ERAS® Society

Enhanced Recovery After Surgery

& how metabolism is key

State of the art lecture

Olle Ljungqvist MD, PhD
Professor of Surgery
Örebro University Hospital
& Karolinska Institutet, Sweden

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Recovery After Surgery
What are we trying to achieve?

Patient back to preoperative function

- **Normal gastrointestinal function**
  - **Normal food intake**
  - **Bowel movement**
- **Pain control**
- **Mobility**

- **No complication**

Insulin & Recovery

Insulin: main anabolic hormone involved in

- **All parts of metabolism**
  - **Glucose control**
  - **Fat metabolism**
  - **Protein**
- **Regulator of return of key functions**
- **Central to development of complications**
- **Affected by many perioperative treatments**

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- **Insulin resistance: a key for understanding and enhancing recovery**

Outline

- **Why Insulin Resistance & Enhanced Recovery?**
- **Insulin resistance**
  - **Recovery**
  - **Complications**
- **Enhanced Recovery After Surgery (ERAS)**
  - **Interaction and protection against insulin resistance**
  - **ERAS and outcomes**

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Recovery After Surgery
What are we trying to achieve?

Patient back to preoperative function

- **Normal GI function and food intake– energy & protein[1]**
  - **Normal food intake**
  - **Bowel movement**
- **Pain control – pain cause insulin resistance[2]**
- **Mobility – bed rest enhance protein breakdown[3]**

- **No complication**

1.Svanfeldt, Clin Nutr 2003; 2.Greisen, Anesthesiology 2001; 3.Biolo G, Am J Clin Nutr 2007

Insulin resistance & complications

- **Elective cardiac surgery, n= 273**
- **Diabetics and non diabetics**

Complications increase with insulin resistance:

50% reduction in insulin sensitivity:

- **5-6 fold increase risk of complications**
- **10 fold risk for infections**

Sato et al, JCEM 2010; 95: 4338-44

Outline

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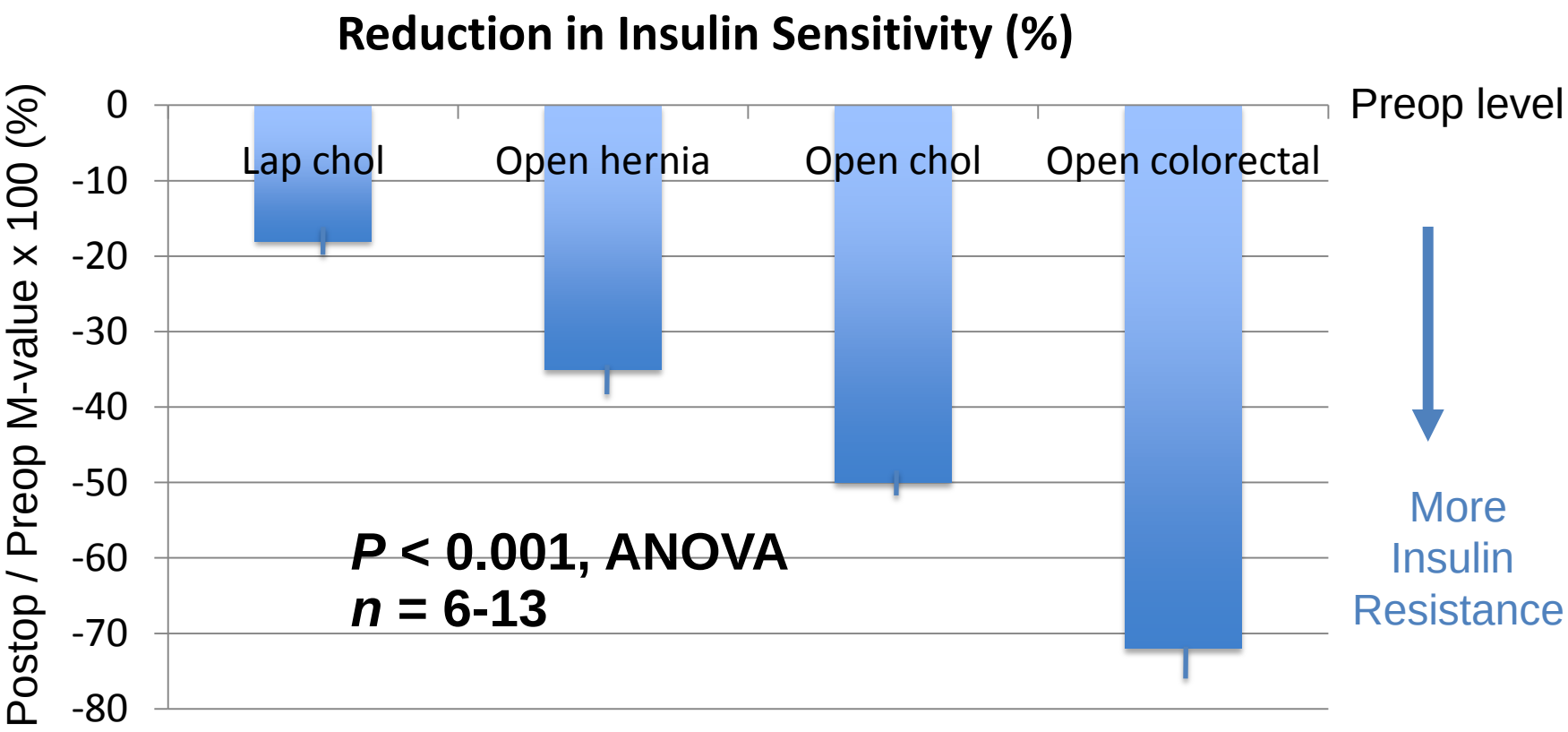
Postoperative Insulin resistance

Defintion:

Below normal metabolic effect of insulin

- **Glucose uptake**
- **Reduction in glucose production**
- **Lipolysis**
- **Protein breakdown / balance**

Insulin sensitivity falls with the magnitude of surgery



Adopted from Thorell et al: Curr Opin Clin Nutr Metab Care 1999

Independent factors predicting length of stay

- **Type of surgery**
- **Perioperative blood loss**
- **Postoperative insulin resistance**

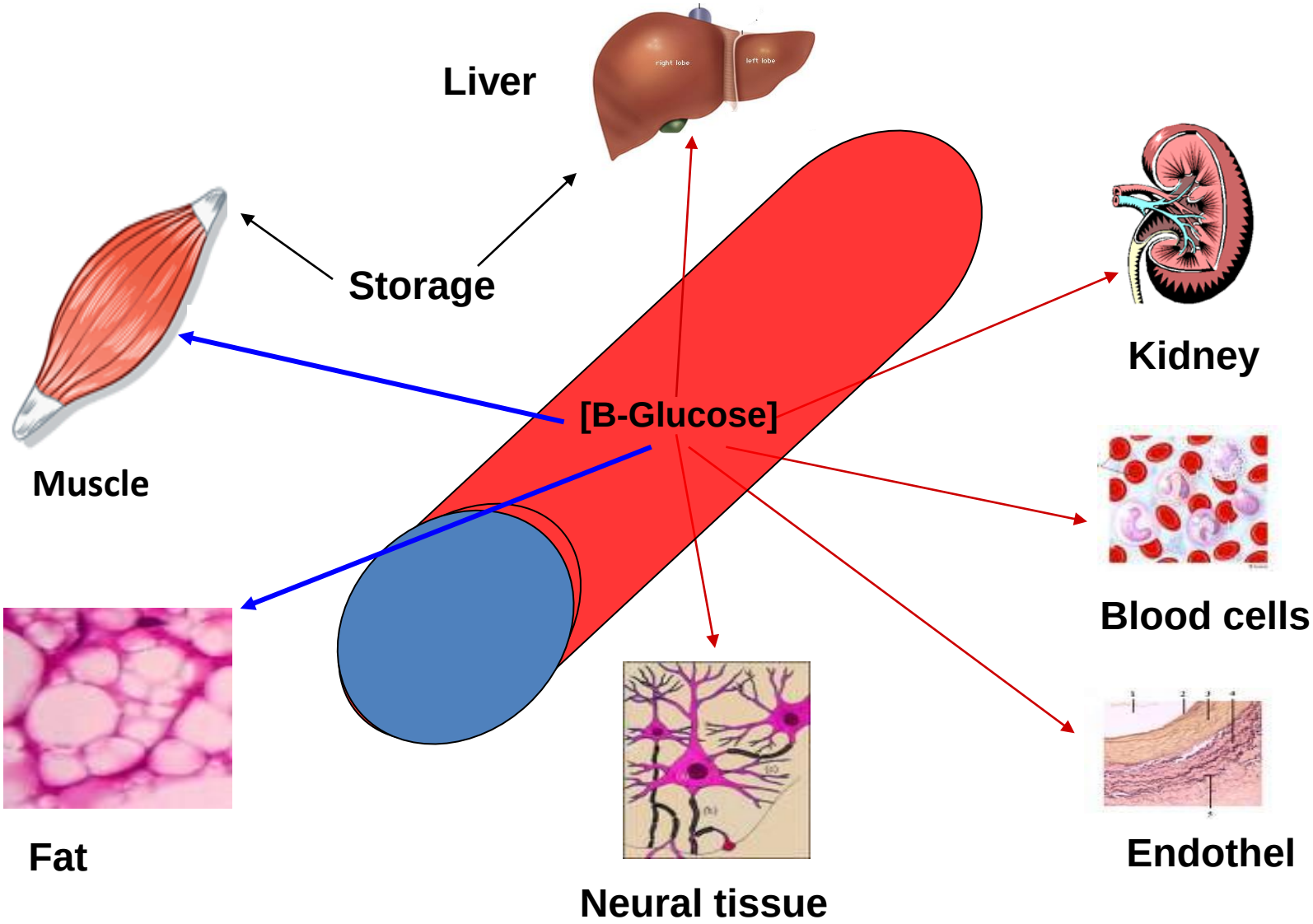
$R^2 = 0.71$, $p < 0.01$

Thorell et al: Curr Opin Clin Nutr Metab Care 1999

Glucose uptake

Insulin regulated

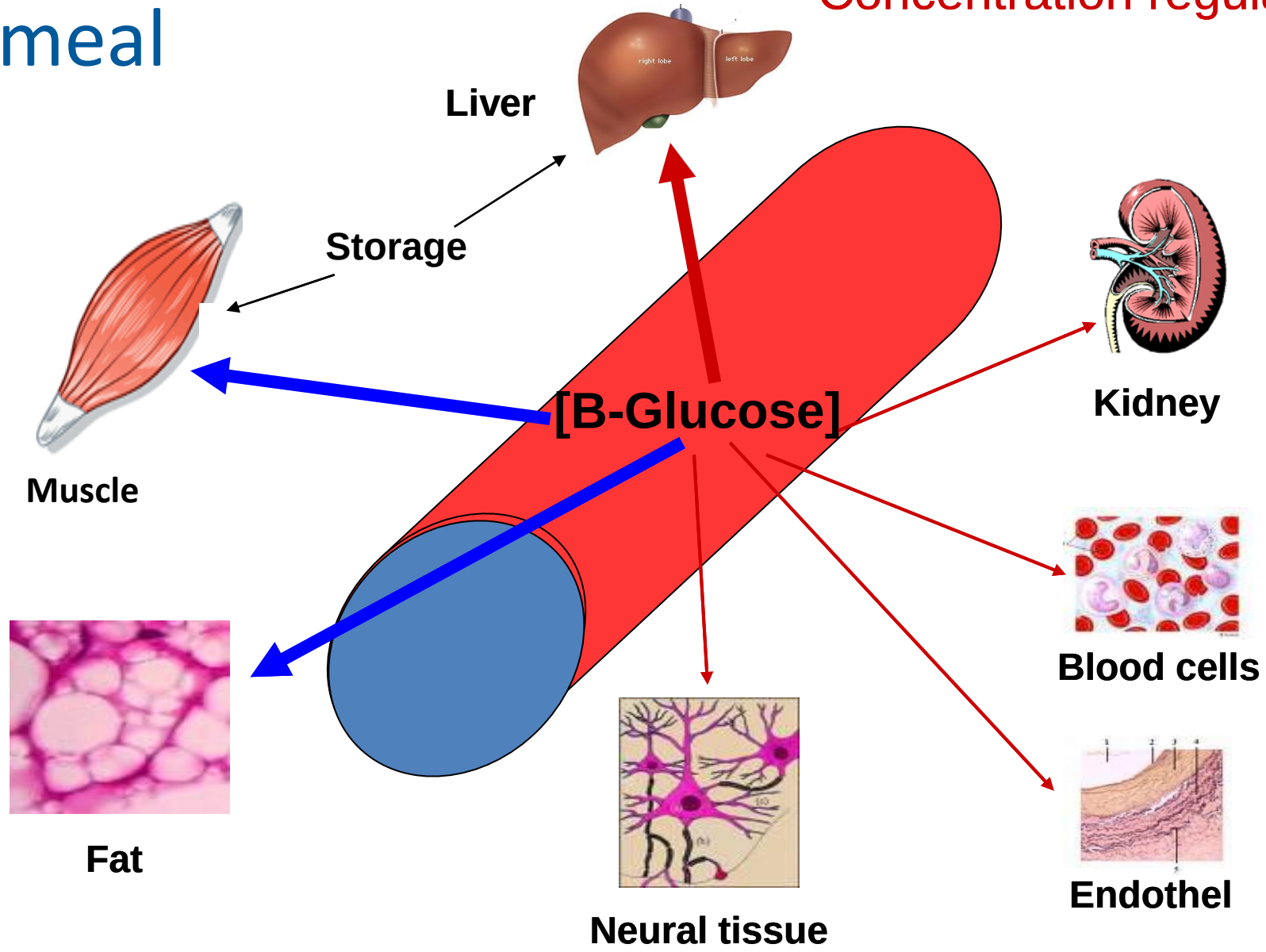
Concentration regulated



Glucose uptake - meal

Insulin regulated

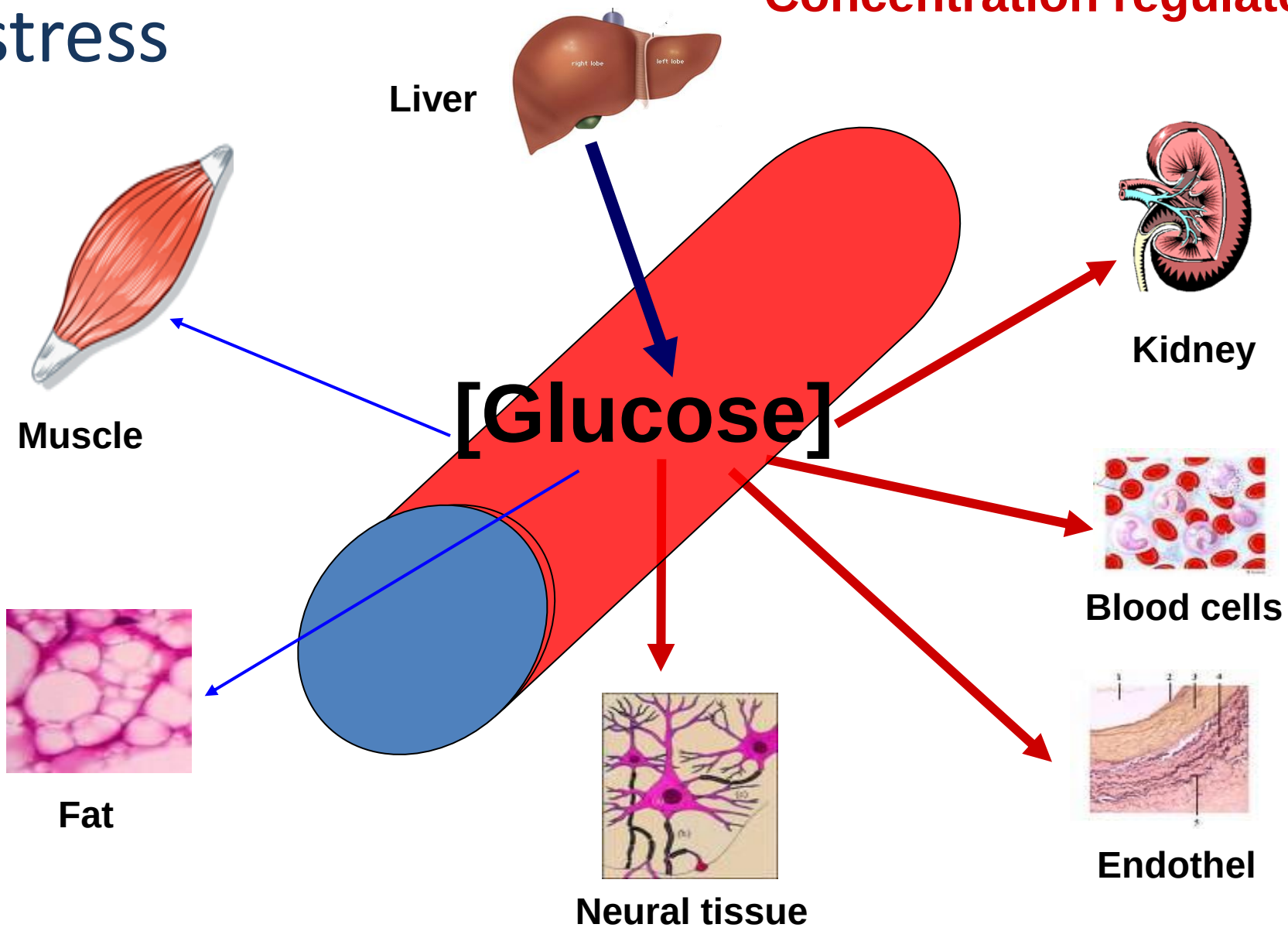
Concentration regulated



Glucose uptake - stress

Insulin regulated

Concentration regulated



Driving forces for hyperglycemia after surgery

	Postop
Hyperglycemia	**+**
Insulin sensitivity	-
Glucose production	**+**
Peripheral glucose uptake	**-**
GLUT4 translocation	-
Glycogen formation	-

Adopted from Ljungqvist et al, Clin Nutr 2001

Driving forces for hyperglycemia after surgery similar to diabetes

	Postop	Type 2 DM
Hyperglycemia	**+**	**+**
Insulin sensitivity	-	-
Glucose production	**+**	**+**
Peripheral glucose uptake	**-**	**-**
GLUT4 translocation	-	-
Glycogen formation	-	-

Adopted from Ljungqvist et al, Clin Nutr 2001

Normalizing insulin action normalizes metabolism

Insulin infusion to normalize:

