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# **Similar outcome with an invasive strategy in men and women with Non-ST-Elevation Acute Coronary Syndromes**

From the Swedish Web-System for Enhancement and Development  
of Evidence-Based Care in Heart Disease Evaluated According to  
Recommended Therapies (SWEDEHEART)

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## Abstract

**Aims.** To assess gender differences in outcome with an early invasive or early non-invasive strategy in patients with Non-ST-elevation Acute Coronary Syndromes (NSTE ACS).

**Methods and Results.** We included 46 455 patients (14 819 women (32%) and 31 636 men (68%)) from the SWEDEHEART register, with NSTE ACS, between 2000 and 2006, and followed them for 1 year.

In the non-invasive strategy arm relative risk (RR) of death was (women vs. men) 1.02 (95% CI, 0.94-1.11) and in the invasive strategy arm 1.12 (95% CI, 0.96-1.29). After adjustment for baseline differences between the genders, with propensity score and discharge medication, there was a similar trend towards better outcome among women in both the early non-invasive cohort (RR 0.90 (95% CI, 0.82-0.99)) and in the early invasive cohort (RR 0.90 (95% CI, 0.76-1.06)), although it did not reach statistical significance in the early invasive cohort. Results were similar with the combined end-point death/MI.

An early invasive treatment was associated with a marked, and similar, mortality reduction in women (HR 0.46, 95% CI (0.38-0.55)) and men (HR 0.45, 95% CI (0.40-0.52)), without interaction with gender.

**Conclusion** In this large cohort of patients with NSTE ACS, reflecting real life management, women and men had similar and better outcome associated with an invasive strategy.

Key words: NSTE ACS, gender, invasive strategy

## Introduction

An early invasive treatment strategy has become the treatment of choice in patients with Non ST-elevation Acute Coronary Syndromes (NSTE ACS). However, gender differences in benefit from an early invasive strategy have been debated and data are conflicting. Three randomized trials, comparing early routine invasive with a selective invasive strategy, have pre-specified analyses according to gender. While the FRISC II trial (Fragmin and Revascularisation during Instability in Coronary artery disease) [1] and RITA 3 trial (Third Randomized Intervention Trial of Unstable Angina) [2] reported a benefit with early intervention for death or myocardial infarction in men but not in women, the TACTICS-TIMI 18 trial (Treat angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy- Thrombolysis In Myocardial Infarction 18) [3] indicated a beneficial effect of early intervention for death or myocardial infarction in both men and women. Finally, the OASIS 5 (Organization to Assess Strategies in Acute Ischemic Syndromes Investigators) women catheterization substudy, [4] showed no difference in the primary outcome between women allocated to a routine invasive compared to a selective invasive strategy, but suggested higher mortality associated with a routine invasive strategy. The aim of this study was to assess gender differences in outcome with an invasive strategy, in a large cohort of unselected patients with NSTE ACS.

## Method

The Swedish Web-System for Enhancement and Development of Evidence-Based Care in heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) (former RIKS-HIA) registers all patients admitted to Swedish coronary care units (CCU). Information is collected prospectively about individual patients' medical history, treatment before admission, management during hospital stay, treatment at discharge and diagnosis is collected. [5] Source data verification is performed in randomly selected patients from about 20 different hospitals annually.

Mortality data were obtained from the National Cause of Death Register and data regarding concomitant diseases, from the National Patient Register.

Reinfarction was defined as rehospitalisation with a discharge diagnosis of myocardial infarction and data were obtained from the SWDEHEART register.

### Study population

We included consecutive patients with elevated biochemical markers (defined as Troponin T (TnT)  $>0.03 \mu\text{g/l}$  or Creatinine Kinase MB  $\geq 5 \mu\text{g/l}$  or Troponin I (TnI) above decision limit for AMI for the method used.) and a discharge diagnosis of acute myocardial infarction (AMI), unstable angina pectoris (UAP) or angina pectoris (AP), admitted between 2000 and 2006. Patients with ST-elevation or left bundle branch block (LBBB) on admission ECG were excluded, as were patients treated with thrombolysis or primary PCI. Because of an increased risk of co-morbidity, potentially interfering with decision to treat invasively or not, patients above the age of 80 were excluded. All patients earlier diagnosed with dementia were also excluded. Only the first registry recorded hospitalization, in agreement with inclusion and exclusion criteria, was included. Analyses were performed on patients that were discharged alive and alive 14 days after admission This was done to avoid bias caused by including

patients in the early non-invasive arm that were so severely ill (including early deaths) that it precluded them from being referred for coronary angiography. However sensitivity analyses were made for different time intervals, including patients that died during the first 14 days after admission.

