

# Improving STEMI outcomes in Denmark

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Denmark

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# Presenter Disclosure Information

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Study funded by Fondation Leducq

***Michael Rahbek Schmidt***

**The following relationships exist related to this presentation:**

***Shareholder in CellAegis inc.***

# Improving STEMI outcomes

Treating faster

Treating better

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

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## A Comparison of Coronary Angioplasty with Fibrinolytic Therapy in Acute Myocardial Infarction

Henning R. Andersen, M.D., Torsten T. Nielsen, M.D., Klaus Rasmussen, M.D., Leif Thuesen, M.D.,  
Henning Kelbaek, M.D., Per Thayssen, M.D., Ulrik Abildgaard, M.D., Flemming Pedersen, M.D.,  
Jan K. Madsen, M.D., Peer Grande, M.D., Anton B. Villadsen, M.D., Lars R. Krusell, M.D., Torben Haghfelt, M.D.,  
Preben Lomholt, M.D., Steen E. Husted, M.D., Else Vigholt, M.D., Henrik K. Kjaergard, M.D.,  
and Leif Spange Mortensen, M.Sc., for the DANAMI-2 Investigators\*

# DENMARK

DANAMI-2

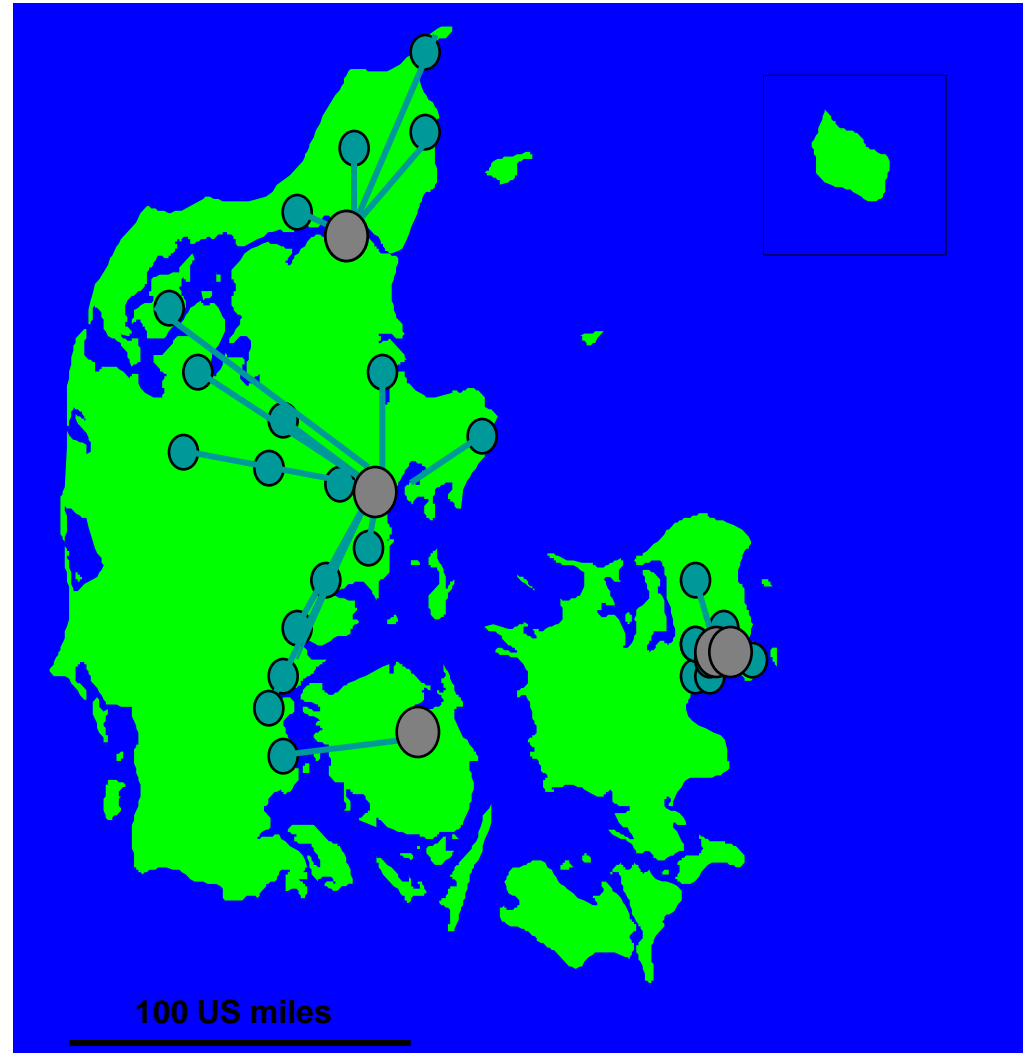
5.5 mill. inhabitants

5 PCI centers

24 referral hospitals

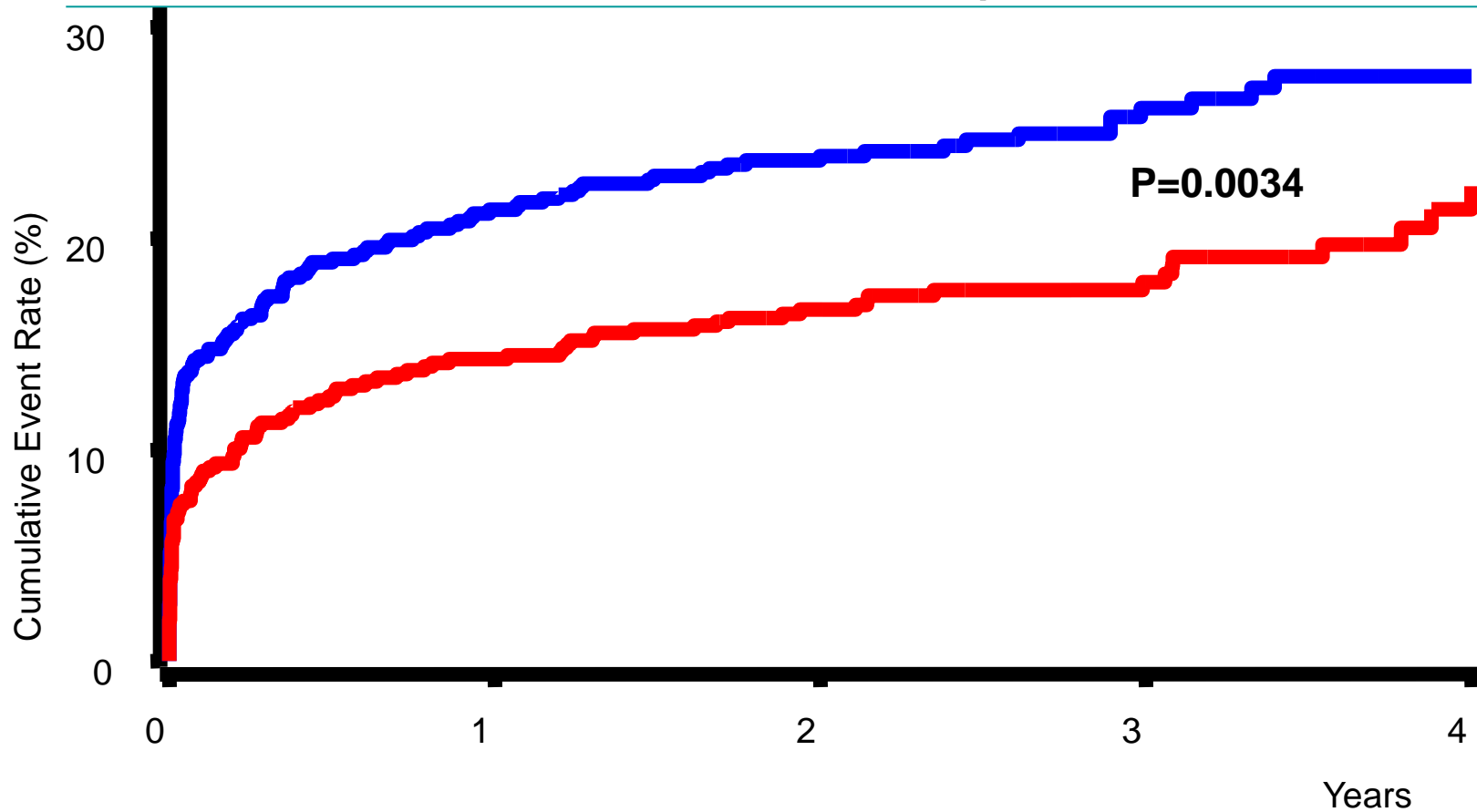
62% of Danish  
population

Transport distance  
up to 95 US miles  
(median 31 miles)



# Combined End Point, Longterm Followup

1,129 Patients from Referral Hospitals



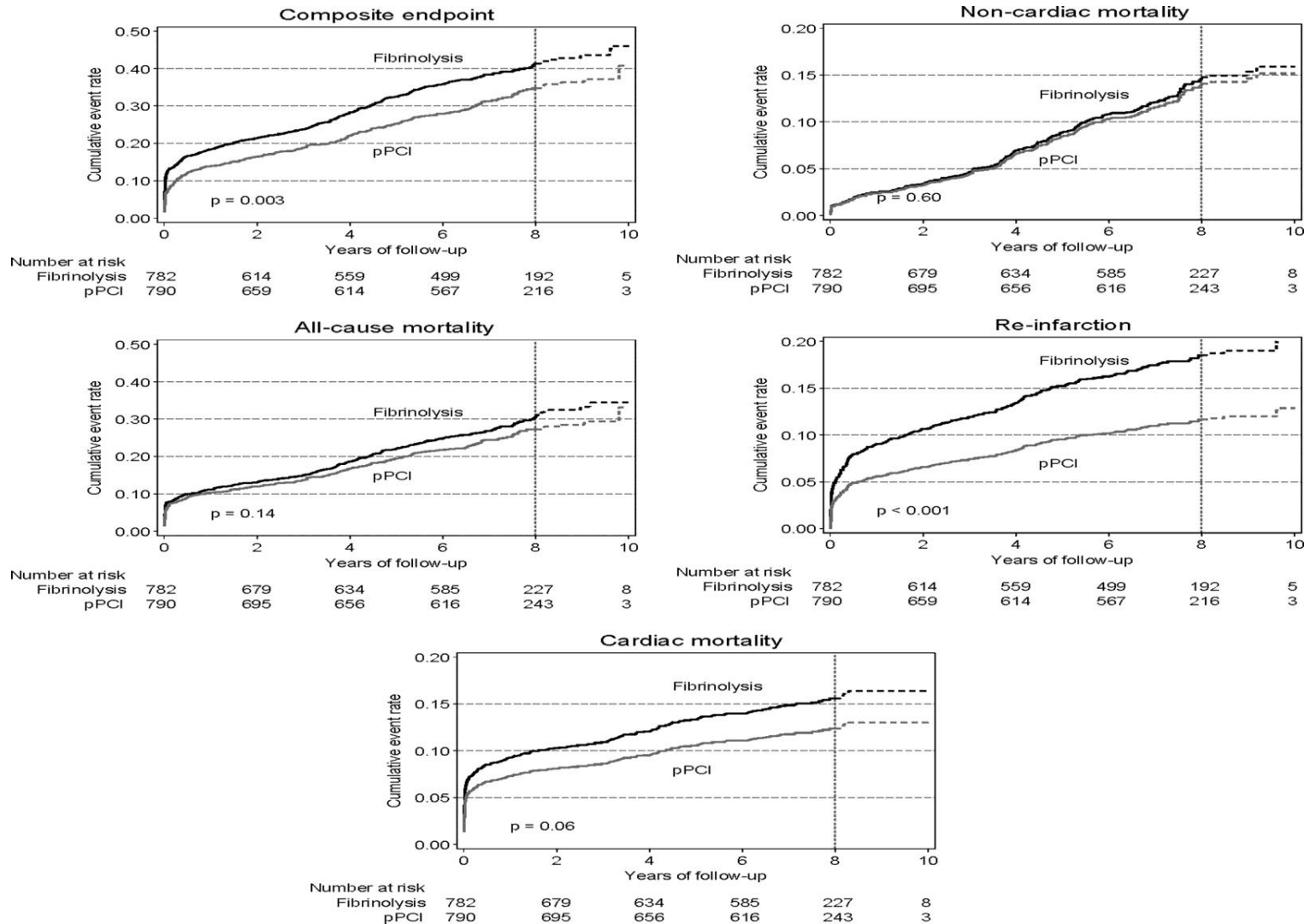
Combined end point: Death or reinfarction or stroke

— Fibrinolysis

— PCI

Andersen et al. NEJM 2003

# Long-term clinical outcome in the DANAMI-2 study



# Improving STEMI outcomes

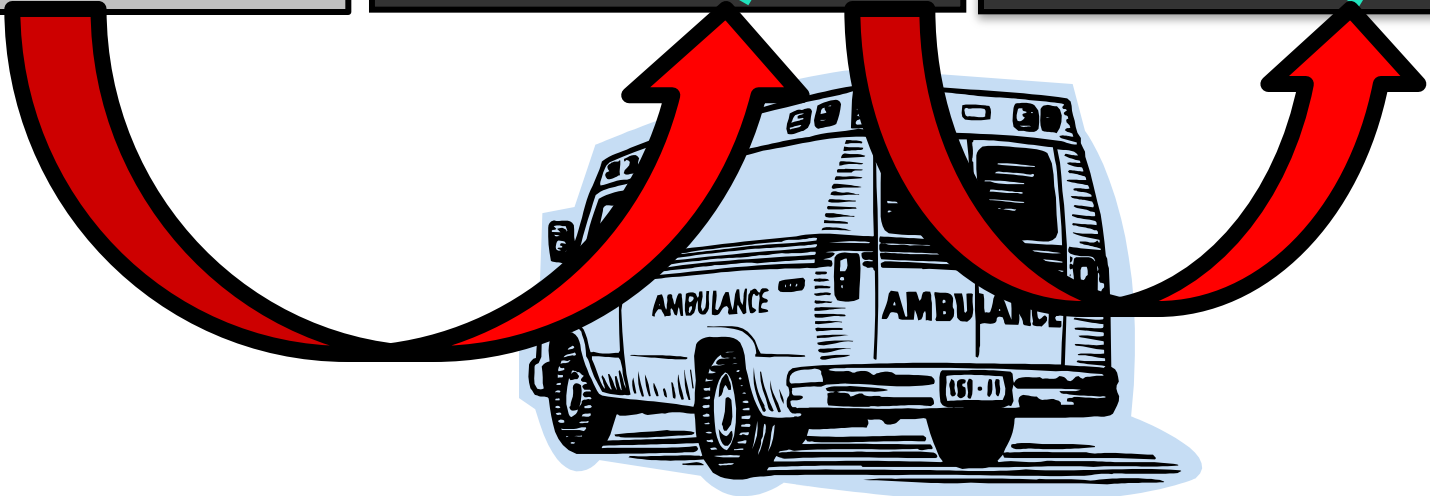
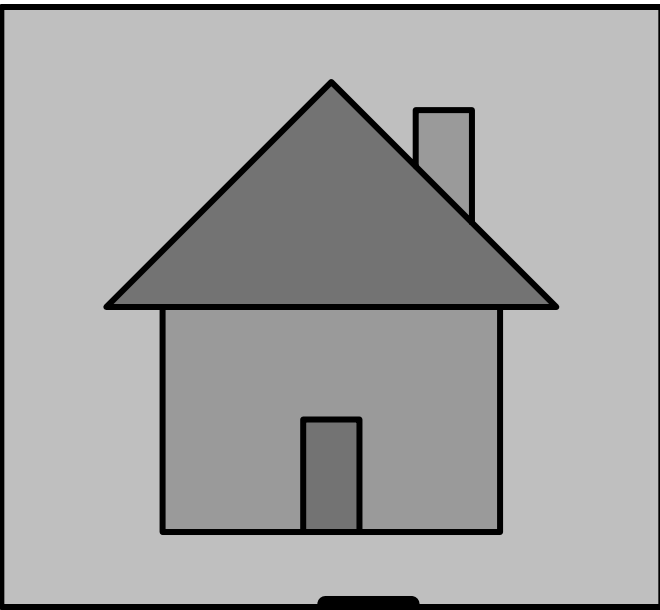
Treating faster



