

# Transportability analyses in Sweden

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# Overview

- Registry based randomized trials
- Why do a transportability/generalizability analysis in Swedish data?

# Registry based randomized trials (R-RCTs)

# SWEDEN

- Sweden has a tax payer funded universal healthcare system
- Everyone that lives in Sweden has a personal number, which is used to capture data every time they use the healthcare system
- There are several mandatory national registers, such as population register, patient register, cause of death register, prescribed drug register etc.
- Also a selection (>100) healthcare quality registries that contain more detailed information on specific diseases. E.g., SWEDEHEART
- Can all be linked using the personal number

## **R-RCT**

Pragmatic randomized trial that uses a clinical registry for one or several major functions for trial conduct and outcomes reporting

- When a clinician is collecting data for a healthcare quality registry, they are notified if the patient is eligible for an ongoing R-RCT
- If they consent, they are randomized to a treatment arm through a randomization module built into the registry

The registry helps to:

- Identify eligible patients
- Randomize
- Collect baseline and procedure characteristics
- Assist with collecting consent forms
- Identify clinical endpoints (there is no “active” follow up)

## WHAT R-RCT'S CAN DO

Evaluate therapeutic options that are available in routine clinical care. We can find out what works best.

## WHAT R-RCT'S CANNOT DO

Cannot design RCTs to experiment new pharmaceutical agents or medical devices.



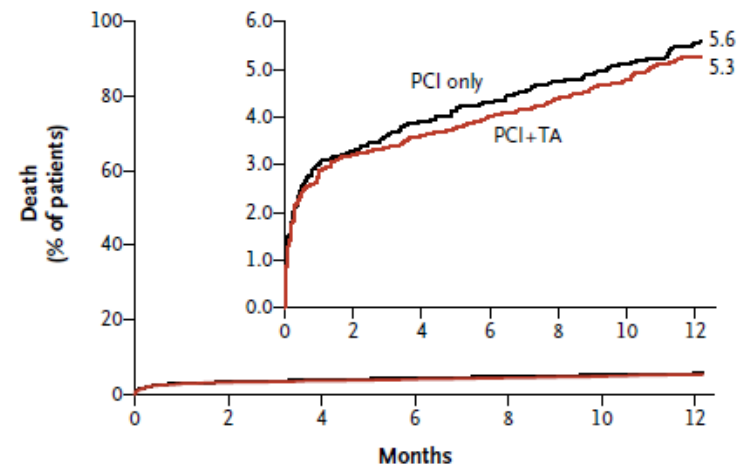
# EXAMPLE

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

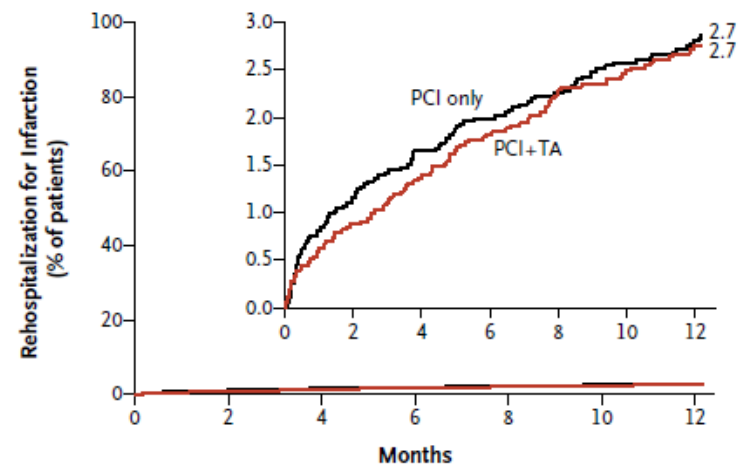
ORIGINAL ARTICLE

## Outcomes 1 Year after Thrombus Aspiration for Myocardial Infarction

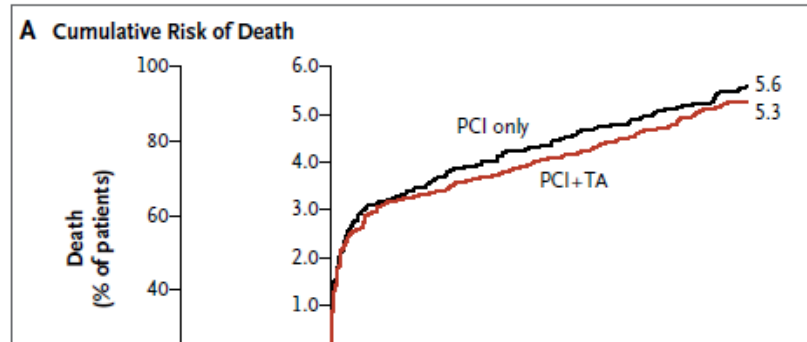
Bo Lagerqvist, M.D., Ph.D., Ole Fröbert, M.D., Ph.D., Göran K. Olivecrona, M.D., Ph.D.,  
Thórarinn Gudnason, M.D., Ph.D., Michael Maeng, M.D., Ph.D., Patrik Alström, M.D.,  
Jonas Andersson, M.D., Ph.D., Fredrik Calais, M.D., Jörg Carlsson, M.D., Ph.D.,  
Olov Collste, M.D., Matthias Götberg, M.D., Ph.D., Peter Hårdhammar, M.D.,  
Dan Ioanes, M.D., Anders Kallryd, M.D., Rickard Linder, M.D., Ph.D.,  
Anders Lundin, M.D., Jacob Odenstedt, M.D., Elmir Omerovic, M.D., Ph.D.,  
Verner Puskar, M.D., Tim Tödt, M.D., Ph.D., Eva Zelleröth, M.D.,  
Ollie Östlund, Ph.D., and Stefan K. James, M.D., Ph.D.

