

# **Assessing the effectiveness of cardiac rehabilitation in patients after myocardial infarction using national-level case-mix data**

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## **Disclosure / Potential conflict of interest**

- *Grant V3-2104 (Slovenian Research Agency/Ministry of Health)*
- *No conflicts pertinent to this presentation*
- *Biased towards cardiac rehabilitation*
- *I am a clinician — not a coding expert, statistician or policy consultant*



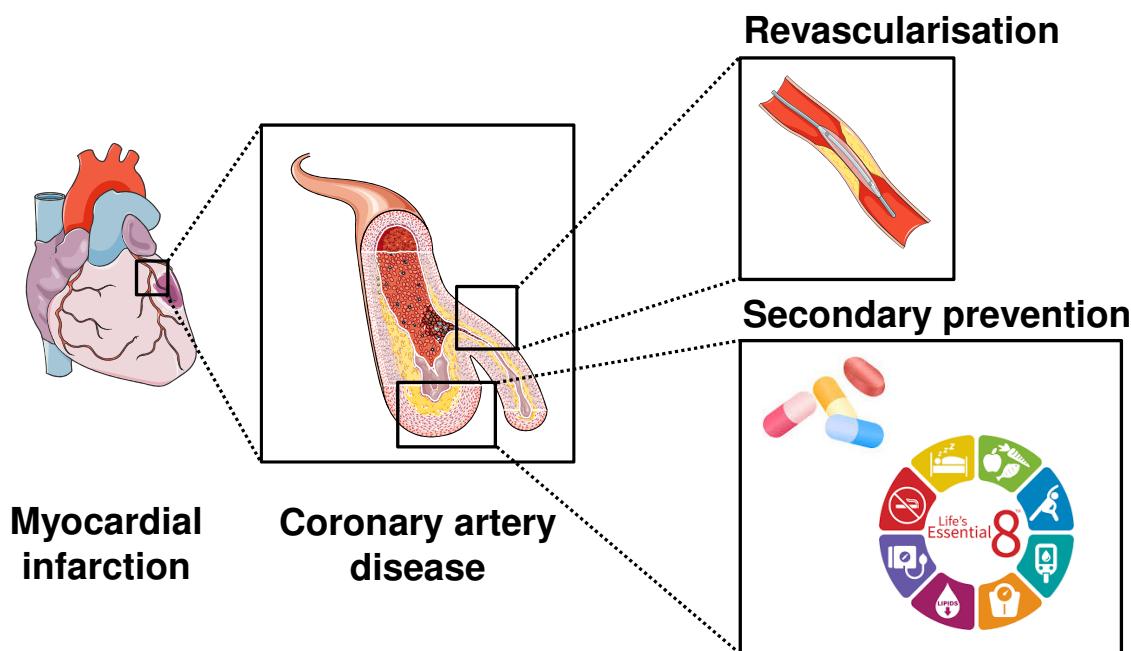
## Outline

- **Why? Myocardial rehabilitation, cardiac rehabilitation and quality of care**
- **How? Methods → from a clinicians perspective**
- **What? Results in context**
- **So what?**

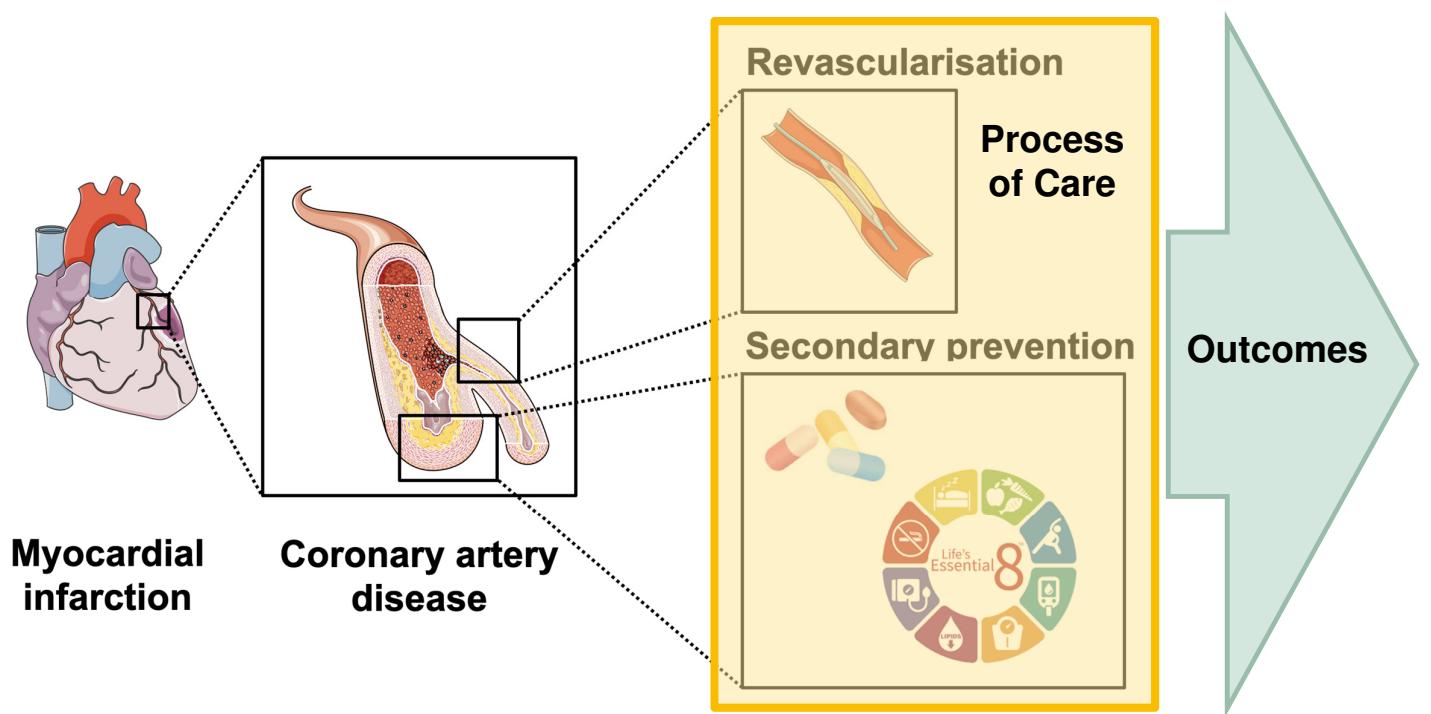
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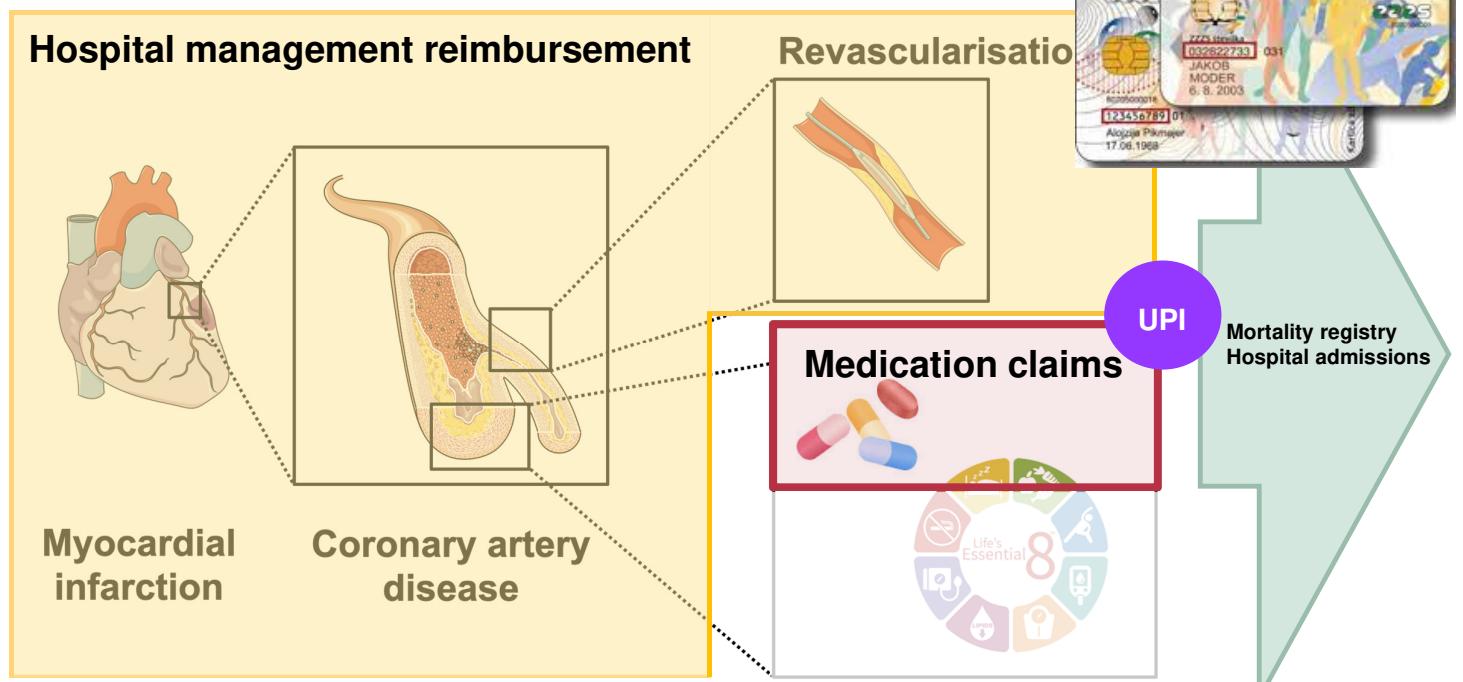
## Myocardial infarction



