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Current management in ACS
Early invasive versus selective invasive

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Disclosures Dr. R.J. de Winter

Grant and / or Research Support

- OrbusNeich

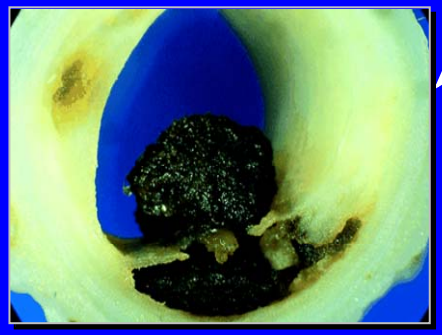
Hamm Lancet 358:1533,2001

Presentation

Ischemic Discomfort

Working Dx

Acute Coronary Syndrome



Davies MJ
Heart 83:361, 2000

ECG

No ST Elevation

NSTEMI

ST Elevation

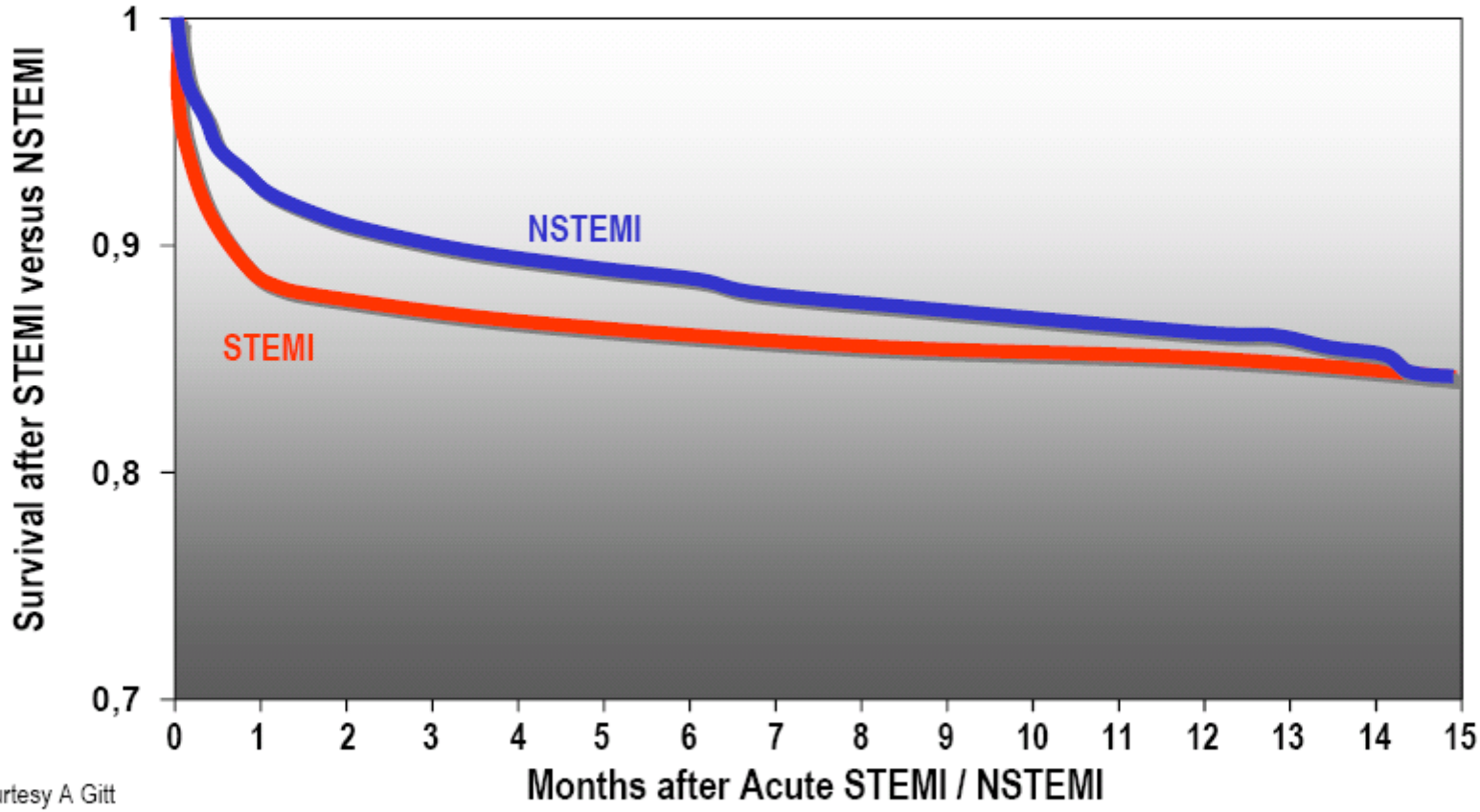
Biochem. Marker

Myocardial Infarction

Final Dx **Unstable Angina** **NQMI** **Qw MI**

Trends and Prognosis in NSTE-ACS

STEMI versus NSTEMI - Cumulative 1 Year Mortality



Courtesy A Gitt

ESC Guidelines for the Management of NSTE-ACS (5)

Treatment

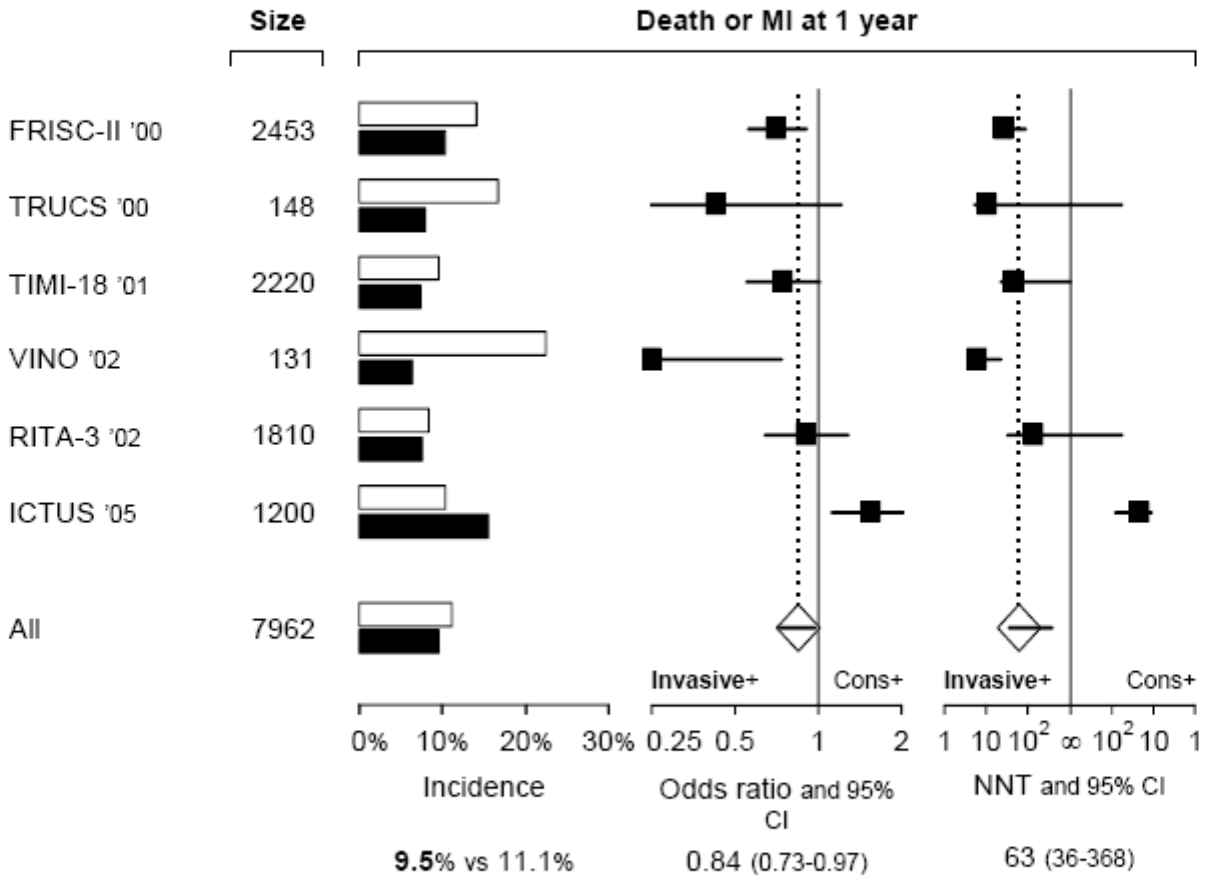
Coronary revascularisation

Invasive vs. Conservative Strategies

1. New data coming from long-term follow-up of RITA-3, FRISC-2 and Mehta meta-analysis show significant risk reduction for death and death & MI at long-term follow-up
2. Early hazard shown in ICTUS trial (excess of death & MI observed within 1st month after revascularisation in immediate invasive group)
3. Early hazard shown in Mehta meta-analysis

ICTUS Lancet 2007;369:827
RITA-3 Lancet 2005;366:914
FRISC 2 Lancet 2000;356:9-16
Mehta JAMA 2005:293:2908

Randomised trials comparing early invasive (dark bars) vs conservative strategy (open bars)



ESC Guidelines for the Management of NSTE-ACS (85)

Recommendations for invasive evaluation and revascularisation (1)

- Urgent coronary angiography is recommended in patients with refractory or recurrent angina associated with dynamic ST deviation, heart failure, life threatening arrhythmias or haemodynamic instability (I - C).

