

# **“Esophageal Cancer, East and West: Same Name, Difference Disease”**



**Asia Medical Forum**

**The Lancet 2007**

**Singapore**

**21 April 2007**

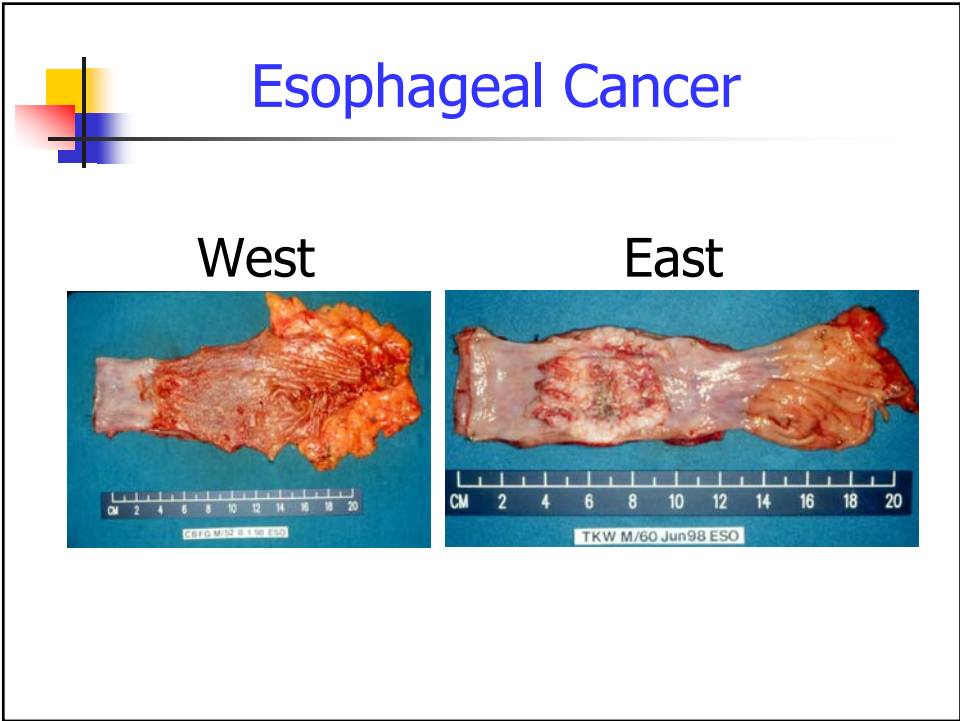
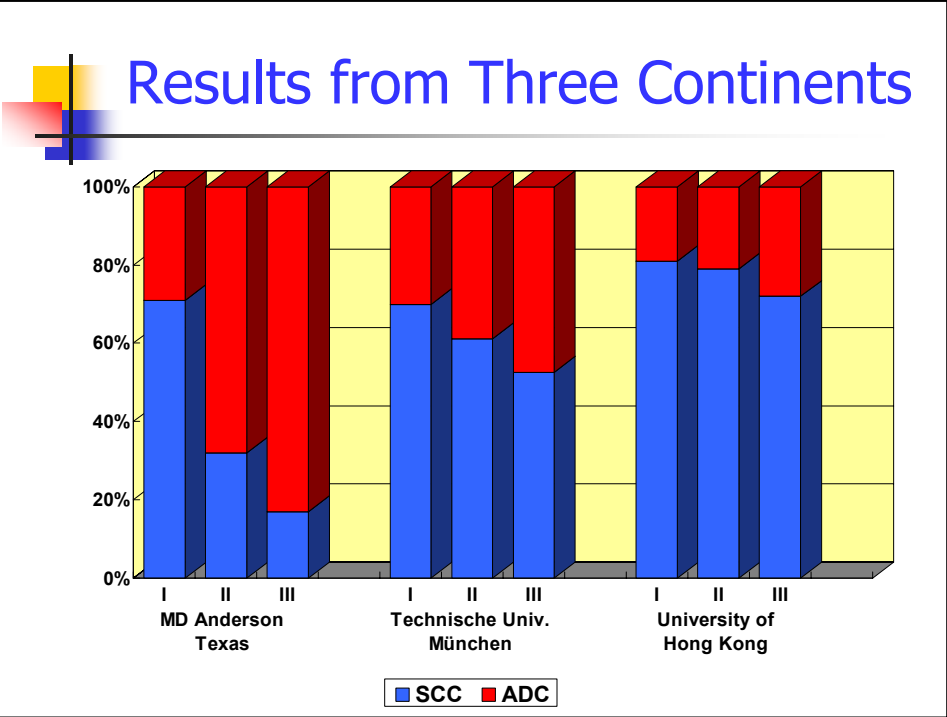
The University of Hong Kong



