



# Prevention & Management of Postoperative and Chemotherapy-induced Complications

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# Disclosure of Speaker`s Interest

**Potential conflict of interest** • **No**

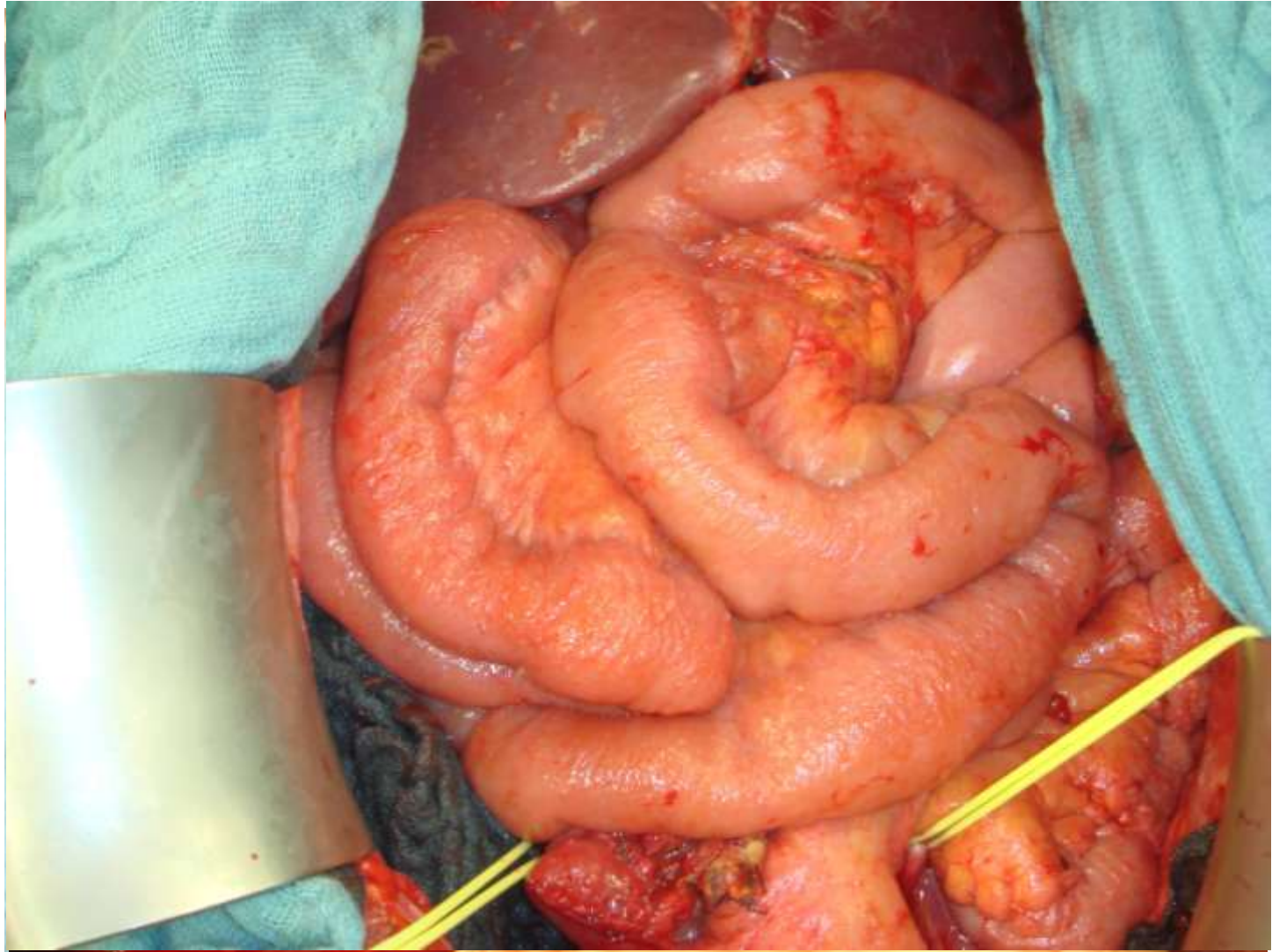
**Potentially relevant company relationships  
in connection with event** • **No**

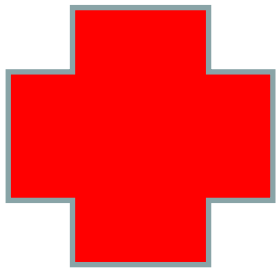
- Sponsorship or research funding • **No**
- Fee or other (financial) payment • **No**
- Shareholder • **No**
- Other relationship, i.e. ... • **No**

# How can we Improve to Reduce Complications ?

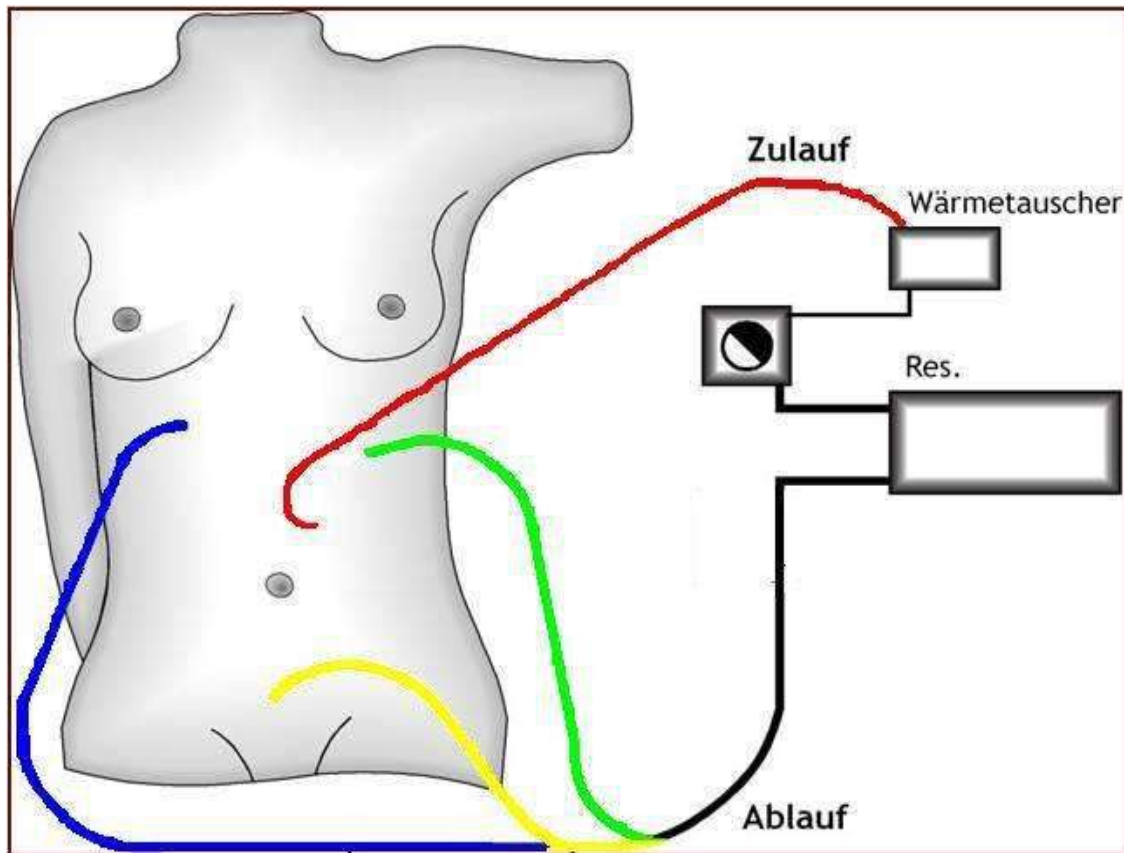
- Analysis of Complications
- Analysis of the Risk Factors
- Management to avoid Complications
- SOP