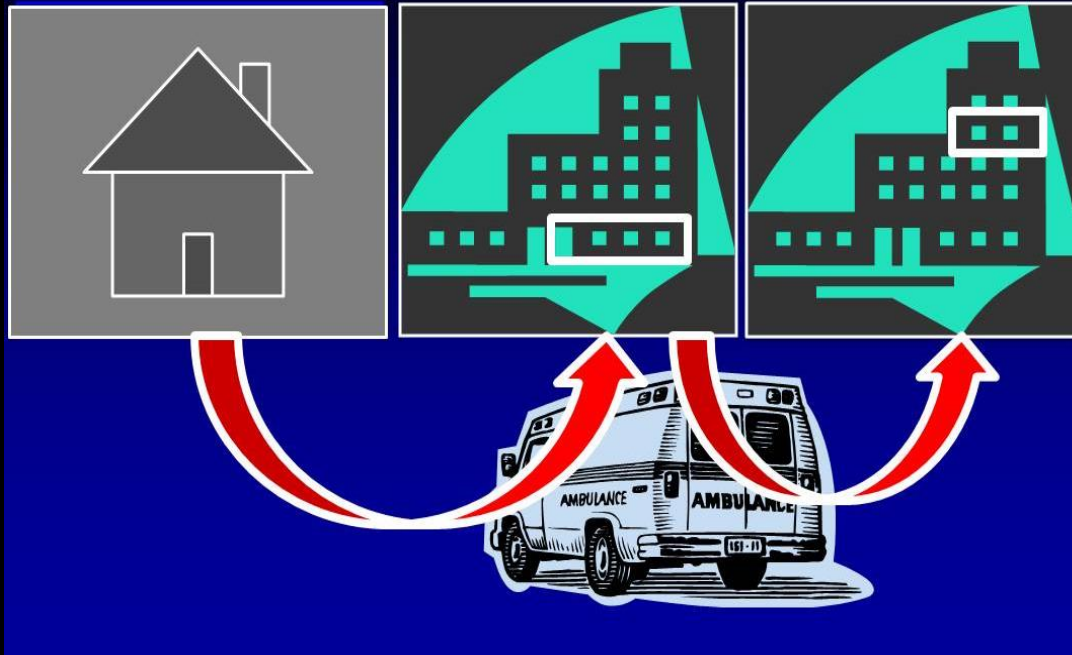
Home

Local hospital  
/ER

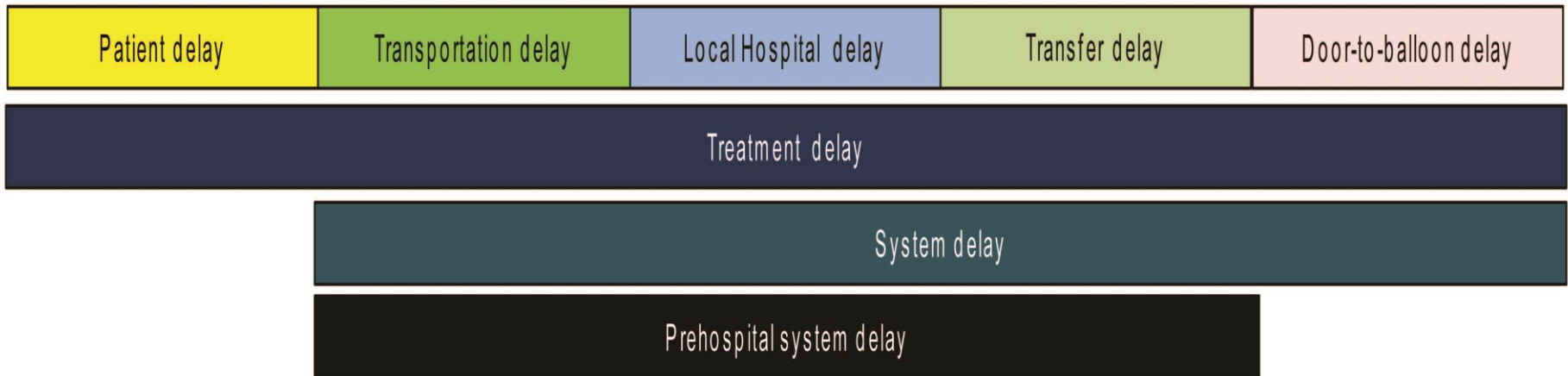
Cath. lab.



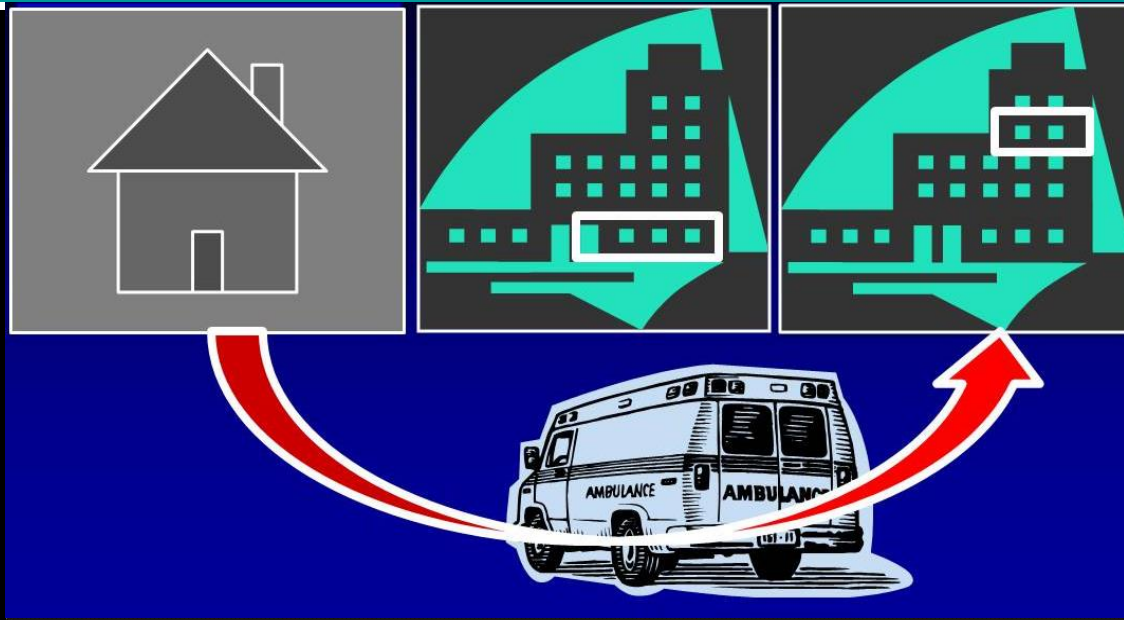
# Delay in pPCI



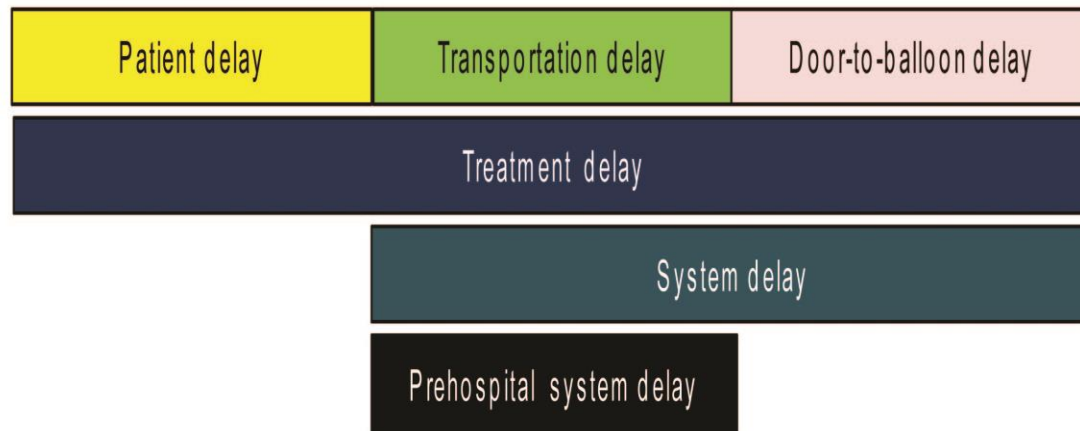
Patients transferred from local hospitals






# Reducing delay in pPCI - Final goal



Patients admitted directly at PCI-centre



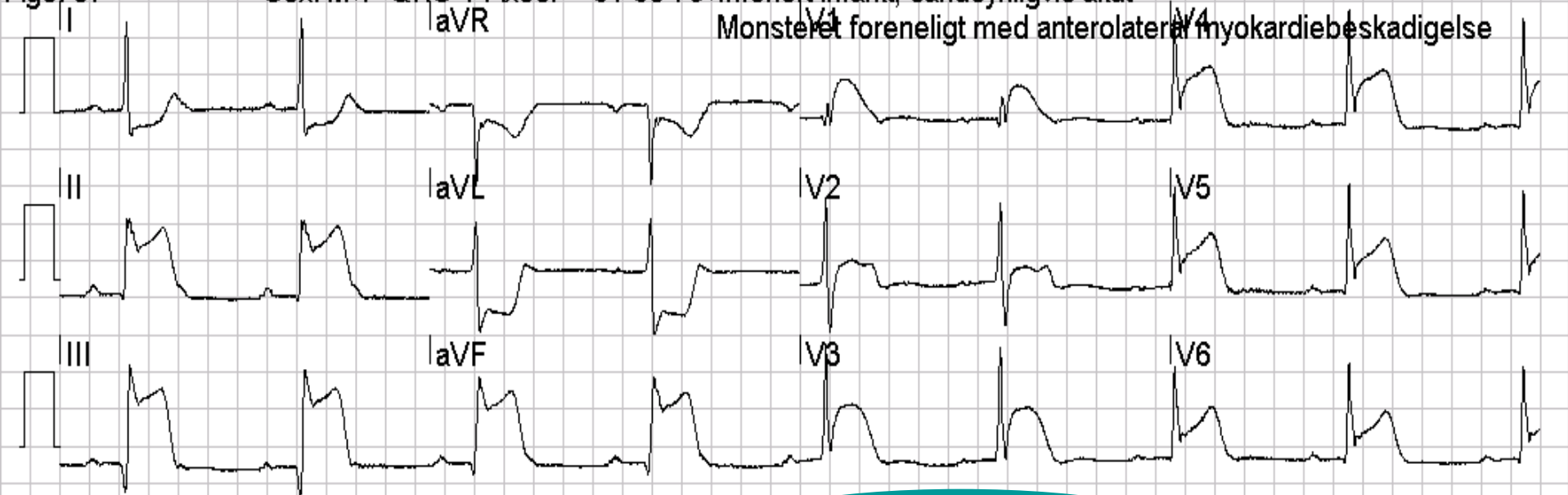
# Stepwise approach – alerting hospitals by telecardiology

-  **Interventional Hospital**
-  **Non-interventional Hospital**
-  **Scene of event**



# Telecardiology

Name: MADSEN;KNUD 12-Lead 1 HR 50bpm \*\*\* SUSPEKT FOR AKUT INFARKT \*\*\*  
ID: 2002112817262900 28-11-2002 17:39:08 Abnormt ekg \*\*Ubekræftet\*\*  
Patient ID: 020545-0165 PR 0.254s QRS 0.128s Sinusbradykardi med 1. grads AV blok  
Incident ID: QT/QTc: 0.454s/0.413s Uspecifikt intraventrikul'rt blok  
Age: 57 Sex: M P-QRS-T Axes: 61 68 79 Inferiort infarkt, sandsynligvis akut  
Monstret foreneligt med anterolateral myokardiebeskadigelse



x1.0 .05-150Hz 25mm/sec

TLF-21215072 RANDERS-3213 011371-090 LP1212650065







# The County of Aarhus:



**Interventional hospital**



**Non-interventional hospital**

**Scene of event**



# Telecardiology

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*Journal of Internal Medicine* 2002; 252: 412–420

## Telemedicine used for remote prehospital diagnosing in patients suspected of acute myocardial infarction

C. J. TERKELSEN<sup>1,2</sup>, B. L. NØRGAARD<sup>2</sup>, J. F. LASSEN<sup>2</sup>, J. C. GERDES<sup>2</sup>, J. P. ANKERSEN<sup>3</sup>, F. RØMER<sup>1</sup>, T. T. NIELSEN<sup>2</sup> & H. R. ANDERSEN<sup>2</sup>

*From the <sup>1</sup>Department of Internal Medicine, Silkeborg Central Hospital, Silkeborg; <sup>2</sup>Department of Cardiology, Skejby University Hospital, Aarhus N; and <sup>3</sup>Falek, Silkeborg; Denmark*

**Conclusions.** It was technically feasible to use telemedicine for remote prehospital diagnosing of patients suspected of AMI. Patients subjected to prehospital diagnosing had shorter door-to-needle times compared with a prospective control group.