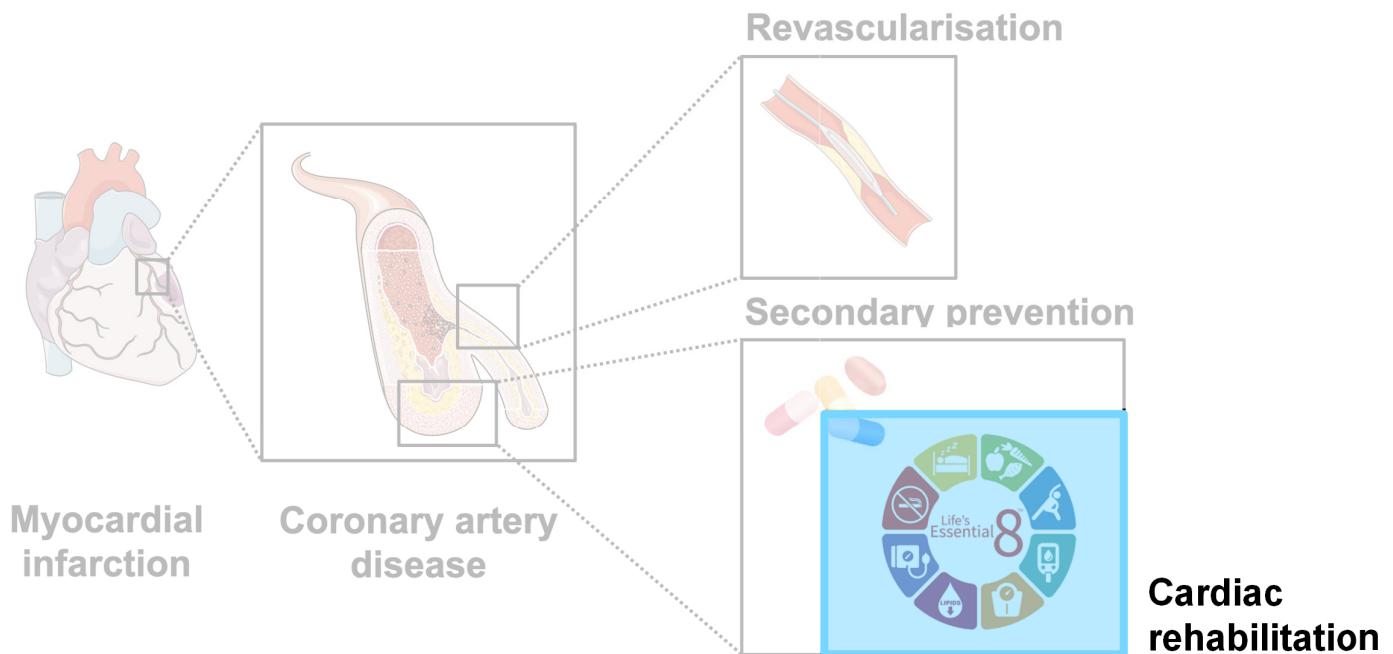
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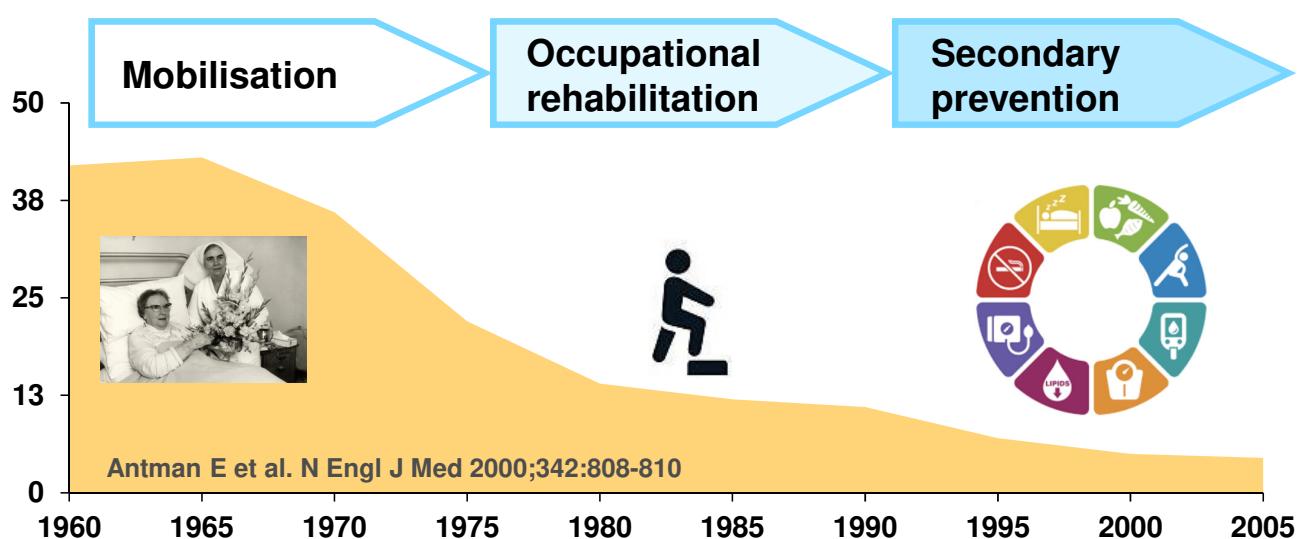
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