Percutanous coronary intervention (PCI) in the elderly

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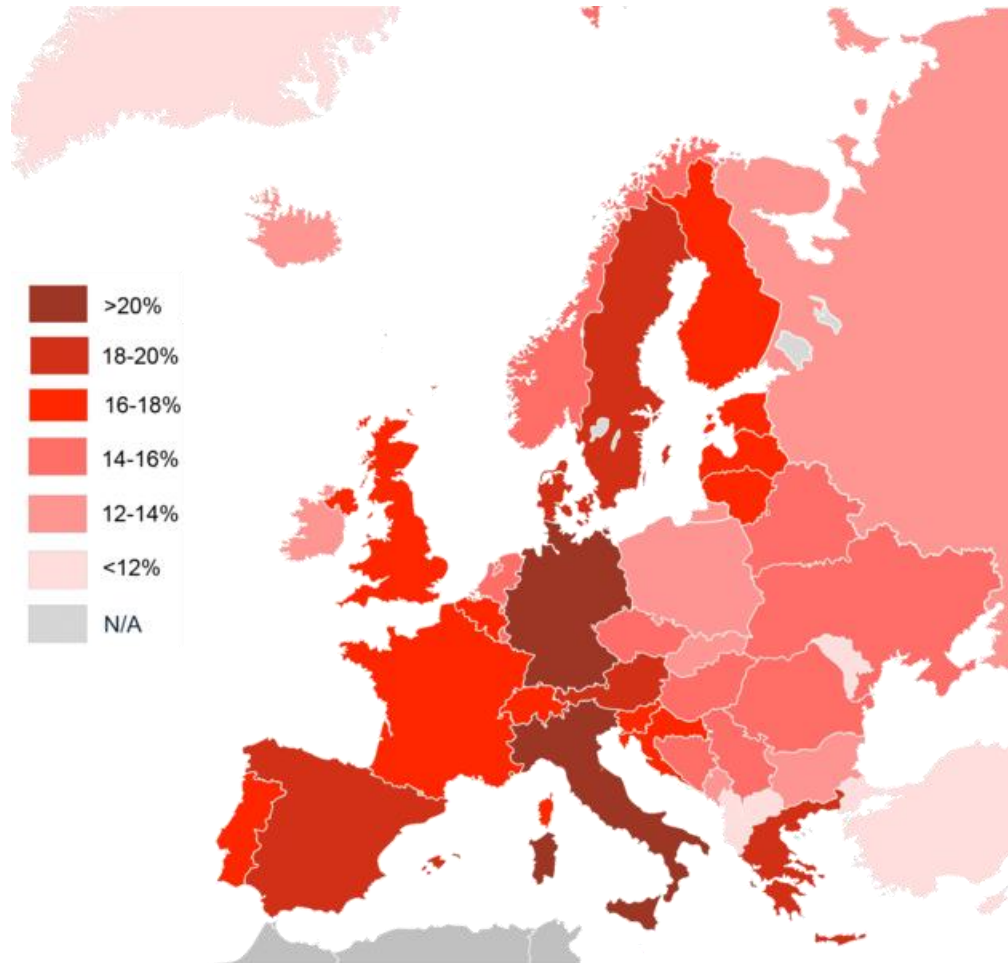
Centre Hospitalier Universitaire Vaudois
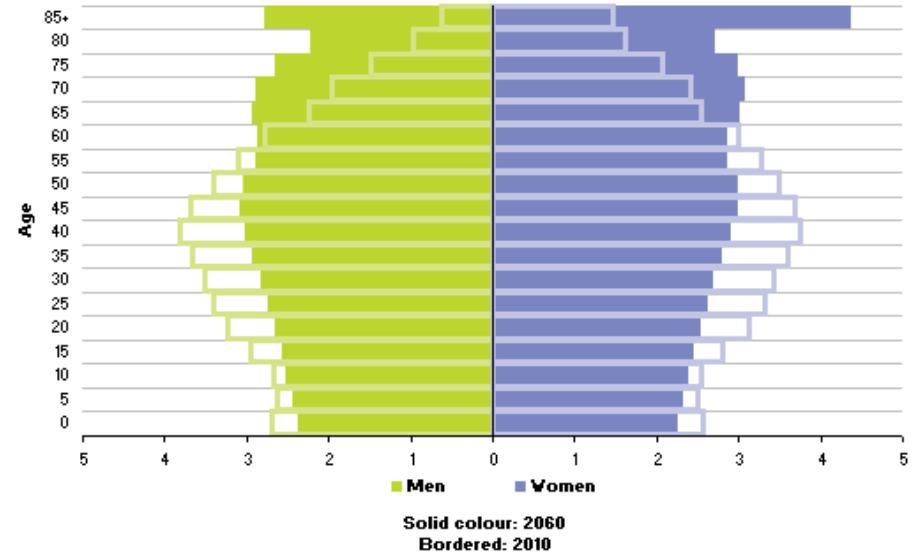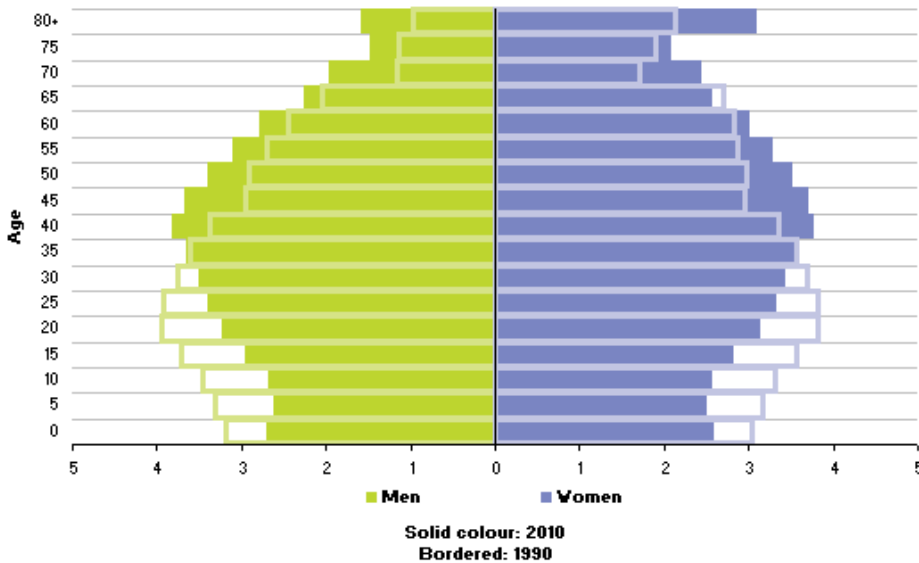
Lausanne, Switzerland

Greying of Europe

Map of Europe showing the percentage of the population over 65 in 2010 for each country
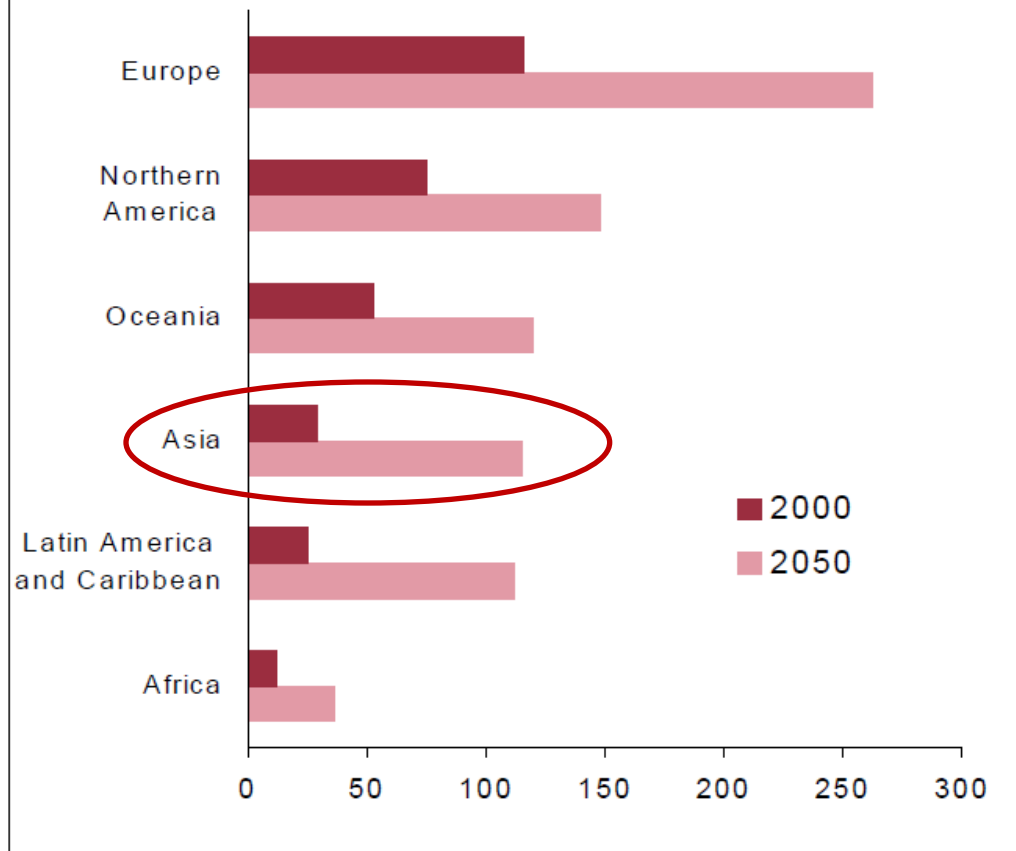
Demographic evolution in Europe