## **Developments that Changed Practice**



1. Epidemiology of cancer
2. Expectation of improved survival
3. Advances in technology
4. Scrutiny by funders and community
5. Critical review of outcome
6. Evidence-based surgery



## Iran



*Pourshams, 2004*



## Golestan (North-east Iran)

370/682 seen in GI clinic has cancer

ESO SCC	60%
ESO ADC	6%
Cardia ADC	16%
Non cardia ADC	16%

Similar to Linxian, China

*Pourshams, 2004*



## GERD and Esophageal Adenocarcinoma

Nationwide, case-controlled study; Sweden

	n	All GERD odds ratio	Severe GERD odds ratio
ESO ADC	189	7.7	43.5
Cardia ADC	262	2.0	4.4
ESO SCC	167	1.1	1.1
Controls	820	-	-

*Lagergren et al, NEJM, 1999*



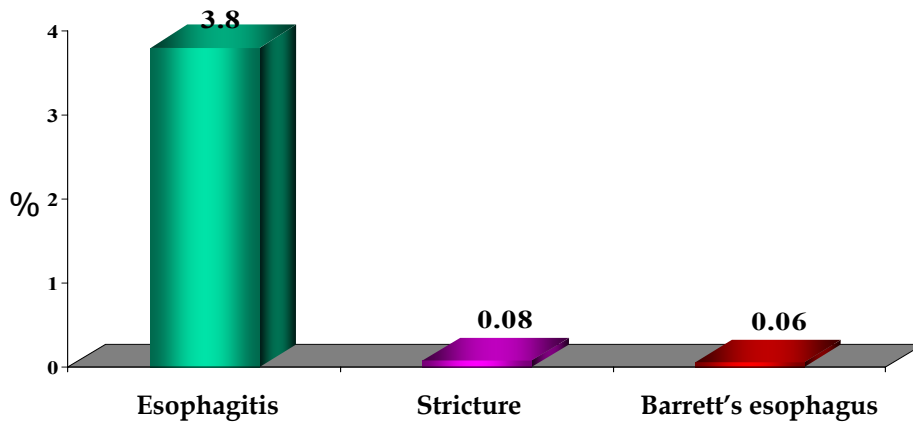
## Body Mass and Esophageal Adenocarcinoma

Nationwide, case-controlled study; Sweden

	n	Highest group odds ratio	Obese odds ratio
ESO ADC	189	7.6	16.2
Cardia ADC	262	2.3	4.3
ESO SCC	167	-	-