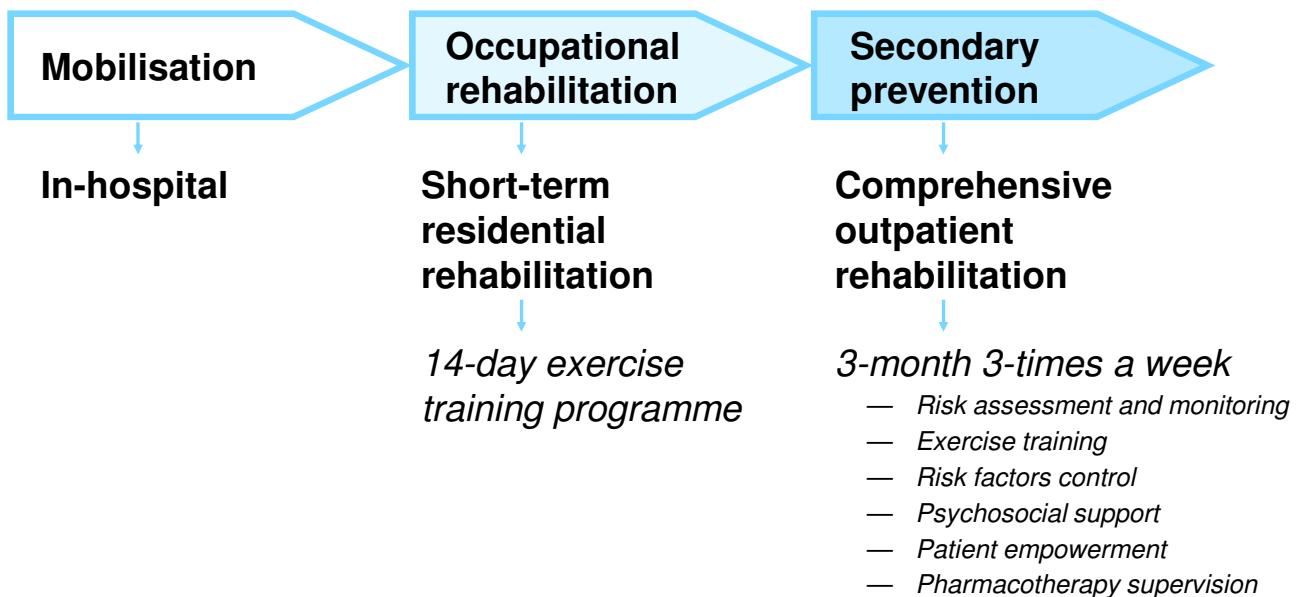
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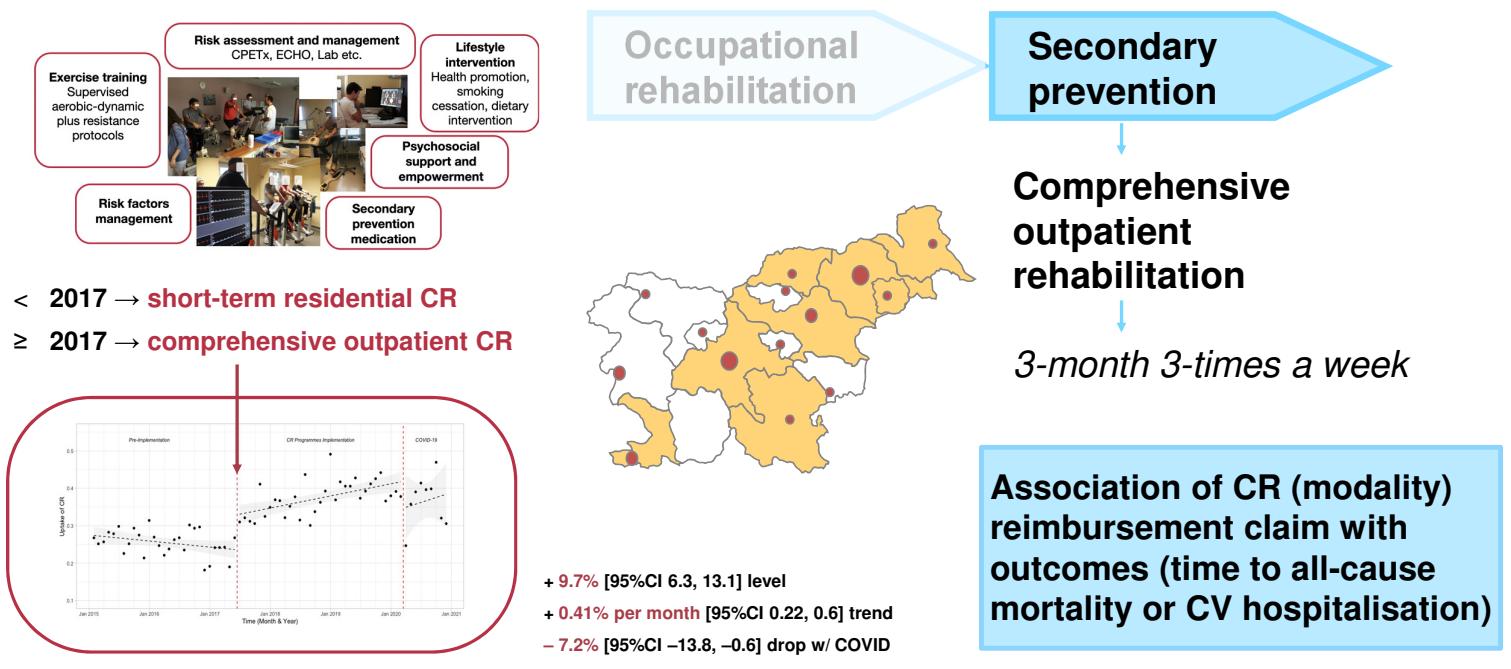
# Cardiac rehabilitation