Patients referred for coronary angiography during 14 days after admission constituted the invasive arm.

Standardized criteria for the diagnoses in accordance with the ESC/ACC/AHA consensus document were used by all participating centers, and were coded according to the International Classification of Diseases, at treating physicians' discretion.[6]

We applied two risk scores to investigate gender differences in outcome according to treatment strategy and risk profile. A slightly modified TIMI-score [7] was calculated TIMI-score. Age >65 years, ST-depression  $\geq 1$  mm, Aspirin treatment on admission, known coronary artery disease (defined as history of AMI or revascularisation), elevated markers (defined as Troponin T  $\geq 0.05$  or CKMB  $\geq 5$ ) and  $\geq 3$  of four risk factors (diabetes, hypertension, smoking and treatment for hyperlipidemia) each gave 1 point. Information on severe angina could not be obtained. Accordingly, patients could have a TIMI score between 0 and 6. We also calculated a FRISC-score Age >65 years, a history of diabetes mellitus, a history of myocardial infarction, ST-segment depression on admission, elevated myocardial damage markers and elevated CRP each gave one point.[8]

### Ethical considerations

All patients for whom data were entered into the SWEDEHEART register were informed of their participation and their right to deny or have data removed later, in accordance to Swedish legislation. Data used for research purposes have had all personal identifiers

removed. The study complies with the Declaration of Helsinki and was approved by the ethics committee.

### Statistical analysis

Group differences based on continuous variables were assessed using the t-test and differences based on categorical variables were assessed using the  $\chi^2$ -test. Our primary outcome was one-year mortality and death/new MI was a secondary outcome. The cumulative risk of death in women and men respectively was calculated using a Cox regression analysis. Separate analyses were made for patients managed with an invasive and non-invasive strategy in the first part of our study. In the second part separate analyses were made for women and men comparing an invasive and a non-invasive strategy.

A propensity score method was used to compensate for the non-randomized study design.[9, 10] A comparison between men and women is not possible to perform in a randomized fashion and baseline differences between the compared study groups were inevitable. The propensity score method produces a summary score of the background characteristics for all patients and was used to balance for baseline differences. The score is usually calculated, in a logistic regression model (given baseline information available), to estimate the probability of being allocated to a certain treatment strategy that is studied, as in the second part of our analysis. When comparing men and women, as in the first part of our study, the score is the estimated probability of being female, given the baseline characteristics that were available. The propensity score model included age, smoking status, previous myocardial infarction (MI), PCI or CABG surgery, history of hypertension, diabetes, congestive heart failure, renal failure, stroke, chronic obstructive pulmonary disease or malignant disease, medical treatment on admission (including ACE inhibitors/Angiotensin receptor blockers, aspirin, clopidogrel,

$\beta$ -blockers, lipid lowering drugs, diuretics, digitalis, long-acting nitroglycerin and calcium antagonists), ST-segment depression, Killip class and year of admission.

To compare risk of mortality and of the combined end-point mortality or myocardial infarction, Cox regression survival analyses were performed including propensity score as a continuous variable and medical treatment at discharge (ACE inhibitors/Angiotensin receptor blockers, aspirin, clopidogrel,  $\beta$ -blockers, statins, diuretics, digitalis, long-acting nitroglycerin and calcium antagonists).

In a similar way difference in outcomes with an early invasive compared to a non-invasive strategy was assessed, with adjustment for propensity for an invasive strategy, and discharge medication.

Results were presented as relative risk (RR) and 95% confidence intervals. Analyses were performed with the statistical software SPSS (version 16.0) and R (version 2.9.0).[11]

## Results

We included 46 455 patients, 14 819 women (32%) and 31 636 men (68%). The proportion treated invasively was 56% for women and 63% for men.

There were significant differences in baseline characteristics between men and women in both treatment strategy arms (Table 1), but they were well balanced after adjustment with a propensity score (data not shown).

Within treatment strategy, we found no significant difference in one-year mortality between women and men. Before adjustment, in the invasive arm, the relative risk (RR) of death (women vs. men) was 1.12 (95% CI, 0.96-1.29) and in the early non-invasive strategy arm 1.02 (95% CI, 0.94-1.11). (Figure 1a and figure 1c)

In both the invasive and non-invasive arms, after adjustment for propensity score and discharge medications, there was a 10% lower risk of death for women. However, it did not reach statistical significance for the invasive arm (RR 0.90 (95% CI, 0.76-1.06)), while it did for the non-invasive arm ((RR 0.90 (95% CI, 0.82-0.99)). (Figure 1b and 1d)

We also calculated the occurrence of the combined outcome death/MI during one year after index admission, but found no significant difference between women and men in the early invasive or in the early conservative cohort, neither before, nor after adjustment.

