



# Heparin versus bivalirudin in patients with non ST-elevation acute coronary syndrome undergoing percutaneous coronary intervention

- a report from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR)

Angerås O<sup>1</sup>, Koul S<sup>2</sup>, Söderbom M<sup>3</sup>, Albertsson P<sup>1</sup>, Råmunddal T<sup>1</sup>, Matejka G<sup>1</sup>, Scherstén F<sup>2</sup>, Oldgren J<sup>4</sup>, James S<sup>4</sup>, Lagerqvist B<sup>4</sup>, Fröbert F<sup>5</sup>, Wedel H<sup>6</sup>, Erlinge D<sup>2</sup>, Omerovic E<sup>1</sup>

**<sup>1</sup>Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden**

<sup>2</sup>Department of Cardiology, Lund University, Lund, Sweden

<sup>3</sup>Department of Economics, University of Gothenburg, Gothenburg, Sweden

<sup>4</sup>Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden

<sup>5</sup>Department of Cardiology, Örebro University Hospital, Örebro, Sweden

<sup>6</sup> Nordic School of Public Health, Gothenburg, Sweden

# Potential conflicts of interests

- Advisory board: AstraZeneca, Bayer
- Institutional research grant: AstraZeneca, Medtronic, Abbott, Merit Medical

# Bivalirudin treatment of choice in NSTEMI-ACS

– ESC NSTEMI-ACS guidelines 2011

Bivalirudin plus provisional GP IIb/IIIa receptor inhibitors are recommended as an alternative to UFH plus GP IIb/IIIa receptor inhibitors in patients with an intended urgent or early invasive strategy, particularly in patients with a high risk of bleeding.	I	B
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– ACC/AHA NSTEMI-ACS guidelines

Class IIa

2. For UA/NSTEMI patients in whom an initial invasive strategy is selected, it is reasonable to omit administration of an IV GP IIb/IIIa inhibitor if bivalirudin is selected as the anticoagulant and at least 300 mg of clopidogrel was administered at least 6 hours earlier than planned catheterization or PCI (57,76,77). (Level of Evidence: B)

# Bivalirudin treatment of choice in NSTE-ACS?

The NEW ENGLAND JOURNAL of MEDICINE 2006

- Bivalirudin vs GPIIb/IIIa inhibitors
- < 60% biomarker positive
- < 60% PCI
- 60% pretreated with clopidogrel
- 6.2% radial access

Ramin Ebrahimi, M.D., Martial Hamon, M.D., Lars H. Rasmussen, M.D.,  
Hans-Jürgen Rupprecht, M.D., James Hoekstra, M.D., Roxana Mehran, M.D.,  
and E. Magnus Ohman, M.D., for the ACUITY Investigators\*

# Anti-thrombotic treatment in NSTEMI-ACS PCI in Sweden 2006-2013



# Bivalirudin vs Heparin in NSTEMI-ACS

randomised trials

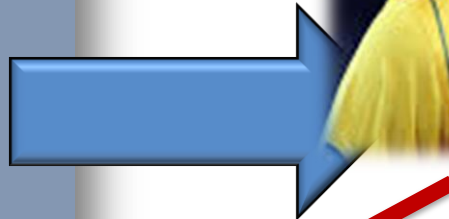
- **BAT trial** (Bittl et al NEJM 1995;333:764-9)
  - 4098 patients randomised 1993-1994
  - Composite endpoint NS
  - Bivalirudin reduced major bleeding
  - Trend for higher mortality in the bivalirudin group ( $p=0.08$ )!
- **ISAR-REACT 3** (Kastrati et al NEJM 2008;359:688-96.)
  - 4570 biomarker negative patients randomised 2005-2008
  - Composite endpoint NS including major bleeding
  - Bivalirudin reduced major bleeding
- All randomised patients had femoral access
- Majority of randomized patients were biomarker negative

# Purpose

- **Purpose: To compare the outcome of heparin alone versus bivalirudin in patients with NSTEMI-ACS undergoing PCI between 2005-2013 and registered in SCAAR**
- **Endpoint: 30-day mortality**

# SCAAR

Swedish Coronary Angiography and Angioplasty Registry



**30 hospitals performing PCI and angiography.  
Financed by Swedish government.  
No support from the industry.**





# SWEDEHEART

RIKS-HIA, SCAAR, SEPHIA och Svenska Hjärtkirurgiregistret som ett register

TILL REGISTRET

KORTINLOGGNING

RIKS-HIA

SCAAR

SEPHIA

HJÄRTKIRURGI

Sök...