- **Blood glucose**

Also controlled:

- **FFA**
- **Urea excretion**
- **Substrate utilization after major surgery**

Insulin resistance the key to catabolism

Brandi LS et al: Clin Sci 1990

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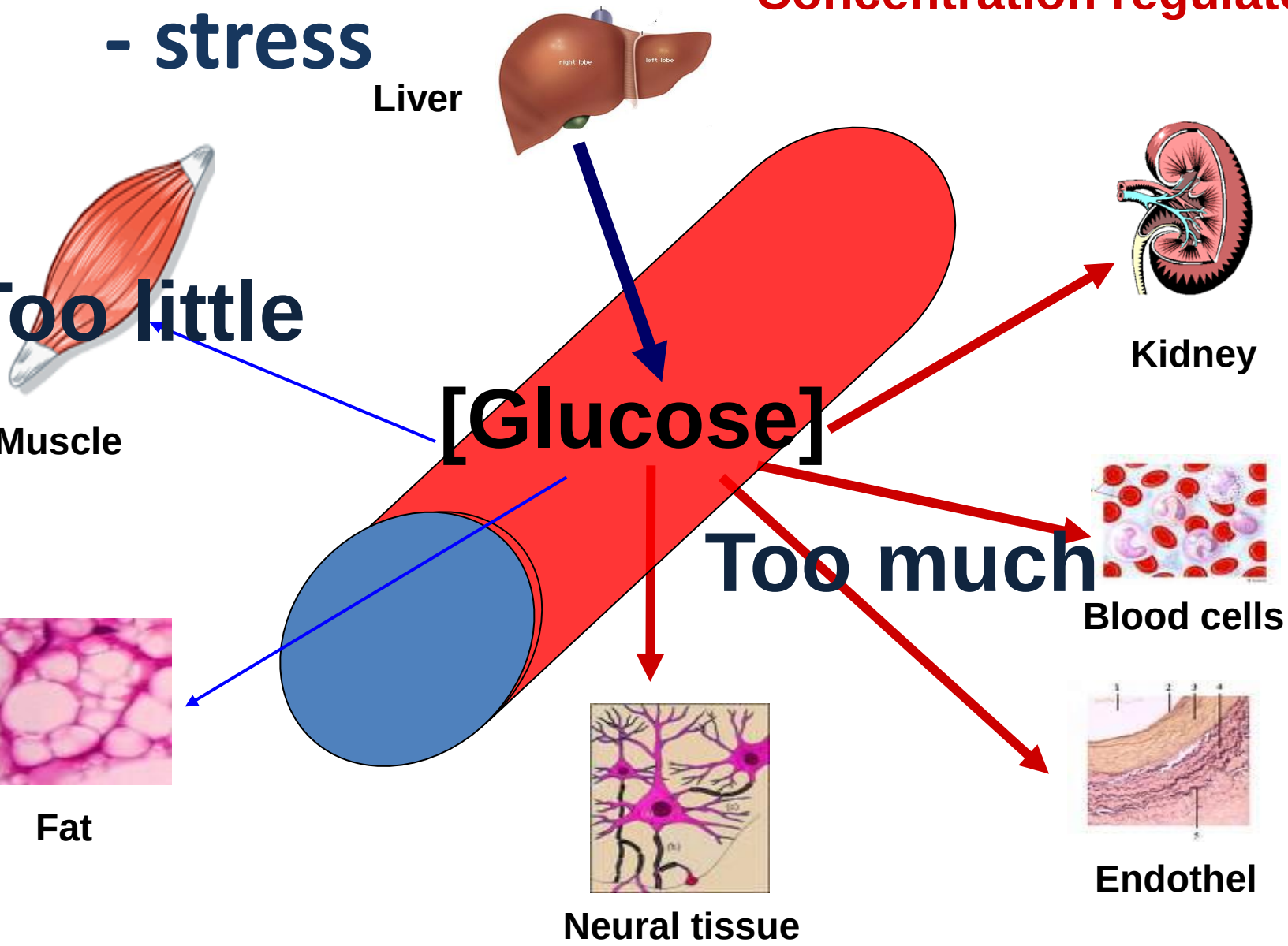
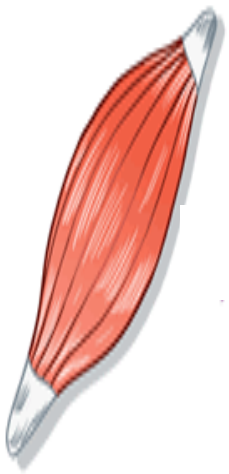
Glucose uptake - stress

Insulin regulated

Concentration regulated



Insulin resistance muscle



- **Reduced glucose uptake**
- **Reduced glycogen storage**
- **Increased protein catabolism**

Insulin resistance muscle

Energy supply uc glucose uptake

Lean body mass y en storage

- **Muscle function** bo m

Mobilisation

Insulin important for wound healing

- **6 patients studied twice, >40% burn injury**
- **Placebo – randomised - cross over design**
- **Hyperinsulinemia**
  - **400-900 microunits/ml for 7 days or placebo**
- **Glucose infusion to normoglycemia**

- **Donor-site healing time reduced**
  - **from 6.5 to 4.7 days, $p < 0.05$**

EJ Pierre et al, J Trauma 1998

Impaired Recovery

Postop (days)	Tissues/cells
Muscle weakness	**muscle**
Infections	leukocytes
Cardiovascular	blood vessels
Renal failure	kidney
Polyneuropathy	nerve tissue

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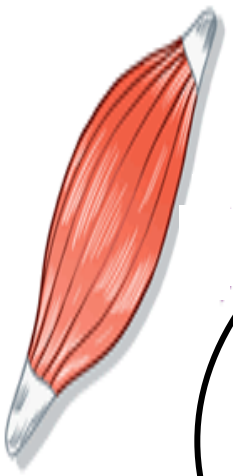
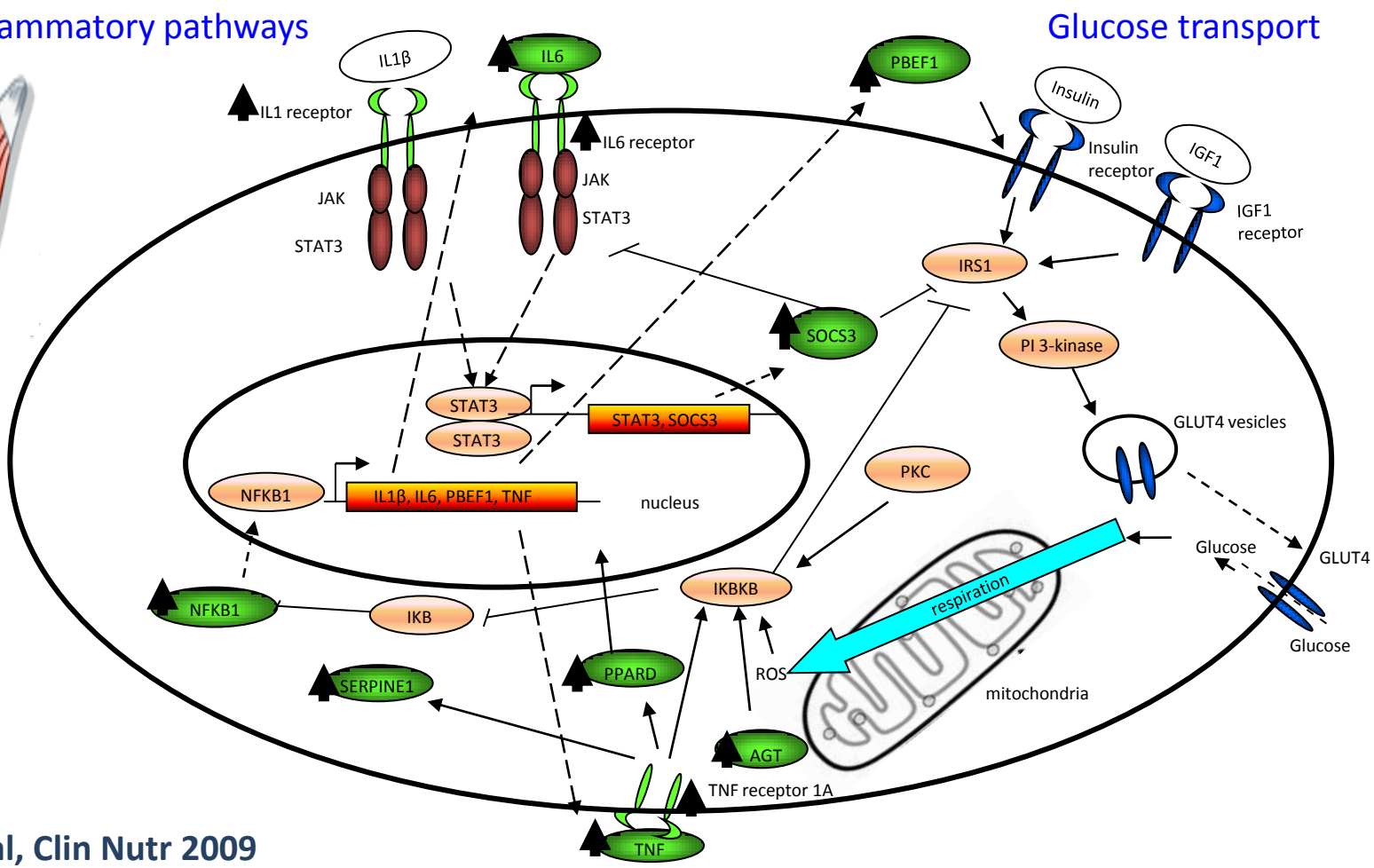
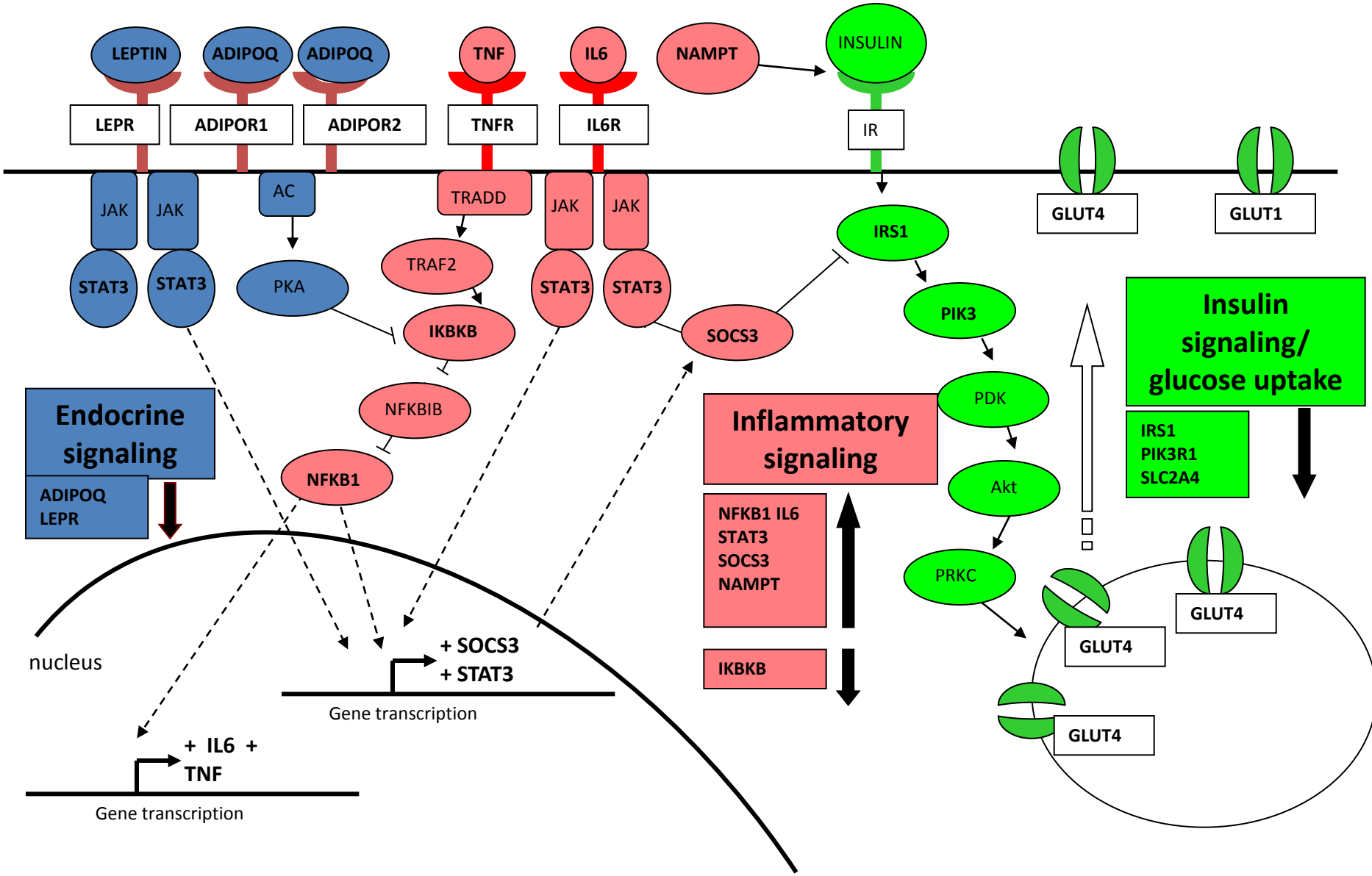
mRNA of inflammatory pathway genes up-regulated in skeletal muscle





Witasp et al, Clin Nutr 2009

Intracellular gene reactions to surgery



Witasp et al, JCEM 2010: 95: 3460-9

Complications

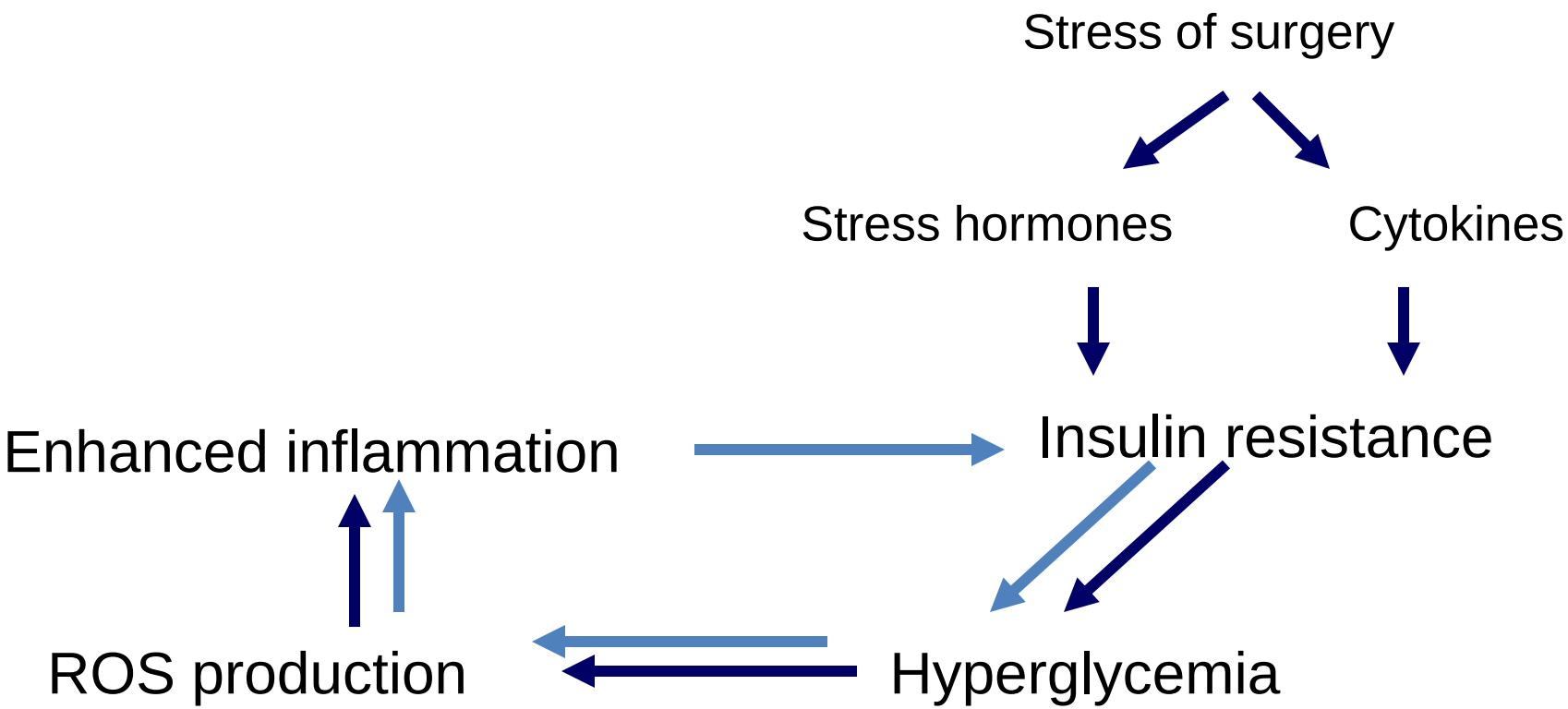
Postop (days)	Tissues/cells
Infections	leukocytes
Cardiovascular	blood vessels
Renal failure	kidney
Polyneuropathy	nerve tissue
Muscle weakness	muscle

Why these organs/cells?