(Figure 2 a-d)

Gender difference in one-year mortality was also assessed according to risk, i.e. calculated TIMI-score and FRISC-score. One-year mortality was higher with increasing risk, according to the both scores. We also found that mortality rates were substantially higher in the non-invasive group, but without significant difference between men and women in any of the risk-score classes. (Table 3)

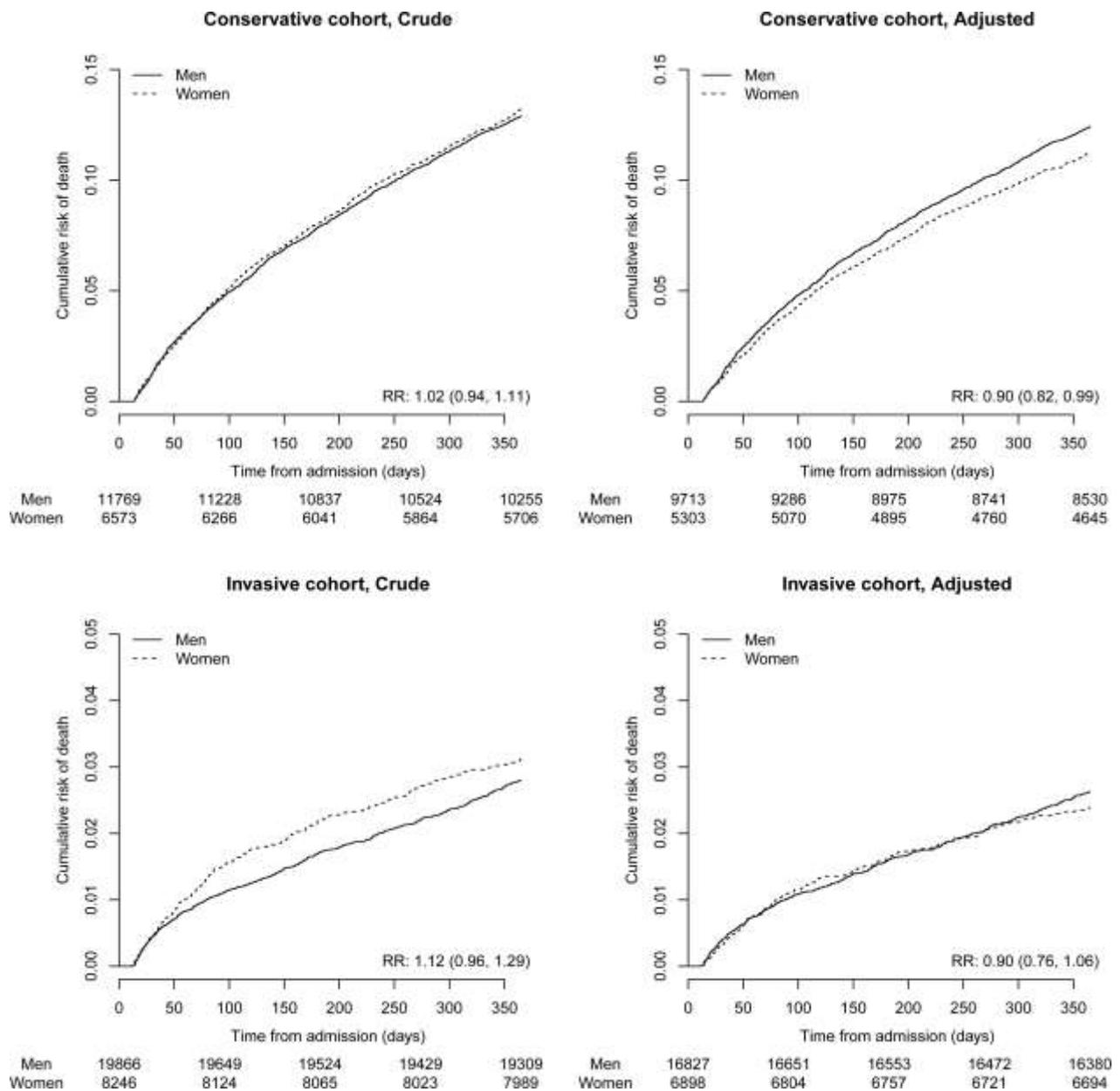


Figure 1  
Crude and adjusted (for propensity score and discharge medication) cumulative risk of death within one year. Women vs. men. RR, Relative Risk.