> Förstasidan

- Nyheter
- Dokument
- Årsrapporter
- Kontakter
- Synpunkter på registret
- Bilder årsmöten
- Om webbplatsen
- Webmaster

PATIENTER / ALLMÄNHET

Information

ENGLISH

Annual report

MONITORER

## Undvik att skapa Vårdkedja där det inte ska skapas en RIKS-HIA del

Fr o m mitten av april har en ökad mängd Startsidor fått en ägare (dvs en specifik sjukhusenhet har fått ansvaret att registrera denna sida).

[Läs mer...](#)

# DETO<sub>2</sub>X

Syrgas eller inte vid hjärtinfarkt?

Anmäl ert sjukhus nu!

[Läs mer](#)

SENASTE NYTT

Ny release 2013-06-10

Undvik att skapa Vårdkedja där det inte ska skapas en RIKS-HIA del

SWEDEHEART uppdatering 2013-04-10

Ny randomiserad studie i SWEDEHEART

Uppdaterad RIKS-HIA manual!

MÖTEN OCH KONGRESSER

MED STÖD AV



<http://www.ucr.uu.se/swedeheart/>

## Swedish Coronary

- 100% coverage
- All coronary angiogram and PCI procedures are registered immediately after procedure
- 200 variables
- Linked to the national cause-specific death registry

The screenshot displays the SWEDEHEART web application interface, which is used for recording and managing coronary artery disease (CAD) procedures. The interface is organized into several panels:

- Left Panel (Patient Overview):** Contains patient information such as ID (19730425-2757), name (Akut vårdkedj), and various medical history fields like "Angio", "Grundupp", "Kliniska bal", "Segment his", "Adjuvant", and "Angiografis".
- Top Panel (Angiogram):** Shows a diagram of the coronary arteries with numbered segments (1-6) and a "TASTE" button for patient selection.
- Right Panel (PCI Details):** Provides a comprehensive list of variables for Percutaneous Coronary Intervention (PCI), categorized into:
  - Diagnostik (v):** Includes fields for "Någon diagnostik vid PCI" and "Sekundärt be".
  - Segmen:** Lists "Segmentnummer", "Graft", and "Nummer på stent".
  - Adjuvant tera:** Details various treatments like "Aortaballongpump", "Stenosklass", "Procedurtyp", "Stent", "Diameter", "Maxtryck ballong", "Stentlängd (mm)", "Stentslut", "Efterdilatation", "Lokal framgång", "Kontrastmedel", "Kontrastmedelsmängd", "Annan kontrastmedels", "Diagnos", "Någon diagnos", "Sekundärt bes", "Adjuvan", "Någon adjuvan", and "Stråldos (Gyom?)".
  - Antitrombotisk medicinering före (inom 24h):** A table listing medications used before PCI, such as "Trombolyt", "ASA", "Clopidogrel/ticlopidin (Plavix/Ticlid)", "Prasugrel (Effient)", "Ticagrelor (Brilique)", "Heparin", "Dalleparin (Fragmin)", "Enoxaparin (Klexane)", "Annan lågmolekylärt heparin", "Bivalirudin (Angiox)", "Fondaparinux (Arixtra)", "Abciximab (Reopro)", and "Eptifibatid (Integinin)".
  - Antitrombotisk medicinering under/direkt i anslutning PCI:** A similar table for medications used during or directly after PCI.

# RANDOMISED REGISTRY CLINICAL TRIAL

## RRCT

SWEDEHEART - Windows Internet Explorer

UCR <https://www.reg.ucr.uu.se/swedeheart/regangiopci.jsp>

Convert Select

Favoriter The Ultimate Idiot Guide! ... Medarbetarportal - Perso... Förslag på webbplatser

SWEDEHEART

Avböjd från operation

**TASTE**

Är patienten lämplig för studien (dvs uppfyller inklusionskriterier och har inga exklusionskriterier)? Ja

Vill patient vara med i Taste-studien Ja

Randomisera & Spara

Spara

Stent  
Meddelande om marknadsföring mailas stent@ucr.uu.se.