- Early (< 72 hours) coronary angiography followed by revascularisation (PCI or CABG) in patients with intermediate to high-risk features is recommended (I - A).

- Routine invasive evaluation of patients without intermediate to high risk features is not recommended (III-C), but non-invasive assessment of inducible ischaemia is advised (I - C).

ESC Guidelines for the Management of NSTE-ACS (86)

ACC / AHA guidelines on nSTE-ACS

3.3. Initial Conservative Versus Initial Invasive Strategies

RECOMMENDATIONS

CLASS I

1. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is indicated in UA/NSTEMI patients who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures). *(Level of Evidence: B)*
2. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is indicated in initially stabilized UA/NSTEMI patients (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events (see Table 11 and Sections 2.2.6 and 3.4.3). *(Level of Evidence: A)*

Management in nSTE-ACS

- ♥ Refractory angina
- ♥ Hemodynamic instability
- ♥ Severe ischemic arrhythmias
- ♥ Early post MI

} Immediate Or Urgent Angiography

- ♥ Atypical chest pain
- ♥ Diagnosis ACS unlikely
- ♥ Contra indications angiography

} No Angiography

Management in nSTE-ACS

- ♥ Refractory angina
- ♥ Hemodynamic instability
- ♥ Severe ischemic arrhythmias
- ♥ Early post MI

} Immediate Or Urgent Angiography

- ♥ **Stabilized on medical therapy**
- ♥ **Intermediate or high risk features**
- ♥ **Assess risk vs benefit**

} **IA IIB**

- ♥ Atypical chest pain
- ♥ Diagnosis ACS unlikely
- ♥ Contra indications angiography

} No Angiography

ACC / AHA guidelines on nSTE-ACS

3.3. Initial Conservative Versus Initial Invasive Strategies

RECOMMENDATIONS

CLASS IIb

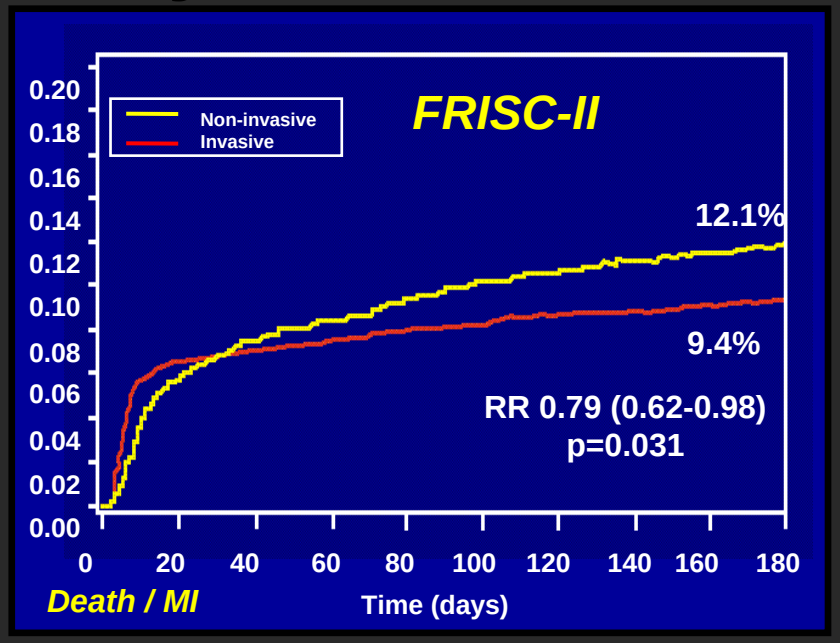
1. In initially stabilized patients, an initially conservative (i.e., a selectively invasive) strategy may be considered as a treatment strategy for UA/NSTEMI patients (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events (see Table 11 and Sections 2.2.6 and 3.4.3) including those who are troponin positive. *(Level of Evidence: B)* The decision to implement an initial conservative (vs. initial invasive) strategy in these patients may be made by considering physician and patient preference. *(Level of Evidence: C)*

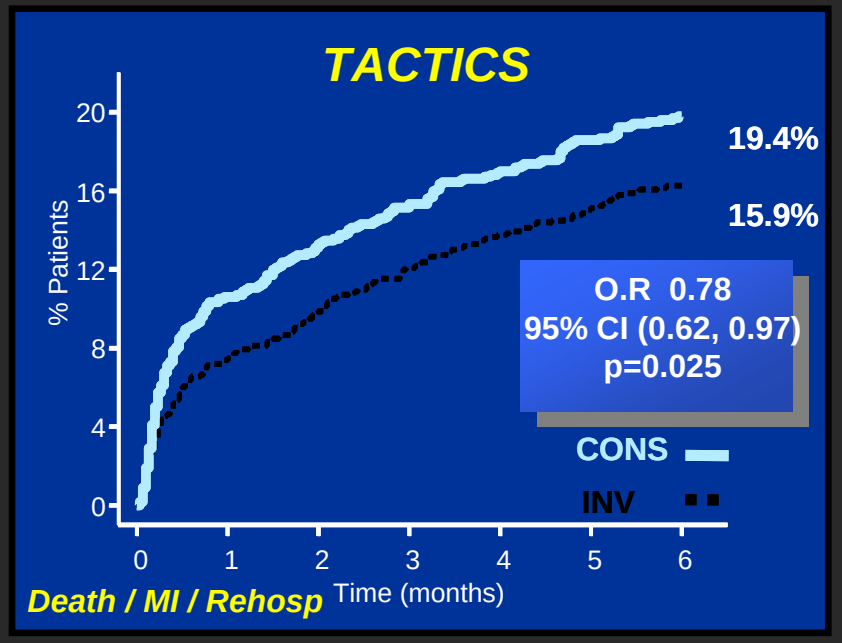
ACC / AHA guidelines on nSTE-ACS

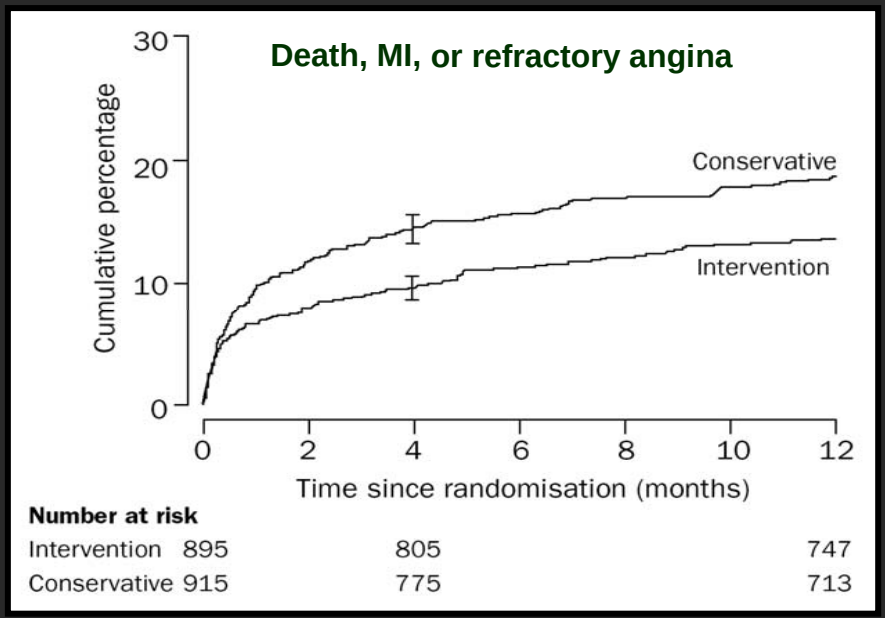
Thus, these guidelines recommend that in initially stabilized UA/NSTEMI patients, an initial conservative (selective invasive) strategy may be considered as a treatment option.