Tissues unprotected to glucose uptake:

- **Uncontrolled inflow of glucose**
- **No storage**
- **Overflow of glycolysis**
- **ROS production**
- **Block of glycolysis & Krebs cycle**
- **Altered gene expression**
- **Enhanced inflammatory response**
- **Vicious circle**

Vicious circle

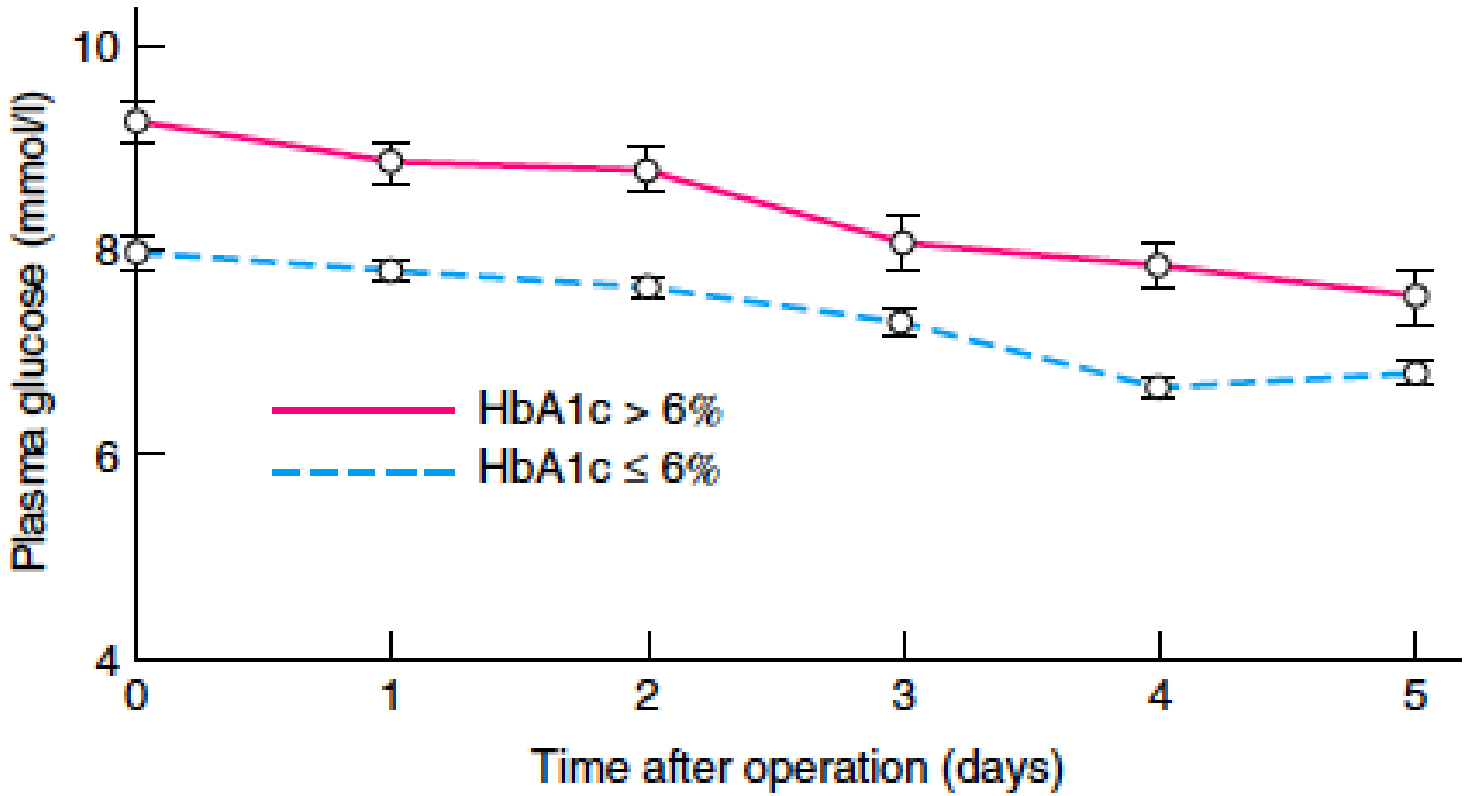


Glucose levels in ERAS & outcomes after surgery

- **120 Consecutive patients**
- **Colorectal surgery**
- **No history of diabetes**
- **Preop HbA1c – above or below 6.1**
- **26% pathologically high (≥ 6.1 mM)**
- **Glucose 5 times daily postop**
- **CRP and complications (30 day follow up)**

Gustafsson et al, BJS 2009: 96; 1358-64

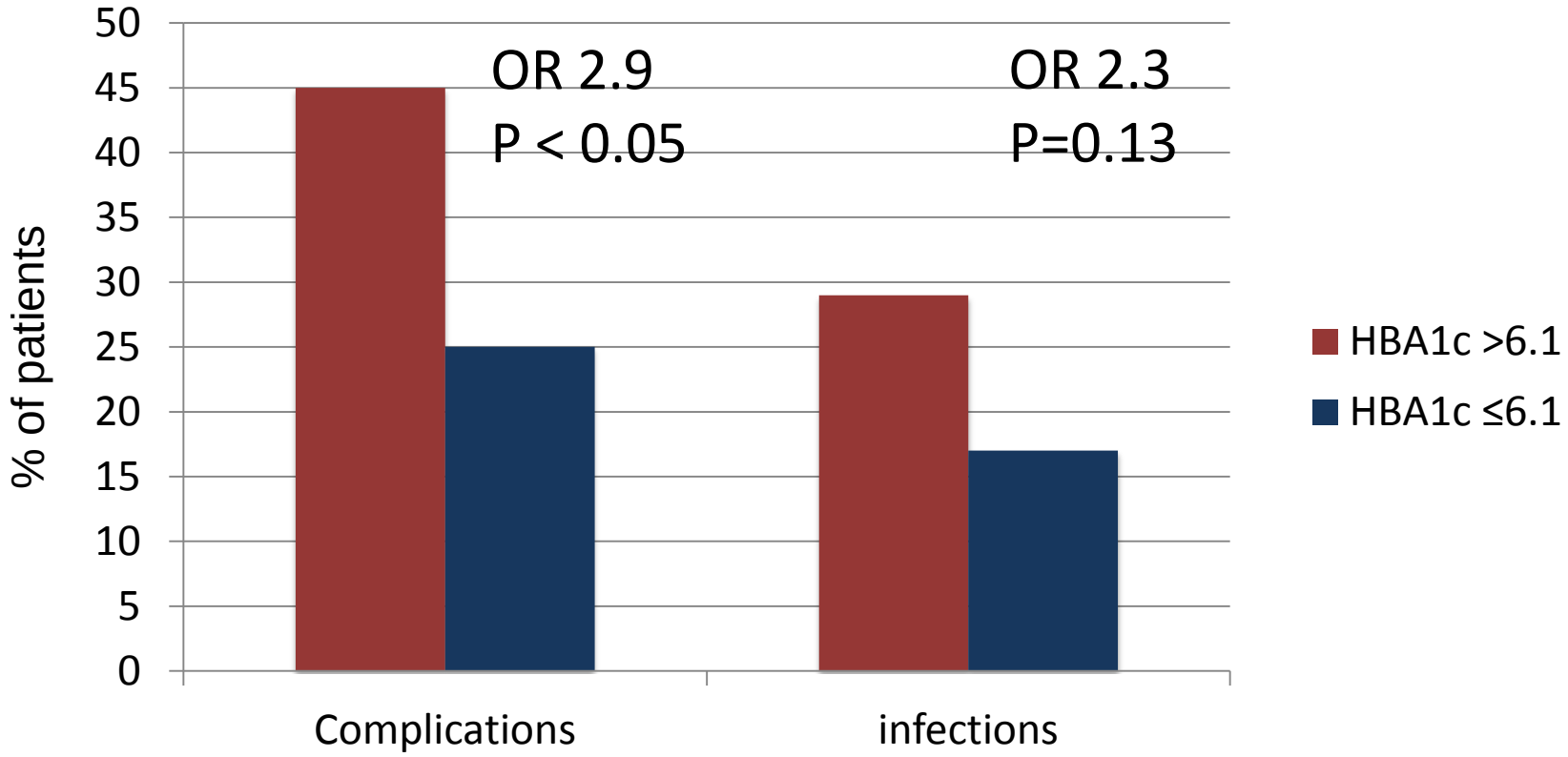
Glucose after major elective surgery



N = 120
1500 kcal/d

Gustafsson et al, BJS 2009: 96; 1358-64

HbA1c, Glucose control and postop complications



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Postoperative insulin resistance increase the risk for complications

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

Complication	OR for every decrease by 1 mg/kg/min (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; 95: 4338-44

Operative Day glucose & outcomes

Colorectal cancer patients, n= 7,576

Glucose level	Outcome	Odds ratio (95% CI)	p value
Moderate (161-200 mg/dl) (8.9-11.1 mmol/l)	**Surgical site infection**	1.44 (1.10-1.87)	<0.01
	Pneumonia	1.37 (1.00-1.87)	<0.05
Severe (>200mg/dl) (>11.1 mmol/l)	**Pneumonia**	1.55 (1.10-2.18)	<0.01
	Re operation	1.37 (1.02-1.87)	<0.05

Jackson et al, JACS 214; 2012

Hyperglycemia impairs immune function

- **Correlation between hyperglycemia and incidence of infection**
- **Diabetics with poor glucose control**
  - **Abnormal granulocyte adherence**
  - **Reduced chemotaxis**
  - **Lower phagocytocis**
  - **Abnormal microbiocidal function**

All above improved by glucose control

Khaodhiar et al, Curr Op Clin Nutr Metab 2: 79-82: 1999

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Fast track surgery ≈> ERAS

- **Multimodal approach to recovery - H Kehlet, DK**
- **A pioneer in fast track surgery**

- **Inspiration and early collaborator in ERAS**

- **ERAS – focus on patient recovery – not speed per se**

***Fearon K et al, Clin Nutr 2005,**

Enhanced Recovery After Surgery Study Group

- **Best practice in perioperative care:**
  - **colon resection,**
  - **rectal resection,**
    - **liver, gastric, pancreas, gynaecology, urology…..**
- **Aims: Enhance recovery**
- **Means:**
  - ***Reduce the stress of surgery***
  - ***Support of function***
- **Evidence Based Protocol***

***Fearon K et al, Clin Nutr 2005, Lassen et al, Arch Surg, 2009**

ERAS Society

3 brand new guidelines 2012

World J Surg
DOI 10.1007/s00268-012-1772-0

World Journal of Surgery

Guidelines for Perioperative Care in Elective Colonic Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations

U. O. Gustafsson · M. J. Scott · W. Schwenk · N. Demartines · D. Roulin · N. Francis · C. E. McNaught · J. MacFie · A. S. Liberman · M. Soop · A. Hill · R. H. Kennedy · D. N. Lobo · K. Fearon · O. Ljungqvist

Colon

World J Surg
DOI 10.1007/s00268-012-1771-1

World Journal of Surgery

Pancreas

Guidelines for Perioperative Care for Pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS®) Society Recommendations

World J Surg
DOI 10.1007/s00268-012-1787-6

World Journal of Surgery

·em Slim · Francesco Carli ·
· · Rowan W. Parks ·
; Demartines · Marco Braga ·

Guidelines for Perioperative Care in Elective Rectal/Pelvic Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations

Rectal

J. Nygren · J. Thacker · F. Carli · K. C. H. Fearon · S. Norderval · D. N. Lobo · O. Ljungqvist · M. Soop · J. Ramirez

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ERAS
Making radical changes

Surgeon:

No bowel prep

Food after surgery

No drains

Early removal u-catheter

No iv fluids, no lines

Early discharge

All evidence based!

Anesthetist:

Carbohydrates no fasting

No premedication

Thoracic Epidural Anesthesia

Balanced fluids

Vasopressors

No or short acting opioids

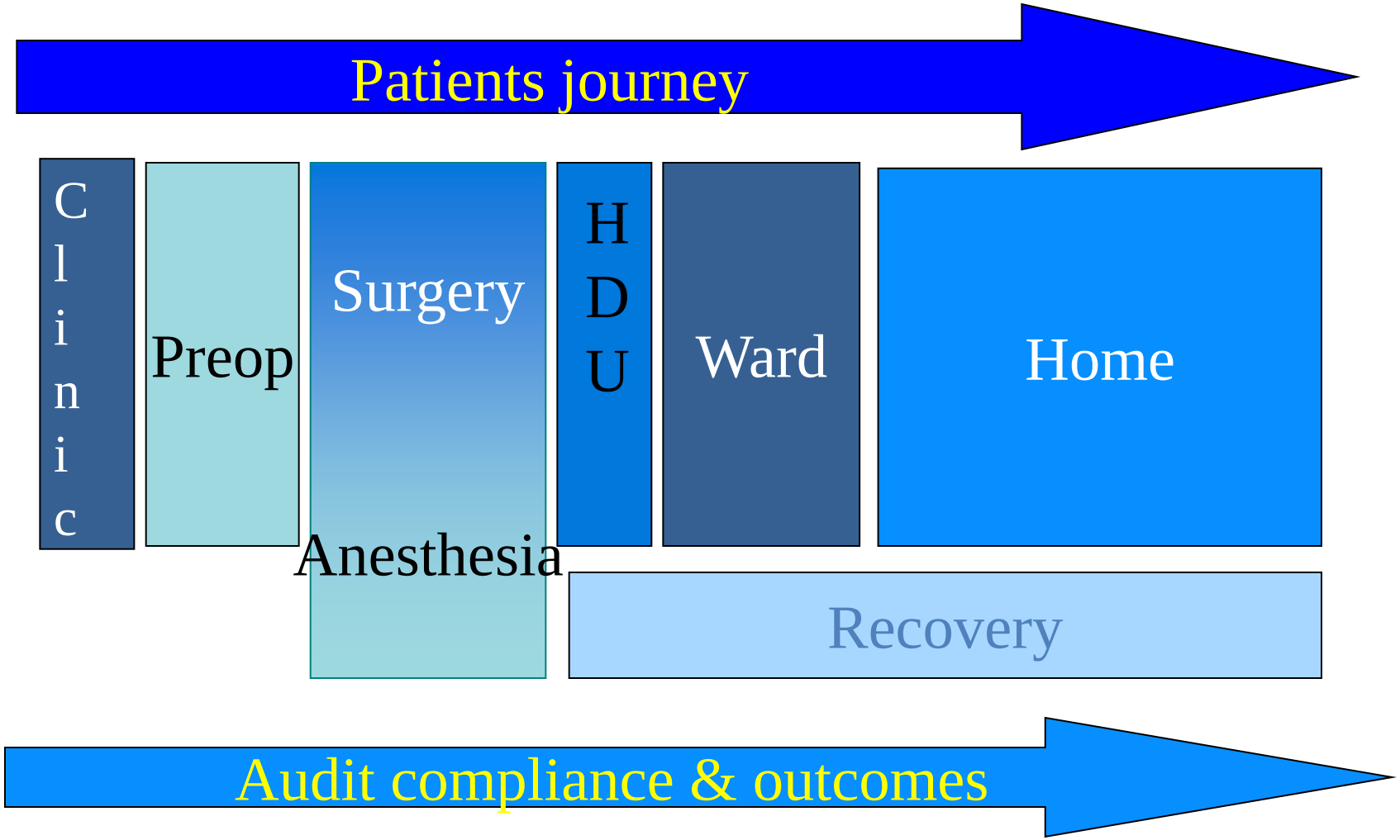
Enhanced Recovery After Surgery ERAS

Standardized protocol for perioperative care

- **Reduce stress**
- **Support function**

- **Evidence based care**
- **Integrated view**
- **Standards**
- **Follow up – audit**

Enhanced Recovery After Surgery



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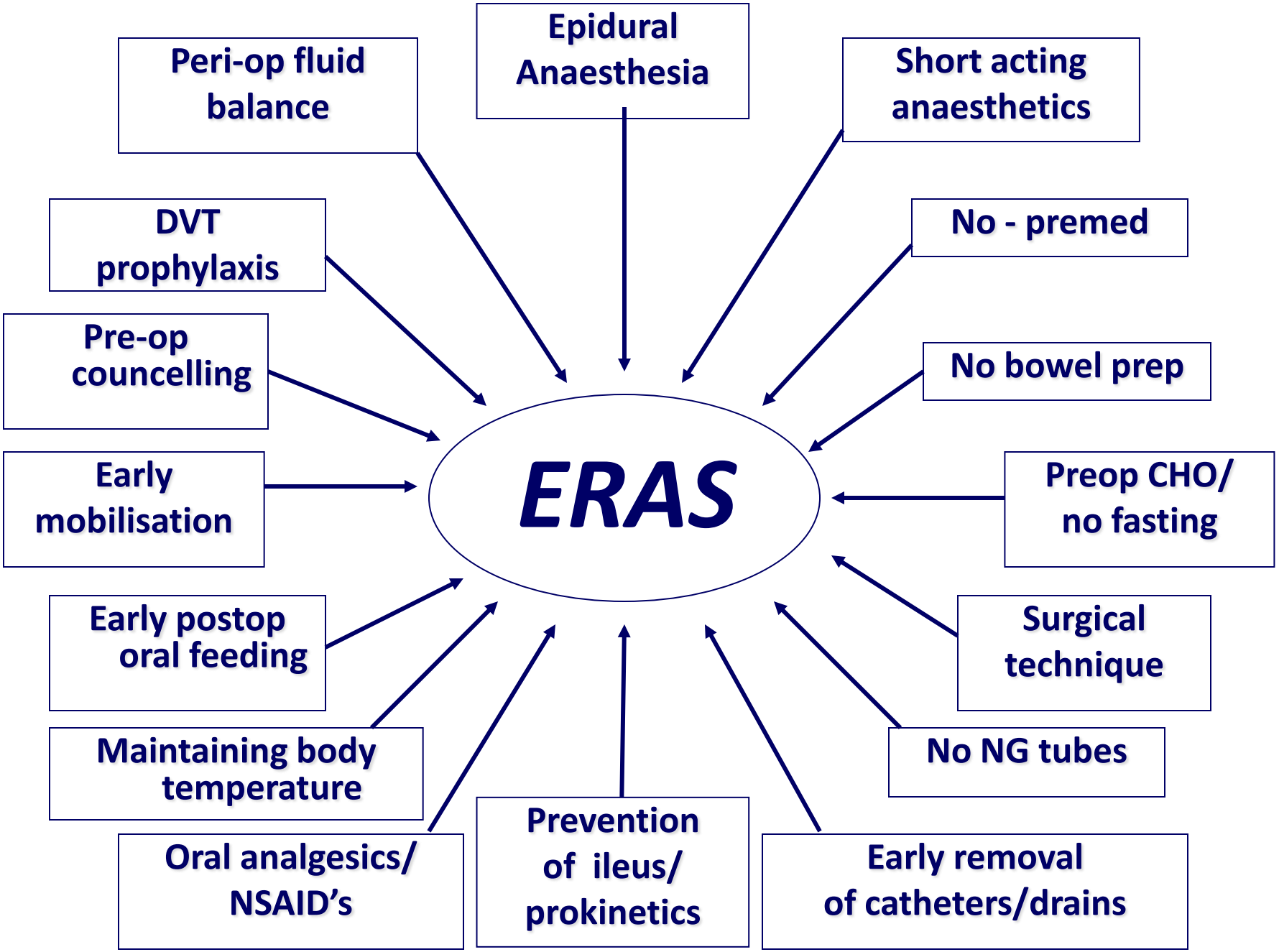
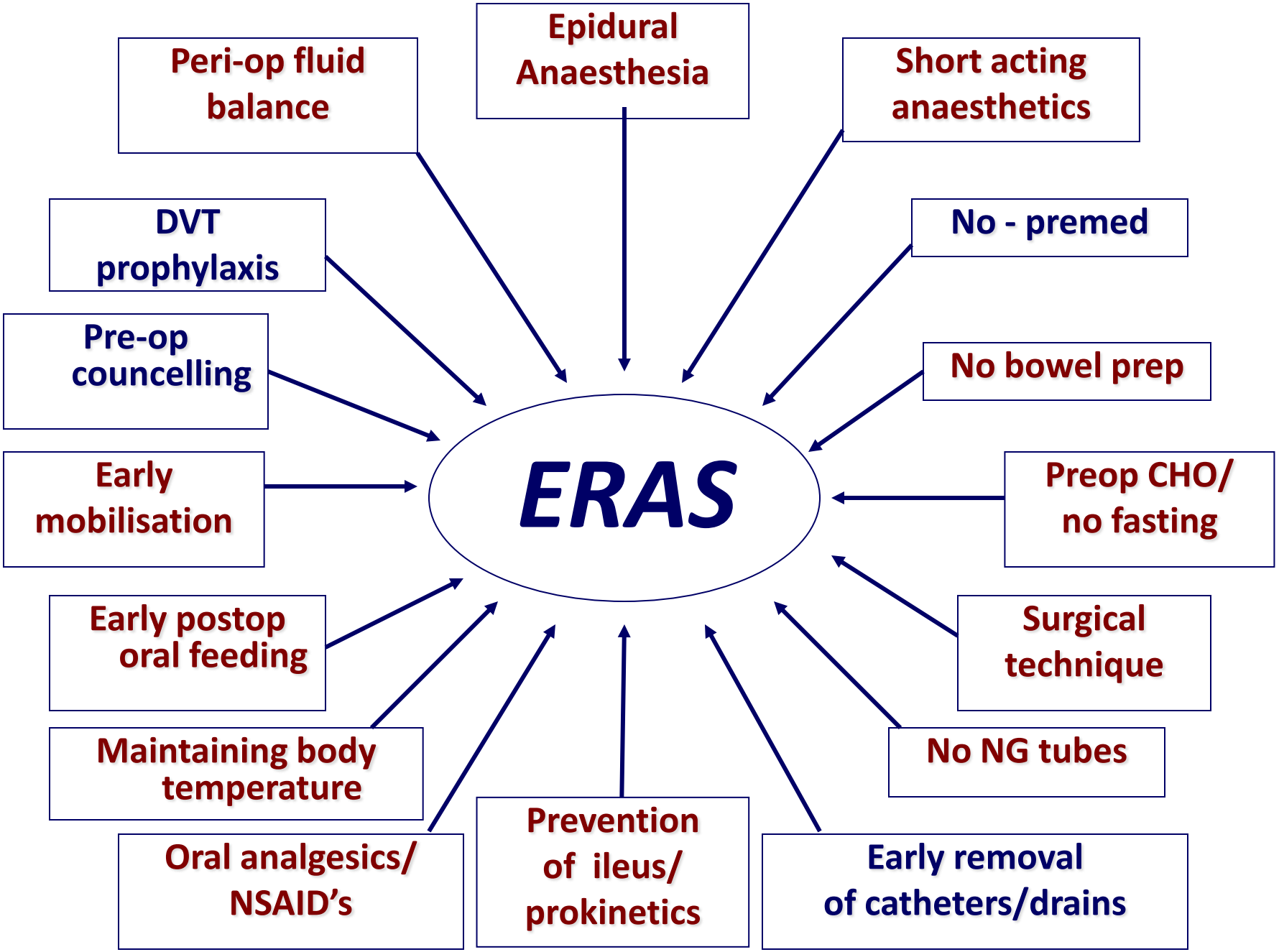


