SUPPLEMENTARY DOCUMENTS

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Supplemental Appendix 1. Members of guidelines' panels

Members of the Primary Panel:

Co-chairs – Drs. P.J. Devereaux, Joel Parlow

Members – Drs. Amal Bessissow, Gregory Bryson, Emmanuelle Duceppe, Michelle Graham, Kristin Lyons, Paul MacDonald, Michael McMullen, Daniel I. Sessler, Sadeesh Srinathan, Kim Styles, Vikas Tandon

Members of the Secondary Panel:

Drs. Rebecca Auer, Mohit Bhandari, Davy Cheng, Peter Choi, Benjamin Chow, Gilles Dagenais, Josée Fafard, Gordon Guyatt, John Harlock, David Hornstein, Michael Jacka, Andrea Kurz, Luc Lanthier, Yannick LeManach, Finlay McAlister, Edward McFalls, Michael McGillion, Marko Mrkobrada, Ameen Patel, Tej Sheth, Maria Tiboni, Duminda Wijeysundera

Supplemental Table 1: Panel members GRADE of recommendation rating and conflicts of interest*

		Bessissow, A	Bryson, G	Devereaux, PJ	Duceppe, E	Graham, M	Lyons, K	MacDonald, P	McMullen, M	Parlow, J	Sessler, D	Srinathan, S	Styles, K	Tandon, V
Preoperative risk prediction	1.Emergency surgery	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP
	2.Urgent/Semi-urgent surgery	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP
	3.Elective surgery	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP
	4.Risk communication	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP	1 VP
	5.Qualitative risk communication	1B	1B	COI	1B	1B	1C	1B	1B	1B	1B	1B	1B	1B
	6.Quantitative risk communication	1B	1B	COI	1B	1C	1C	2C	1C	1C	1B	1B	1B	1B
	7.Clinical risk indices	2C	2C	2C	2C	2C	2C	2C	2C	2C	2C	2C	2C	2C
	8.NT-proBNP/BNP	1B	1B	COI	COI	1B	1B	1B	1B	1B	COI	COI	1B	1B
	9.Resting echocardiography	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C

	10.Coronary CT angiogram	1B	1B	COI	1B	1B	1B	1B	1B	1B	1B	1A	1B	COI
	11.Exercise testing	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C
	12.Cardio-pulmonary exercise testing	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C
	13.Stress echocardiography	2C	1C	1C	2B	1C	1C	1C	1C	1C	1B	1C	1C	1C
	14.Nuclear stress imaging	1C	1B	1B	2B	1B	1B	1B	1B	1B	1B	1B	1B	1B
Preoperative risk modification	15.ASA initiation	1A	1A	COI	1A	COI	1A	COI	1A	COI	COI	COI	1A	1A
	16.ASA continuation	1A	1A	COI	1A	COI	1A	COI	1A	COI	COI	COI	1A	1A
	17.β-blocker initiation	1A	COI	COI	1A	1A	1A	COI	1A	COI	1A	1A	1A	1A
	18.β-blocker continuation	2C	COI	COI	2C	2C	2C	2C	2B	2B	2C	2C	2C	2C
	19.α-2 agonist initiation	1A	1A	COI	1A	COI	1A	COI	1A	COI	COI	COI	1A	1A
	20.CCB initiation	2C	2C	2C	2C	2C	2C	2C	2C	2C	2C	2C	2C	2C