In a subset of patients in the early invasive arm, with complete angiographic data (7 057 women and 16 854 men) men had more severe coronary artery disease, with a higher rate of 3-vessel/left main disease and lower rates of no significant stenosis. (Table 4)

To further explore gender differences among the invasively treated patients we analyzed outcome according to degree of coronary artery disease and mode of revascularisation. We found no significant difference between the genders with similar degree of coronary artery

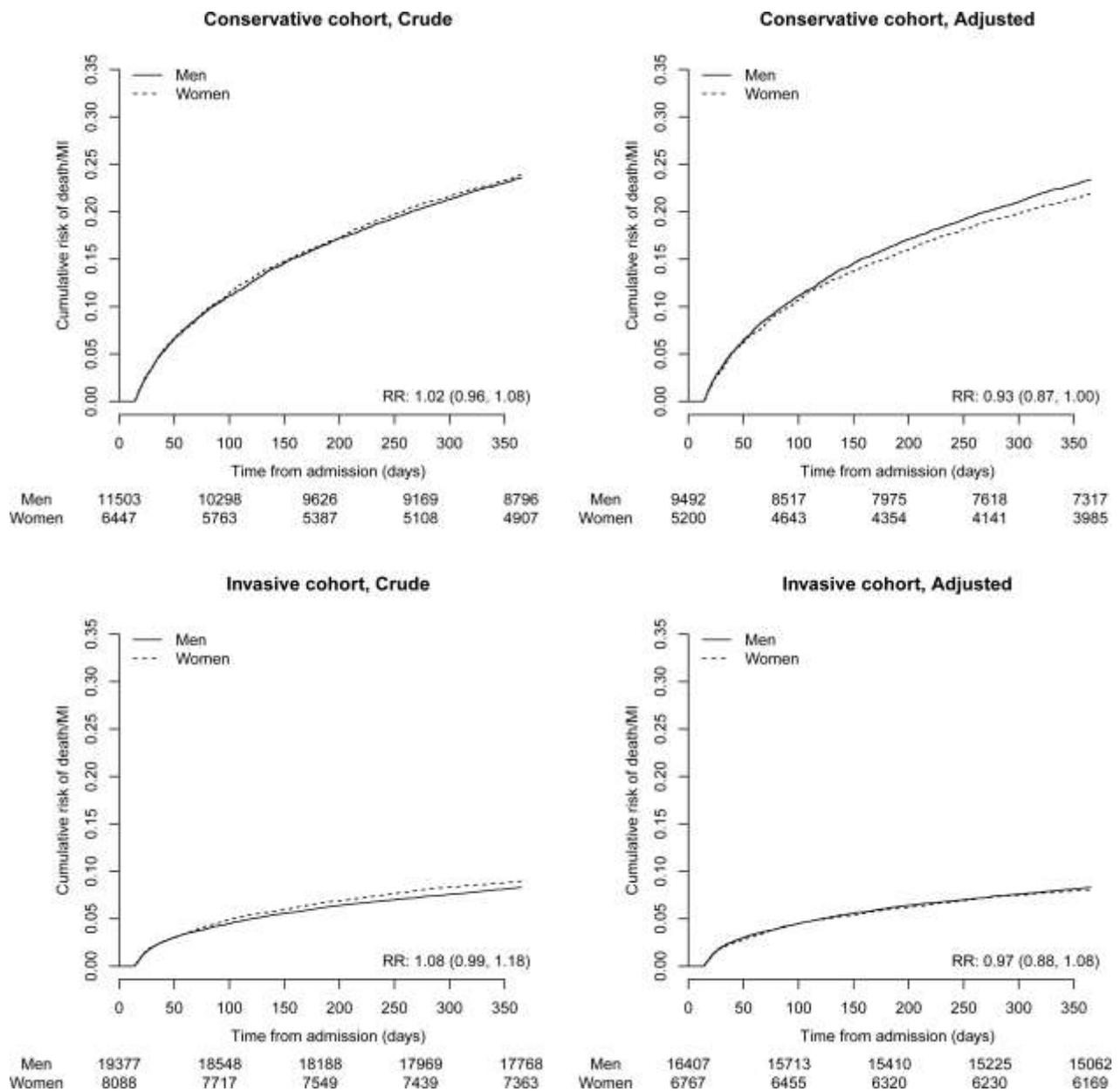


Figure 2  
Crude and adjusted (for propensity score and discharge medication) cumulative risk of death/MI within one year. Women vs. men. RR, Relative Risk.

