Supplemental material (SM)

Effectiveness of Comprehensive Cardiac Rehabilitation in CAD-Patients Treated According to Contemporary Evidence Based Medicine – Update of the Cardiac Rehabilitation Outcome Study (CROS-II)

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Table SM 1: CROS inclusion criteria (PICOs)

Population (P)	**(1) After ACS, (2) After CABG, (3) Mixed population**
Age	No restriction
Time of index events	1995 or later*
Minimal standards of acute treatment	in-hospital standard therapy according to actual guidelines
Intervention (I)	**Multi-component cardiac rehabilitation (CR)**
Start	Not later than 3 months after hospital discharge
Supervision	CR must be under supervision and responsibility of a rehabilitation center (center-based CR)
Definition of "multi-component"	CR including supervised and structured physical exercise at least twice a week as basic requirement plus at least one, preferably more, of the following components: Information, motivational techniques, education, psychological support and interventions, social and vocational support
CR setting	In-patient, out-patient or mixed. Tele-rehabilitation will be included as long as the major part of CR sessions is center-based and all other predefined criteria are fulfilled
Control (C)	**Usual care**
Definition	Patients with index event, but not participating in CR. Patients of the control group may be supervised by general practitioners and/or resident cardiologists. They also may participate in non-structured and non-supervised exercise programs outside a CR program.
Outcomes (O); clinical course after the index event	
Primary outcome	(1) Total mortality
Secondary outcomes	(2) Cardiovascular mortality (3) Major cardiovascular and cerebrovascular events (MACCE = combined endpoint of death, non – fatal myocardial infarction, non – fatal stroke (4) Non – fatal myocardial infarction (5) Non – fatal stroke (6) Hospital readmission for any reason (7) Unplanned hospital readmission for any cardiovascular event (8) Unplanned coronary revascularization (9) Cardiovascular mortality + admission for any cardiovascular event (10) All combined endpoints including fatal and non-fatal events not predefined (amendment by the CROS steering committee January 18th, 2015)
Observation period	6 months or more after hospital discharge
Study designs and biometry	
Study designs included	Randomized controlled trials (RCT); prospective and retrospective cohort studies with a control group (pCCT, rCCT)
Biometry	Cohort studies must provide a description of data sources, should have used methods to reduce risk of selection bias, e.g. linear regression analysis, propensity score methods, should provide information on dealing with patients lost at follow-up and missing data

* Studies including patients before and after 1995 were only included into the analysis, if the vast majority of patients was treated in 1995 or later

Table SM 2: Search sources

Medline: Search interface: PubMed – Date of search: Sept 4 2018
(includes segments "Medline", "Pubmed – as supplied by publisher", "PubMed- in process", "PubMed – pubmednotmedline")

#1 "Acute Coronary Syndrome"[mh] OR "Angina, Unstable"[mh] OR "Coronary Occlusion"[mh] OR "Coronary Thrombosis"[mh] OR "Myocardial Infarction"[mh] OR "Myocardial Revascularization"[mh] OR myocardial infarct*[tiab] OR coronary infarct*[tiab] OR cardiac infarct*[tiab] OR heart infarct*[tiab] OR postmyocardial infarct*[tiab] OR "post-MI"[tiab] OR heart attack*[tiab] OR coronary attack*[tiab] OR cardiac attack*[tiab] OR myocardial attack*[tiab] OR cardiac event*[tiab] OR coronary event*[tiab] OR myocardial event*[tiab] OR coronary syndrome*[tiab] OR cardiac syndrome*[tiab] OR myocardial syndrome*[tiab] OR "bypass grafting"[tiab] OR "coronary artery bypass"[tiab] OR "coronary bypass"[tiab] OR "cardiac bypass"[tiab] OR coronary thromb*[tiab] OR intracoronary thromb*[tiab] OR coronary angioplast*[tiab] OR intracoronary angioplast*[tiab] OR cardiac angioplast*[tiab] OR coronary stent*[tiab] OR intracoronary stent*[tiab] OR cardiac stent*[tiab] OR coronary intervention*[tiab] OR intracoronary intervention*[tiab] OR cardiac intervention*[tiab] OR coronary reperfusion*[tiab] OR intracoronary reperfusion*[tiab] OR cardiac reperfusion*[tiab] OR myocardial revasculari*[tiab] OR coronary revasculari*[tiab] OR cardiac revasculari*[tiab] OR "myocardial stunning"[tiab] OR "cardiac stunning"[tiab]

#2 "Rehabilitation"[mh] OR "Rehabilitation"[sh] OR "Rehabilitation Centers"[mh:noexp] OR "Secondary Prevention"[mh] OR rehabilitat*[tiab] OR rehab[tiab] OR cardiorehabilit*[tiab] OR secondary prevent*[tiab] OR program[tiab] OR programme[tiab] OR programs[tiab] OR programmes[tiab]

#3 #1 AND #2

#4 "cardiac rehabilitation"[tiab]

#5 #3 OR #4

#6 *[Cochrane HSSS filter]* (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals[mh] NOT humans[mh])

#7 *[Own filter]* "cohort studies"[mh:noexp] OR "follow-up studies"[mh] OR "longitudinal studies"[mh] OR "prospective studies"[mh] OR cohort*[tiab] OR prospectiv*[tiab] OR longitudinal*[tiab] OR follow-up*[tiab] OR followup*[tiab] OR "retrospective studies"[mh] OR retrospectiv*[tiab]

#8 #6 OR #7

#9 #5 AND #8

#10 #9 AND medline[sb]

#11 #5 NOT medline[sb]

#12 #10 OR #11

#13 #12 NOT pmcbook

#14 2015/12/15:2018/12/31[edat]

#15 #13 AND #14

Embase: Search interface: Ovid SP – Date of search: Sept 4 2018 (Embase 1974 to 2018 August 31)

#1 exp acute coronary syndrome/ or coronary artery thrombosis/ or exp percutaneous coronary intervention/ or exp unstable angina pectoris/ or exp heart infarction/ or exp coronary artery surgery/

#2 (myocardial infarct* or coronary infarct* or cardiac infarct* or heart infarct* or postmyocardial infarct* or post-MI or heart attack* or coronary attack* or cardiac attack* or cardiac event* or coronary event* or coronary syndrome or cardiac syndrome or bypass grafting or coronary artery bypass or coronary bypass or cardiac bypass or coronary thromb* or intracoronary thromb* or coronary angioplast* or intracoronary angioplast* or cardiac angioplast* or coronary stent* or intracoronary stent* or cardiac stent* or coronary intervention* or intracoronary intervention* or cardiac intervention* or coronary reperfusion* or intracoronary reperfusion* or cardiac reperfusion* or myocardial revasculari* or coronary revasculari* or cardiac revasculari* or myocardial stunning or cardiac stunning).tw.

#3 1 or 2

#4 rehabilitation/ or heart rehabilitation/ or functional assessment/ or functional training/ or rehabilitation center/ or secondary prevention/

#5 (rehabilitat* or rehab or cardiorehabilit*).tw.

#6 4 or 5

#7 3 and 6

#8 "cardiac rehabilitation".tw.

#9 7 or 8

#10 limit 9 to yr=1995-Current

#11 *[Wong 2006 Embase filter]* random*.tw. or clinical trial*.mp. or exp health care quality/

#12 *[Own filter]* cohort analysis/ or longitudinal study/ or prospective study/ or follow up/ or retrospective study/ or (cohort* or prospectiv* or longitudinal* or follow-up* or followup* or retrospectiv*).tw.

#13 11 or 12

#14 10 and 13

#15 (201512* or 2016* or 2017* or 2018*).dc.

#16 14 and 15

#17 remove duplicates from 16

Cochrane Central Register of Controlled Trials: Search interface: Cochrane Library – Date of search: Sept 04 2018 (Issue 8 of 12, 2018)

#1 MeSH descriptor: [Acute Coronary Syndrome] explode all trees

#2 MeSH descriptor: [Angina, Unstable] explode all trees

#3 MeSH descriptor: [Coronary Occlusion] explode all trees

#4 MeSH descriptor: [Coronary Thrombosis] explode all trees

#5 MeSH descriptor: [Myocardial Infarction] explode all trees

#6	MeSH descriptor: [Myocardial Revascularization] explode all trees
#7	("myocardial infarct*" or "coronary infarct*" or "cardiac infarct*" or "heart infarct*" or "postmyocardial infarct*" or "post-MI" or "AMI" or "STEMI" or "NSTEMI" or "heart attack*" or "coronary attack*" or "cardiac attack*" or "myocardial attack*" or "cardiac event*" or "coronary event*" or "myocardial event*" or "coronary syndrome*" or "cardiac syndrome*" or "myocardial syndrome*" or "bypass grafting" or "coronary artery bypass" or "coronary bypass" or "cardiac bypass" or "CABG" or "coronary thromb*" or "intracoronary thromb*" or "coronary angioplast*" or "intracoronary angioplast*" or "cardiac angioplast*" or "coronary stent*" or "intracoronary stent*" or "cardiac stent*" or "PCI" or "coronary intervention*" or "intracoronary intervention*" or "cardiac intervention*" or "coronary reperfusion*" or "intracoronary reperfusion*" or "cardiac reperfusion*" or "myocardial revasculari*" or "coronary revasculari*" or "cardiac revasculari*" or "myocardial stunning" or "cardiac stunning"):ti,ab,kw
#8	#1 or #2 or #3 or #4 or #5 or #6 or #7
#9	MeSH descriptor: [Rehabilitation] explode all trees
#10	Any MeSH descriptor with qualifier(s): [Rehabilitation - RH]
#11	MeSH descriptor: [Rehabilitation Centers] explode all trees
#12	MeSH descriptor: [Secondary Prevention] explode all trees
#13	("rehabilitat*" or "rehab" or "cardiorehabilit*" or "secondary prevent*" or "program" or "programme" or "programs" or "programmes"):ti,ab,kw
#14	#9 or #10 or #11 or #12 or #13
#15	("cardiac rehabilitation"):ti,ab,kw
#16	#8 and #14
#17	#15 or #16
#18	with Cochrane Library publication date from Dec 2015 to Sep 2018

ICTRP (International Clinical Trials Registry Platform): Search interface: ICTRP Search Portal (http://apps.who.int/trialsearch/) – Date of search: Sept 4 2018

[Each line was run and exported separately, only records from Dec 2015 onwards were exported]

(#1)

myocardial infarct* AND rehab* OR coronary infarct* AND rehab* OR cardiac infarct* AND rehab* OR heart infarct* AND rehab* OR postmyocardial infarct* AND rehab* OR post-MI AND rehab* OR heart attack* AND rehab* OR coronary attack* AND rehab* OR cardiac attack* AND rehab* OR myocardial attack* AND rehab* OR cardiac event* AND rehab* OR coronary event* AND rehab* OR myocardial event* AND rehab* OR coronary syndrome* AND rehab* OR cardiac syndrome* AND rehab* OR myocardial syndrome* AND rehab* OR bypass grafting AND rehab* OR coronary artery bypass AND rehab* OR coronary bypass AND rehab* OR cardiac bypass AND rehab* OR coronary thromb* AND rehab* OR intracoronary thromb* AND rehab* OR coronary angioplast* AND rehab* OR intracoronary angioplast* AND rehab* OR cardiac angioplast* AND rehab* OR coronary stent* AND rehab* OR intracoronary stent* AND rehab* OR cardiac stent* AND rehab* OR coronary intervention* AND rehab* OR intracoronary intervention* AND rehab* OR cardiac intervention* AND rehab* OR coronary reperfusion* AND rehab* OR intracoronary reperfusion* AND rehab* OR cardiac reperfusion* AND rehab* OR myocardial revasculari* AND rehab* OR coronary revasculari* AND rehab* OR cardiac revasculari* AND rehab* OR myocardial stunning AND rehab* OR cardiac stunning AND rehab* OR AMI AND rehab* OR STEMI AND rehab* OR NSTEMI AND rehab* OR PCI AND rehab* OR CABG AND rehab* OR PTCA

AND rehab* OR unstable angina AND rehab*

(#2)
myocardial infarct* AND program* OR coronary infarct* AND program* OR cardiac infarct* AND program* OR heart infarct* AND program* OR postmyocardial infarct* AND program* OR post-MI AND program* OR heart attack* AND program* OR coronary attack* AND program* OR cardiac attack* AND program* OR myocardial attack* AND program* OR cardiac event* AND program* OR coronary event* AND program* OR myocardial event* AND program* OR coronary syndrome* AND program* OR cardiac syndrome* AND program* OR myocardial syndrome* AND program* OR bypass grafting AND program* OR coronary artery bypass AND program* OR coronary bypass AND program* OR cardiac bypass AND program* OR coronary thromb* AND program* OR intracoronary thromb* AND program* OR coronary angioplast* AND program* OR intracoronary angioplast* AND program*

(#3)
cardiac angioplast* AND program* OR coronary stent* AND program* OR intracoronary stent* AND program* OR cardiac stent* AND program* OR coronary intervention* AND program* OR intracoronary intervention* AND program* OR cardiac intervention* AND program* OR coronary reperfusion* AND program* OR intracoronary reperfusion* AND program* OR cardiac reperfusion* AND program* OR myocardial revasculari* AND program* OR coronary revasculari* AND program* OR cardiac revasculari* AND program* OR myocardial stunning AND program* OR cardiac stunning AND program* OR AMI AND program* OR STEMI AND program* OR NSTEMI AND program* OR PCI AND program* OR CABG AND program* OR PTCA AND program* OR unstable angina AND program*

(#4)
cardiac rehabilitation

Footnotes:

Cochrane HSSS filter: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-maximizing version, 2008 revision (available at: http://handbook.cochrane.org/)

Own filter: Own cohort study filter based on two (unvalidated) search filters: BMJ Cohort Filter (available at: http://clinicalevidence.bmj.com/x/set/static/ebm/learn/665076.html) and University of Texas Cohort Filter (available at: http://libguides.sph.uth.tmc.edu/ovid_medline_filters)

Wong 2006 Embase filter: Wong SS, Wilczynski NL, Haynes RB. Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE. *Journal of the Medical Library Association* 2006;94(1):41-7.