Greying of Europe

Evolution from 1990-2010 and anticipated future evolution 2010-2060

Demographic evolution in the world

Figure 15. Number of persons 65 or over per hundred children under 15: major areas, 2000 and 2050
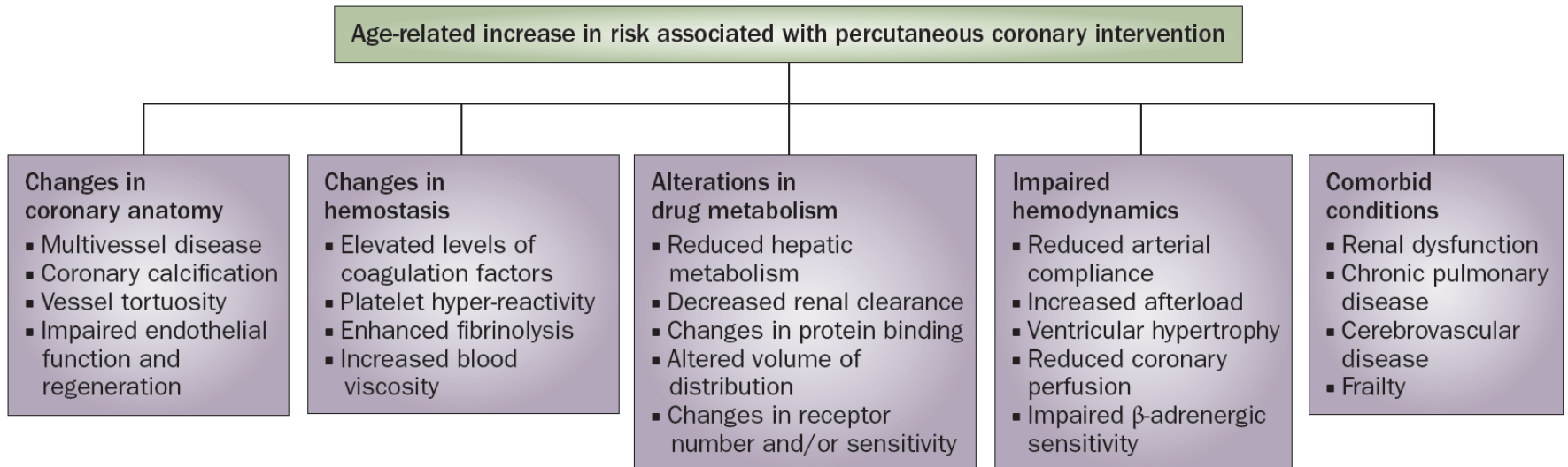
Aging and coronary artery disease

- Elderly: > 75 years
- Most interventional studies regardless of clinical context focus on patients 50-65 years ('healthy worker population')

- Age is a chronological descriptor that is only incompletely associated with an individual's physiological age
- Nevertheless, age is an independent risk factor for coronary artery disease
  - Age as a risk factor *an sich*
  - Classical risk factors that increase with age
  - Difficult to separate these 2 interlinked entities
- Therefore, cardiovascular disease remains the leading cause of morbidity and mortality among the elderly
- 25% of all PCI's in patients > 75 years; 12% in patients > 80 years

Treatment paradox in the elderly

- In *urgent* settings older patients more often present with ACS, with longer intervals from the onset of symptoms to presentation, frequently complain of atypical symptoms and frequently present with non-diagnostic ECG's

- In *elective* settings older patients are less often referred for cath compared to younger patients ('first do no harm') so often late referral and more extensive coronary artery disease

- 'Treatment paradox': the more elderly, the more high risk a patient is, the less frequently angiography and revascularization are used; although in this subset of patients the benefits of an invasive strategy can even be higher than in younger patients

PCI in the elderly in general

Multiple physiological changes occurring with age augment the risk of adverse outcomes with PCI, even in elective setting

Age-related increase in risk associated with percutaneous coronary intervention

Changes in coronary anatomy
- Multivessel disease
- Coronary calcification
- Vessel tortuosity
- Impaired endothelial function and regeneration

Changes in hemostasis
- Elevated levels of coagulation factors
- Platelet hyper-reactivity
- Enhanced fibrinolysis
- Increased blood viscosity

Alterations in drug metabolism
- Reduced hepatic metabolism
- Decreased renal clearance
- Changes in protein binding
- Altered volume of distribution
- Changes in receptor number and/or sensitivity

Impaired hemodynamics
- Reduced arterial compliance
- Increased afterload
- Ventricular hypertrophy
- Reduced coronary perfusion
- Impaired β-adrenergic sensitivity

Comorbid conditions
- Renal dysfunction
- Chronic pulmonary disease
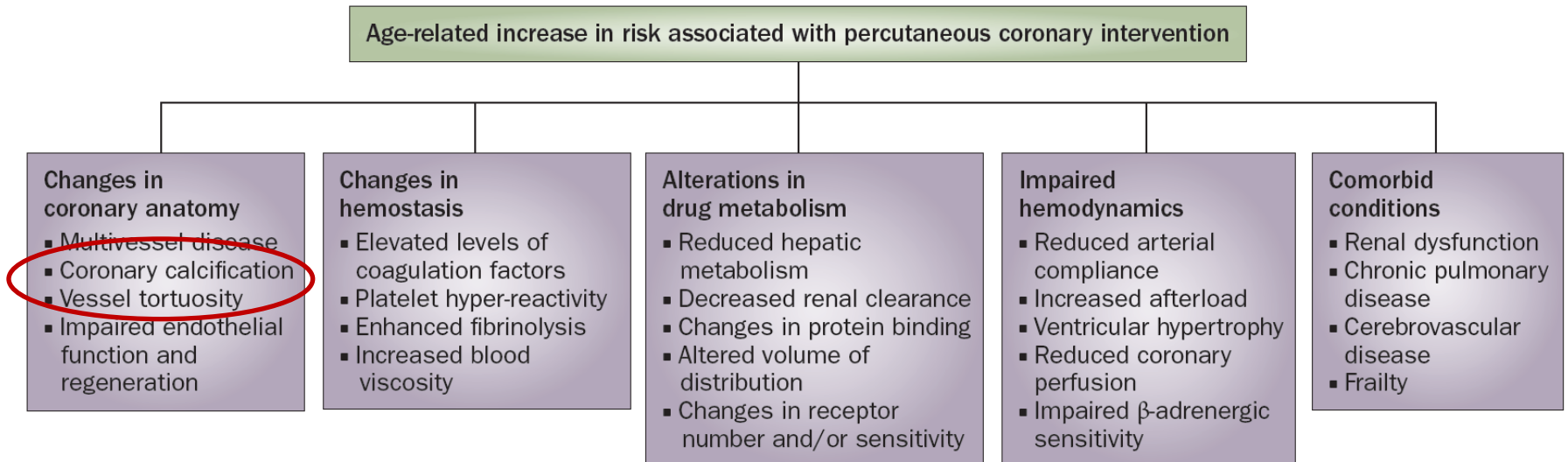- Cerebrovascular disease
- Frailty