	21.ACEI/ARB continuation	1C	1C	1C	1C	1C	2C	1C	1C	1C	1C	1C	1C	1C
	22.Statin continuation	1B	COI	COI	1B	1B	1B	1B	1B	1B	1B	1B	1B	1B
	23.Coronary revascularisation	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C	1C
	24.Smoking cessation	1C	1C	1C	IE	IE	IE	1C	1C	1C	1C	1C	1C	1C
Postoperative monitoring	25.Troponin	COI	1B	COI	COI	COI	1B	1B	1B	1B	COI	COI	1B	COI
	26.ECG	2C	2C	2C	2C	2C	2C	2C	1C	2C	2C	2C	2C	2C
	27.Telemetry	COI	IE	COI	IE	IE	IE	IE	IE	IE	COI	IE	IE	IE
	28.Pulmonary artery catheter	1B	1B	1B	1B	1B	1B	1B	1B	1B	1B	1B	1B	1B
	29.Shared-care models	2C	2B	2B	2B	2C	2C	2B	2C	2C	2C	2C	2C	2B
Management of postoperative events	30.ASA	1B	1B	COI	1B	1B	1B	1B	1B	1B	1B	1B	1B	1B
	31.Statin	1B	1B	COI	1B	1B	1B	1B	1B	1B	1B	1B	1B	1B

*No member had a financial conflict of interest. All conflicts of interest were intellectual conflicts. Members in conflict of interest participated in the discussion but recused themselves from the vote. No external or industry funding was received for the development of these guidelines. Internal funding was used for the face-to-face meeting.

All members voted in the same direction for all recommendation (i.e., either “for” or “against”).

1 = strong recommendation, 2 = conditional recommendation, A = high-quality evidence, B = moderate-quality evidence, C = low/very low-quality of evidence. ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blockers, ASA = acetylsalicylic acid, BNP = brain natriuretic peptide, CCB = calcium channel blocker, COI = conflict of interest, CT = computed tomography, ECG = electrocardiogram, IE = panel member felt there was insufficient evidence to support a GRADE recommendation, NT-proBNP = N-terminal pro-brain natriuretic peptide, VP = recommendation based on values and preferences.

Supplemental Table 2: Grading strength of recommendation and quality of evidence rating

Grade of Recommendation*	Benefit vs Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or *vice versa*	Evidence for at least one critical outcome from observational studies, case series, or from RCTS with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence from observational studies	Best action may differ depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate

Weak recommendation, low/very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTS with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

* We use the wording *we recommend* for strong recommendations (Grade 1) and *we suggest* for weak recommendations (Grade 2).
This table was re-produced with approval from CHEST. Also, we have substituted the word "conditional" for "weak" in relation to our recommendations.

Supplemental Table 3: Summary of findings for communicating perioperative cardiac risk

Author year	Type of study	Population	Study characteristics	Results	Comments
QUALITATIVE RISK COMMUNICATION					
Taher[1] 2002	cross-sectional survey	104 members of the Canadian Society of Internal Medicine who routinely performed preoperative risk assessments	mailed survey with questions on risk communication, interventions used to reduce risk, and routine use of cardiac risk indices questionnaire validation: questionnaire pilot tested with 5 internists	**Risk communication to patient** 96% communicated their preoperative cardiac risk assessment to their patients 77% only communicated risk subjectively (i.e., low, moderate, high risk) **Definition of risk category** when asked to provide estimate of risk respondents provided: 8 different definitions of low risk (range <1% to <20%) 27 different definitions of moderate risk (range 1-2% to 20-50%) 12 different definitions of high risk (range >5% to >50%)	response rate 38% respondents compared to non-respondents were more likely to have an academic position (69% vs 53%; p<0.001) and be in group practice (67% vs 41%, p<0.001)
Man-Son-Hing 2002[2]	RCT	198 volunteers aged 60–80 years	participants asked to imagine having atrial fibrillation randomized to decision aid on probability of stroke and major bleeding when taking warfarin, aspirin, or no therapy: (1) quantitatively (numerically and graphically) or (2) qualitatively (e.g. very low, moderate, high).	**Decisional conflict scale** participants reviewing quantitative risk information scored better on the informed subscale of the decisional conflict scale (P < 0.05) participants using the quantitative decision aids felt more informed than those using the qualitative decision aid	the decisional conflict scale measured participants' uncertainty about which therapy to choose, modifiable factors contributing to uncertainty (such as feeling informed, clear about values and supported in decision-making), and perceived