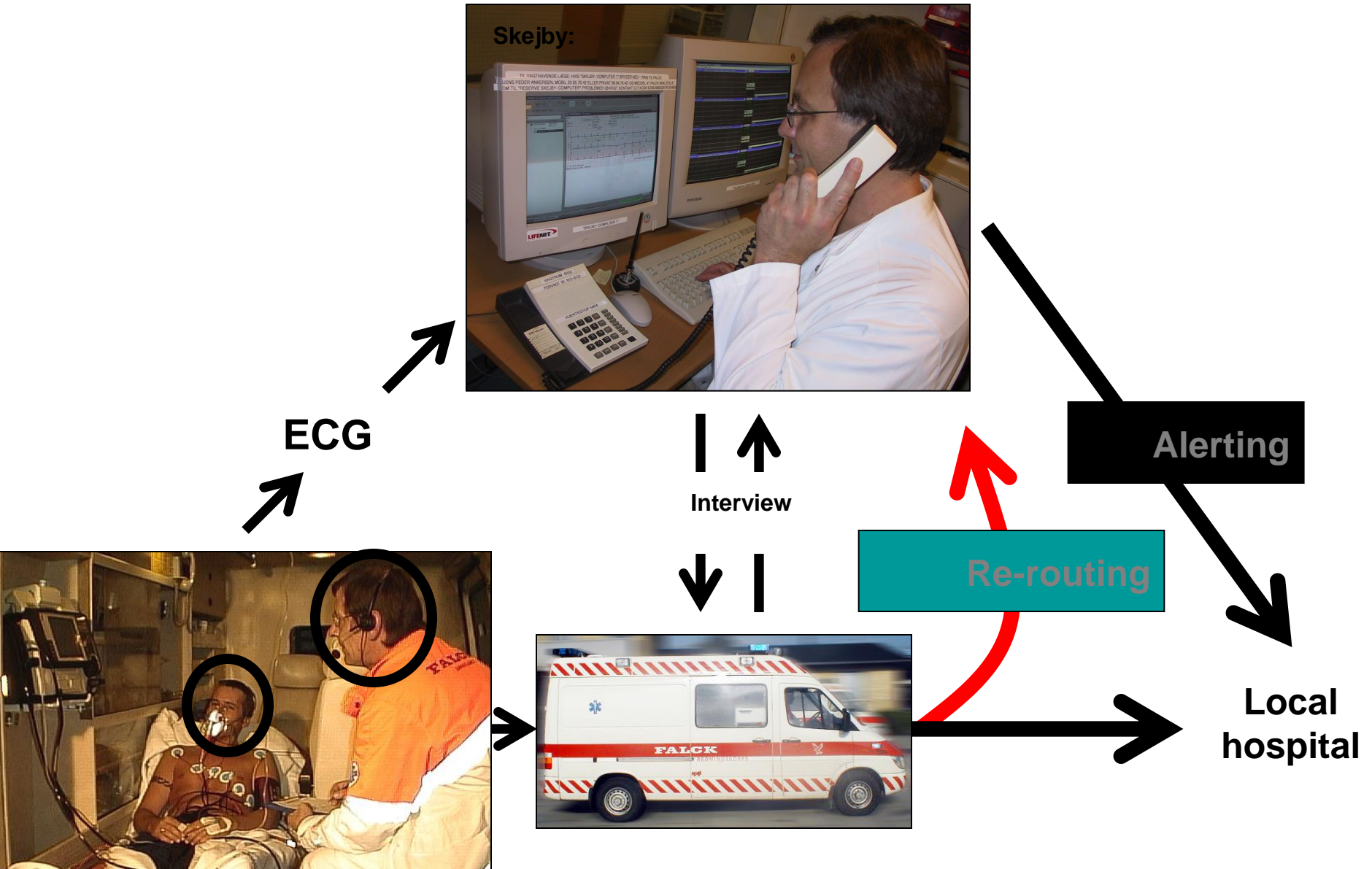
# Extended telecardiology



ECG



# Extended telecardiology



# Current strategy



**Interventional Hospital**



**Non-interventional Hospital**



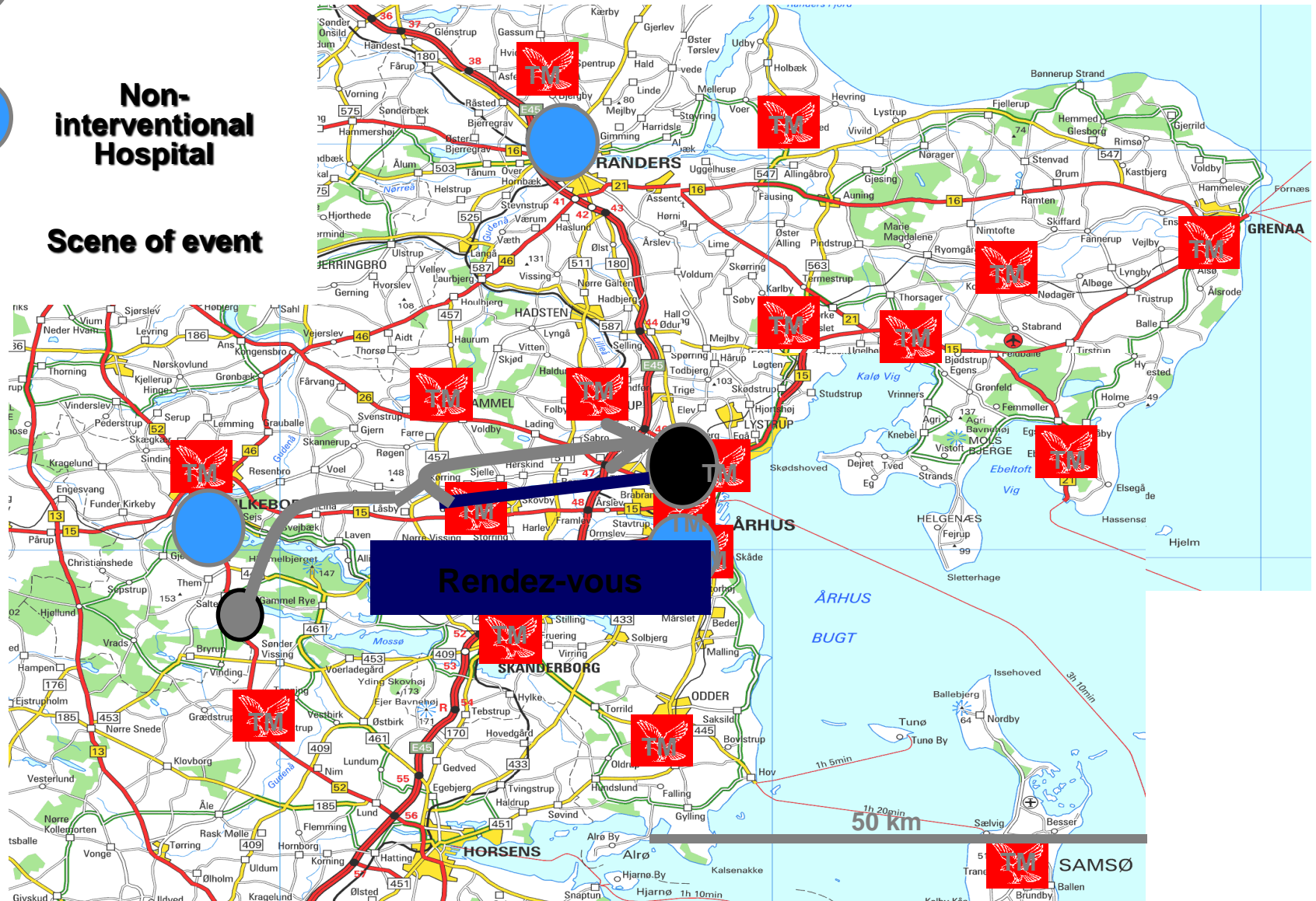
**Scene of event**



**Telemedicine ambulances**

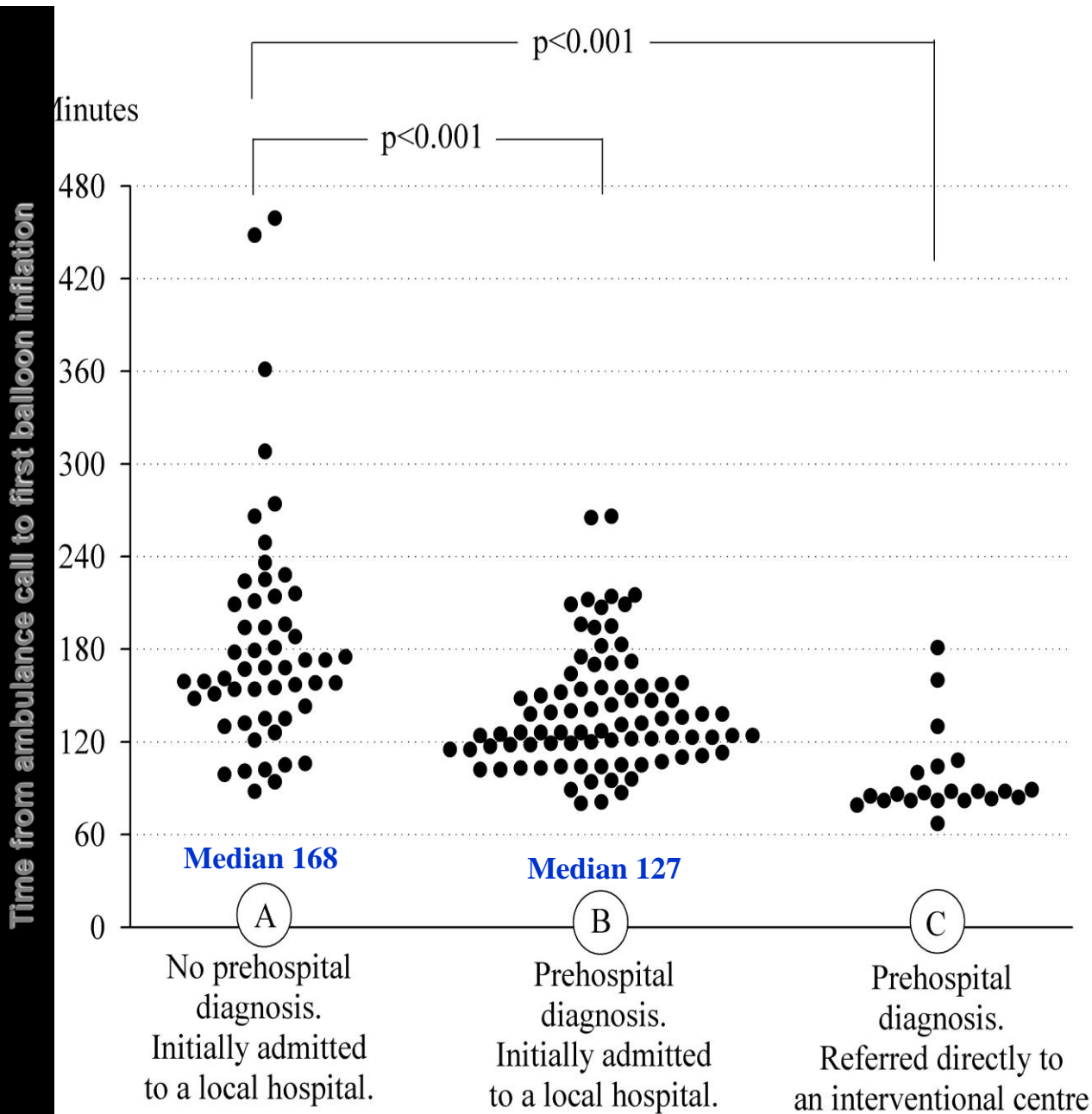


**Regular ambulances**

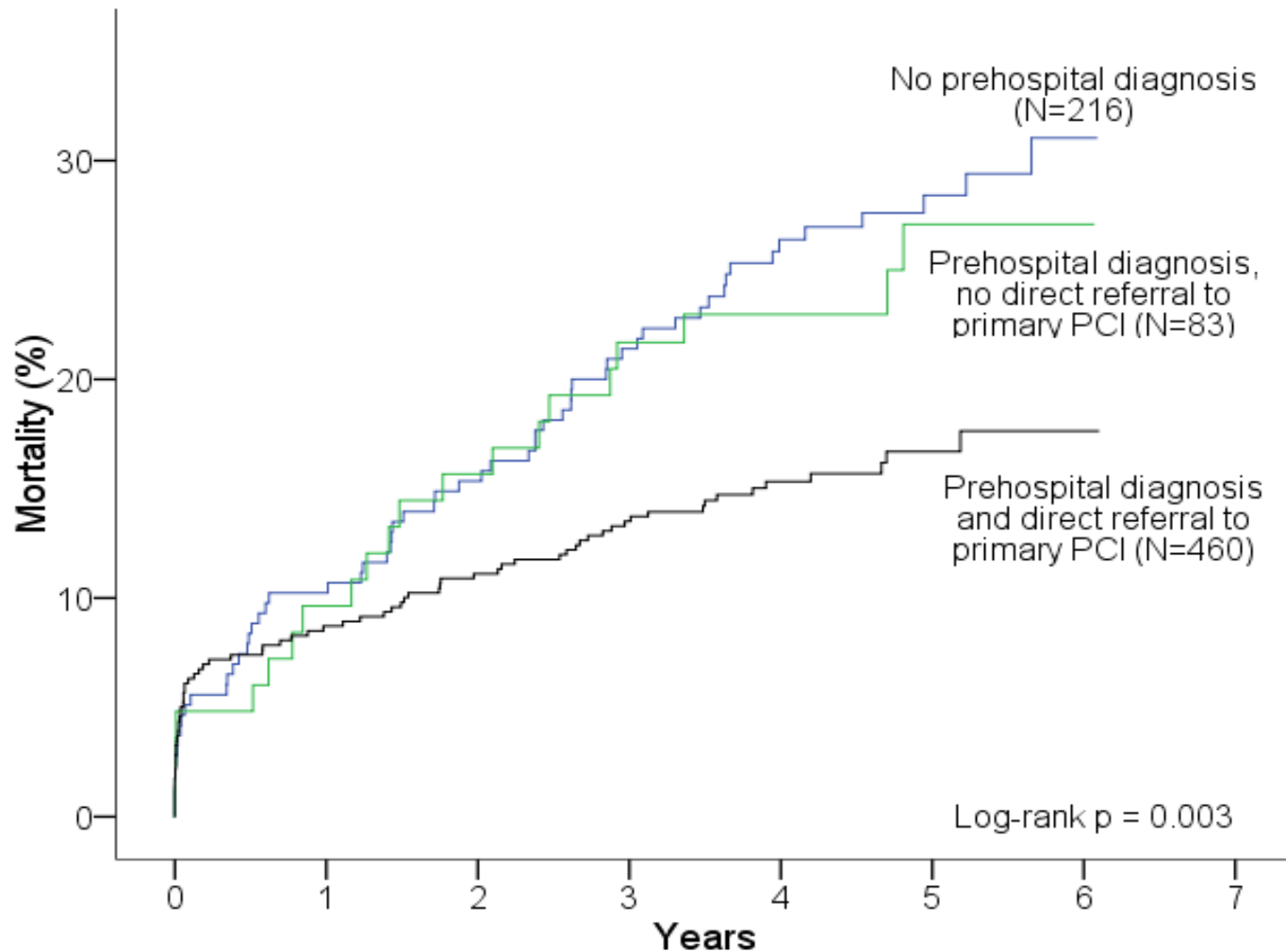




# Triage to cath. lab.



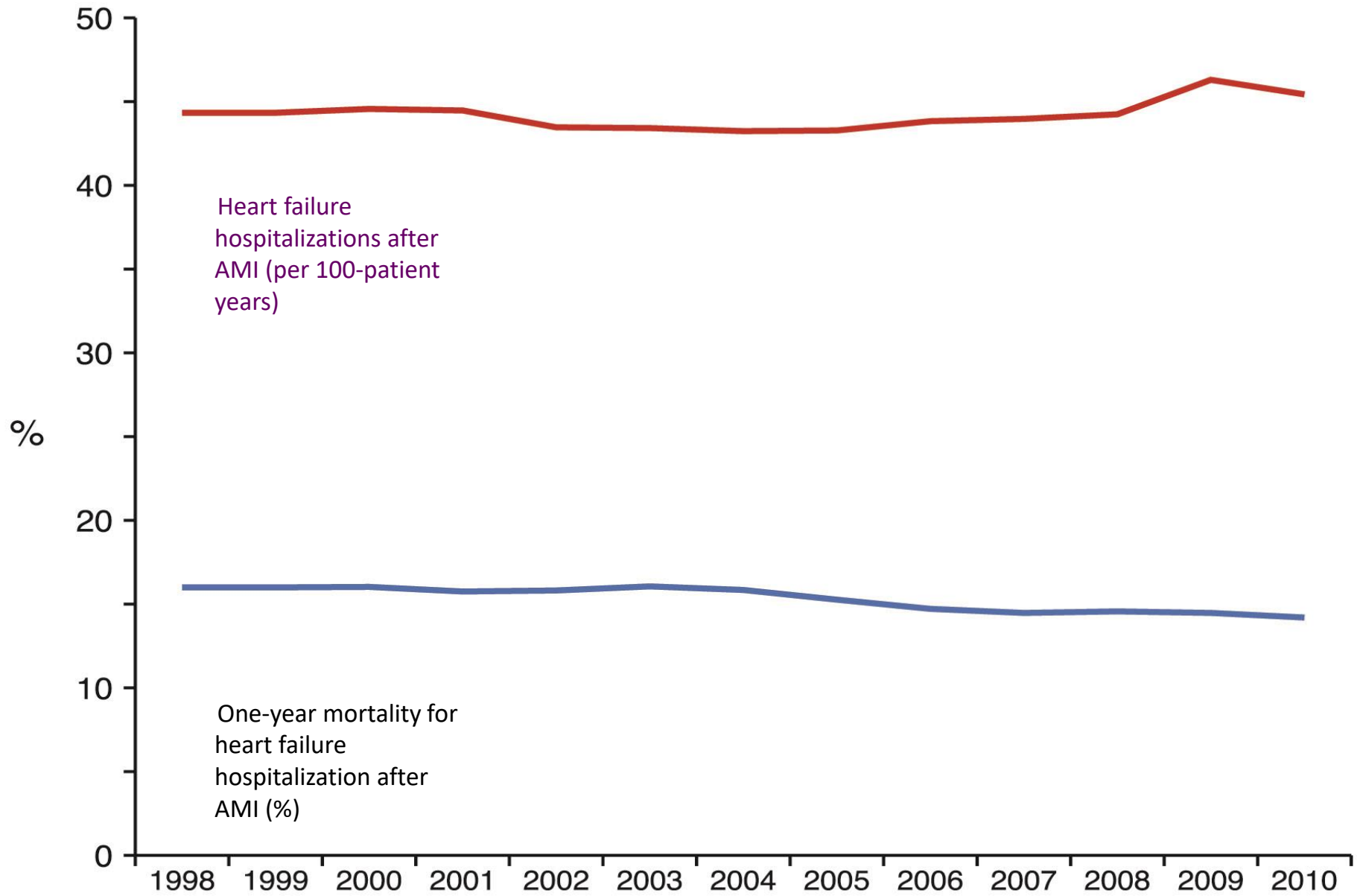
# Impact on mortality



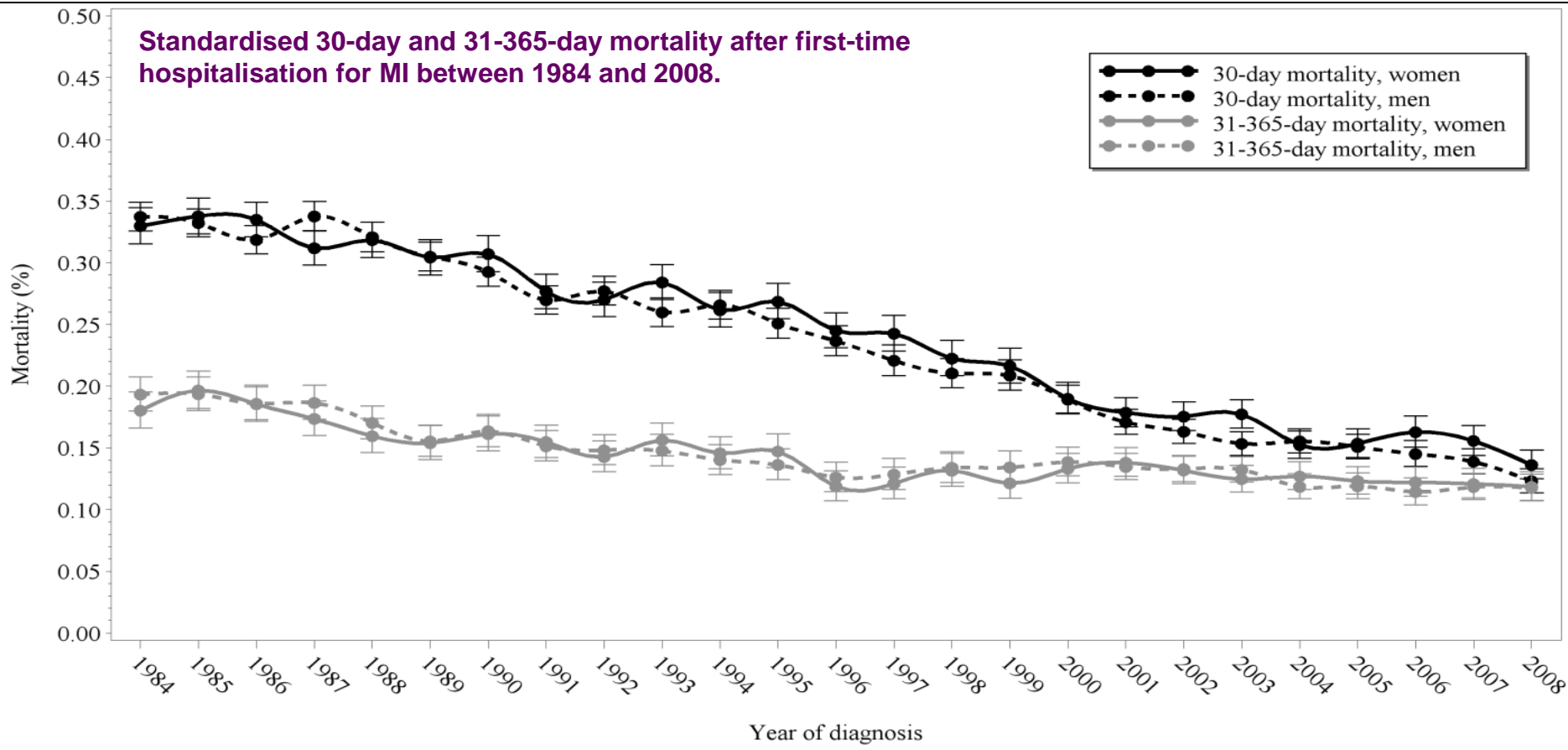
# Summary

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- **Prehospital diagnosis of STEMI**  
Telemedicine
- **Direct transportation of Patients to primary PCI**  
Bypassing local non-invasive hospitals  