PCI

Operatör

Segment

# Thrombus Aspiration in ST- Elevation myocardial infarction in Scandinavia (**TASTE** trial)

*Main results at 30 days*

Ole Fröbert, MD, PhD - on behalf of the **TASTE** investigators

Department of Cardiology  
Örebro University Hospital  
Sweden

ORIGINAL ARTICLE

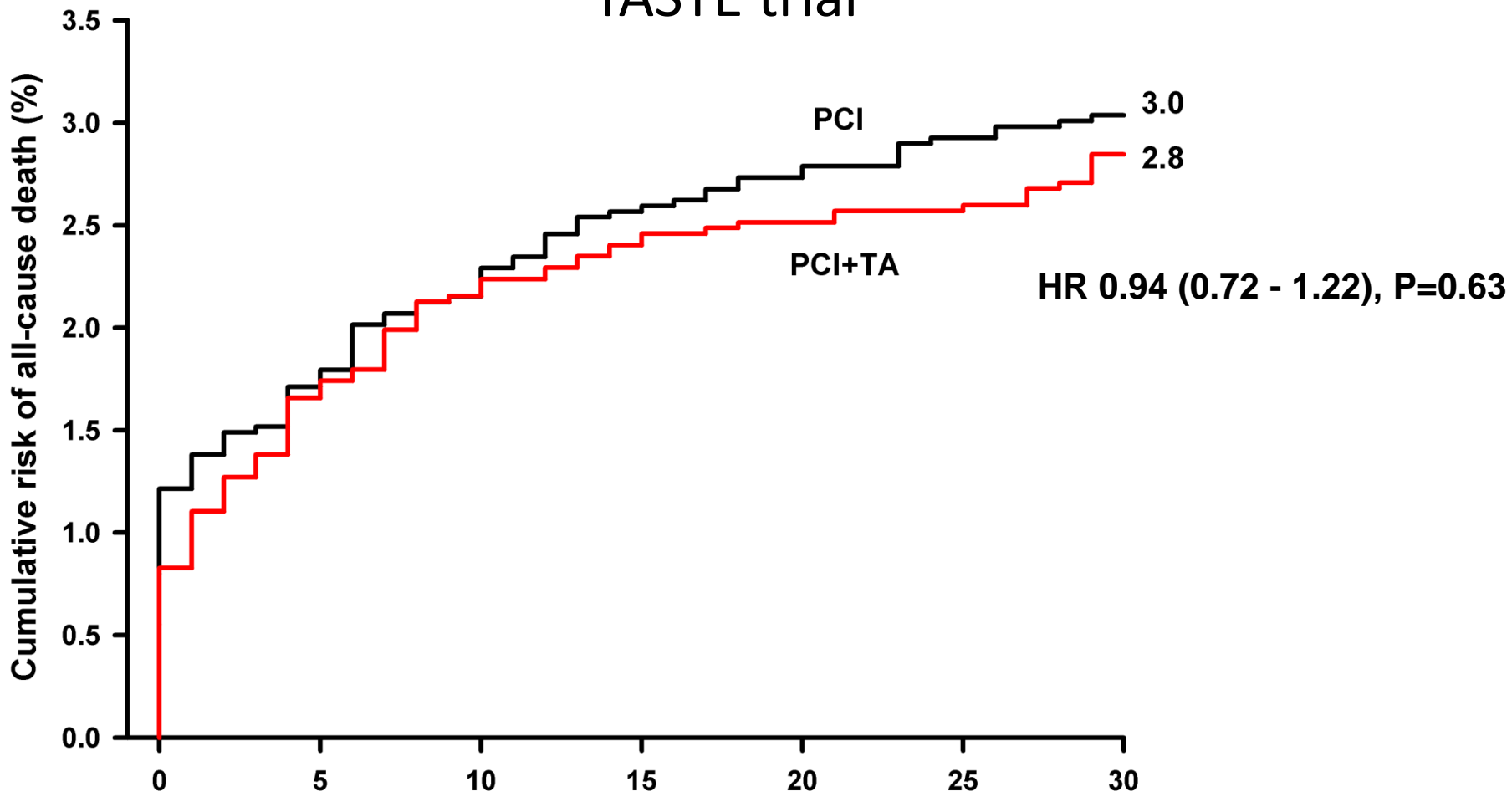
# Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