# Appendix Cancer + Carcinomatosis





# Hyperthermic intraperiton. Chemotherapy (HIPEC)

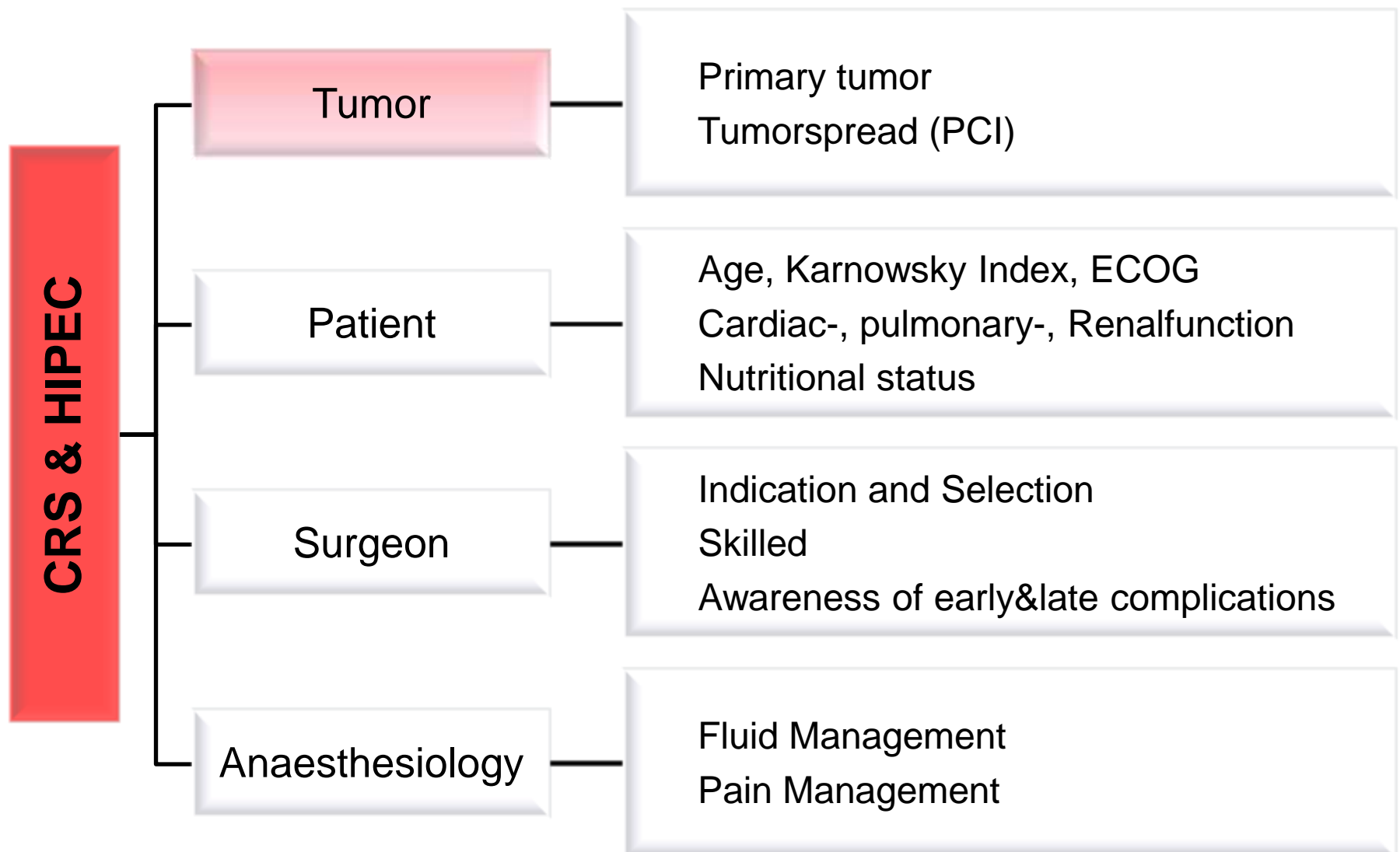


# Related Complications

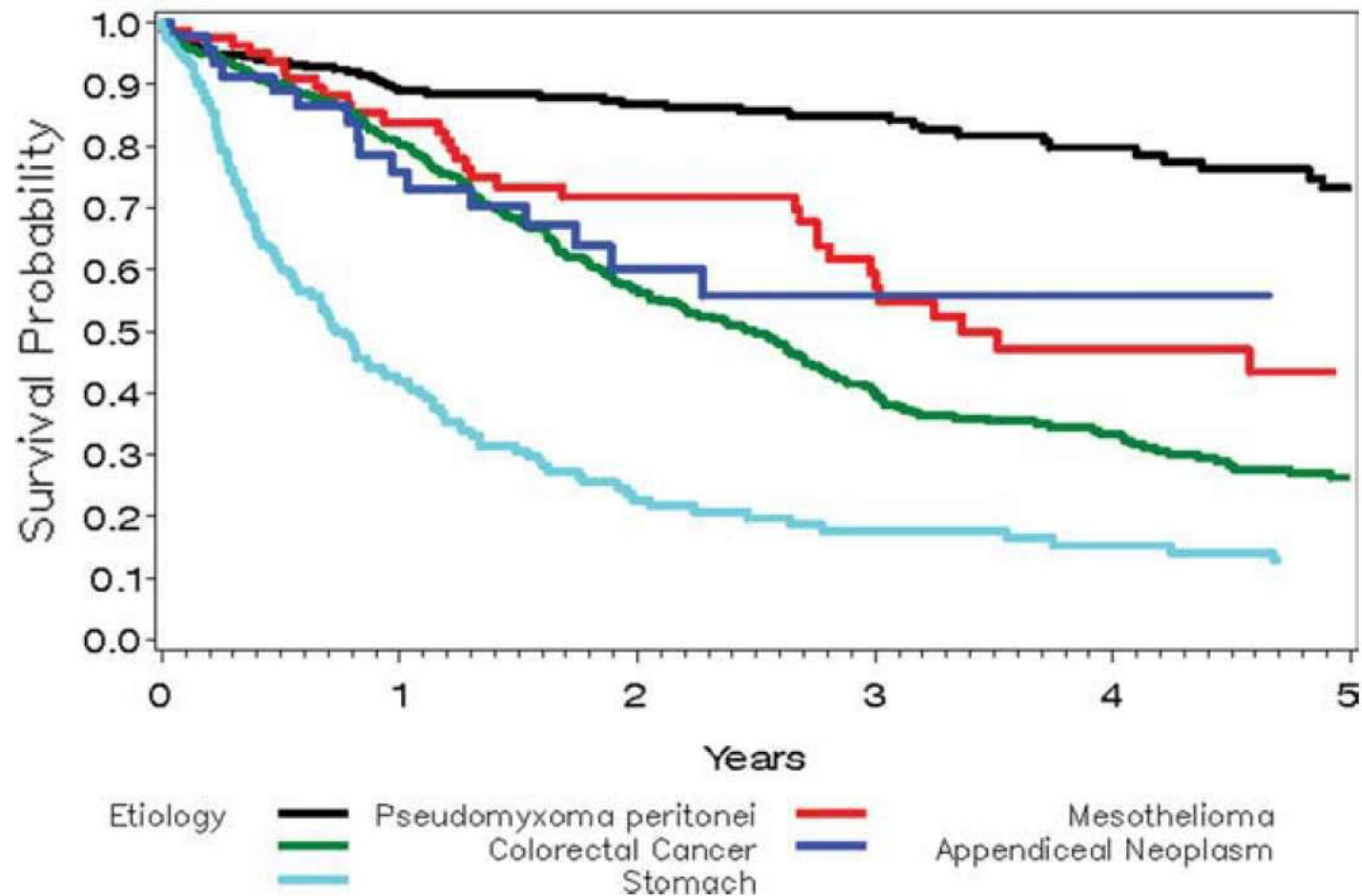
| Surgical                       | Non-surgical            | Chemotherapy            |
|--------------------------------|-------------------------|-------------------------|
| Surgical site infections (SSI) | DVT                     | Leucopenia              |
| Post OP Bleeding               | LAE                     | Neuropathy              |
| Ileus                          | Pneumonia               | Renal Insufficiency     |
| Abcess                         | Urinary tract infection | Post-operative Bleeding |
| Fistula                        |                         |                         |
| Bowel perforation              |                         |                         |
| Anastomotic insufficiency      |                         |                         |
| Sepsis                         |                         |                         |
| Re-Operation                   |                         |                         |



# Risk Factors related to



# PM: Prognostic Value of Primary Cancer



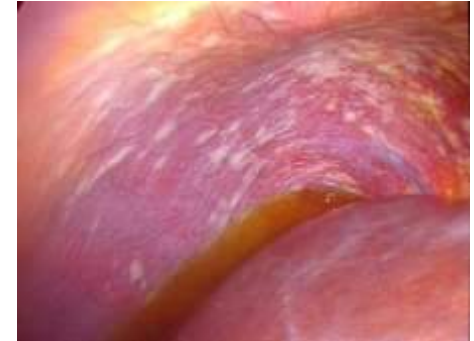
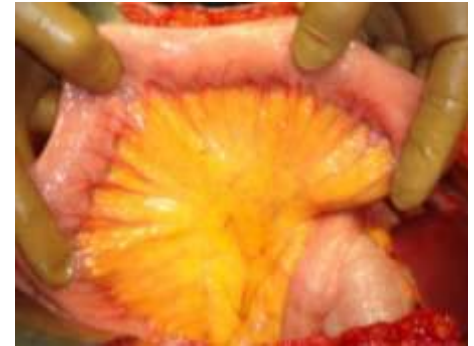
Glehen O et al. Cancer 116:5608 (2010)



# Selection for Peritoneal Metastasis (PM)

## Differentiation

- Mucinous PM
- Non mucinous PM
- Growth pattern
- Signet cell
- .....