**A Cumulative Risk of Death****No. at Risk**

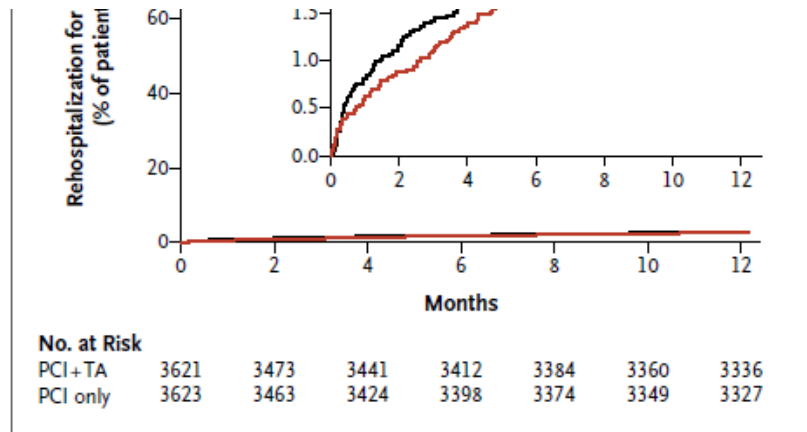
PCI+TA	3621	3500	3485	3470	3456	3440	3425
PCI only	3623	3503	3481	3466	3450	3435	3420

**B Cumulative Risk of Rehospitalization for Infarction****No. at Risk**

PCI+TA	3621	3473	3441	3412	3384	3360	3336
PCI only	3623	3463	3424	3398	3374	3349	3327



**NO DIFFERENCE IN RISK OF DEATH OR  
MOCARDIAL INFARCTION BY 1 YEAR BETWEEN  
THOSE RANDOMIZED TO THROMBUS  
ASPIRATION OR NO THROMBUS ASPIRATION**



TASTE used the SWEDEHEART registry to:

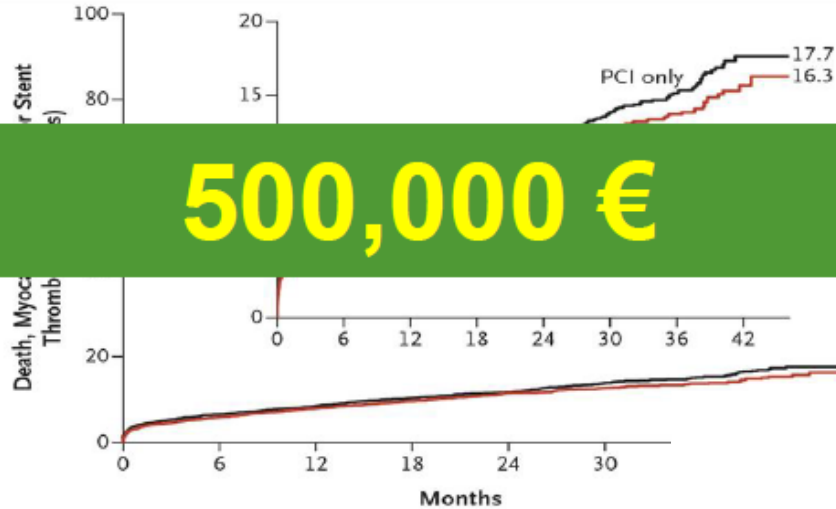
- Identify eligible patients that had an MI and underwent PCI
- Randomize individuals to thrombus aspiration or no thrombus aspiration
- Collect baseline characteristics
- Assist with collecting consent forms
- Identify clinical endpoints of death and myocardial infarction

Embedding the trial within a registry meant TASTE was

**CHEAP & QUICK**

*TASTE*

## Registry-based Follow-up



No. at Risk								
PCI+TA	3623	3404	3328	2821	2180	1505	864	184
PCI only	3621	3386	3315	2796	2200	1494	862	190