Table SM 3a: Studies selected for quantitative analysis (CROS I, search until Dec 2015, and CROS II, search until Sep 2018); baseline study characteristics and overall results

Study Publication year Country	Study design	Population (P): **a.** Data sources **b.** Number of included participants (N) **c.** Index events **d.** Inclusion period **e.** Other inclusion criteria and characteristics **f.** Age (y, mean±SD or as stated) **g.** Gender (male, %)	Intervention (I): **a.** Number (n) **b.** Structured and multi-component CR (SMC-CR)? **c.** Start after index event **d.** Duration (time period and/or total number of CR sessions) **e.** Frequency (CR exercise sessions per wk) **f.** CR-setting	Control (C): **a.** Number (n) **b.** Treatment, characteristics	Outcome (O): **a.** Follow-up period **b.** Outcomes according to the CROS criteria (numbers according to table 1) **c.** Other outcomes	Overall results, with respect to endpoints 1–10 as defined by CROS. Definitions are given at the end of the table*	Remarks
(1) Boulay P et al. 2004[1] Canada	p/r CCT	a. Institutional b. n=128 c. AMI d. probably after 1995 e. aged ≤ 75 y, EF > 35%, first ischemic event f. 53.8±9.9 (CR+, phase II) 54.3±10.3 (CR+,phase II+III) 56.5±9.7 (no CR) g. 86.5 (CR+, phase II) 78.4 (CR+, phase II+III) 77.8 (no CR)	a. n=37 (phase II) n=37 (phase II+III) b. SMC-CR c. ≤ 1 wk after discharge (phase II) d. 12 wk (phase II) at least 9 mo (phase III) e. n=2 f. outpatient (phase II, III)	a. n=54 b. UC, AMI within 1 y before start of the study	a. 1 y post AMI b. (4), (7) c. number of emergency room visits for chest pain or suspicion for cardiac-related symptoms, recurrences of fatal and non-fatal AMI, duration of hospital stay	*Event rate (%)* Endpoint 7: no CR: 37 CR+ phase II: 29.7 CR+ phase II+III: 16.2 p<0.05 Endpoint 4: Control: 5.6 CR phase II: 0 CR phase II+III: 2.7 p<0.05	- different time periods for CR and control group (prospective and retrospective evaluation) - inclusion period confirmed by authors
(2) Norris CM et al. 2004[2] Canada	rCCS	a. Data linkage: Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) with the Northern Alberta Cardiac Rehabilitation Program (NACRP)	a. n=1,470 b. SMC-CR c. 88.65±78.09 d Median 54 d (information by author) d. 12 wk (information by author) e. n=2–3 (information by	a. n=3,611 b. UC	a. 1, 2, 6 y b. (1) c. –	*HR (95% CI)* Endpoint 1: 0.79 (0.64–0.98) in favor to CR+ p=0.036	- description of CR obtained by author

		b. n=5,081 c. mixed population: catheterization for AP, ACS, followed by PCI, CABG or medical therapy d. 01/1995–12/1999 e. ≥ 6 mo survival after index event f. 60.8 (CR+) 64.2 (no CR) g. 80.7 (CR+) 75.2 (no CR)	author) f. outpatient				
(3) Kutner NG et al. 2006[3] USA	rCCS	a. United States Renal Data System (USRDS) b. n=6,215 n=1,855 aged < 65y n=4,353 aged > 65y n=7 lost at follow-up c. CABG d. 01/01/1998–31/12/2002 e. HD patients surviving ≥ 90 days post-surgery f. 67.9±10.3 (total) g. 61.4 (total)	a. n=193 (10.4 % of the population < 65y) n=431 (9.9 % of the population > 65y) b. not clear, includes physical exercise supervised or not supervised c. 88±100 d d. total: 36 CR sessions within 12 wk e. n=3 f. outpatient	a. n=5,581 b. UC	a. up to 6 y b. (1),(2) c. –	*HR (95% CI)* Endpoint 1: 0.65 (0.56–0.76) in favor to CR+ p<0.001 Endpoint 2: 0.64 (0.51–0.81) in favor to CR+ p<0.001	NOS 7 description of CR incomplete multi component CR as defined by CROS not witnessed - author contacted but no reply
(4) Milani RV et al. 2007[4] USA	rCCS	a. Ochsner Medical Center, New Orleans b. n=701 c. coronary events, including AMI (39 %), CABG (35 %), PCI (44%) d. 01/2000–07/2005 e. including depressive patients	a. n=522 b. SMC-CR c. 2–6 wk after index event d. 12 wk, total: 36 sessions e. n=3 f. outpatient	a. n=179 b. UC after non completion of 2 wks CR (< 5 sessions)	a. 1,296 ± 551 d (range: 109–2,188 d) b. (1) c. Cardiovascular risk factors, psychological parameters, quality of life	*Event rate (% CR+/no CR)* Endpoint 1: 8/30 p=0.0005 (subgroup of depressed patients)	- no mortality data from the whole study group (with and without depression) available - contact to author not successful

		f. 64±11 (total) g. 72 (total)					
(5) Nielsen KM et al. 2008[5] Denmark	rCCS	a. Coronary care unit at Aarhus Sygehus, Municipality of Aarhus cohort, Denmark, aged 30–69 y b. n=200 c. AMI d. 01/04/2000–31/03/2002 e. ≥ 30 d survival after AMI f. Mdn 59.8 (CR+) Mdn 59.7 (no CR) g. 71.5 (CR+), na (no CR)	a. n=145 b. SMC-CR c. 1–2 wk after hospital admission d. 6 wk (phase II) e. n=2 exercise sessions + education, life style and psychosocial support f. outpatient	a. n=55 b. CR non-attenders, UC	a. 1 and 2 y b. (1), (4) c. –	*Event rate (% CR+/no CR)* Endpoint 1 after 1y: 2.1/14.5, p=0.001 Endpoint 1 after 2y: 2.8/21.8, p=0.0001 Endpoint 4 after 1y: 22.1/10.9, p=0.07	
(6) Alter DA et al. 2009[6] Canada	rCCS	a. Data linkage: Toronto Rehabilitation Institutes, Clinical Registry (UNIX platform), Canadian Institute of Health Information Discharge Abstract Database (DAD), Ontario Health Insurance Plan, and Registered Persons Database b. n=4,084 c. primary index event ACS (97.7 %), CHF and others (2.3 %) d. 06/01/1999–10/12/2003 e. death or readmissions within 1 y after index event were excluded f. 59.4±10	a. n=2,042 b. SMC-CR c. 89 d average d. 12 mo, total: 26–36 sessions e. n=1 on-site exercise session + monitored home-based sessions and education f. outpatient	a. n=2,042 b. CR non-attenders matched for index events, medical history, age, gender, socio-economic status, geographical region; UC	a. 2 y + 5.2 y (mean) (4.0–6.6) y b. (1) (ITT analysis) c. effect of CR in various subgroups; effect of CR completion and non-completion	*HR (95% CI)* Endpoint 1: total: 0.47 (0.32–0.68); p<0.001 ≤65y: 0.59 (0.35–0.97); p=0.04 ≥66y: 0.31 (0.17–0.56); p<0.001 high risk: 0.57 (0.36–0.90); p=0.02 low risk: 0.57 (0.17–1.95); p=0.31 CR non completers:0.71 (0.29–1.71), p=0.41 CR completers: 0.28 (0.13–0.60), p<0.001 (below 1.00 is in favor to CR+)	- follow-up started 1 y after index event

		g. 87.4					
(7) Hansen D et al. 2009[7] Belgium	pCCS	a. hospital files and general practitioners b. n=238 c. successful CABG d. 01/1998–10/2002 e. blanking period: 4 wk post CABG, exclusion: symptomatic patients, co-morbidity of prognostic relevance f. 65.0± 9.0 (CR+) 66.2±8.3 (no CR) g. 69.8 (CR+) 67.7 (no CR)	a. n=149 b. SMC-CR c. 1–2 wk after discharge d. 3 mo, total ≥ 24 sessions e. n=3 + psychological/educational interventions f. outpatient	a. n=89 b. UC	a. 2 y b. (1), (4), (8), (10) c. –	*Event rate (% CR+/no CR)* <u>Endpoint 1:</u> 0.7/5.4, p<0.05 <u>Endpoint 4:</u> 0.0/3.2, p<0.05 <u>Endpoint 8:</u> with PCI: 4.0/6.5 With CABG: 0.0/0.7 <u>Endpoint 10:</u> 4.7/14.0	NOS 6 potential selection bias by using 2 medical centers offering CR or not - inclusion period by information from the author
(8) Suaya JA et al. 2009[8] USA	rCCS	a. Data linkage: Medicare's National Claims History File, Medicare's master enrollment database, American Hospital Association b. n=601,099 n=70,040 matched pairs c. mixed population: AMI (37.1 %), CABG (35.4 %), PCI (21.0 %), others d. through 1997 e. age ≥ 65 y, hospital stay ≤ 30d, surviving ≥ 30 d after discharge f. 65–74 y: 65.2 % 75–84 Y: 32.7 % ≥ 85 y: 2.1 % a. 63.6	a. n=70,040 b. SMC-CR c. not reported d. average: 24 CR sessions low CR users: 1–24 sessions high CR users: ≥ 25 sessions e. not reported f. outpatient	a. n=70,040 b. Nonusers of CR matched on AMI, PCI and CABG and demographics	a. 1 + 5 y after discharge from index hospitalization b. (1) c. –	*Event rate (% CR+/no CR)* <u>Endpoint 1 after 1y:</u> Propensity-based matching: 2.2/5.3 Regression modelling: 4.8/10.9 <u>Endpoint 1 after 5y:</u> Propensity-based matching: 16.3/24.6 Regression modelling: 28.1/38.0 p<0.0001 for all	- description of CR is limited to the "use of CR services defined by Medicare reimbursement for at least 1 CR session within 1 y of follow-up" - CR content is not reported in publication but known as multi-component through official Medicare sites: ww.massgeneral.org; https://www.medicare.gov/cardiac-