PCI in the elderly in general

Multiple physiological changes occurring with age augment the risk of adverse outcomes with PCI, even in elective setting

| Age-related increase in risk associated with percutaneous coronary intervention				
Changes in coronary anatomy	**Changes in hemostasis**	**Alterations in drug metabolism**	**Impaired hemodynamics**	**Comorbid conditions**
▪ Multivessel disease ▪ Coronary calcification ▪ Vessel tortuosity ▪ Impaired endothelial function and regeneration	▪ Elevated levels of coagulation factors ▪ Platelet hyper-reactivity ▪ Enhanced fibrinolysis ▪ Increased blood viscosity	▪ Reduced hepatic metabolism ▪ Decreased renal clearance ▪ Changes in protein binding ▪ Altered volume of distribution ▪ Changes in receptor number and/or sensitivity	▪ Reduced arterial compliance ▪ Increased afterload ▪ Ventricular hypertrophy ▪ Reduced coronary perfusion ▪ Impaired β-adrenergic sensitivity	▪ Renal dysfunction ▪ Chronic pulmonary disease ▪ Cerebrovascular disease ▪ Frailty

PCI in the elderly in general

- Elderly patients are more likely to have complex, multivessel disease necessitating more challenging multilesion interventions

- Age is a significant predictor of coronary calcification and tortuosity:
  - increased frequency of periprocedural complications, decreased success rates, inadequate stent expansion and thus increased restenosis rates
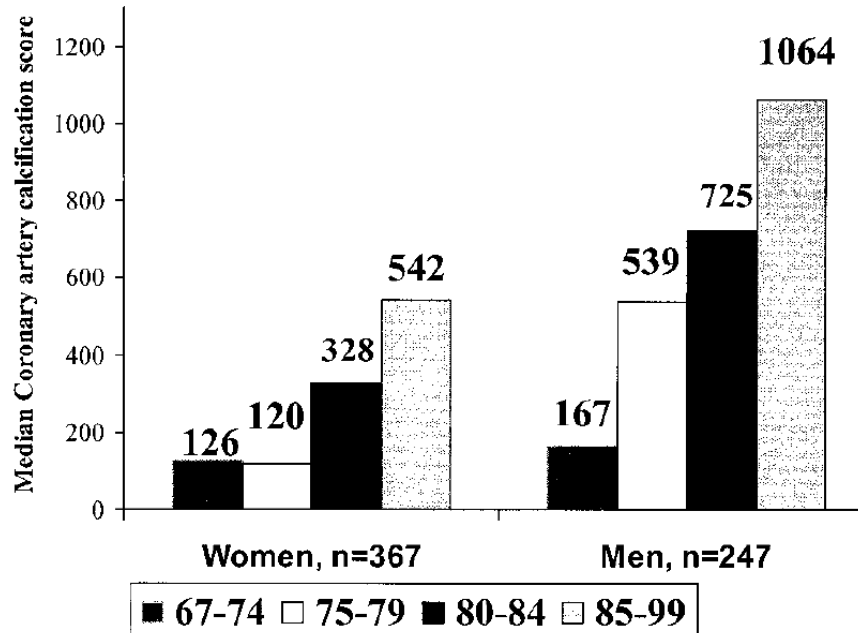
PCI in the elderly in general

- Well documented worse outcome for PCI in the elderly compared to younger patients
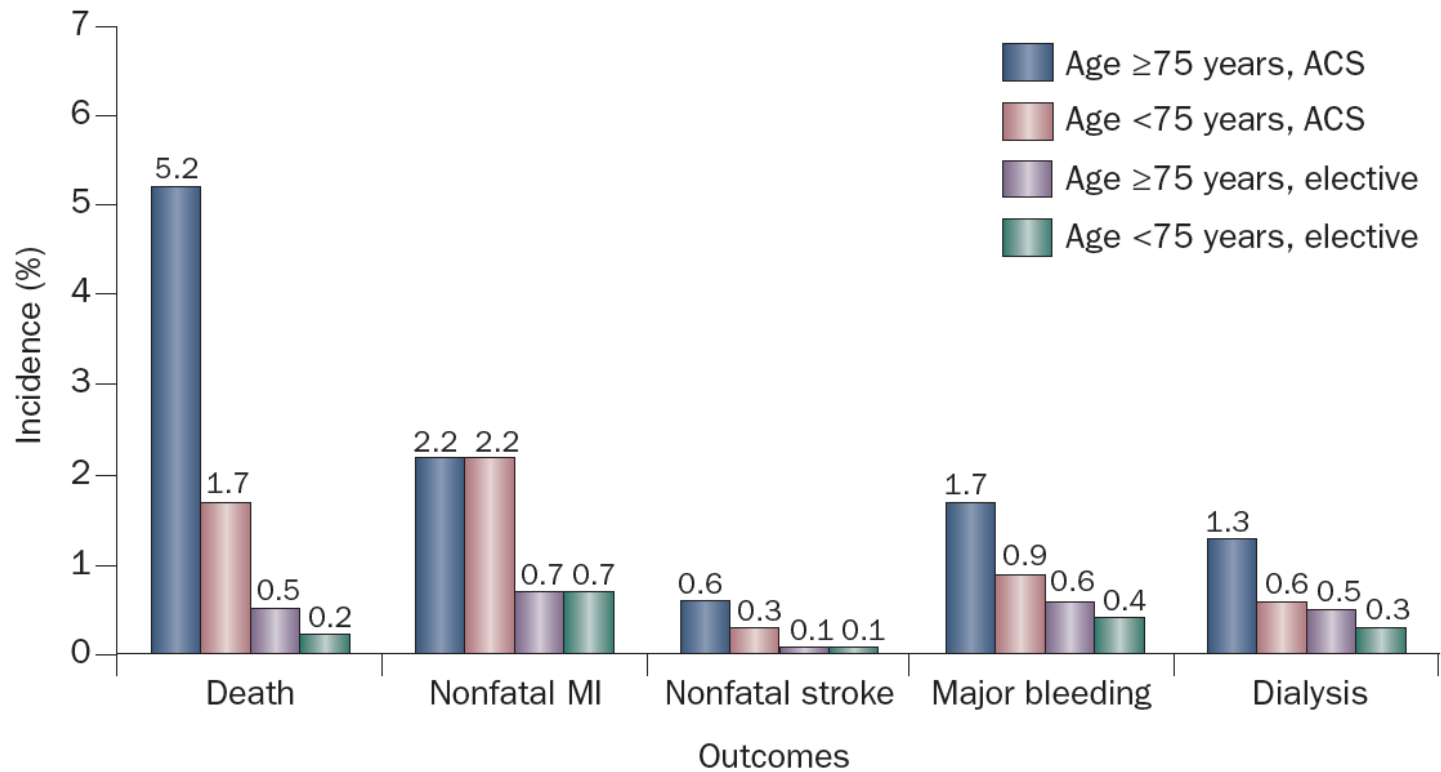
PCI in the elderly in general

- Well documented worse outcome for PCI in the elderly compared to younger patients but a significant downtrend in PCI-associated mortality in the modern era, most prominent in patients > 80 years
  - Improved patient selection
  - Evolution of revascularization techniques
  - Broader use of evidence-based periprocedural medications
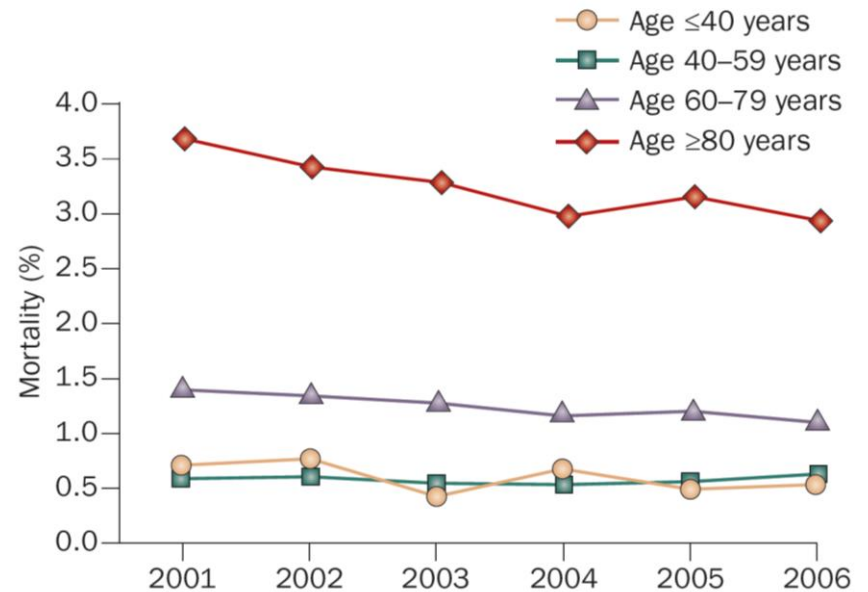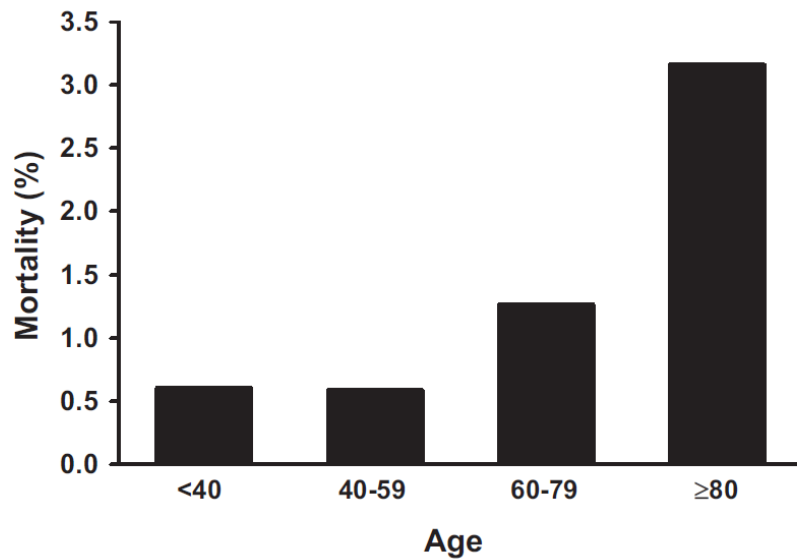
Elective PCI