1<sup>st</sup> patient: June 2010

30 centers

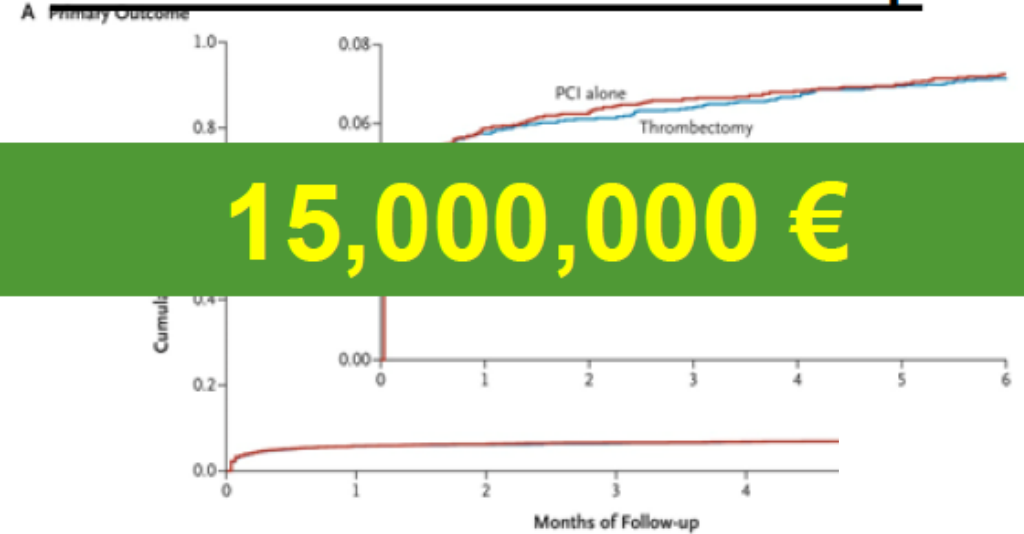
33 months to full enrollment

Fröbert et al. N Engl J Med 2013 Oct 24;369(17):1587-97

Lagerqvist B et al. N Engl J Med 2014;371:1111-1120



## Standard site-based Follow-up



No. at Risk							
Thrombectomy	5033	4734	4696	4678	4662	4647	4628
PCI alone	5030	4727	4688	4666	4653	4642	4618

1<sup>st</sup> patient: August 2010

87 centers

48 months to full enrollment

Jolly SS et al. N Engl J Med 2015;372:1389-1398



Why undertake a  
generalizability/transportability  
analysis in Swedish data?