# Cardiac rehabilitation



# Cardiac rehabilitation



# Cardiac rehabilitation: Evidence (trials)

- Complex, evolving intervention
- Not as interesting as medications or procedures
- Not for everyone (referral, adherence)
- Small scale trials focusing on surrogate outcomes (e.g., exercise capacity)

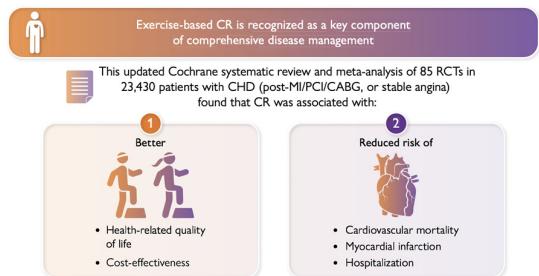


European Heart Journal (2023) 44, 452–469  
<https://doi.org/10.1093/eurheartj/e hac747>

## META-ANALYSIS Ischaemic heart disease

### Exercise-based cardiac rehabilitation for coronary heart disease: a meta-analysis

Grace O. Dibben <sup>1\*</sup>, James Faulkner<sup>2</sup>, Neil Oldridge<sup>3</sup>, Karen Rees<sup>4</sup>,  
David R. Thompson <sup>5</sup>, Ann-Dorthe Zwisler <sup>6,7,8</sup>, and Rod S. Taylor<sup>1,9</sup>



Dibben G et al. European Heart Journal (2023) 44, 452–469

# Cardiac rehabilitation: Evidence (observ)

	HR (95% CI)	Method	Reference
Ejisvogels, 2022	0.59; 0.52–0.68	IPTW logistic, 26 171 pts	JAMA. 2020;3(7):e2011686
Suaya, 2009	0.59; 0.35–0.97	PSM, 2024 pts	J Am Coll Cardiol 2009;54(1):25-33
Martin, 2012	0.59; 0.49–0.70	PSM, 2900 pts	Circulation 2012;126(6):677-87
Sunamura, 2018	0.61; 0.46–0.81	PSM, 1159 pts	Eur Heart J Qual Care Clin Outcomes 2018;4(3):168-72
de Vries, 2015	0.65; 0.56–0.77	IPTW GBM, 11 014 pts	Eur Heart J 2015;36(24):1519-28

- Two-group comparisons (CR vs. No CR)
- Diverse CR modalities (comprehensive outpatient-type)
- Different healthcare systems (e.g., CR coverage varies)

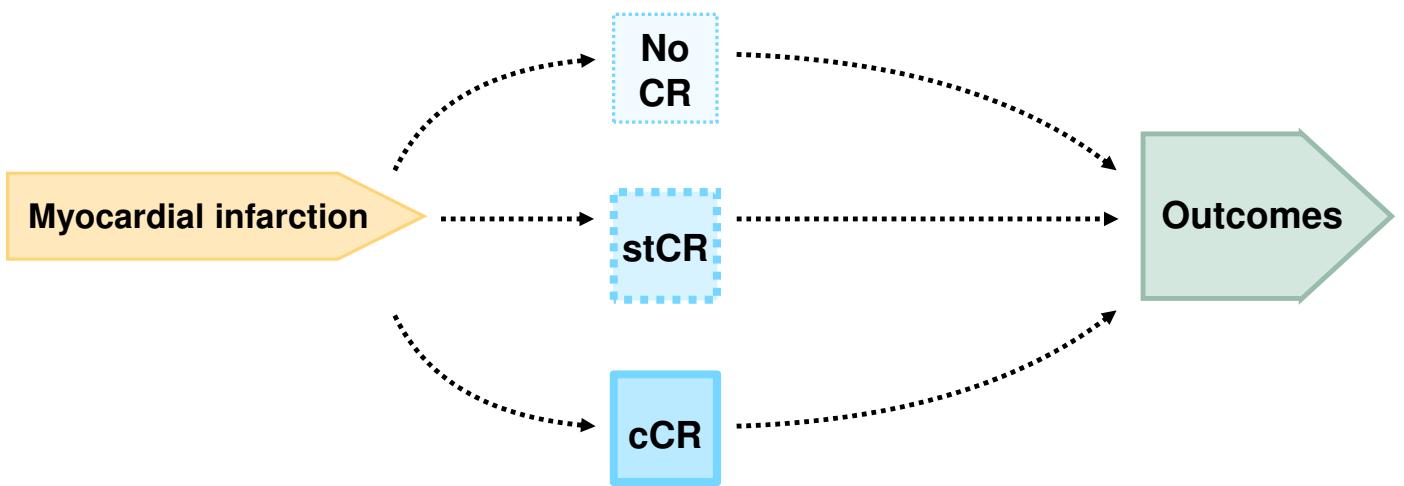
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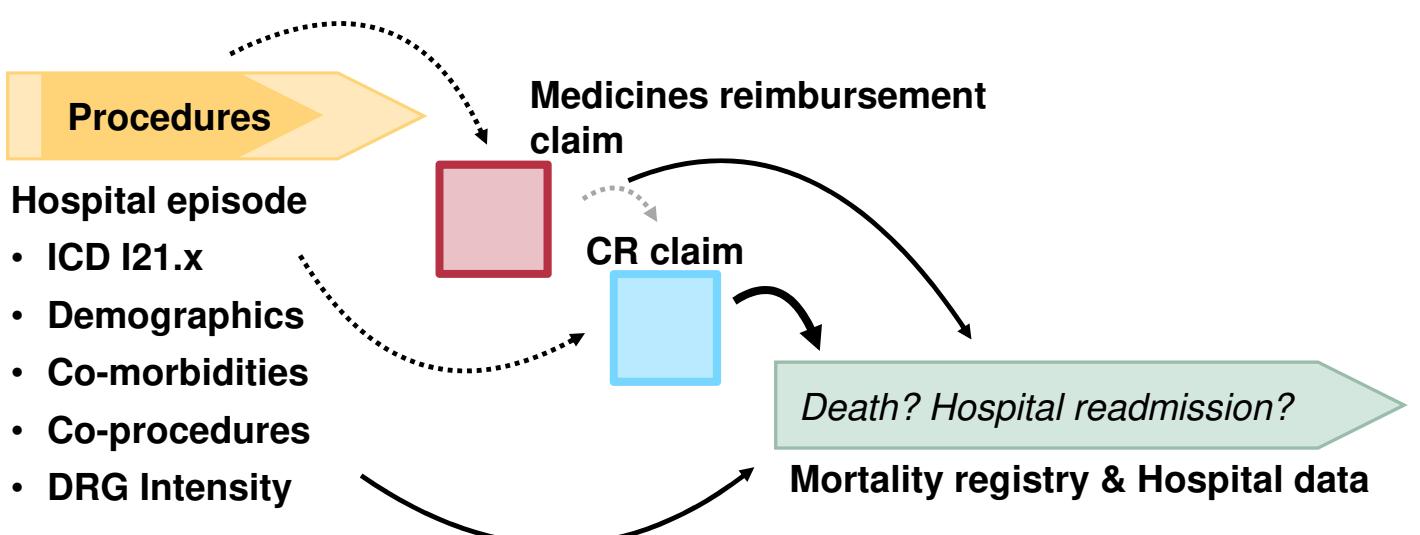
## Methods