Ole Fröbert, M.D., Ph.D., Bo Lagerqvist, M.D., Ph.D., Göran K. Olivecrona, M.D., Ph.D.,  
Elmir Omerovic, M.D., Ph.D., Thorarinn Gudnason, M.D., Ph.D.,  
Michael Maeng, M.D., Ph.D., Mikael Aasa, M.D., Ph.D., Oskar Angerås, M.D.,  
Fredrik Calais, M.D., Mikael Danielewicz, M.D., David Erlinge, M.D., Ph.D.,  
Lars Hellsten, M.D., Ulf Jensen, M.D., Ph.D., Agneta C. Johansson, M.D.,  
Amra Kåregren, M.D., Johan Nilsson, M.D., Ph.D., Lotta Robertson, M.D.,  
Lennart Sandhall, M.D., Iwar Sjögren, M.D., Ollie Östlund, Ph.D.,  
Jan Harnek, M.D., Ph.D., and Stefan K. James, M.D., Ph.D.

This article was published on September 1,  
2013, at [NEJM.org](http://NEJM.org).

# All-cause mortality at 30 days

## TASTE trial



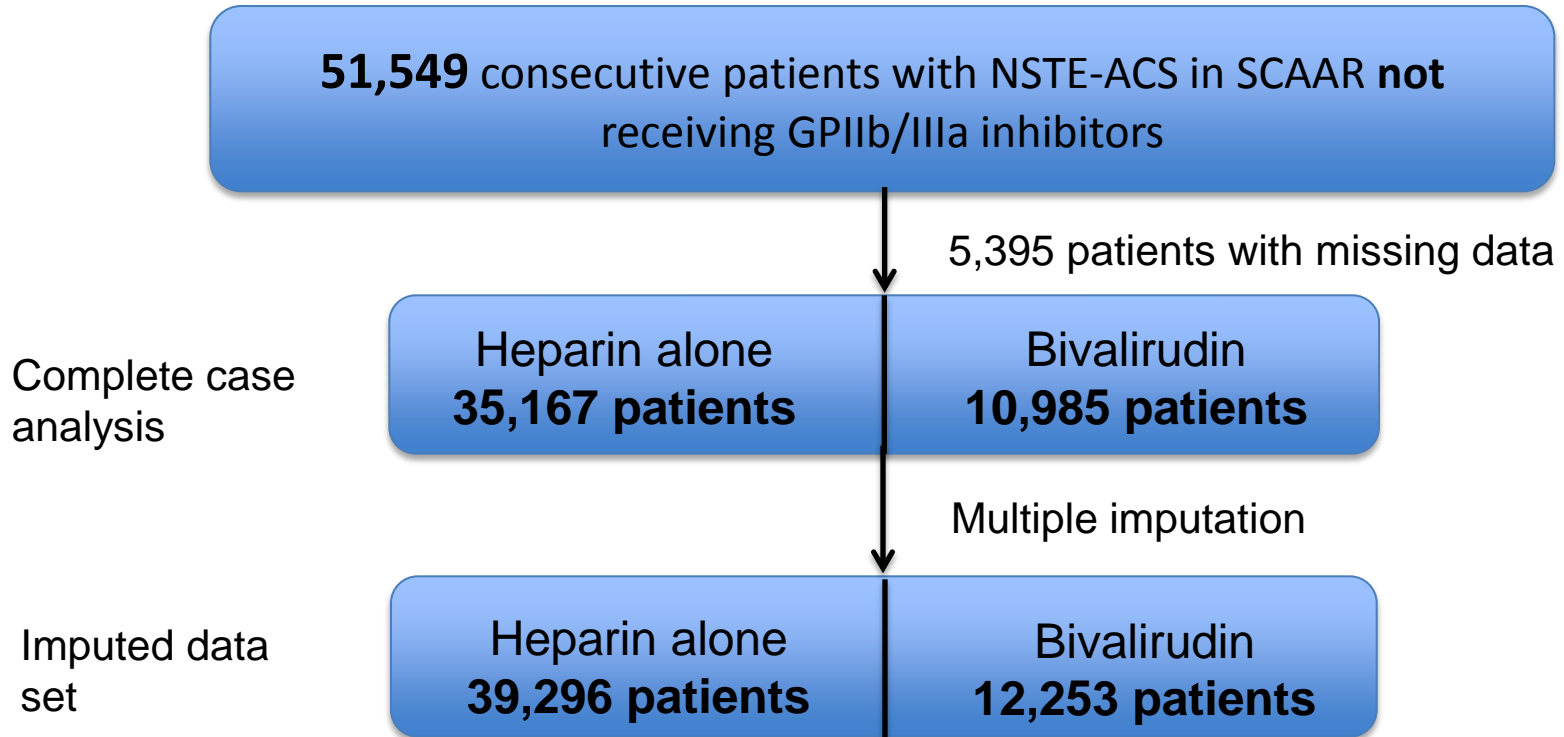
### No. at Risk

PCI+TA	3621	3568	3540	3532	3526	3524	3519
PCI	3623	3567	3545	3530	3523	3517	3513

*TASTE*

# Study design

heparin vs. bivalirudin



# Baseline characteristics

	UH/LMWH (n=39,298)	Bivalirudin (n=12,252)	p-value	p-value after ps- score adjustment	Missing (n)
Age (mean±SD)	67.6 ± 11	68.3 ± 11	<0.001	0.56	185
Female (%)	28	30	0.004	0.90	0
Treated hypertension (%)	59	56	<0.001	0.79	546
Treated hyperlipidemia (%)	56	54	0.02	0.85	629