Bypassing CCU and ER at the PCI-centre.
- **PCI centre organisation**  
24-7 service, short activation time of card. lab. personel  
(door-to-balloon-time <30 min.)
- **Reduces mortality**



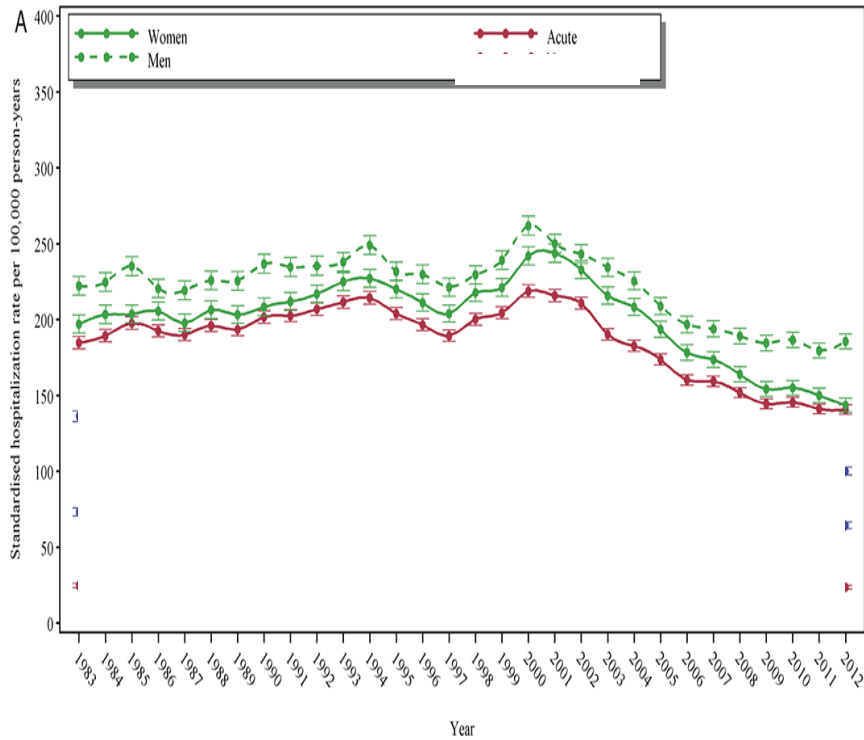
# Mortality from MI



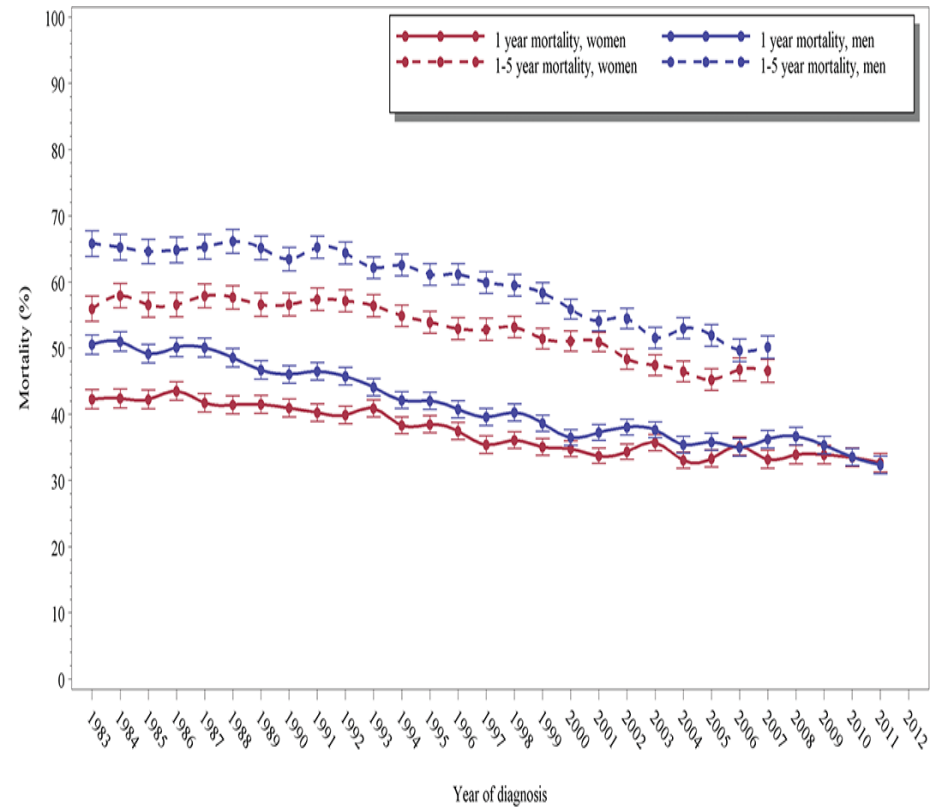


# Trends in heart failure in DK

## Incidence



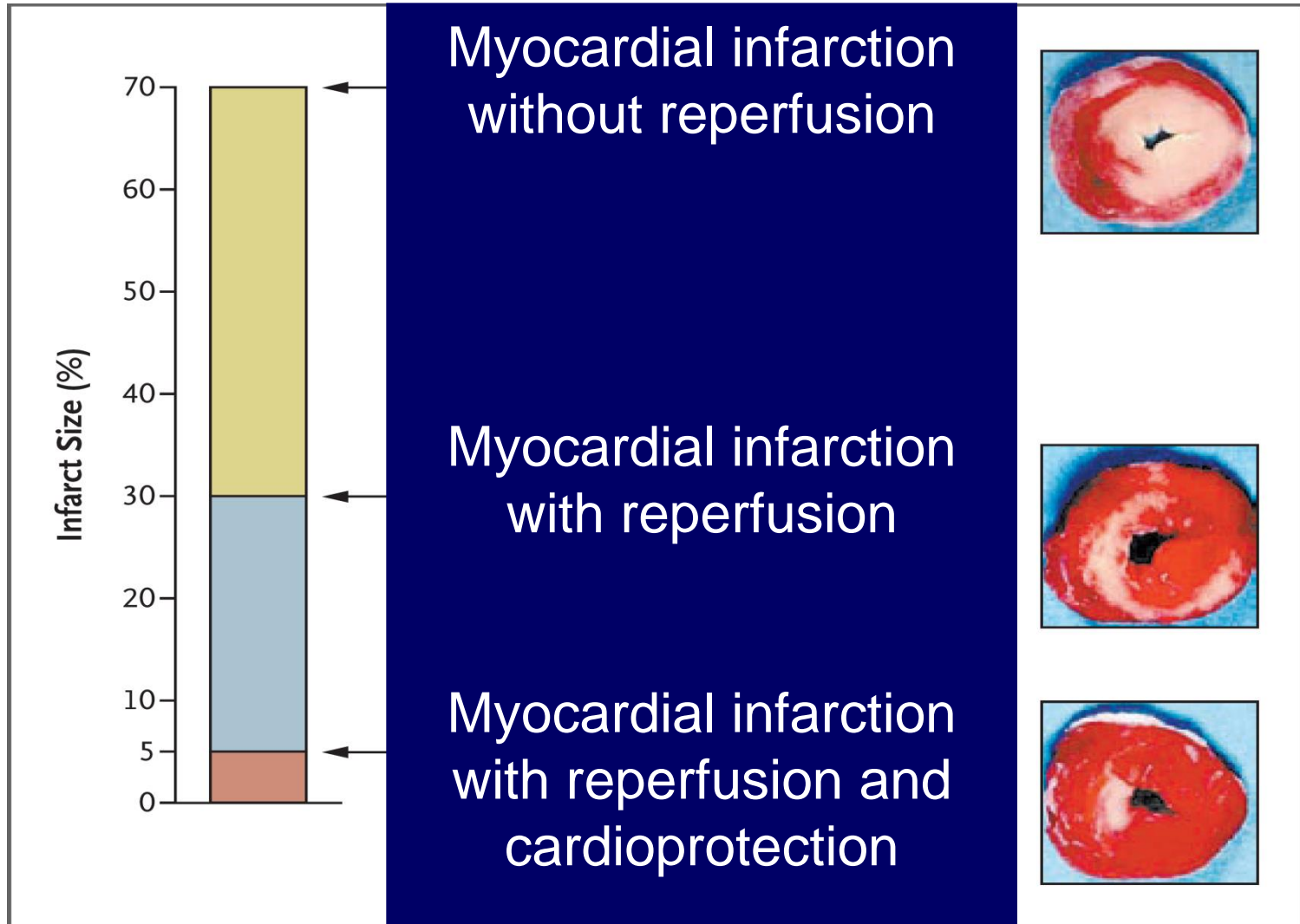
## Mortality



R 6000

Treating better

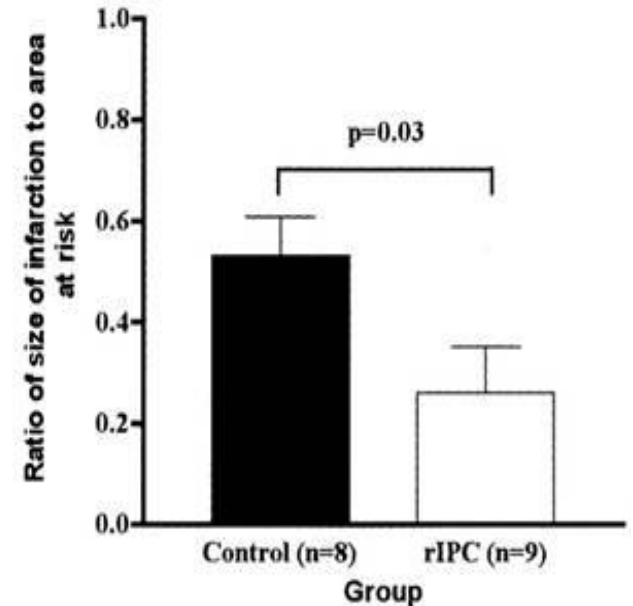
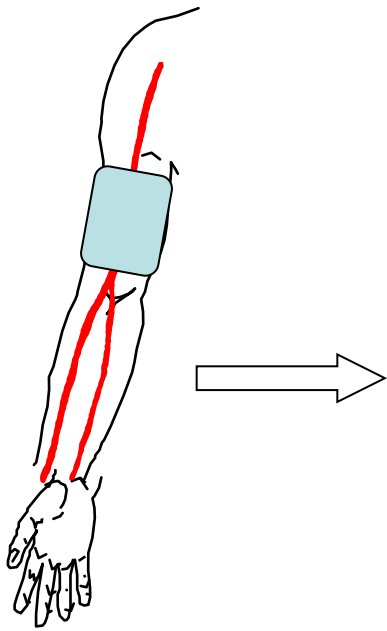
# Experimental Theory



*Murry et al, Circulation, 1986*

*Yellon and Hausenloy, NEJM, 2007*

# Remote Preconditioning

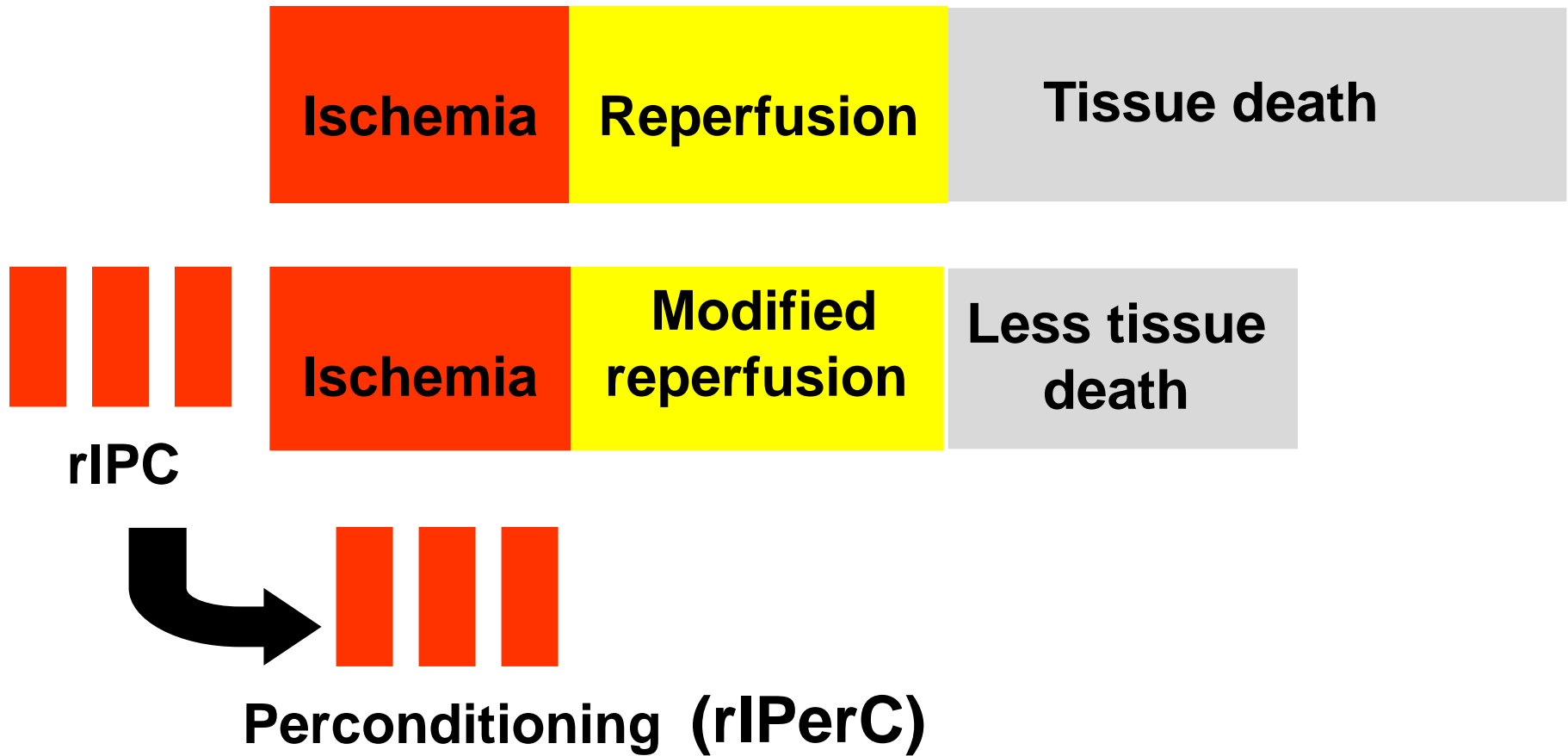


Four cycles of 5 minutes of upper limb ischemia induced by blood pressure cuff inflation (200 mm Hg)