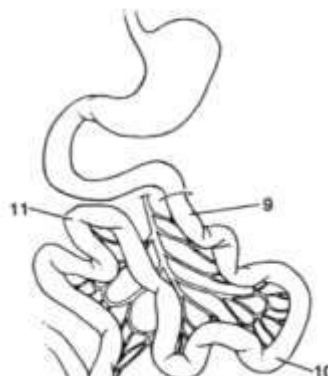


# Tumor-related Risk Factors

- Primary cancer
  - (CRC, Gastric Cancer,
  - Mesothelioma, Pseudomyxoma)
- PCI
- Number of quadrant peritonectomy
- Duration of surgery
- Transfusion
- .....

| <u>Regions</u>   | <u>Lesion Size</u> | <u>Lesion Size Score</u> |
|------------------|--------------------|--------------------------|
| 0 Central        | _____              | LS 0 No tumor seen       |
| 1 Right Upper    | _____              | LS 1 Tumor up to 0.5 cm  |
| 2 Epigastrium    | _____              | LS 2 Tumor up to 5.0 cm  |
| 3 Left Upper     | _____              | LS 3 Tumor > 5.0 cm      |
| 4 Left Flank     | _____              | or confluence            |
| 5 Left Lower     | _____              |                          |
| 6 Pelvis         | _____              |                          |
| 7 Right Lower    | _____              |                          |
| 8 Right Flank    | _____              |                          |
| 9 Upper Jejunum  | _____              |                          |
| 10 Lower Jejunum | _____              |                          |
| 11 Upper Ileum   | _____              |                          |
| 12 Lower Ileum   | _____              |                          |

PCI ☐

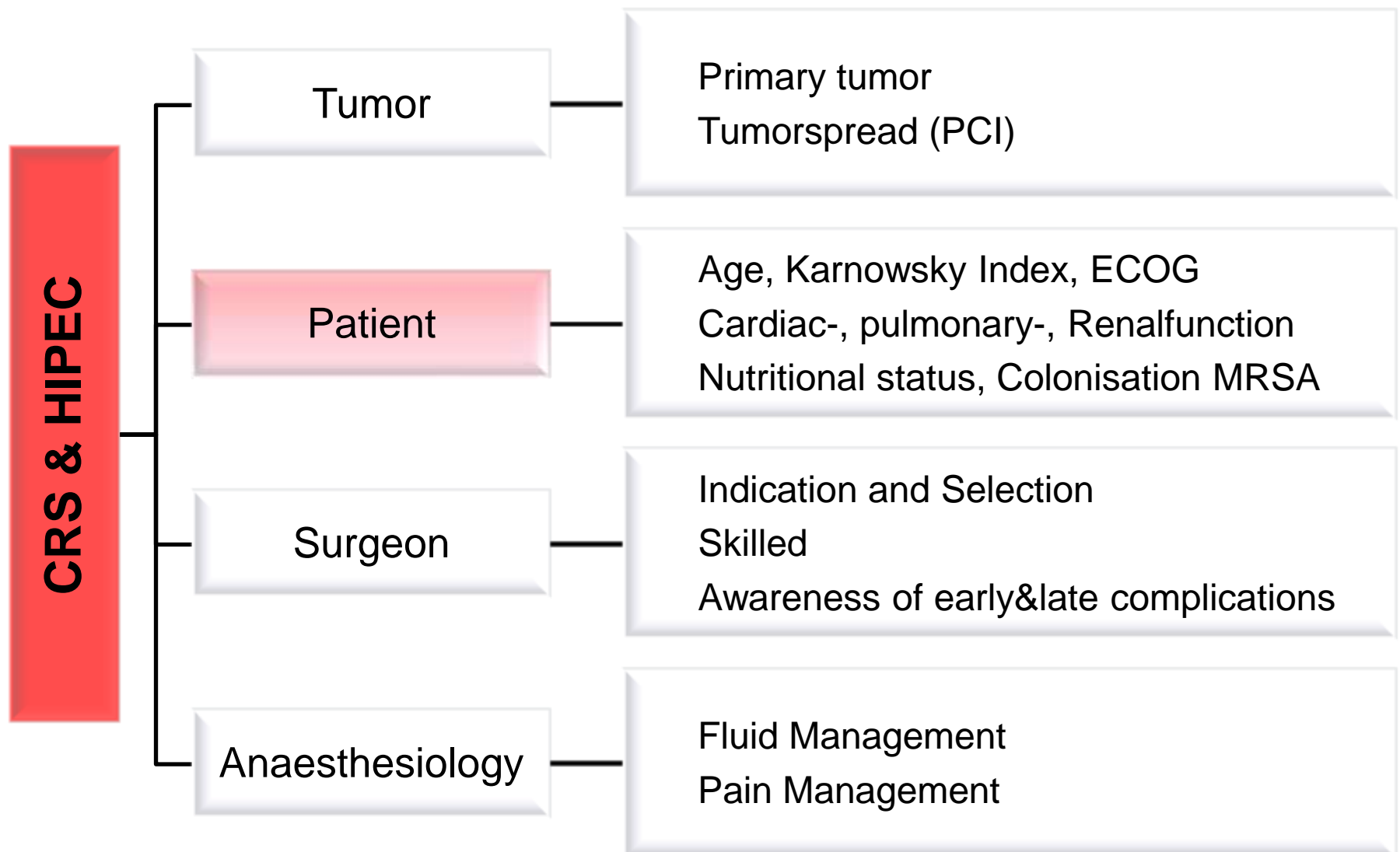



# Risk Factors for Perioperative Outcome

| Variables   |              | No Grade III/IV | Grade III/IV | p      |
|-------------|--------------|-----------------|--------------|--------|
| Diagnosis   | CRC          | 38              | 17           |        |
|             | Pseudomyxoma | 72              | 64           |        |
|             | Mesothelioma | 14              | 16           |        |
|             | OTH          | 12              | 10           | 0,04   |
| OP duration | ≤ 9h         | 82              | 37           |        |
|             | > 9h         | 37              | 52           | <0,001 |
| Transfusion | < 6 U        | 99              | 53           |        |
|             | > 6 U        | 37              | 54           | <0,001 |

Chua TC, Ann Surg 251:101(2010)

# Risk Factors related to

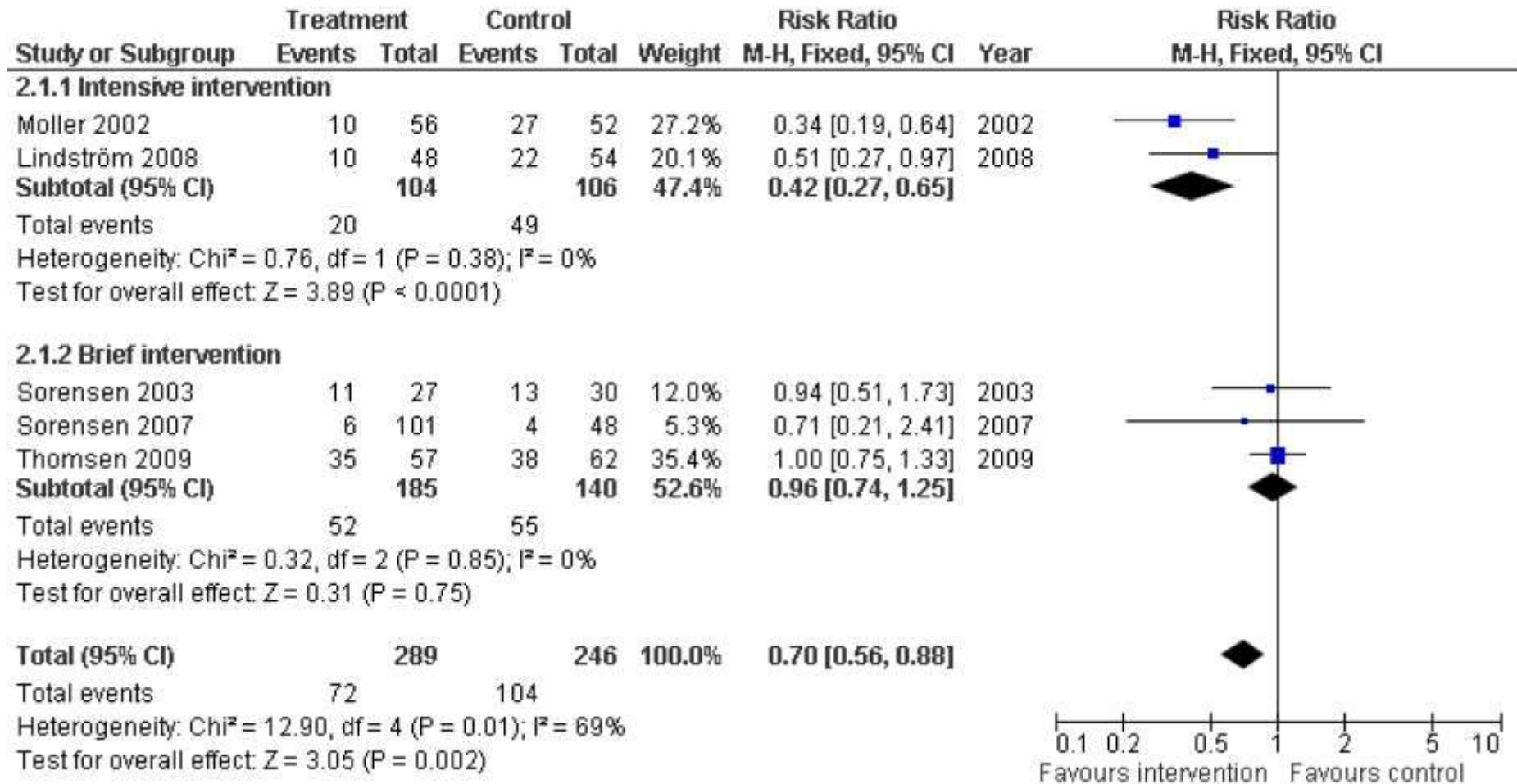


# Risk-Evaluation

- Smoking?
- Lung function test
- Echocardiography
- Creatinin clearance
- Nutritional index
- Colonisation
- Fitness

