Hvordan bruke resultater fra kvalitetsregistre for å endre klinisk praksis?

Claes Held, MD PhD
Kardiologkliniken
Uppsala Clinical Research Center
Akademiska Sjukhuset
Uppsala
SWEDEHEART

Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies

www.swedeheart.org
SWEDHEART - Organisation

Public Health Care providers (SALAR) → Swedeheart Steering-group → Registry-center UCR

Acute Coronary Care (RIKS-HIA) Working group
Angiography & PCI (SCAAR) Working group
Heart Surgery Working group
Secondary prevention SEPHIA Working group
Catheter-based Valve-intervention Working group
Cardio-genetics Working group

71 hospitals → 30 hospitals → 8 hospitals → 71 hospitals → 7 hospitals → ? hospitals
## SWEDHEART - Coverage

<table>
<thead>
<tr>
<th>Service</th>
<th>Hospitals</th>
<th>Patients</th>
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<tbody>
<tr>
<td>Heart Surgery</td>
<td>100 %</td>
<td>100 %</td>
</tr>
<tr>
<td>Angiography &amp; PCI (SCAAR)</td>
<td>100 %</td>
<td>100 %</td>
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<tr>
<td>Acute coronary syndrome (RIKS-HIA)</td>
<td>100 %</td>
<td>90 %</td>
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<tr>
<td>Secondary prevention (SEPHIA)</td>
<td>100 %</td>
<td>70 %</td>
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<tr>
<td>Cath.-based valve-intervention</td>
<td>100%</td>
<td>100%</td>
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</table>
Caregiver

Electronic Health Records

On-line reports to caregivers, patients, policy-makers, public

Patient

Other health registries

Decision-support

Biobank

Register

Research database

Publications
Årsrapporter


<table>
<thead>
<tr>
<th>År</th>
<th>Actilyse</th>
<th>Metalyse</th>
<th>Rapilysin</th>
<th>Streptokinas</th>
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<table>
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<tr>
<th>År</th>
<th>Avlidne inom 30 dgr</th>
<th>Avlidne inom 1 år</th>
<th>Sjukhus</th>
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<tr>
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<td>10%</td>
<td>20%</td>
<td>Sjukhus Avesta</td>
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<td>15%</td>
<td>25%</td>
<td>Sjukhus Piteå</td>
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<td>1996</td>
<td>20%</td>
<td>30%</td>
<td>Sjukhus Umea</td>
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<tr>
<td>1997</td>
<td>25%</td>
<td>35%</td>
<td>Sjukhus Örebro</td>
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<td>30%</td>
<td>40%</td>
<td>Sjukhus Linköping</td>
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<td>35%</td>
<td>45%</td>
<td>Sjukhus Malmö</td>
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<tr>
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<td>40%</td>
<td>50%</td>
<td>Sjukhus Göteborg</td>
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<tr>
<td>2001</td>
<td>45%</td>
<td>55%</td>
<td>Sjukhus Helsingborg</td>
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<tr>
<td>2002</td>
<td>50%</td>
<td>60%</td>
<td>Sjukhus Västra Frölunda</td>
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<td>2003</td>
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<td>65%</td>
<td>Sjukhus Trelleborg</td>
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<tr>
<td>2004</td>
<td>60%</td>
<td>70%</td>
<td>Sjukhus Kristianstad</td>
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<tr>
<td>2005</td>
<td>65%</td>
<td>75%</td>
<td>Sjukhus Karlskrona</td>
</tr>
<tr>
<td>2006</td>
<td>70%</td>
<td>80%</td>
<td>Sjukhus Oskarshamn</td>
</tr>
</tbody>
</table>

Snitt=10.0% med >=20 patienter i urvalet, 2006 - 2007 (medelvärde, 95% konfidensintervall).