					effective decision-making
Marteau 2000[3]	RCT	209 pregnant women with low risk results following a serum screening test for Down syndrome	letter sent to inform about the result using either numerical (i.e., chance of having a baby with Down syndrome is: 1 in XXX) or qualitative probabilities (i.e., chance of having a baby with Down syndrome is: low)	**Understanding of the results** Numerical : 97% (94/ 97) understood result Qualitative: 91% (102/112) understood result 6% absolute difference (95% CI, 0% - 12%) p=0.04	
QUANTITATIVE RISK COMMUNICATION					
Trevena 2006[2]	systematic review on communicating with patients about evidence	patients making healthcare decisions (included surgical and nonsurgical settings)	high quality RCTs and systematic reviews of RCTs addressing one of following research questions: 1) What are the most effective communication tools to improve patient understanding of 'evidence'? 2) What are the most effective formats to represent probabilistic information to improve patient understanding of 'evidence'? 3) What are the most effective strategies to elicit patient preferences/beliefs/values relating to 'evidence'?	**Effective tools for communicating with patients about evidence** (10 systematic reviews and additional 17 trials) - using most available communication tools is better than no communication tool for increasing knowledge about health care - more likely to increase understanding if structured, tailored and/or interactive tool **Effective formats for communicating probabilistic information** (15 RCTs) - patients have more accurate perception of risk if probabilistic information presented as numbers like event rates (natural frequencies), rather than words, probabilities or summarized as effect measures such as relative risk reduction - illustrations such as cartoons, or graphs (vertical bar charts) appear to aid understanding **Effective strategies for eliciting patient preferences** (1 systematic review and 3 RCTs) - decision aids and decision analysis appear to be effective tools for eliciting preferences	total of 10 systematic reviews and additional 30 RCTS addressing at least one of the research questions

CI = confidence interval, RCT = randomized controlled trial.

Supplemental Table 4: GRADE quality assessment for communicating perioperative cardiac risk

Quality Assessment						Summary of Evidence	
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled Estimate**	**Quality of evidence**
QUALITATIVE RISK COMMUNICATION							
104 (1 study)[1]	Serious limitation[(1)]	No serious limitation	No serious limitation	No serious limitation	Potential[(2)]	N/A	Low
QUANTITATIVE RISK COMMUNICATION							
10 systematic reviews and 30 RCTs[2]	No serious limitation	No serious limitation	Serious limitation[(3)]	No serious limitation	No serious limitation	N/A	Moderate

N/A = not applicable

1. Low response rate, at risk of selection bias
2. Only one study found on the topic
3. Evidence included studies from surgical and non-surgical settings.

Supplemental Table 5: Summary of findings for clinical risk indices

Author	Population	Total No. patients	Design	Length of follow-up after surgery	Predictors	Systematic outcome monitoring	Outcome Results	Comments
REVISED CARDIAC RISK INDEX (RCRI)								
Ford 2010[4]	noncardiac surgery	792,740	meta-analysis that included 24 studies, up to 2008	majority followed for a maximum of 30 days	prognostic capabilities of the individual components of the RCRI were not evaluated in the meta-analysis	12 of 24 studies used systematic surveillance for cardiac complications	**Major cardiac complications** **Noncardiac surgery** 18 studies (124,032 patients) Median AUC 0.69 (IQR 0.62-0.75), I^2=82% type of surgery was the only study variable found to explain heterogeneity in meta-regression **Nonvascular mixed surgery** 10 studies (9743 patients) Pooled AUC 0.75 (CI, 0.72–0.79), I^2=48% **Vascular surgery** 7 studies (5696 patients) Pooled AUC 0.64 (CI, 0.61-0.68), I^2=29%	studies from Poldermans' group were included in the meta-analysis but provided similar results to the other studies
Rao 2012[5]	patients referred to cardiology aged ≥40 years undergoing many different types of	853	prospective cohort study	not reported	**Insulin therapy** aOR 1.07 (95% CI, 0.44-2.57) **CAD** aOR 4.98 (95% CI, 2.04-12.16) **CHF** aOR 1.09 (95% CI, 0.13-9.52)	troponin was measured in intermediate and high-risk patients, and in others if symptomatic	**Major cardiovascular events**: Events/Total: 26/853 (3%) RCRI: AUC 0.65 **RCRI score** OR (95% CI) (No. events/total) 1 : OR 1.00 (5/304) 2 : OR 1.22 (0.38–3.88) (7/347) 3 : OR 4.23 (1.42–12.60) (10/150)	major CV events**:** ACS, pulmonary edema, cardiac death; possible selection bias