# Risk Reduction: Nicotin replacement

## Complications



Thomsen T, The Cochrane Collaboration, Issue 9 (2010)



# NRS = Nutritional Risk Screening

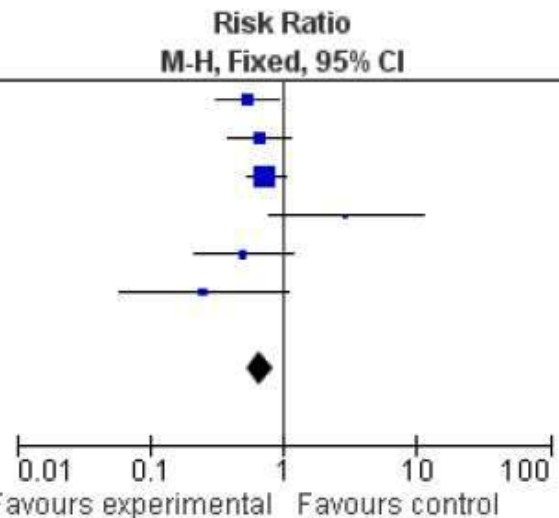
## Severe nutritional Risk:

- Weight loss > 10 to 15 % in between the last 6 months
- BMI < 18,5 kg/m<sup>2</sup>
- Serumalbumin < 30g/l
- Scoring:
  - Subjective Global Assessment: Grad C
  - Nutritional Risk Screening (NRS) ≥ 3 Punkte

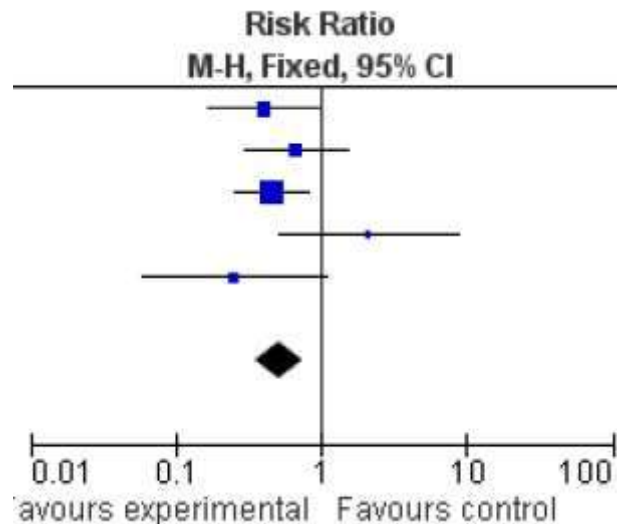
# Risk Reduction: Pre-operative Nutrition

Immunonutrition  
VS  
No additional nutrition

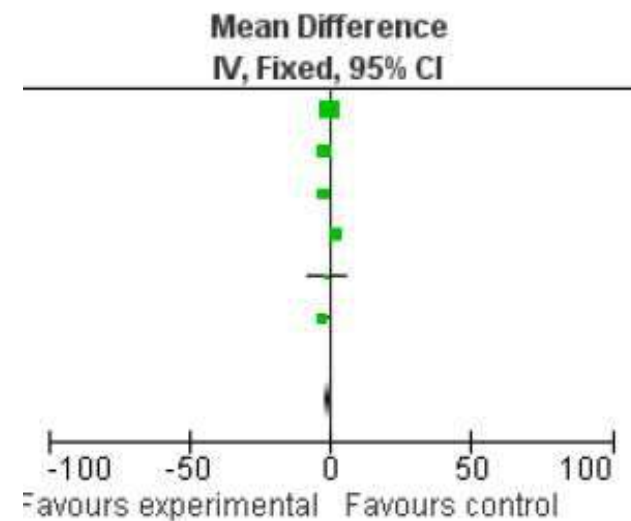
## Complications



## SSI



## Hospital Stay



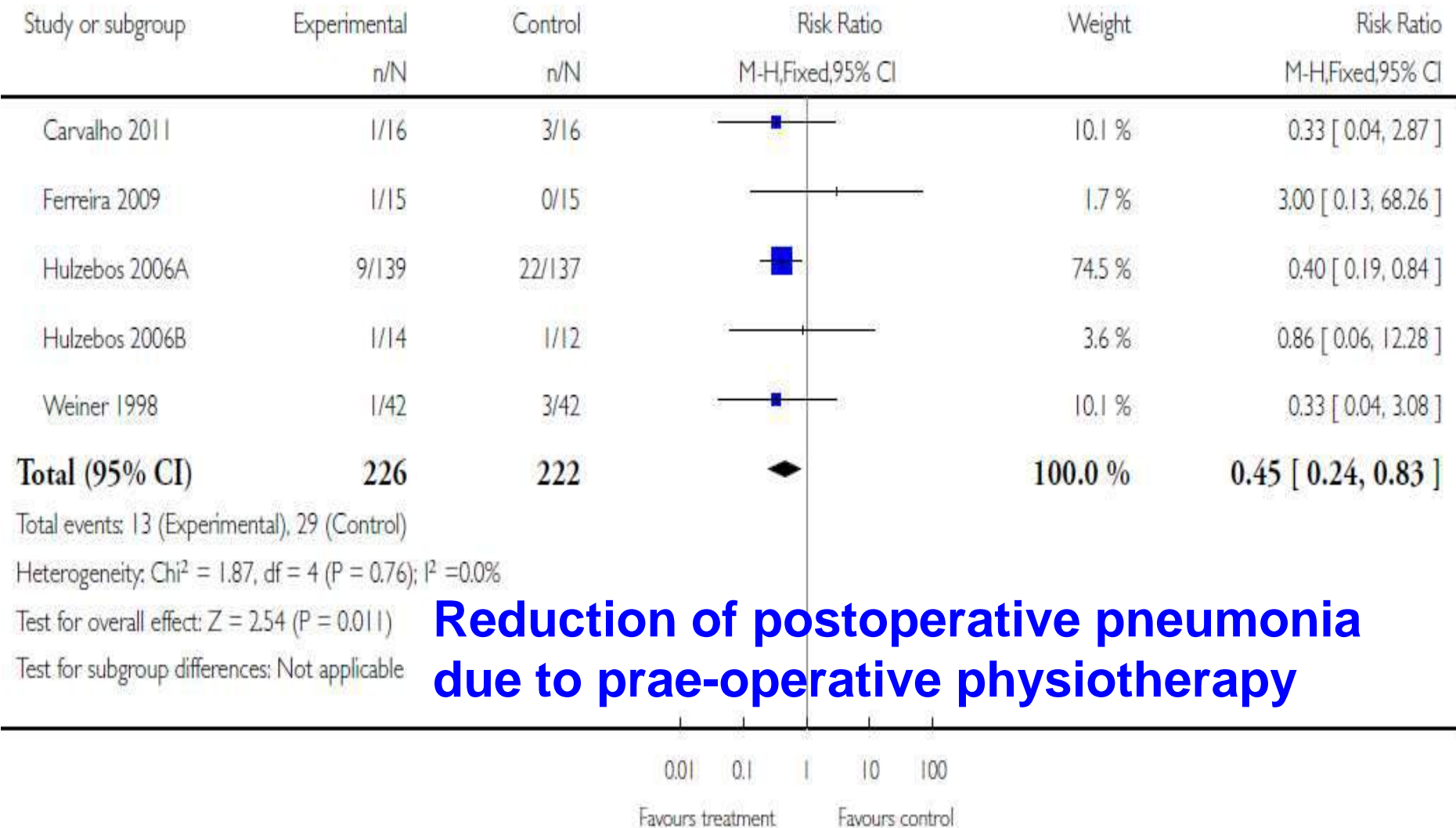
Burden S, The Cochrane Collaboration, Issue 11(2012)

# MRSA Screening in Patients on Risk

- MRSA colonisation is associated with
  - Hospitalisation elsewhere
  - Clostridium difficile infection
  - Vancomycin-resistant Enterococci carrier
  - Comorbidity: kardiac, pulmonary, renal, immune deficiency

McKinnell JA, Infect Control Hosp Epidemiol 34:1077 (2013)