*Lagergren et al, Ann Intern Med, 1999*

## Erosive Esophagitis in Hong Kong 16606 patients in QMH

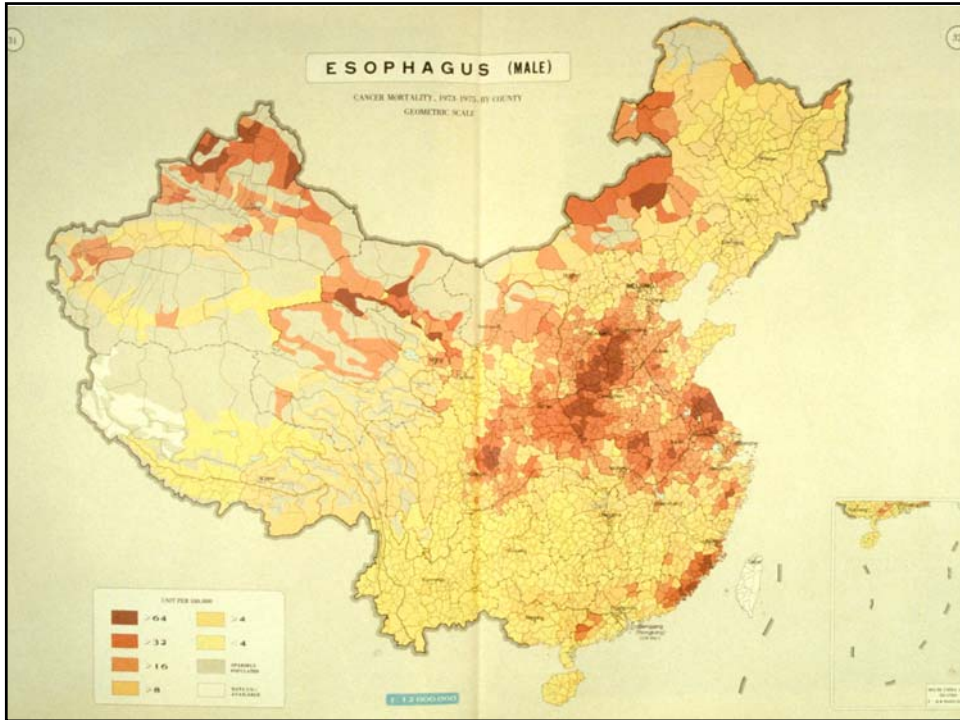


*Wu et al, HKU GI Group*

## BMI Worldwide

BMI > 25 kg/m<sup>2</sup>

Hong Kong	17.4%
Philippine	20.2%
Japan	21.3%
Canada	48.2%
Germany	49.2%
U.S.	58.5%



*Int. J. Cancer*: 102, 271–274 (2002)  
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Publication of the International Union Against Cancer

## MORTALITY AND INCIDENCE TRENDS FROM ESOPHAGUS CANCER IN SELECTED GEOGRAPHIC AREAS OF CHINA CIRCA 1970–90

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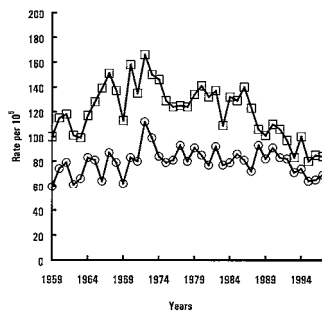


FIGURE 2 – Age-standardized incidence trends from both combination of esophageal cancer and cardiac cancer by gender in Linxian, North China, 1959–97. □, male; ○, female.

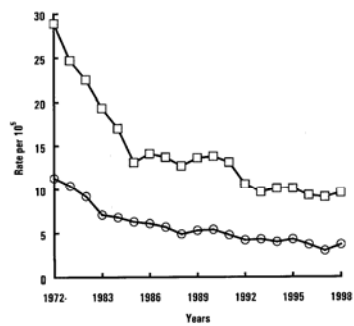


FIGURE 4 – Age-standardized incidence trends from esophageal cancer by gender in urban Shanghai, China, 1972–98. □, male; ○, female.



## Risk Factors

	<b>ADC (West)</b>	<b>SCC (East)</b>
Barrett's esophagus	++++	-
Weekly reflux symptoms	+++	-
Obesity	++	-
Tobacco use	++	+++
Alcohol use	-	+++
Poverty	-	++
History of head and neck cancer	-	++++
Frequent consumption of extremely hot beverages	-	+
Chronic disease of esophagus	-	++++

*Enzinger et al, NEJM, 2003*



## Challenges in 1980's

- Operative mortality high
- Complications serious
- Alternative treatment unsafe
- Quality of life low priority