- As in younger patients there is only in selected subgroups a *prognostic* benefit for revascularization when added to optimal medical therapy.
  - 'High anatomical risk' patients
  - 'High clinical risk' patients

	Subset of CAD by anatomy	Class[a]	Level[b]
For prognosis	Left main >50%[d]	I	A
	Any proximal LAD >50%[d]	I	A
	2VD or 3VD with impaired LV function[d]	I	B
	Proven large area of ischaemia (>10% LV)	I	B
	Single remaining patent vessel >50% stenosis[d]	I	C

- However PCI has proven to be a very effective tool in *symptomatic* relief. This is even more important in an old population in which improving prognostic outcome is more or less obsolete.

Elective PCI

TIME study

- Trial of invasive vs medical therapy in elderly patients
- RCT in patients > 75 years with chest pain refractory to at least 2 antianginal drugs
- Follow-up 6 months and 1 year
- Primary endpoint: QOL and death+MI+hospital admission

JAMA 2003; 289: 1117-23
Lancet 2001; 358: 951-57
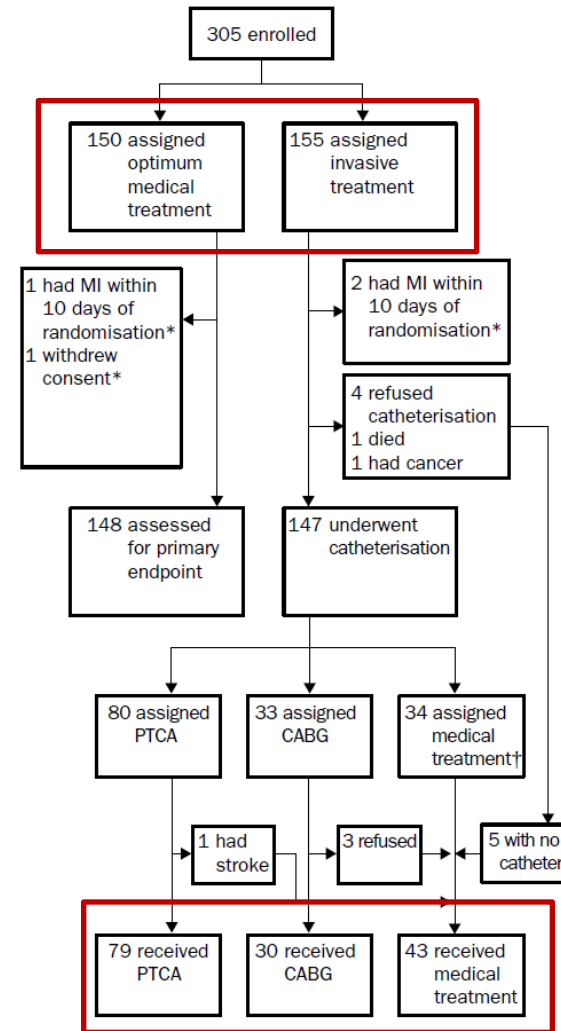
Elective PCI

TIME study – 6 months outcome

- MACE was lower in the interventional group, predominantly due to lower need for rehospitalization for angina

- Elderly patients benefit from revascularization in terms of QOL and symptom relief

- There is a small peri-interventional mortality hazard
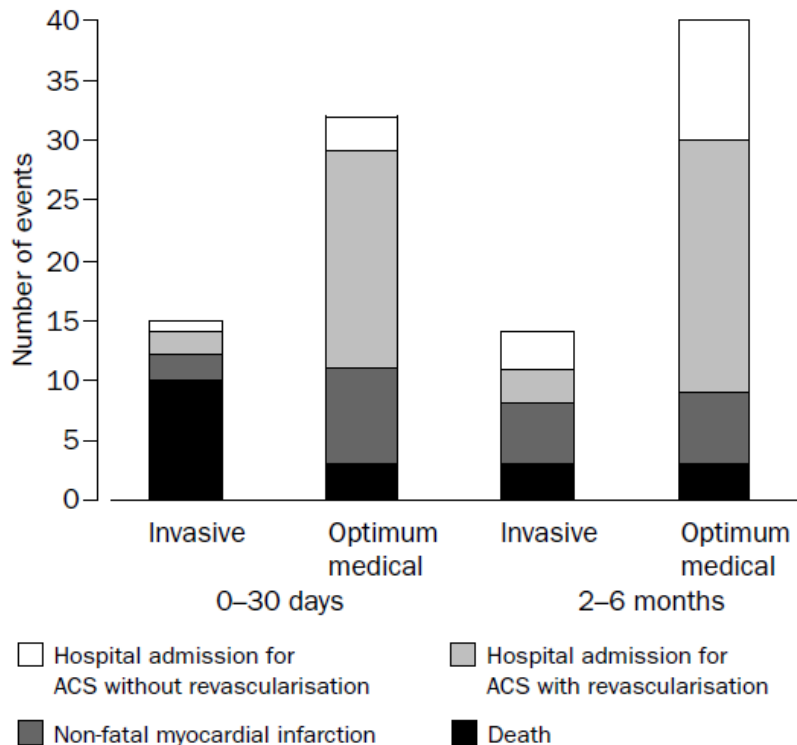
	Invasive strategy (n=153)	Optimum medical strategy (n=148)	p
Death	13	6	0·15*
Non-fatal infarctions	12	17	0·46†
Hospital admissions for ACS			
Without revascularisation	5	18	0·006†
With revascularisation	10	55	<0·0001†
Total major adverse cardiac events	40	96	<0·0001†

ACS=acute coronary syndrome. *Fisher's exact test. †Wilcoxon-Mann-Whitney test.

Elective PCI

TIME study – 1 year outcome

- No difference in QOL between 2 groups
- Overall MACE rate remains significantly higher in medical treatment group, predominantly due to increased hospitalization for ACS

Figure 2. Time to Death or Nonfatal Myocardial Infarction (MI) in Both Treatment Groups

Proportion With Death or MI vs Days After Inclusion. Invasive. Log Rank P = .71. Optimized Medical.
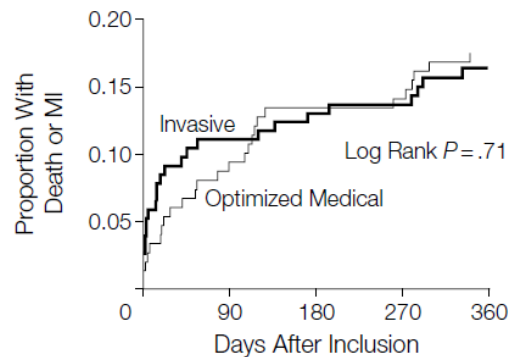
No. at Risk

Optimized Medical	148	135	128	127	122
Invasive	153	136	133	132	99

Note the small early hazard in invasive patients (thick line), which is balanced during later follow-up (optimized medical therapy, thin line).