disease. Before adjustment, but not after, women had higher mortality if treated with PCI. The observed difference seemed to be due to older age and comorbidity. On the other hand, among medically treated patients, after adjustment, women had lower mortality compared to their male counterparts. (Table 5)

In our main analyses patients had to be alive the first 14 days after admission to be included, but we also performed sensitivity analyses for several time-points after admission (day 0-365,

1-365, 30-365 and 45-365). In all time intervals there was a similar relative risk for women vs. men, within treatment strategy. In the invasive arm the crude relative risk for death, for women vs. men, varied from 1.14 (0.96-1.34) day 45-365 to 1.19 (1.05-1.134) day 1-365. In the invasive arm there was an indication of worse outcome for women, before but not after, adjustment. On the other hand, in the non-invasive arm, there was an indication of better outcome for women after but not before adjustment. (Table 6)

We also assessed outcomes with an invasive vs. a non-invasive treatment strategy. The adjusted relative risks of death for an invasive vs. a non-invasive strategy were similar for women (RR=0.46, 95%CI (0.38-0.55) and men (RR=0.45, 95% CI (0.40-0.52)). The corresponding result for death/MI were also similar, (RR=0.57, 95%CI (0.51-0.64) for women and (RR=0.60, 95% CI (0.56-0.65)) for men. Tests for interaction between gender and treatment strategy were non-significant.

## Discussion

There were two major findings in this large cohort of patients, reflecting real-life management.

First, there was a lack of statistically significant difference between the genders with an early invasive strategy, with a relative risk (women vs. men) of one-year mortality of 1.12 (95% CI, 0.96-1.29), after adjustment 0.90 (95% CI, 0.76-1.06). In the non-invasive arm there was also no significant difference (RR 1.02, 95% CI 0.94-1.11), but adjustment indicated lower mortality in women (RR 0.90, 95% CI 0.82-0.99). With a composite end-point, including death or MI, the corresponding results after adjustment were 0.97 (95% CI, 0.88-1.08) in the invasive and 0.93 (95% CI 0.87-1.00) in the non-invasive cohort.

Second, early invasive treatment was associated with a marked, and similar, mortality reduction in women (HR 0.46, 95% CI (0.38-0.55)) and men (HR 0.45, 95% CI (0.40-0.52)), without interaction with gender.

In accordance with our findings, male sex was an independent risk factor for death/MI in the non-invasive strategy arm in the FRISC II trial. [1] However the indication of harm for women treated invasively, that was found in three earlier randomized trials, could not be found in the present study.[1, 2, 4]

The TACTICS TIMI 18-trial indicated similar benefit for men and women, but restricted to high-risk patients with elevated troponins.[3] The importance of troponin elevation in potential benefit of an invasive strategy was supported by a recent meta-analysis by O'Donoghue et al including 8 randomized trials.[12] In patients with elevated markers the odds of the combined end-point death/MI was significantly lower with an invasive strategy for men (OR, 0.64; 95% CI, 0.51-0.81) and directionally consistent but not statistically significant for women (OR, 0.77; 95% CI, 0.47-1.25). On the other hand, for marker-negative men there was a non-significant benefit while there was an indication of possible harm for

marker-negative women with an invasive strategy. In our study all patients had elevated biomarkers and our results, with similar risk reduction for women (RR=0.57, 95% CI (0.51-0.64)) and men (RR=0.60, 95% CI (0.56-0.65)) associated with an invasive strategy, fits well with the meta-analysis by O'Donoghue et al.

Risk-scores have been used to identify patients that benefit the most from an invasive approach.[8] In the present study we found no difference in mortality between the genders in any of the risk-score classes, neither with invasive nor with non-invasive treatment.

Difference in degree of coronary disease has been proposed as a reason for observed difference in outcome between the genders with an invasive strategy.[3] In agreement with earlier findings we found important differences between women and men in degree of coronary artery disease and hence in revascularisation.[1-3, 13] Invasively treated women were much more likely to have no significant stenosis on the angiogram (22% vs. 7%) and consequently more likely to receive medical treatment after angiography (41.5 % vs. 32.3%). The higher proportion of a significant stenosis in men may explain that after adjustment, medically treated women had better outcome than medically treated men RR, 0.78; 95% CI, (0.61-0.98) while there was no difference in mortality if the degree of coronary artery disease was similar.

