep blockade
    - Permit lower insufflation pressures (8 mmHg)
    - Produce cardiorespiratory effects
    - Produce less pain, PONV
    - Permit improved surgical access
  - Confirm reversal (microaspiration)
  - Sugammadex
- Depth of Anaesthesia (BIS)
  - Triple low
  - Effect on POCD and delirium

The Future

Anaesthesia and cancer outcome

- Regional anesthesia potentially improves outcome for some specialties (breast and prostate)

- ERAS patients may be fitter for adjuvant treatment more quickly (eg chemotherapy)

Day AR. *Colorectal Disease* 2014

- Sympathetic block may improve cellular immunity

- Drug effects
  - Morphine and effects on NK cells
  - lidoocaine demethylates DNA cancer cells

Analgesic effect on cancer outcome

- Not so far in Colorectal in retrospective analysis

British Journal of Anaesthesia **109** (2): 185–90 (2012)
Advance Access publication 23 April 2012 · doi:10.1093/bja/aes106

BJA

CLINICAL PRACTICE

Retrospective analysis of the effect of postoperative analgesia on survival in patients after laparoscopic resection of colorectal cancer

A. Day[1*], R. Smith[1], I. Jourdan[1], W. Fawcett[2], M. Scott[2] and T. Rockall[1]

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[2] Department of Anaesthesia, The Royal Surrey County Hospital, Egerton Road, Guildford GU2 7XX, UK

- Nor gynecological (ovarian or cervical)

Long term survival

- Can we improve long term survival?

British Journal of Anaesthesia **109** (5): 671–4 (2012)
doi:10.1093/bja/aes358

EDITORIAL I

Enhanced recovery: more than just reducing length of stay?

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Summary

- Challenge dogma to produce evidence-based pathways
- Pathway adherence is crucial
- Avoidance of complications crucial
- MIS
  - As surgery changes so re-examine pathway
- Fluids
- Analgesia:
  - As surgery changes so does analgesia
- Active management of problems
  - PONV
  - Hypotension
  - Poor mobility
- Why is patient still
  - In pyjamas
  - In hospital

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