Figure 3. Rates of Major Adverse Clinical Events (MACE) Over Time

Proportion With MACE vs Days After Inclusion. Optimized Medical. Log Rank P <.001. Invasive.
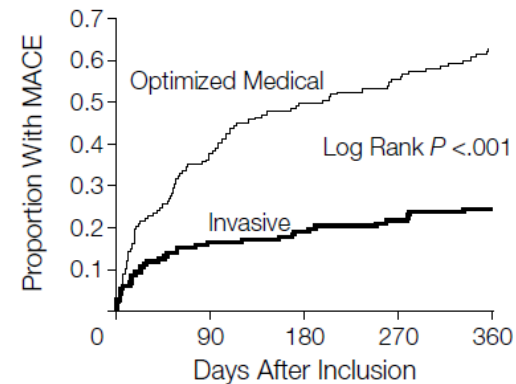
No. at Risk

Optimized Medical	148	92	74	66	55
Invasive	153	128	124	120	90

MACE curves continue to diverge throughout 12 months due to an increasing number of late revascularizations in optimized medical therapy patients.

Elective PCI

TIME study – economical analysis

- The invasive strategy was cost-effective over a one-year observation period compared to medical therapy
- The early increased revasc. costs are balanced by increased private practitioner's charges and symptom driven late revascularizations in the medical group
- Increased intervention costs should not be an argument against invasive strategy in an elderly patient with symptomatic CAD
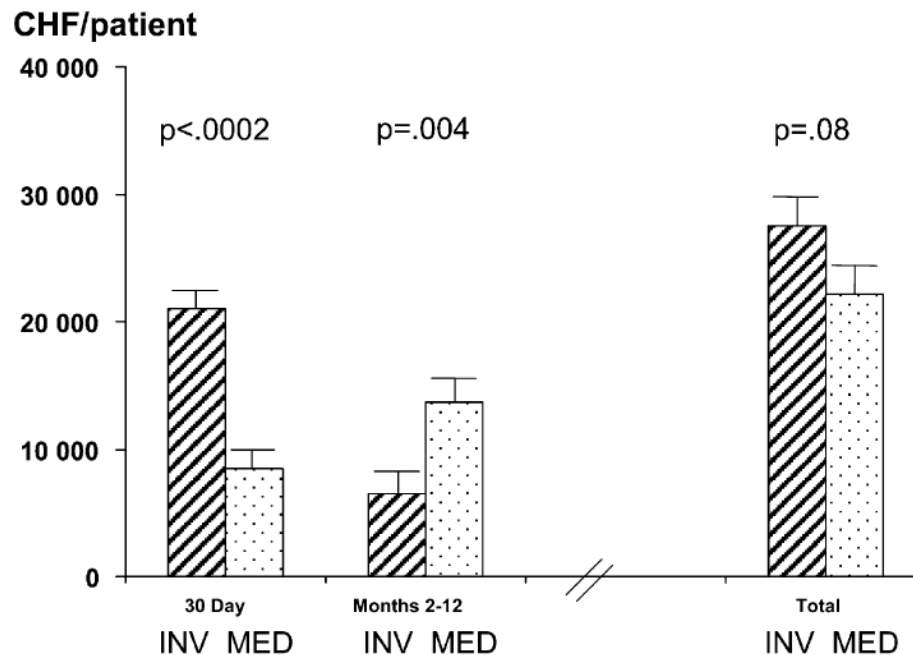
Elective PCI

APPROACH registry

- 'Alberta provincial project for outcomes assessment in coronary heart disease': clinical data collection initiative capturing all pts. undergoing cath. in the province of Alberta since 1995
- 21573 pts. of which 6181 > 70 years
- Seattle angina questionnaire (SAQ)

Outcomes	Age (years)		
	<70	70–79	≥80
Exertional capacity (OR; 95%CI)	1.48; 1.32–1.66	1.45; 1.20–1.76	1.79; 1.04–3.10
Anginal frequency (OR; 95%CI)	1.70; 1.51–1.90	1.97; 1.63–2.40	2.03; 1.24–3.32
Anginal stability (OR; 95%CI)	1.80; 1.64–1.99	2.16; 1.82–2.55	1.86; 1.19–2.88
Quality of life (OR; 95%CI)	1.56; 1.41–1.73	1.69; 1.42–2.02	1.70; 1.07–2.71
Treatment satisfaction (OR; 95%CI)	1.77; 1.55–2.02	1.96; 1.53–2.50	1.62; 0.79–3.36

Table 1 | Quality of life after coronary revascularization versus medical therapy

ORs above 1.0 reflect better odds of having higher scores on the relevant measurements, as assessed using the Seattle Angina Questionnaire. Abbreviation: OR, odds ratio. Modified from Graham, M. M. *et al.* Quality of life after coronary revascularization in the elderly. *Eur. Heart J.*, 2006, **27**, 1690–1698, by permission of Oxford University Press.[76]

PCI vs. CABG

- Recent meta-analysis: pooled individual patient data from 10 randomised trials to compare the effectiveness of CABG with PCI according to patients' basline characteristics (n= 7812)
- Mortality-HR PCI vs. CABG: < 55 years: 1.25; 55-65 years: 0.90; > 65 years: 0.82 in favor of CABG

Lancet 2009; 373: 1190-97
JACC 2012; 60:2150-7
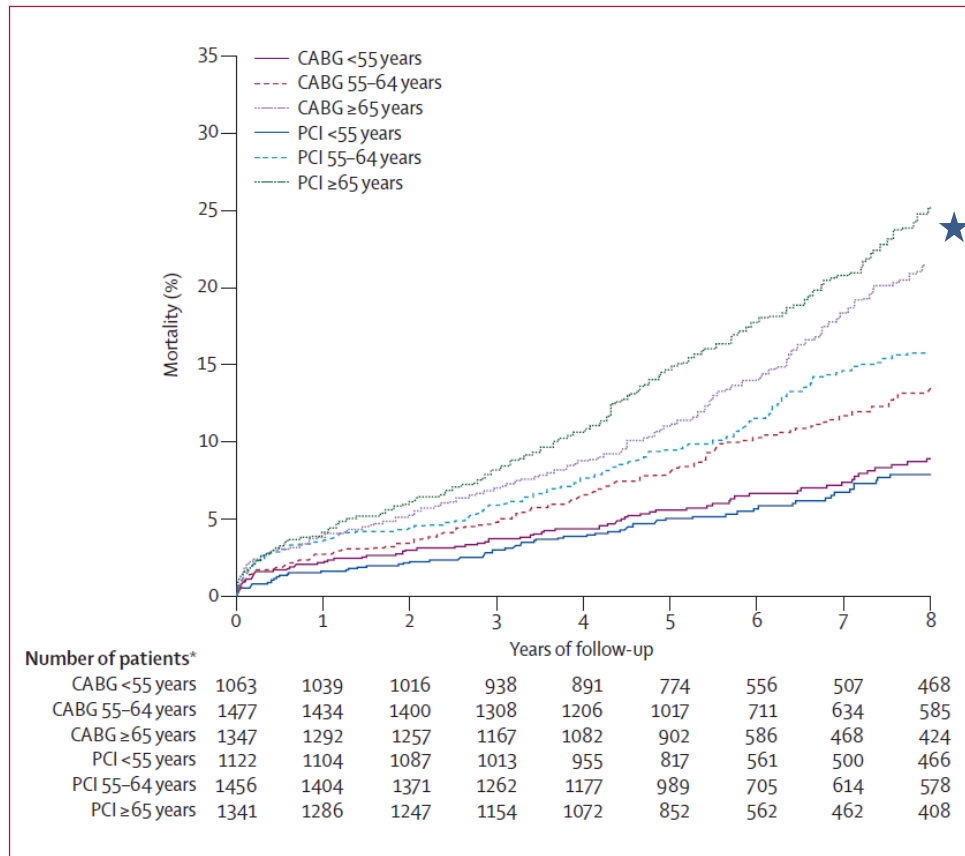
PCI vs. CABG

- Besides a possible beneficial effect of CABG on mortality in the elderly, it is also very effective in symptom control and in mainting independence

- 73 consecutive octogenerians underwent CABG; QOL and performance measures were evaluated

- Karnofsky scale: capacity for independent living

TABLE 3 Karnofsky Performance Scale

|	
100	Normal, no complaints, no evidence of disease
90	Able to carry on normal activity: minor symptoms of disease
80	Normal activity with effort: some symptoms of disease
70	Cares for self: unable to carry on normal activity or active work
60	Requires occasional assistance but is able to care for needs
50	Requires considerable assistance and frequent medical care
40	Disabled: requires special care and assistance
30	Severely disabled: hospitalization is indicated, death not imminent
20	Very sick, hospitalization necessary: active treatment necessary
10	Moribund, fatal processes progressing rapidly
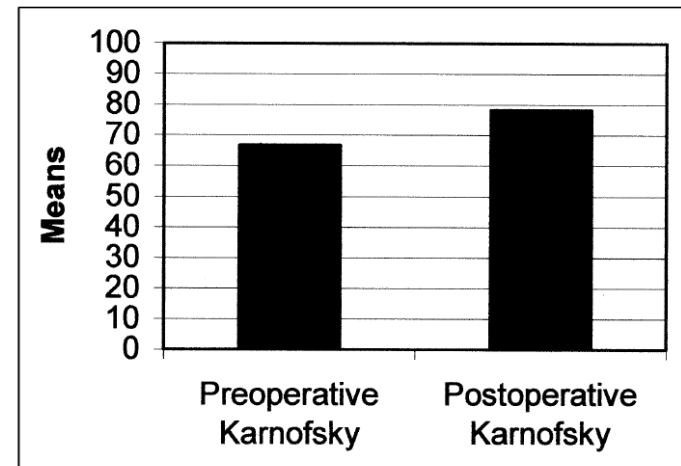
FIGURE 1. Means of pre- and postoperative Karnofsky performance status scores measuring functional status. Significance value is based on paired Student's t test ($p < 0.05$).