*Kharbanda R et al. Circulation 2002;106:2881-3*

# Remote Perconditioning Hypothesis

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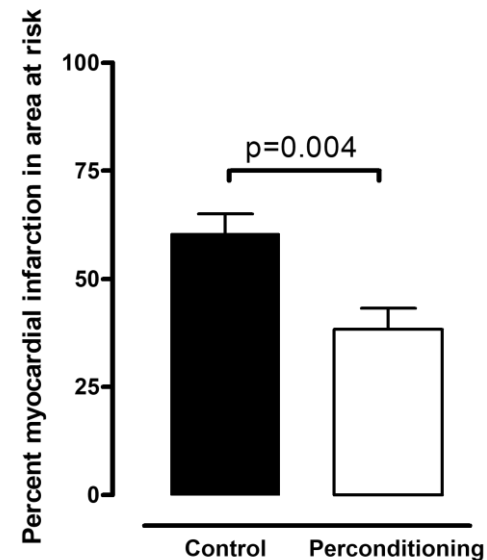
*Schmidt et al, Am J Physiol, 2007; 292:H1883-90*

# Intermittent peripheral tissue ischemia during coronary ischemia reduces myocardial infarction through a $K_{ATP}$ -dependent mechanism: first demonstration of remote ischemic preconditioning

M. R. Schmidt,<sup>1,2</sup> M. Smerup,<sup>1</sup> I. E. Konstantinov,<sup>2</sup> M. Shimizu,<sup>2</sup> J. Li,<sup>2</sup> M. Cheung,<sup>2</sup> P. A. White,<sup>3</sup> S. B. Kristiansen,<sup>1</sup> K. Sorensen,<sup>1</sup> V. Dzavik,<sup>4</sup> A. N. Redington,<sup>2</sup> and R. K. Kharbanda<sup>3,4,5</sup>

<sup>1</sup>Aarhus University Hospital, Skejby, Denmark; <sup>2</sup>Hospital for Sick Children and <sup>4</sup>University Health Network, Toronto, Ontario, Canada; and <sup>3</sup>Papworth Hospital and <sup>5</sup>University of Cambridge, Cambridge, United Kingdom

Submitted 11 June 2006; accepted in final form 10 December 2006



# Clinical study (CONDI)

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- AIM:
  - To determine whether RIC in the ambulance during transfer to primary PCI reduces myocardial reperfusion injury and infarct size in patients with first STEMI

# Referral area

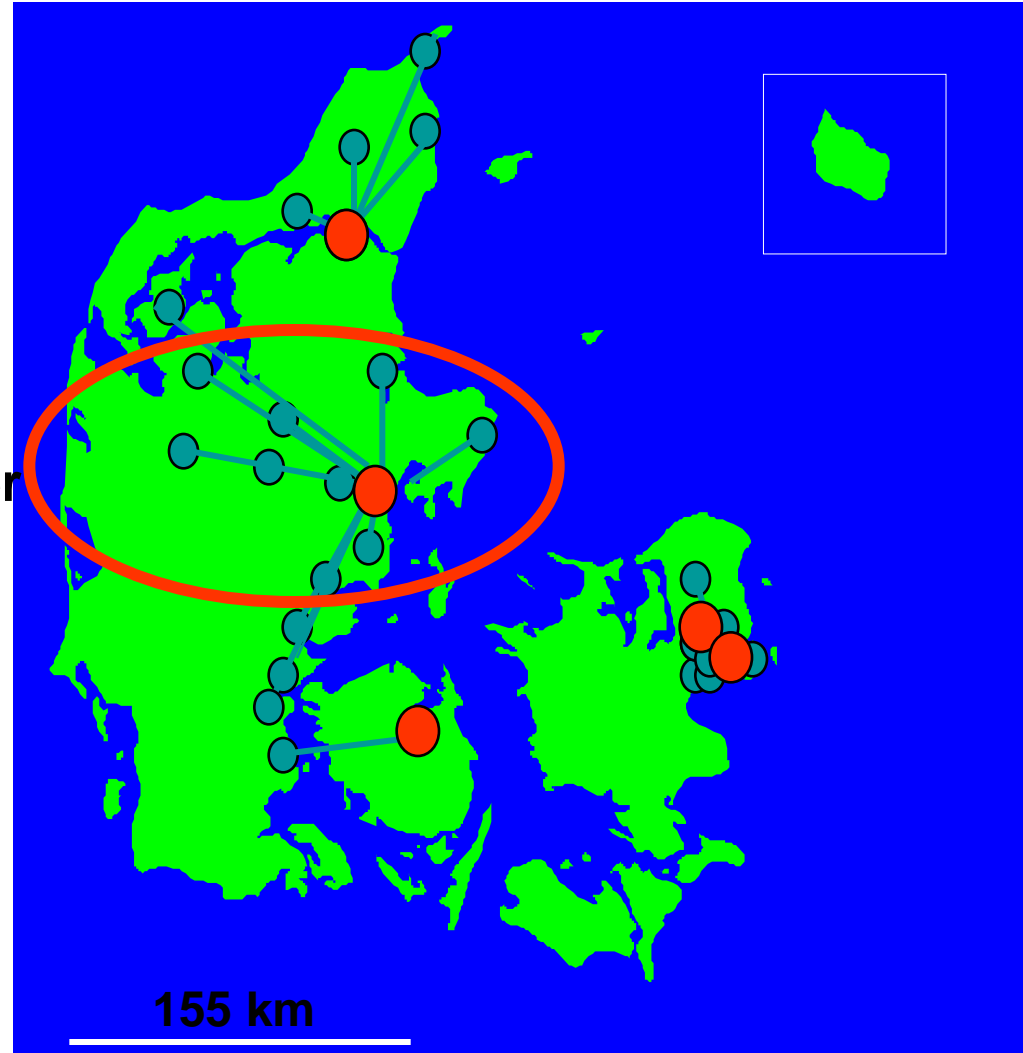
1.2 mill. inhabitants

600 STEMI per year

15% STEMI patients with first admission at the invasive center

85% STEMI patients are transferred for primary PCI

Maximum transport distance:  
150-160 km (100 miles)





# Patient Recruitment and Randomization



ECG

Randomization



Patient



Ambulance



# Inclusion Criteria

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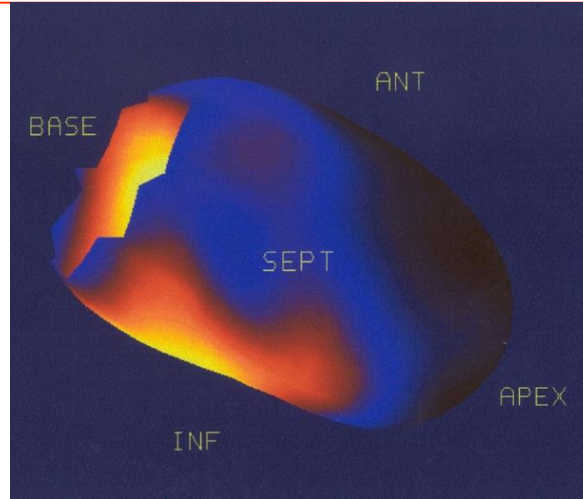
- Symptoms lasting  $> 30$  minutes and  $< 12$  hours
- ST-segment elevation  $\geq 0.1$  mV in 2 contiguous leads
- Age  $\geq 18$  years
- Informed consent

# Exclusion Criteria

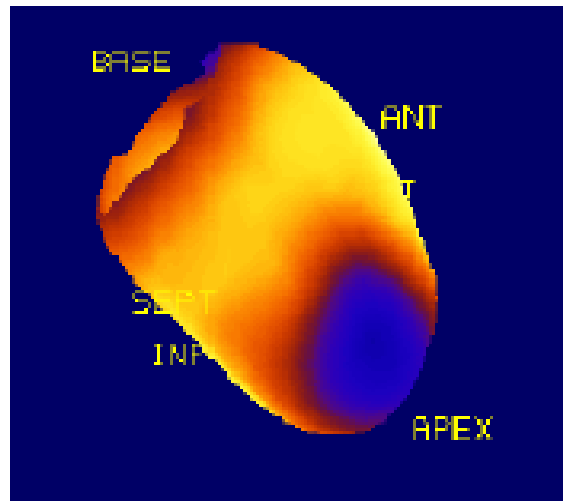
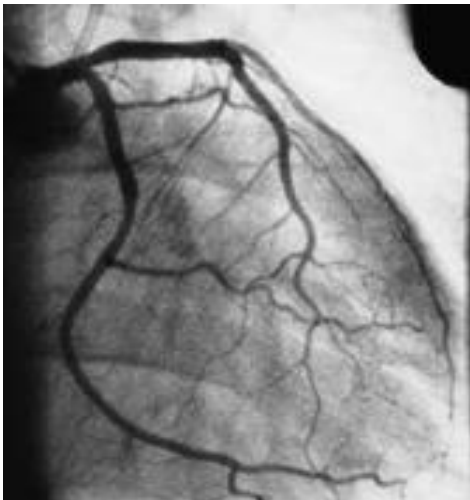
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- Previous myocardial infarction
- Left bundle-branch block
- Previous coronary-artery bypass surgery
- Patient treated with cooling, mechanical ventilation or patients who have had cardiac arrest
- Severe heart failure requiring intra-aortic balloon pump
- Patients with A-V-shunts (hemodialysis)

# Primary Endpoint: Myocardial Salvage Index



Acute scan:  
Area-at-risk  
(AAR)



**Salvage index =  
(AAR-FIS)/AAR**

One month scan:  
Final infarct size  
(FIS)

Pre-hospital  
randomization  
n=333

PCI only  
(n=167)

rIPerC  
(n=166)

22 did not meet  
inclusion criteria

19 did not meet  
inclusion criteria

PCI only  
(n=145)

rIPerC  
(n=147)

20 previous MI

21 previous MI

PCI only  
(n=125)

rIPerC  
(n=126)

3 dead

3 dead

11 consent withdrawn

11 consent withdrawn

1 CABG

3 CABG

110 final infarct size  
69 with salvage index

109 final infarct size  
73 with salvage index

# Clinical Characteristics

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	PCI only (n=125)	riPerC (n=126)	P Value
Age, year (mean)	62±12	63±12	0.71
Male sex (%)	75	77	0.71
Diabetes Mellitus (%)	9	9	0.97
Current smoker (%)	57	56	0.67
Hypertension (%)	31	39	0.01
Statin Tx (%)	20	16	0.47
Symptom to balloon time, min (median [IQR])	185 [134; 309]	188 [132; 302]	0.98

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# Remote ischaemic conditioning before hospital admission, as a complement to angioplasty, and effect on myocardial salvage in patients with acute myocardial infarction: a randomised trial

Hans Erik Bøtker, Rajesh Kharbanda, Michael R Schmidt, Morten Bettcher, Anne K Kaltoft, Christian J Terkelsen, Kim Munk, Niels H Andersen, Troels M Hansen, Sven Trautner, Jens Flensted Lassen, Evald Høj Christiansen, Lars R Kruse, Steen D Kristensen, Leif Thuesen, Søren S Nielsen, Michael Rehling, Henrik Toft Sørensen, Andrew N Redington, Torsten T Nielsen

## Summary

**Background** Remote ischaemic preconditioning attenuates cardiac injury at elective surgery and angioplasty. We tested the hypothesis that remote ischaemic conditioning during evolving ST-elevation myocardial infarction, and done before primary percutaneous coronary intervention, increases myocardial salvage.

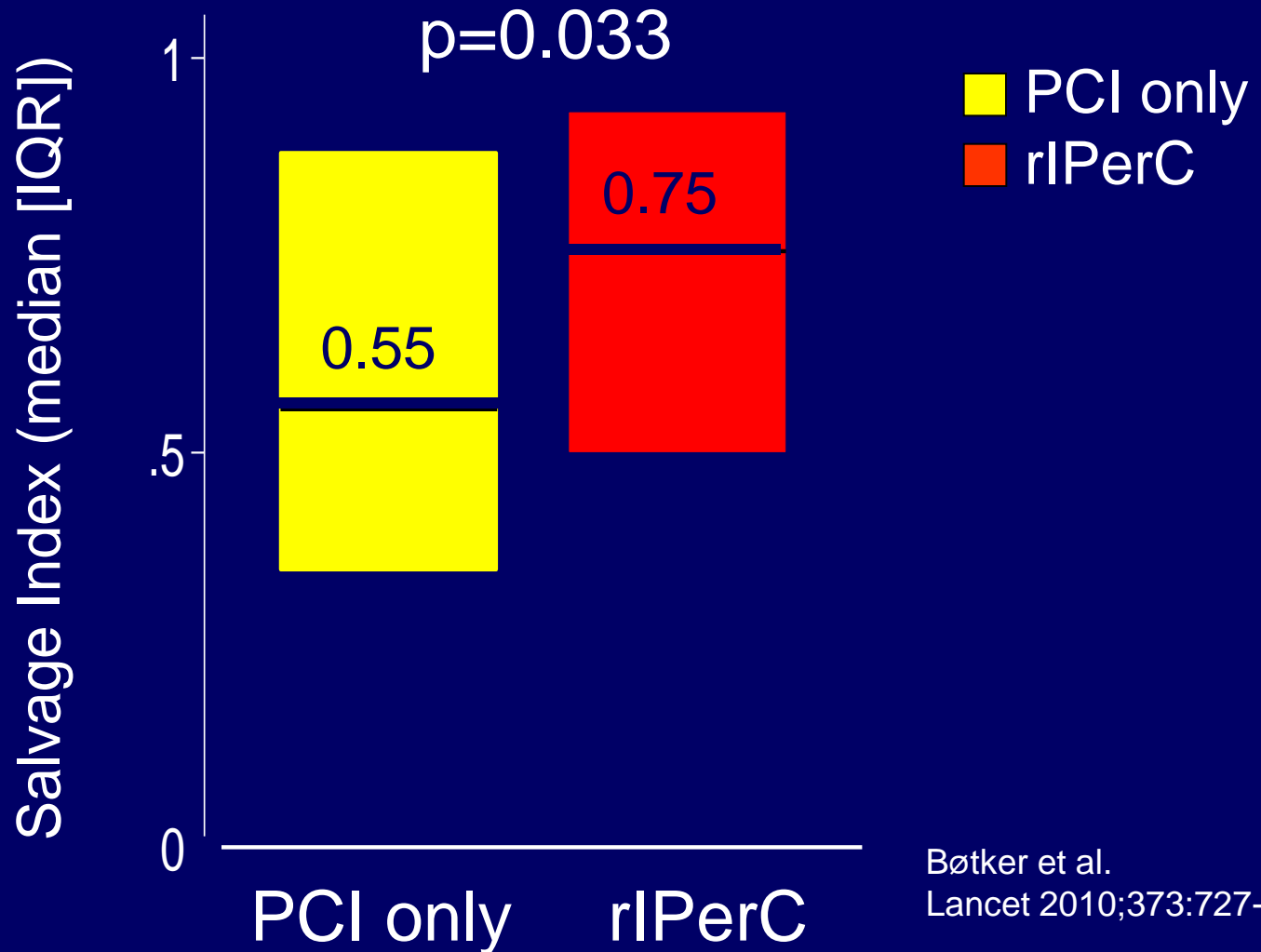
**Methods** 333 consecutive adult patients with a suspected first acute myocardial infarction were randomly assigned in a 1:1 ratio by computerised block randomisation to receive primary percutaneous coronary intervention with (n=166 patients) versus without (n=167) remote conditioning (intermittent arm ischaemia through four cycles of 5-min inflation and 5-min deflation of a blood-pressure cuff). Allocation was concealed with opaque sealed envelopes. Patients received remote conditioning during transport to hospital, and primary percutaneous coronary intervention in hospital. The primary endpoint was myocardial salvage index at 30 days after primary percutaneous coronary intervention, measured by myocardial perfusion imaging as the proportion of the area at risk salvaged by treatment; analysis was per protocol. This study is registered with ClinicalTrials.gov, number NCT00435266.