Fearon et al, Clin Nutr, 2005



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ERAS elements to reduce insulin resistance

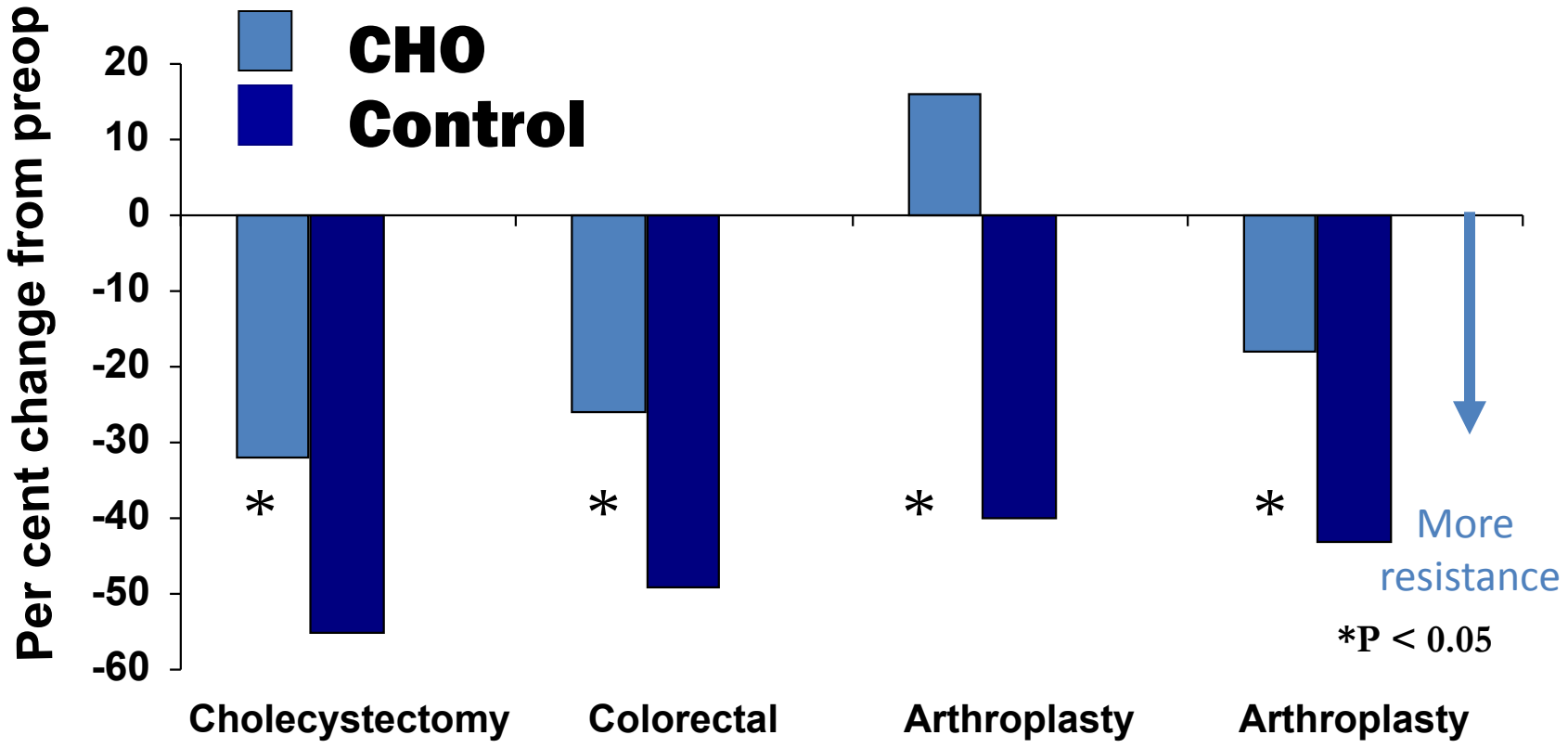
Preoperative

- **Preoperative carbohydrates**
- **Epidural anesthesia**

Postoperative

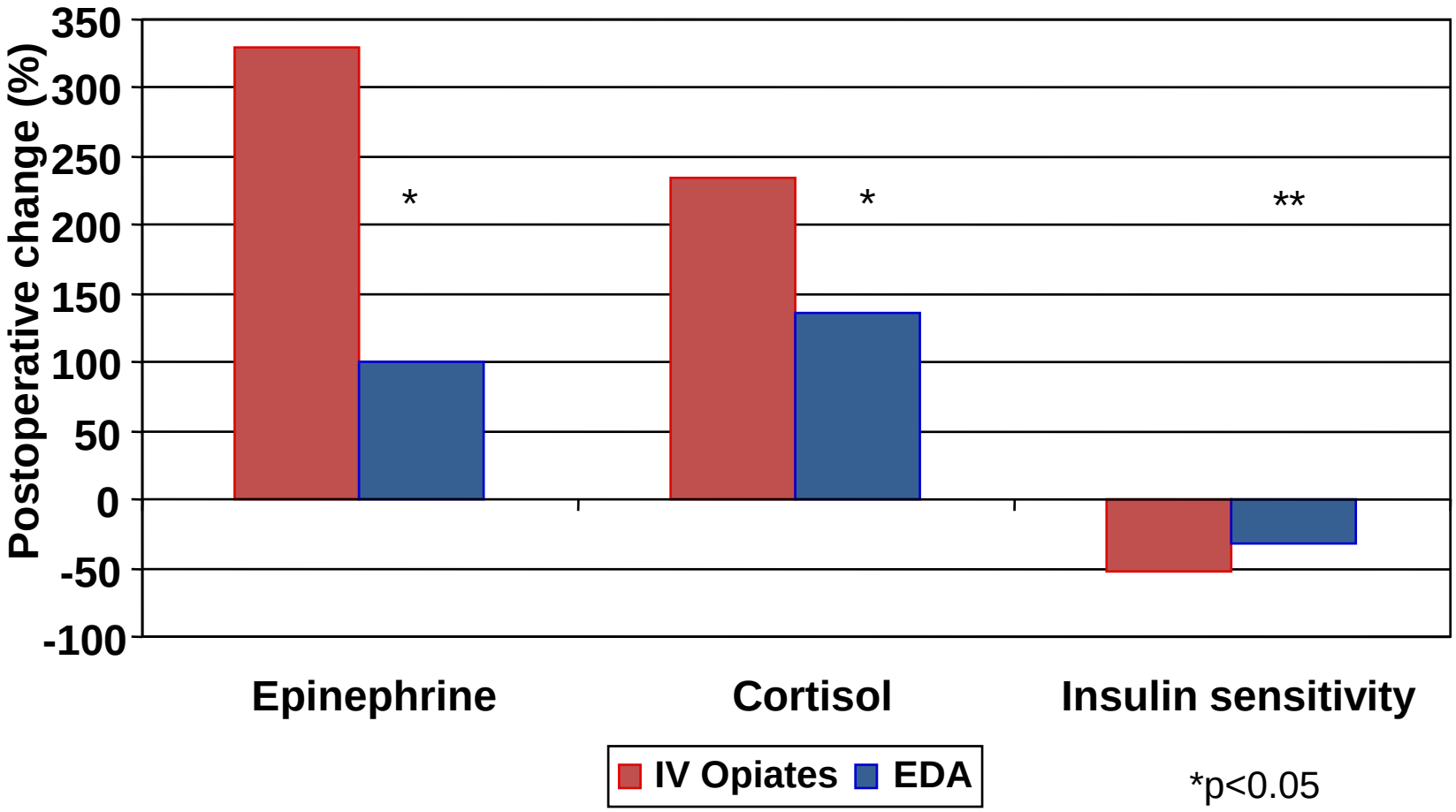
- **Pain control**
- **Early postop feeding**

Preoperative CHO reduces postop insulin resistance



Nygren et al: Curr Opin Clin Nutr Metab Care 2001

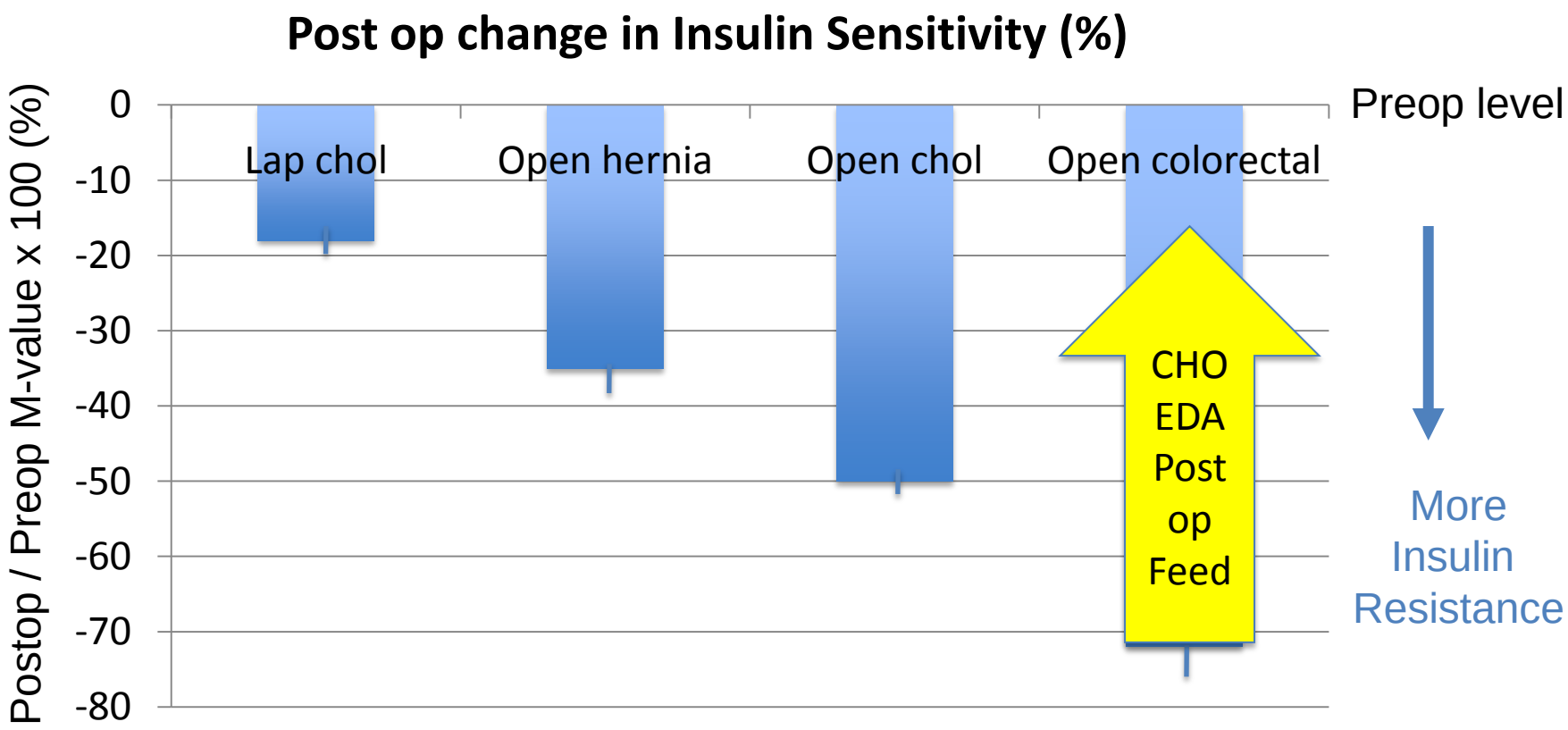
EDA reduces postoperative insulin resistance



*p<0.05
**p<0.01

Uchida, Br J Surg 1988

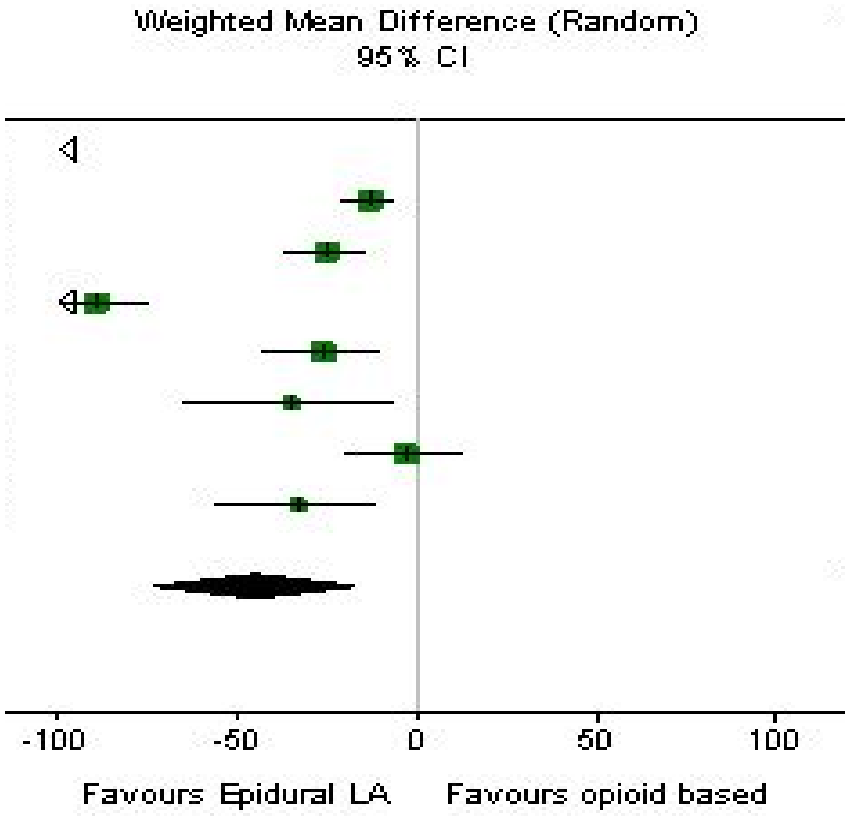
Insulin sensitivity improved with pre op Carb, EDA + post op feed



From Thorell et al: Curr Opin Clin Nutr Metab Care 1999, Soop M et al, Br J Surg, 2004