Our results suggested worse outcome among women actually treated invasively after angiography but the observed difference appears to be explained by difference in age, since after adjustment for age alone the difference was abolished. In the FRISC II trial the higher event rate in invasively treated women seemed to be largely due to a higher rate of death (9.9% vs. 1.2%) and MI (12% vs. 5%) associated with CABG surgery. Also, a substantially higher proportion of the patients allocated to the invasive arm in the FRISC II trial had CABG performed (29% and 37% for women and men respectively) compared to patients in the invasive group in our study (6.8 % and 9.3 %). Whether worse outcome in women with

CABG is explained by difference in coronary artery size, comorbidity, or yet other factors, is still not clear. In the FRISC II trial and TACTICS TIMI-18 trial there was no difference in outcome between the genders in patients undergoing PCI. In contrast, the OASIS 5 WSS, at 2-year follow-up, indicated worse outcome in PCI-treated patients, similar to those undergoing CABG. Our study indicates that there may be a higher rate of adverse outcome associated with higher age and comorbidity, but not gender per se, in both PCI and CABG-treated patients, a finding that merits further studies.

The current study was an observational study of real life clinical practice with a substantial number of patients treated in an early non-invasive way. The proportion of patients treated with an early invasive strategy was however similar to, or even higher than, earlier observational studies.[14-16] For both men and women, invasive treatment was associated with a markedly lower event rate. This was true both for mortality and the combined end-point death/MI and was maintained even after multiple adjustments. However, a larger proportion of men than women were referred for catheterization (63% vs. 56%).

Better outcome with an invasive strategy observed in our study does not necessarily mean that all patients would have the lower event rate with an invasive strategy. Hence, the optimal proportion of women and men referred for early angiography, especially older patients, taking risk for a new ischemic event as well as procedural complications into account, remains to be decided.

## Strengths and limitations

The most important strength with this study with the present study is that it reflects everyday clinical practice for a whole country, including all types of hospitals. Another strength is the large number of patients making proper adjustment for baseline differences possible. There are however limitations. This is an observational study and patients have been allocated to the invasive and non-invasive group based on a clinical decision. Hence individuals with the highest risk for procedural complications may not have been referred for invasive treatment. Although data have been extensively adjusted for a large number of potential confounding variables it is not possible to adjust for variables not included in the register.

## Conclusion

In this large cohort of patients with NSTEMI ACS, reflecting real life management, women and men had similar and better outcome associated with an invasive strategy. Further studies are warranted to find the most optimal treatment strategy for women and men with different risk profiles.

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**Table 1 Baseline Characteristics**

	Early non-invasive strategy			Early invasive strategy		
	Women (n=6 573)	Men (n=11 770)	P-value	Women (n=8 246)	Men (n=19 886)	P-value
Age, mean (year $\pm$ SD)	70.3 $\pm$ 8.4	68.0 $\pm$ 9.3	<0.001	66.0 $\pm$ 9.7	63.5 $\pm$ 9.7	<0.001
<b>Risk factors</b>						
Hypertension	44.9	39.6	<0.001	46.0	38.0	<0.001
Diabetes	31.3	28.2	<0.001	23.4	20.8	<0.001
Current Smoker	21.7	23.5	0.006	27.0	25.7	0.023
History of MI	32.6	41.8	<0.001	19.5	25.7	<0.001
History of PCI/CABG	14.8	23.5	<0.001	12.5	17.9	<0.001
<b>Medical history</b>						
Stroke	13.2	14.8	0.003	6.4	6.0	0.280
Renal failure	3.5	4.7	<0.001	1.2	1.2	0.855
COPD	15.7	10.6	<0.001	9.0	5.5	<0.001
Heart failure	18.3	17.7	0.269	6.1	5.4	0.034
Cancer last 3 years	3.8	5.1	<0.001	2.3	2.4	0.646
<b>Medication on admission</b>						
ACE-I/ARB	28.5	29.7	0.085	24.5	24.0	0.423
Aspirin	47.3	49.9	0.001	40.3	42.3	0.011
Clopidogrel	4.4	5.0	0.073	7.6	6.9	0.031
Warfarin	6.8	8.0	0.003	3.1	4.1	<0.001
$\beta$ -blocker	47.2	48.1	0.264	43.6	41.3	<0.001
Digitalis	7.4	6.6	0.041	2.5	2.4	0.709
Diuretic	41.3	30.5	<0.001	24.8	15.0	<0.001
Statin	28.9	31.5	<0.001	28.6	29.6	0.092
Long acting nitro	25.5	24.1	0.035	16.7	15.2	0.003
<b>In-hospital events</b>						
Shock on arrival	3.1	3.0	0.518	1.8	1.4	0.014
Killip Class I	74.4	78.4		88.0	91.3	
Killip Class II	16.6	14.4		8.0	5.9	
Killip Class III	5.8	4.2		2.2	1.4	
Killip Class IV	3.2	3.0	<0.001	1.8	1.4	<0.001
ST-depression*	36.9	33.0	<0.001	34.2	32.8	0.026

Data are given as percentages unless otherwise indicated. SD, standard deviation; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; ARB, angiotensin receptor blocker; ACE-I, angiotensin-converting enzyme inhibitor. \*Defined as  $\geq 1$  mm depression of the ST-segment in  $\geq 2$  leads.