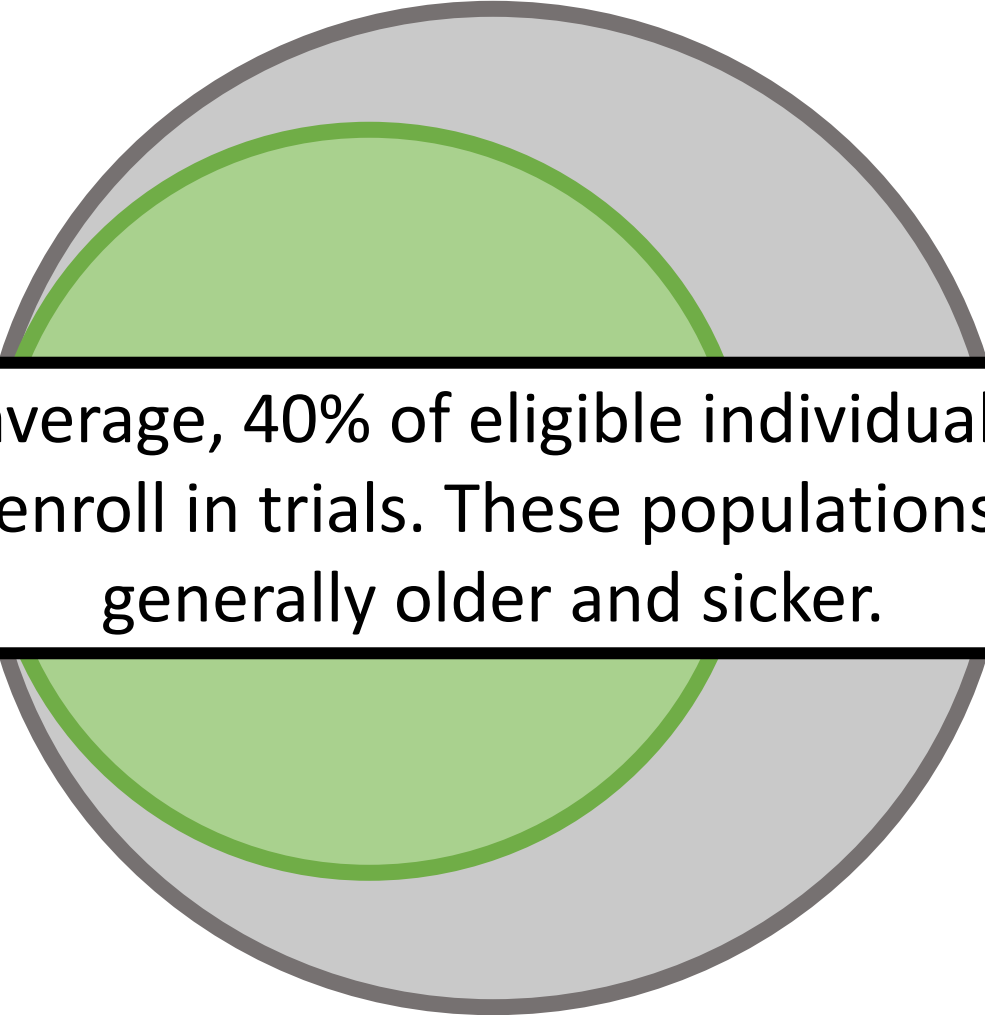


There remain questions around external validity  
when we undertake R-RCTs

TARGET POPULATION



## TARGET POPULATION



On average, 40% of eligible individuals do not enroll in trials. These populations are generally older and sicker.

## TARGET POPULATION

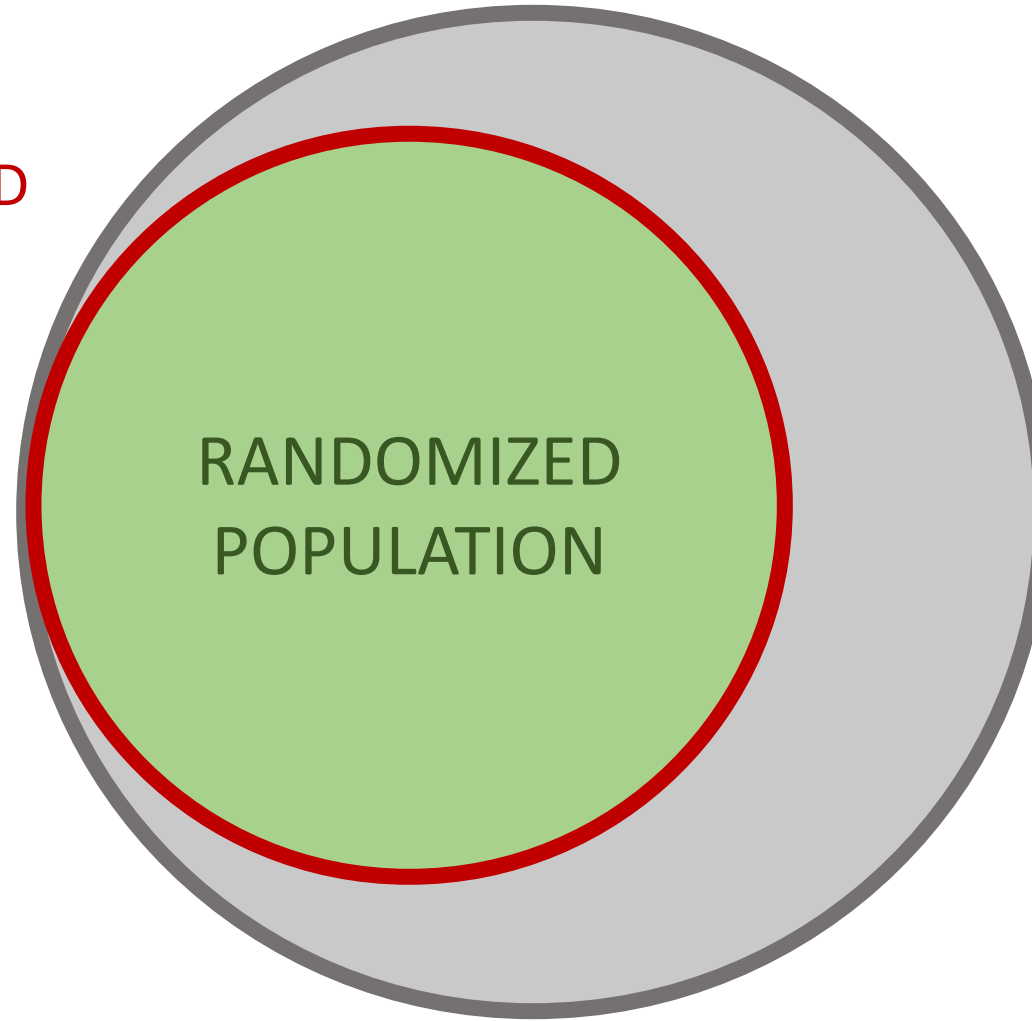
A diagram consisting of a large gray semi-circle with a dark gray outline. Inside this semi-circle, there is a smaller green semi-circle with a green outline, positioned horizontally in the center. The green semi-circle is partially obscured by a white rectangular box with a black border that contains text.