ACC / AHA guidelines

Early invasive strategy in nSTE-ACS







RITA-3

Routine *I* nvasive versus

Sele *C* tive invasive

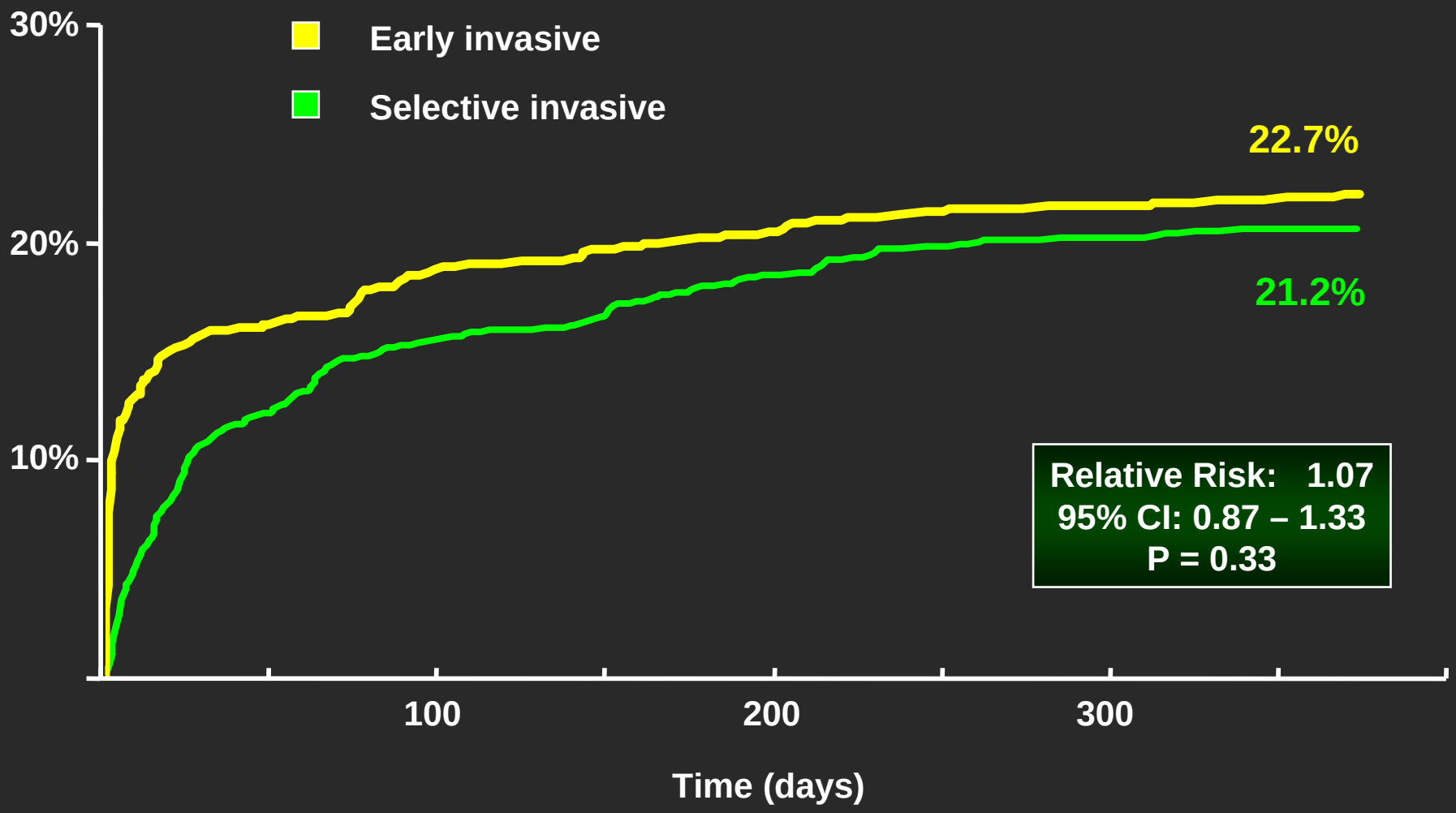
T reatment in

U nstable coronary

S yndromes

- 1200 patients enrolled, 2001-2003
- Era of stents, GP2b/3a, clopidogrel
- Prospectively 100% troponin positive pts
- High volume centers
- Intensive medical therapy

Death, MI, Rehospitalization for ACS



De winter RJ et al. NEJM 2005;353:1095-104

Events at one year

	Early invasive (%)	Selective invasive (%)	Relative Risk	P-value
Death	2.5	2.5	0.99	0.97
MI	15.0	10.0	1.50	0.005
Rehosp. angina	7.4	10.9	0.68	0.037
Primary endpoint	22.7	21.2	1.07	0.33
Procedure related	11.3	5.4	2.09	0.001
Spontaneous	3.7	4.6	0.80	0.45

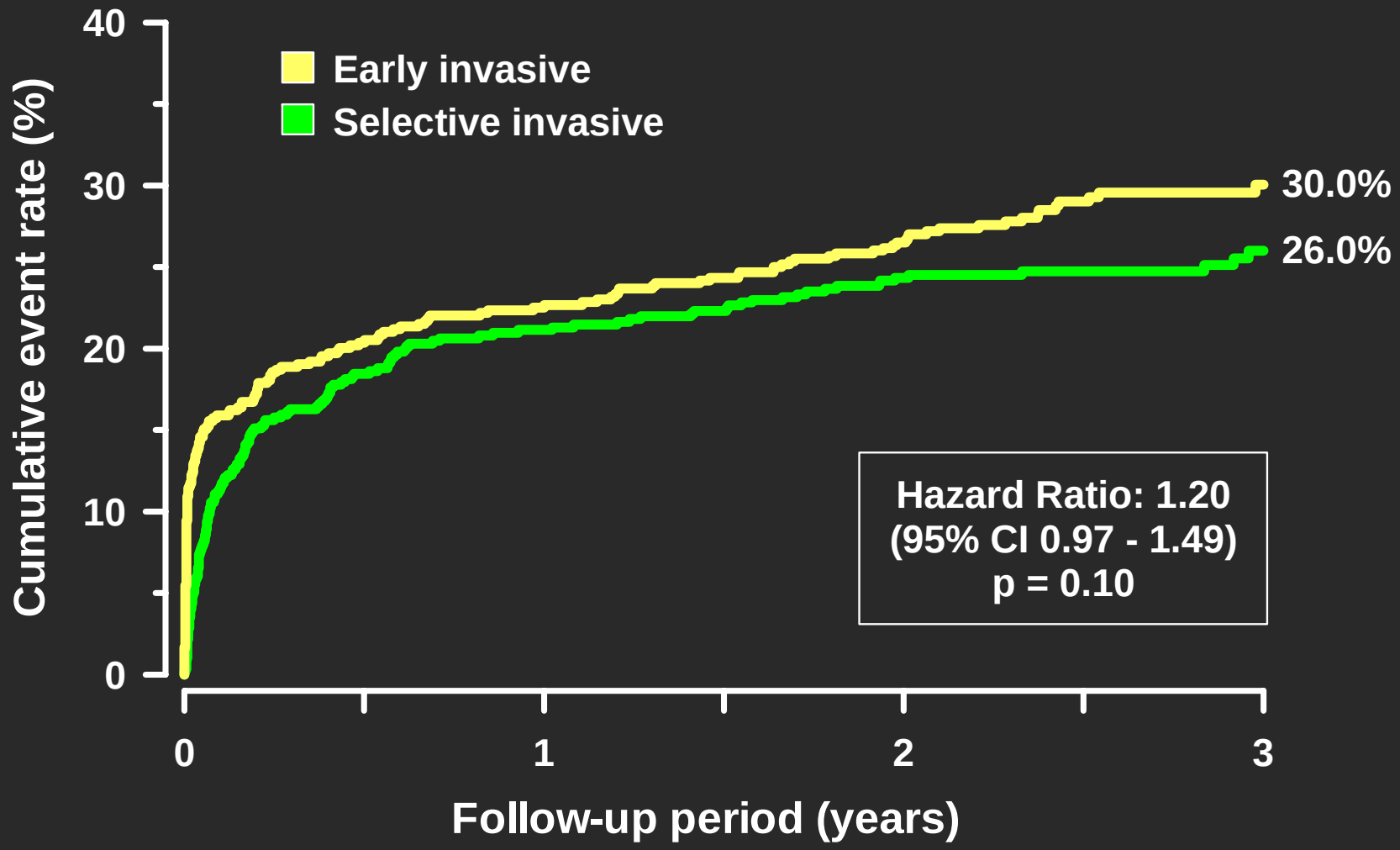
Three / four Year Follow up

- Prospectively planned long term follow up
- Telephone interview, outpatient visits
- Events documented by hospital records
- Death and cause of death confirmed with National Central Bureau of Death Statistics
- Clinical Endpoint Committee