# Risk Reduction: Physiotherapy (Heart - OP)



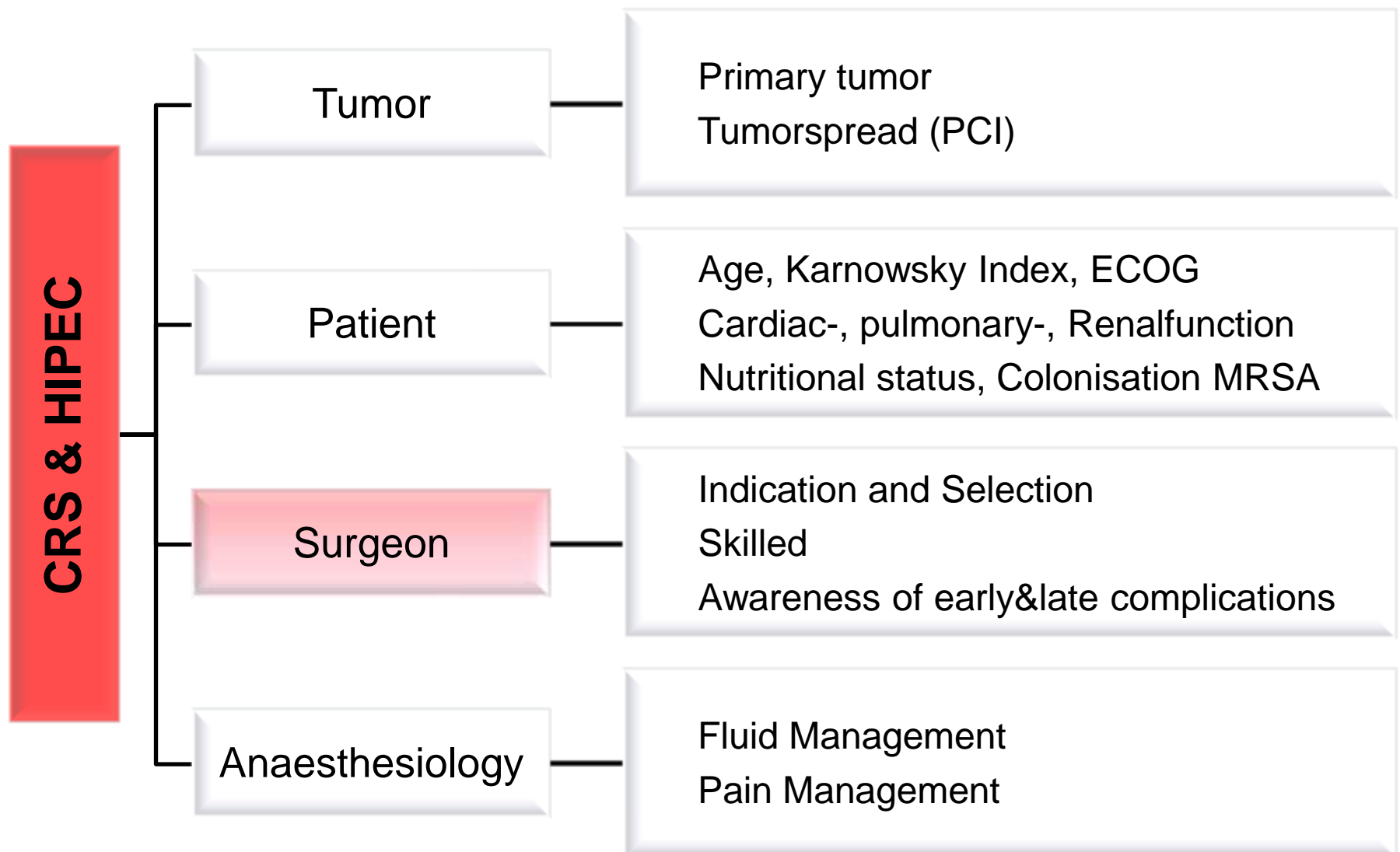
Hulzebos EHJ, The Cochrane Collaboration, Issue 11(2012)

# Summary – Patients-related Risk Factors

- Pulmonary and cardiac risk evaluation important
- Risk – Reduction needs time
  - Nicotin replacement
  - Physiotherapy
  - Nutrition (EN, PEN, Immunonutrition)
  - Microbes screening, body washing

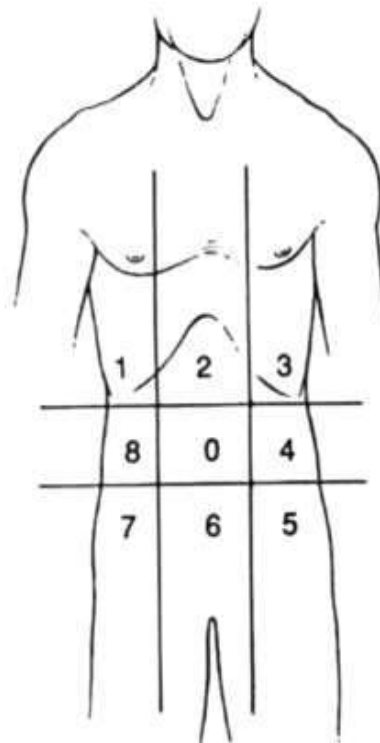
**Reduction of morbidity and mortality is documented**

# Risk Factors related to





# Peritoneal Cancer Index (PCI)



| <u>Regions</u>   | <u>Lesion Size</u> |
|------------------|--------------------|
| 0 Central        | <u>3</u>           |
| 1 Right Upper    | <u>2</u>           |
| 2 Epigastrium    | <u>2</u>           |
| 3 Left Upper     | <u>2</u>           |
| 4 Left Flank     | <u>1</u>           |
| 5 Left Lower     | <u>2</u>           |
| 6 Pelvis         | <u>2</u>           |
| 7 Right Lower    | <u>2</u>           |
| 8 Right Flank    | <u>3</u>           |
| 9 Upper Jejunum  | <u>  </u>          |
| 10 Lower Jejunum | <u>2</u>           |
| 11 Upper Ileum   | <u>  </u>          |
| 12 Lower Ileum   | <u>  </u>          |

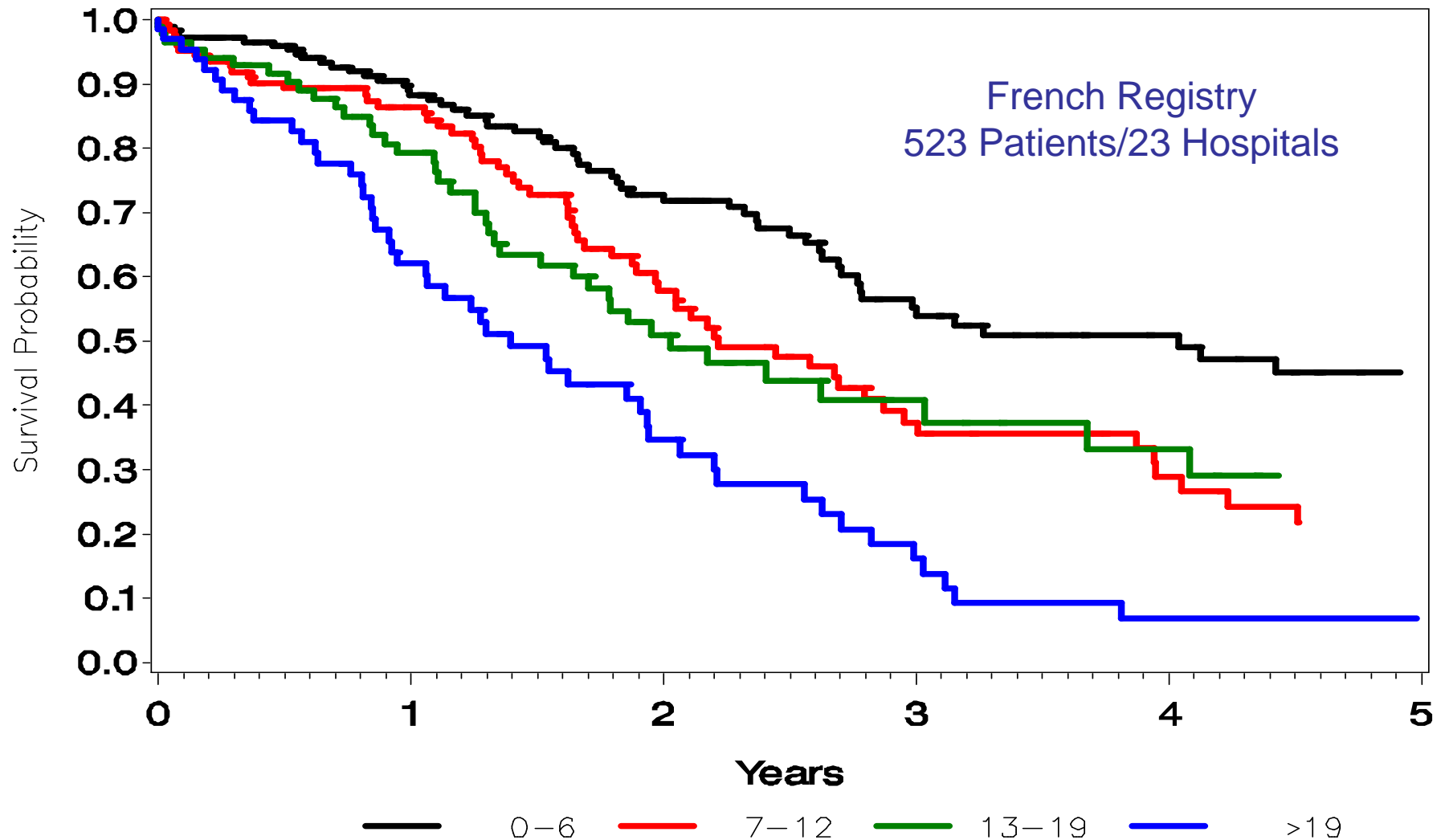
**PCI**

**19**

Peritoneal Surface Oncology Group (PSOG) 14:128 (2007)