PCI vs. CABG

- Despite these beneficial effects of CABG in the elderly it remains a treatment modality with a non-negligable peri-operative mortality and morbidity; older patients are at increased risk of perioperative MI, renal failure , nosocomial infections, prolonged ventilation and ICU stay and postoperative delirium.

- Especially post-operative neuro-cognitive functioning is a major concern (periprocedural neurological complications 0,4% in PCI vs. 3,5% in CABG) with a significant incidence of both short-and long term cognitive impairment affecting functional status.

- In conclusion, surgical revascularization should remain an option only for a selected population of highly functing elderly patients with few comorbidities. If the acute peri-operative phase with an increased risk of mortality/morbidity has been passed, elderly patients in particular can benefit from surgical revascularization.

Unstable angina/NSTEMI

- In European registries of NSTE-ACS > 30% of patients are aged > 75 years. Despite this high proportion , the elderly represent < 20% of all patients in recent NSTE-ACS trials. Even when elderly are included, those randomized have substantially less co-morbidity than patients encountered in daily clinical practice ('trial' vs 'community' population).

- Clinical presentation is often atypical with only mild symptoms, dyspnea as the predominant complaint and often a non-diagnostic ECG.

Chest Pain and Initial Diagnosis
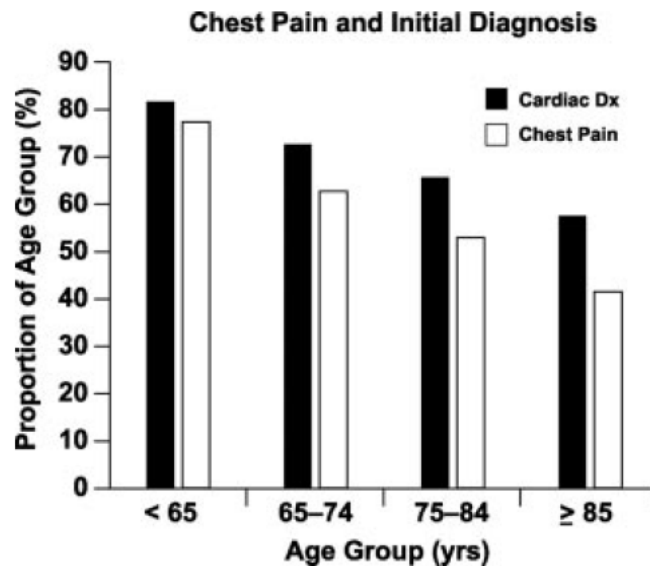
Unstable angina/NSTEMI

- Age is of one of the most important predictors of morbidity (heart and renal failure, bleeding, stroke) and mortality in NSTE-ACS
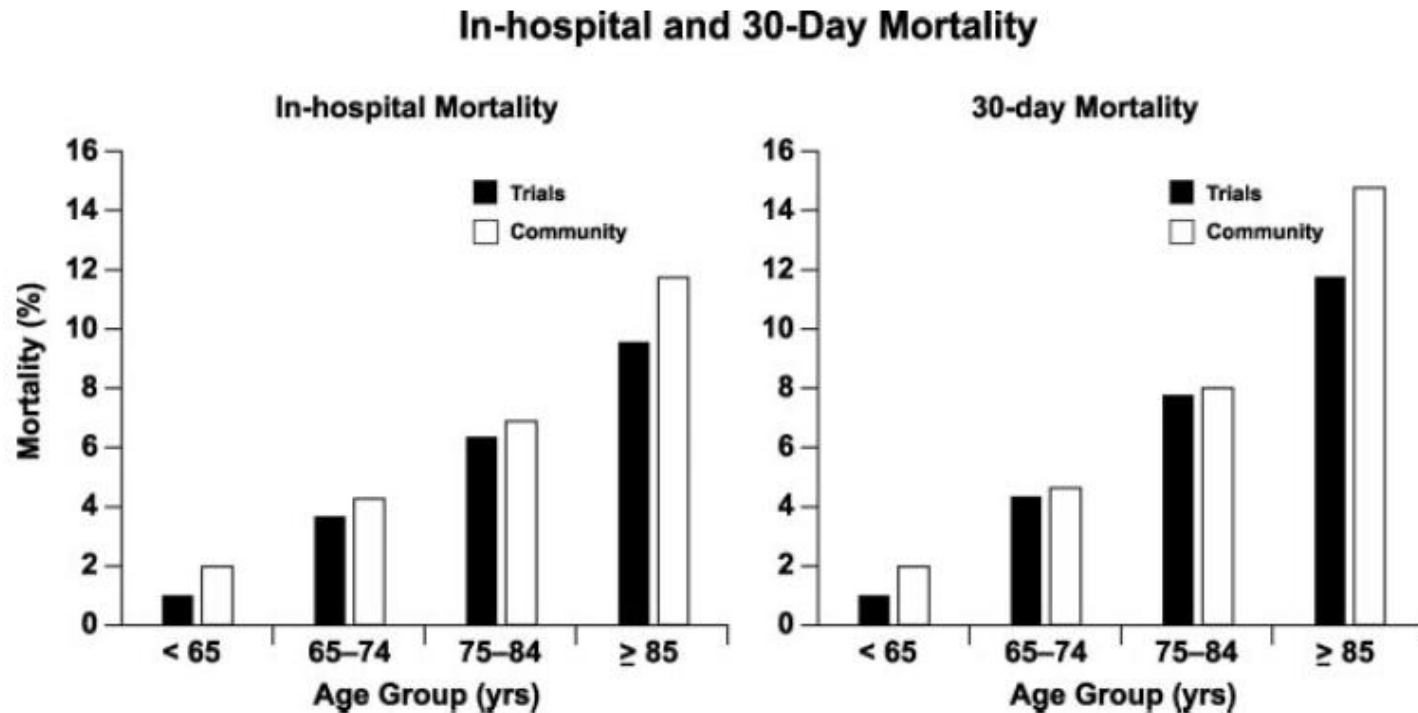

'trial': VIGOUR trials; 'community': GRACE registry

- TACTICS –TIMI 18
  - RCT in 2220 patients with NSTE-ACS
  - Medical therapy and coronary angiography at 4-48h vs. Medical therapy and predischarge exercise testing (ASA, Heparine, Tirofiban)
  - Endpoints: death, MI, hospitalization, stroke, bleeding; analysis in function of age groups after 30 days and 6 months
  - Results: major bleeding rates were higher in patients > 75 years of age with early invasive strategy (16,6% vs. 6,5%; p=0,009)
 - But improved ischemic outcomes with increasing age