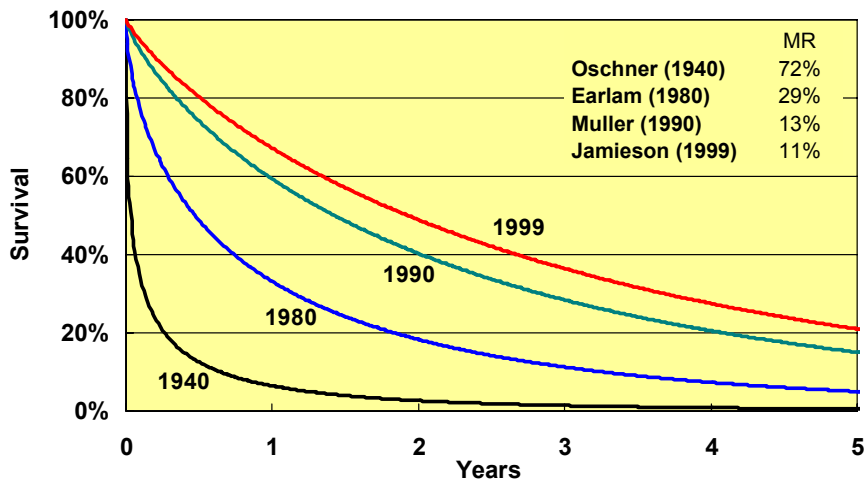


## 25 Years Later

- Mortality reduced to almost zero
- Complications better managed
- Alternative treatment more effective
- Quality of life an important goal

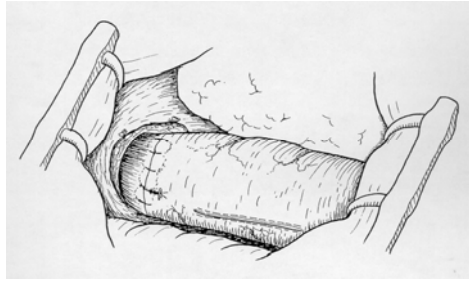
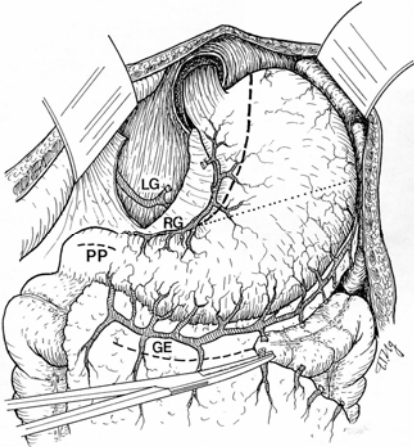