# Long Term Results

Survival according to the Extent of the Peritoneal Carcinomatosis ( $p < 0.0001$ )



# Contra Indication to CRS

- **Cytoreductive surgery**
  - CCR 0-1 not achievable
  - High risk for small bowel perforation
  - Distant metastases (Liver, Lung, Bone, ...)
  - All contraindication for large general surgery
- **No skilled Surgeon and no skilled Team**

# Learning Curve

- Potential risk factor for patients outcome is the surgeon...
- Extended learning time!
- Stable CCR0-1-results and low morbidity after 140 procedures CRS+HIPEC

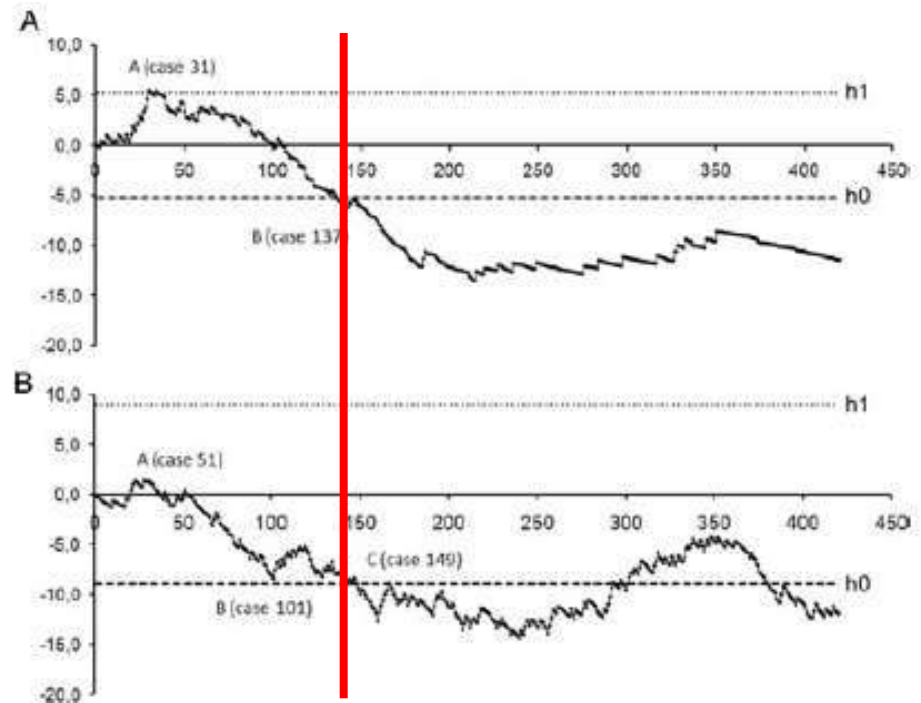
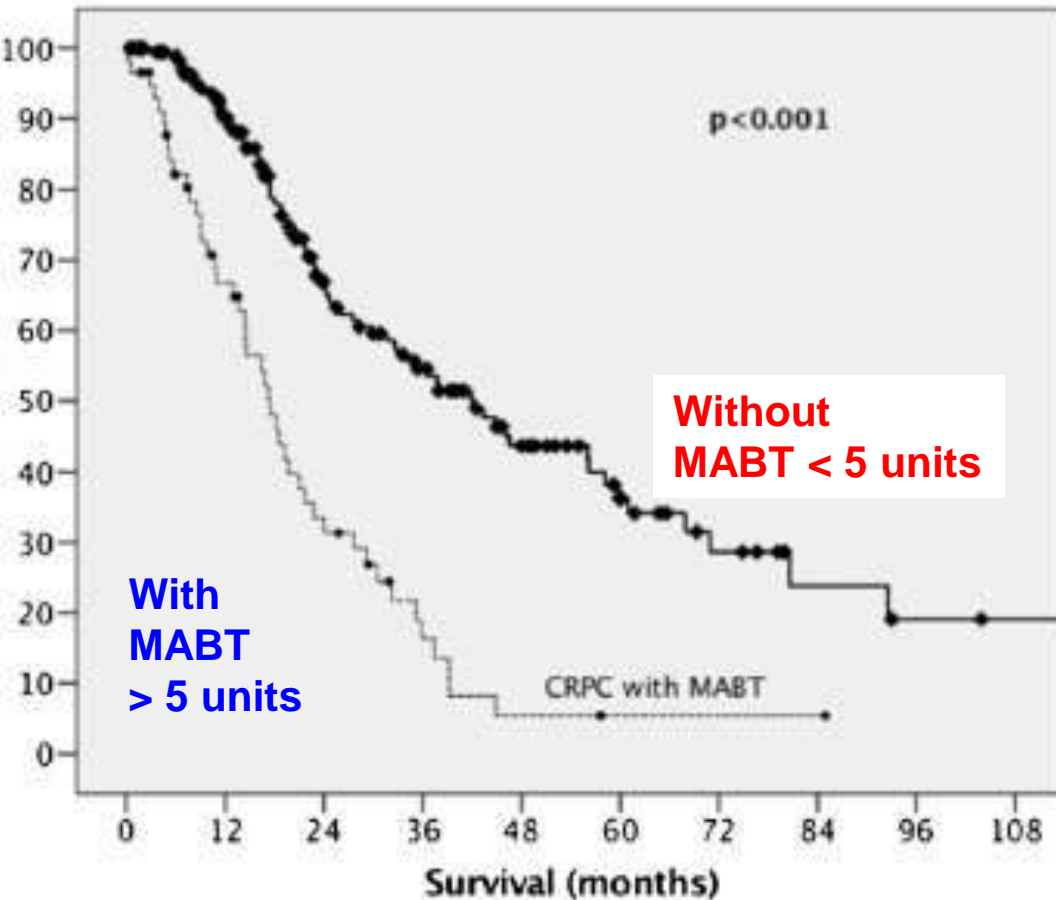


FIGURE 1. The x axis represents operation number, not calendar time. The y axis represents a cumulative score resultant from calculation involving risk-adjusted log likelihood ratios. h0: lower boundary of control limit; h1: upper boundary of control limit. The lower boundaries were surpassed by the RA-SPRT plots at the 137th (A) and 149th (B) cases, respectively, for incomplete cytoreduction and G3-5 morbidities. A, Incomplete cytoreduction rates (RA-SPRT). B, G3-5 postoperative morbidity rates (RA-SPRT).