Medication during follow up

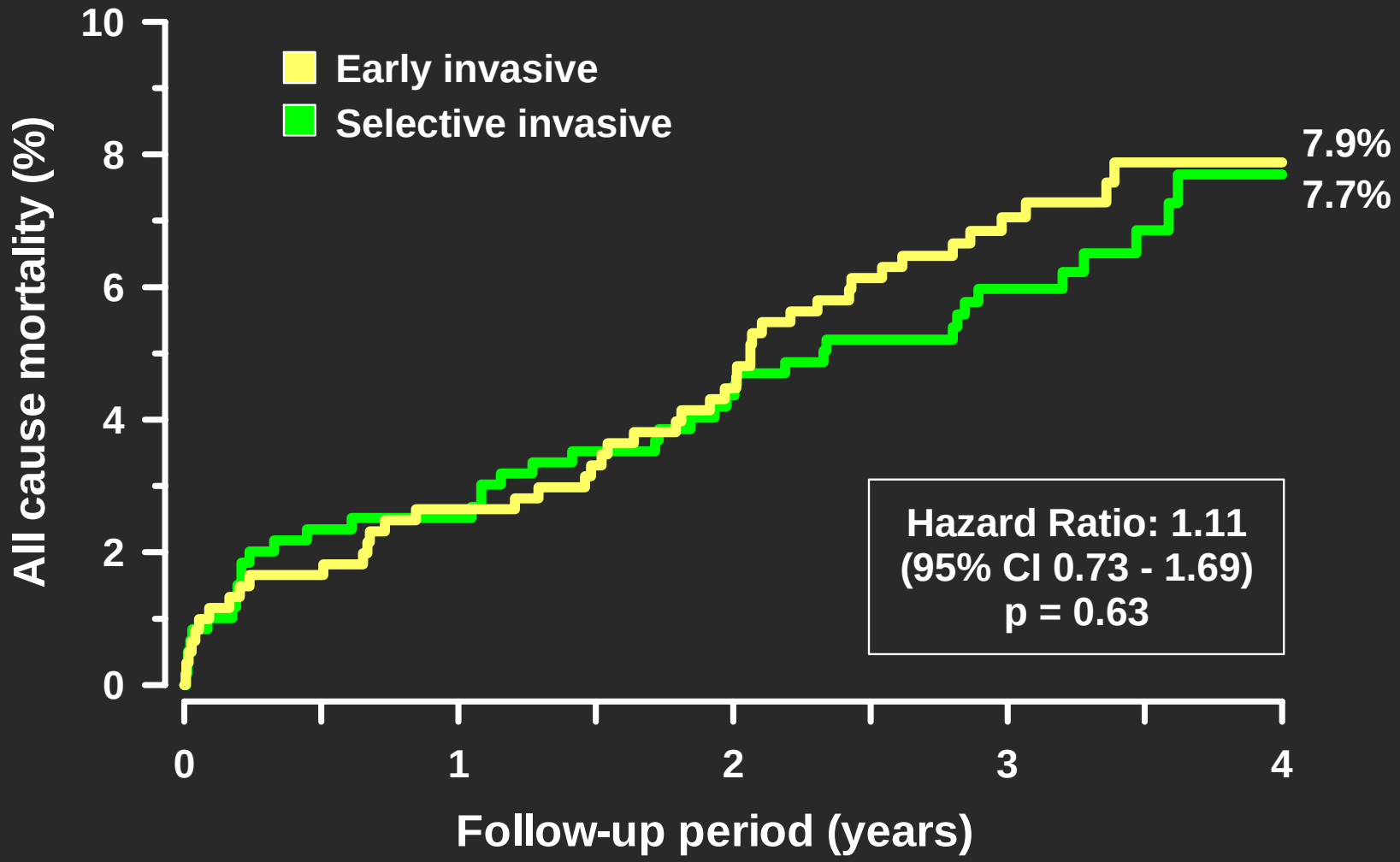
	Discharge	1 y	Long term FU
Aspirin %	93	93	91
ACE-inh. %	31	34	29
Beta-blockers %	88	79	72
Statins %	92	94	93