Figur 28f. 1-årsmortalitet vid hjärtinfarkt, <80 år, per sjukhus.
<table>
<thead>
<tr>
<th>Quality indicator</th>
<th>0,5 points</th>
<th>1 points</th>
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<tbody>
<tr>
<td>Reperfusion for STEMI/LBBB</td>
<td>80%</td>
<td>85%</td>
</tr>
<tr>
<td>Reperfusion for STEMI/LBBB within recommended time (PCI within 90 min and</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>thrombolysis within 30 min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary angiogram for target population with NSTEMI</td>
<td>75%</td>
<td>80%</td>
</tr>
<tr>
<td>LMW Heparin/ Heparin/ Fondaparinux for NSTEMI</td>
<td>90%</td>
<td>95%</td>
</tr>
<tr>
<td>ASA, other platelet inhibitor or anticoag for MI</td>
<td>90%</td>
<td>95%</td>
</tr>
<tr>
<td>P2Y12-blocker for NSTEMI</td>
<td>85%</td>
<td>90%</td>
</tr>
<tr>
<td>Betablocker for MI</td>
<td>85%</td>
<td>90%</td>
</tr>
<tr>
<td>Lipid lowering post MI</td>
<td>90%</td>
<td>95%</td>
</tr>
<tr>
<td>ACE-inh/ARB for target population post MI</td>
<td>85%</td>
<td>90%</td>
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</tbody>
</table>
RIKS-HIA Quality Index

2005

2011
Hospital Scores On The Swedish Coronary Care Registry Quality Index, 2005–09

Index scores become public

- All hospitals (N = 69)
- Below-average hospitals as of 2007 (n = 34)

Larsson et al. Health Affairs 2012; 31(1)
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<tr>
<td>ACEinh/ARB for target population post MI</td>
<td>85%</td>
<td>90%</td>
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<tr>
<td>Proportion &lt; 75 y with sec prev</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>Proportion quit smoking 12-14 m</td>
<td>60%</td>
<td>70%</td>
</tr>
<tr>
<td>Physical training program 12-14 m</td>
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<td>60%</td>
</tr>
<tr>
<td>LDL &lt;2.5 mmol/L 12-14 m</td>
<td>60%</td>
<td>70%</td>
</tr>
<tr>
<td>BP &lt; 140 mmHg 12-14 m</td>
<td>70%</td>
<td>75%</td>
</tr>
</tbody>
</table>
Forskning under 2000-talet Swedeheart stigande antal publikationer, bl.a.

Nationwide Cohort Study of Risk of Ischemic Heart Disease in Patients With Celiac Disease

Jonas F. Ludvigsson, MD, PhD; Stefan James, MD, PhD; Johan Askling, MD, PhD; Ulf Stenestrand, MD, PhD; Erik Ingelsson, MD, PhD

Background—Studies on ischemic heart disease (IHD) incidence in individuals with celiac disease (CD) are contradictory and do not take small intestinal pathology into account.

Methods and Results—In this Swedish population-based cohort study, we examined the risk of IHD in patients with CD based on small intestinal histopathology. We defined IHD as death or incident disease in myocardial infarction or angina pectoris in Swedish national registers. In 2006 there were 32 690 new cases of CD, about one-third of which were diagnosed after the age of 20 years.

Association Between Admission Supine Systolic Blood Pressure and 1-Year Mortality in Patients Admitted to the Intensive Care Unit for Acute Chest Pain

Ulf Stenestrand, MD, PhD
Magnus Wijkman, MD
Max Fréderiksson, MD
Fredrik H. Nyström, MD, PhD

Context—High resting blood pressure (BP) is among the best studied and established risk factors for cardiovascular disease. However, little is known about the relationship between BP under acute stress, such as in acute chest pain, and subsequent mortality.

Objective—To study long-term mortality related to supine BP in patients admitted to the intensive care unit for acute chest pain.

Design—Prospective, observational cohort study.

Influence of Renal Function on the Effects of Early Revascularization in Non–ST-Elevation Myocardial Infarction

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

Karolina Sanner, MD; Pia Lundman, MD, PhD; Stefan H. Jacobsson, MD, PhD; Staffan Schöni, MD; Johan Lindbäck, MSc; Ulf Stenestrand, MD, PhD; Lars Wallentin, MD, PhD; Tomas Jernberg

Background—It is unknown whether patients with acute myocardial infarction who are transferred to intensive care units within 24 hours of symptom onset have better outcomes than do those who are transferred within 24 to 48 hours of symptom onset.