							rehab-programs.html
(9) Jünger C et al. 2010[9] Germany	rCCS	a. Acute Coronary Syndrome Registry (ACOS), including 155 hospitals in Germany b. STEMI, n=2,432 NSTEMI, n=2,115 c. STEMI, NSTEMI d. 06/2000–12/2002 e. alive at hospital discharge f. Mdn: STEMI 63.2 (CR+) 70.0 (no CR) NSTEMI 66.3 (CR+) 71.3 (no CR) g. STEMI 73.6 (CR+); 70.0 (no CR) NSTEMI 71.5 (CR+); 63.6 (no CR)	a. STEMI n=1,649 NSTEMI n=1,107 b. SMC-CR c. ≤ 2 wk after hospital discharge d. 3–4 wk e. ≥ 5 exercise sessions per wk + education, motivation, psychosocial support f. Inpatient	a. STEMI n=783 NSTEMI n=1,008 b. Usual care (General practitioner, control by cardiologists)	a. 1 y b. (1), (3), (10) c. –	*OR (95% CI)* Endpoint 1: STEMI: 0.41 (0.28–0.60) NSTEMI: 0.53 (0.38–0.76) Endpoint 3: STEMI: 0.66 (0.49–0.89) NSTEMI: 0.73 (0.55–0.98) Endpoint 10: STEMI: 0.58 (0.42–0.79) NSTEMI: 0.71(0.53–0.97) p<0.001 for all calculations	- CR controlled by German pension funds; the numbers of exercise sessions represent a minimum - Evaluation of deceased patients: retrospective questionnaires and/or telephone calls for assessment of CR-participation with help of relatives, not verified by medical records - high risk of selection bias
(10) Goel K et al. 2011[10] USA	rCCS	a. Mayo Clinic PCI registry (Rochester area, Olmsted County) + database of the Mayo Clinic CR program b. n=2,395, n=719 matched pairs c. PCI (elective, urgent or emergency due to ACS) d. 01/01/1994-30/06/2008 e. – f. 62.5±11.7 (CR+) 66.8±13.5 (no CR)	a. n=964 (entire cohort) n=719 (matched pairs) b. SMC-CR c. within 3 mo after index event d. total: Mdn 13 sessions e. not reported f. outpatient	a. n=1,431 (entire cohort) n=719 (matched pairs) b. UC	a. Mdn 6.3 y b. (1),(2),(4), (8), (10) c. –	*HR (95% CI)* Propensity score stratification: Endpoint 1: 0.53 (0.42–0.67) p<0.001 Endpoint 2: 0.61(0.41–0.91) p<0.016 Endpoint 4: 1.07(0.85–1.36) p<0.56 Endpoint 8:	- study includes a small part of patients in 1994; - mixed population including stable CAD patients - no detailed description of CR, but SMC-CR confirmed by author - per definition in the study, CR could

		g. 72 (CR+) 66 (no CR)				1.06(0.90–1.25) p=0.47 <u>Endpoint 10: death, AMI, PCI, CABG:</u> 0.85(0.74–0.98) p=0.022 Matched groups analysis: <u>Endpoint 1:</u> 0.54 (0.41–0.71) p<0.001 <u>Endpoint 2:</u> 0.69(0.44–1.07) p=0.095 <u>Endpoint 4:</u> 1.11(0.84–1.45) p=0.47 <u>Endpoint 8:</u> 1.16(0.96–1.39) p=0.13 <u>Endpoint 10: death, AMI, PCI, CABG:</u> 0.92(0.78–1.07) p=0.28	be of low volume - "repeat PCI/CABG" as calculated in the study was regarded as CROS endpoint number 8
(11) Kim C et al. 2011[11] Korea	pCCS	a. Sanggye Paik Hospital, Seoul, Korea b. n=141 c. AMI d. 01/2006–12/2007 e. PCI or CABG, exclusion: stroke, cancer, neuro-musculoskeletal symptoms f. 61.9±10.7 (CR+) 64.5±12.8 (no CR)	a. n=69 b. SMC-CR c. not reported d. 6–8 wk, hospital monitored, followed by monitored home based exercise e. not reported f. outpatient	a. n=72 b. UC	a. 1 y b. (1),(6),(8),(10) c. –	*Event rate (% CR+/no CR)* <u>Endpoint 1:</u> 1.4/1.04; p=0.95 <u>Endpoint 6:</u> 0.0/3.0; p=0.49 <u>Endpoint 8:</u> 6.0/10.0; p=0.53 <u>Endpoint 10:</u> 10.0/24.0; p=0.033	- endpoint (10) was defined as "recurrence", which was a composite of re-hospitalization, re-ACS, coronary angiography, PCI, CABG, and death - start after index event and CR

		g. 71 (CR+) 83 (no CR)					exercise frequency not reported - contact to author not successful
(12) Schwaab B et al. 2011[12] Germany	rCCS	a. secondary selection of participants from the TeleGuard trial,(40) b. n=1,474 c. mixed population (AMI, stable AP, elective or emergency PCI, CABG) d. 2001–2004 e. participation in the TeleGuard trial f. 64.1±9.6 (CR+) 62.2±10.3 (no CR) g. 73.7 (CR+) 76.9 (no CR)	a. n=794 b. SMC-CR c. ≤2 wk after hospital discharge d. 3–4 wk e. > 5 exercise sessions per wk + education, psychosocial support f. inpatient (majority)	a. n=679 b. UC	a. 1 y upon CR start b. Primary endpoint: (10) Secondary endpoints: (1), (4), (6), (8) c. –	*Event rate (% CR+/no CR)* Endpoint 1: 2.1/2.4; p=0.014 Endpoint 4: 1.8/3.8; p=0.015 Endpoint 6: 31.8/38.0; p=0.013 *OR (95% CI)* Endpoint 10: 0.73 (0.59–0.91) p=0.005 in favor to CR+	- Exercise frequency is not reported but CR follows regulations of German pension funds (numbers represent a minimum as confirmed by author) - Self-reported CR-participation, not verified - potential selection bias due to 56.4% CABG patients in the CR+ group vs only 27.9 % CABG patients in the control group (“no CR”) - suspicion of underrepresentation of NSTEMI-patients in both groups
(13) Martin BJ et al. 2012[13] Canada	pCCS	a. data linkage: Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH), Cardiac	a. n=2,900 (entire population) n=2,256 (matched pairs) b. SMC-CR	a. n=2,986 (entire population) n=2,256 (matched pairs) b. no CR and non-	a. Mdn: 5.37, up to 14 y b. (1),(6),(7) c. Emergency room visits without	*HR (95% CI)* Endpoint 1: Adjusted: 0.59 (0.49–0.70) Propensity matched:	- Information on CR content not included in publication but obtained from

		Wellness Institute of Calgary (CWIC) inpatient and emergency databases; Canada b. n=5,886 c. population (ACS +stable AP, others) d. 01/07/1996–31/01/2009 e. exclusion: aged < 18 y, no official health number, surviving < 6 mo after index event f. 60.1 (CR+) 61.1 (no CR) g. 83.8 (CR+) 74.7 (no CR)	c. 105.8 days (mean from referral to CR enrolment) d. 12 wk, total: 21.9±10.2 sessions e. n=2–3 supervised exercise session per wk + resistance training + non supervised sessions at home f. outpatient	completers of CR c. UC	hospitalization	0.67 (0.54–0.81) Endpoint 6: CR+ completion: 0.77 (0.71–0.84) CR non completers: 1.30 (1.13–1.49) Endpoint 7: CR+ completion: 0.68 (0.55–0.83) CR non completers: 0.87 (0.64–1.19)	author
(14) West RR et al. 2012[14] United Kingdom	pRCT	a. multi-center based b. n=1,813 c. AMI d. 08/1997–04/2000 e. discharged home within 28 d f. 64.2±11.2 (CR+) 64.7±10.9 (no CR) g. 72.6 (CR+) 74.4 (no CR)	a. n=903 b. SMC-CR c. not reported d. mean: 20 h within 6–8 wk e. n =1–2 per wk f. outpatient	a. n=910 b. UC	a. 1 y, 2y until 7–9 y b. (1),(4), (5), (7), (10) c. quality of life (SF36), life style	*RR (95% CI)* Endpoint 1 after 1y: 1.16 (0.79–1.69) Endpoint 1 after 2y: 0.98 (0.74–1.30) Endpoint 1 after 7–9 y: 0.99 (0.85–1.15) Endpoint 10 after 1 y: 0.96 (0.88–1.07) Endpoints 4, 5, 7: no differences between CR and control	- high risk of under-powering - early closure of enrollment due to limited funding: from an anticipated total of 6,000 patients only 1,813 patients were included into the study
(15) Beauchamp A et al. 2013[15] Australia	rCCS	a. a sample of participants of an earlier study(42) b. n=544 c. mixed population: AMI, CABG and PCI d. 1996–1997	a. n= 281 b. SMC-CR c. not reported d. total: 6–12 CR sessions (each session: 1 h exercise + 1 h	a. n=263 b. UC	a. 14 y b. (1) c. –	*HR (95% CI)* Endpoint 1: 1.58 (1.16–2.15) p=0.004 in favor to CR +	- mortality was ascertained through linkage to the Australian National Death Index

		e. survival within 1 y after index event f. 60.9±10.1 (CR+) 64.2±12.3 (no CR) g. 77 (CR+) 69 (no CR)	education) e. not reported f. outpatient				- no external validation of clinical characteristics - CR duration and frequency of sessions not reported
(16) Lee HY et al. 2013[16] Korea	pCCS	a. Sanggye Paik Hospital, Seoul, Korea b. n=74 c. AMI after successful PCI with drug-eluting stent d. 11/2007–05/2009 e. Age 50–75 y excluded if prior revascularization, cardiovascular or other comorbidities- f. 58.8±10.8 (CR+) 60.3±8.7 (no CR) g. 81.8 (CR+) 83.8 (no CR)	a. n=37 b. not reported c. within 4 wk d. 6 wk including structured and supervised exercise, followed by community-based and self-managed exercise (total 9 mo) e. n=3 per wk f. outpatient	a. n=37 (similar age as CR+) b. UC	a. 9 mo b. (2),(4), (10) c. coronary restenosis as primary endpoint	*Event quantity (n CR+/no CR)* Endpoint 2: 0/1, p=0.33 Endpoint 4: 0/0 Endpoint 10: 1/6, p=0.20	- Multi-component CR not reported in detail - small numbers of study participants
(17) Marzolini S et al. 2013[17] Canada	pCCS	a. secondary analysis of CR CARE survey comparing CR-participation by referral strategy (medically stable patients from 11 hospitals between Windsor, Sudbury, Ottawa, Ontario);(45) linkage to medical charts and administrative data bases b. n=851 c. ACS d. 2006-2008	a. n=424 b. SMC c. data not available d. data not available e. data not available f. outpatient	a. n=427 b. UC	a. Mdn: 2.7 y b. (1), (10) c. –	*HR (95% CI)* Endpoint 1: 3.91 (1.23–12.36) in favor to CR+ Endpoint 10: no significant differences	- self-reported CR-participation - information on CR-content given by author, data on CR start, duration and intensity are not available

		e. musculoskeletal comorbidities f. 64.8±9.7 (CR+) 68.1±10.6 (no CR) g. 78.1 (CR+) 64.7 (no CR)				
(18) Pack QP et al. 2013[18] USA	rCCS	a. database of the Division of Cardiovascular Surgery, Mayo Clinic, Rochester including consecutive residents of Olmstedt County b. n=846 c. CABG d. 01/1996–12/2007 e. Exclusion if combined procedure or discharged to a long-term facility f. 64.4±10.3 (CR+) 68.3±11.0 (no CR) g. 78 (CR+) 73 (no CR)	a. n=582 b. SMC-CR c. majority within 1 mo Mdn: 10 d d. Mdn: 55 d total: Mdn 14 sessions e. n=3 exercise sessions (30–45 min each) + encouragement to exercise for 30min/d on "non CR" days f. outpatient	a. n=264 b. UC	a. 9.0±3.7 y b. (1) c. –	*HR (95% CI)* Endpoint 1: 0.54 (0.40–0.74) p<0.001 in favor to CR+	- CR attendance was ascertained by Mayo Clinic data base - patients were considered to have participated in CR if they attended at least 1 outpatient session within 6 months of the index CABG surgery
(19) Coll-Fernández R et al. 2014[19] Spain	pCCS	a. Risk Factors and Arterial Disease (FRENA) registry, Spain(47) b. n=1,043 c. AMI d. 5/2003–8/2012 e. patients with a first AMI occurring < 3 mo prior to enrollment were considered f. 56.0±10.0 (CR+) 67.0±13.0 (no CR) g. 90 (CR+)	a. n=521 b. based on international clinical practice guidelines, but no standardized protocol for all hospitals c. < 3 mo after AMI d. not reported e. not reported f. outpatient	a. n=522 b. UC	a. Mean: 18 mo b. (1), (10) c. –	*HR (95% CI)* Endpoint 1: 0.08 (0.01-0.63) p=0.16 Endpoint 10: 0.65 (0.30.1.42) p=0.28	- Part of the information with respect to study design were obtained from author