Death, MI, rehospitalization for ACS
Three year follow up



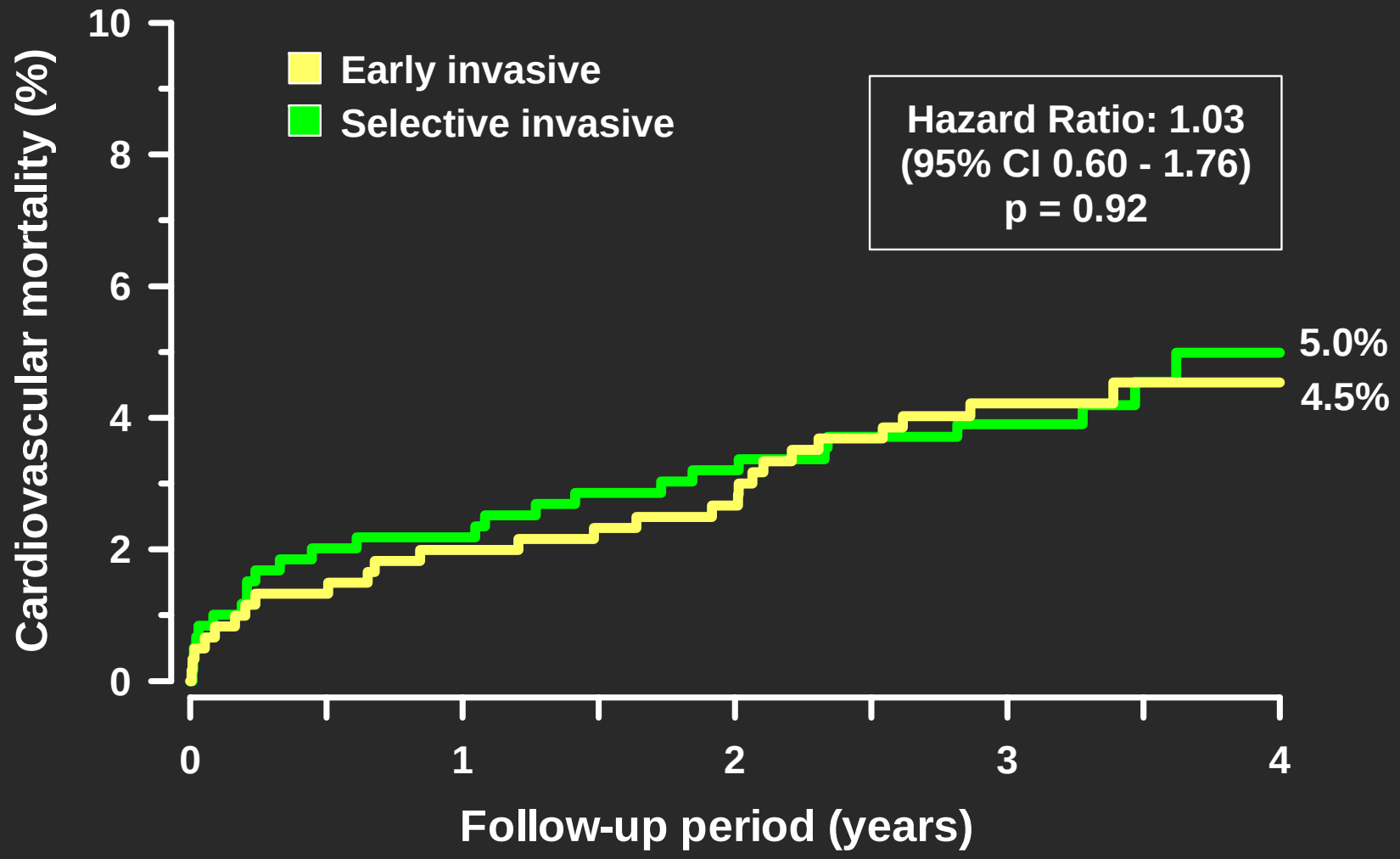
Hirsch A et al, Lancet 2007;367:827-35

All Cause Mortality



Hirsch A et al, Lancet 2007;367:827-35

Cardiovascular Mortality

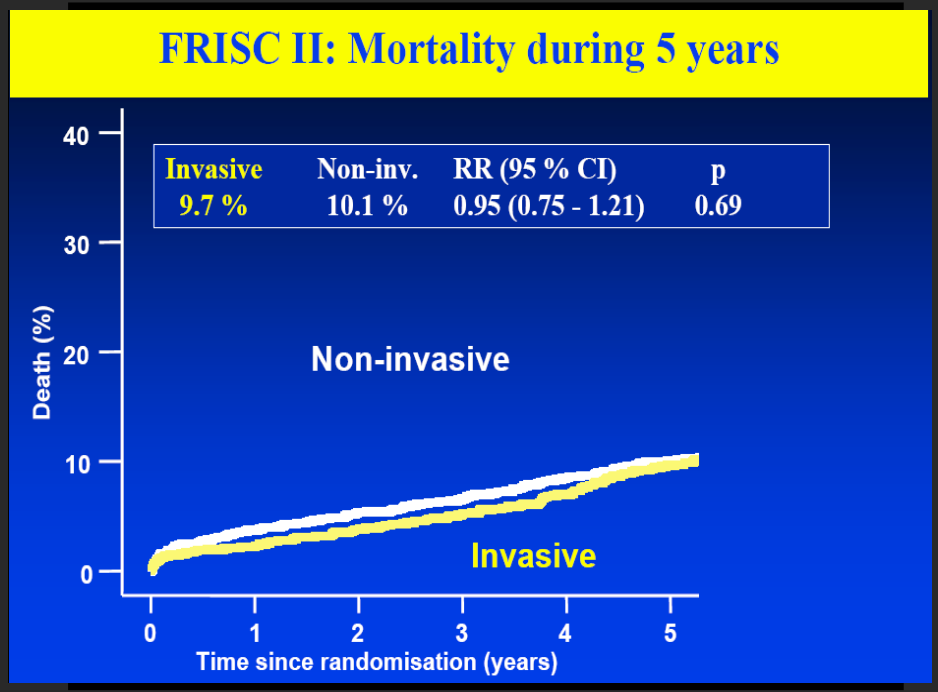


Hirsch A et al, Lancet 2007;367:827-35

Early invasive strategy in nSTE-ACS

Mortality reduction

FRISC-II, five year FU



Lagerquist et al. Lancet 2006;368:998-1004

RITA-3, five year FU

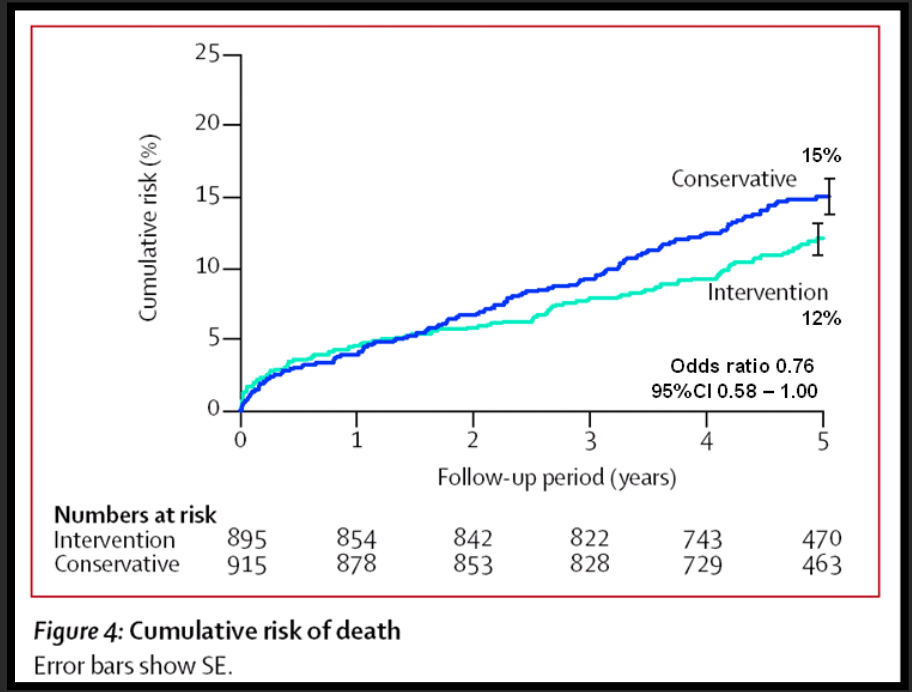
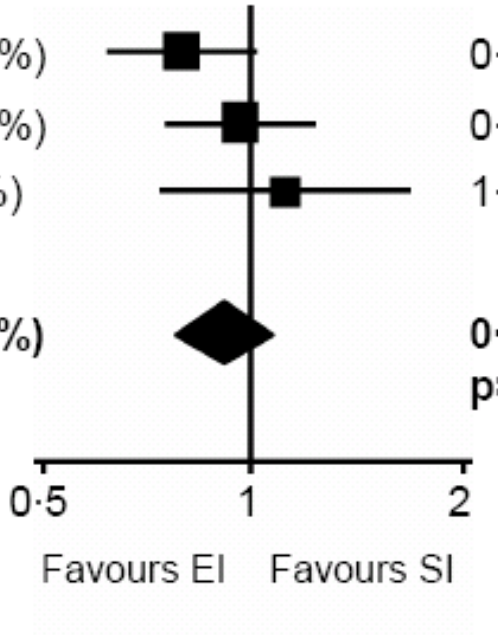


Figure 4: Cumulative risk of death
Error bars show SE.

Fox et al. Lancet 2005;366:914-20

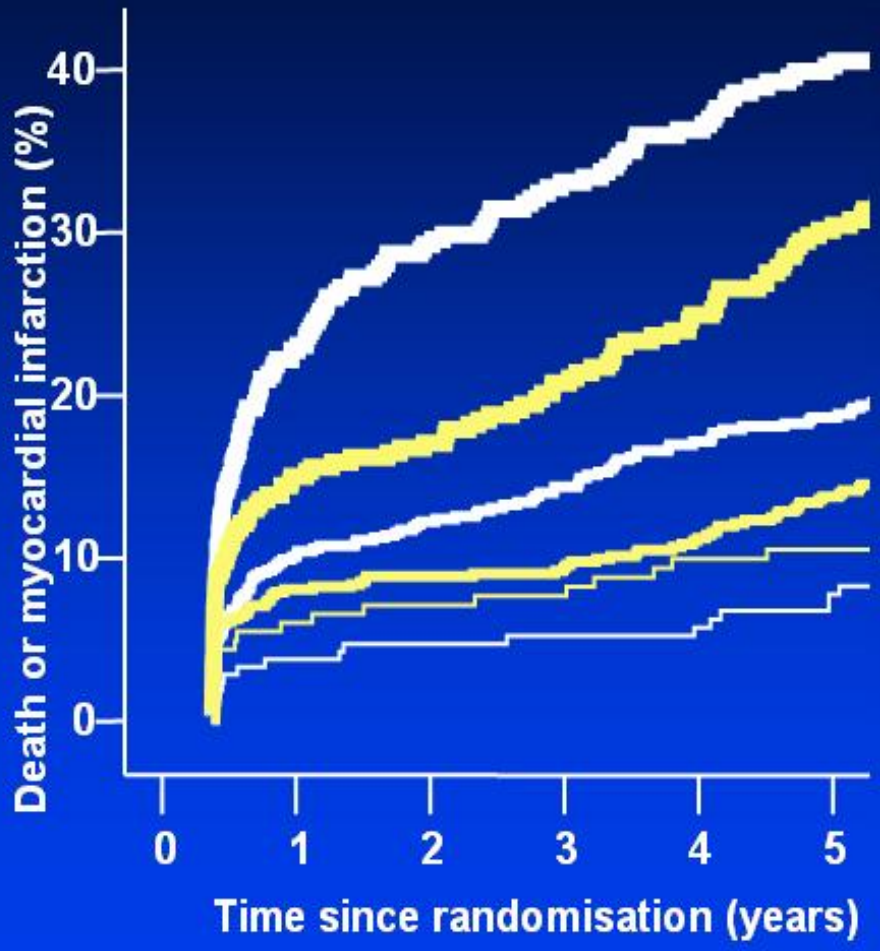
Meta-analysis of RCT with long term FU

Study	Early Invasive deaths/N (%)	Selective Invasive deaths/N (%)	Relative Risk (95% CI)	RR (fixed) (95% CI)
RITA 3[4]	102/895 (11·4%)	132/915 (14·4%)		0·79 (0·62–1·01)
FRISC-II[5]	117/1222 (9·6%)	124/1235 (10·0%)		0·95 (0·75–1·21)
ICTUS	45/604 (7·4%)	40/596 (6·7%)		1·11 (0·74–1·67)
Total	**264/2721 (9·7%)**	**296/2746 (10·8%)**		**0·90 (0·77–1·06) p=0·20**