Long-Term Outcomes with Drug-Eluting Stents versus Bare-Metal Stents in Sweden

Bo Lagerqvist, MD, Ph.D., Stefan K. James, M.D., Ph.D., Ulf Stenestrand, M.D., Ph.D., Johan Lindbäck, M.Sc., Tage Nilsson, M.D., Ph.D., and Lars Wallentin, M.D., Ph.D., for the SCAAR Study Group

Long-term Outcome of Primary Percutaneous Coronary Intervention vs Prehospital In-Hospital Thrombolysis for Patients With ST-Elevation Myocardial Infarction

Ulf Stenestrand, MD, PhD; Johan Lindbäck, MSc; and Lars Wallentin

Anticoagulation Therapy in Atrial Fibrillation in Combination With Acute Myocardial Infarction Influences Long-Term Outcome

A Prospective Cohort Study From the Register of Information and Knowledge About Swedish Heart Intensive Care Admissions (RIKS-HIA)

Ulf Stenestrand, MD, PhD; Johan Lindbäck, MSc; Lars Wallentin

Early revascularisation and 1-year survival in 14-day survivors of acute myocardial infarction: a prospective cohort study

Ulf Stenestrand, Lars Wallentin

Introduction
Background Randomised trials of early revascularisation in acute coronary syndromes have yielded conflicting results.

Long-Term Safety and Efficacy of Drug-Eluting versus Bare-Metal Stents in Sweden

Stefan K. James, M.D., Ph.D., Ulf Stenestrand, M.D., Ph.D., Johan Lindbäck, M.Sc., Jörg Carlsson, M.D., Ph.D., Fredrik Schöni, M.D., Ph.D., Tage Nilsson, M.D., Ph.D., Lars Wallentin, M.D., Ph.D., and Bo Lagerqvist, M.D., Ph.D., for the SCAAR Study Group

Association Between Adoption of Evidence-Based Treatment and Survival for Patients With ST-Elevation Myocardial Infarction

Tomas Jernberg, MD, PhD
Pia Johansson, MD, PhD
Claes Held, MD, Ph.D.

Context—Only limited information is available on the impact of implementing new evidence-based and guideline-adherent care in real-life healthcare systems.

Objective—To describe.
Publications from SWEDHEART in 2015 - 58 vetenskapliga artiklar
Register av intresse inom kardiovaskulär forskning

- The National Board of Health and Welfare (Socialstyrelsen)
  - The national registry of causes of death (Dödsorsaksregistret)
  - The national patient register (Patientregistret)
  - The Swedish prescribed drug register (Läkemedelsregistret)
- Statistics Sweden (SCB)
  - eg. marital status, country of birth, income, educational level
- The Swedish Social Insurance Agency (Försäkringskassan)
- The National Quality Registers (about 100 at present)
Observational (registry) studies

**Strengths**

- Unselected populations – high degree of generalizability
- Clinical important, “hard” endpoints
- Large cohorts allow rare endpoints
- Not expensive

**Weaknesses**

- Less good data quality
- “Missing data” – selection biases
- Confounders impossible to adjust for
- Advanced statistics – “black box”
# Differences between registries and clinical studies

<table>
<thead>
<tr>
<th>Quality registries (patientdatalag, Personuppgifftslag)</th>
<th>Clinical studies (GCP)</th>
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<tbody>
<tr>
<td>Data must be deleted if requested from the patients</td>
<td>Data collected until the patient ask for withdrawal must not be deleted</td>
</tr>
<tr>
<td>Data must be deleted after a certain time if not approved otherwise</td>
<td>Data must be stored as long as it may be of interest to perform new data analysis</td>
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<tr>
<td>Data in the registry can be changed</td>
<td>Data in the study database must not be changed after “clean file”</td>
</tr>
<tr>
<td>Changes in the registry do not have to be logged.</td>
<td>Changes in the study database have to be logged until ”clean file” (audit trail)</td>
</tr>
<tr>
<td>Access to data must be logged to ensure a caregiver-patient relation</td>
<td>Access to data must not be logged to ensure a caregiver-patient relation but for audit trail</td>
</tr>
</tbody>
</table>
Randomized Clinical Trials - RCT

**Strengths**
- Correctly design studies with adequate power – “gold standard” to compare treatments
- No “confounding”

**Weaknesses**
- Very expensive – long time to plan and perform
- Often surrogate endpoint
- Selected centers, selected doctors
- Selected patients
  - Inclusion- and exclusions criteria
  - Selection based on doctors’ preferences.
- Patients are much more carefully monitored
- Often sponsored by pharma company – only studies with an financial interest

Balance between benefit and harm may be different
The concept of Register-based Randomized Clinical Trials (RRCT).