		71 (no CR)				
(20) Prince DZ et al. 2014[20] USA	rCCS	a. Montefiore Medical Center, New York b. n=822 c. mixed population (AMI, CAD, CHF, stable AP, valvular heart disease) d. 01/05/2001–31/01/2011 e. – f. 61.6±10.8 (CR+) 61.6±12.6 (noCR) g. 63.1 (CR+) 58.1 (no CR)	a. n=488 b. not reported c. not reported d. not reported e. total (mean±SD): 21.6±13.5 f. outpatient	a. n=334 b. UC	a. up to 14 y b. (1) c. predictors of CR initiation, adherence and completion	Endpoint 1: in favor to CR+, p=0.0022	- description of CR incomplete, SMC-CR therefore not witnessed - duration of follow-up not exactly defined - steps to reduce selection bias between CR+ and no CR are unclear
(21) Rauch B et al. 2014[21] Germany	pCCS	a. OMEGA trial data base(49) b. n=3,560 c. AMI d. 10/2003–06/2007 e. >3 mo survival after index event f. Mdn: 62 (CR+) 69 (no CR) g. 76.4 (CR+) 71.1 (no CR)	a. n=2,513 b. SMC-CR c. ≤2 wk after hospital discharge (according to the German CR system, but not witnessed by OMEGA data base) d. 3–4 wk e. ≥5 exercise sessions + education, motivation, psychosocial support f. inpatient (vast majority)	a. n=1,047 b. UC	a. 4–12 mo after index event b. (1), (2), (3), (4), (5), (6), (8) c. PCI/CABG, heart failure, medication, laboratory tests	*OR (95% CI)* Endpoint 1: 0.46 (0.27–0.77) in favor to CR+ Endpoint 2: 0.43 (0.23–0.79) in favor to CR+ Endpoint 3: 0.53 (0.38–0.75) in favor to CR+ Endpoint 4: 0.72 (0.43–1.21) Endpoint 5: 0.35 (0.15–0.84) in favor to CR+ Endpoint 6: 0.96 (0.81–1.13) Endpoint 8: 1.00 (0.78–1.27)	- CR content and volume controlled by German pension funds - self-reported CR-participation by predefined structured interviews
(22) Goel K et al. 2015[22] USA	rCCS	a. Institutional, Mayo Clinic, Rochester Minnesota b. n=201	a. n=94 b. SMC-CR c. not reported	a. n=107 b. UC	a. 6.8±2.8 y b. (1)	*HR (95% CI)* Endpoint 1: 0.48 (0.27–0.83)	

		c. CABG + heart valve surgery d. 1996-2007 e. Olmsted country residents, aged ≥ 18 y, discharged alive f. 71.5±9.0 (CR+) 73.8±12.0 (no CR) g. 78 (CR+) 57 (no CR)	d. 12 wk (phase II), in addition phase III recommended total: Mdn 13 e. n=1–3 per wk f. outpatient			p=0.009 in favor to CR+, adjusted for propensity scores and mortality risk factors	
(23) De Vries H et al. 2015[23] The Netherlands	rCCS	a. Institutional, Dutch health insurance firm, Achmea Zorg en Gezondheid b. n=35,919 c. ACS, and/or PCI, CABG and/or valve surgery d. 01/01/2007–01/06/2010 e. Alive + insured 365 days before and 180 days after event f. 63.4±10.8 (CR+) 68.1±13.2 (no CR) g. 75 (CR+) 58 (no CR)	a. n=11,014 b. SMC-CR c. within 180 d after index event d. 6–12 wk e. n=2.3 exercise sessions per wk + education, psychology, social support, physiotherapy according to Dutch guidelines f. outpatient	a. n=24,905 b. UC	a. 4 y b. (1)	*HR (±95%CI)* <u>Endpoint 1:</u> Total population: 0.65 (0.56–0.77) p<0.01 in favor to CR+, adjusted for propensity scores and mortality risk factors <u>Subpopulations:</u> CABG/valve surgery: 0.55 (0.42–0.74) p<0.01 ACS: 0.68 (0.57–0.82) p<0.01	- Extensive management of confounding by automated variable selection out of 919 potential confounders

(24) Meurs M et al. 2015[24] The Netherlands	rCCS	a. Secondary selection out of two studies: DepreMI, MIND-IT(51, 52) b. n=1,702 c. After AMI with or without depression d. 09/1997–09/2000; 09/1999–11/2002 e. none f. 57±10 (CR+) 65±11 (no CR) g. 83 (CR+) 75 (no CR)	a. n=878 b. SMC-CR c. Mean 63 d after AMI d. 9 we average e. n=2.2 ± 1.6 exercise sessions per wk f. outpatient	a. n=824		a. 6 y (mean) b. (1), (6)	*HR (±95%CI)* <u>Endpoint 1:</u> Total population: 0.83 (0.54–1.30) p=0.41 Non depressed patients: 1.09 (0.63–1.89) p=0.74 Depressed patients: 0.48 (0.28–0.84) p=0.01 HR below 1.0 is in favor to CR+	- NOS 5 - Information of CR-content, duration and intensity obtained from author by request
(25) Schlitt A et al. 2015[25] Germany	rCCS	a. Secondary analysis of two RCTs with other primary objectives (54) b. n=1,798 c. Mixed population: Stable CAD, ACS, CABG, heart failure others d. 2007–2011, 2007–2009 e. >18 y, live expectancy > 12 mo	a. n=552 b. SMC-CR c. Within 180 d after index event as outlined in publication; within 1 mo after index event like ACS or CABG according rules of German authorities d. Not reported: 3–4 we according rules of German authorities e. Not reported: > 5 exercise sessions per week to be supposed f. inpatient (majority) and outpatient	a. n=1,246 b. UC		a. 136±71 wk b. (1)	*HR (± 95% CI)* <u>Endpoint 1:</u> 0.067 (0.025–0.180) p<0.001	- NOS 4 - High risk of selection bias, as study is a secondary evaluation of two RCTs with other objectives[63,64] - CR not described in detail within the publication but following minimal standards given by German pension funds and confirmed by author
(26) Espinosa	pCCS	a. Institutional, Hospital	a. n=113	a. n=40		a. 1 y1 y post AMI	*Event rate*	- Only patients with

Caliani S et al. 2004[26] Spain		Clínico Universitario Virgen de la Victoria, Málaga, Spain. b. N=153 c. AMI d. not stated; after 1995 e. control group did not accept CR program f. 49.9±8.4 (CR+) 53.5±9.5 (no CR) g. 93.5	b. SMC-CR c. Immediately after discharge (phase I) d. 12 wk (phase II) at least 9 mo (phase III) e. n=3 (24 sessions) + educational talks, dietary and nutritional advice, psychological support (3mo, phase II). Maintenance phase III until 12 mo f. primary care centre (phase II, III)	b. CR non-attenders	b. (10) c. Quality of life, exercise capacity, body mass index	*(%CR+/noCR))* Endpoint 10 (angina, hospitalization, re-infarction, cardiac insufficiency and/or death): 6.7/ 6.7 (p=NS)	low-risk MI - CR by patients' decision - CR supervised by "family doctor" not by cardiologist - CR program accredited by Cardiology Spanish Society
(27) Lee JY et al. 2016[27] Canada	pCCS	a. Data linkage: ASAN Medical Center-Left MAIN Revascularization registry (single-center retrospective database) b. N=3,040 c. mixed population: patients with unprotected LMCA stenosis >50% with subjective or objective ischemia; ACS (64.2%), silent ischemia (8%), stable AP (27.8%) d. 01/01/1995–31/12/2010 e. Patients treated with PCI (37.7%), CABG (49.1%) or medically (13.2%); end of follow-up 31/08/2014 f. 60.8±10.3 (CR+) 62.4±10.5 (no CR)	a. n=596 n=507 (matched pairs) b. SMC-CR c. Within 3 mo after index hospitalization (phase II) d. 3 mo (36 sessions) e. n=3 f. outpatient	a. n=2,444 n=507 (matched pairs) b. CR non-attenders	a. Mdn 7.3y (IQR, 4.4- 10.2y) b. (1),(2),(4),(5),(8) c. Risk factors' modification, exercise capacity, QoL, return to work, psychological results	*Event rate (%CR+/noCR))* Endpoint 1: 13.3/ 18.5 Endpoint 2: 10.4/ 15.5 Endpoint 4: 3.0/ 6.7 p<0.001 for all Endpoint 5: 2.0/ 3.4 p=0.07 Endpoint 8: 7.3/ 10.9 p=0.006 *HR (95% CI) after multivariate analysis* Endpoint 1: 0.70 (0.49–1.00); p=0.05 Endpoint 2: 0.69 (0.48–0.97); p=0.03 Endpoints 4, 5, 8: p=NS *HR (95% CI)* *p*ropensity-matched	- participation in CR was defined as attending at least one outpatient CR session (phase II) within 3 mo after index hospitalization

		g. 76.2 (CR+) 72.9 (no CR)				pairs Endpoint 1: 0.62 (0.43–0.89); p=0.009 Endpoint 2: 0.54 (0.36–0.80); p=0.002 Endpoints 4, 5, 8: p=NS	
(28) Aronov DM et al. 2017[28] Russia	RCT	a. Institutional Moscow Centre of Interventional Cardioangiology. b. N=36 c. patients with IHD who had undergone CABG d. not stated; after 1995 e. -- f. 58.6±7.0 (CR+) 55.9±7.0 (no CR) g. 100	a. n=18 b. SMC-CR (educational program + physical training) c. 2–8 wk after CABG (mean 7.8±1.6 wk) d. 4 mo e. n=3 f. monitored (medical supervision) or not-monitored (home based)	a. n=18 b. CR non-attenders; only educational program available	a. 1 y b. (1), (6), (8), (10) c. Exercise and echocardiography parameters, lipd levels, QoL, AP attacks, return to work	*Event (nr CR+/nr no CR)* Endpoint 1: 0/0 Endpoint 6: 1/3 Endpoint 8: 1/1 Endpoint 10 (AP, MI, re-vascularization, hospitalization for IHD exacerbation): 2/7	- publication in Russian language (translations received from Cochrane Russia and a private agency) - no statistical analyses of the results - CR had educational component only - contact to author not successful
(29) Hautala AJ et al. 2017[29] Finland	RCT	a. EFEX-CARE (Effectiveness of Exercise Cardiac Rehabilitation) database of the Finnish Health care setting b. N=204 c. ACS d. 02/2011–05/2014 e. Exclusion criteria: NYHA ≥III, scheduled or emergency CABG, UA, severe peripheral atherosclerosis, diabetic retinopathy or	a. n=109 (drop-out, n=31) b. SMC-CR c. within 1 wk after hospital discharge d. 1 y e. n=4-5 (1 in hospital session per wk and home-based sessions for 6 mo; thereafter home based only) + information, motivation, education, social and vocational support	a. n=95 (drop-out, n=25) b. UC	a. 1 y b. (10) c. Health care costs, quality-adjusted life years, cost-effectiveness	*Event rate (%CR+/no CR)* Endpoint 10 after 1y: (combination of death, recurrent acute coronary event, or hospitalization for HF) 4.6/16.8, p=0.004	- Center-based CR under supervision of cardiologists and physiotherapists, all components of SMC-CR were available to most of the patients, no information about psychological support (information provided by the author)

		neuropathy, inability to perform regular home-based exercises (i.e. severe musculoskeletal problems) f. 60±11 (CR+), 62±9 (no CR) g. 73 (CR+), 71 (no CR)	f. outpatient				
(30) Doimo S et al. 2018[30] Italy	rCCS	a. Patients discharged from two tertiary hospitals b. N=1,280 c. mixed population; STEMI (n=378), NSTEMI (n=265), CABG with or without valve surgery (n=353) or planned PCI (n=284) d. 01/01/2009–31/12/2010 e. Non-residents in the region or with severe non-cardiac comorbidities (i.e. end-stage tumors), dementia, or immobilized patients, were excluded from the CR group. 13% of eligible patients did not attend CR f. 68±11 (CR+), 66±12 (no CR) g. 68 (CR+), 75 (no CR)	a. n=839; STEMI (n=251), NSTEMI (n=162), CABG (n=243), PCI (n=183) b. SMC-CR c. 89 d (average) d. 5 mo (average) e. 1st part (10 sessions of 45min of cyclette training 2 times/wk for 5 wks); 2nd part (18 sessions of 45min of gym training 3 times/wk for 6wks) supervised by trained nurse and physiotherapist. Other components: Lifestyle counseling at every visit + nutritional advice once/mo + psychological support f. outpatient	a. n=441; STEMI (n=127), NSTEMI (n=103), CABG (n=110), PCI (n=101) b. CR non-attenders receiving all other components of CR	a. Mdn 82 mo (IQR 60 – 89 mo) b. PEP: (9) SEP: (1), (2), (6) c. effect of CR in various subgroups	*Event rate (%CR+/no CR)* Endpoint 1: 17/18 (p=0.861) Endpoint 2: 6/6 (p=0.623) Endpoint 6: 15/27 (p<0.001)) Endpoint 9: 18/30 (p<0.001)) *HR (95% CI)* Endpoint 9: 0.578 (0.432–0.773); p<0.001 *Event rate, propensity matched analysis (%CR+/ no CR)* Endpoint 1: 10/19 (p=0.002) Endpoint 2: 2/7 (p=0.008) Endpoint 6: 25/11 (p<0.001)) Endpoint 9: 29/13 (p<0.001))	- Group allocation by different hospitals - Multivariable regression model and propensity score matching analysis (covariates: age, sex, hypertension, LVEF, DM, smoking, CKD, dyslipidaemia, previous PCI, previous ACS, BB, ACEi/ARB, statins/ezetimibe) - statistical analysis does not address cardiovascular mortality adequately - 5-year composite endpoint as primary outcome (hospitalization for cardiovascular causes and cardiovascular mortality)