## Survival



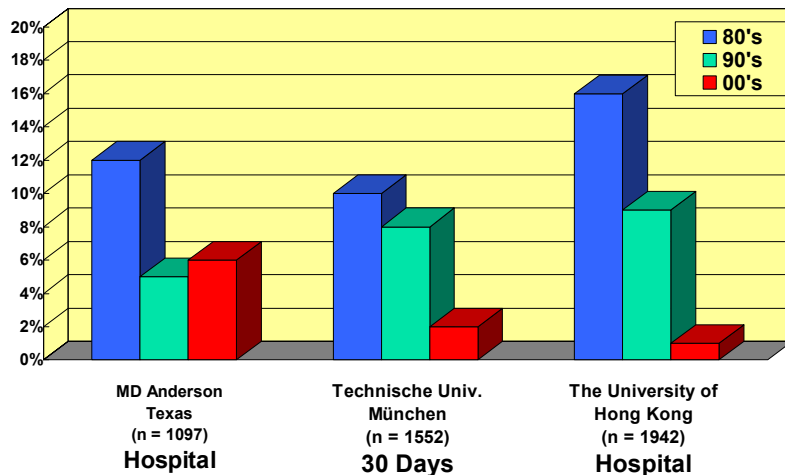


# Lewis Tanner Operation



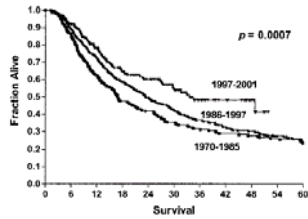
# Results from Three Continents

## Mortality Rates

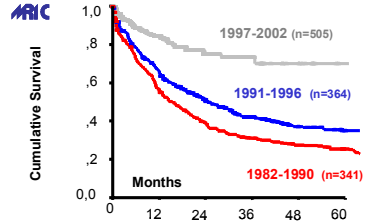


# Survival after Resection

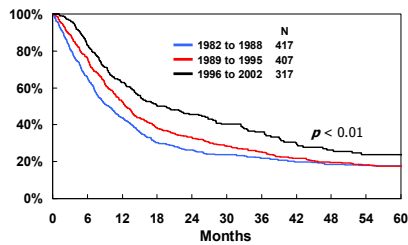
## University of Texas



## University of Munich

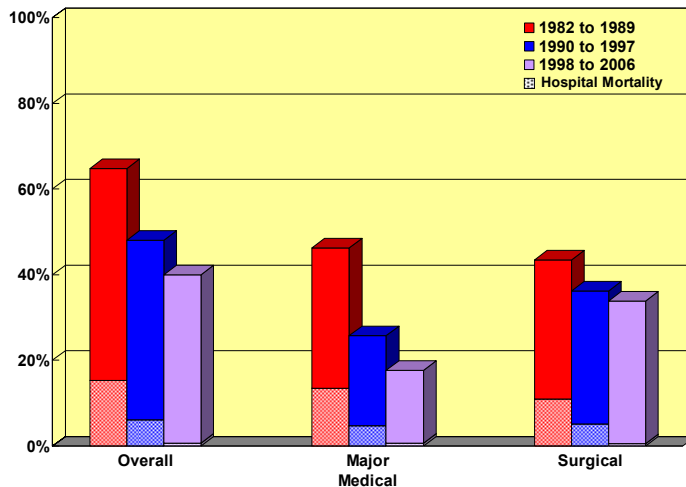


## University of Hong Kong



# Complications and Mortality

Resections = 1363





## Advances in Technology

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- Imaging
- Localisation
- Anesthesiology/monitoring
- Stapler and other devices
- CUSA, Argon beam, others
- MIS and sentinel node
- Endoscopic capabilities
- Intensive care facilities

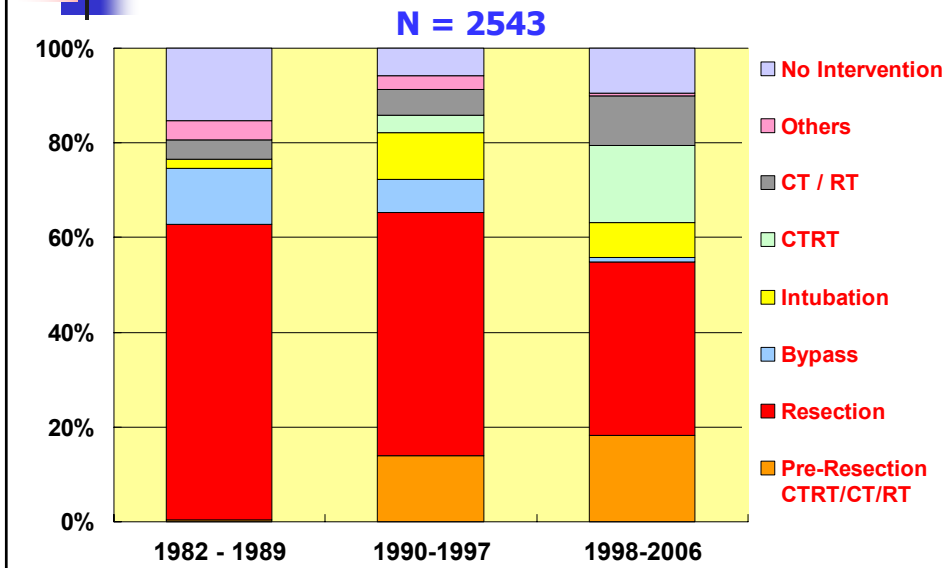


## Advances in Technology

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- Antibiotics
- Epidural analgesic
- Pain relief
- Haemostatic sealants
- Chemotherapy and other drugs
- Radiotherapy and focused beams
- Molecular methods in pathology
- Rapid retrieval of data