**Table 2 Diagnosis and Medication at discharge**

	Non-invasive strategy			Invasive strategy		
	Women (n=6 573) (%)	Men (n=11 770) (%)	P- value	Women (n=8 246) (%)	Men (n=19 866) (%)	P- value
<b>Diagnosis</b>						
NSTEMI	73.2	73.0		78.4	78.7	
UAP	5.8	6.4		14.4	14.9	
AP	21.0	20.6	0.289	7.2	6.4	0.051
<b>Medication</b>						
ACE-I/ARB	47.3	48.1	0.270	48.6	49.8	0.077
Aspirin	80.6	82.3	0.003	91.1	92.7	<0.001
Clopidogrel	19.2	18.8	0.526	61.0	62.1	0.105
Oral anticoagulant	10.0	10.7	0.117	4.6	4.6	0.994
β-blocker	82.3	84.4	<0.001	87.6	89.3	<0.001
Calcium channel antagonist	19.7	19.0	0.279	16.9	15.3	0.001
Digitalis	8.9	8.1	0.056	2.9	2.5	0.042
Diuretic	52.1	41.9	<0.001	29.4	20.2	<0.001
Statin	60.5	61.5	0.182	81.9	84.1	<0.001
Long acting Nitroglycerin	38.8	37.9	0.235	25.6	23.1	<0.001

Data are given as percentages unless otherwise indicated. Data are given as percentages unless otherwise indicated. NSTEMI, Non ST-Elevation Myocardial Infarction; UAP, Unstable Angina Pectoris; AP, Angina Pectoris; ARB, angiotensin receptor blocker; ACE-I, angiotensin-converting enzyme inhibitor.

**Table 3 One year mortality according to treatment strategy, risk score and gender**

<b>Non-invasive strategy</b>			
	<b>Women (n=6 573) (%)</b>	<b>Men (n=11 770) (%)</b>	<b>p-value</b>
<b>TIMI-score</b>			
TIMI 0-2	8.5	8.0	0.482
TIMI 3-4	15.1	14.7	0.534
TIMI 5-6	20.6	21.2	0.753
<b>FRISC-score</b>			
FRISC 0-1	3.8	4.1	0.729
FRISC 2-3	11.3	11.3	0.869
FRISC 4-5	22.9	23.5	0.648
<b>Invasive strategy</b>			
	<b>Women (n=8 246) (%)</b>	<b>Men (n=19 866) (%)</b>	<b>p-value</b>
<b>TIMI-score</b>			
TIMI 0-2	1.9	1.6	0.206
TIMI 3-4	4.2	4.1	0.880
TIMI 5-6	7.3	5.5	0.151
<b>FRISC-Score</b>			
FRISC 0-1	1.0	1.0	0.963
FRISC 2-3	3.3	3.2	0.738
FRISC 4-5	7.3	6.6	0.434

Data are presented as percentages. TIMI-score (0 to 6 points) and FRISC-score (0 to 5 points) (for information on included variables, see methods).

**Table 4 Angiographic data for invasively managed patients**

<b>Degree of coronary disease</b>			
	<b>Women (n=7 057) (%)</b>	<b>Men (n=16 854) (%)</b>	<b>P-value</b>
Normal	21.6	6.9	
/atheromatosis			
1-2 vessel disease	52.0	57.5	
3-vessel/main stem disease	26.4	35.6	<0.001
<b>Treatment after angiography</b>			
	<b>Women (n=8 246) (%)</b>	<b>Men (n=19 866) (%)</b>	<b>P-value</b>
Medical treatment	41.5	32.3	
PCI	51.7	58.4	
CABG	6.8	9.3	<0.001

Abbreviations: PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting. Complete data on angiography findings were available for 85% of the early invasively treated patients. Treatment after angiography is reported for all early invasively treated patients.