(31) Sunamura M et al. 2018[31] The Netherlands	rCCS	a. Patients from Erasmus Medical Centre (no CR), Rotterdam were propensity score matched with patients from Capri Cardiac Rehabilitation Cater, Rotterdam (CR+) b. N=3,958 c. ACS followed by primary PCI d. 2003 - 2011 e. Excluded: patients with cardiogenic shock (2.3%) and with early (within 60 d post-PCI) death (5.2%) f. 59.0±9.9 (CR+), 58.8±11.83 (no CR) g. 77 (CR+), 78 (no CR)	a. n=1,159 b. SMC-CR c. Mdn 4-6 wk d. 12 wk e. n=2 (1.5h group exercise session). Other components: verbal and written instructions on how to deal with exercise, diet, smoking cessation, and stress management. Individual consultations with psychiatrist, psychologist, and social workers was available if necessary. Complete CR if attended at least 75% of the physical program f. outpatient	a. n=1,159 b. no CR participants	a. Mdn 10 y 4-12 y (range) b. (1) c. Mortality rates of CR completion vs non-completion	*Cumulative rates (% CR+/no CR)* Endpoint 1 at 5 y: 6.4/10.4 Endpoint 1 at 10 y: 14.7/23.5 HR (95% CI) Endpoint 1 at 10y: (unadjusted) 0.56 (0.43-0.73) (adjusted) 0.61 (0.46-0.81); p<0.001	- Propensity score matching analysis 1:1 (covariates: age, sex, STEMI, current smoking, family history of CAD, HTN, hypercholesterolemia, DM, prior MI, prior history of PCI or CABG, proximal LAD lesion, socioeconomic status)

Descriptive values of metric variables are given in mean or mean plus standard deviation (SD), if applicable. Other calculations are noted in the table. Mdn, median; N, number of total population, n, number of subpopulation; na, not applicable (not published); d, days; wk, week(s); mo, month(s); y, year(s)
AMI, acute myocardial infarction; AP, angina pectoris; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CHF, congestive heart failure; CR, cardiac rehabilitation; EF, ejection fraction; EP, endpoint; HD, hemodialysis; HREA, hospital readmission for any reason; IG, intervention group; ITT, intention to treat; MACE, major adverse cardiac events (death, non-fatal reinfarction); MACCE, major adverse cardiac and cerebrovascular events (death, non-fatal reinfarction and stroke); pCCS, prospective controlled cohort trial; PCI, percutaneous coronary intervention; PEP, primary endpoint; rCCS, retrospective controlled cohort trial; RCT, randomized controlled trial; SEP, secondary endpoint; SMC-CR, structured and multi-component CR; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; UC, usual care including ambulatory supervision by family doctor and/or cardiologist, and may also include advise to exercise at home

Table SM 3b: Studies selected for quantitative analysis (CROS I, search until Dec 2015, and CROS II, search until Sep 2018); reported exercise volumes

Study, Publication year, Country	Study design	CR phase II duration (weeks)	Physical exercise sessions per week	Sum of CR sessions	Population
(1) Boulay P et al. 2004[1], Canada	p/rCCT	12	2	24	ACS
(2) Norris CM et al. 2004[2], Canada	rCCS	12	2-3	24-36	mixed
(3) Kutner NG et al. 2006[3], USA	rCCS	12	3	36	CABG
(4) Milani RV et al. 2007[4], USA	rCCS	12	3	36	mixed
(5) Nielsen KM et al. 2008[5], Denmark	rCCS	6	2	12	ACS
(6) Alter DA et al. 2009[6], Canada	rCCS	52		26-36	ACS
(7) Hansen D et al. 2009[7], Belgium	pCCS	13	3	minimum 24; 48±25 (mean±SD)	CABG
(8) Suaya JA et al. 2009[8], USA	rCCS		Not reported	average 24; Low: 1-24, High: ≥25	mixed
(9) Jünger C et al. 2010[9], Germany	rCCS	3-4	>5	>20	ACS
(10) Goel K et al. 2011[10], USA	rCCS	Not reported	13 mdn	Not reported	ACS
(11) Kim C et al. 2011[11], Korea	pCCS	6-8	Not reported	Not reported	ACS
(12) Schwaab B et al. 2011[12], Germany	rCCS	3-4	>5	>20	mixed
(13) Martin BJ et al. 2012[13], Canada	pCCS	12	2-3	24-36; average 21.9; non completers: average 6.7	mixed
(14) West RR et al. 2012[14], United Kingdom	pRCT	6-8	1-2	6-16	ACS
(15) Beauchamp A et al. 2013[15], Australia	rCCS	Not reported	Not reported	6-12	mixed
(16) Lee HY et al. 2013[16], Korea	pCCS	6	3	18	ACS
(17) Marzolini S et al. 2013[17], Canada	pCCS	Not reported	Not reported	Not reported	ACS
(18) Pack QP et al. 2013[18], USA	rCCS	7.8 mdn	3	14 mdn	CABG
(19) Coll-Fernández R et al. 2014[19], Spain	pCCS	Not reported	Not reported	Not reported	ACS
(20) Prince DZ et al. 2014[20], USA	rCCS	Not reported	Not reported	21.6±13.5 (mean±SD), minimum 18	mixed
(21) Rauch B et al. 2014[21], Germany	pCCS	3-4	>5	>20	ACS
(22) Goel K et al. 2015[22], USA	rCCS	12	1-3	13 mdn (8-20)	CABG
(23) De Vries H et al. 2015[23], The Netherlands	rCCS	6-12	2.3	13.8-27.6	mixed
(24) Meurs M et al. 2015[24], The Netherlands	rCCS	9	2.2 average	19.8	ACS

(25) Schlitt A et al. 2015[25], Germany	rCCS	3-4	>5	>20	mixed
(26) Espinosa Caliani S et al. 2004[26], Spain	pCCS	not reported	3	24	ACS
(27) Lee JY et al. 2016[27], Canada	pCCS	12	3	36	mixed
(28) Aronov DM et al. 2017[28], Russia	RCT	16	3	48	CABG
(29) Hautala AJ et al. 2017[29], Finland	RCT	26	1 centre-based (+ 3-4 home-based)	26 centre-based (+ 78-104 home-based)	ACS
(30) Doimo S et al. 2018[30], Italy	rCCS	22	2-3	28	mixed
(31) Sunamura M et al. 2018[31], The Netherlands	rCCS	12, 6 minimum	2	24	ACS

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CR, cardiac rehabilitation; mdn, median; pCCS, prospective controlled cohort trial; rCCS, retrospective controlled cohort trial; RCT, randomized controlled trial; SD, standard deviation

Table SM 4: Excluded studies and justification for exclusion

Study (abstracts and design papers of studies included into CROS meta-analysis are not listed in this table) **CO**, study was included into Cochrane meta-analysis 2016[32,33]	**Reason for exclusion based on** (P) Population (I) Intervention (C) Controls (O) Outcomes (OR) Other reasons	**Study selection level:** PS = **P**re**S**election FTE = **F**ull **T**ext **E**valuation SSE = **S**tructured **S**tudy **E**valuation PS (+) = Only conference abstract available, but study and potential publication has to be followed **Final search:** **Sep 04 2018**
1995		
Bondestam E et al.[34]	(P) Population recruited before 1995	PS
Cannistra LB et al.[35]	(C) No control without CR	PS
Gohlke-Bärwolf C et al.[36]	(OR) No original study	PS
Hamalainen H et al.[37]	(P) Index event before 1995	PS
Scherwitz LW et al.[38]	(P) Population recruited before 1995	PS
Heller LF et al.[39]	(I) No comprehensive CR	PS
1996		
Jones DA et al.[40]	(P) Population recruited before 1995	PS
Lidell E et al.[41]	(P) Population recruited before 1995	PS
MRFIT publishers[42]	(P) Population recruited before 1995	PS
Allen JK et al.[43]	(O) No prognostic outcomes as defined by CROS	PS
Engblom E et al.[44] **CO**	(P) Population recruited before 1995	PS
Rugulies R et al[45]	(C) No control as defined by CROS	PS
Speccia C et al.[46] **CO**	(P) Population recruited from 1992–1995	PS
1997		
Ornish lifestyle program [47]	(OR) No original study	PS
Almeida P et al.[48]	(O) No prognostic outcomes	PS
Bundy C [49]	(OR) Only commentary	PS
Engblom E et al.[50]	(P) Population recruited before 1995	PS
Frasure-Smith et al.[51]	(I) No intervention as defined by CROS	PS
Kozlov ID et al.[52]	(P) Inclusion period to a significant part before 1995 (O) No prognostic outcomes	PS
Lee SS[53]	(O) No prognostic outcomes	PS
Niebauer J et al.[54]	(P) Population recruited before 1995	PS
Roseler et al.[55]	(P) Population recruited 1993–1995 (I) Only phase III CR	PS
Tanabe K et al.[56]	(OR) Full paper not available	PS
Van Dixhoom J et al.[57]	(P) Population recruited before 1995	PS
1998		
Ali A et al.[58]	(O) No prognostic outcomes as defined by CROS	PS
Bell JM[59] **CO**	(C) No control according to CROS criteria	PS + FTE
Campbell NC et al.[60]	(I) No exercise	PS
Carlsson R et al. [61] **CO**	(O) No predefined prognostic outcomes (only surrogate parameters)	PS + FTE
Fattirolli F et al.[62]	(OR) Only description of study design (O) Outcomes do not meet CROS criteria	PS
Jitpraphai C et al.[63]	(P) Population recruited before 1995	PS
Jolly K et al. (SHIP) [64]	(O) No prognostic outcomes	PS
Nahhas GT et al.[65]	(OR) Only abstract	PS
Ornish D et al.[66]	(P) Trial conducted before 1995	PS

Ornish D [67]	(P)	Population recruited before 1995	PS + FTE
Walters J et al.[68]	(P)	Population recruited before 1995	PS
	(I)	Phase I rehabilitation	
1999			
Stahle A et al.[69] **CO**	(I)	Only exercise	PS
Ma H et al.[70]	(C)	Not control according to CROS criteria	PS
Lisspers J et al.[71]	(P)	Population recruited 1993–1995	PS
Jolly K et al.[72]	(O)	No outcomes as defined by CROS	PS
Johnston M et al.[73]	(O)	No outcomes as defined by CROS	PS
Hofman Bang C et al.[74] **CO**	(P)	Population recruited 1993–1995	PS
Dugmore LD et al.[75] **CO**	(P)	Population recruited before 1995	PS
Bethell HJN et al.[76]	(P)	Population recruited before 1995	PS
Wallner S et al.[77]	(P)	Population recruited in 1994–1995	PS
van Dixhoorn JJ et al.[78]	(P)	Population recruitment before 1995	PS
Takahashi H et al.[79]	(P)	Population recruitment before 1995	PS
2000			
Allison TG et al. CHEER [80]	(I)	Intervention without exercise	PS
Epstein AM et al.[81]	(OR)	Only abstract	PS
See also Goss JR et al.[82]	(O)	No prognostic outcomes	
Fridlund B et al.[83]	(O)	No outcomes as defined by CROS	PS
Hata R et al.[84]	(OR)	Only abstract, full paper not found	PS
Naughton J et al. [85]	(P)	Population recruited before 1995	PS
Pater C et al. CORE study [86]	(OR)	Only study design, publication of study results not found	PS
Steffen-Batey L et al.[87]	(P)	Population recruited before 1995	PS
Corpus Christi Heart Project			
Toobert DJ et al.[88] **CO**	(O)	Health related quality of life	PS
Women's Lifestyle Heart Trial			
2001			
Baessler A et al.[89]	(P)	Index events before 1995	PS + FTE
Belardinelli R et al.[90] **CO**	(P)	Population recruited before 1995	PS
ETICA trial	(I)	Only exercise	
Denollet J et al.[91]	(P)	Population recruited before 1995	PS
Fonarow GC et al.[92]	(I)	Intervention does not meet CROS criteria	PS
CHAMP			
Hedbäck B et al.[93]	(P)	Population recruited before 1995	PS
Higgins HC et al.[94] **CO**	(P)	Patients after PCI	PS
	(O)	No predefined prognostic outcomes	
Whellan DJ et al.[95]	(P)	Index event does not meet CROS criteria and took place before 1995 in a significant part of patients	PS
Sharma B et al.[96]	(P)	Population recruited 1991–1996	PS
2002			
Buchwalsky G et al.[97]	(I)	Phase III rehabilitation	PS
Desmarais PL et al.[98]	(C)	No control	PS
Goss JR et al.[82]	(O)	No clinical events	PS + FTE
Hall JP et al.[99]	(O)	No clinical events	
Kavanagh T et al.[100]	(P)	Recruitment before 1995	PS
La Rovere MT et al.[101] **CO**	(P)	Recruitment before 1995	PS
Oldridge N et al.[102]	(OR)	Meta-analysis	PS
Warren TF [103]	(P)	Index events before 1995	PS
Winberg B et al.[104]	(P)	Patient`s inclusion period to a significant part before 1995	PS + FTE
Wright DJ et al.[105]	(O)	Outcomes do not meet CROS criteria	PS
2003			
Afrasiabi SG et al.[106]	(O)	No prognostic outcomes as defined by CROS	PS + FTE
Aldana SG et al.[107]	(O)	Outcomes do not meet CROS criteria	PS
(Ornish programme)			