## Main Treatment

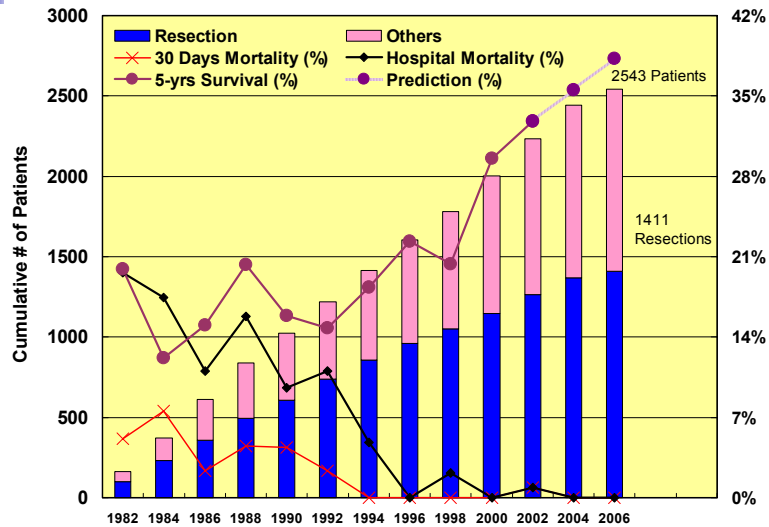


## Factors Improving Outcome

- Hospital volume
- Surgeon volume
- Qualified anesthetists
- Epidural analgesia
- Bachelor degree of nurses
- Daily ward round
- Fluid restriction
- Normal albumin level



## Hospital Volume, Mortality and Survival



## National Surgical Quality Improvement Program (NSQIP)

11 years; VA hospital

30 day mortality      ↓28%

Postop morbidity      ↓43%

*Harris et al, Bulletin ACS, 2004*



## Hong Kong Esophagectomy Mortality Rate

First audit (1997-2001) 11.2%

Second audit (2002-2006) 5.5%

High volume 4.8%

Mid volume 5.0%

Low volume 8.7%



## Preoperative Chemotherapy

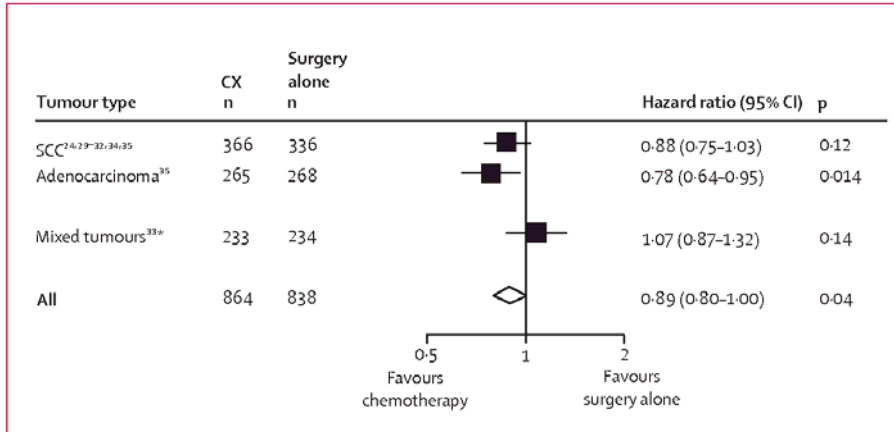
Meta-analysis; 11 RCTs; 1976 patients

- CT + S → lower resection rate
- higher R<sub>0</sub> resections
- no increase in MR
- no survival benefit

*Urschel et al, AJS, 2002*



## Meta-analysis of NCT vs Surgery

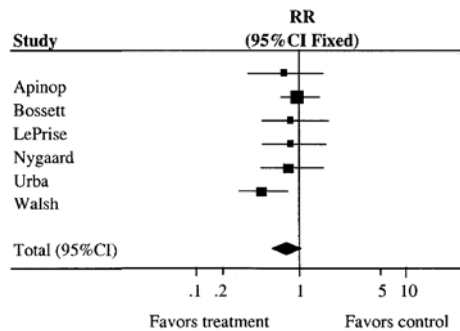


*Gebski et al, Lancet Oncol, 2007*



## Neoadjuvant CRT for Esophageal Cancer

Meta-analysis of RCT; 1966-2003; 374/364 patients



Test for heterogeneity: chi-square=5.08 ( $P=.41$ )