Prior MI (%)	28	26	<0.001	0.70	908
Prior PCI (%)	19	16	<0.001	0.51	21
Ex-smokers (%)	40	37	<0.001	0.70	1,929
Active smokers (%)	20	20	0.53	0.90	1,929
Prior CABG (%)	11	11	0.05	0.87	10
Diabetes (%)	21	20	0.02	0.94	150
ASA (%)	97	97	0.008	0.74	15
Clopidogrel/Ticagrelor/ Prasugrel (%)	94	92	<0.001	0.29	35
Pretreated with UH/LMWH/Fondaparinux (%)	54	55	0.08	0.91	28
Warfarin (%)	2.2	1.6	<0.001	0.48	5
Positive biomarkers (%)	74	80	<0.001	0.29	1,515



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	UH/LMWH (n=39,298)	Bivalirudin (n=12,252)	P-value	p-value after ps- score adjustment	Missing (n)
UH/LMWH/Fondaparinux during the procedure (%)	100	28	n/a	n/a	0
<b>Access site</b>					
Femoral (%)	47	47	0.45	0.80	0
Radial (%)	53	53	0.45	0.80	0
<b>Angiographical findings</b>					
One vessel disease (%)	47	43	<0.001	0.50	249
Two vessel disease (%)	30	31	0.12	0.89	249
Three vessel disease (%)	18	20	<0.001	0.75	249
Left main stem disease (%)	4.8	6.1	<0.001	0.50	249
Complete revascularization (%)	66	60	<0.001	0.30	430
Use of stent (%)	92	94	<0.001	0.59	0
Use of DES (%)	48	41	<0.001	0.43	0

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# Statistical models

(adjustment for confounders)