Chiashi K et al.[108]	(P)	Inclusion of study participants before 1995	PS
Frenn M et al.[109]	(P)	No index event	PS + FTE
ISRCTN73884263	(OR)	Design paper	PS
BRUM study [110]	(C)	Control does not meet CROS criteria	
Johansen S et al.[111]	(I)	No structured and supervised exercise	PS
Marchionni N et al.[112] **CO**	(O)	No outcomes as defined by CROS	PS
Murchie P et al.[113]	(P)	Patients with CAD, no index events described	PS + FTE
	(I)	No structured exercise	
Pasquali SK et al.[114]	(O)	Functional status as primary endpoint. Rehospitalization as secondary endpoint biased by premature deaths not evaluated	PS + FTE
Sundin O et al.[115]	(O)	No prognostic outcomes	PS
	(C)	No control as defined by CROS	
Vitcenda M [116]	(C)	No control as defined by CROS	PS
VHSG Vestfold Heartcare Study Group [117] **CO**	(P)	Mixed population with a large part of chronic CAD	PS + FTE
	(O)	No outcomes as defined by CROS, calculating the 5-years CAD risk according to the WOSCOPS study algorithm	
Young W et al.[118]	(I)	Intervention does not meet CROS criteria	PS
2004			
Ballegaard S et al.[119]	(P)	Population does not meet CROS criteria	PS
	(I)	no structured and supervised Exercise	
Hambrecht R et al.[120] **CO**	(P)	Only stable angina pectoris	PS
	(I)	Only exercise	
ISRCTN74601515 [121]	(OR)	Study registration (DANREHAB TRIAL), see also Zwisler AD et al. 2005[90] and Zwisler AD et al.2008[91]	PS
	(P)	Population does not meet CROS criteria	
Jiang X[122]	(P)	No index event as described by CROS	PS
	(O)	Follow-up too short (3 months)	
Kotseva K et al.[123]	(O)	No prognostic outcomes	PS
Murchie P et al.[124]	(I)	No structured supervised exercise	PS
Piestrzeniewicz K et al.[125]	(C)	No control as defined by CROS	PS + FTE
Sundarajan V et al.[126]	(OR)	design problems: linkage of two data bases resulted in classification error in 30% of the participants	PS + FTE
Witt BJ et al.[127]	(P)	Population recruited from 1982–1998	PS + FTE
Yu CM et al.[128]	(O)	No prognostic outcome	PS
2005			
Austin J et al.[129]	(P)	No index events as defined by CROS	PS
Briffa TG et al.[130] **CO**	(O)	no prognostic outcomes (costs, HRQL)	PS + FTE
Dendale P et al.[131]	(P)	No index events as described by CROSS	PS + FTE
Lisspers J et al.[132]	(P)	Index events do not meet CROS criteria	PS + FTE
Maroto Montero JM et al.[133] **CO**	(P)	Inclusion period starts before 1995	PS + FTE
Raftery JP et al.[134]	(I)	No structured exercise	PS + FTE
Sinclair AJ et al.[135]	(I)	Intervention does not meet CROS criteria	PS
Zwisler AD et al.[136]	(OR)	DANREHAB trial, design paper; See publication of results in 2008 [137]	PS
	(P)	Population does not meet CROS Criteria (including risk patients without proven CAD)	
2006			
Bhaskaran A et al.[138]	(OR)	Meeting abstract; full paper not found	PS
Herdy AH et al.[139]	(OR)	Meeting abstract See publication of results in 2008[108]	PS

	(I)	Intervention does not meet CROS criteria	
	(O)	outcomes do not meet CROS criteria	
Kappagoda CT et al.[140]	(P)	No index event as defined by CROS	
	(C)	No controls as defined by CROS	
Kovoor P et al.[141] **CO**	(P)	selectively low risk patients	PS + FTE + SSE
	(I)	minimal frequency of exercise as defined by CROS may not have been achieved	
	(O)	Primary outcome does not meet CROS criteria	
Lear SA et al.[142]	(O)	Outcomes do not meet CROS criteria	PS
Soerensen C et al.[143]	(OR)	Only abstract; full paper based on this title has not been found; compare Nielsen KM et al.2008[113]	PS
Viswanathan K et al.[144]	(OR)	Only abstract; full paper not found	PS
Zhang YM et al.[145]	(I)	Phase I CR in hospital	PS
2007			
Carrol DL et al.[146]	(I)	Intervention does not meet CROS criteria	PS
Hua ST et al.[147]	(OR)	Meeting abstract	PS
	(O)	outcomes do not meet CROS criteria	
Jiang X et al.[148]	(I)	Intervention does not meet CROS criteria	PS
	(O)	No prognostic outcomes	
Macchi C et al.[149]	(C)	No control without CR	PS
Merenich JA et al.[150]	(I)	No supervised and professionally controlled exercise sessions	PS + FTE
Suaya JA et al.[151]	(O)	Outcomes do not meet CROS criteria	PS + FTE
2008			
Batista IBI et al.[152]	(OR)	Only abstract, full paper not found	PS
Canyon S et al.[153]	(P)	Mixed population including patients only at CAD risk	PS + FTE + SSE
Delaney EK et al.[154]	(P)	No index events as defined by CROS	PS + FTE
	(I)	No regular supervised exercise	
Dendale P et al.[155]	(P)	Primarily patients after elective PCI	PS + FTE
Giannuzzi P et al.[156]	(I)	Phase III rehabilitation	PS
Herdy AH et al.[157]	(I)	phase I rehabilitation	PS
	(O)	No outcomes as defined by CROS	
Huang Y et al.[158]	(P)	Population overlaps with Kutner et al.2006[128]	PS + FTE + SSE
Kummel M et al.[159]	(I)	No structured exercise	PS
Naser A et al.[160]	(O)	No outcomes as defined by CROS	PS
Silva RC et al.[161]	(I)	No structured exercise sessions	
Zwisler AD et al.[137]	(P)	Mixed population not following CROS criteria, and including patients without proven CAD	PS + FTE + SSE
2009			
Cortes OL [162]	(OR)	Systematic review	PS
Edstrom-Pluss C et al.[163]	(C)	No control group defined by CROS	PS
	(I)	Evaluation of extended CR	
Giallauria F et al.[164]	(C)	No control group without CR	PS
	(I)	Phase III rehabilitation	
Jolly et al.[165]	(C)	No control group as defined by CROS	PS + FTE
BRUM study	(O)	No prognostic outcomes	
King M et al.[166]	(C)	No control group	PS
Lafitte M et al.[167]	(I)	No exercise based CR	PS + FTE
CEPTA programme	(C)	No control	
2010			
Hammill BG et al.[168]	(C)	No control as defined by CROS	PS
Hansen D et al.[169]	(O)	No control as defined by CROS	PS
NCT01075867 [170]	(OR)	Study design	PS

ELIPSE programme	(I)	Intervention does not meet CROS criteria	
Onishi T et al.[171]	(I)	CR starts too late after index event; exercise intensity is too low	PS + FTE
Silberman A et al.[172]	(P)	No index events as defined by CROS	PS
SogaY et al.[173]	(P)	Only patients after elective PCI	PS
	(O)	Outcome is safety of CR after PCI	
2011			
Boyden T F et al.[174]	(OR)	Conference abstract	PS
	(C)	No control without CR; see Doll, JA et al.2015 [175]	
Gulliksson M et al.[176]	(I)	No exercise based CR	PS
JPRN-UMIN000005177 [177]	(P)	No index event as defined by CROS	PS
Lam G et al.[178]	(O)	Follow-up too short	PS
Lewinter C et al.[179]	(OR)	Conference abstract; see also Lewinter C et al.2012 [180]	PS
	(I)	Evaluation of CR referral rather than CR attendance	
Milani RV et al.[181]	(P)	Population is a subset of depressed heart failure patients	PS
Moreno-Palanco MA et al.[182]	(P)	Population includes stroke patients	PS
MIRVAS study	(I)	No structured and supervised exercise	
Piso B et al.[183]	(I)	Phase III cardiac rehabilitation	PS
Pluss CE et al.[184]	(C)	No control group without CR	PS
Soga Y et al.[185]	(P)	Index event does not meet CROS criteria	PS
2012			
Armstrong MJ et al.[186]	(OR)	Conference abstract, See Armstrong MJ et al.2015	PS
	(P)	Population overlaps with the study published by Martin, BJ 2012[13,187]	
Franklin BA [188]	(OR)	Comment referring to West RR et al.[14]	PS
Ghroubi S et al.[189]	(OR)	Conference abstract	PS
	(O)	Outcomes do not meet CROS criteria	
Iliou MC et al.[190] French FAST-MI study	(OR)	Conference abstract, see also Pouche, M et al.2013 (abstract), [191] and Pouche, M et al.2015 [192]	PS
Kubilius R et al.[193]	(P)	Population does not meet CROS criteria	PS
Lewinter C et al.[180]	(I)	Evaluation of CR referral rather than attendance	PS
Mayer-Berger W et al.[194]	(I)	Phase III cardiac rehabilitation	PS
Naranjo-Estupinan NF et al.[195]	(OR)	pCCS with a low number of participants and a high grade of asymmetric distribution within three study arms; no further information from authors available	PS + FTE + SSE
Ou HT & Balkrishnan R [196]	(OR)	Conference abstract,	**PS (+)**
	(O)	Effect of CR after AMI on cost effectiveness and rehospitalization	
Parashar S et al.[197]	(O)	No prognostic outcomes	PS
Rangel I et al.[198]	(C)	Control does not meet CROS criteria	PS
Rideout A et al.[199]	(I)	Pre-surgical rehabilitation	PS
Suzuki T et al.[200]	(P)	No predefined index event	PS + FTE
2013			
Carrington MJ et al.[201]	(I)	No comprehensive CR as defined by CROS	PS
Gambogi R et al.[202]	(OR)	Conference abstract,	**PS (+)**
	(I)	Effect of CR on clinical course, survival and revascularization	
Hung RK et al.[203]	(I)	No comprehensive CR as defined by CROS	PS
Jorstad HT[204] RESPONSE trial	(I)	No structured exercise as defined by CROS	PS