**Findings** 82 patients were excluded on arrival at hospital because they did not meet inclusion criteria, 32 were lost to follow-up, and 77 did not complete the follow-up with data for salvage index. Median salvage index was 0.75 (IQR 0.50–0.93, n=73) in the remote conditioning group versus 0.55 (0.35–0.88, n=69) in the control group, with median difference of 0.10 (95% CI 0.01–0.22; p=0.0333); mean salvage index was 0.69 (SD 0.27) versus 0.57 (0.26), with mean difference of 0.12 (95% CI 0.01–0.21; p=0.0333). Major adverse coronary events were death (n=3 per group), reinfarction (n=1 per group), and heart failure (n=3 per group).

**Interpretation** Remote ischaemic conditioning before hospital admission increases myocardial salvage, and has a favourable safety profile. Our findings merit a larger trial to establish the effect of remote conditioning on clinical outcomes.

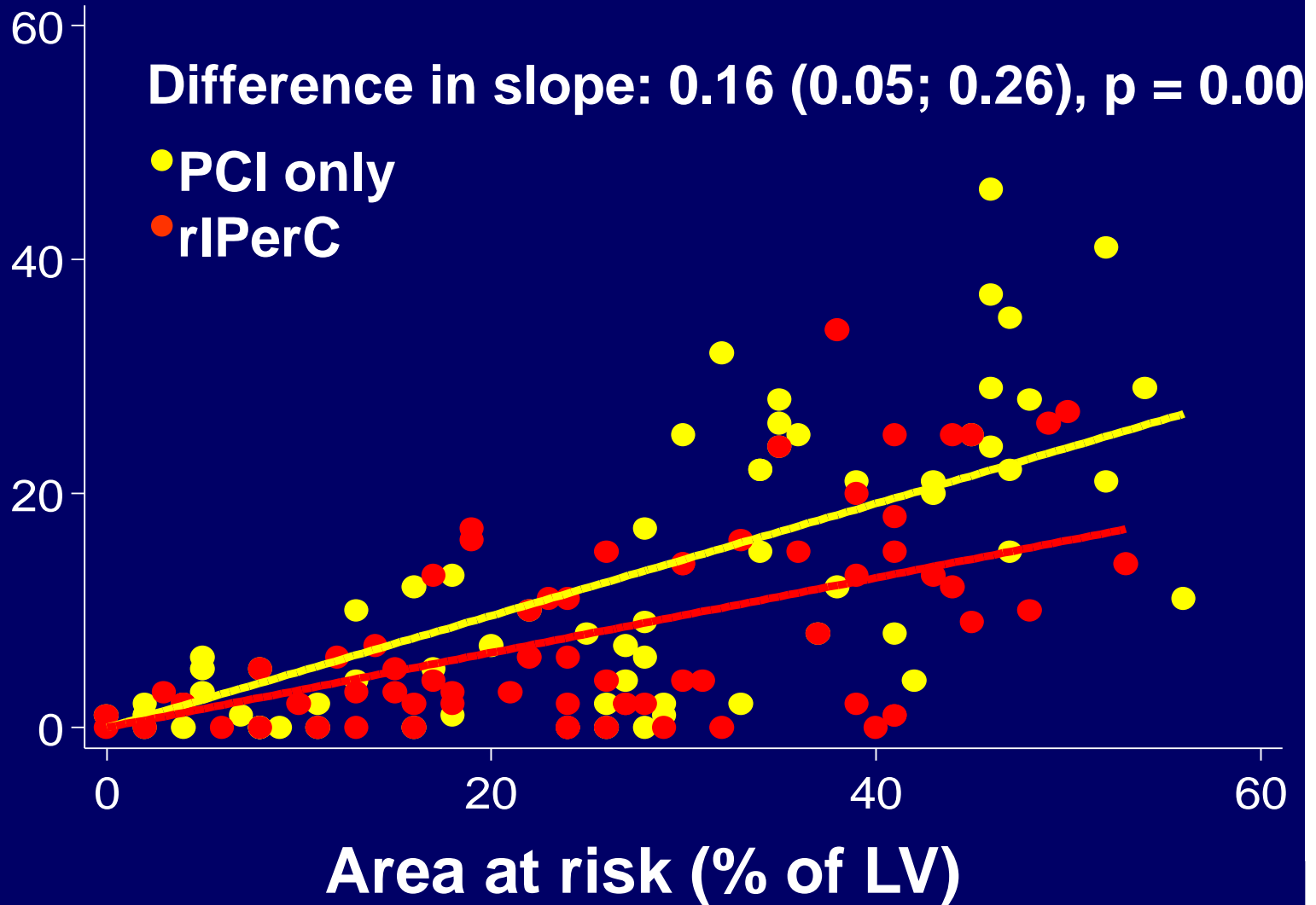
**Funding** Fondation Leducq.

# Primary Endpoint: Myocardial Salvage Index





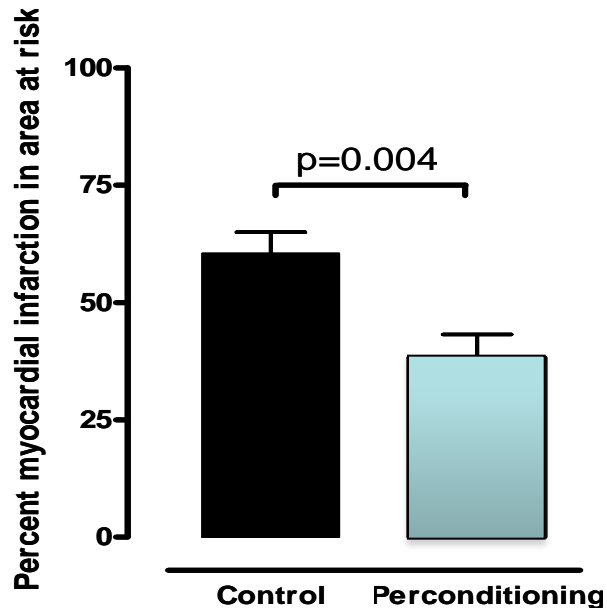
# Relation Between AAR and FIS



# Remote ischemic preconditioning



## Experimental



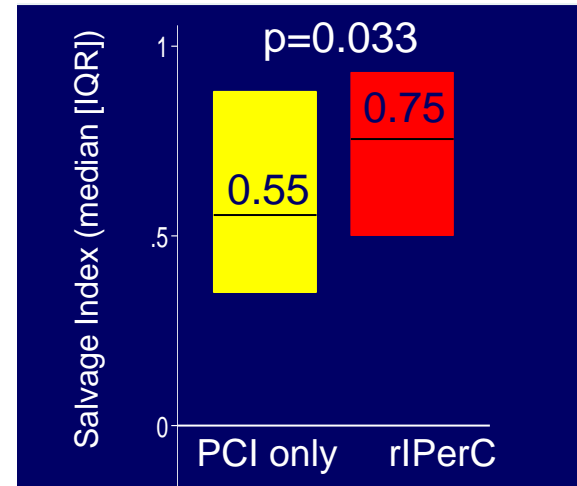
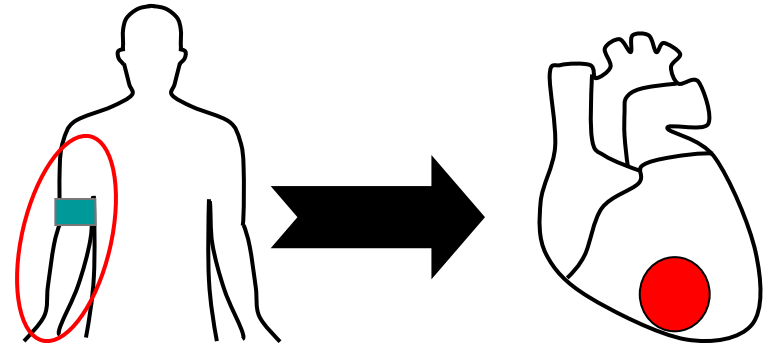
Schmidt MR et al. Am J Physiol Heart Circ Physiol 2007;292:H1883-90.

## STEMI

## Clinical



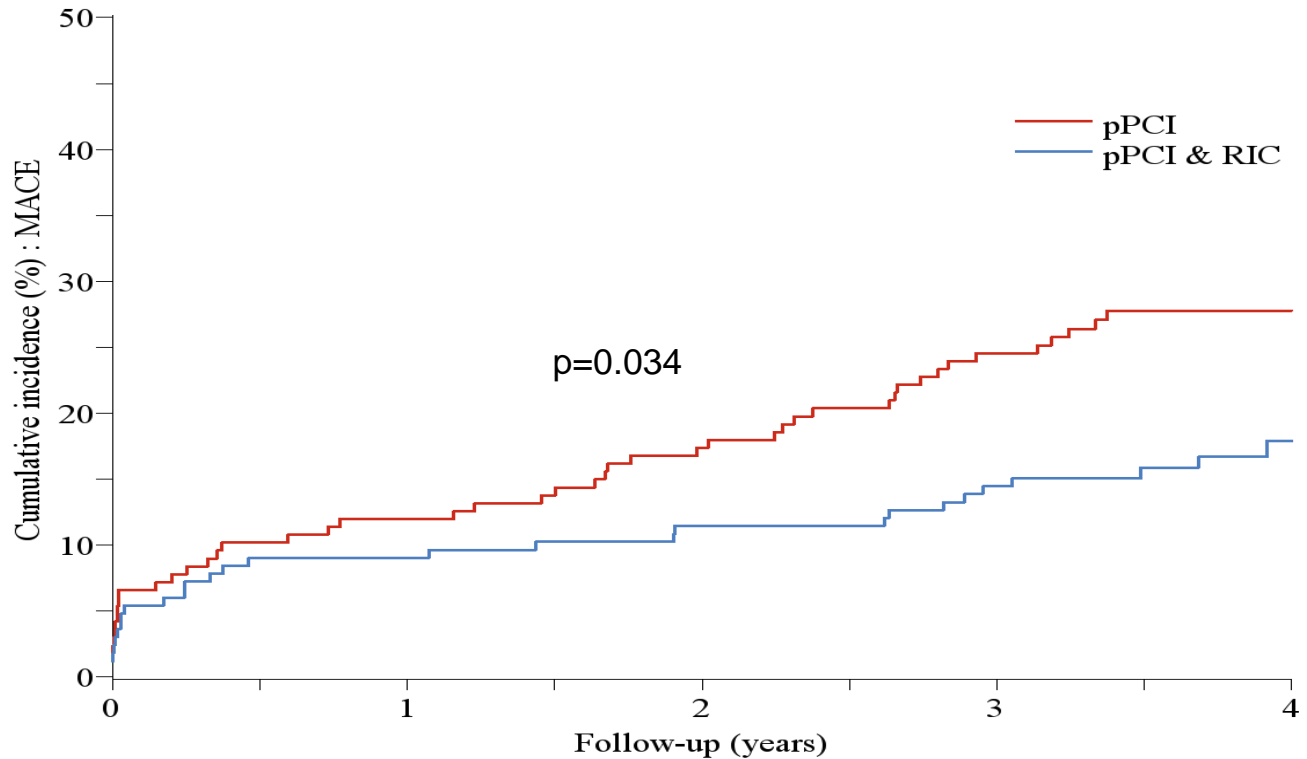
Remote preconditioning during ambulance transport in patients with STEMI before pPCI