- Causal assumptions
- Variable selection
- Propensity score estimation and diagnostics
- Inverse probability of treatment weights
- Cox proportional hazards modelling

# Cardiac rehabilitation and outcomes



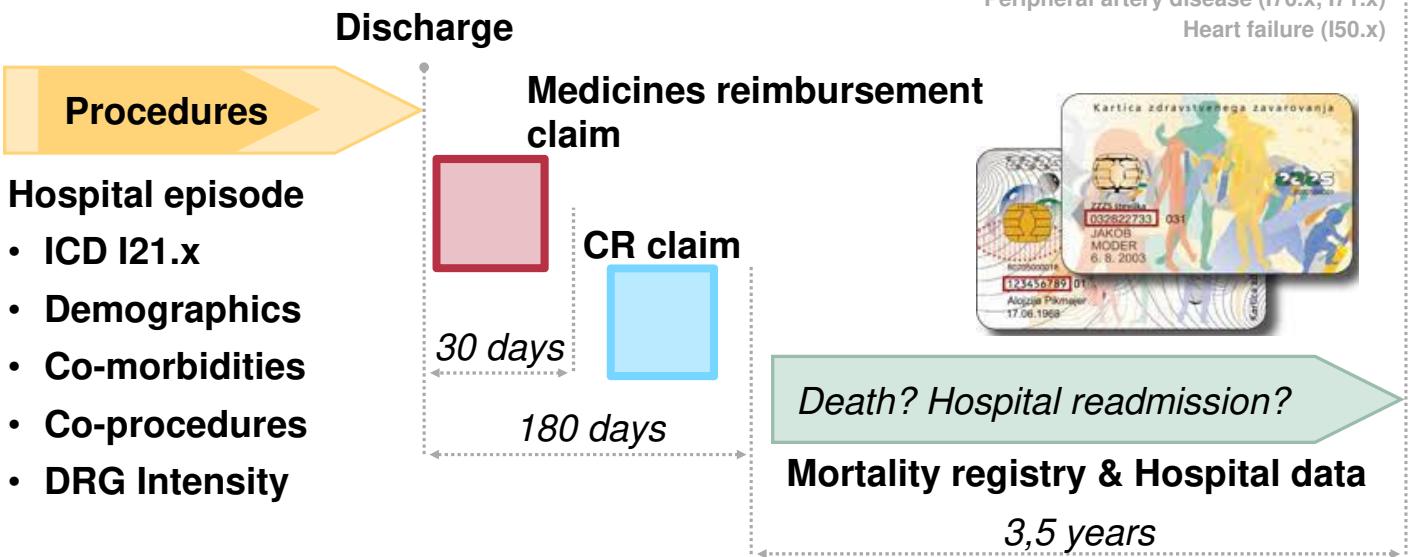
## Causal assumptions



# Definitions

## Index event

Admission between Jan 1 2015 and Jun 30 2021



# Variables selection?

## Cardiac Rehabilitation

- No CR
- Short-term Residential
- Comprehensive Outpatient

~

- Age, Sex,
- Infarct type, Atrial fibrillation, Heart Failure, Residual Ischaemia,
- Diabetes mellitus, Arterial hypertension,
- Depression, Dementia, Cancer, CKD, COPD/Asthma,
- Revascularisation procedure,
- Antithrombotic, Lipid-lowering, Beta Blocker, RAAS Therapy,
- Length of Stay, DRG Intensity,
- Total Number of Diagnoses, Total Number of Procedures,

**Evidence-based predictors of CR participation & outcomes, reviewed by expert panel**

# Are covariates valid?

- Biomedical rationale
- Professional Standards & Good Clinical Practice
- Reimbursement

- Age, Sex,
- Infarct type, Atrial fibrillation, Heart Failure, Residual Ischaemia,
- Diabetes mellitus, Arterial hypertension,
- Depression, Dementia, Cancer, CKD, COPD/Asthma,
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External control

Registry comparison

*Evidence-based predictors of CR participation & outcomes, reviewed by expert panel*

# Are covariates valid?

Cardiac Rehabilitation

— No CR

— S

— C

- Major determinants
- Complex diagnoses
- Non-cardiovascular
- Meds prescription?

- Age, Sex, **Confident?**
- Infarct type, Atrial fibrillation, **Likely?**
- Diabetes mellitus, Arterial hypertension, **Likely?**
- Depression, Dementia, Cancer, CKD, COPD/Asthma, **Likely?**
- Revascularisation procedure, **Confident?**
- Antithrombotic, Lipid-lowering, Beta Blocker, RAAS Therapy,
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*Evidence-based predictors of CR participation & outcomes, reviewed by expert panel*