	noncardiac surgery				**CKD** aOR 1.26 (95% CI, 0.39-4.11)		4 : OR 4.93 (1.28–19.02) (4/52)	
Andersson 2015[6]	many different types of noncardiac surgery	447,352	retrospective register-based study	30 days	**Individual RCRI components:** **high-risk surgery** aOR 2.70 (95% CI, 2.46–2.96) **CAD** aOR 3.30 (95% CI, 2.96–3.69) **CHF** aOR 2.65 (95% CI, 2.29–3.06) **CVD** aOR 10.02 (95% CI, 9.08–11.05) **insulin** aOR 1.62 (95% CI, 1.37–1.93) **CKD** aOR 1.45 (95% CI, 1.33–1.59)	no	**Major cardiovascular events**: Events/Total: 2275/447,352 (0.51%) RCRI: AUC 0.76	major CV events: nonfatal MI, nonfatal ischemic stroke, or CV death (ICD-10 codes)
Park 2011[7]	consecutive patients with cardiac consult and echo-cardiography before elective noncardiac surgery	1923	prospective cohort study	30 days	prognostic capabilities of the individual components of the RCRI were not evaluated in the this study	troponin was measured at the end of the surgical day and 24 hours later	**Major cardiovascular events**: Events/Total: 280/1923 (14.6%) RCRI: AUC 0.62 (95% CI, 0.60-0.64) Other variables in the multivariable model: age, sex, functional status ≥3, diabetes, heart failure, stroke, evidence of ischemic heart disease or history of revascularization, emergency surgery, and vascular surgery	major CV events: MI, pulmonary edema, or primary CV death

Gupta 2011[8]	various types of noncardiac surgery	257,385	retrospective NSQIP study	30 days	**high-risk surgery** aOR 2.01 (95% CI, 1.81-2.23) **CHF** aOR 3.26 (95% CI, 2.67-3.98) **CAD** aOR 3.02 (95% CI, 2.51-3.64) **CVD** aOR 1.92 (95% CI, 1.67-2.20) **insulin** aOR 1.27 (95% CI, 1.10-1.46) **CKD** aOR 4.86 (95% CI, 4.31-5.49)	no	**MI or cardiac arrest:** Events/Total: 1401/257,385 (0.54%) RCRI: AUC 0.75	MI definition: 1) ST elevation, new LBBB, or new Q waves or 2) troponin elevation >3x ULN
Choi 2010[9]	consecutive patients undergoing major noncardiac surgery who were referred for cardiac consult and ≥1 CV risk factor or abnormal ECG	2304	prospective cohort study	30 days	RCRI >2 was associated with increased risk of major CV event after adjustment for age, sex, and traditional clinical risk factors (aRR 1.50 (95% CI, 1.17-1.91)	troponin was measured at the end of the surgical day and 24 hours later	**Major CV events** RCRI >2: AUC 0.59	major CV event: MI, pulmonary edema, or CV death
Davis 2013[10]	noncardiac surgery, age ≥50 years,	9519	administrative database	not reported	prognostic capabilities of the individual	no	**Major CV events:** Events/Total: 200/9519 (2.1%)	Major CV events: MI, pulmonary