Epidural - less paralysis

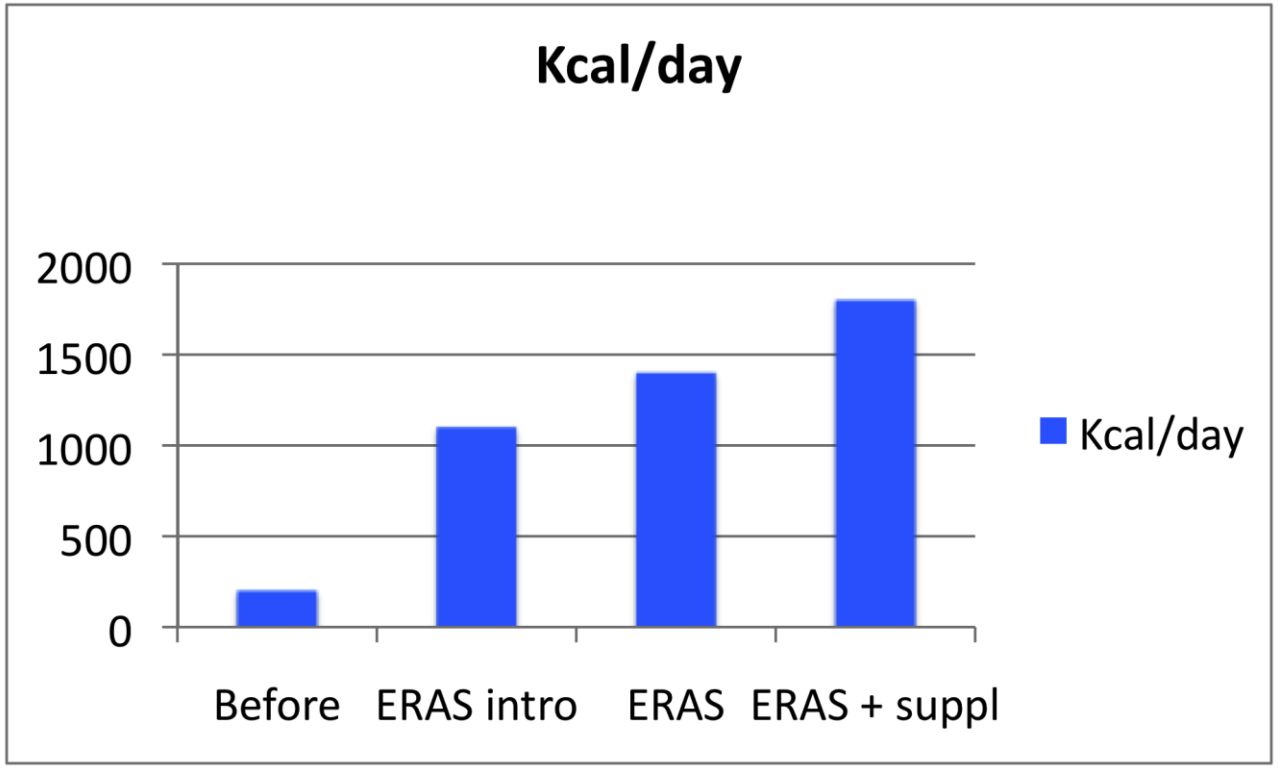
EDA vs. Iv opiates



Jorgensen Cochr Database Syst Rev 2004

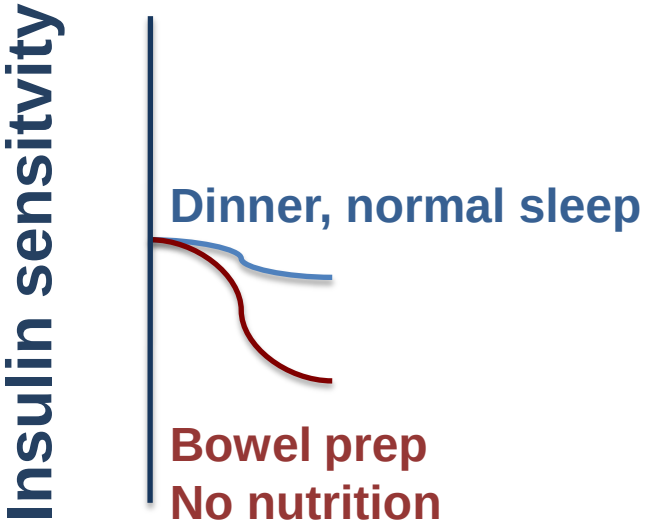
ERAS: oral intake development

(mean intake postop day 1-4)