Unstable angina/NSTEMI

- TACTICS –TIMI 18
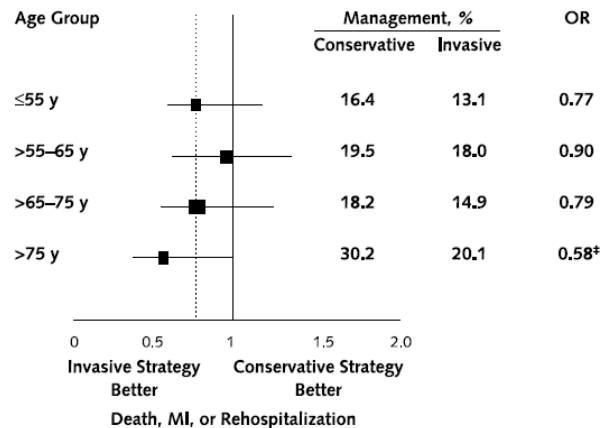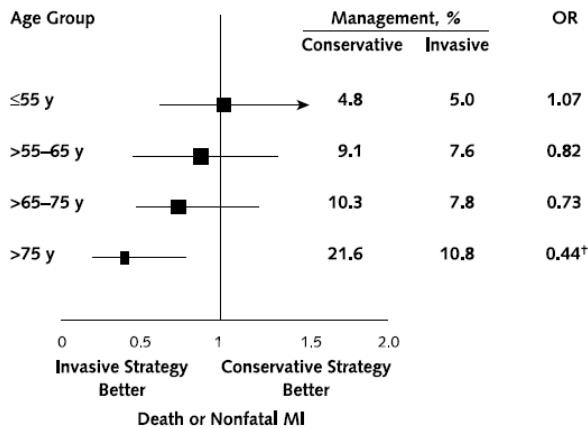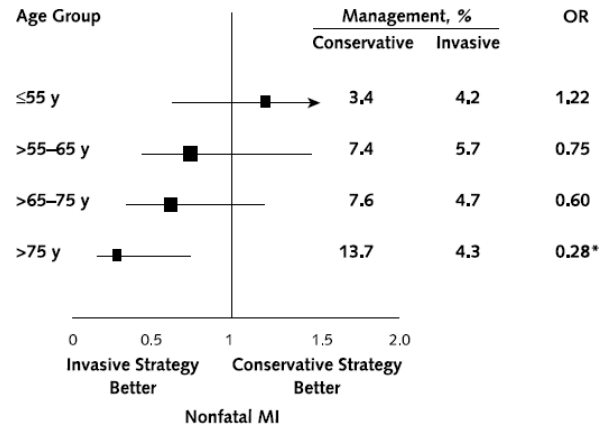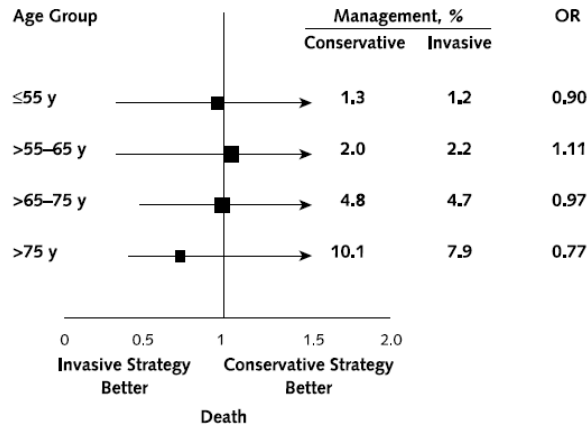
Unstable angina/NSTEMI

- CRUSADE registry
  - 56963 patients in 443 US hospitals with NSTE-ACS
  - Lower risk of in-hospital mortality was observed among elderly patients treated with early invasive strategy (<48h after admission) compared to conservative approach (OR 0.79)

- Despite data both from registries and clinical trials indicative for a better outcome in the elderly with NSTE-ACS with an invasive strategy, most older patients do not undergo revascularization

JACC 2005; 46: 1479-87
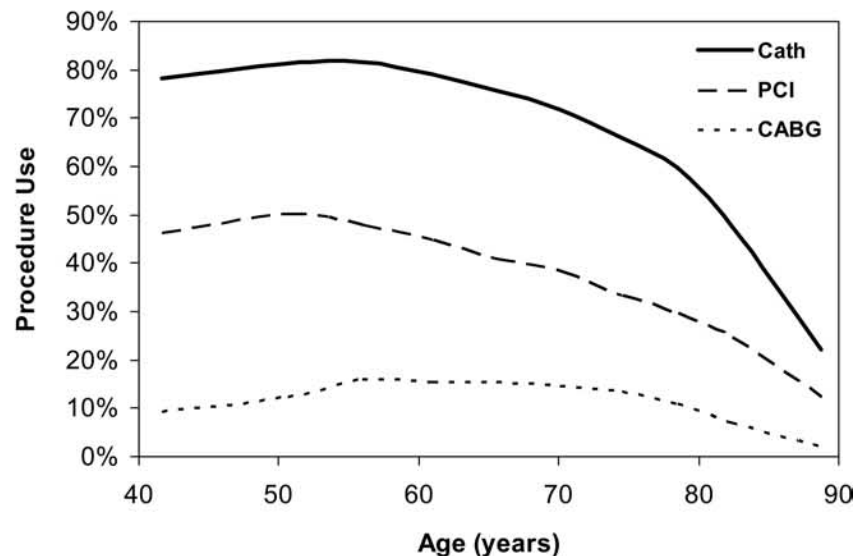
- The same holds true for elderly patients compared with NSTEMI:
  - Underrepresentation in clinical trials
  - Often atypical clinical presentation leading to a delay in diagnosis
  - Increasing mortality with increasing age
  - Undertreatment
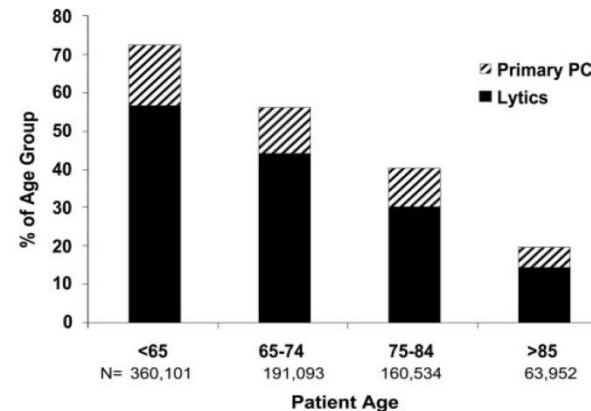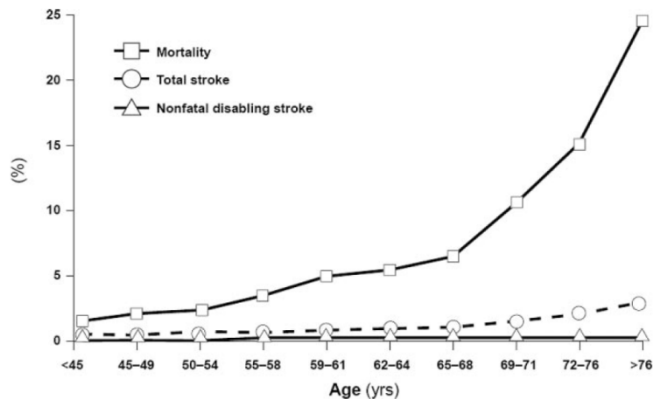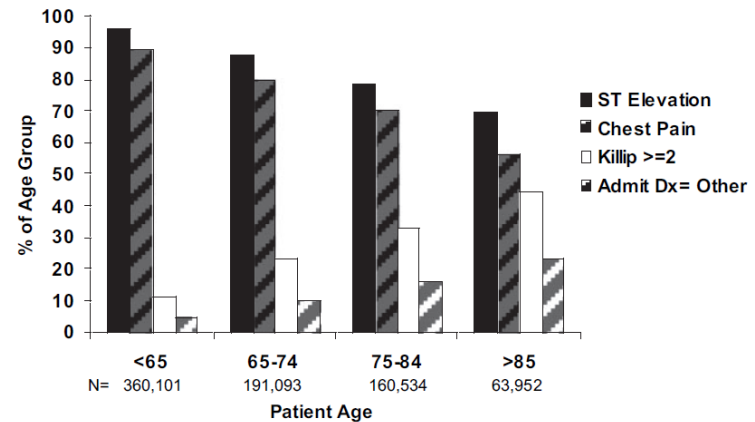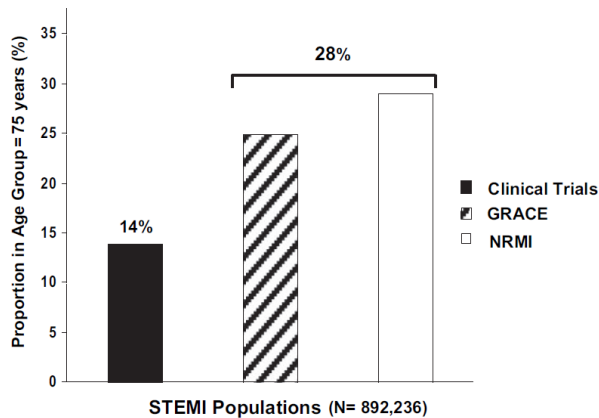
- There is lack of STEMI trials specifically investigating the treatment of STEMI in the elderly. It mostly concerns the comparison between PCI vs. thrombolysis. In general (besides of a few random exceptions) the benefits observed with PCI compared to thrombolysis in the treatment of STEMI are the same compared to younger patients as shown in a recent meta-analysis (n= 6763, 22 trials)
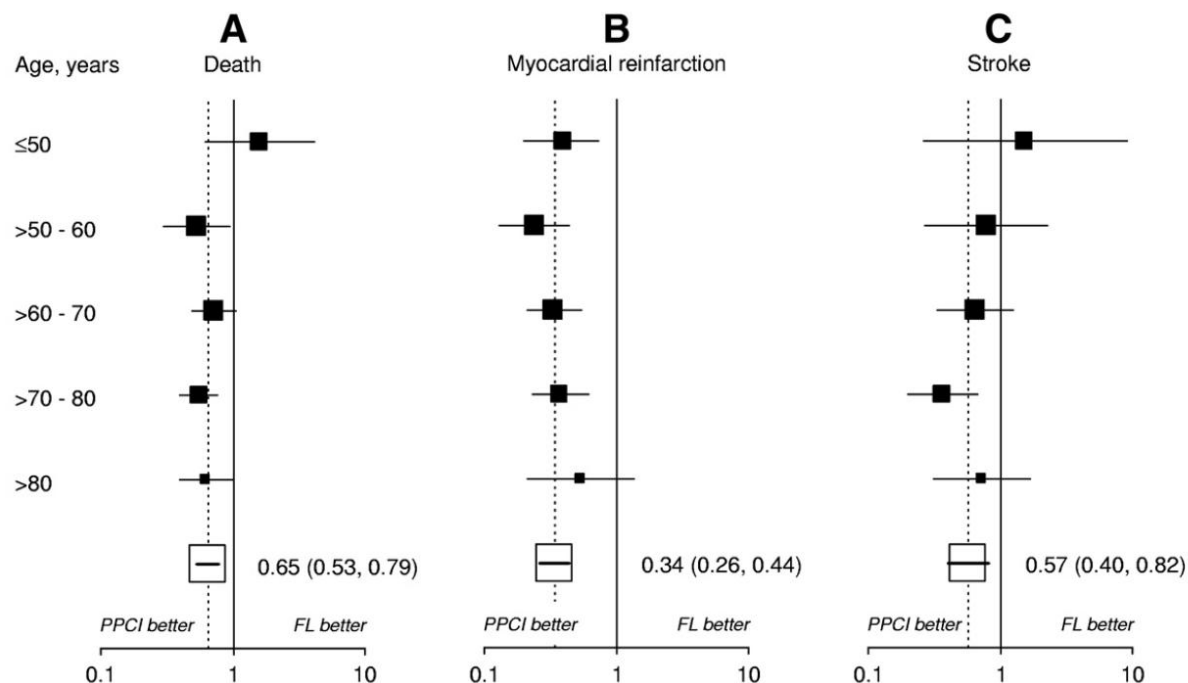