Kotseva K et al.[205] EUROASPIRE III	(O)	No prognostic outcomes	PS
Lear SA et al.[206]	(OR)	conference abstract, not to be followed	PS
	(I)	Internet-based prevention program	
	(O)	no outcomes as defined by CROS	
Longobardi G et al.[207]	(OR)	Only abstract, not to be followed	PS
	(I)	Prognostic effect of physical exercise levels before a cardiac event	
Martin BJ et al.[208]	(I)	Study compares fitness levels	PS
Meisinger C et al.[209]	(I)	No structured and supervised Exercise	PS
Mudrick DW et al.[210]	(OR)	Conference abstract,	**PS (+)**
	(O)	Effect of CR and hospital Readmission	
Murphy BM et al. [211]	(I)	No structured supervised exercise	PS
Naci H et al.[212]	(OR)	Meta-analysis	PS
Panovsky R et al.[213]	(P)	Only patients with chronic CAD included	PS + FTE + SSE
	(C)	No control as defined by CROS	
Pouche M et al.[191] French FAST-MI study	(OR)	Conference abstract, see also Pouche M et al.2015 (165)	PS
	(I)	CR referral rather than Participation	
Russo N et al.[214]	(OR)	Conference abstract, not to be followed	PS
	(C)	No control	
Santaularia N et al.[215]	(OR)	Study design RCT to evaluate the effect of a structured exercise program in CAD patients with ischemia	**PS (+)**
Sobolev M. et al.[216]	(OR)	Conference abstract	**PS (+)**
	(O)	Comparison of re-hospitalization rates between CR attenders and non-attenders	
Turkstra E et al.[217]	(I)	Intervention does not meet CROS criteria	PS
	(O)	Health related quality of life and physical activity	
Vervueren PL et al.[218] French MONICA registry	(OR)	Conference abstract	**PS (+)**
2014			
ACTRN12614000284662 [219] Central Australian heart protection Study	(OR)	Registration of study design	**PS (+)**
	(I)	Prognostic effect of a family based secondary prevention program after ACS	
Alter DA et al.[220]	(C)	No comparison between CR and non CR	PS
Anderson LJ & Taylor RS [221]	(OR)	Review of meta-analyses	PS
Cobo Gomez N et al.[222]	(P)	No index events as defined by CROS	PS
Dunlay SM et al.[223]	(P)	Recruitment 1987–2010	PS + FTE + SSE
Otero Chulian E et al.[224]	(OR)	Conference abstract, to be followed	**PS (+)**
Expósito-Tirado JA et al.[225]	(C)	No control as defined by CROS	PS
Kamath DY et al.[226]	(OR)	Design paper, not to be followed	PS
	(I)	Intervention does not meet CROS Criteria	
Karmali KN et al.[227]	(OR)	Update of a Cochrane review	PS
Kim SS et al.[228]	(I)	No structured and supervised Exercise	PS + FTE
Kureshi F et al.[229]	(OR)	Conference abstract, Effect of CR on health status scores and mortality after AMI	**PS (+)**
Lewinter C et al.[230]	(I)	CR referral rather than CR Attendance; see also Lewinter C et al.2011 and 2012, [179,180]	PS + FTE + SSE
Lewinter C et al.[231]	(OR)	Conference abstract	PS
DANREHAB trial	(P)	Only heart failure patients without primary ACS	
Lubinskaya E et al.[232]	(OR)	Conference abstract, effect of CR on cost effectiveness including prognosis	**PS (+)**
Martin BJ et al.[233]	(P)	Overlap of population with earlier publications, see Martin BJ et al.2012 [13]	PS + FTE + SSE
Maddison R et al.[234] **CO**	(I)	Intervention does not meet CROS criteria	PS

REMOTE-CR	(C)	no controls as defined by CROS	
	(O)	no outcomes as defined by CROS	
Ramirez -Moreno A et al.[235]	(OR)	Conference abstract, not to be followed	PS
	(C)	no control group	
	(O)	RCT evaluating CR compliance rather than CR attendance.	
Santoalha JM et al.[236]	(OR)	conference abstract, to be followed	**PS (+)**
	(C)	control group represents patients with low CR adherence and completing <30% of scheduled CR program	
Sharma R et al.[237]	(OR)	Conference abstract	**PS (+)**
APPROACH registry	(P)	APPROACH registry 2002–2012	
2015			
ACTRN12615001247561[238]	(OR)	Registration of study design	**PS (+)**
Ammendrup FD et al.[239]	(C)	No control group without CR	**PS**
Armstrong MJ et al.[240]	(P)	Population Overlap of population compared to study of Martin et al.2012 (confirmed by author)	PS + FTE
Bubnova M et al.[241]	(OR)	Conference abstract	**PS (+)**
	(I)	Intervention might not follow CROS criteria of multi-component CR	
Chen HM et al.[242]	(I)	Only phase I cardiac rehabilitation	PS + FTE + SSE
Chew DP et al.[243]	(OR)	Design paper	PS
	(I)	Application of risk stratification tool, no multi-component CR	
Colbert JD et al.[244]	(P)	Population considerably overlaps with	PS + FTE
APPROACH and CWIC registry		Martin BJ et al.as confirmed by authors	
Cobo Gomez N et al.[245]	(OR)	Conference abstract	**PS (+)**
	(O)	Mortality and events after PCI in patients with incomplete re-vascularization	
Cobo Gomez N et al.[246]	(OR)	Conference abstract,	**PS (+)**
	(P)	Patients with ischemic cardiomyopathy and reduced LV-function	
Coll-Fernandez R. et al.[247]	(OR)	Conference abstract	PS
	(P)	Population with a large overlap to a previous study of the same group, Coll-Fernandez, R et al.2014[214]	
Deljanin Ilic M et al.[248]	(OR)	Conference abstract	PS
	(C)	No control group as defined by CROS	
Doll JA et al.[175]	(C)	No control group without CR	PS + FTE
ACTION Registry-GWTG			
Gencer B et al.[249]	(OR)	Conference abstract	PS
Swiss ELIPS program	(I)	Intervention does not meet CROS Criteria	
Goto Y et al.[250]	(OR)	Conference abstract	PS
Kadda O et al.[251]	(I)	No CR program as defined by CROS, predominantly life style instruction program	PS + FTE
Kim HJ et al.[252]	(P)	Patients after myocardial infarction with diabetes mellitus	PS
	(C)	Patients after myocardial infarction without diabetes mellitus	
	(O)	No prognostic outcomes as defined by CROS	
Kirchberger I et al.[253]	(I)	Case management intervention	PS
Klainman S et al.[254]	(OR)	Conference abstract	PS
Landry M et al.[255]	(C)	No control without CR	PS
	(O)	No prognostic outcome	
McPhee PG et al.[256]	(C)	No control group without CR	PS
	(O)	No prognostic outcome	
Medina-Inojosa JR et al.[257]	(I)	No comprehensive CR as defined by CROS	PS

	(C)	No control group without CR	
NCT02584192 [258]	(OR)	Trial registration	PS
	(O)	No prognostic outcomes as defined by CROS	
Nishitani-Yokoyan M et al.[259]	(O)	No prognostic outcomes as defined by CROS	PS
NTR5306[260]	(OR)	Trial registration, not to be followed	PS
	(C)	No control group	
Pouche M et al.[192]	(I)	Only evaluation of CR referral, but not CR attendance	PS + FTE
French FAST-MI registry		(confirmed by author)	
Romero Reyes MJ et al.[261]	(OR)	Conference abstract,	**PS (+)**
	(P)	Only elective PCI?	
Sanchez Martinez M et al.[262]	(OR)	Conference abstract	PS
	(O)	No prognostic outcomes	
Vataman EB et al.[263]	(OR)	Conference abstract	**PS (+)**
	(O)	Rehospitalization rate	
Wang W et al.[264]	(OR)	Conference abstract	PS
	(I)	home based self-management program, no structured supervised exercise	
	(O)	Risk parameters and unplanned use of health services	
2016			
Andion Ogando R et al.[265]	(OR)	Conference abstract	PS
Andjic M et al.[266]	(C)	No control group	PS
	(O)	No prognostic outcomes as defined by CROS	
Ding R et al.[267]	(OR)	Conference abstract	PS
Dong Z et al.[268]	(I)	Early rehabilitation (phase I)	
Fukui S et al.[269]	(P)	Patients with inoerable chronic thromboembolic pulmonary hypertension	
	(O)	No prognostic outcomes	
Gostoli S et al.[270]	(O)	No prognostic outcomes as defined by CROS	PS + FTE
Goto Y et al.[271]	(C)	No control group	PS
	(OR)	Group allocation by outcome	
Hassan AM et al.[272]	(O)	No prognostic outcomes as defined by CROS	PS
Hirsch K et al.[273]	(OR)	Protocol of a registry	PS
Højskov IE et al.[274]	(O)	No prognostic outcomes	PS
Hou WH et al.[275]	(I)	No information about CR details available	PS + FTE
Huber D et al.[276]	(I)	No CR as defined by CROS	PS
	(C)	No relevant control group	
	(O)	No prognostic outcomes	
Iles-Smith H et al.[277]	(C)	No control without CR	PS
	(O)	No prognostic outcomes	
	(OR)	Qualitative study design	
JPRN-UMIN000021393[278]	(O)	No prognostic outcome as defined by CROS	PS
	(OR)	Study registration	
Kikkenborg BS et al.[279]	(P)	Patients with first time ICD implantation	PS
	(O)	No prognostic outcomes as defined by CROS	
Kuo LY et al.[280]	(I)	Exercise-based CR without further components	PS
	(OR)	Dose-response relationship	
Kureshi F et al.[281]	(I)	No information about CR details available	PS + FTE
Loprinzi PD et al.[282]	(I)	No cardiac rehabilitation	PS
Mandic S et al.[283]	(P)	Patients with CAD, ACS excluded	PS + FTE
	(O)	No prognostic outcomes as defined by CROS	
Marcassa C et al.[284]	(C)	No control group as defined by CROS (CR cohort has been compared with general population including healthy persons)	PS + FTE
Nakayama A et al.[285]	(OR)	Conference abstract	PS
Nedkoff L et al.[286]	(I)	No cardiac rehabilitation	PS

	(C)	No control without CR	
	(OR)	Comparison survival in diabetic/non diabetic patients after AMi	
Panovsky R et al.[287]	(OR)	Conference abstract	PS
Philippe F et al.[288]	(I)	No cardiac rehabilitation	PS
Pope M et al.[289]	(OR)	Comparison between UK and other countries, no investigation of impact of a CR program	PS
Reibis R et al.[290]	(C)	No control without CR	PS
	(O)	No prognostic outcomes	
	(OR)	No follow up after CR	
Sabbag A et al.[291]	(OR)	Investigation of CR referral trends over time	PS
Sharma R et al.[292]	(P)	Patients with coronary angiogram showing CAD	PS + FTE
Silveira C et al.[293]	(OR)	Conference abstract	PS
Sjolin I et al.[294]	(OR)	Conference abstract	PS
Sunamura M et al.[295]	(OR)	Conference abstract	**PS (+)**
Taylor C et al.[296]	(I)	Exercise only	PS
	(C)	No control group without CR	
	(OR)	Investigation of association between cardiorespiratory fitness and mortality	
Van Halewijn G et al.[297]	(I)	Exercise rehabilitation	PS
	(OR)	Meta-analasys	
Varnfield M et al.[298]	(I)	Home-based CR program	PS
	(O)	No prognostic outcome	
Vibulchai N et al.[299]	(I)	Intervention without supervised exercise	PS
	(O)	No prognostic outcome	
Xavier D et al.[300]	(I)	Intervention without supervised exercise	PS
	(O)	No prognostic outcome	
Yuriy Dovgalyuk Y et al.[301]	(C)	No control group without CR	PS
2017			
Ades PA et al.[302]	(OR)	Initiative to increase uptake of CR and prevent cardiovascular events	PS
Almeida Morais L et al.[303]	(OR)	Conference abstract	**PS (+)**
Alrohaibani A et al.[304]	(OR)	Conference abstract	**PS (+)**
Alter DA et al.[305]	(P)	Mixed population including stable patients and heart failure, population overlap with Alter et al. 2009[6] (Apr 1-Dec 31, 2003),	PS + FTE
	(I)	CR session frequency only 1/week	
	(OR)	non fitting group design: 4 groups (non referred control, nonparticipants, low dose, high dose)	
Biery D et al.[306]	(OR)	Conference abstract	**PS (+)**
Bravo-EscobarR et al.[307]	(I)	Home-based mixed surveillance program	PS
	(C)	Exercise-based CR in hospital	
	(O)	No prognostic outcome	
Burazor I et al.[308]	(C)	No control group without CR	PS
Chernomordik FD et al.[309]	(OR)	Matched group comparison for CR referral, participation not verified, no information about CR uptake after 30 days after hospital discharge, start of CR not clear, group cross-over possible	PS + FTE
Claes J et al.[310]	(I)	Home-based CR	PS
	(C)	Center-based exercise program or usual care	
	(OR)	Systematic review	
CTRI/2017/03/008022[311]	(I)	Counseling on CR apects	PS
	(OR)	Trial registration	
Dabek J et al.[312]	(C)	No control group without CR	PS