If the characteristic differences of those that do and do not enroll in the trial are also modifiers of the treatment effect

Then, we do not have external validity and our treatment effect may differ between the trial and target populations

TARGET POPULATION

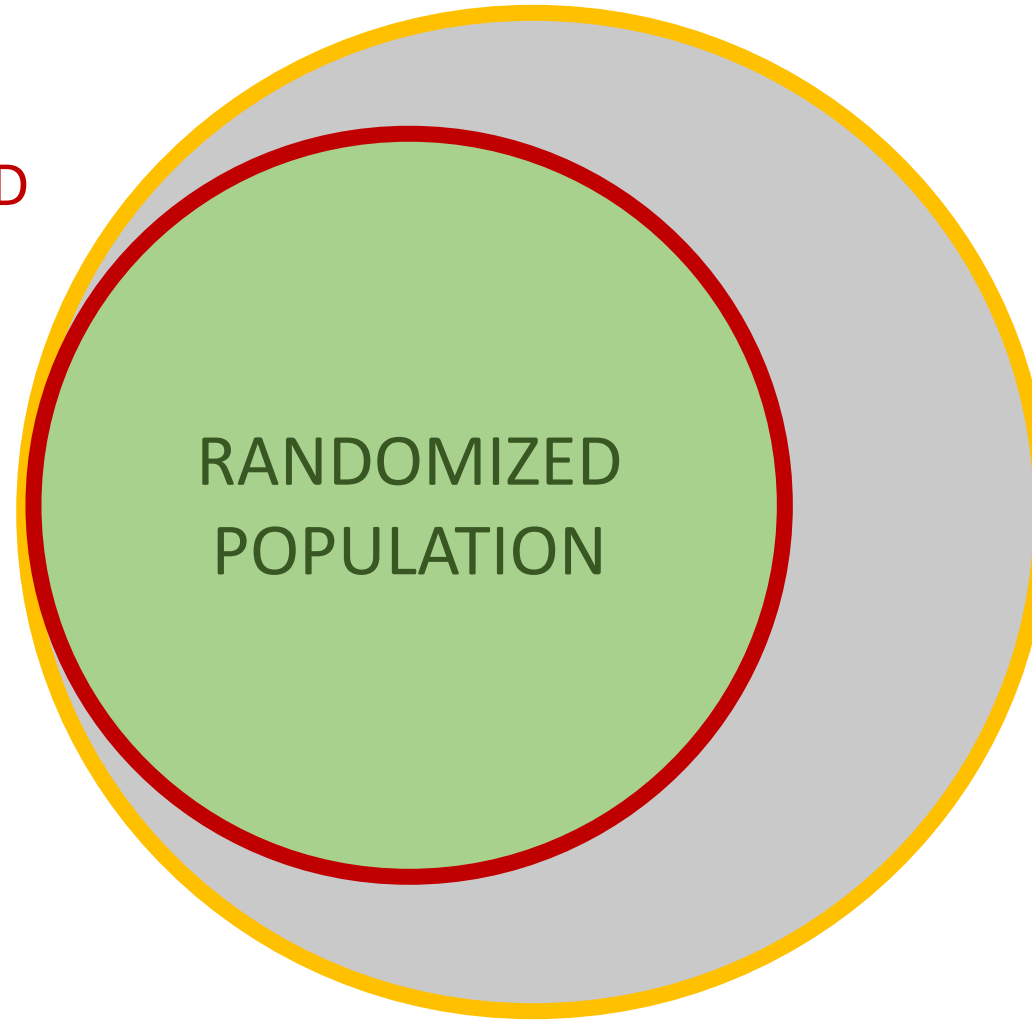
**TRADITIONAL RCT**  
BASELINE DATA COLLECTED  
IN RANDOMIZED  
POPULATION



TARGET POPULATION

**TRADITIONAL RCT**

BASELINE DATA COLLECTED  
IN RANDOMIZED  
POPULATION