## 1. **Complete case analysis** adjusted for propensity score

Multilevel logistic regression

## 2. **Imputed data** set adjusted for propensity score

Missing data imputed by multiple imputation model

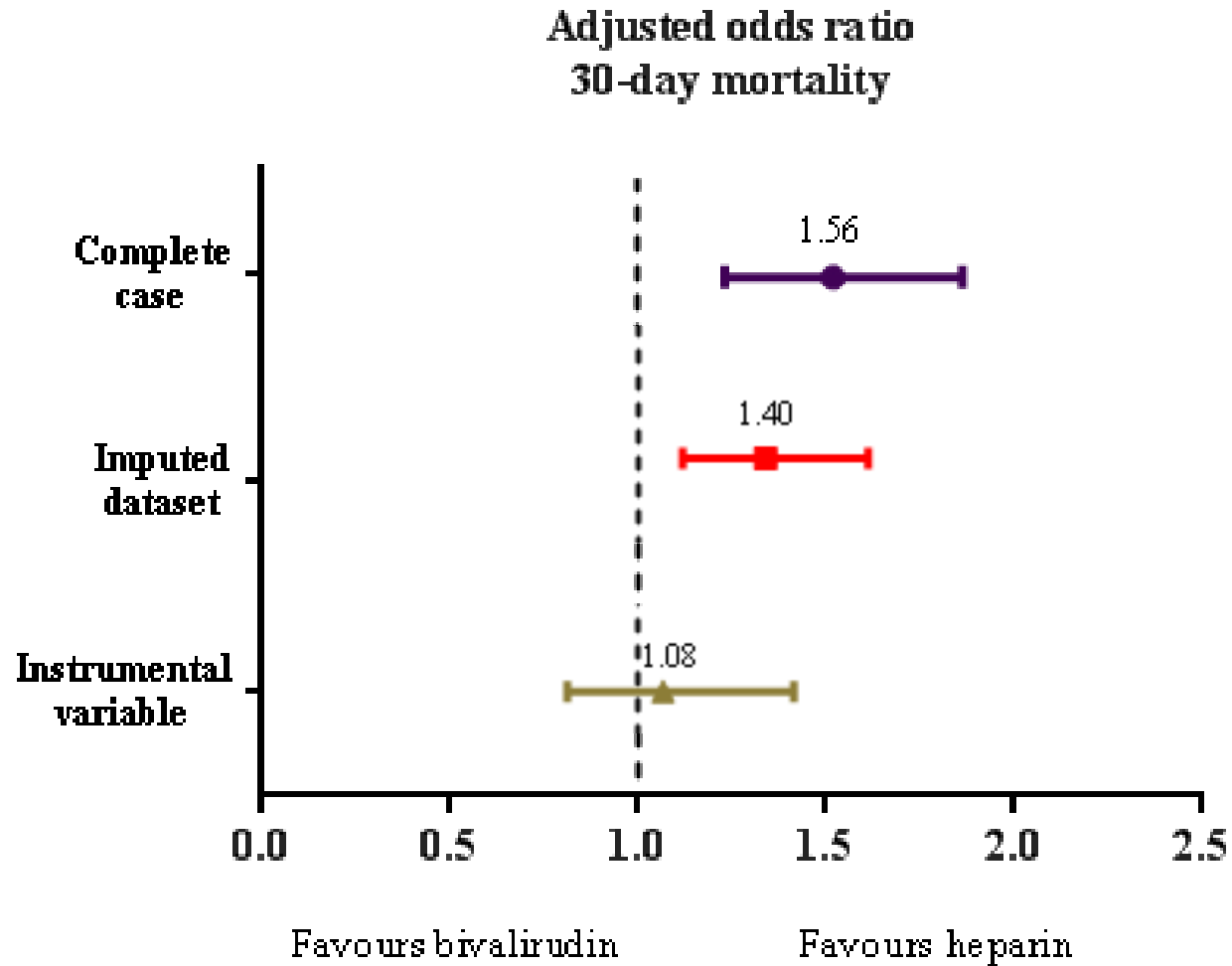
Multilevel logistic regression

## 3. **Instrumental variable analysis**

To adjust for unknown/unmeasured confounders!

Adjusted for: age, biomarkers, procedural success, hypertension, hyperlipidemia, gender, antiplatelet therapy, warfarin therapy, UFH/LMWH treatment, prior CABG, prior MI, prior PCI, diabetes, smoking, year, angiographic findings, access site, usage of DES, CTO procedure, completeness of revascularization)

# Results



# Conclusion

- Our large observational study **questions the superiority of bivalirudin** over heparin in the absence of GP IIb/IIIa blockade in patients with NSTEMI-ACS undergoing PCI.
- **A prospective randomized trial** evaluating bivalirudin vs heparin is highly warranted.
- **The register-based randomized clinical trial VALIDATE-SWEDEHEART** comparing bivalirudin to heparin in patients pretreated with novel ADP-receptor blockers (n=6000) is under way.



# Planned RRCTs in SCAAR

REAL-SWEDEHEART

STEMI  
N=3450



R



Radial  
N=1725

Femoral  
N=1725

Primary outcome: death at  
180 days

VALIDATE-SWEDEHEART

STEMI N=3000  
NSTEMI N=3000



R



Heparin  
alone  
N=3000

Bivalirudin  
N=3000

Primary outcome: death,  
MI or major bleeding at  
180 days