Insulin sensitivity
Day before surgery

ERAS Care

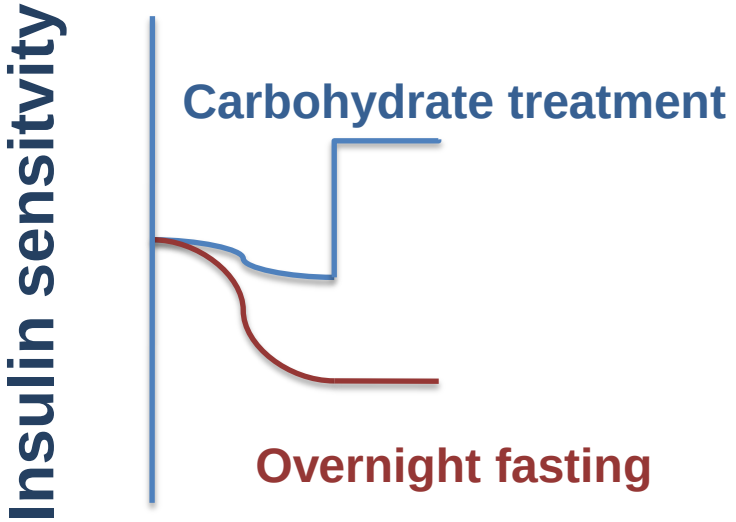


Traditional care

Insulin sensitivity
Morning of surgery

ERAS Care

Dinner, normal sleep



Bowel prep
No nutrition

Traditional care

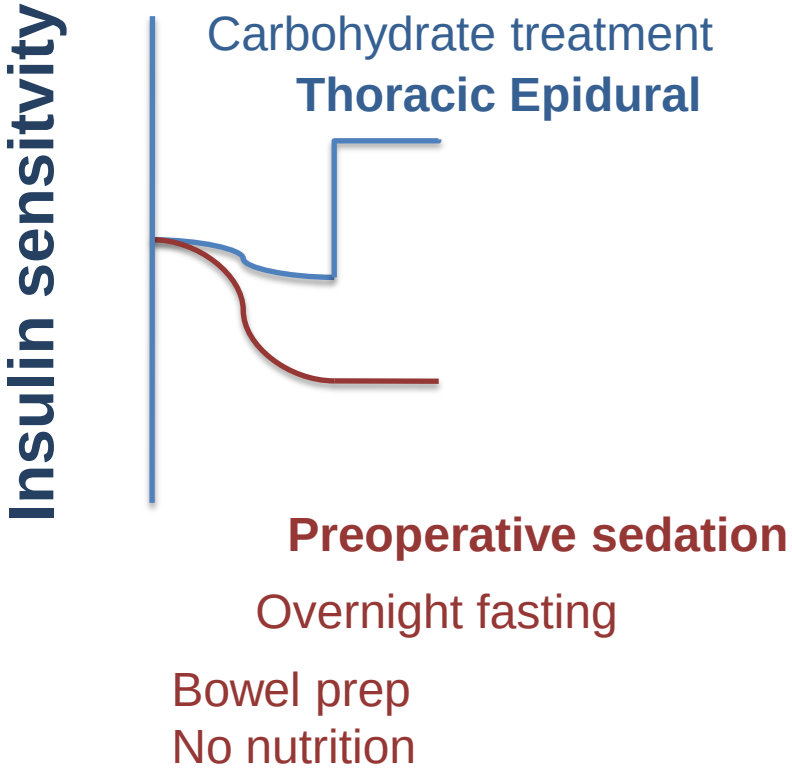
Insulin sensitivity
Anesthesia start

ERAS Care

Dinner, normal sleep

Carbohydrate treatment

Thoracic Epidural



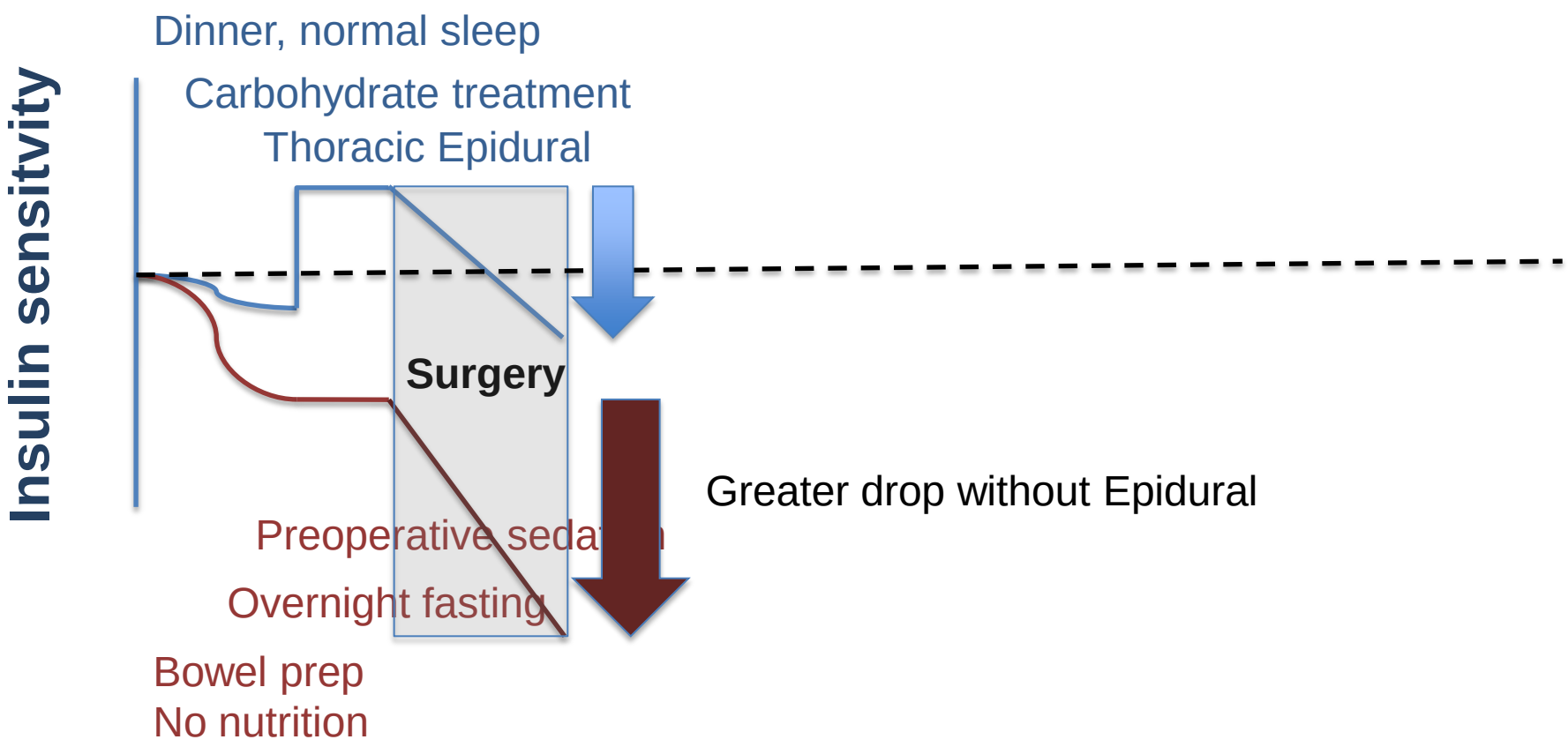
Preoperative sedation

Overnight fasting

Bowel prep
No nutrition

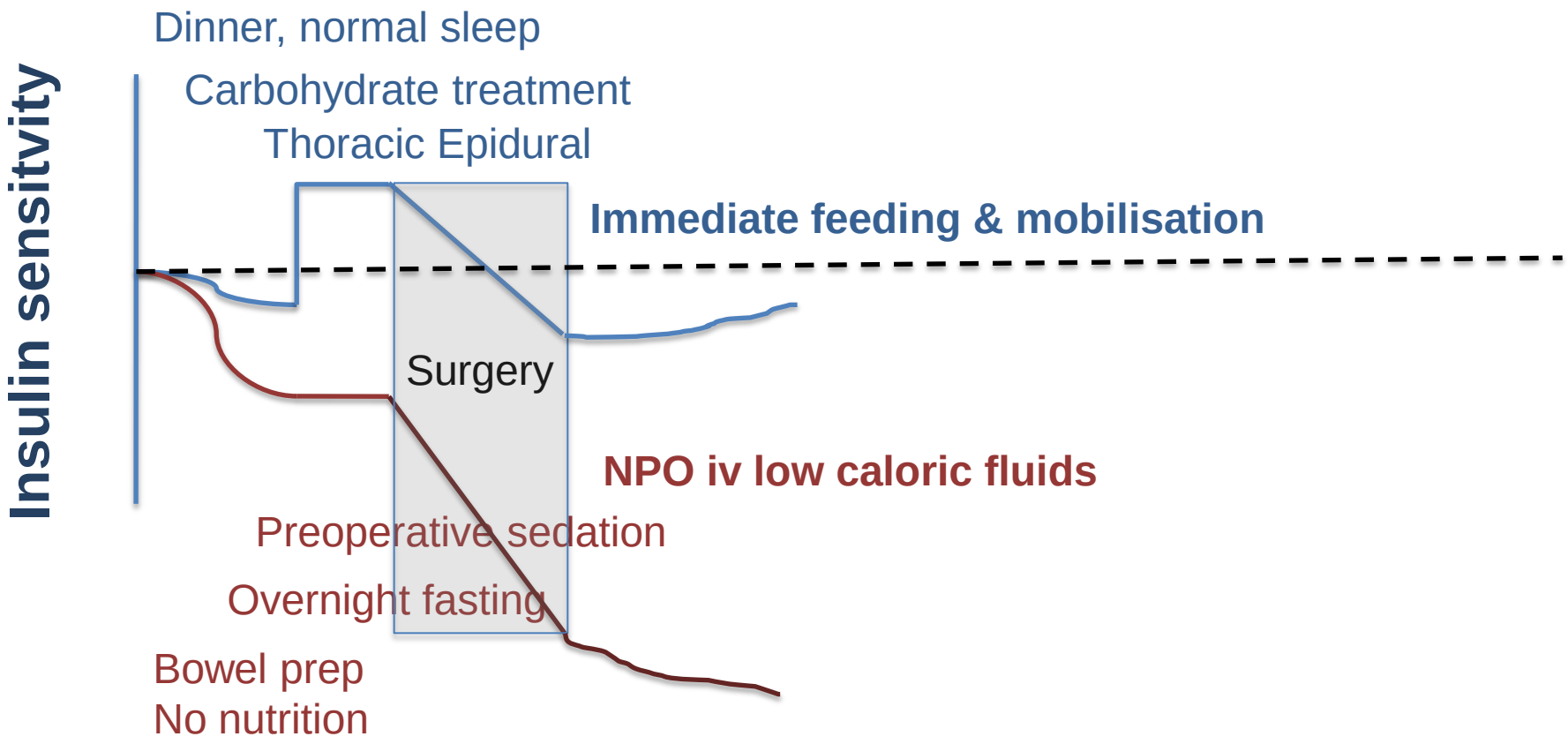
Traditional care

Insulin sensitivity
Reaction to surgery



Insulin sensitivity

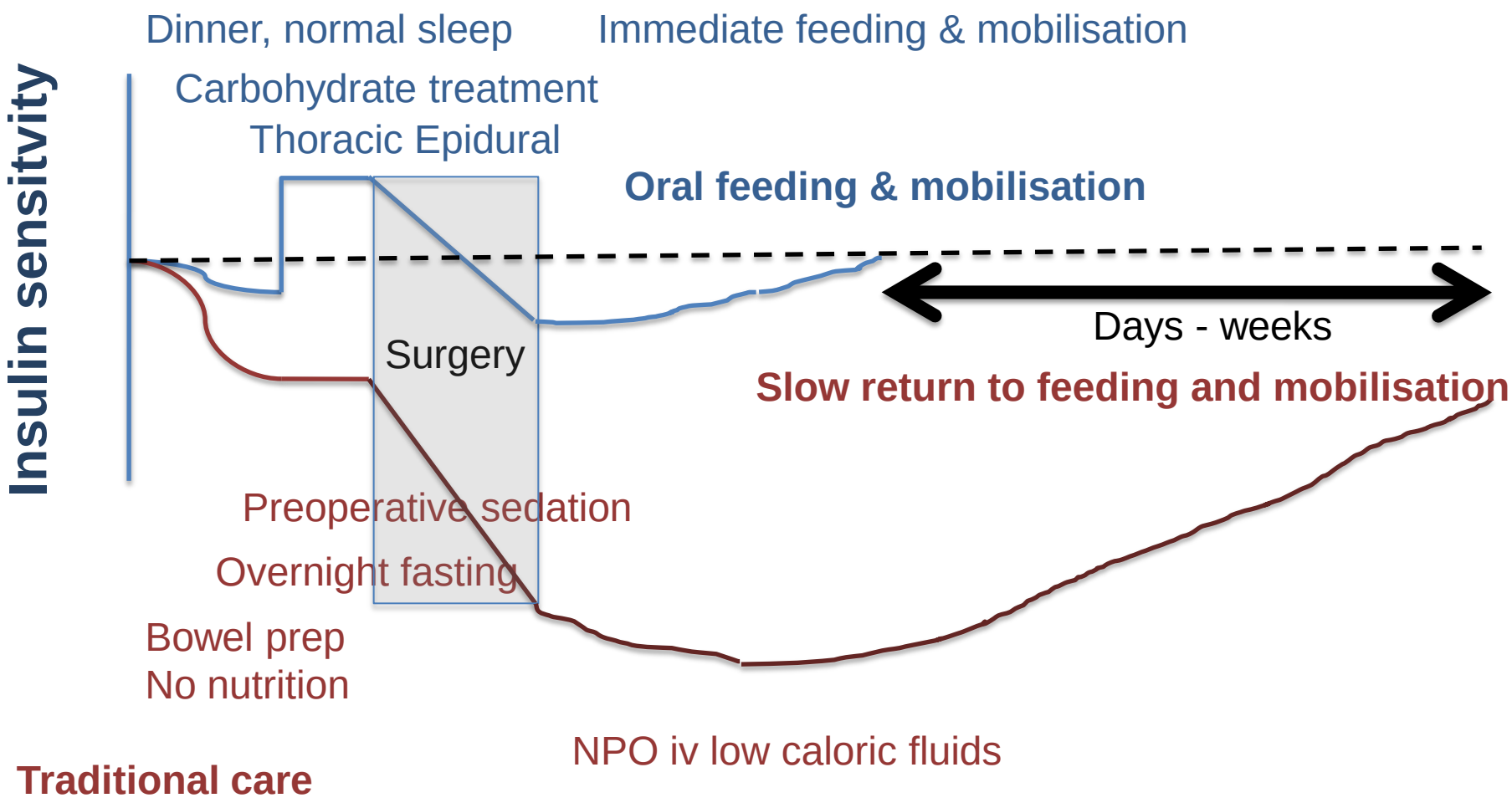
ERAS Care Afternoon of surgery



Traditional care

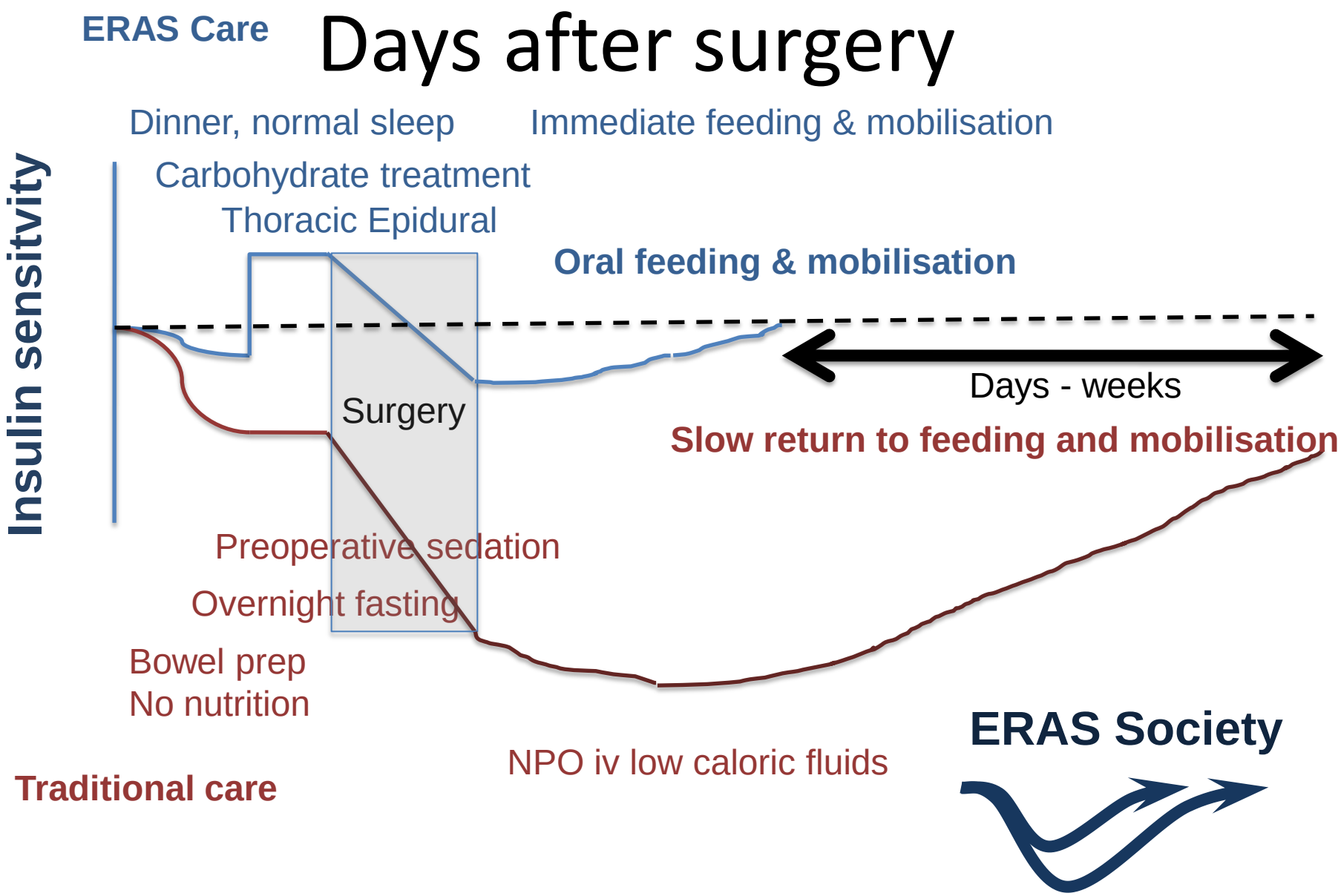
Insulin sensitivity

Days after surgery



Ljungqvist, JPEN 2012

Insulin sensitivity



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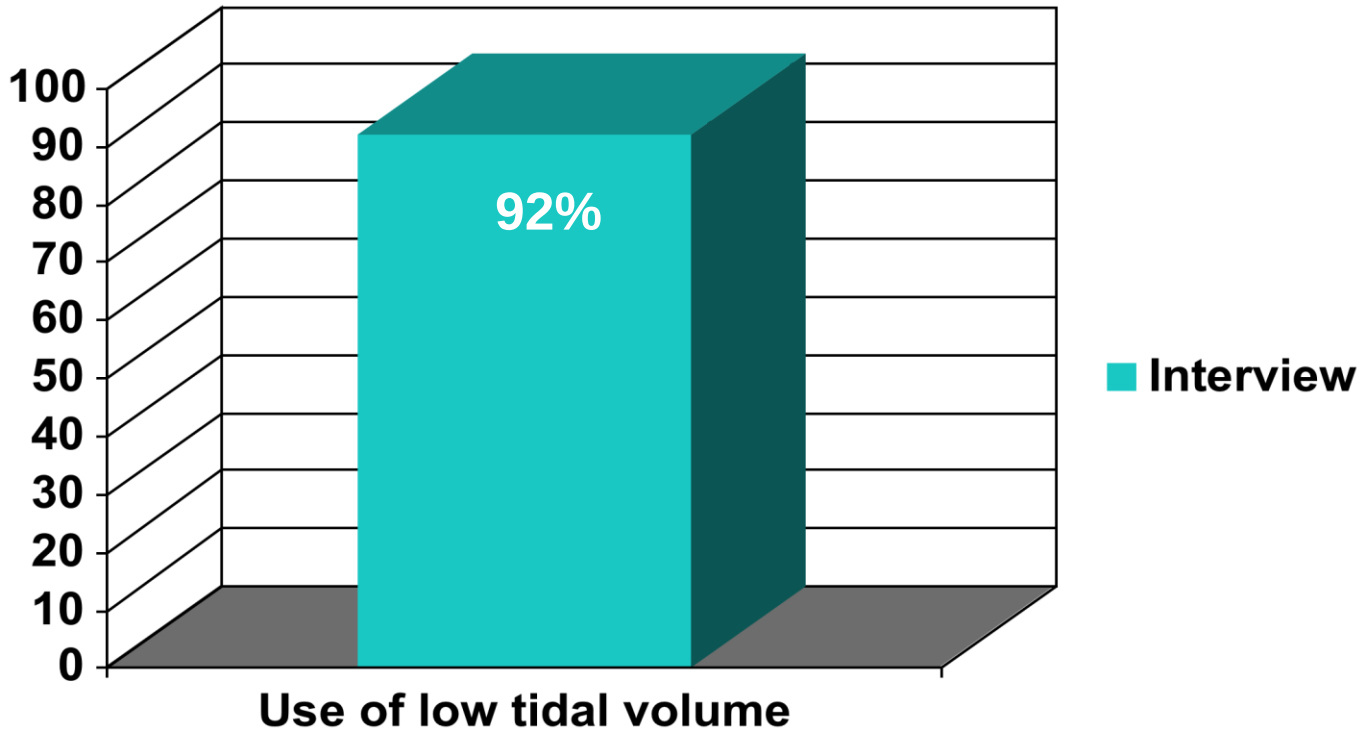
  - **Closely related to common postoperative complications**
- **ERAS presents EBM protocols to enhance recovery**
  - **Minimize insulin resistance & support anabolism**
  - **ERAS and outomes**

Outline

- **Issues remain, but new insights and possibilities**
- **Insulin resistance counteracts recovery**
- **Insulin resistance is central to stress metabolism**
  - **Reduces wound healing and muscle function recovery**
  - **Closely related to common postoperative complications**
- **ERAS presents EBM protocols to enhance recovery**
  - **Minimize insulin resistance & support anabolism**
  - **ERAS and outcomes**

Real life
Adherence to Best practice

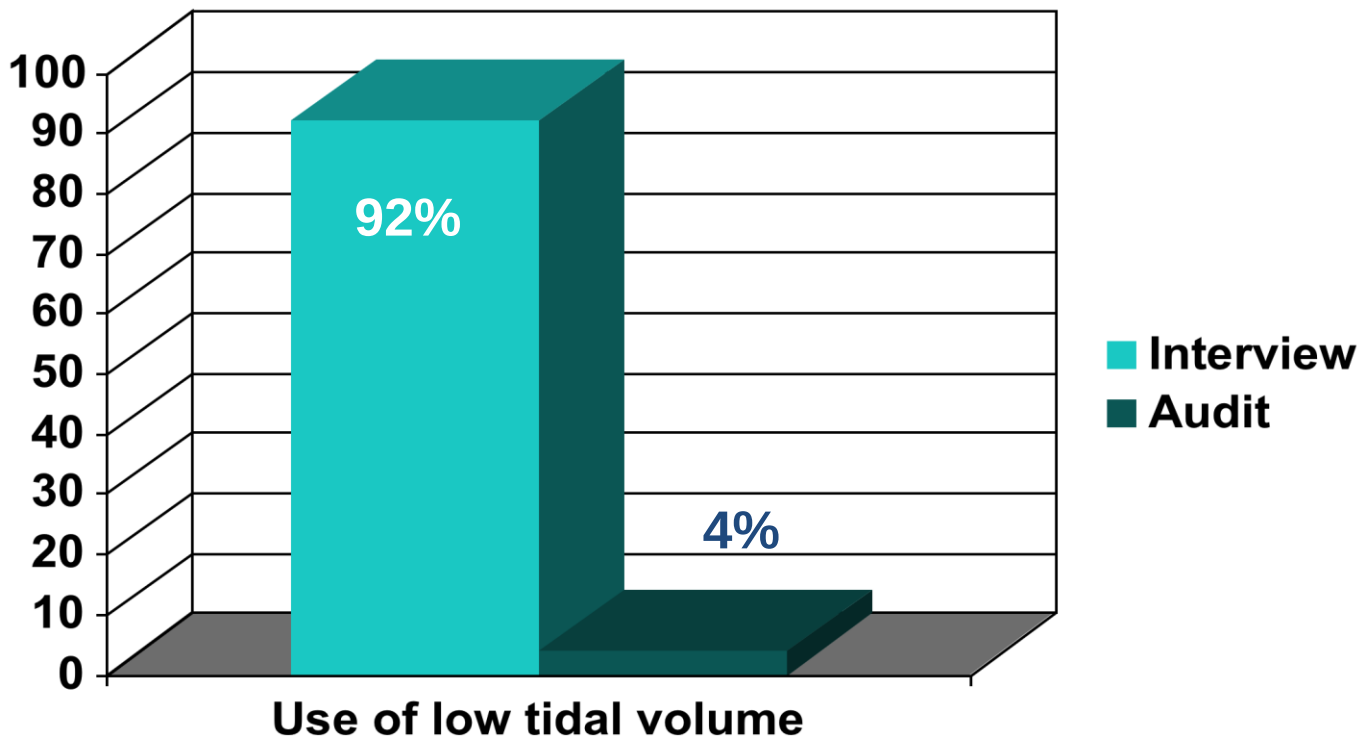
The German ”Prevalence” Study in ICU



M M Levy, ASPEN 2007

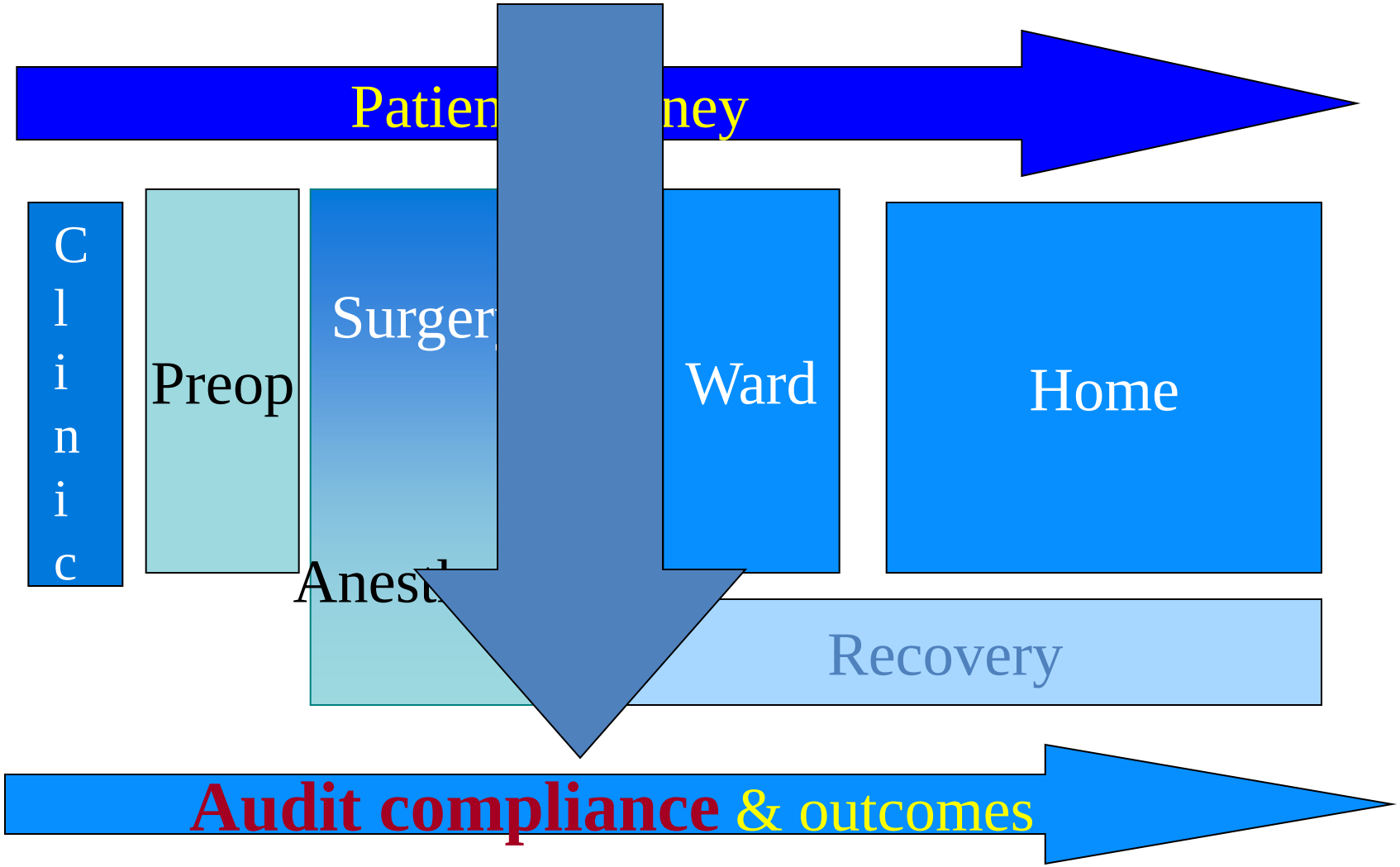
Implementing change
Adherence to Best practice

The German ”Prevalence”Study



M M Levy, ASPEN 2007

ERAS: Audit the change



ERAS implementation

Login gateway | QlikView – AccessPoint | A & R Total.qvw | A & R Demo

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2010 | 2011 | 2012

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

More Time Dimensions

Admission Records in Selection: 183 of 183

Zoom in/out | Reset

Compliance

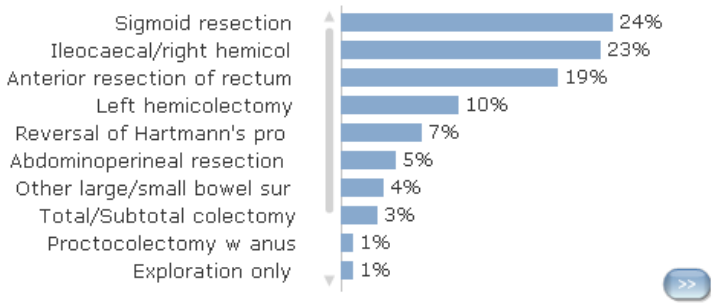
PreOp	IntraOp	PostOp

Surgical approach	
Procedure group	Colorectal and small bo
Primary operation	
Mode of surgery	
Mortality	
Reoperations	
Adverse events	
Complication group	
Complication	
Intensive care	
Compliance measur	
Consultant surgeon	
ERAS no.	

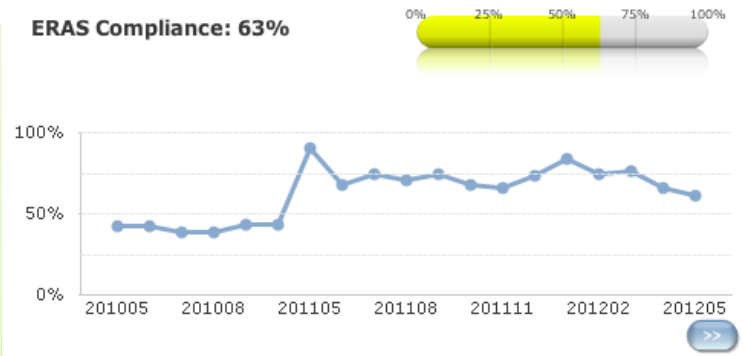
Current Selections

Fields	Values

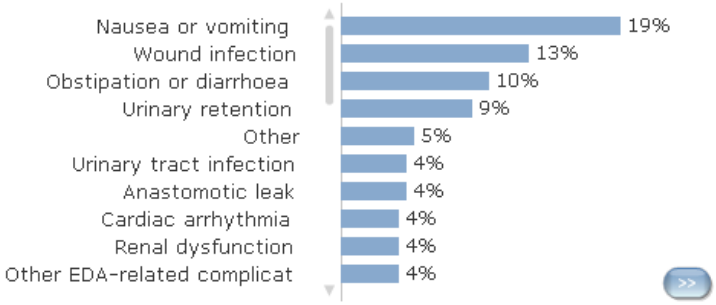
Primary Operation



ERAS Compliance: 63%

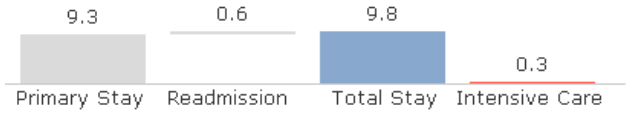


Complications (Primary and Follow-up)



LOS & ICU (Average)

Including Follow-up	Occurence (%)
Reoperations	7.1%
Mortality	1.1%
Anastomotic leaks	4.4%



Before ERAS: Outcomes

A & R Demo

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Statistics ERASsociety | QlikView An...AccessPoint | ERAS Society | IP Test DataBitar | DN | SvD | SAS | Lufthansa | Arlanda | Väder NO | SL | PubMed | SEB

Login gateway | QlikView – AccessPoint | A & R Total.qvw | A & R Demo

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2010 | 2011 | 2012

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

More Time Dimensions

Admission Records in Selection: 50 of 183

Zoom in/out | Reset

Compliance

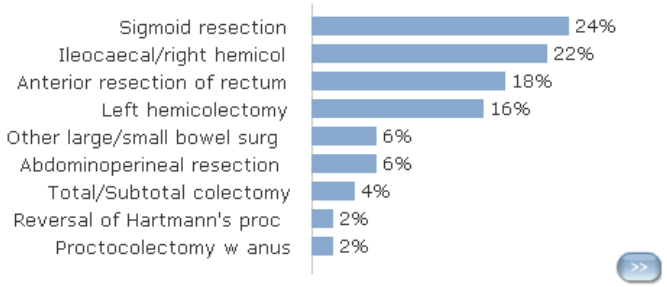
PreOp	IntraOp	PostOp

Surgical approach
Procedure group
Primary operation
Mode of surgery
Mortality
Reoperations
Adverse events
Complication group
Complication
Intensive care
Compliance measur
Consultant surgeon
ERAS no.