**R-RCT**

BASELINE DATA COLLECTED  
IN WHOLE TARGET  
POULATION

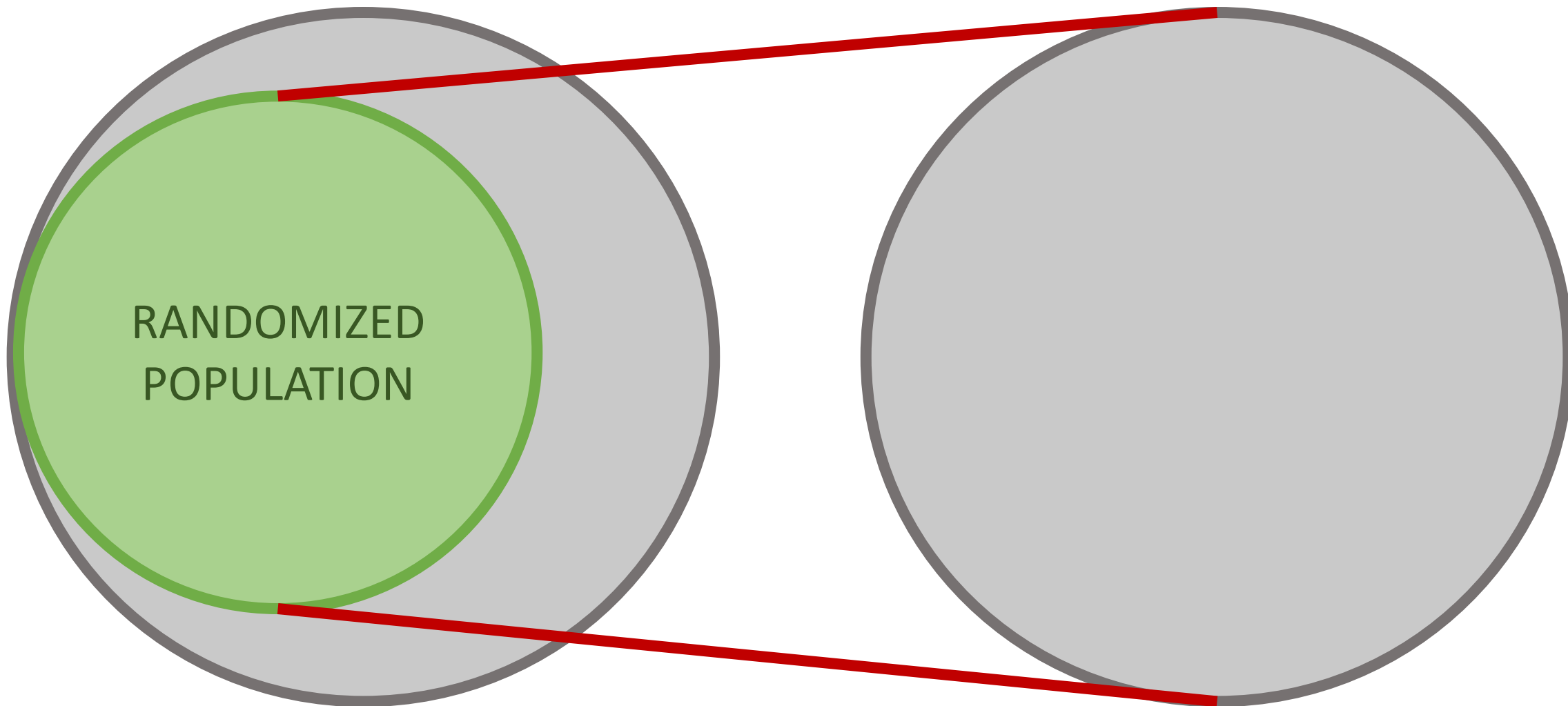
When a trial is embedded within a registry:

- Baseline characteristics are collected in all eligible individuals as part of the standard data collection for the registry
- The data generating mechanism is the same for everyone, regardless of if they take part in the trial
- We can get **the same** baseline data for individuals that were and were not randomized