- Uses registries for data-capture and follow up.

- A randomization-module within the registry
Registry-based RCT (R-RCT)

- Combines the advantages of Quality Registries and Randomized Clinical Trials (RCT)
- Complements but does not replace RCT
- Patients may be identified in the registry and recruitment is facilitated by the system, leading to faster and more efficient enrollment and higher population coverage.
- Site participation using standard workflow and IT-systems
Registry-based RCT (R-RCT)

- High generalizability
  - Broad inclusion criteria
  - Few exclusion criteria
  - Comparison with those not included

- Lower costs by use of already existing:
  - Data collection platforms
    - Quality registries
    - Other health registries
  - Monitor organisation
  - collaboration network / research organization

- Long-term outcome by the use of other health registries
## Study design

<table>
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<th>R-RCT</th>
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<td>+</td>
</tr>
<tr>
<td>Device – CE mark, used</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Device, first in man</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Approved drugs used in clinical practise</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Drugs for new indication</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>New drugs</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>
R-RCTs are suitable when:

- open label randomization
- treatments that are already used in clinical practice
- limited monitoring is necessary
- central adjudication is not necessary.
- “Simple questions – simple endpoints”
- limited funding available
R-RCTs are **not** suitable when:

- careful safety monitoring and follow-up are necessary
- “blinding” of treatment is required
- high demand for data quality
- strictly defined endpoints and central adjudication is required
The spectrum from RRCT to RCT

New indication for a drug

RRCT
- Blinding
- Safety reporting
- Monitoring
- Adjudication of events

RCT
Some examples of recent RRCT
Prospective Registry based Randomized Clinical Trials (R-RCT) – a new concept for clinical research

Stefan James, Uppsala University

Ole Fröbert, Örebro University, Göran Olivecrona, Lund University, David Erlinge, Lund University, Tomas Jernberg, Karolinska Institute, Stockholm, Bertil Lindahl, Uppsala University, Lars Wallentin, Uppsala University, Bo Lagerqvist, Uppsala University

Sweden
When registering a STEMI during PCI, the system suggests randomization.
Two questions to answer:
- Informed consent?
- Inclusion / Exclusion criteria?
Patients with suspected STEMI referred to primary PCI
N = 7200

STEMI diagnosis confirmed at coronary angiography. Informed consent obtained

Online 1:1 randomization in SCAAR, guidewire advancement, i.c. nitroglycerin

Thrombus aspiration and PCI  
PCI alone

Immediately after PCI: TIMI flow grade

30 days: all-cause death

1, 2, 5 and 10 years: all-cause death and additional secondary endpoints

Fröbert et al, AHJ 2009
**TASTE** inclusion rate

![Graph showing the number of patients over time for All primary PCI:s and Randomized groups. The graph indicates a steady increase in patients from 2006 to 2013. There are 7244 patients in total.]
All patients with STEMI in Sweden and Iceland undergoing primary or rescue PCI. N=11 709 *

Enrolled in TASTE N=7259

N=3621 assigned to thrombus aspiration
N=3399 underwent thrombus aspiration
N=222 underwent conventional PCI
N=3445 underwent conventional PCI
N=1162 underwent thrombus aspiration
N=3535 underwent conventional PCI
N=3621 were followed up
N=3623 were followed up

Enrolled in Denmark N=247

Erroneous enrollments N=15

Randomized in TASTE N=7244

N=3623 were followed up
N=1162 were followed up
N=3535 were followed up

Not enrolled N=4697

N=3623 assigned to conventional PCI
N=3535 underwent conventional PCI
N=1162 underwent thrombus aspiration
N=3445 underwent conventional PCI

No patients (0) were lost to follow-up of the primary outcome!
All-cause mortality at 30 days

Per protocol analysis based on actual treatment:

HR 0.94 (0.72 - 1.22), P=0.63

HR 0.88 (0.66 - 1.17), P=0.38
The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research?

Michael S. Lauer, M.D., and Ralph B. D’Agostino, Sr., Ph.D.