Kusamura et al., Ann Surg 2012

# Massive Allogenic Blood Transfusion

Cumulative Survival %

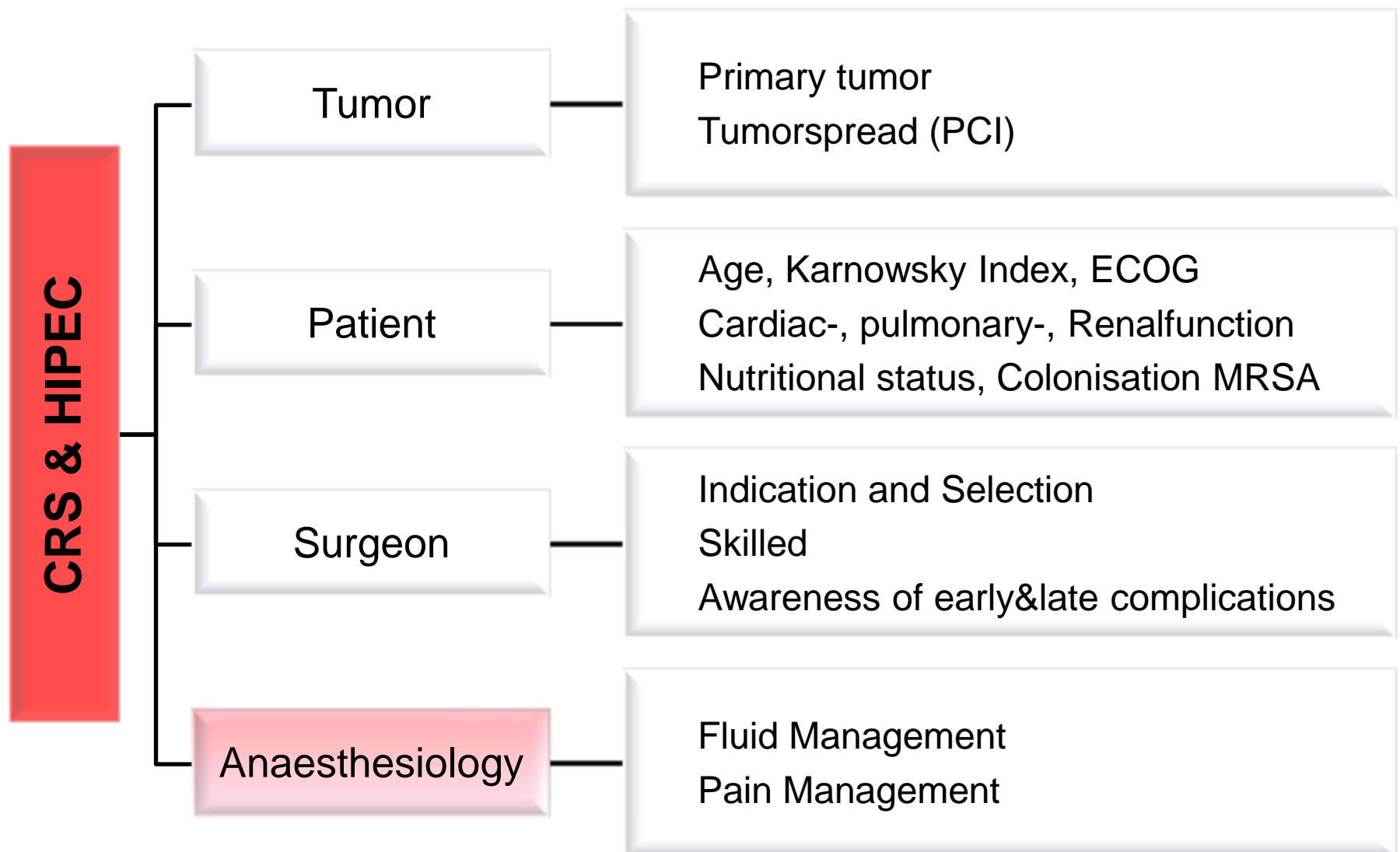


## Significantly associated with MABT

- Infection
- Intra-abdominell collection
- Grade III/IV morbidity
- Length of ICU stay > 4 d
- Length of hospital stay > 28 d
- In-hospital mortality

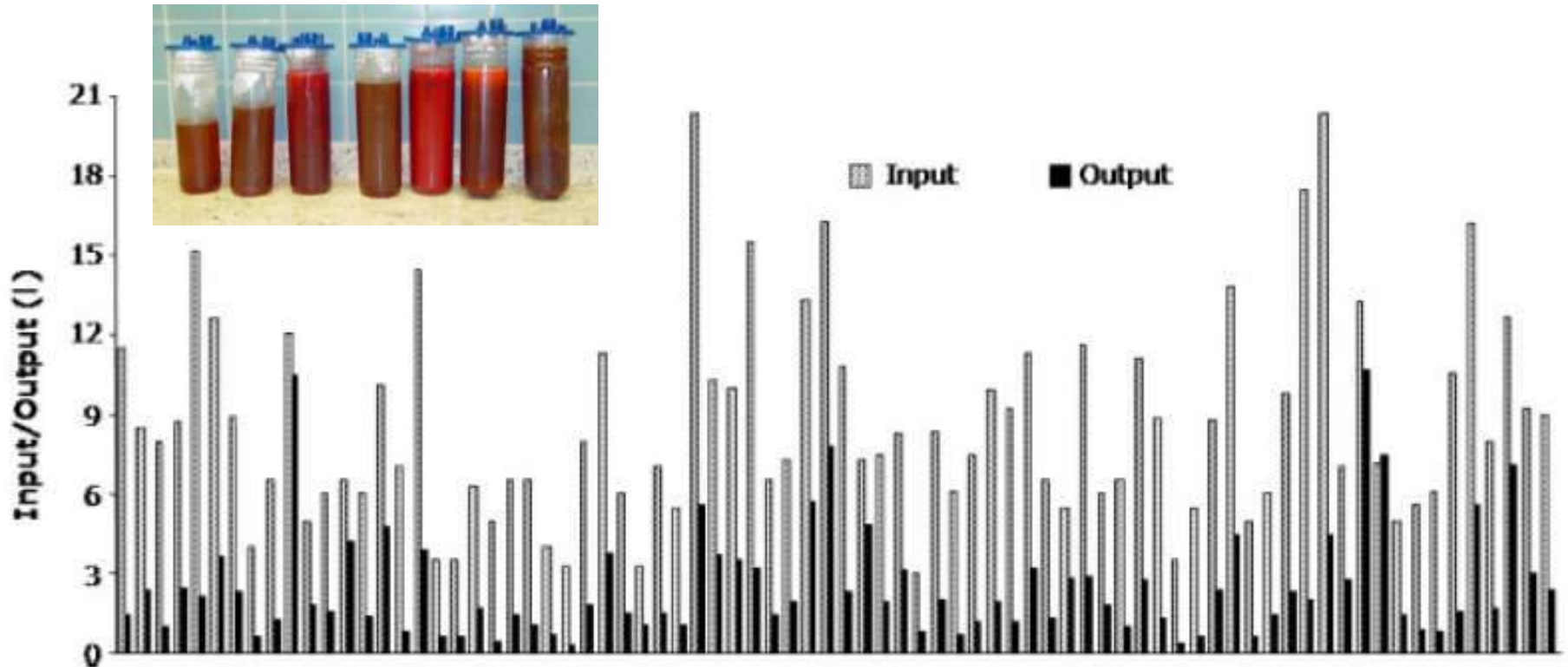
Saxena A., J Gastrointest Surg DOI 10.1007/s11605-017-3444-8 (2017)

# Risk Factors related to





# Intraoperative Fluid Turnover n=78



Fluid Turnover ~ 12 ml / kg x h

Schmidt C, JSO 100:297 (2009)

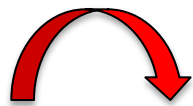
# Monitoring and Goals

- **Goals for volume therapy**
  - Filling pressures (CVP, PAOP)
    - no prediction of volume responsiveness
  - Stroke volume (cardiac output)
    - goal for titrated volume therapy
  - Static volume parameters (GEDI, ELVI)
    - safety limits
- **Goals for hemodynamic therapy**
  - Oxygen delivery
    - avoid oxygen debt
  - Lactate
    - late warning sign

Given by Prof. Sanders

# SIRS and hemodynamic changes

- SIRS continues into postoperative period
  - vasodilation
  - loss of systemic vascular resistance (SVR)
  - capillary leak
- Aggravated in combination with epidural anaesthesia



- **Management:**

- advanced hemodynamic monitoring
- vasopressor support
- fluid replacement

Cooksley TJ , World J Surg Oncol. 9:169 (2011)

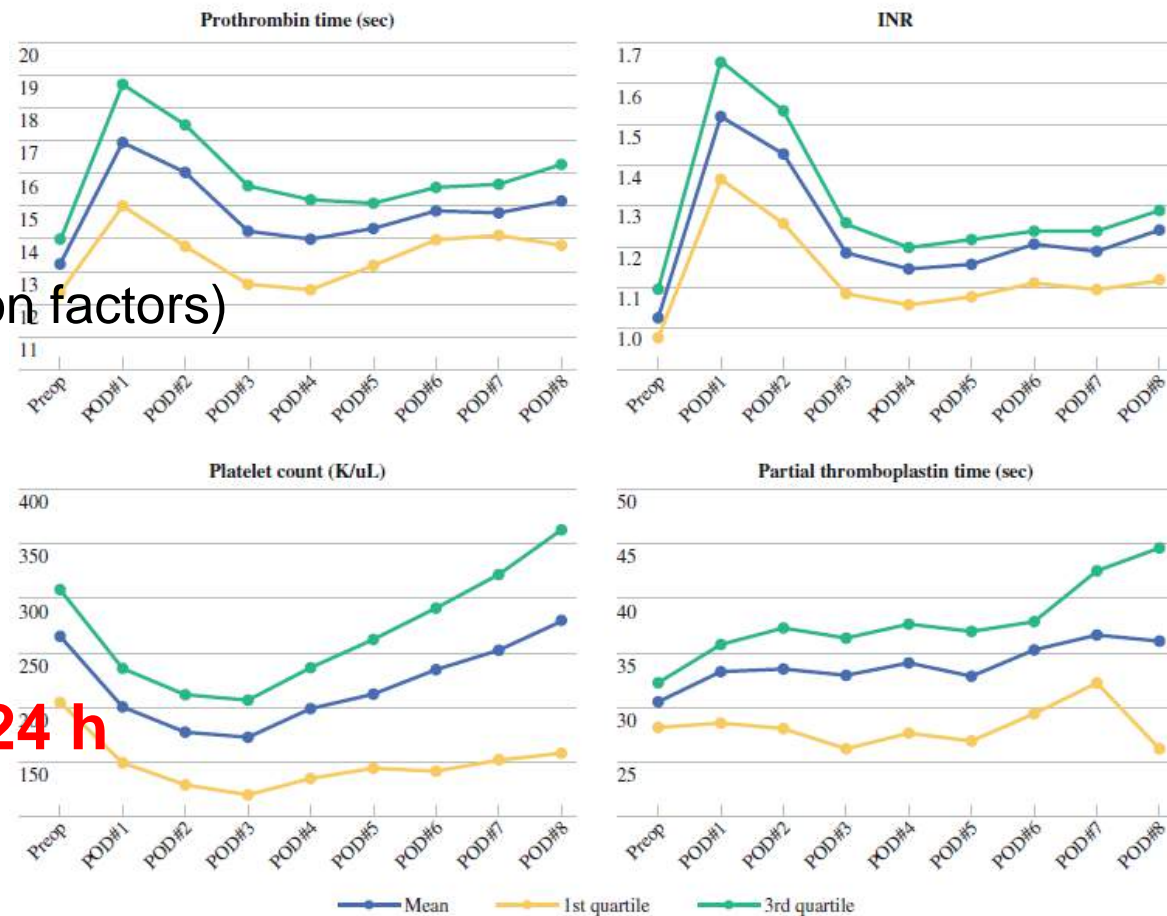
# Postoperative Coagulopathy

## ● Reasons:

- blood loss
- (loss of coagulation factors)
- dilution effects
- thrombocytopenia (chemo-induced)