Figure 1. Incidence of Death, MI, Stroke/Treatment According to Age

Relation between allocated treatment (primary percutaneous coronary intervention [PPCI] vs. fibrinolysis [FL]) and the incidence of death (**A**), myocardial infarction (MI) (**B**), and stroke (**C**) at 30 days according to age category. Data represent adjusted odds ratios and 95% confidence intervals.

- Importantly, guidelines set no age-limit on the optimal treatment of STEMI. So, increasing age cannot be seen as a contra-indication or as a drawback for a full invasive approach.

**Table 11   Primary PCI: indications and procedural aspects**

Recommendations	Class[a]	Level[b]	Ref[c]
Indications for primary PCI			
Primary PCI is the recommended reperfusion therapy over fibrinolysis if performed by an experienced team within 120 min of FMC.	I	A	69, 99
Primary PCI is indicated for patients with severe acute heart failure or cardiogenic shock, unless the expected PCI related delay is excessive and the patient presents early after symptom onset.	I	B	100
Procedural aspects of primary PCI			
Stenting is recommended (over balloon angioplasty alone) for primary PCI.	I	A	101, 102
Primary PCI should be limited to the culprit vessel with the exception of cardiogenic shock and persistent ischaemia after PCI of the supposed culprit lesion.	IIa	B	75, 103–105
If performed by an experienced radial operator, radial access should be preferred over femoral access.	IIa	B	78, 79
If the patient has no contraindications to prolonged DAPT (indication for oral anticoagulation, or estimated high long-term bleeding risk) and is likely to be compliant, DES should be preferred over BMS.	IIa	A	80, 82, 106, 107
Routine thrombus aspiration should be considered.	IIa	B	83–85
Routine use of distal protection devices is not recommended.	III	C	86, 108
Routine use of IABP (in patients without shock) is not recommended.	III	A	97, 98

Pharmacology

- A variety of traditional and novel antithrombotic (antithrombin and antiplatelet) agents are currently available to minimize procedure-related thrombotic events , although their selection more often reflects consideration of bleeding risk.

- Elderly patients are particularly at high risk of bleeding, predominantly due to decreased renal function and relative overdosage of antithrombotics.

- Type and dose of an antithrombotic agent need to be tailored to each individual patient undergoing PCI according to the anticipated bleeding risk. Risk algorithms could be of particular interest:

Variable	Points Assigned
ACS type	
ST-elevation MI	10
Non–ST-elevation MI/unstable angina	3
Cardiogenic shock	8
Female gender	6
Previous CHF	5
No previous PCI	4
NYHA class IV CHF	4
Peripheral vascular disease	2
Age, y	
66–75	2
76–85	5
≥85	8
Estimated glomerular filtration rate	1 (per 10 unit decrease if <90)

CHF indicates congestive heart failure; NYHA, New York Heart Association.
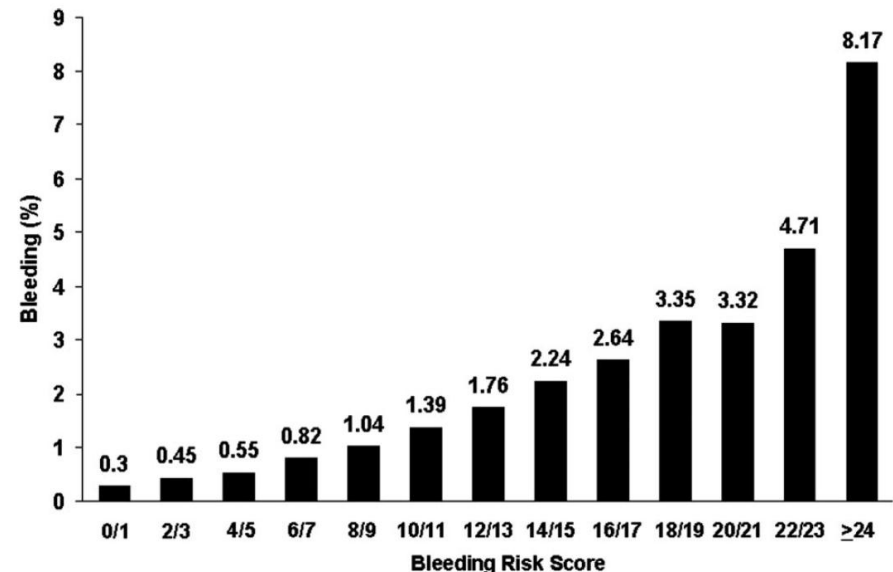
Conclusion

- There is an important greying demographic evolution in the Western world and within a few decades also in the Asian continent. Since the incidence of coronary artery disease augments exponentially with increasing age, PCI will be done more and more in the (very) elderly.

- Multiple physiological changes occurring with age augment the risk of adverse outcomes with PCI, both in elective and urgent setting. This means there is a well known peri-interventional mortality and morbidity risk associated with PCI in the elderly. This is often a reason physicians are reluctant of an invasive treatment of CAD in the older patient. However, in the last decade this peri-interventional risk is decreasing due to better patient selection and evolution of revascularization techniques.

- Furthermore there can be a prognostic benefit and there is certainly a very significant symptomatic benefit in the elderly with PCI that is even more pronounced compared to younger patients predominantly due to the more important coronary disease burden in older patients.

- All this means an invasive strategy should not be withheld on the basis of an advanced age only, but should be done taking into account co-moborbidities, clinical presentation and patient's wishes.