The randomized trial is one of the most powerful tools clinical researchers possess, a tool that enables them to evaluate the effectiveness of new (or established) therapies while accounting for United States and abroad have collected vast amounts of data from patients with acute coronary syndromes, stable coronary disease, and heart failure, as well as...
Eligible patient*: in ambulance, ED or cath lab
N=6600

*Inclusion criteria:
- symptoms suggestive of AMI within 6h
- SpO2 ≥ 90%
- ≥ 30y
- ECG changes indicating ischemia and/or elevated troponin levels

Oxygen
6l/min for (6-)12h via Oxymask

Air

Primary Endpoint: 1-year total mortality

Additional secondary endpoint and sub studies
Data analysis through SWEDHEART registry and national mortality registry

Funding: Swedish Research council (VR)
Oxygen Therapy in Suspected Acute Myocardial Infarction

Robin Hofmann, M.D., Stefan K. James, M.D., Ph.D., Tomas Jernberg, M.D., Ph.D., Bertil Lindahl, M.D., Ph.D., David Erlinge, M.D., Ph.D., Nils Witt, M.D., Ph.D., Gabriel Arefalk, M.D., Mats Frick, M.D., Ph.D., Joakim Alfredsson, M.D., Ph.D., Lennart Nilsson, M.D., Ph.D., Annica Ravn-Fischer, M.D., Ph.D., Elmir Ormerovic, M.D., Ph.D., Thomas Kellerth, M.D., David Sparv, B.Sc., Ulf Ekelund, M.D., Ph.D., Rickard Linder, M.D., Ph.D., Mattias Ekström, M.D., Ph.D., Jörg Lauermann, M.D., Urban Haaga, B.Sc., John Pernow, M.D., Ph.D., Ollie Östlund, Ph.D., Johan Herlitz, M.D., Ph.D., and Leif Svensson, M.D., Ph.D., for the DETO2X–SWEDEHEART Investigators*
Figure 2. Kaplan–Meier Curves for Death from Any Cause.

Kaplan–Meier curves are shown for the cumulative probability of death from any cause up to 365 days after randomization among patients assigned to oxygen or ambient air. The proportional-hazards assumption was subjected to post hoc testing by inserting a linear treatment–time interaction in the Cox proportional-hazards model, which did not noticeably improve the model fit (P=0.61). The inset shows the same data on an expanded y axis.
STEMI or NSTEMI
Treatment with ticagrelor or prasugrel pre-PCI

Heparin only
(acrossing to local PM)

Bivalirudin
(Heparin max 5000U)

Primary endpoint: Death, MI, Major bleeding at 6 months.
Bivalirudin versus Heparin Monotherapy in Myocardial Infarction

Figure 1. Primary End-Point Events during 180 Days of Follow-up.

The Kaplan–Meier curves show the cumulative probability of the primary end point, which was a composite of death, myocardial infarction, or major bleeding (Panel A), as well as the cumulative probability of each component of the primary end point (Panels B, C, and D), during 180 days of follow-up. The insets show the same data on an enlarged y axis.
SPIRRIT- HFPEF

Patients enrolled from ~11,018 eligible patients in registry
N=3583

R 1:1

Spirinolactone
Standard of care

Event driven 1073 events

Primary Endpoint: All cause death,
Secondary efficacy endpoints: HF hospitalization and other cardiovascular outcomes
Safety endpoints related to renal function and potassium

- Stable chronic HF
- Age ≥ 50 years
- EF ≥ 40%
- NT-proBNP
  - > 300 (sinus rhythm);
  - > 750 (AF)
Total n=4052 patients
2026 patients in each arm

Exclude:
- Previous CABG
- Left main disease
- Shock

Primary PCI of STEMI or high-risk NSTEMI
+ Residual non-culprit disease

Non-CTO
≥ 1 non-culprit lesions
non-culprit vessels at least 2.5mm on angiography (50-99%)

1:1 Randomization

Index admission FFR-guided PCI to non-culprit lesions*

Initial conservative management of non-culprit lesions

Trial follow-up for endpoints at 30d and at least 1 year

Admission meaning initial PCI-capable unit or after transfer to another PCI-capable unit

Böhm, James et al
Patients with STEMI or NSTEMI referred to coronary angiography
N = 4400

PCI / coronary angiography

Online 1:1 randomization

Influenza vaccination  Placebo vaccination

1 year: Composite of time to all-cause death, new AMI and stent thrombosis + secondary endpoints