Bøtker et al. Lancet 2010; 373: 727-34

# Long-term clinical effect

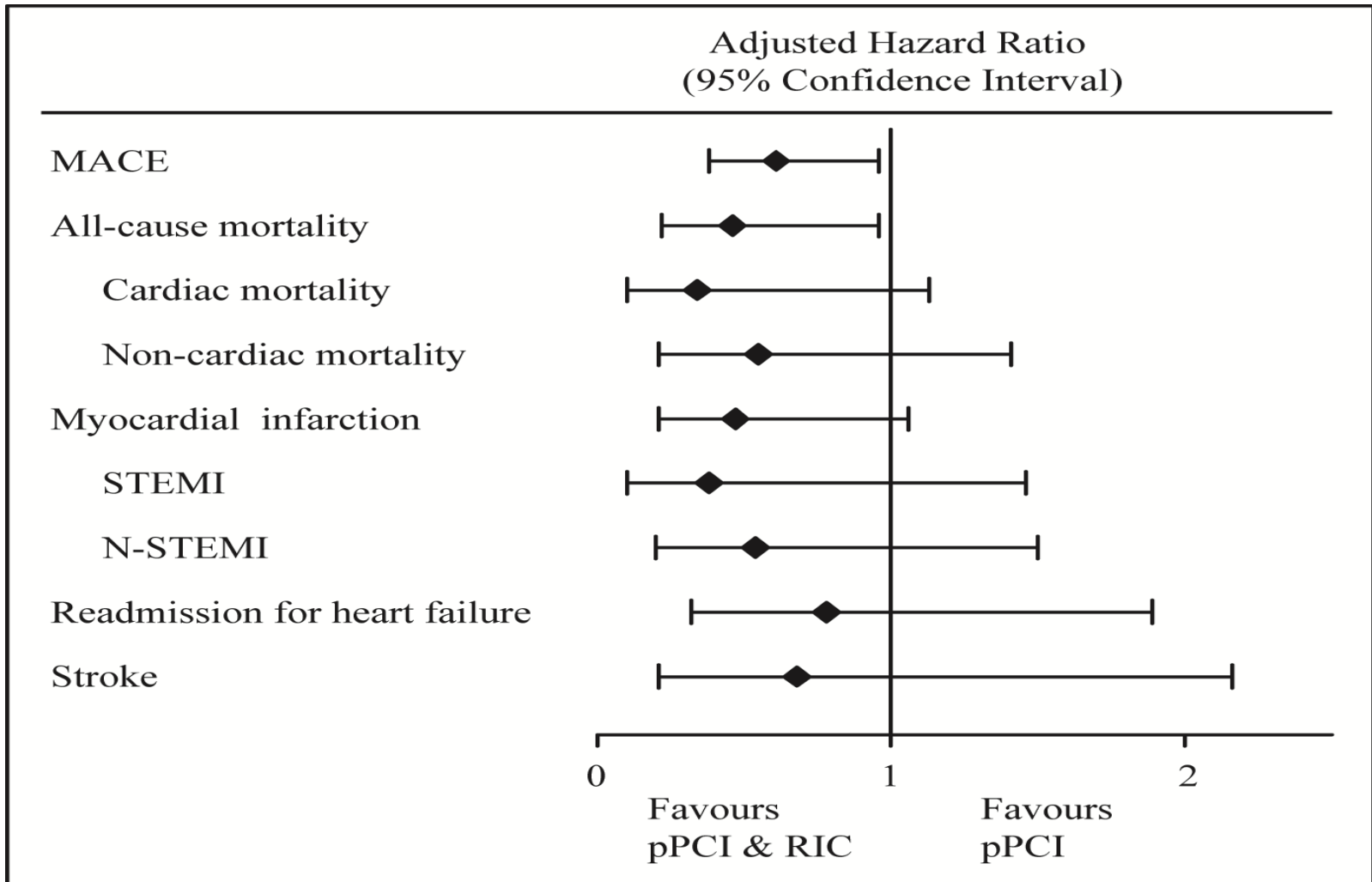
## Cummulative occurrence of MACE



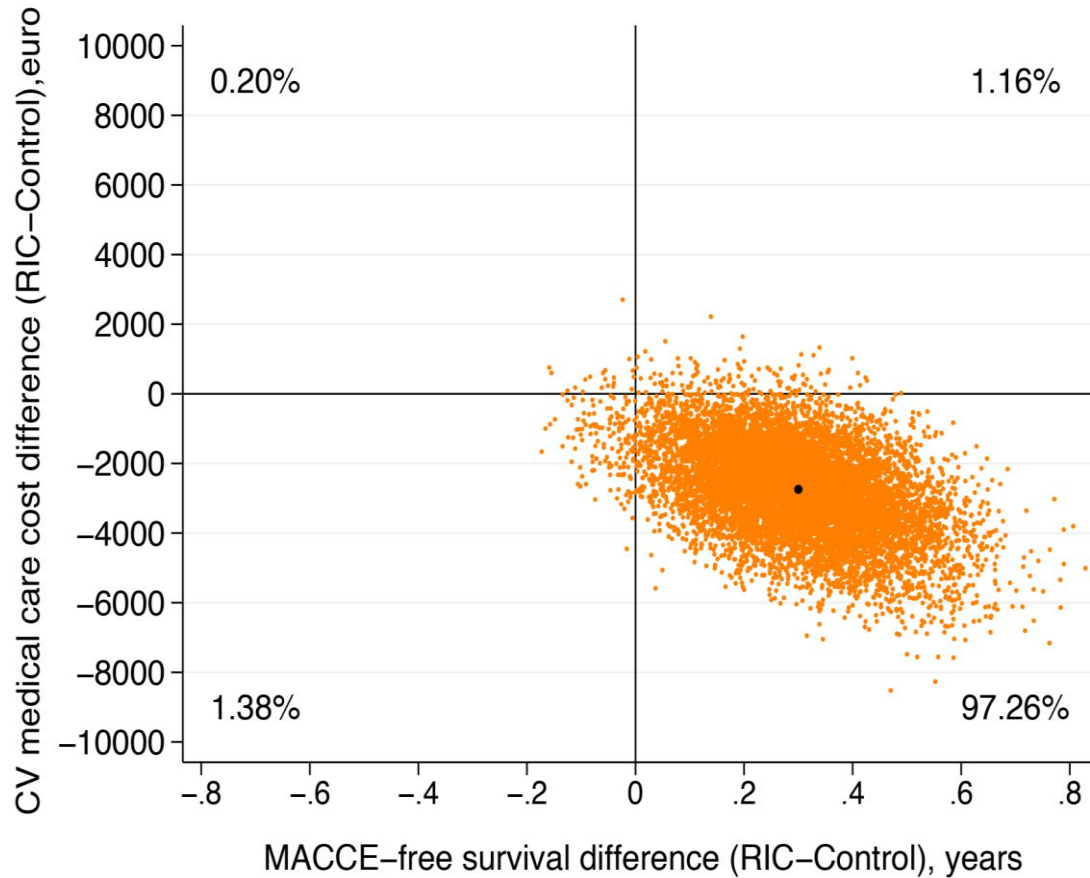
Patients at risk :

pPCI & RIC	166	152	148	143	59
pPCI	167	148	139	127	57

# Long-term effect of RIC



# Cost-effectiveness



CONDI 2, Aarhus Universitets  
Hospital



# RIC in STEMI

Study	No of patients (control/RIC)	RIC regimen	Endpoint	Outcome
Botker et al 2010	69/73	Upper limb 4 cycles I/R (5/5 min)	Salvage index (SPECT)	20% increase in salvage index
Munk et al 2010	110/108	Upper limb 4 cycles I/R (5/5 min)	LVEF at 30 days	5% increase in LVEF in anterior infarcts
Rentoukas et al 2010	30/33	Upper limb 3 cycles I/R (5/5 min)	ST-segment resolution	20% increase in proportion of patients achieving full ST-segment resolution
Crimi et al 2013	50/50	Lower limb 3 cycles I/R (5/5 min)	CK-MB (AUC 72 h after PCI)	20% reduction of CK-MB release
Prunier et al 2014	17/18	Upper limb 4 cycles I/R (5/5 min)	CK-MB (AUC 72 h after PCI)	31% reduction of CK-MB release
Sloth et al 2014	167/166	Upper limb 4 cycles I/R (5/5 min)	MACCE at 4 yr	12% reduction in MACCE
Yellon et al 2015	260/260	Upper limb 4 cycles I/R (5/5 min)	TnT (AUC 24 h after PCI)	17% reduction of TnT release
Eitel et al 2015	232/232/232	Upper limb 3 cycles I/R (5/5 min) + local post CON	Salvage index (MRI)	23 % increase in salvage index
White et al 2015	40/43	Upper limb 4 cycles I/R (5/5 min)	Myocardial edema (MRI)	27 % reduction in myocardial edema

# Conclusions

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- Remote ischemic conditioning during evolving ST-elevation myocardial infarction is feasible, increases myocardial salvage and infarct size in large infarcts with primary PCI
- This simple and safe intervention has the potential to reduce mortality and morbidity in STEMI patients and merits a larger trial powered to detect these clinical endpoints

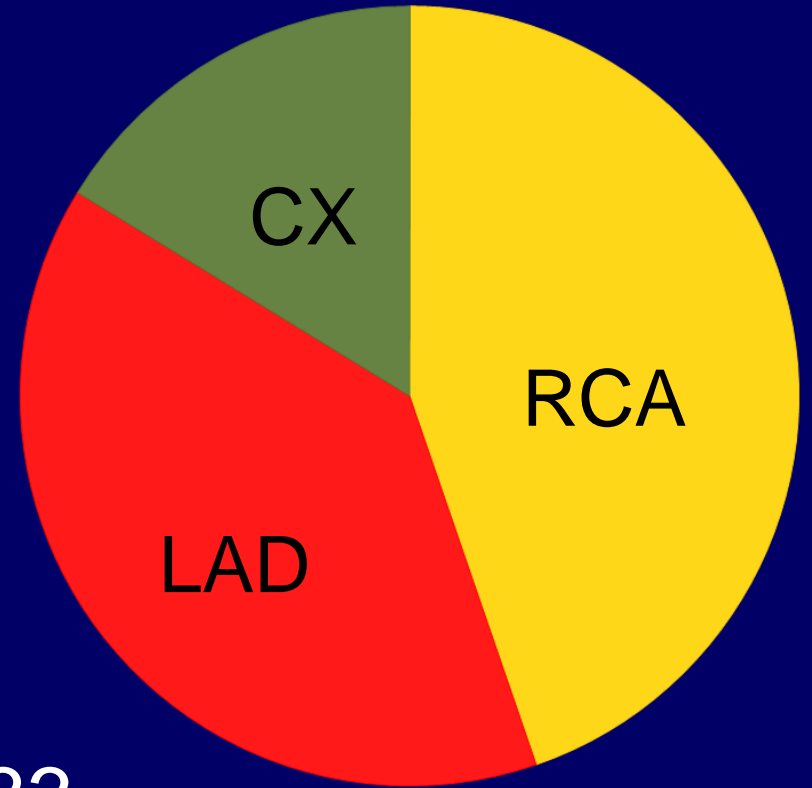
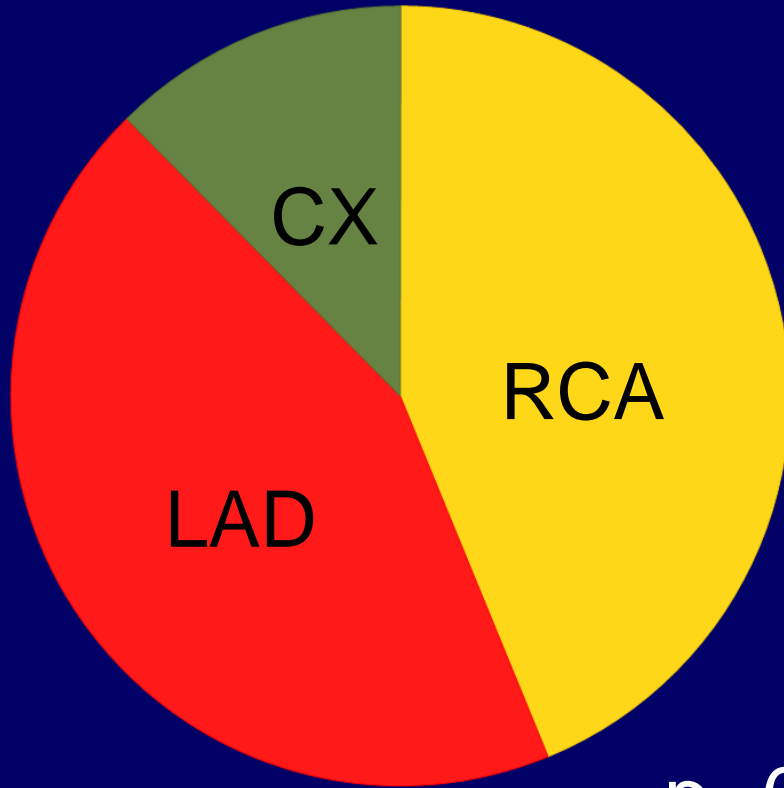
# CONDI 2 – ERIC-PPCI

- Remote ischemic conditioning in STEMI
- Clinical outcomes
- >5000 patients
- Inclusion complete early 2018
- Final 2019