	screened in preoperative clinic, length of stay ≥2 days				components of the RCRI were not evaluated in the this study		RCRI : AUC 0.79 (95% CI, 0.76-0.83)	edema, or primary cardiac arrest
NSQIP MICA								
Gupta 2011[8]	various types of noncardiac and cardiac surgery*	211,410 patients (derivation) 257,385 patients (validation)	retrospective NSQIP study	30 days	ASA class, dependent functional status, increasing age, abnormal creatinine (>1.5 mg/dL), and type of surgery were independent predictors of death or MI	no	**MI or death** **Derivation cohort**: Events/Total: 1371/211,410 (0.65%) C-statistic 0.88 **Validation cohor**t: Events/Total: 1401/257,385 (0.54%) C-statistic 0.87 **Vascular surgery only** (n=26,183) C-statistic 0.75 Other variables in the multivariable model: ASA class, dependent functional status, increasing age, abnormal creatinine (>1.5 mg/dL), and type of surgery (20 categories of surgery)	MI definition: 1) ST elevation, new LBBB, or new Q waves or 2) troponin elevation >3x ULN * 0.3% cardiac surgery
ACS NSQIP								
Bilimoria 2013[11]	various types of noncardiac and cardiac surgery	1,414,006	retrospective NSQIP study	unclear	N/R	no	**Mortality** Events: 18,909 (1.3%) C-statistic: 0.94 **Cardiac events** Events: 10,676 (0.8%)	cardiac event: cardiac arrest or MI

							C-statistic: 0.89	

aOR = adjusted odds ratio, ACS = acute coronary syndrome, ASA = American Society of Anesthesiologists, AUC = area under the receiver operator curve, CAD = coronary artery disease, CVD = cerebrovascular disease, CKD = chronic kidney disease, CI = confidence interval, CHF = congestive heart failure, CRP = C-reactive protein, CV = cardiovascular, ICD = international code of diseases, LBBB = left bundle branch block, LR = likelihood ratio, MACE = major adverse cardiac events, MI = myocardial infarction, MINS = myocardial injury after noncardiac surgery, N/R = not reported, NSQIP = National Surgical Quality Improvement Program, NT-proBNP = N-terminal pro-brain natriuretic peptide, RCRI = Revised Cardiac Risk Index, ULN = upper limit of normal.

Supplemental Table 6. GRADE quality assessment for clinical risk indices

Quality Assessment						Summary of Evidence	
No. of participants (No. of studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**AUC**	**Quality of evidence**
REVISED CARDIAC RISK INDEX							
MAJOR CARDIOVASCULAR COMPLICATIONS							
3176 (5 studies)[12-16]	Serious limitation[(1)]	Serious limitation[(2)]	No serious limitation	No serious limitation	Not detected	Median AUC 0.69 (IQR 0.62-0.75)	Low
NSQIP MICA							
MI AND CARDIAC ARREST							
468,795 (1 study)[8]	Very serious limitation[(3)]	No serious limitation	No serious limitation	No serious limitation	Not detected	AUC 0.88	Low
ACS NSQIP							
MI AND CARDIAC ARREST							
1,414,006 (1 study)[11]	Very serious limitation[(3)]	No serious limitation	No serious limitation	No serious limitation	Not detected	AUC 0.90	Low

AUC = area under the receiver operator curve, CI = confidence interval, IQR = interquartile range, MI = myocardial infarction, MICA = myocardial infarction or cardiac arrest, NSQIP = National Surgical Quality Improvement Program.

1. Only a minority of studies were high-quality studies (i.e., prospective design, low risk of selection bias, systematic outcome assessment and blinded outcome adjudication).
2. I^2=82% in meta-analysis by Ford et al.

3. Risk of bias since not prospective design, no systematic monitoring of outcomes in all patients and no blinded adjudication of event. Further, has not been validated since the original publication. Includes ASA class which high potential for inter-rater variability.