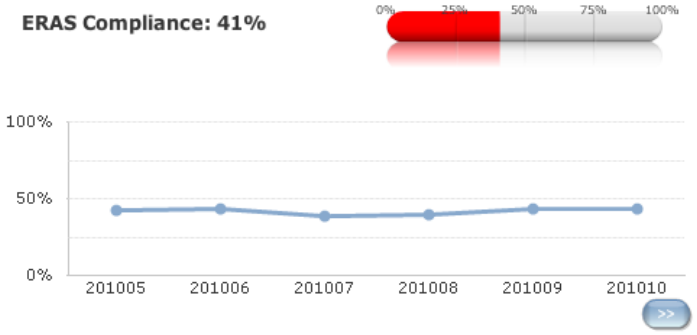
Current Selections

Fields	Values
Year	2010

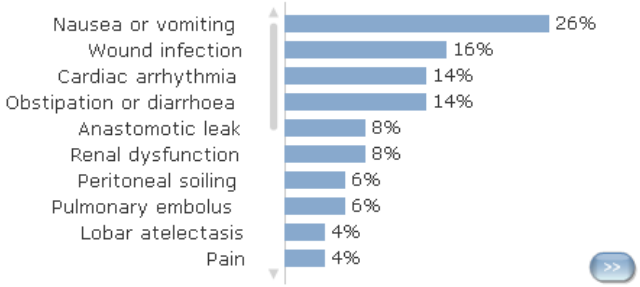
Primary Operation



ERAS Compliance: 41%

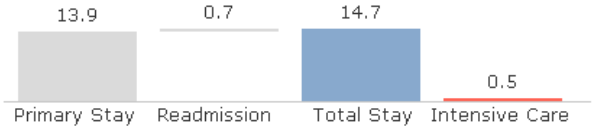


Complications (Primary and Follow-up)



LOS & ICU (Average)

Including Follow-up	Occurence (%)
Reoperations	10.0%
Mortality	2.0%
Anastomotic leaks	8.0%



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Before ERAS: Compliance

A & R Demo

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Statistics ERASsociety | QlikView An...AccessPoint | ERAS Society | IP Test DataBitar | DN | SvD | SAS | Lufthansa | Arlanda | Väder NO | SL | PubMed | SEB

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2010 | 2011 | 2012

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

More Time Dimensions

Admission Records in Selection: 50 of 183

Zoom in/out | Reset | <<

Search

Compliance

PreOp	IntraOp	PostOp

Surgical approach
Procedure group
Primary operation
Mode of surgery
Mortality
Reoperations
Adverse events
Complication group
Complication
Intensive care
Compliance measur
Consultant surgeon
ERAS no.

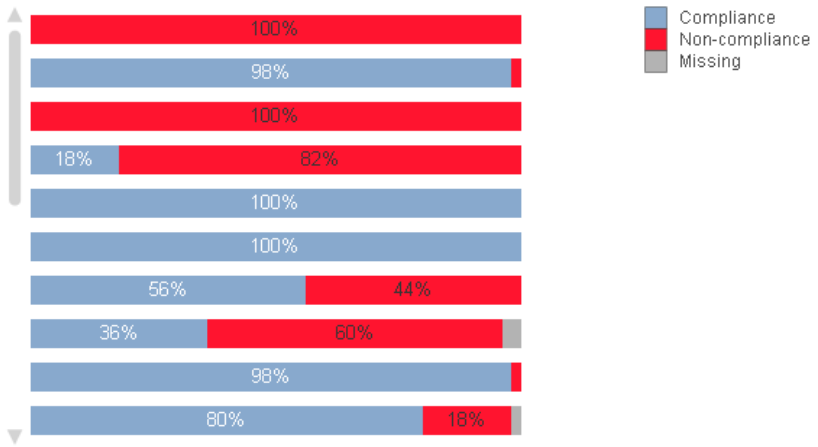
Current Selections

Fields	Values
Year	2010

By Care Element

Percent Compliant

Compliance Measure



By Periop Phase | Compliance & Total L... | Mobilisation D0 and D1

Compliance vs Total... | By Periop Phase | Compliance Trend by...

After ERAS: Outcomes

A & R Demo

https://eias.eras.pro/QvAJAXZfc/opendoc.htm?document=A%20%26%20R%20Demo%20Test.qvw&host=QVS

Statistics ERASsociety | QlikView An...AccessPoint | ERAS Society | IP Test DataBitar | DN | SvD | SAS | Lufthansa | Arlanda | Väder NO | SL | PubMed | SEB

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ERAS® Interactive Audit System

2010 | 2011 | 2012

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

More Time Dimensions

Admission Records in Selection: 70 of 183

Zoom in/out | Reset

Compliance

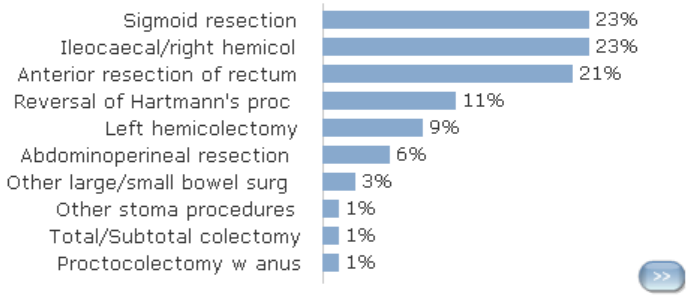
PreOp	IntraOp	PostOp

Surgical approach
Procedure group
Primary operation
Mode of surgery
Mortality
Reoperations
Adverse events
Complication group
Complication
Intensive care
Compliance measur
Consultant surgeon
ERAS no.

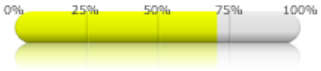
Current Selections

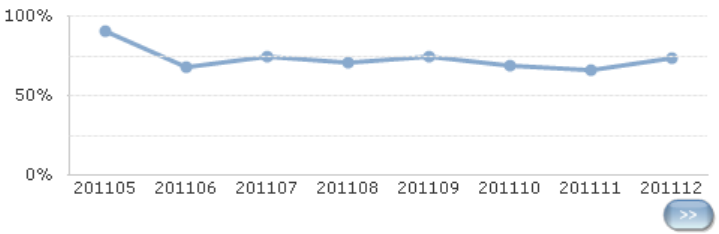
Fields	Values
Year	2011

Primary Operation

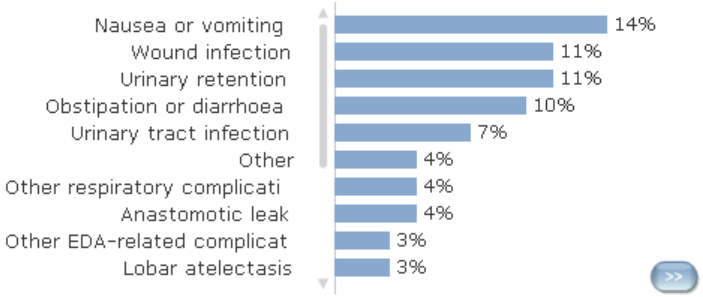


ERAS Compliance: 71%



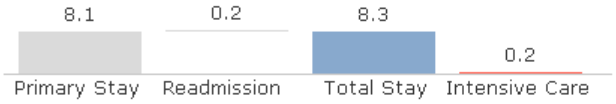


Complications (Primary and Follow-up)



LOS & ICU (Average)

Including Follow-up	Occurence (%)
Reoperations	5.7%
Mortality	0.0%
Anastomotic leaks	4.3%



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After ERAS: Compliance

A & R Demo

https://eias.eras.pro/QvAJAXZfc/opendoc.htm?document=A%20%26%20R%20Demo%20Test.qvw&host=QVS

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Login gateway | QlikView – AccessPoint | A & R Total.qvw | A & R Demo

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2010 | 2011 | 2012

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

More Time Dimensions

Admission Records in Selection: 70 of 183

Zoom in/out | Reset

Search

Compliance

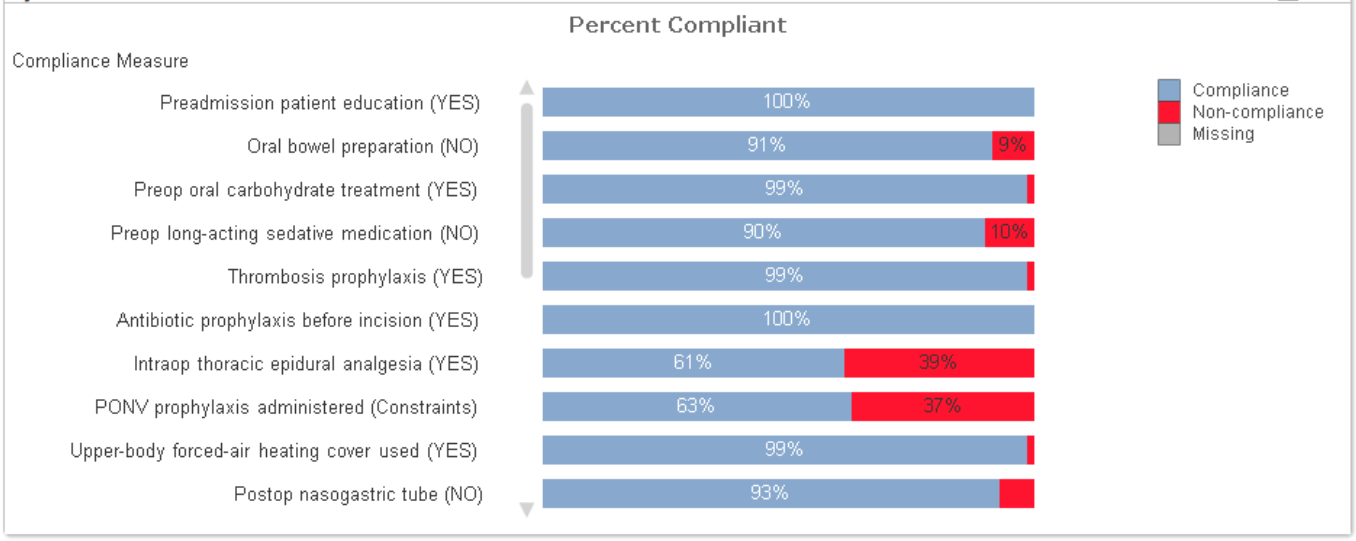
PreOp	IntraOp	PostOp

Surgical approach
Procedure group
Primary operation
Mode of surgery
Mortality
Reoperations
Adverse events
Complication group
Complication
Intensive care
Compliance measur
Consultant surgeon
ERAS no.

Current Selections

Fields	Values
Year	2011

By Care Element



By Periop Phase | Compliance & Total L... | Mobilisation D0 and D1

Compliance vs Total... | By Periop Phase | Compliance Trend by...

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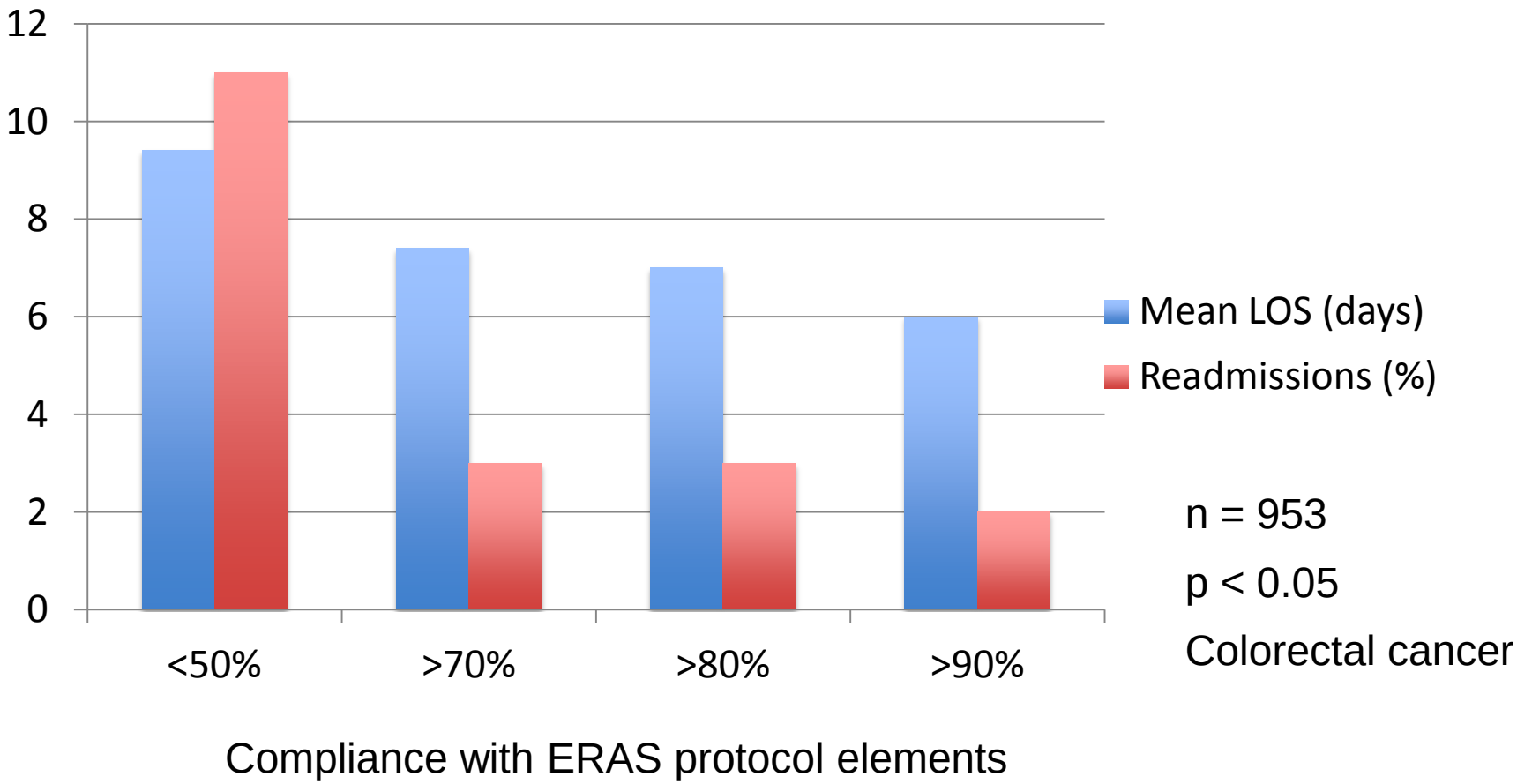
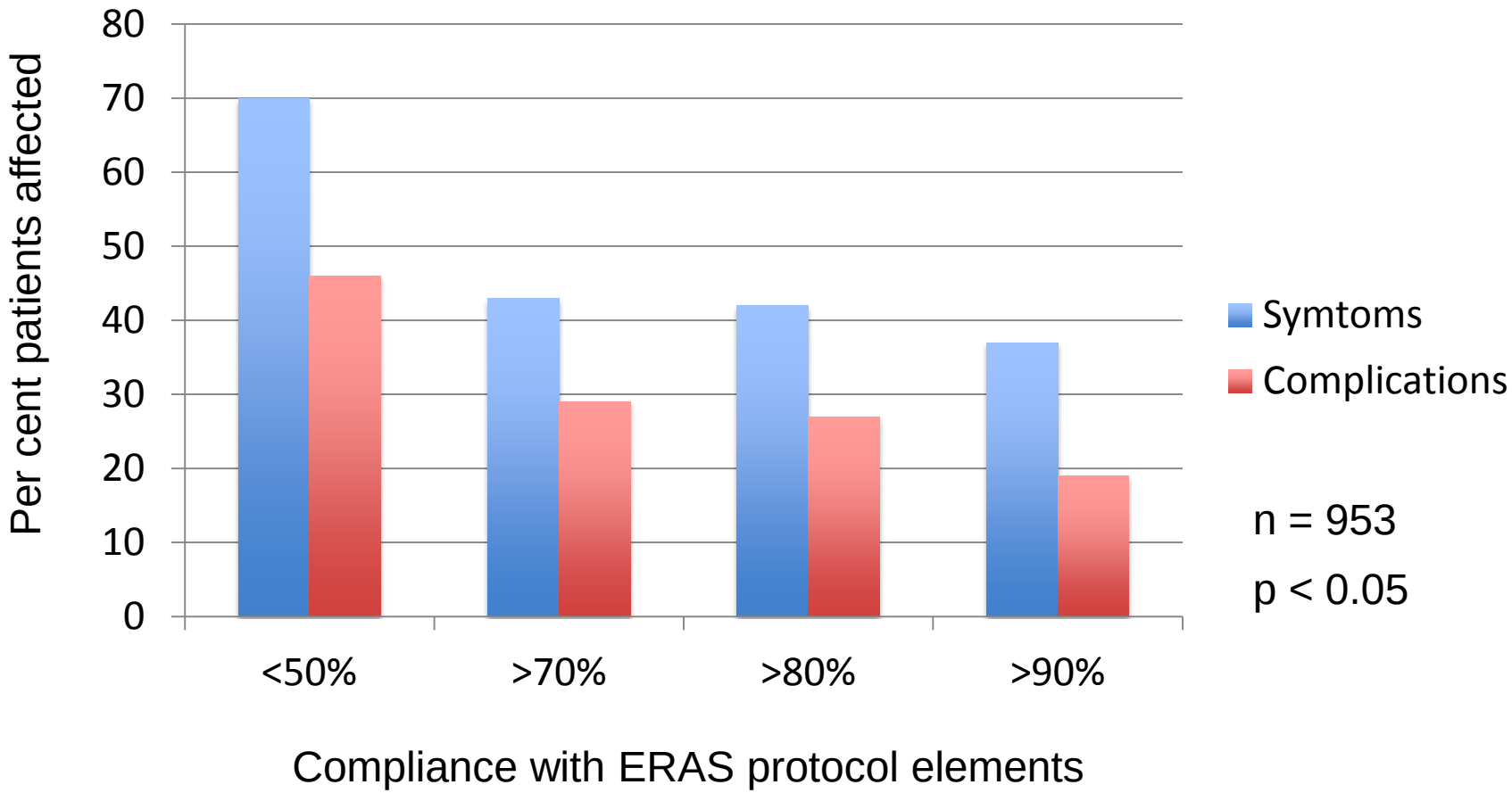
Length of stay & Readmissions vs. ERAS compliance