Early invasive strategy in nSTE-ACS

Death or MI during 5 years and Risk



High risk (Frisc score 4-7) 30%

Invasive	Non-inv.	RR (95 % CI)
32.7 %	41.6 %	0.79 (0.64 - 0.97)

Medium risk (Frisc score 2-3) 53%

Invasive	Non-inv.	RR (95 % CI)
14.6 %	20.4 %	0.72 (0.55 - 1.13)

Low risk (Frisc score 0-1) 17%

Invasive	Non-inv.	RR (95 % CI)
10.3 %	8.2 %	1.26 (0.66 – 2.40)

FRISC score (sum of):

- Age > 65 years
- Male gender
- Diabetes mellitus
- Previous MI
- ST-depression
- Elevated troponin
- Elevated Il-6 / CRP

Lagerqvist B et al. Heart 2004

Lagerquist et al. Lancet 2006;368:998-1004

Management in nSTE-ACS

- ♥ No clear mortality benefit
  - √ FRISC-II: benefit lost at 5 yrs
  - √ RITA-3: no benefit 2yrs, benefit 5yrs NS
  - √ ICTUS: no benefit at 4 yrs
- ♥ Reduction in MI (high risk patients)
  - √ Against background of optimized medical therapy, late benefit lost (ICTUS)
- ♥ Reduction in angina, rehospitalization

Women ? Elderly ?

Recommendations for Special Populations

Elderly

- Elderly patients (>75 years) often have atypical symptoms. Active screening for NSTE-ACS should be initiated at lower levels of suspicion than among younger (<75 years) patients (I-C).

- Treatment decisions in the elderly should be tailored according to estimated life expectancy, patient wishes and co-morbidities to minimize risk and improve morbidity and mortality outcomes in this frail but high-risk population. (I – C)

- Elderly patients should be considered for routine early invasive strategy, after careful evaluation of their inherent raised risk of procedure-related complications, especially during CABG (I – B).

Management in nSTE-ACS

ACC / AHA

Elderly

RECOMMENDATIONS

CLASS I

1. Older patients with UA/NSTEMI should be evaluated for appropriate acute and long-term therapeutic interventions in a similar manner as younger patients with UA/NSTEMI. *(Level of Evidence: A)*
2. Decisions on management of older patients with UA/NSTEMI should not be based solely on chronologic age but should be patient-centered, with consideration given to general health, functional and cognitive status, comorbidities, life expectancy, and patient preferences and goals. *(Level of Evidence: B)*

4. Older UA/NSTEMI patients face increased early procedural risks with revascularization relative to younger patients, yet the overall benefits from invasive strategies are equal to or perhaps greater in older adults and are recommended. *(Level of Evidence: B)*

CLASS I

1. Women with UA/NSTEMI should be managed with the same pharmacological therapy as men both in the hospital and for secondary prevention, with attention to antiplatelet and anticoagulant doses based on weight and renal function; doses of renally cleared medications should be based on estimated creatinine clearance. *(Level of Evidence: B)*
2. Recommended indications for noninvasive testing in women with UA/NSTEMI are similar to those for men. *(Level of Evidence: B)*
3. For women with high-risk features, recommendations for invasive strategy are similar to those of men. See Section 3.3. *(Level of Evidence: B)*
4. In women with low-risk features, a conservative strategy is recommended. *(Level of Evidence: B)*

Women

- **Women should be evaluated and treated in the same way as men, with special attention to co-morbidities (I-B).**

Gender differences in ACS

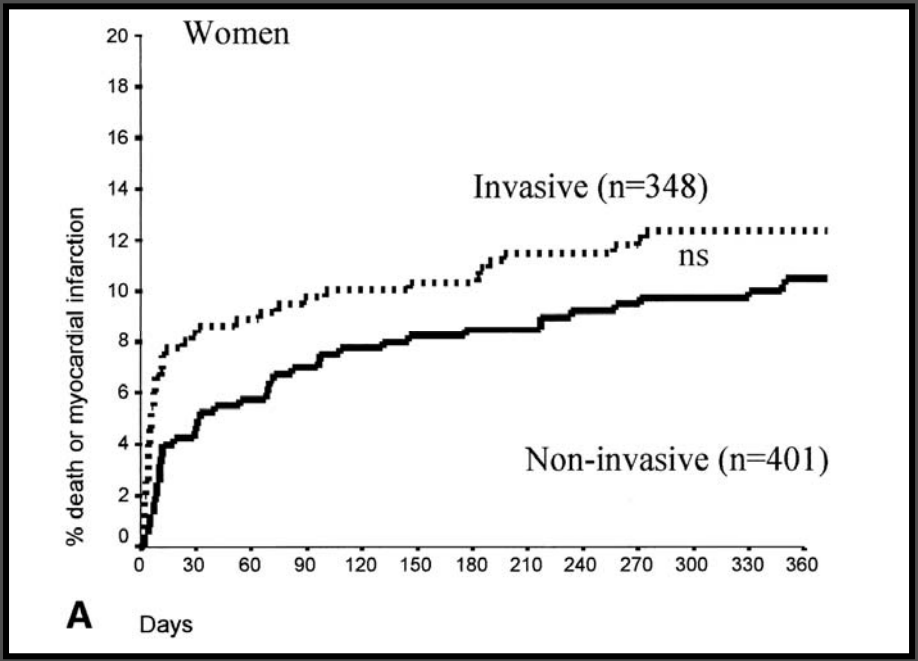
Women differ from men in risk profile

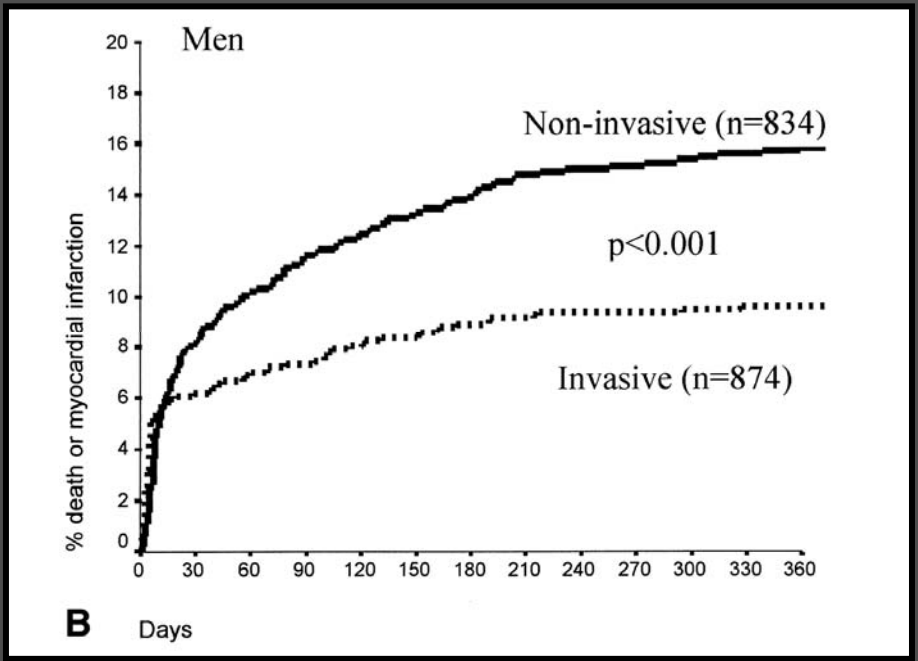
- ♥ Older
- ♥ More co-morbidities: diabetes, hypertension
- ♥ More often have normal coronary arteries
- ♥ Less likely to be (former) smokers
- ♥ More often have normal ejection fraction
- ♥ Less likely to undergo invasive therapy
- ♥ More often have bleeding complications

Early invasive strategy in nSTE-ACS

Do Women benefit from invasive treatment?