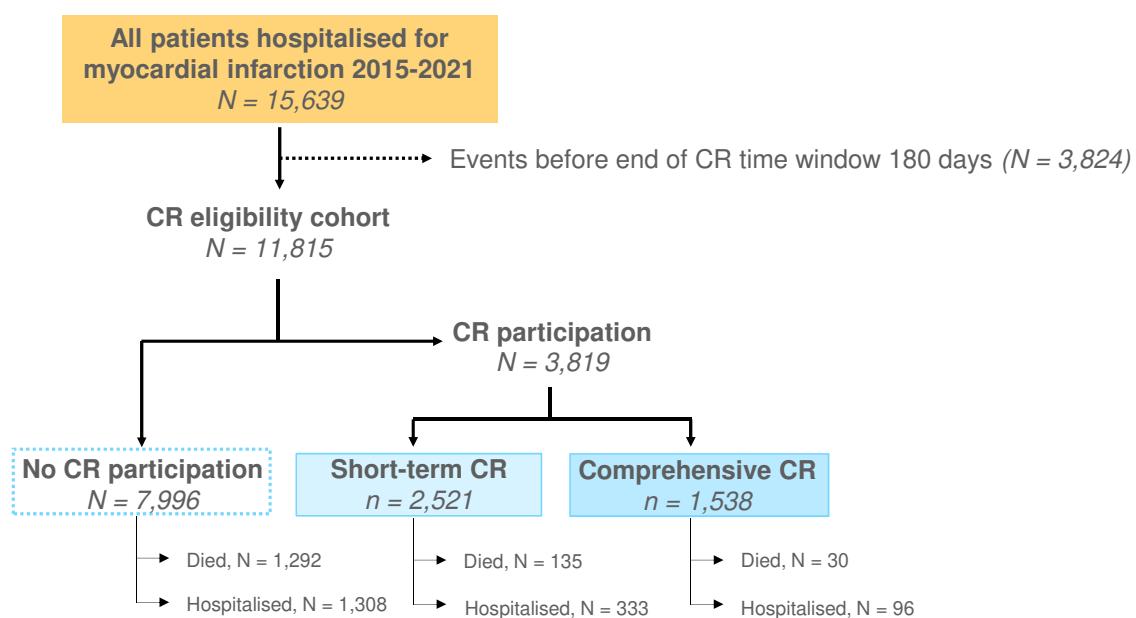
# Is this all?

- Smoking?
- Exercise capacity?
- Diet?
- Obesity?
- Socio-economic status?
- Laboratory values?

- Age, Sex,
- Infarct type, Atrial fibrillation, Heart Failure, Residual Ischaemia,
- Diabetes mellitus, Arterial hypertension,
- Depression, Dementia, Cancer, CKD, COPD/Asthma,
- Revascularisation procedure,
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**Evidence-based predictors of CR participation & outcomes, reviewed by expert panel**

## Flowchart & Baseline



# Flowchart & Baseline

Characteristic	Overall N = 11 815	No CR N = 7 996	Short-term N = 2 281	Comprehensive N = 1 538	p-value
Age	66 (57-77)	69 (59-79)	63 (55-71)	58 (52-66)	<0.0001
Sex (male)	7 882 (67%)	5 030 (63%)	1 676 (73%)	1 176 (76%)	<0.0001
STEMI	5 431 (46%)	3 112 (39%)	1 410 (62%)	909 (59%)	<0.0001
Diabetes	2 631 (22%)	1 827 (23%)	564 (25%)	240 (16%)	<0.0001
Arterial Hypertension	7 245 (61%)	5 030 (63%)	1 384 (61%)	831 (54%)	<0.0001
Atrial Fibrillation	1 481 (13%)	1 147 (14%)	260 (11%)	74 (4.8%)	<0.0001
Heart Failure	2 094 (18%)	1 366 (17%)	539 (24%)	189 (12%)	<0.0001
Depression	811 (6.9%)	585 (7.3%)	147 (6.4%)	79 (5.1%)	0.0056
Dementia	264 (2.2%)	258 (3.2%)	5 (0.2%)	1 (<0.1%)	<0.0001
Malignancy	358 (3.0%)	285 (3.6%)	51 (2.2%)	22 (1.4%)	<0.0001
Chronic Kidney Disease	966 (8.2%)	768 (9.6%)	155 (6.8%)	43 (2.8%)	<0.0001
COPD or Asthma	1 038 (8.8%)	748 (9.4%)	191 (8.4%)	99 (6.4%)	0.0008
Antiplatelet Therapy	11 212 (95%)	7 493 (94%)	2 189 (96%)	1 530 (99%)	<0.0001
Lipid-Lowering Therapy	9 727 (82%)	6 250 (78%)	2 018 (88%)	1 459 (95%)	<0.0001
RAAS Inhibitors	8 544 (72%)	5 629 (70%)	1 714 (75%)	1 201 (78%)	<0.0001
Beta Blockers	8 834 (75%)	5 682 (71%)	1 871 (82%)	1 281 (83%)	<0.0001
Antiischemic Therapy	2 381 (20%)	1 660 (21%)	479 (21%)	242 (16%)	<0.0001
Revascularisation	10 319 (87%)	6 731 (84%)	2 119 (93%)	1 469 (96%)	<0.0001
Number of Diagnoses	4 (2-5)	4 (2-5)	4 (3-6)	3 (2-4)	<0.0001
Number of Procedures	15 (9-19)	13 (7-18)	16 (10-20)	17 (13-20)	<0.0001
Length of Stay >5 days	6 242 (53%)	4 098 (51%)	1 508 (66%)	636 (41%)	<0.0001
DRG Intensity	3.4 (2.4-3.8)	3.2 (2.3-3.8)	3.4 (2.7-4.2)	3.6 (3.2-3.8)	<0.0001

Younger

Men

Less co-morbidities

More intensive baseline management

## Propensity score estimation

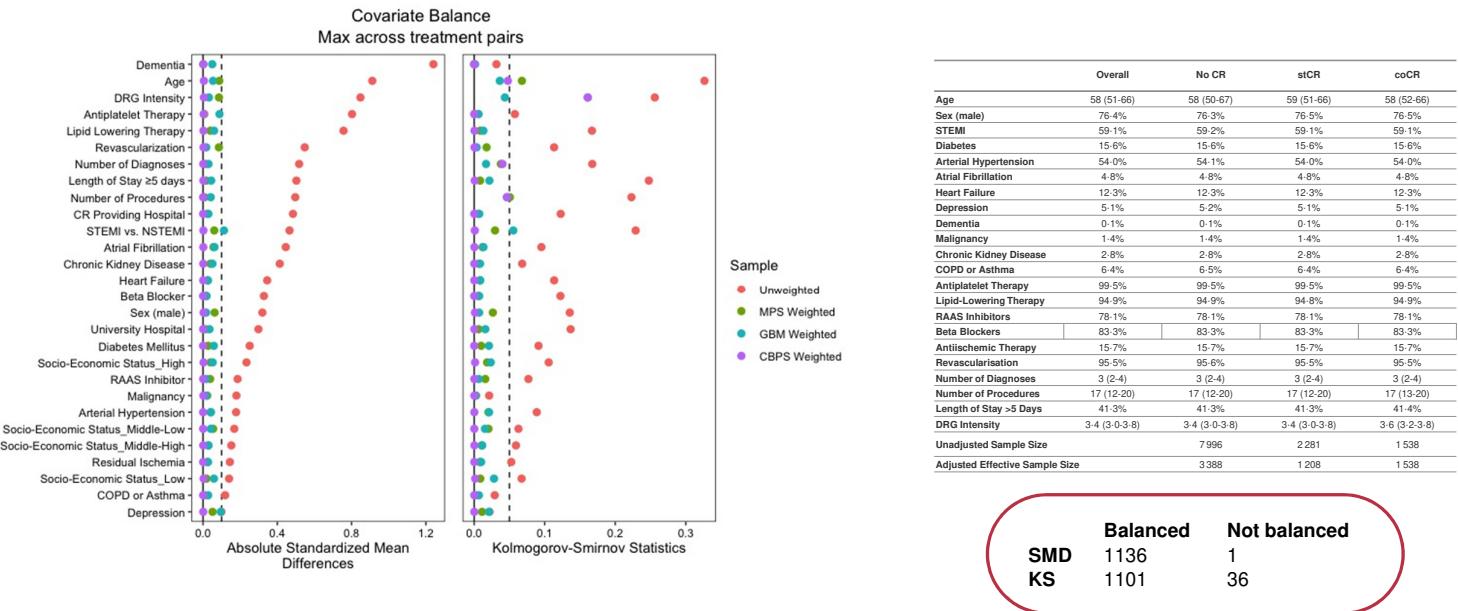
- **Multinomial logistic** → “Well, that seems easy enough for a simple clinician ...”
- **General boosted model<sup>1</sup>** → “Excuse me?”
- **Covariate balancing propensity score<sup>2</sup>** → “Que?!”
- **Other (e.g., entropy balancing propensity score<sup>3</sup>)** → “OK, you lost me ...”