	(O)	No prognostic outcome	
Dondo TB et al.[313]	(C)	No control group without CR	PS + FTE
	(OR)	No controlled cohort trial, investigation of CR enrollment as predictor of survival; no CR description or standardization	
Du L et al.[314]	(P)	Patients with stable coronary artery disease	PS
	(I)	No CR as defined by CROS	
	(OR)	Meta-analysis	
Ehrman JK et al.[315]	(P)	Patients with reduced ejection fraction	PS
Fors A et al.[316]	(I)	No CR as defined by CROS	PS
Frohmader TJ et al.[317]	(I)	Home-based CR	PS
	(C)	No control group without CR	
	(O)	No prognostic outcome	
Gabelhouse J et al.[318]	(I)	Hybrid CR with supervised/unsupervised exercise	PS
	(C)	Traditional CR	
	(O)	No prognostic outcome	
Harun MR et al.[319]	(P)	Patients with metabolic syndrome in CR	PS
	(C)	No control group without CR	
	(O)	No prognostic outcome	
Hoejskov I et al.[320]	(O)	No prognostic outcome	PS
Ishida T et al.[321]	(C)	No control group without CR	PS
	(O)	No prognostic outcome	
Jamal UJ[322]	(I)	Home-based CR	PS
	(O)	No prognostic outcome as defined by CROS	
	(OR)	Conference abstract	
Kachur S et al.[323]	(OR)	Review	PS
Khoury M et al.[324]	(OR)	Conference abstract, no comparision of CR vs no CR	PS
Klein J et al.[325]	(P)	stable CAD, elective PCI only, ACS excluded	PS
Kyuno E et al.[326]	(OR)	Conference abstract	**PS (+)**
Larsen TR et al.[327]	(OR)	Conference abstract	PS
Lee BJ et al.[328]	(O)	No prognostic outcome	PS
Lloyd-Jones DM et al.[329]	(OR)	Initiative to increase uptake of CR and prevent cardiovascular events; description of tool estimation of benefits of therapies	PS
Ma J et al.[330]	(OR)	Conference abstract	**PS (+)**
Marcos-Forniol E et al.[331]	(I)	No CR as defined by CROS	PS + FTE
Marta Braga M et al.[332]	(C)	No control group without CR	PS
	(O)	No prognostic outcome	
	(OR)	Comparison of obese/non obese patients	
Minneboo M et al.[333]	(O)	No prognostic outcome	PS
Pardaens S et al.[334]	(OR)	Investigation of impact of drop-out of CR on event-free survival	PS
Peurois J et al.[335]	(OR)	Conference abstract	PS
Pieters K et al.[336]	(O)	No prognostic outcome as defined by CROS	PS
Prince SA et al.[337]	(C)	No control group without CR	PS
Puymirat E et al.[338]	(OR)	No controlled cohort study of effects of CR	PS
Taylor C et al.[339]	(I)	Exercise only	PS
	(C)	No control group without CR	
	(OR)	Investigation of the effect of exercise dose	
Zhao M et al.[340]	(OR)	Investigation of cardioprotective medication use	PS
Zullo MD et al.[341]	(OR)	Investigation of the association between depression and CR participation	PS
2018			
Bertelsen JB et al.[342]	(I)	No comprehensive rehabilitation as specified by CROS	PS

	(O)	No prognostic outcomes as defined by CROS	
Cao R et al.[343]	(O)	No prognostic outcomes as defined by CROS	PS
	(OR)	Only abstract	
Colantonio LD et al.[344]	(O)	No prognostic outcomes as defined by CROS	PS
	(OR)	Study design, abstract only	
Cordero A et al.[345]	(I)	No comprehensive rehabilitation as specified by CROS	PS + FTE
Dorje T et al.[346]	(OR)	Study protocol	PS
Flint K et al.[347]	(I)	Patient reported record of CR participation with no detail about timing from discharge to start, duration or structure of CR	PS + FTE
Ghisi GLM et al.[348]	(OR)	Letter to the editors	PS
Krstacic G et al.[349]	(OR)	Conference abstract	**PS (+)**
Kruchinova SV et al.[350]	(OR)	Conference abstract	**PS (+)**
Li S et al.[351]	(OR)	Study investigates referral only	PS + FTE
Long L et al.[352]	(OR)	Systematic review	PS
Maessen M et al.[353]	(OR)	Conference abstract	**PS (+)**
Moore N et al.[354]	(OR)	Conference abstract	**PS (+)**
Nilsson BB et al.[355]	(O)	No prognostic outcomes as defined by CROS	PS
Toshie Tanaka T et al.[356]	(OR)	Conference abstract	**PS (+)**

Table SM 5: Study evaluation: Newcastle – Ottawa Scale (NOS)

Study	Basic design	Selection of the participants					Comparability of the cohorts	outcomes				Sum of positive adjudications (+)
			Representativeness of exposed cohort *	Selection of control	Ascertainment of exposure	Outcome not present at start of study †	Controls for most important factors, Inter-vention and controls are taken from the same cohort		Assessment of outcomes	Follow-up long enough?	Adequacy of follow-up	
Boulay P et al.[1]	rCCS		+	0	+	0	**0**		0	+	0	**3**
Norris CM et al.[2]	rCCS		+	+	+	0	**+**		+	+	+	**8**
Kutner NG et al.[3]	rCCS		0	+	+	0	**+**		+	+	+	**7**
Milani RV et al.[4]	rCCS		0	+	+	0	**+**		+	+	0	**6**
Nielsen KM et al.[5]	rCCS		+	+	+	0	**+**		+	+	+	**8**
Alter DA et al.[6]	rCCS		+	+	+	0	**+**		+	+	+	**8**
Hansen D et al.[7]	pCCS		+	0	+	+	**0**		+	+	+	**6**
Suaya JA et al.[8]	rCCS		+	+	+	0	**+**		+	+	+	**7**
Jünger J et al.[9]	rCCS		+	+	+	0	**+**		+	+	+	**7**
Goel K et al.[10]	rCCS		+	+	+	0	**+**		+	+	+	**7**
Kim C et al.[11]	pCCS		0	+	0	+	**+**		0	+	+	**4**
Schwaab B et al.[12]	rCCS		0	+	+	0	**+**		+	+	+	**6**
Martin BJ et al.[13]	pCCS		+	+	+	+	**+**		+	+	0	**7**
Beauchamp A et al.[15]	rCCS		+	+	+	0	**+**		+	+	+	**7**
Lee HY et al.[16]	pCCS		+	+	+	+	**+**		+	+	+	**8**
Marzolini S et al.[17]	pCCS		+	+	+	+	**+**		+	+	+	**8**
Pack QR et al.[18]	rCCS		+	+	+	0	**+**		+	+	+	**7**
Coll-Fernandez R et al.[19]	pCCS		+	+	+	+	**+**		+	+	+	**8**
Prince DZ et al.[20]	rCCS		+	+	+	0	**0**		+	+	+	**6**
Rauch B et al.[21]	pCCS		+	+	+	+	**+**		+	+	+	**8**
Goel K et al.[22]	rCCS		+	+	+	0	**+**		+	+	+	**7**
De Vries H et al.[23]	rCCS		+	+	+	0	**+**		+	+	+	**7**
Meurs M et al.[24]	rCCS		0	+	+	0	**+**		+	+	0	**5**
Schlitt A et al.[25]	rCCS		0	+	0	0	**+**		+	+	0	**4**
Lee JY et al.[27]	pCCS		+	+	+	+	**+**		+	+	0	**7**
Espinosa Caliani S et al.[26]	pCCS		+	+	+	+	**0**		+	+	0	**6**
Doimo S et al.[30]	rCCS		+	0	+	0	**+**		+	+	0	**5**
Sunamura M et al.[31]	rCCS		+	0	+	+	**+**		+	+	+	**7**

*representativeness was regarded to be limited if the population was recruited form pre-existing studies with differing goals. † retrospective studies were adjudicated with "O"

Table SM 6: Sensitivity analyses for all-cause mortality analyses

Population	Design	Reason for sensitivity analysis	HR (95% CI)	OR (95% CI) pooling method	Statistical heterogeneity: I-squared tau-squared p-value
ACS	rCCS	Meurs M et al.2015: data of independent groups used [24]	0.59 (0.48-0.73)		25.2%; 0.012; p=0.26
ACS	rCCS	Nielsen KM et al.2008: rates for 1-year mortality used [5]		0.25 (0.15-0.40) MH *	17.1%; 0.052; p=0.27
CABG	rCCS	De Vries H et al.2015: data of independent groups used [23]	0.62 (0.54-0.71)		0.0%; 0.0; p=0.43
CABG	rCCS	Goel K et al.2013: data of independent groups used [18]	0.60 (0.52-0.68)		10.0%; 0.002; p=0.34
MIXED	rCCS	Goel K et al.2011: data of propensity score stratification used [10]	0.52 (0.36-0.76)		84.8%; 0.14; p<0.01
MIXED	rCCS	Schlitt A et al.2015: data of independent groups used [25]	0.45 (0.27-0.77)		92.8%; 0.331 p<0.0001
MIXED	rCCS	Norris CM et al, 2004: rates for matched groups used[2]		0. 70 (0.37-1.32) MH	91.6%; 0.3241; p<0.01
MIXED	pCCS	Martin BJ et al.2012: data of independent groups used [13]	0.59 (0.50-0.70)		0.0%; 0.0; p=0.75

* MH, Mantel-Haenszel method used for pooling

Table SM 7: Checklist according to MOOSE and PRISMA statements

MOOSE statement[357]		**PRISMA statement[358]**	
Section, topic	**Described in manuscript: yes/no; comments**	**Section, topic**	**Described in manuscript: yes/no; comments**
		Title	Yes
		Structured summary	Yes
Reporting of Background		**Introduction**	
Problem definition	Yes, Introduction	Rational	Yes
Hypothesis	Yes, Introduction	Objectives	Yes
Description of study outcomes	Yes, Methods, Table SM1		
Type of intervention	Yes, Methods, Table SM1		
Type of study designs	Yes, Methods, Table SM1		
Study population	Yes, Methods, Table SM1		
Reporting of Search Strategy			
Qualification of searchers	Yes, Methods		
Search strategy, time period	Yes, Methods, Supplemental Material Table SM 2		
Effort to include all available studies	Yes, Methods, Figure 1, Table 1, Supplemental Material Table SM 3a		
Data bases searched	Yes, Summary, Methods, Supplemental Material, Table SM 2		
Search software used	Yes, Methods		
Use of hand-searching	Yes, routinely done in reference lists of selected studies		
List of citations located and excluded	Yes, Table 1 and Supplemental Material, Table SM 2, SM 3a		
Methods of handling abstracts and unpublished studies	Yes, Supplemental Material, Table SM4		
Description of contact to authors	Yes, Table 1, Supplemental Material Table SM 3a		
Reporting of Methods		**Reporting of Methods**	
Appropriateness of studies assessed	Yes, Table 1	Protocol and registration	Yes; PROSPERO CRD42014007084
Rational for selection and coding od data	Yes, Methods	Eligibility criteria, PICOS	Yes, Methods, Table 1
Documentation of how data were classified and coded	Yes, Methods, Figure 1	Information sources	Yes; Methods, Supplemental Material Table SM 2
Assessment of confounding	Yes, Methods, Tables 3a, 3b, Supplemental Material Table SM4	Search	Electronic search strategy described in Methods, Supplemental Material, Table SM2
Assessment of study quality	Yes, Methods, Tables 3a, 3b, SM5	Study selection	Yes; Methods, Fig. 1; Supplemental Material. Tables SM2, SM4

Assessment of heterogeneity	Yes, Methods, Figure 2, Table 2	Data collection process	Yes; Methods
Description of statistical methods	Yes, Methods	Data items	Yes, Methods, Table SM 1 (predefined PICOs)
Appropriate Figures and Tables	Yes	Risk of bias in individual studies	Yes; Methods, Tables 3a, 3b; Supplemental Material, Table SM 5
		Summary measures	Yes, Methods; Results
		Synthesis of results	Yes, Methods
		Risk of bias across the studies	Yes, Methods
		Additional analyses	Yes, sensitivity analyses, Supplemental Material, Table SM 5
Reporting of Results		**Reporting of Results**	
		Study selection	Yes, Results, Figure 1
Giving descriptive information for each study included	Yes, Table 1, Supplemental Material Table SM 3a	Study characteristics	Yes, Table
		Results of individual studies	Yes, Table SM 1
		Risk of bias within the studies	Yes, Tables 3a,b; Suppl. Material, Table SM 5
Graphics and tables summarizing results	Yes, Figure 2, Table 2	Synthesis	Yes, Figure 2, Table 2
Indication of statistical uncertainty	Yes, Figure 2, Table 2	Risk of bias across studies	Addressed, see “statistical analysis” in Methods
Results of sensitivity testing	Yes, Results, Supplemental Material, Table SM 6	Additional analyses	Yes, sensitivity analysis, Supplemental Material Table SM 6
Reporting of Discussion		**Reporting of Discussion**	
Quantitative assessment of bias	Yes	Summary of evidence	Yes
Justification of exclusion	Yes	Limitations	Not explicitly, adressed in discussion.
Assessment of quality	Yes		
Reporting of Conclusions			
Consideration of alternative explanations	Yes	Conclusions	Yes
Generalization of the conclusions	Yes	General interpretation and implications	Yes
Guidelines for future research	Yes		
Disclosure of funding source	Yes	**Funding**	Yes

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