FRISC-II



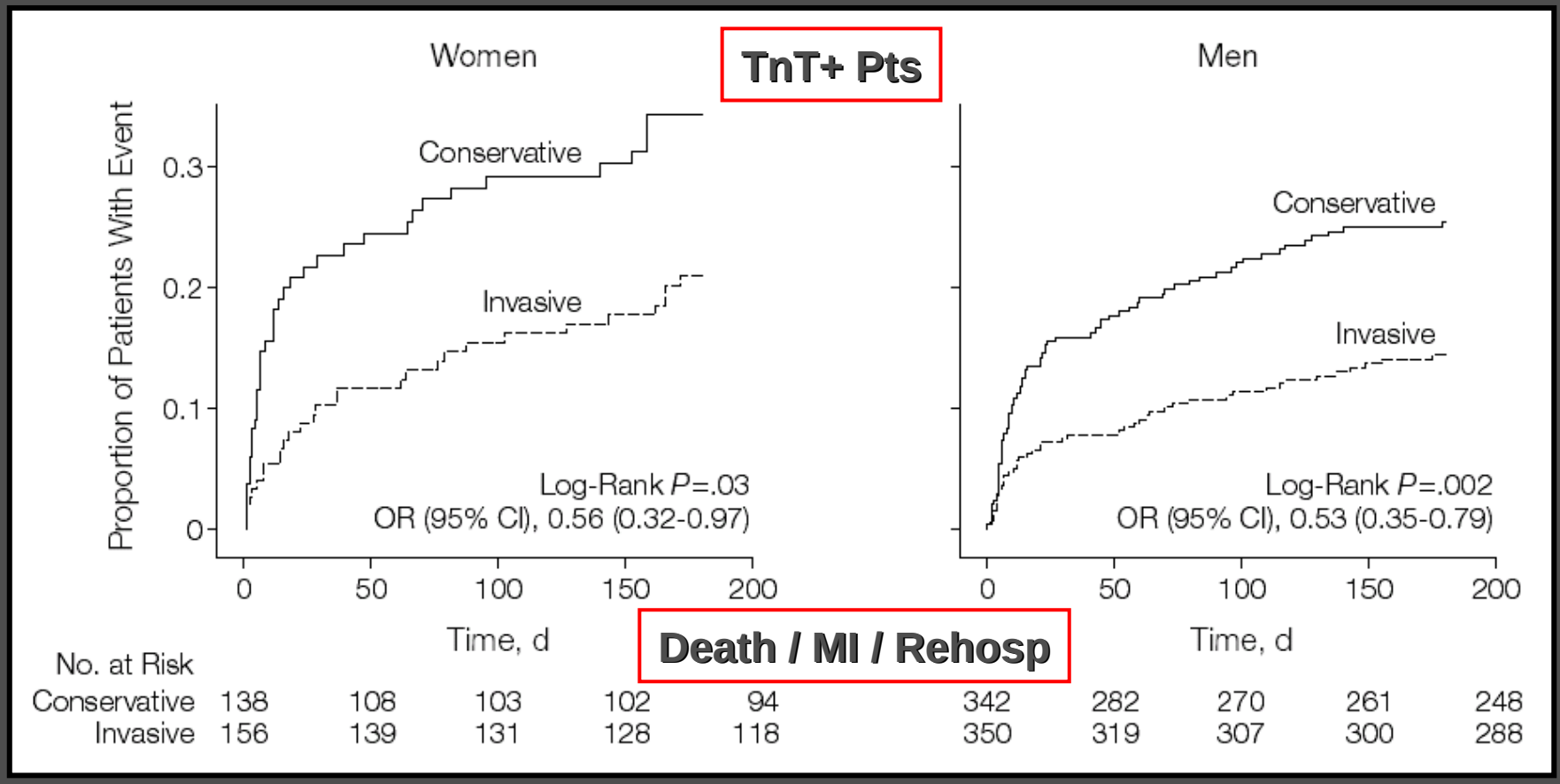


Death / MI

Early invasive strategy in nSTE-ACS

Do Women benefit from invasive treatment?

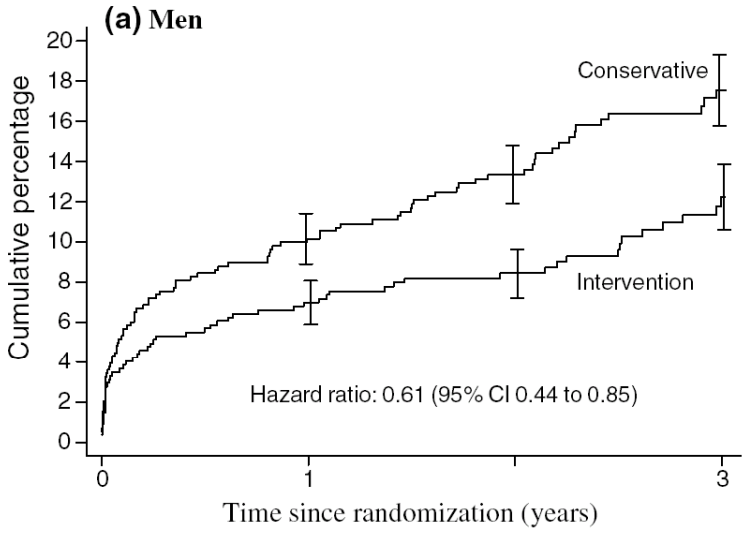
TACTICS-TIMI18

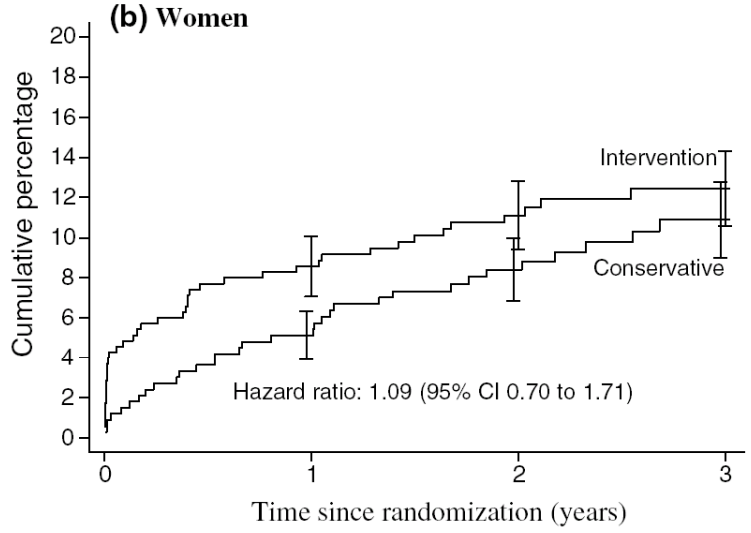


Early invasive strategy in nSTE-ACS

Do Women benefit from invasive treatment?

RITA-3





Intervention	545	491	354	189	350	316	228	125
Conservative	583	507	356	194	332	305	230	119

Death / MI

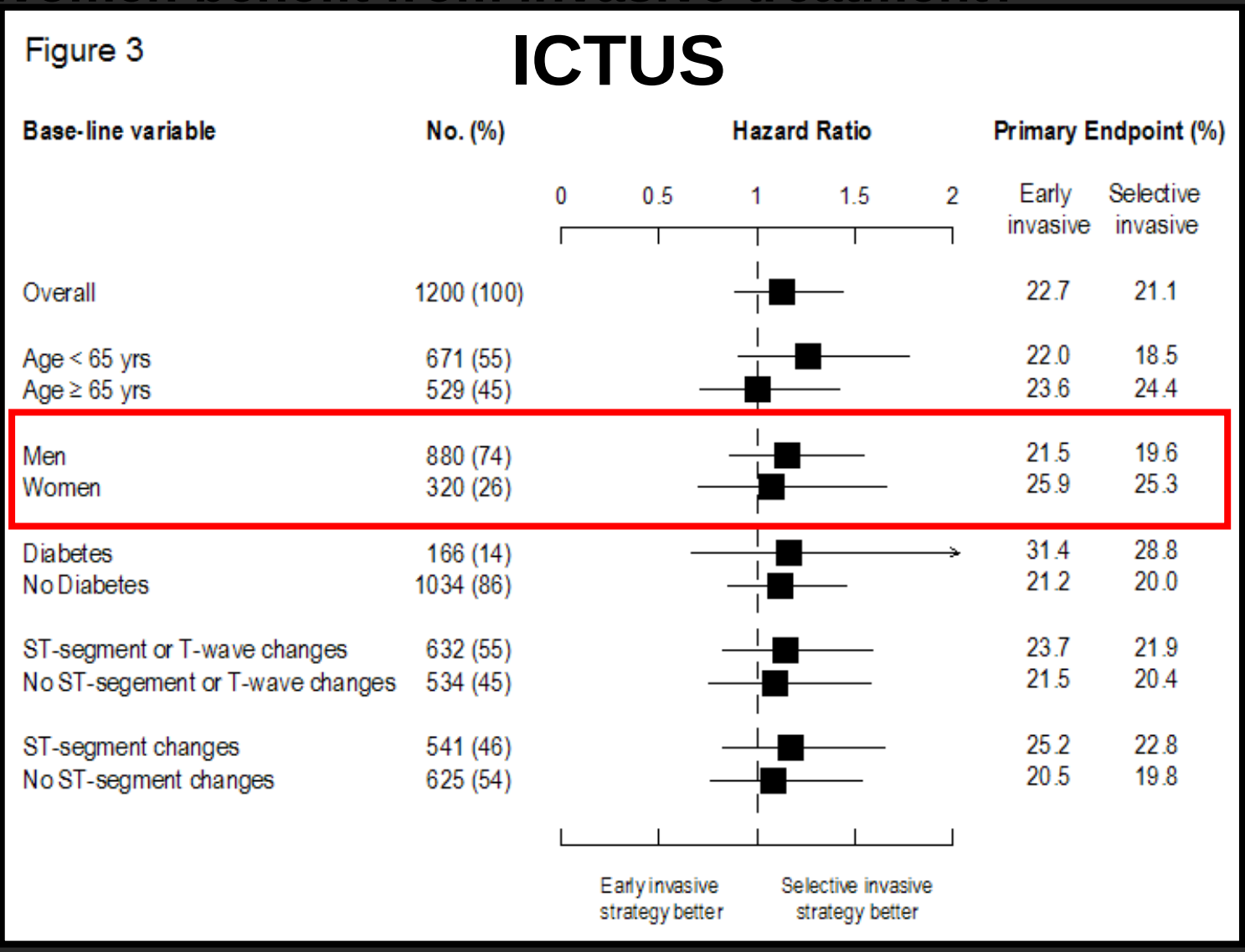
Fig. 1 Cumulative risk of death or myocardial infarction by gender.