2, 3 and 5 years: Exploratory endpoints
Study endpoints

• Primary composite endpoint:
  o **All-cause death**,  
  o **Hospitalization for a new myocardial infarction** or  
  o **Stent thrombosis**

- within 1 year in patients with STEMI or NSTEMI undergoing coronary angiography/PCI

• Secondary endpoints: time to cardiovascular death, revascularization, stroke or rehospitalization for heart failure till 1 year

• Exploratory endpoint assessment after 1 year
REDUCE-SWEDEHEART

- en ny och enkel R-RCT där alla sjukhus kan delta

REDUCE-SWEDEHEART

Studerar frågan om effekten av beta-blockad eller ej till patienter med hjärtinfarkt och normal systolisk vänsterkammarfunktion
Patients with **myocardial infarction**, undergoing angiography and if appropriate revascularization and **LV-EF ≥ 50%**, included in SWEDHEART

**Informed consent**

**Randomization**

n = 7000

**Oral Beta-blockade**

(Metoprolol Succinate or Bisoprolol)

n = 3500

**No Beta-blockade**

N = 3500

**Primary endpoint:** Death or non-fatal MI

(Event driven ITT, expected median follow-up of 2 years)

**Secondary endpoints:** Death, cardiovascular death, MI, HF, atrial fibrillation

(Safety data, PROM)
Patient med akut hjärtinfarkt

Kranskärlsröntgen

Stenos ≥50%

Stenos <50%

MINOCA-BAT

REDCeSWEDHEART
Patient som uppfyller alla inklusionsmen inga exklusionskriterier

Informert samtycke. Randomisering dag 1-14
N=3400

- Både ACEI/ARB och Beta-blockad
  N=850
- Enbart ACEI/ARB
  N=850
- Enbart Beta-blockad
  N=850
- Ingen ACEI/ARB eller Beta-blockad
  N=850

All annan behandling: Optimal sekundärprevention med målnivåer enligt guideliens

12 månader: besök/telefonsamtal/brev
Följsamhet till läkemedel och utvärderingar av substudier (separata protokoll)

4 år (i medel): uppföljning i register
Primärt kombinerat utfallsmått: död och återinläggning pga hjärtinfarkt, ischemisk stroke eller hjärtsvikt
TACSI study design

Patient data capture in registries

-4 days  0  30 days  365 days  2 y  3 y  5 y
Primary endpoints

• Primary efficacy endpoint: Time to MACE (all cause death, myocardial infarction, stroke, new revascularization) within 12 months after inclusion

• Primary safety endpoint: Bleeding requiring hospitalization

• Endpoints assessed 1, 12, 24, 36, 60 and 120 months after inclusion.
Future developments that may change the conditions for RRCTs

• Improvement of the proportion actually included: >95%

• Improvement of data quality: Logical and statistical controls, 7 monitors are now employed.

• Improve PROM (patient reported outcome measures) and PREM modules

• Integration between electronic health records and the registry

• Building a biobank around Swedeheart

• International collaboration
Konklusion

- Användandet av och offentliggörande av kvalitetsindex per sjukhus i register leder till successiv förbättring av vårdkvaliteten
- R-RCT är ett nytt koncept som revolutionerat klinisk forskning och möjliggör studier med viktiga frågeställningar till en bråkdel av kostnaden jämfört med traditionella RCT
- Internationella guidelines har redan förändrats pga RRCT-resultat:
  - TASTE-studien ledde till ändrade guidelines för trombsugning vid primär PCI till att inte användas rutinmässigt
  - DETOX-studien har ändrat guidelines till att inte rekommendera syrgas rutinmässigt till pat med misstänkt hjärtinfarkt och saturation >90%
  - VALIDATE har påverkat guidelines till att nedgradera Bivalirudin vs Heparin vid AKS
Konklusion

• Stort behov av randomiserade prövningar (RCT) speciellt för evaluering av vårdstrategier, devices, etablerade farmakologiska terapier

• Klassiska RCT görs ofta inte i breda representativa patientpopulationer

• Nationella kliniska register är starka nätverk för samarbete och enrollerar kompletta patientpopulationer

• Prospektiva Registerbaserade Randomiserade Clinical Trials (RRCT) är en ny utvecklingsmöjlighet för klinisk forskning

• RRCT är idealisk för att studera en kliniskt viktig hypotes med hårda endpoints
Thank you!