**Table 5 Outcome in subgroups of invasively managed patients****One year mortality according to angiographic finding**

	<b>Women (n=7 057) (%)</b>	<b>Men (n=16 854) (%)</b>	<b>RR (95% CI) Women vs Men</b>	<b>RR (95% CI) Adjusted For age</b>	<b>RR (95% CI) Full Adjustment*</b>
Normal /atheromatosis	2.0	1.8	1.129 (0.649- 0.965)	1.007 (0.574- 1.768)	0.819 (0.433- 1.551)
1-2 vessel disease	2.0	1.6	1.247 (0.944- 1.647)	1.045 (0.789- 1.385)	0.965 (0.707- 1.319)
3-vessel/main stem disease	5.1	4.5	1.142 (0.904- 1.442)	1.014 (0.801- 1.284)	0.910 (0.688- 1.202)

**One year mortality according to treatment after angiography**

	<b>Women (n=8 246) (%)</b>	<b>Men (n=19 866) (%)</b>	<b>RR (95% CI) Women vs Men</b>	<b>RR (95% CI) Adjusted for age</b>	<b>RR (95% CI) Full Adjustment*</b>
Medical treatment	4.0	4.6	0.886 (0.724- 1.085)	0.838 (0.684- 1.027)	<b>0.775</b> <b>(0.614-</b> <b>0.980)</b>
PCI	2.3	1.8	<b>1.287</b> <b>(1.015-</b> <b>1.633)</b>	1.062 (0.835- 1.350)	1.056 (0.803- 1.389)
CABG	3.7	2.8	1.345 (0.810- 2.232)	1.132 (0.678- 1.890)	0.909 (0.489- 1.689)

PCI, percutaneous coronary intervention; CABG, coronary artery by-pass grafting; RR, Relative Risk; CI, Confidence interval. Complete data on angiography findings were available for 85% of the early invasively treated patients. Treatment after angiography is reported for all early invasively treated patients. \*Adjustment with propensity score (see methods) and discharge medication.

**Table 6 Sensitivity analyses. One year mortality in different time intervals**

<b>Non-invasive strategy</b>				
	<b>Women</b> (n=7 024) (%)	<b>Men</b> (n=12 590) (%)	<b>RR</b> (95% CI) Crude Women vs Men	<b>RR</b> (95% CI) Adjusted for propensity score
0-365	18.6	18.4	1.010 (0.943-1.080)	<b>0.895</b> <b>(0.827-0.968)</b>
1-365	18.1	17.8	1.015 (0.947-1.088)	<b>0.898</b> <b>(0.829-0.973)</b>
15-365	13.6	13.2	1.031 (0.950-1.120)	0.931 (0.847-1.024)
30-365	12.3	11.9	1.034 (0.948-1.128)	0.940 (0.851-1.040)
45-365	11.3	10.7	1.052 (0.960-1.153)	0.939 (0.844-1.044)
<b>Invasive strategy</b>				
	<b>Women</b> (n=8 377) (%)	<b>Men</b> (n=20 099) (%)	<b>RR</b> (95% CI) Crude Women vs Men	<b>RR</b> (95% CI) Adjusted for propensity score
0-365	4.5	3.8	<b>1.186</b> <b>(1.048-1.342)</b>	0.943 (0.818-1.086)
1-365	4.4	3.8	<b>1.178</b> <b>(1.040-1.334)</b>	0.934 (0.810-1.078)
15-365	3.2	2.8	1.118 (0.966-1.295)	0.902 (0.764-1.066)
30-365	2.8	2.4	1.168 (0.997-1.368)	0.985 (0.825-1.178)
<b>45-365</b>	2.5	2.2	1.136 (0.961-1.343)	0.962 (0.797-1.162)

RR, Relative Risk; CI, Confidence interval.

Cox regression analysis crude, adjusted for age and adjusted for Propensity score (see methods section).

**Table 7 One-year Outcome Invasive vs. non-invasive strategy**

	<b>Invasive</b> n= 28 112 (%)	<b>Non-invasive</b> n= 18 343 (%)	RR (95% CI) Crude	RR (95% CI) Adjusted	Interaction p-value
<b>Death</b>					
<b>Women</b>	3.1	13.2	0.227 (0.197- 0.261)	0.456 (0.381- 0.545)	0.611
<b>Men</b>	2.8	12.9	0.206 (0.187- 0.227)	0.453 (0.399- 0.515)	
<b>Death/MI</b>					
<b>Women</b>	10.7	25.3	0.395 (0.364- 0.429)	0.572 (0.514- 0.636)	0.684
<b>Men</b>	10.5	25.0	0.394 (0.373- 0.417)	0.603 (0.560- 0.649)	

RR, Relative Risk; CI, Confidence interval.

Cox regression analysis, crude and adjusted for Propensity score (see methods) and discharge medication.

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## Conflict of interest

None declared

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## Selection of study population among all myocardial infarction patients