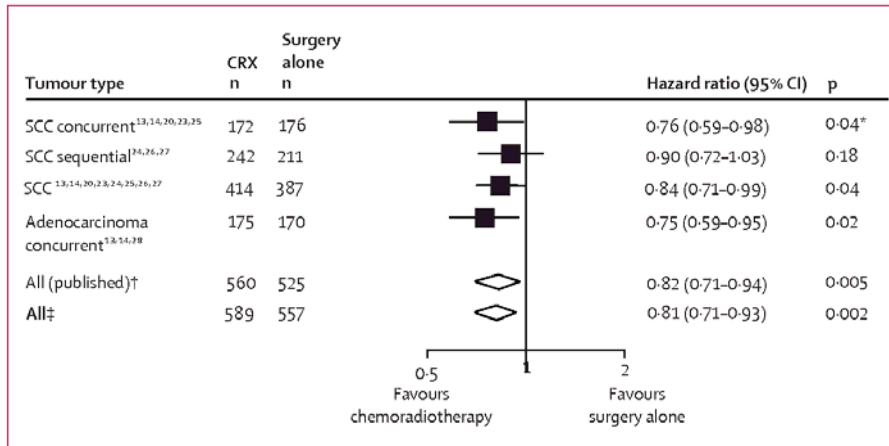
Test for overall effect:  $z=1.84$  ( $P=.07$ )

**Small, non-statistically improvement with NCRT**

*Greer et al, Surgery, 2005*



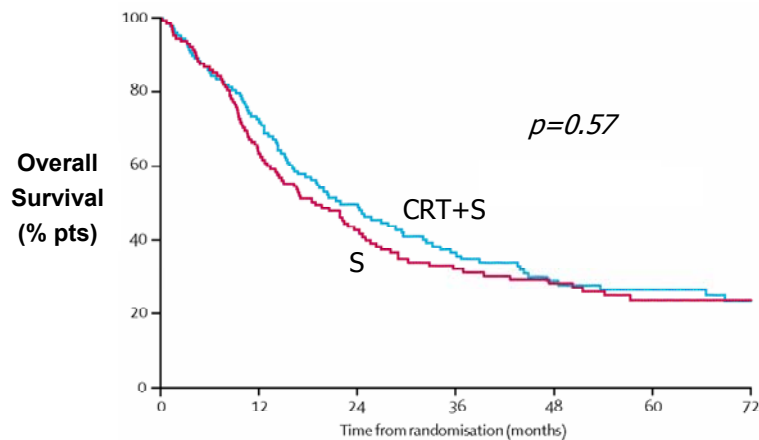
## Meta-analysis of NCRT vs Surgery



*Gebski et al, Lancet Oncol, 2007*



## CRT+Surgery vs Surgery

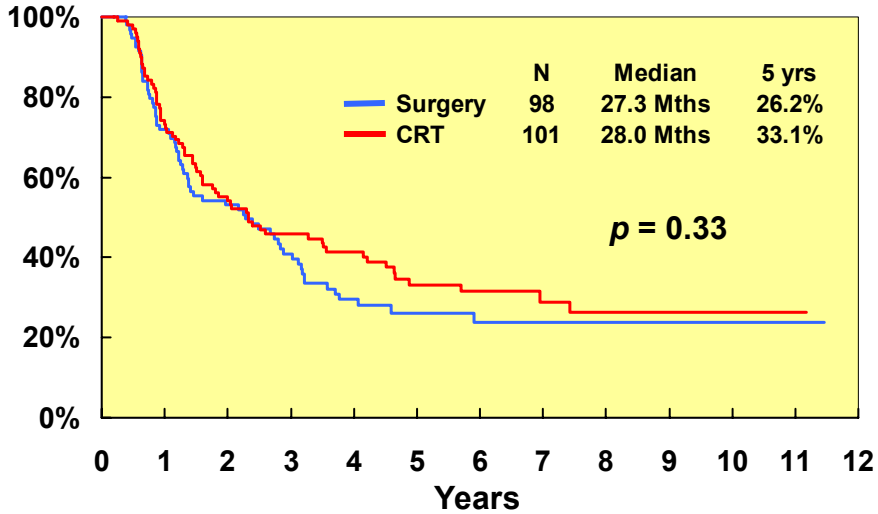


*Burmeister et al, Lancet Oncol, 2005*

3 cases were excluded after reviewing of records recently (i.e. n = 202 - 3 = 199)