TARGET POPULATION

TARGET POPULATION

RANDOMIZED  
POPULATION



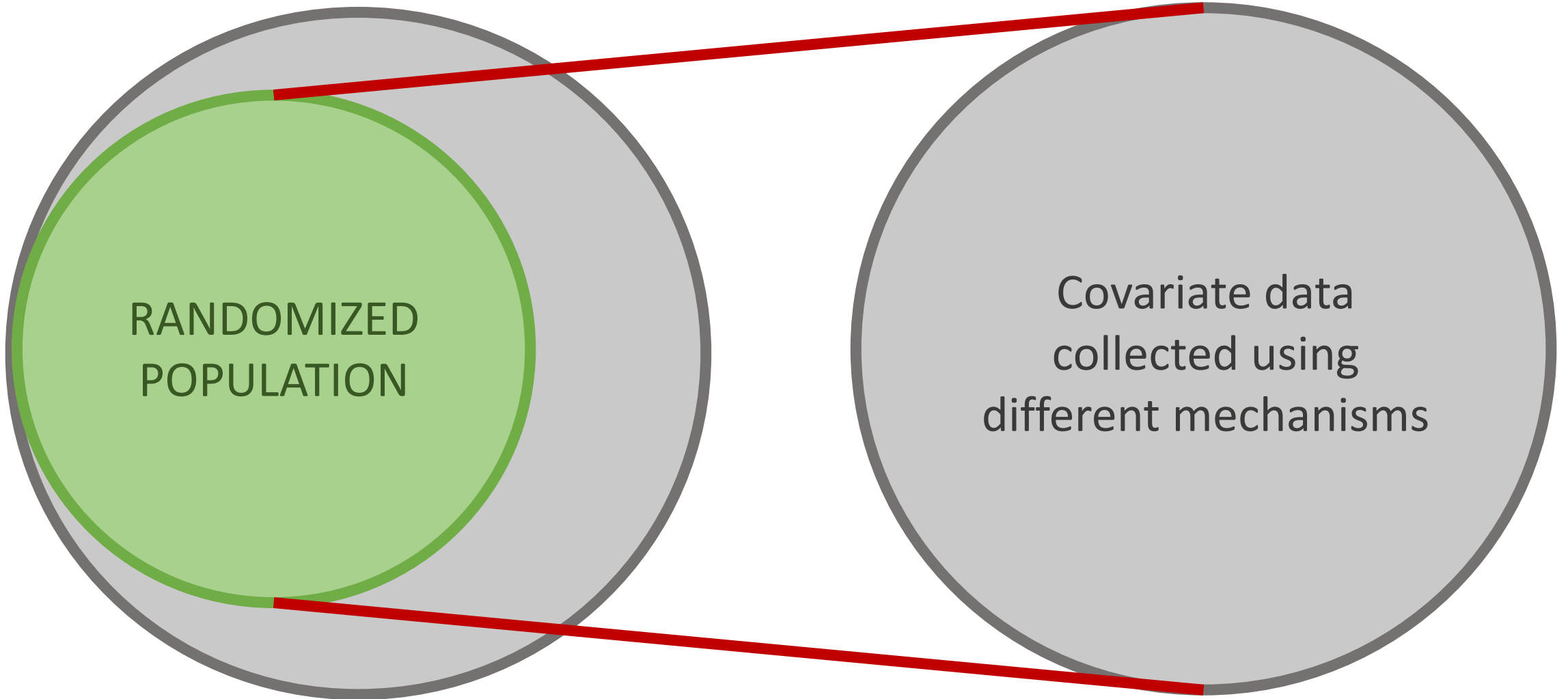


TARGET POPULATION

TARGET POPULATION

RANDOMIZED  
POPULATION

Covariate data  
collected using  
different mechanisms



TARGET POPULATION

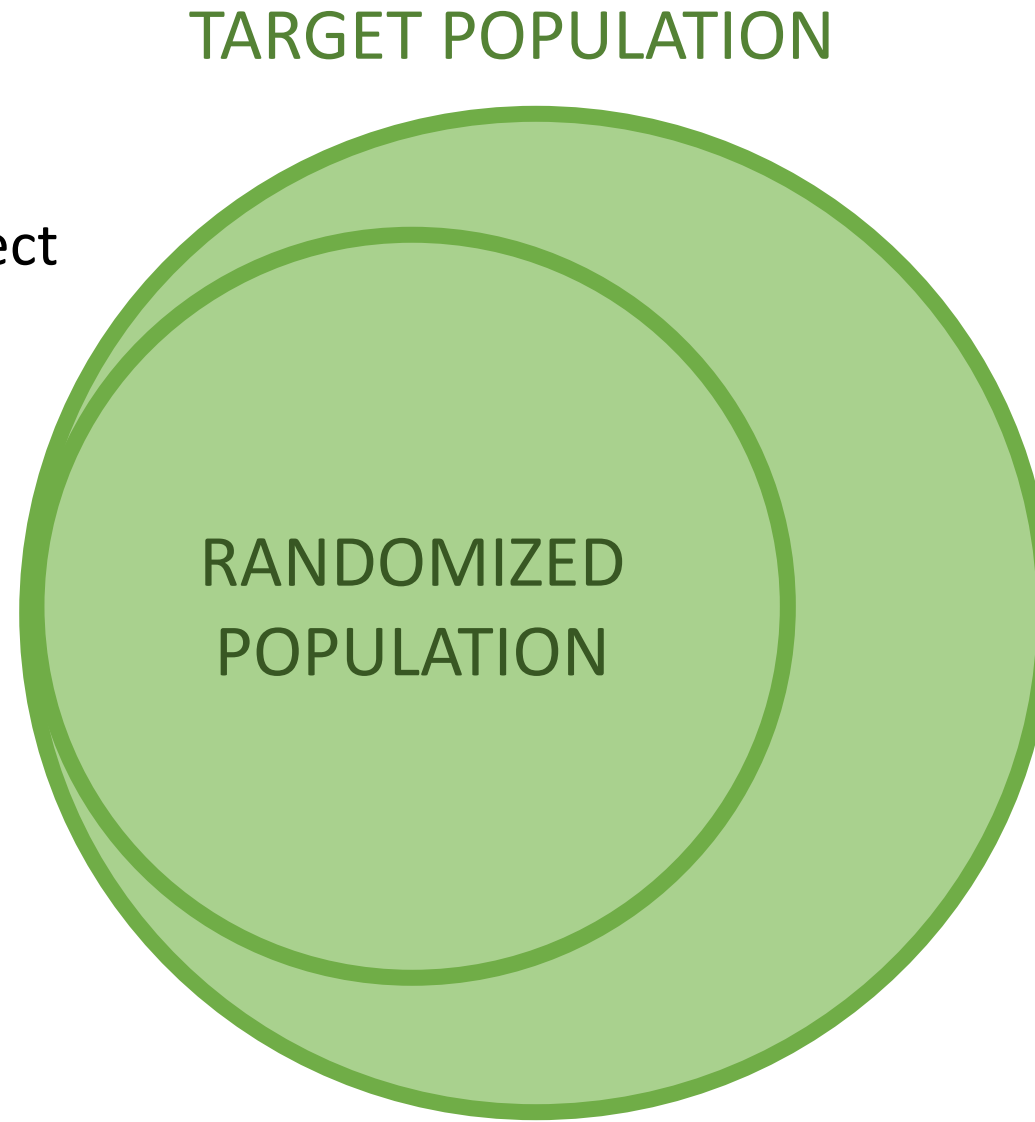
TARGET POPULATION

We make an assumption that the covariates from the trial and the target population are measuring the same thing.