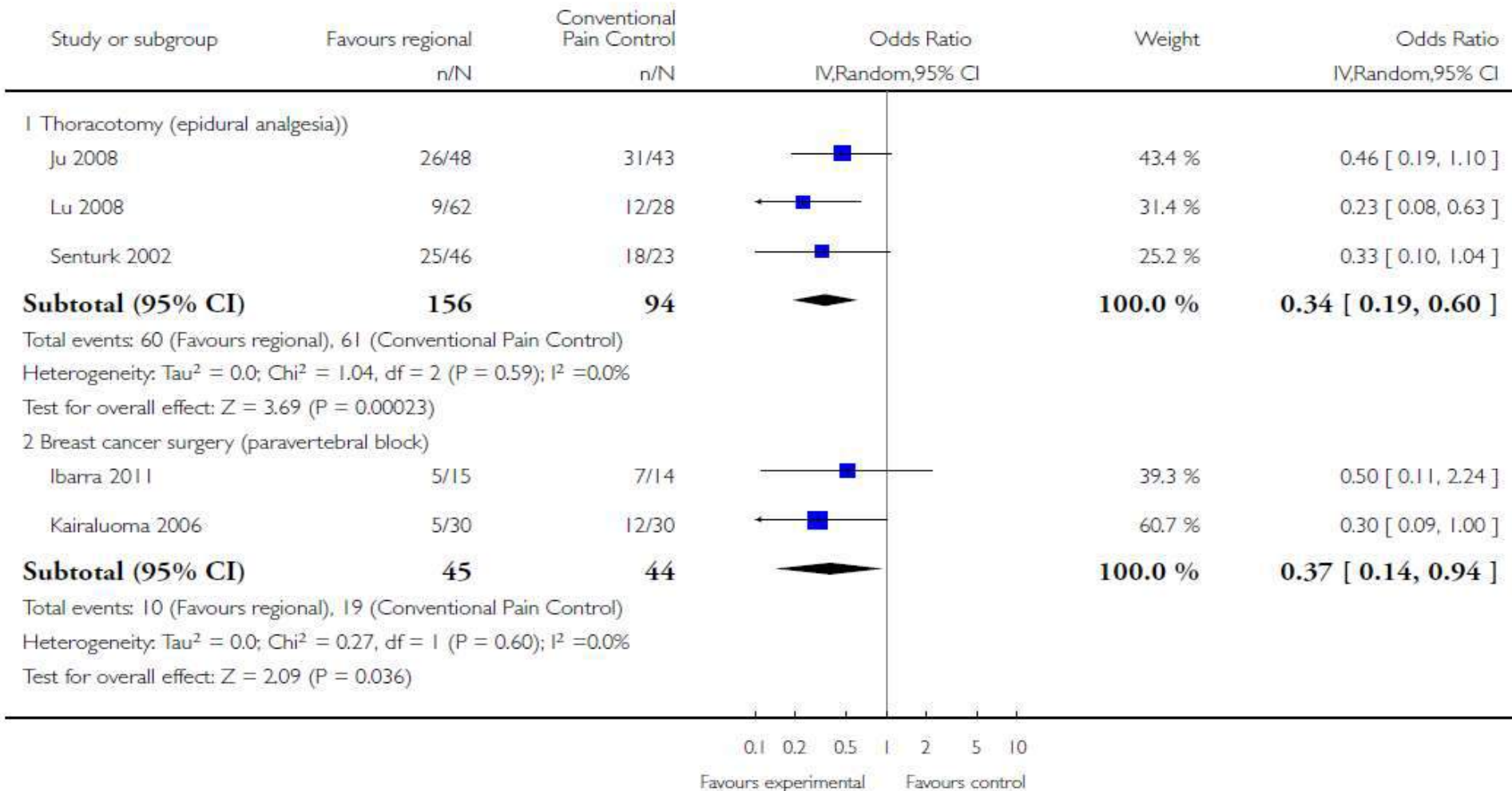
**Peak after 24 h**



Owusu-Agyemang P, Ann Surg Oncol. (2013)

# Local and regional Analgesia

## Reduction of pain



Andreae MH, The Cochrane Collaboration (2012)

# Impaired Bowel Function

## Nausea and Vomiting

- up to 13 days postoperatively
- Causes:
  - anesthesia related nausea and vomiting (PONV)
  - chemotherapy associated nausea



- **Management:**
  - prophylactic use of antiemetics (Ondansetron, DHB)
  - pain control with epidural anesthesia

Arekelian E, EJSO 37:897 (2011)



# Impaired Bowel Function

## Post-OP Ileus

- Causes:

- surgical procedure and mechanical handling of the gut
- increased sympathetic tone
- pain
- release of inflammatory mediators
- paralysis due to use of opioids



- **Management:**

- pain control and sympaticolysis with epidural anesthesia

Shi WZ, Acta Anaesthesiol Scand 58:923 (2014)

# Chemo-induced Toxicity - Nephrotoxicity

- Frequency from none<sup>(1)</sup> to 3,7%<sup>(2)</sup> up to 19%<sup>(3)</sup>
- Especially platinum containing substances
- Significant risk factors of Acute Kidney Insufficiency:
  - low intraoperative Urinary Output
  - angiotensin II receptor antagonist use (eg Sartane)
  - hypertension



- **Management:** forced diuresis already intraoperatively

(1)Cooksley TJ, World J Surg Oncol. 9:169 (2011)

(2)Hakeam HA, Renal Fail 10:1486 (2014)

(3)Canda AE, Ann Surg Oncol 4:1082 (2013)

# Chemo-induced Toxicity

## Immunosuppression, Leucopenia and Infection

- Haematotoxicity of 14 – 20 %
- Even after single dosage possible
- Independent from extend of peritonectomy
- Nadir of bone marrow suppression ~ 14 day post-op
- Severe Leucopenia decrease of granulocytes  $< 0,5\mu\text{g/l}$ 
  - stimulation of granulopoiesis with Filgrastim (= NEUPOGEN®)
- **Sepsis is the leading cause of mortality**

Pelz JO, Chirurg. 84:957 (2013) ; Cooksley TJ World J Surg Oncol. (2011)

# ERAS: Enhanced recovery after surgery

- Involve the nutrition in the therapeutical Master Plan
- Screening of the metabolic risk (NRS, BIA)
- Avoid longer fasting periods
- Start nutrition at the earliest possible point after the operation
- Minimize katabolic stress
- Measure blood sugar level
- Early mobilization to stimulate protein synthesis and muscle function

# What influences the hospital stay?

- Early extubation
- Analgesia + epidural catheter
  - Nausea – Vomiting (PONV vs Chemotherapy)
  - Pain
  - Delayed gastric emptying (DGE)
  - Flatus
  - Defecation
- Short period of drainage
- Short stay on ICU
- Infection
- Early start of fluid / nutrition
- Early mobilisation

# Conclusions

## Peri-operative Management in CRS and HIPEC

- Standardized protocols are helpful
- SOP are recommended - be generated within the team
- Preoperatively main goal is risk evaluation and reduction
- Intraoperatively main topic fluid and pain management
- Postoperatively early recovery concepts, if possible

# 5th Course Perioperative Management

**Modul 1:** Perioperative management during cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of peritoneal malignancy

**01.-02.12.2017**

Deadline for registration

Deadline: 10. October 2016

**Modul 2:** Live Demonstration of Patients Treatment

**04.-06.12.2017**

(limited Number of Participants)

## SAVE THE DATE



Management of Hyperthermic  
Intraperitoneal Chemotherapy (HIPEC)  
after Cytoreductive Surgery (CRS)

**15.-17.02.2018**

**2018**

HAMBURG



**Further information:**  
**[www.essoweb.org](http://www.essoweb.org)**  
**[ana.galan@essoweb.org](mailto:ana.galan@essoweb.org)**