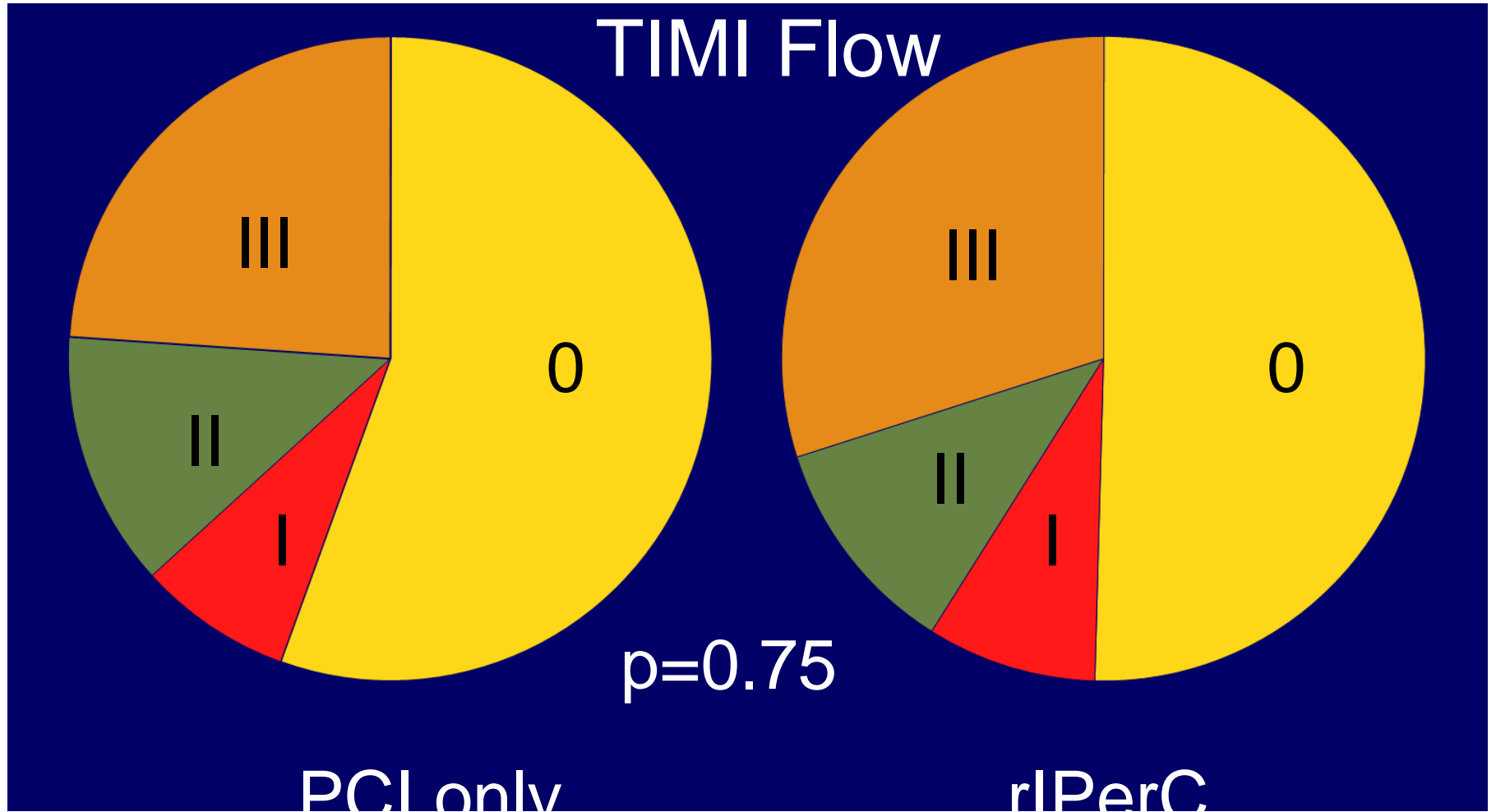
**THANK YOU**

# Infarct Related Artery

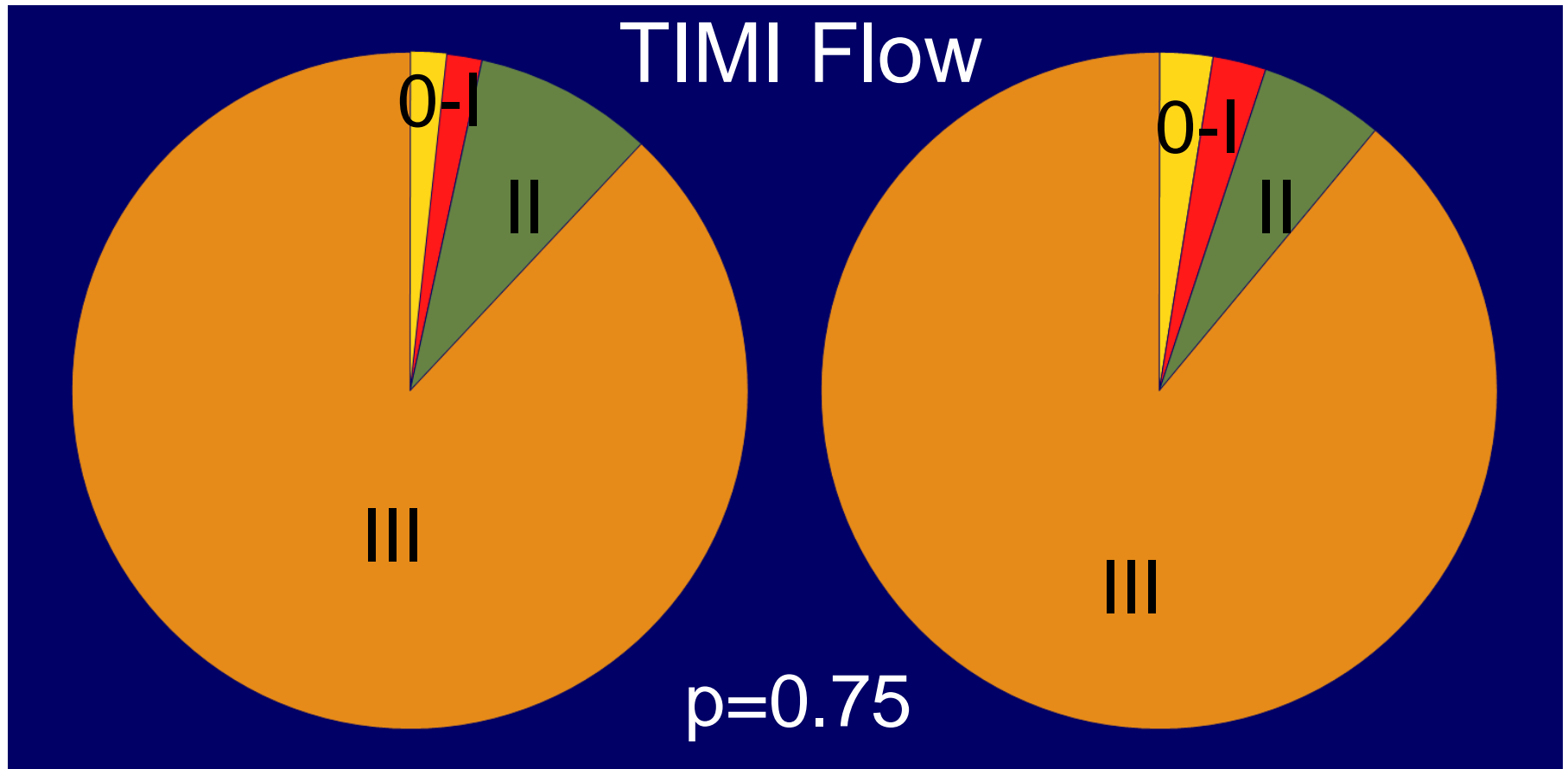


$p=0.83$

# Vessel Patency before PCI



# Vessel Patency after PCI





# Current strategy



**Interventional hospital**



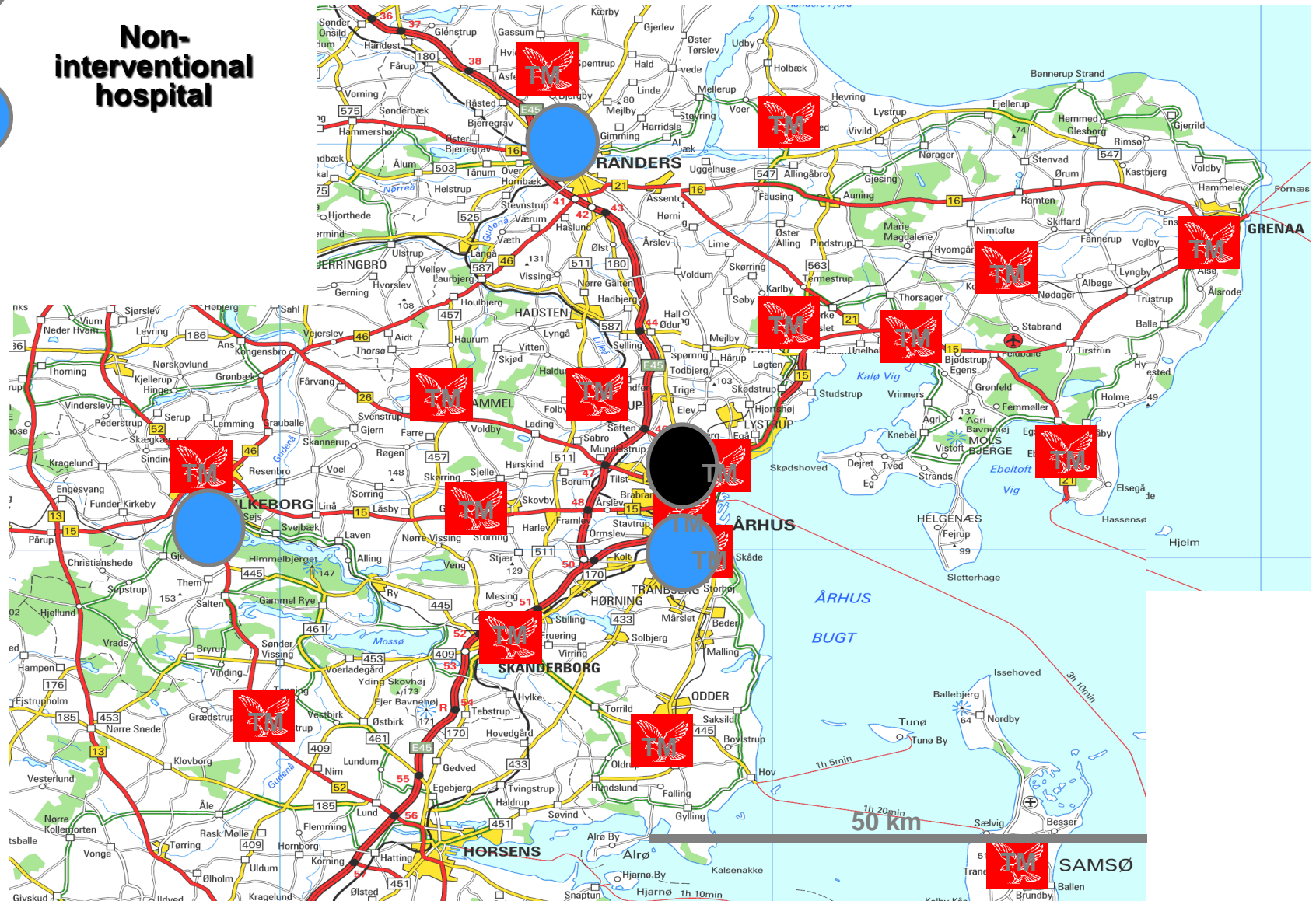
**Non-interventional hospital**



**Telemedicine ambulances**



**Regular ambulances**



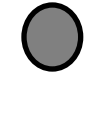
# Current strategy



**Interventional hospital**



**Non-interventional hospital**



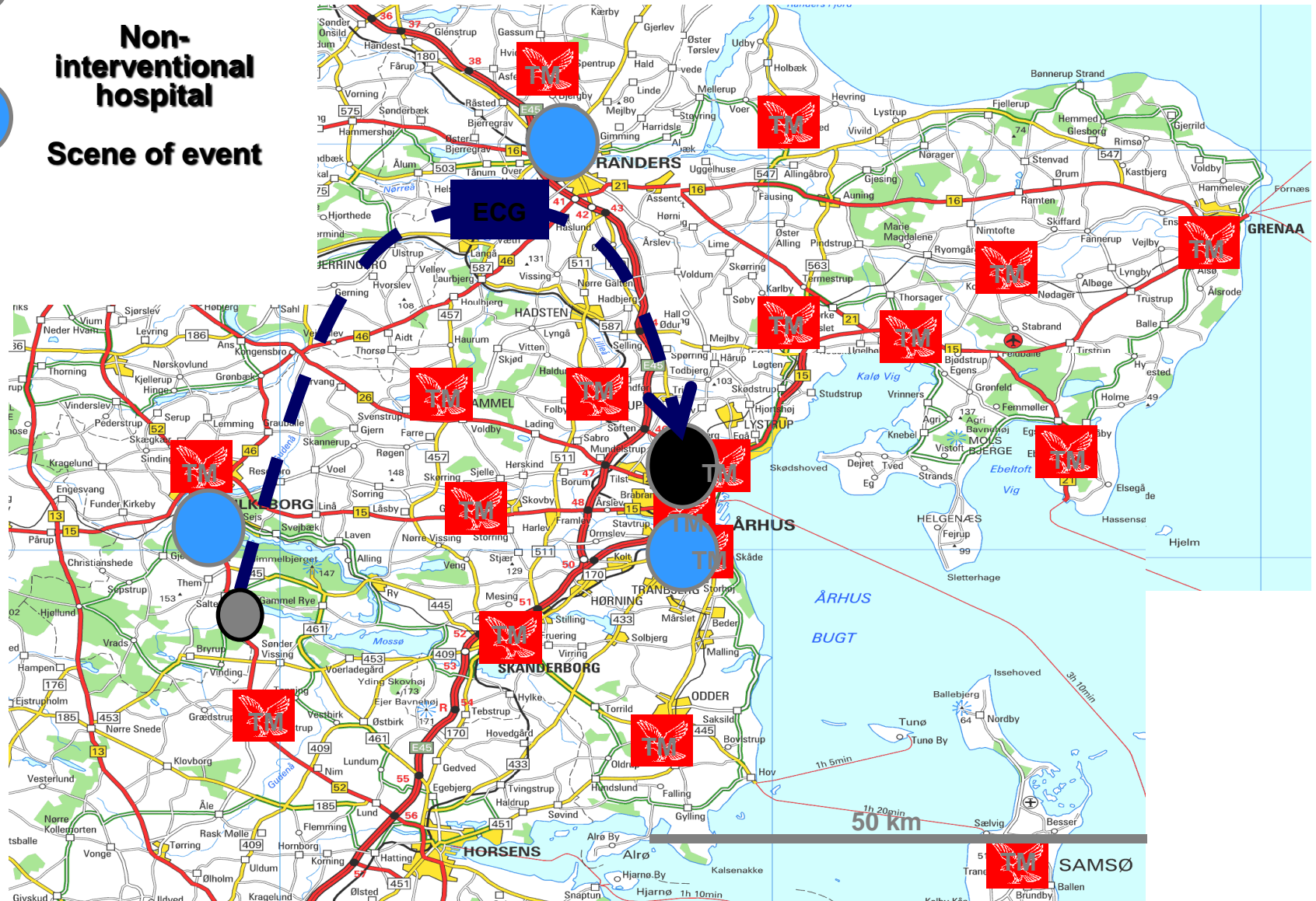
**Scene of event**



**Telemedicine ambulances**



**Regular ambulances**





# Current strategy



**Interventional hospital**



**Non-interventional hospital**



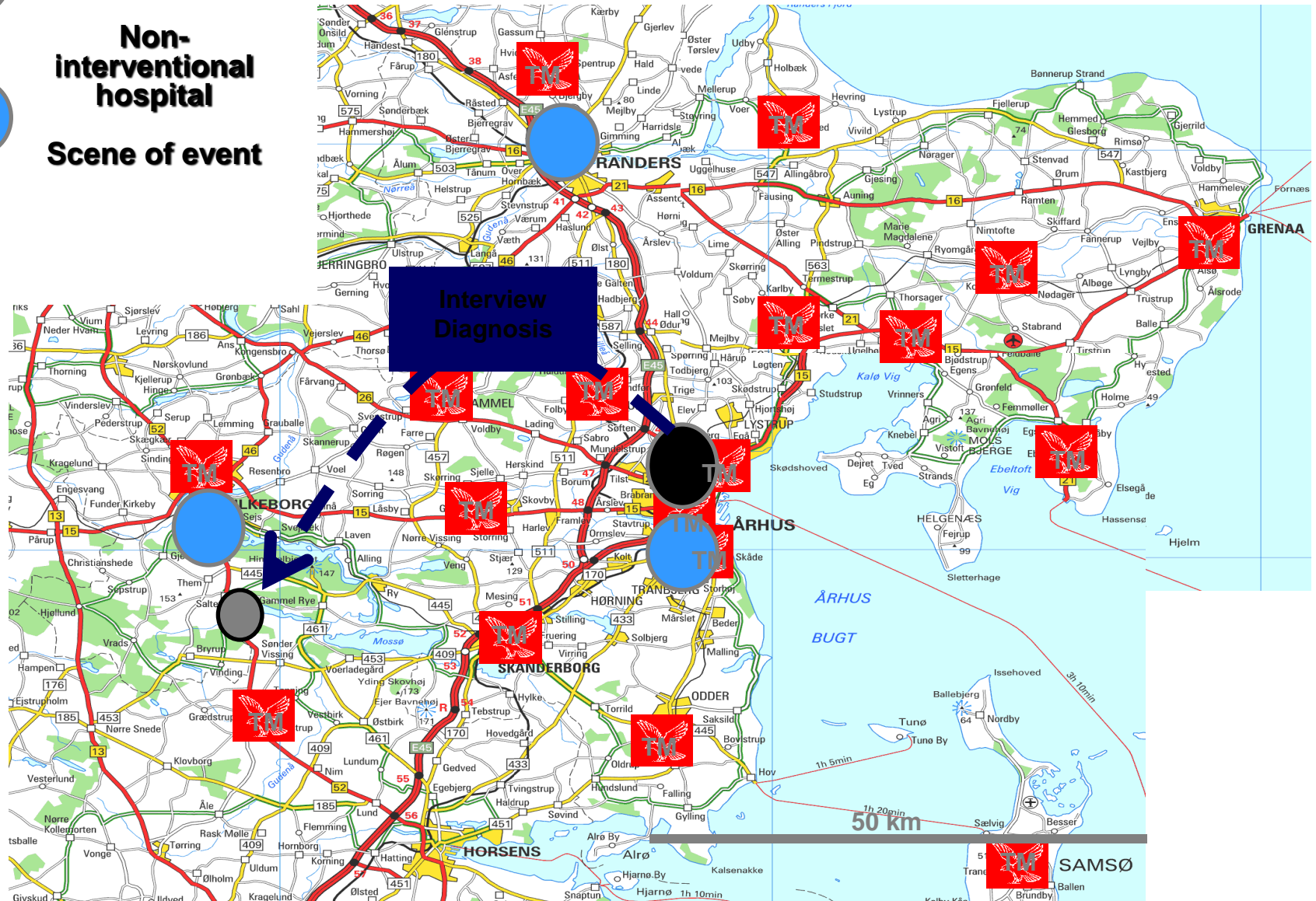
**Scene of event**



**Telemedicine ambulances**



**Regular ambulances**





# Current strategy



**Interventional hospital**



**Non-interventional hospital**



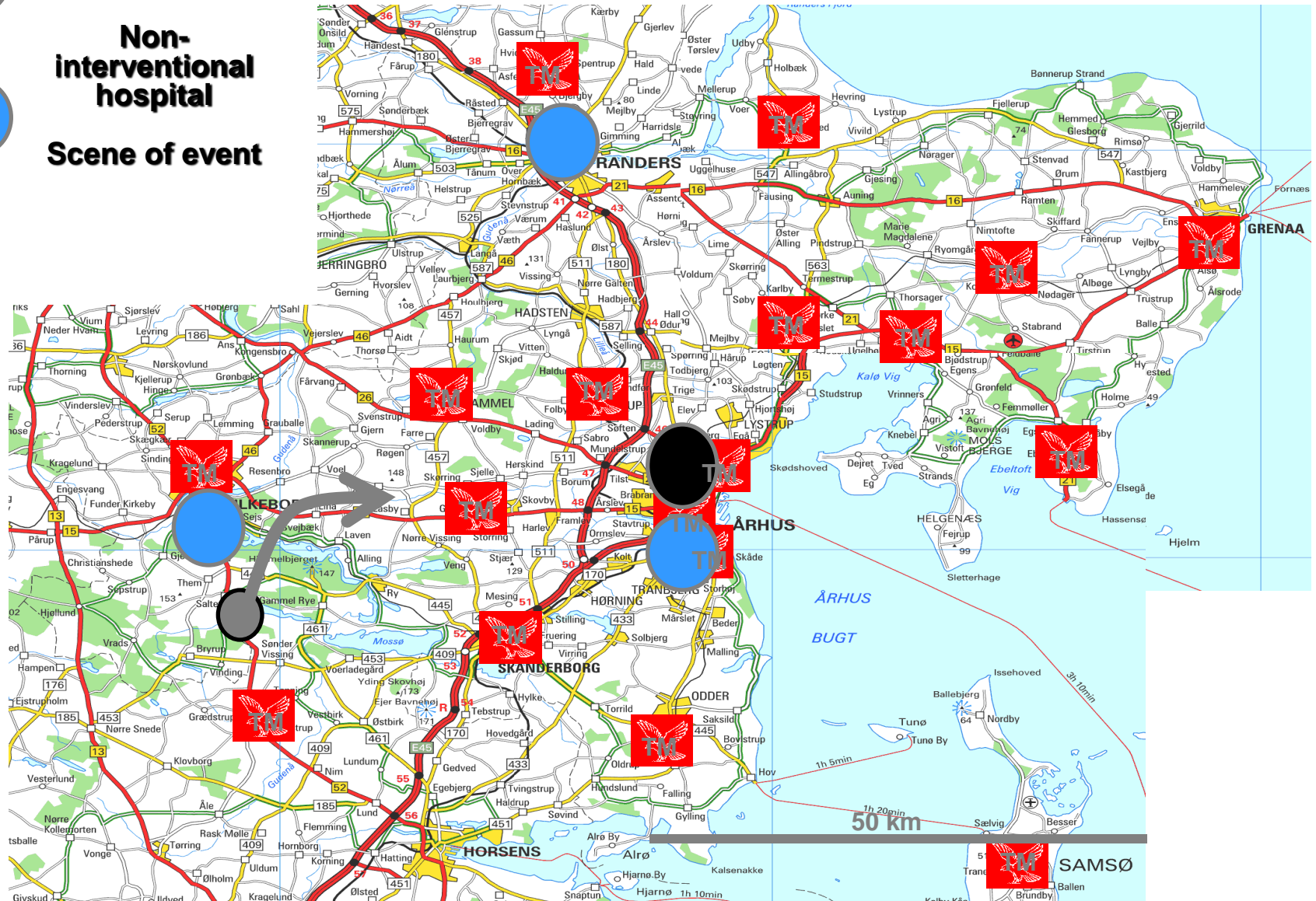
**Scene of event**



**Telemedicine ambulances**



**Regular ambulances**



# Current strategy



**Interventional hospital**



**Non-interventional hospital**



**Scene of event**



**Telemedicine ambulances**



**Regular ambulances**