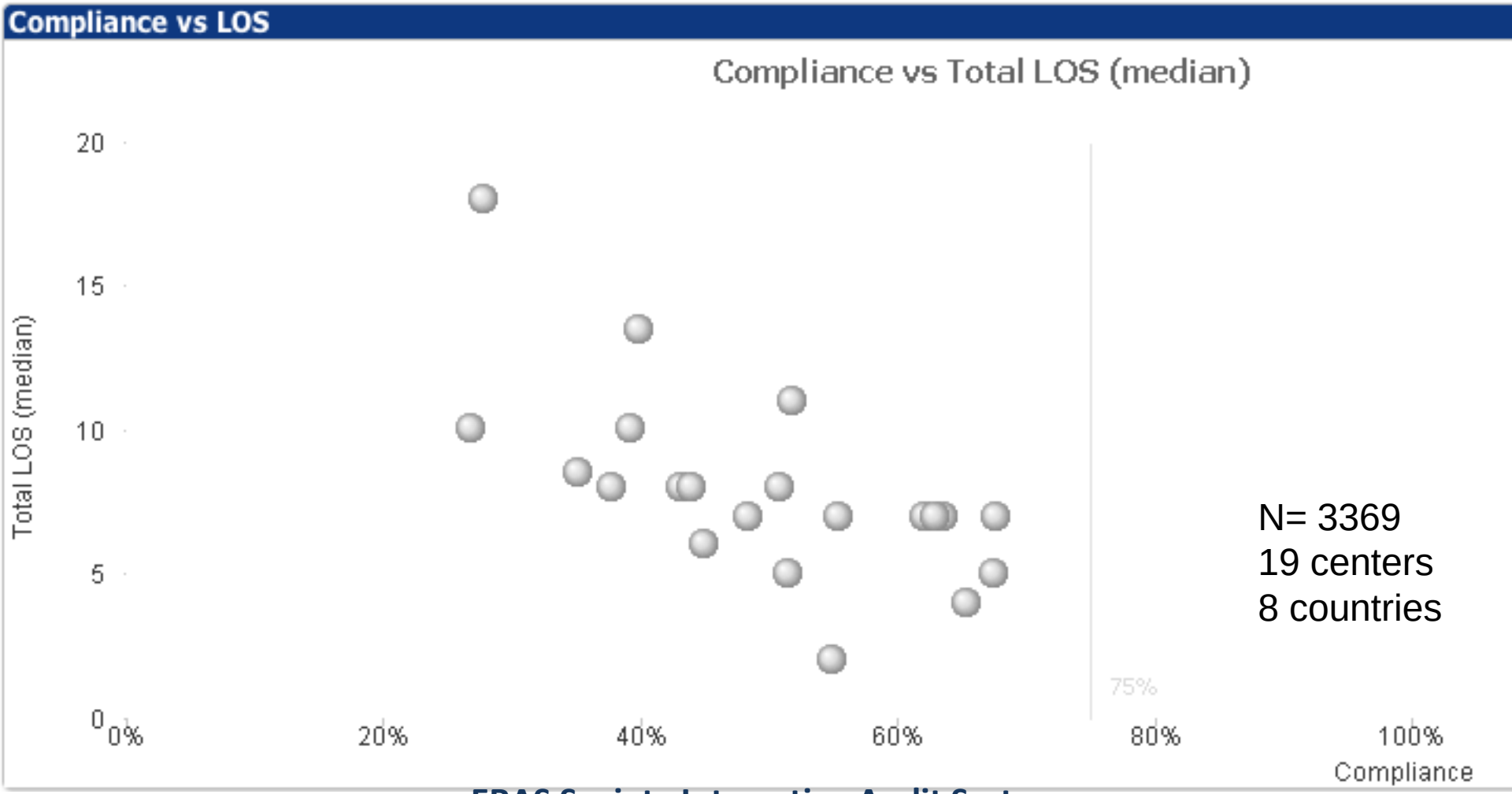
Gustafsson et al, Arch Surg, 2011

Complications & Symtoms vs. ERAS compliance



Gustafsson et al, Arch Surg, 2011

ERAS Compliance vs LOS



N= 3369
19 centers
8 countries

ERAS Society Interactive Audit System

ERAS reduce length of stay

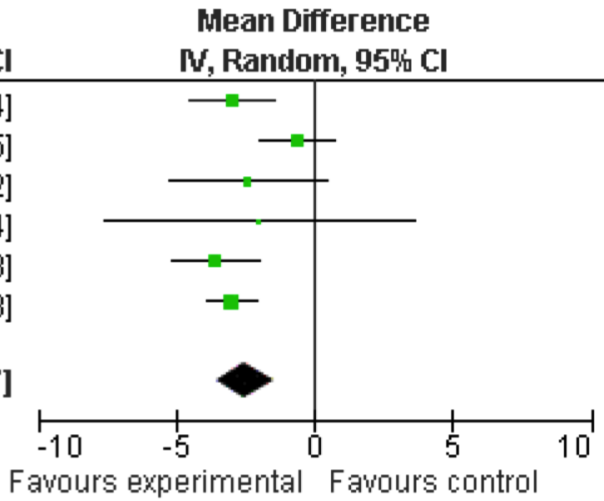
Length of stay reduced by 2.5 days

Meta analysis 452 patients, 6 RCTs, 4 countries

	ERAS			TC				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Anderson 2003	4	1.8	14	7	2.1	11	19.3%	-3.00 [-4.56, -1.44]
Delaney 2003	5.2	2.5	31	5.8	3	33	21.7%	-0.60 [-1.95, 0.75]
Gatt2005	6.6	4.4	19	9	4.6	20	9.6%	-2.40 [-5.22, 0.42]
Khoo 2007	5	8.5	35	7	14.75	35	3.1%	-2.00 [-7.64, 3.64]
Muller2009	6.7	4.84	76	10.3	4.97	75	19.2%	-3.60 [-5.17, -2.03]
Serclova2009	7.4	1.3	51	10.4	3.1	52	27.1%	-3.00 [-3.92, -2.08]
Total (95% CI)			**226**			**226**	**100.0%**	**-2.51 [-3.54, -1.47]**

Heterogeneity: Tau² = 0.80; Chi² = 11.04, df = 5 (P = 0.05); I² = 55%

Test for overall effect: Z = 4.76 (P < 0.00001)



Varadhan et al, Clin Nutr 2010

ERAS reduce complications

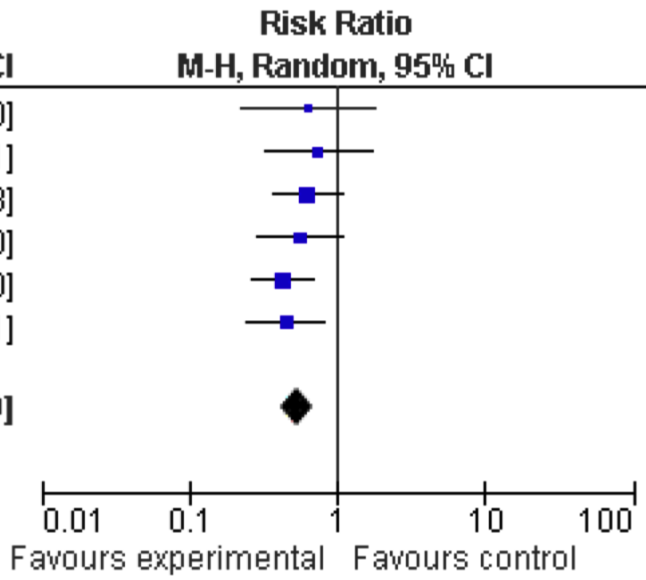
Complications down by half

Meta analysis 452 patients, 6 RCTs, 4 countries

Study or Subgroup	ERAS Events	ERAS Total	TC Events	TC Total	Weight	Risk Ratio M-H, Random, 95% CI
Anderson 2003	4	14	5	11	6.0%	0.63 [0.22, 1.80]
Delaney 2003	7	31	10	33	9.6%	0.75 [0.32, 1.71]
Gatt2005	9	19	15	20	23.1%	0.63 [0.37, 1.08]
Khoo 2007	9	35	16	35	14.9%	0.56 [0.29, 1.10]
Muller2009	16	76	37	75	27.5%	0.43 [0.26, 0.70]
Serclova2009	11	51	25	52	18.8%	0.45 [0.25, 0.81]
Total (95% CI)		**226**		**226**	**100.0%**	**0.53 [0.41, 0.69]**
Total events	56		108			

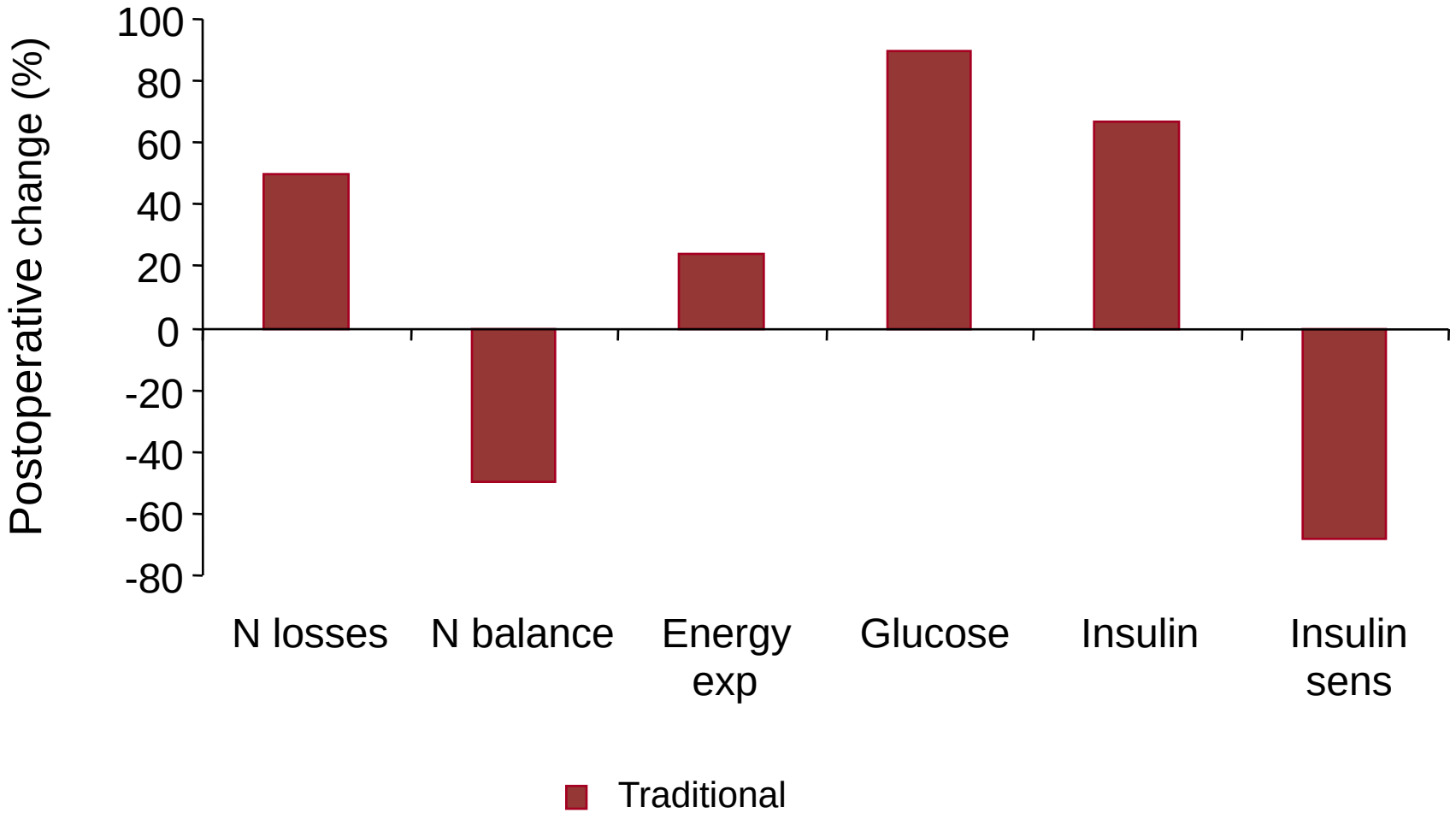
Heterogeneity: Tau² = 0.00; Chi² = 2.26, df = 5 (P = 0.81); I² = 0%

Test for overall effect: Z = 4.81 (P < 0.00001)

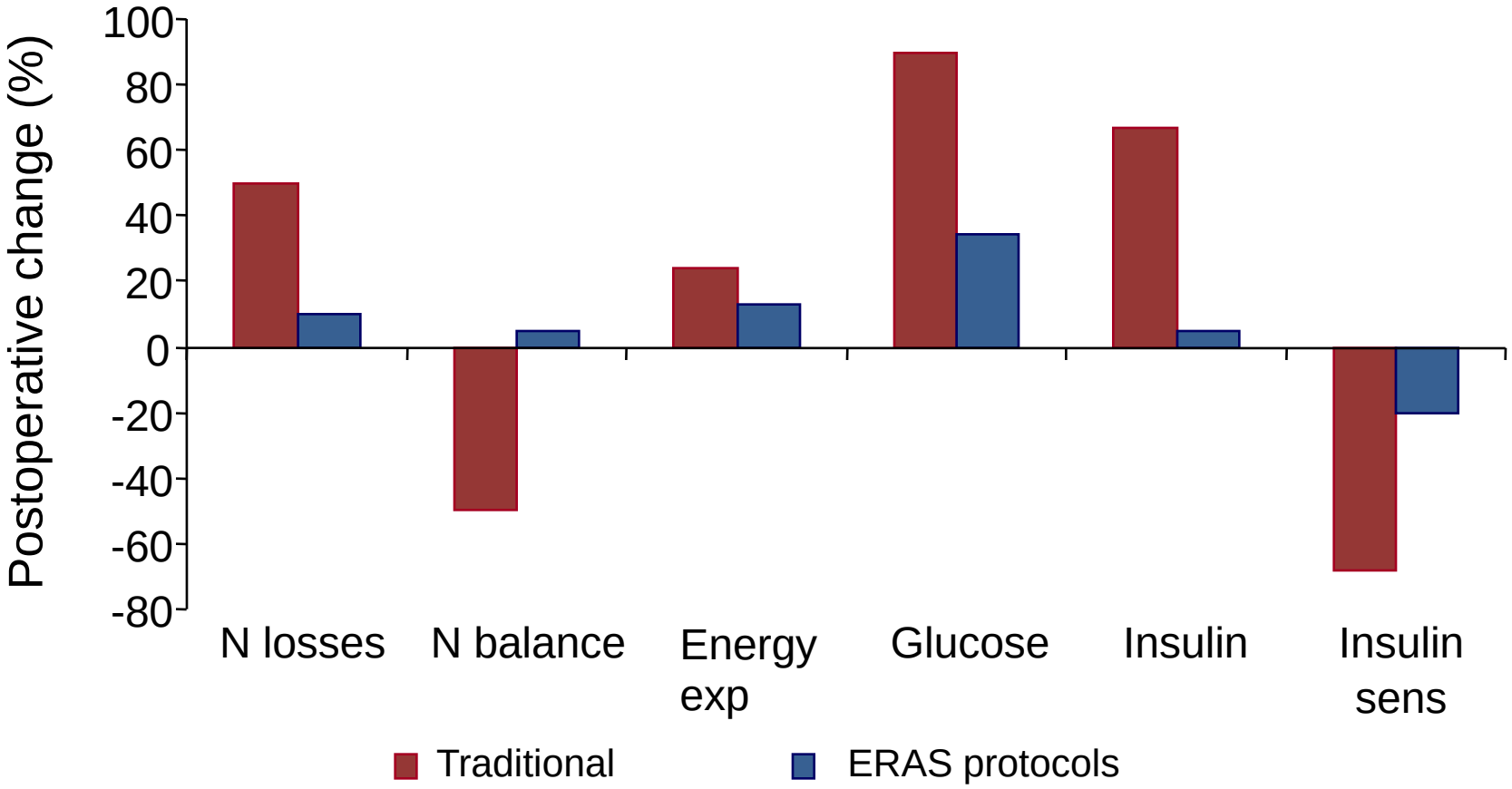


Varadhan et al, Clin Nutr 2010

Metabolic response to surgery in traditional perioperative care



Metabolic response to surgery in traditional perioperative care vs. ERAS protocols



Outline

- **Insulin resistance counteracts recovery**
- **Insulin resistance is central to stress metabolism**
  - **Reduces healing and muscle function recovery**
  - **Closely related to common postoperative complications**
- **ERAS presents EBM protocols to enhance recovery**
  - **Interaction and protection against insulin resistance**
  - **Structured interactive audit increase compliance and improve outcomes by minimizing metabolic stress**

Conclusions

Enhanced Recovery After Surgery is achieved by

- **Using Evidence Based Protocols for perioperative care**

ERAS

- **Improves outcomes**
  - **Faster return of function**
  - **Reduce complications**

A Key mechanism:

- **Minimize insulin resistance**

Conclusions

Enhanced Recovery After Surgery is achieved by

- **Using Evidence Based Protocols for perioperative care**

ERAS

- **Improves outcomes**
  - **Faster return of function**
  - **Reduce complications**

A Key mechanism:

- **Minimize insulin resistance**
- ***Metabolism and Nutrition is back on the surgical agenda***

2nd ERAS World congress

Valencia Spain
April 23-26, 2014

World class speakers

BJS Henrik Kehlet Lecture

Pre congress course:
Implementation

www.erassociety.org

ERAS Society

1st ERAS Congress
Enhanced Recovery After Surgery

5-7 October 2012

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