1. Imai K, Ratkovic M. J R Statist Soc 2014;76(1):243-263.

2. McCaffrey DF et al. Stat Med 2013;32(19):338-3414.

3. Heinmueller J. Political Analysis 2012; 20:25–46.

# Balance diagnostics



Greifer N. WeightIt: Weighting for Covariate Balance in Observational Studies. <https://ngreifer.github.io/WeightIt/>, <https://github.com/ngreifer/WeightIt.2023>.  
 Greifer N. Covariate Balance Tables and Plots. <https://ngreifer.github.io/cobalt/>, <https://github.com/ngreifer/cobalt.2023>.

## IPTW — ATE or ATT?

- Selected population — enrolment, adherence, completion
  - Standard of care → 60% of patients after MI
    - Statins → 90% of patients
    - Mediterranean-type diet → 100% of patients
- Interested in **comprehensive CR** (i.e., focus = newly introduced intervention)

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## Effectiveness estimates?

Characteristic	Multinomial			GBM			CBPS			Adjusted Unweighted			Unadjusted Weighted		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Comprehensive CR	0.58	0.48 to 0.70	<0.0001	0.60	0.49 to 0.74	<0.0001	0.58	0.47 to 0.70	<0.0001	0.58	0.48 to 0.70	<0.0001	0.57	0.47 to 0.62	<0.0001
Short-term CR	0.78	0.67 to 0.91	0.002	0.84	0.70 to 0.99	0.046	0.79	0.68 to 0.93	0.0033	0.72	0.64 to 0.80	<0.0001	0.81	0.69 to 0.94	0.007
Age	1.02	1.01 to 1.03	<0.0001	1.02	1.01 to 1.03	<0.0001	1.02	1.01 to 1.03	<0.0001	1.03	1.02 to 1.03	<0.0001			
Sex (male)	1.17	0.99 to 1.38	0.066	1.24	1.04 to 1.47	0.014	1.15	0.98 to 1.36	0.088	1.15	1.06 to 1.25	0.006			
STEMI	1.02	0.88 to 1.19	0.75	0.98	0.83 to 1.17	0.84	1.02	0.88 to 1.19	0.77	0.96	0.88 to 1.04	0.28			
Diabetes	1.29	1.10 to 1.52	0.0022	1.38	1.15 to 1.67	0.0005	1.26	1.06 to 1.49	0.0071	1.23	1.13 to 1.34	<0.0001			
Arterial Hypertension	0.85	0.72 to 1.00	0.046	0.80	0.67 to 0.96	0.017	0.84	0.72 to 0.99	0.039	0.88	0.81 to 0.96	0.0037			
Atrial Fibrillation	1.11	0.89 to 1.38	0.35	1.03	0.81 to 1.30	0.83	1.13	0.91 to 1.40	0.26	1.04	0.95 to 1.15	0.39			
Heart Failure	1.23	1.03 to 1.46	0.021	1.24	1.02 to 1.51	0.031	1.22	1.03 to 1.44	0.021	1.29	1.17 to 1.41	<0.0001			
Residual Ischaemia	1.12	0.96 to 1.32	0.15	1.20	1.00 to 1.44	0.055	1.14	0.97 to 1.34	0.11	1.14	1.05 to 1.25	0.0025			
Depression	1.54	1.18 to 2.01	0.0013	1.59	1.19 to 2.11	0.0015	1.53	1.19 to 1.97	0.0008	1.25	1.09 to 1.42	0.0009			
Dementia	2.25	0.66 to 7.72	0.20	1.62	0.63 to 4.18	0.32	2.22	0.66 to 7.41	0.20	1.24	1.04 to 1.47	0.017			
Malignancy	1.37	0.93 to 2.03	0.11	1.20	0.80 to 1.78	0.38	1.39	0.96 to 2.01	0.082	1.44	1.23 to 1.70	<0.0001			
Chronic Kidney Disease	1.06	0.82 to 1.37	0.67	1.06	0.81 to 1.39	0.67	1.08	0.84 to 1.38	0.56	1.29	1.15 to 1.44	<0.0001			
COPD or Asthma	1.16	0.93 to 1.45	0.19	1.15	0.92 to 1.44	0.23	1.16	0.93 to 1.45	0.19	1.20	1.07 to 1.35	0.0018			
Antiplatelet Therapy	1.27	0.83 to 1.96	0.27	1.23	0.85 to 1.79	0.28	1.31	0.85 to 2.03	0.22	1.12	0.95 to 1.31	0.17			
Lipid-Lowering Therapy	0.83	0.67 to 1.04	0.10	0.79	0.62 to 1.01	0.062	0.83	0.67 to 1.03	0.085	0.73	0.66 to 0.81	<0.0001			
RAAS Inhibitors	0.91	0.77 to 1.09	0.32	0.93	0.78 to 1.12	0.44	0.93	0.78 to 1.11	0.42	0.87	0.80 to 0.95	0.0015			
Beta Blockers	0.95	0.80 to 1.14	0.61	0.89	0.73 to 1.08	0.22	0.93	0.78 to 1.12	0.47	0.98	0.90 to 1.07	0.63			
Revascularisation	1.04	0.77 to 1.42	0.79	1.19	0.85 to 1.65	0.31	0.98	0.73 to 1.30	0.87	0.73	0.65 to 0.82	<0.0001			
Number of Diagnoses	1.07	1.03 to 1.11	0.0004	1.07	1.03 to 1.11	0.0003	1.07	1.04 to 1.11	<0.0001	1.06	1.04 to 1.07	<0.0001			
Number of Procedures	0.99	0.98 to 1.01	0.24	1.00	0.98 to 1.01	0.60	0.99	0.98 to 1.01	0.31	1.00	0.99 to 1.01	0.52			
Length of Stay	1.18	1.01 to 1.38	0.036	1.29	1.09 to 1.54	0.0032	1.16	1.00 to 1.36	0.051	1.16	1.06 to 1.26	0.0008			
DRG Intensity	1.03	0.97 to 1.09	0.29	1.03	0.99 to 1.07	0.22	1.03	0.98 to 1.07	0.25	1.02	1.00 to 1.04	0.11			