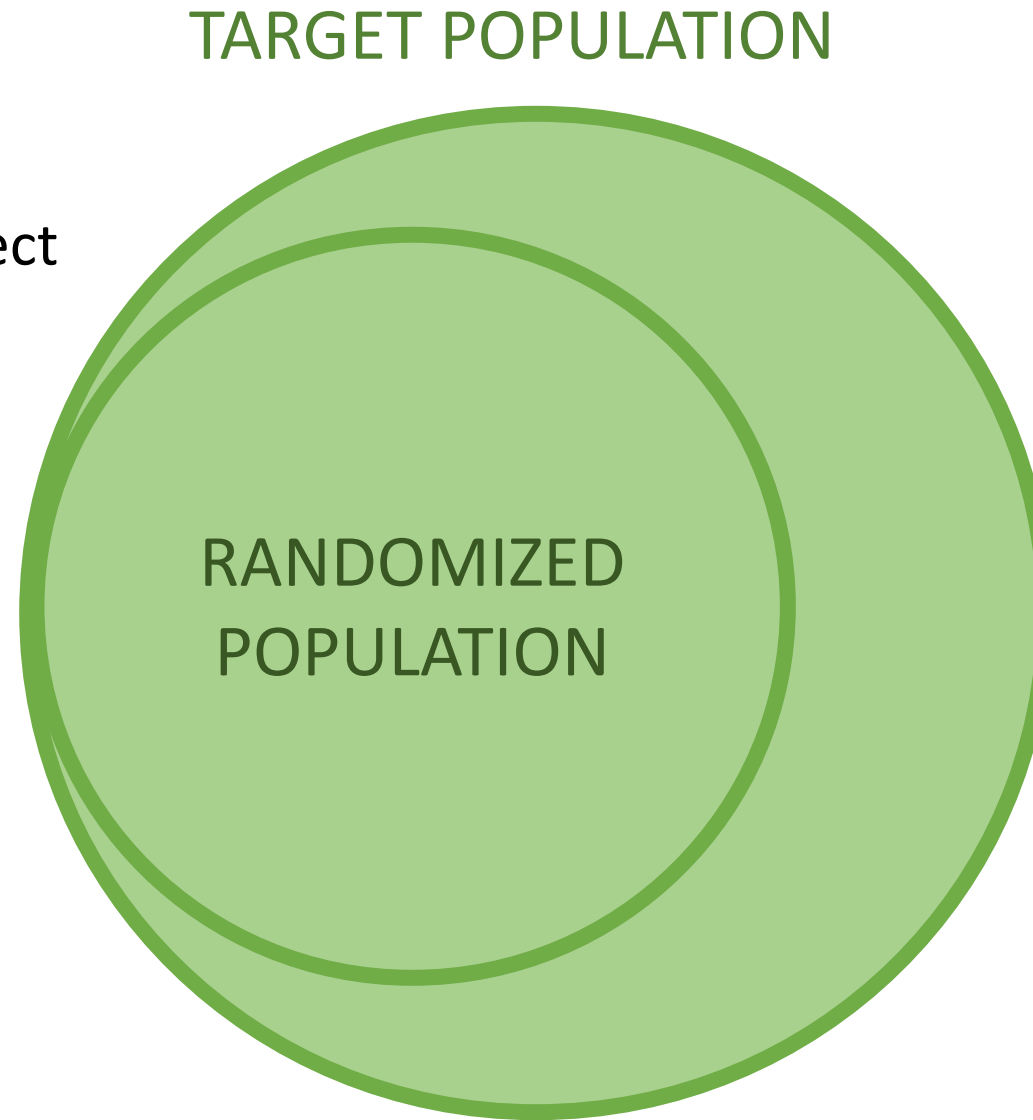
But, if you are using data from different countries/healthcare systems they may not be

e.g., there may be different diagnosis or prescribing thresholds

Use baseline data on the potential modifiers of treatment effect to transport (generalize) effect estimates from the randomized to the target population



Use baseline data on the potential modifiers of treatment effect to transport (generalize) effect estimates from the randomized to the target population



As data are collected in the same way, we don't have to make assumptions that the trial data and observational data are collecting the same info, because THEY ARE

# Why undertake a transportability/generalizability analysis in Sweden (or anywhere else that undertakes R-RCTs)?

- There are currently a lot of R-RCTs being undertaken in Sweden (cardiology, cancer, respiratory diseases etc.)
- But these trials still cannot experiment on everyone eligible for the treatments under study – our target population
- We can use data from the SAME registries and perform transportability analyses to estimate the effects in those not included in the R-RCTs
- Because the data are collected from the same registry, we do not have to make assumptions about the data generating mechanisms



QUESTIONS?