Early invasive strategy in nSTE-ACS

Do Women benefit from invasive treatment?

Figure 3

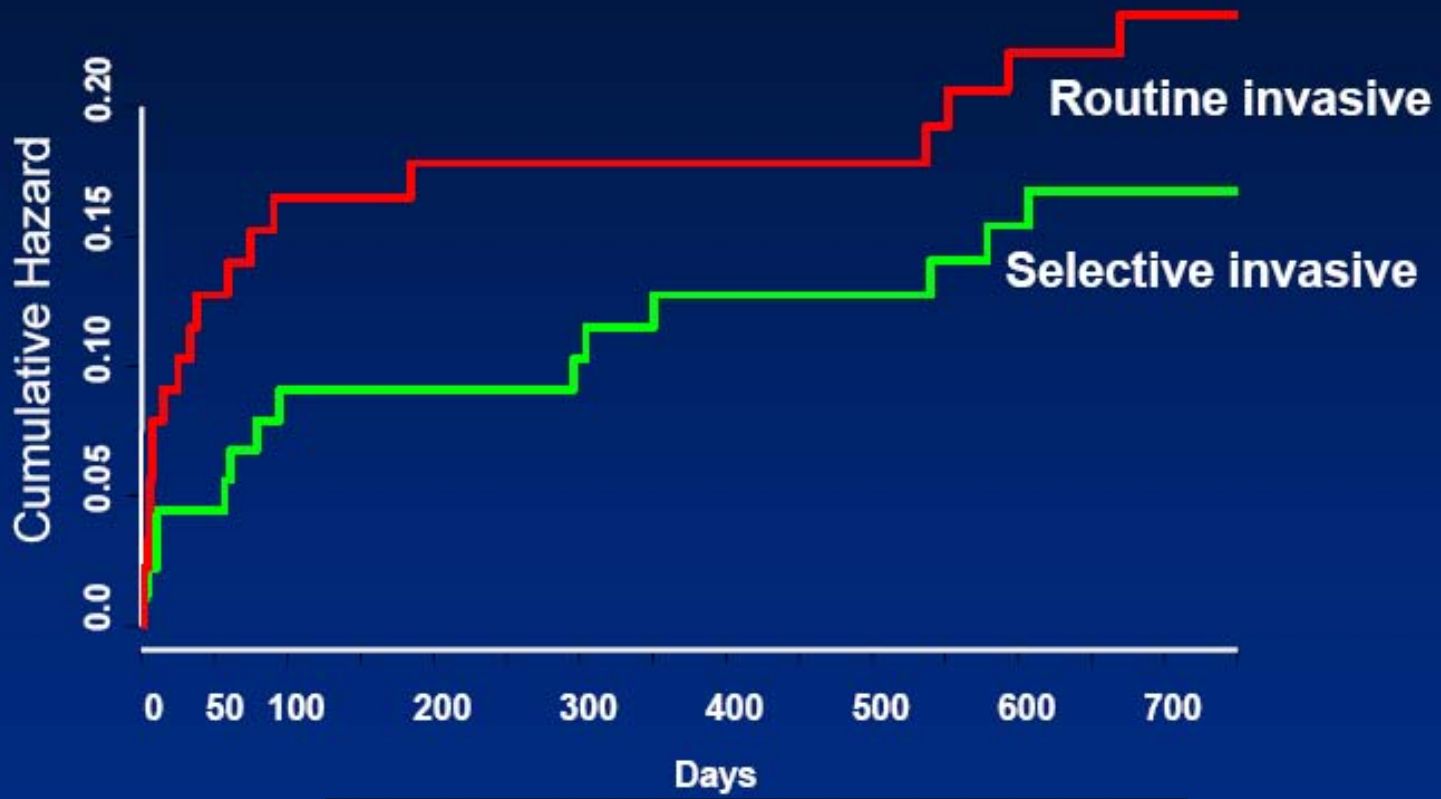
ICTUS



De winter RJ et al. NEJM 2005;353:1095-104

Death/MI/Stroke

MICHELANGELO: OASIS 5
Women's Substudy



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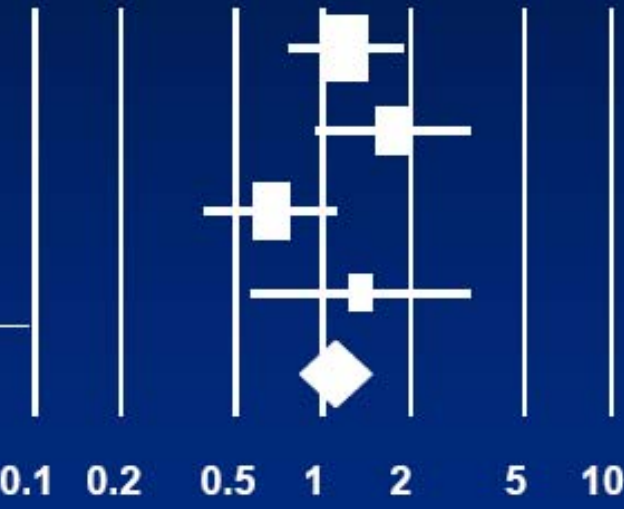
Meta analysis - Death/MI

Study name	Death or MI / Total Routine Invasive	Selective Invasive	Odds ratio	Lower limit	Upper limit	p-Value
FRISC II	43 / 348	42 / 401	1.21	0.77	1.89	0.42
RITA 3	30 / 350	17 / 332	1.74	0.94	3.21	0.08
TACTICS	26 / 395	35 / 362	0.66	0.39	1.12	0.12
OASIS 5	13 / 92	10 / 92	1.35	0.56	3.25	0.50
	112 /1185	104/1187	1.11	0.83	1.47	0.48

Statistics for each study

Odds ratio and 95% CI



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Early invasive strategy in nSTE-ACS

Do Women benefit from invasive treatment?

- ♥ Differences in clinical profiles
- ♥ Non-randomized data show no clear benefit
- ♥ Randomized data conflicting results
- ♥ Higher incidence of complications
- ♥ The question remains unanswered

Management in nSTE-ACS

- ♥ Refractory angina
- ♥ Hemodynamic instability
- ♥ Severe ischemic arrhythmias
- ♥ Early post MI

} Immediate Or Urgent Angiography

- ♥ Atypical chest pain
- ♥ Diagnosis ACS unlikely
- ♥ Contra indications angiography

} No Angiography

Management in nSTE-ACS

- ♥ Refractory angina
- ♥ Hemodynamic instability
- ♥ Severe ischemic arrhythmias
- ♥ Early post MI

} Immediate Or Urgent Angiography

- ♥ **Stabilized on medical therapy**
- ♥ **Intermediate or high risk features**
- ♥ **Assess risk vs benefit**

} **IA IIB**

- ♥ Atypical chest pain
- ♥ Diagnosis ACS unlikely
- ♥ Contra indications angiography

} No Angiography

ACC / AHA guidelines on nSTE-ACS 2007

Thus, these guidelines recommend that in initially stabilized UA/NSTEMI patients, an initial conservative (selective invasive) strategy may be considered as a treatment option.

Elderly !

Women ?