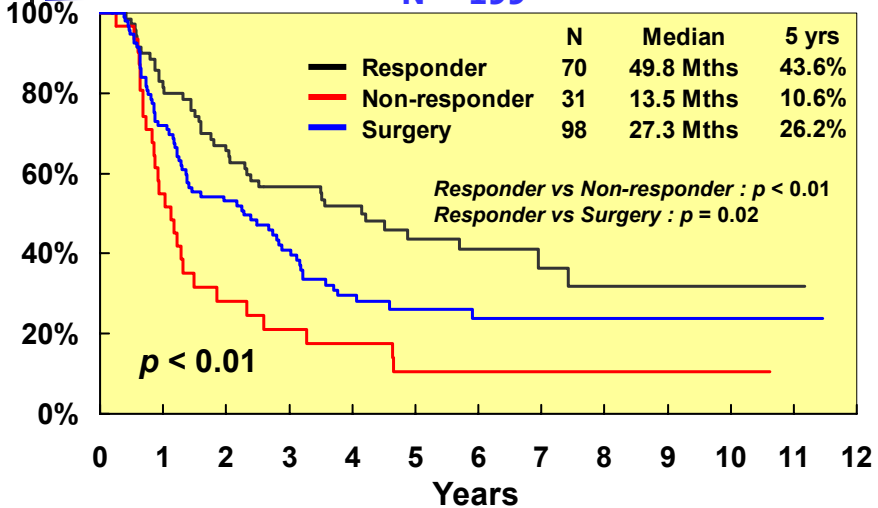
## CRT Trial – Overall Survival

N = 199



## CRT Trial – Overall Survival

N = 199



Responders: With Resection , Japanese Classification Grade II/III (i.e. <33% viable tumour cells)  
Without Resection, Clinical assessment of >50% reduction in primary & NOT M1



## Additional Treatment

“..... despite the widespread use of preoperative chemotherapy and radiotherapy, there remains no proof of principle that this strategy is effective in patients with esophageal cancer.”

*Enzinger et al, NEJM, 2003*



## Advanced Esophageal Cancer (SCC)

	n	2 yrs Survival	Median Survival	MR during treatment
German Trial				
CRT + OP	89	75%	>37.6 m	14.4%
CRT	88	74%	39.9 m	8.1%
French Trial				
CRT + OP	129	34%	17.7 m	9%
CRT	130	40%	19.3 m	1%

*Stahl et al, ASCO, 2003*

*Bonnetain et al, ASCO, 2003*



## Long-Term Toxicity After CRT

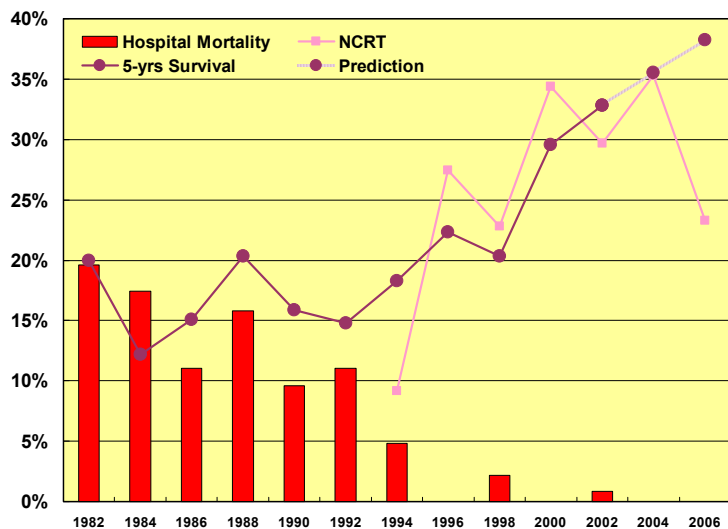
78 complete responders

	≥G3 toxicity	Median time
Pneumonitis	4%	5 mths
Pleural effusion	10%	15 mths
Pericarditis	10%	18 mths

*Ishikura et al, J Clin Oncol, 2005*



## Hospital mortality, NCRT and Survival





## Perspectives

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- Esophageal cancer can be prevented
- Early diagnosis by molecular techniques
- Effective drugs, agents and delivery systems
- Prediction of individual response
- Zero mortality of treatment
- Good quality of life
- Evidence of benefit by trials
- Ensure value for money