HR = Hazard Ratio, CI = Confidence Interval, CR = Cardiac rehabilitation, STEMI = ST-elevation myocardial infarction, COPD = Chronic obstructive pulmonary disease, RAAS = Renin-angiotensin system

# Effectiveness estimates?

Characteristic	Multinomial			GBM			CBPS			Adjusted Unweighted			Unadjusted Weighted		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
	CR	Multinomial		GBM			CBPS			Adj. Unweighted			Unadj. Weighted		
coCR	<b>0.58</b>	<b>0.48 to 0.70</b>	<b>0.60</b>	<b>0.49 to 0.74</b>	<b>0.58</b>	<b>0.47 to 0.70</b>	<b>0.58</b>	<b>0.48 to 0.70</b>	<b>0.57</b>	<b>0.47 to 0.62</b>					
srCR	<b>0.78</b>	<b>0.67 to 0.91</b>	<b>0.84</b>	<b>0.70 to 0.99</b>	<b>0.79</b>	<b>0.68 to 0.93</b>	<b>0.72</b>	<b>0.64 to 0.80</b>	<b>0.81</b>	<b>0.69 to 0.94</b>					
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Heart Failure	1.23	1.03 to 1.46	0.021	1.24	1.02 to 1.51	0.031	1.22	1.03 to 1.44	0.021	1.29	1.17 to 1.41	<0.0001			
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Depression	1.54	1.18 to 2.01	0.0013	1.59	1.19 to 2.11	0.0015	1.53	1.19 to 1.97	0.0008	1.25	1.09 to 1.42	0.0009			
Dementia	2.25	0.66 to 7.72	0.20	1.62	0.63 to 4.18	0.32	2.22	0.66 to 7.41	0.20	1.24	1.04 to 1.47	0.017			
Malignancy	1.37	0.93 to 2.03	0.11	1.20	0.80 to 1.78	0.38	1.39	0.96 to 2.01	0.082	1.44	1.23 to 1.70	<0.0001			
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Number of Procedures	0.99	0.98 to 1.01	0.24	1.00	0.98 to 1.01	0.60	0.99	0.98 to 1.01	0.31	1.00	0.99 to 1.01	0.52			
Length of Stay	1.18	1.01 to 1.38	0.036	1.29	1.09 to 1.54	0.0032	1.16	1.00 to 1.36	0.051	1.16	1.06 to 1.26	0.0008			
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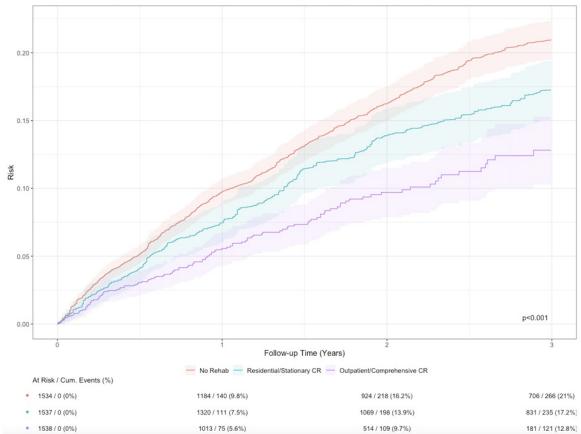
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srCR	<b>0.78</b>	<b>0.67 to 0.91</b>	<b>0.84</b>	<b>0.70 to 0.99</b>	<b>0.79</b>	<b>0.68 to 0.93</b>

	HR (95% CI)	Method	Reference
Ejisvogels, 2022	<b>0.59; 0.52–0.68</b>	IPTW logistic, 26 171 pts	JAMA. 2020;3(7):e2011686
Suaya, 2009	<b>0.59; 0.35–0.97</b>	PSM, 2024 pts	J Am Coll Cardiol 2009;54(1):25-33
Martin, 2012	<b>0.59; 0.49–0.70</b>	PSM, 2900 pts	Circulation 2012;126(6):677-87
Sunamura, 2018	<b>0.61; 0.46–0.81</b>	PSM, 1159 pts	Eur Heart J Qual Care Clin Outcomes 2018;4(3):168-72
de Vries, 2015	<b>0.65; 0.56–0.77</b>	IPTW GBM, 11 014 pts	Eur Heart J 2015;36(24):1519-28

- Two-group comparisons (CR vs. No CR)
- Diverse CR modalities (comprehensive outpatient-type)
- Different healthcare systems (e.g., CR coverage varies)
- Different covariates selection

# Effectiveness estimates to inform clinical management and health policies



21% → 505 events / 3 yrs  
17.2% → ↓67 events → NNR 26  
12.8% → ↓143 events → NNR 12

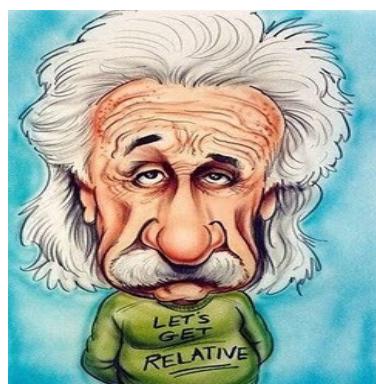
## Outline

- Why? Myocardial rehabilitation, cardiac rehabilitation and quality of care
- How? Methods → from a clinicians perspective
- What? Results in context
- So what?

# Conclusions

- CR is associated with reduced time-to-event HR for all-cause mortality and CV hospitalisations
  - *Estimated effectiveness larger for comprehensive CR*
  - *If patients resemble those referred to comprehensive CR*
- Confident in the estimated effectiveness enough to:
  - Inform medical community
  - Promote cardiologists to refer to CR
  - Provide healthcare insurance with evidence of effectiveness-for-payment
- Observational study (association, not causation)
- Dataset large in size, but limited in scope:
  - Derived from administrative data sources
  - Unmeasured covariates? (e.g, smoking, diet, exercise capacity)
  - Limited to all-cause mortality and CV hospitalisations, and not capturing other relevant outcomes (e.g., exercise improvement, quality of life)

Thank you!



Intelectuals solve problems.  
Geniuses prevent them.

A. Einstein

Questions?