Supplemental Table 7. The risk of myocardial infarction, cardiac arrest, or death according to the RCRI score in high-quality external validation studies*

Author	Design	Risk outcome detection bias	Type surgery	Primary outcome	RCRI 0 point		RCRI 1 point		RCRI 2 points		RCRI ≥3 points	
					No. events	No. patients	No. events	No. patients	No. events	No. patients	No. events	No. patients
Rajagopalan 2008[13]	Prospective	No	Vascular	MI	3	42	14	61	9	28	2	5
Ausset 2008[14]	Prospective	No	Orthopedic	MI	6	60	2	15	2	11	1	2
Devereaux 2011[15]	Prospective	No	Mixed	CV death, nonfatal MI, nonfatal cardiac arrest	10	452	23	291	4	76	16	44
Sheth 2015[16]	Prospective	No	Mixed	Death, MI	15	320	29	407	19	178	11	50
Le Manach 2005[12]	Retrospective	No	AAA	MI	0	0	14	607	34	380	7	146
Major cardiac events			**TOTAL**		**34**	**874**	**83**	**1382**	**68**	**673**	**37**	**247**
			Pooled Event Rate (95% CI)		**3.9% (2.8%-5.4%)**		**6.0% (4.9%-7.4%)**		**10.1% (8.1%-12.6%)**		**15.0% (11.1%-20.0%)**	

AAA = aortic abdominal aneurysm, CI = confidence interval, CV = cardiovascular, MI = myocardial infarction, RCRI = Revised Cardiac Risk Index.

*Studies included if: performed systematic outcome monitoring (i.e. troponin monitoring), reported on cardiac events (i.e., MI, cardiac arrest and/or death), and reported number of patients and cardiac events for each RCRI score.

Supplemental Table 8. Summary of findings for preoperative NT-proBNP/BNP

Author	No. patients (No. studies)	Design (type surgery)	Type of Natriuretic Peptide	Results	Comments
COMPOSITE DEATH AND NON-FATAL MYOCARDIAL INFARCTION					
Rodseth 2014[17]	2179 patients (18 studies)	individual patient data meta-analysis (4 studies mixed or major general surgery, 3 orthopedic, 3 thoracic, 2 urologic, 6 vascular)	NT-proBNP (10 studies) BNP (8 studies)	**Death or nonfatal MI at 30 days**: Overall incidence 10.8% (235/2179) **No. events/Total** Positive NT-proBNP/BNP*: 166/763 (21.8%) Negative NT-proBNP/BNP*: 69/1416 (4.9%) aOR 3.40 (95% CI, 2.57-4.47) p< 0.001 Other variables in the model: RCRI, urgent/ emergent surgery Assuming a baseline risk of death or nonfatal MI of 7.7%, the overall absolute net reclassification in a sample of 1,000 patients is that a preoperative natriuretic peptide measurement will result in a more appropriate risk estimate in 155 patients (based on risk categories of <5%, 5-10%, >10-15%, and >15%) compared to a clinical model	*Positive NT-proBNP ≥300 ng/L *Positive BNP ≥92 mg/l NP threshold value associated with lowest p value for death and MI for BNP was 92 mg/l and for NTproBNP was 300 ng/l
MYOCARDIAL INFARCTION					
Rodseth 2011[18]	850 patients (6 studies)	individual patient data meta-analysis (vascular surgery)	NT-proBNP (1 study, n=218 patients) BNP (5 studies, n=632 patients)	**Nonfatal MI at 30 days**: ORs for NP higher than the threshold: aOR 7.5 (95% CI, 4.1-13.6)* no measure of heterogeneity reported	General optimal test threshold: BNP =116 pg/ml and NT-proBNP= 277.5 pg/ml

CARDIAC MORTALITY					
Rodseth 2011[18]	850 patients (6 studies)	see above	see above	**Cardiac death at 30 days**: ORs for NP higher than the threshold: aOR 4.3 (95% CI, 1.7-11.3) no measure of heterogeneity reported	General optimal test threshold: BNP =116 pg/ml and NT-proBNP= 277.5 pg/ml
Ryding 2009[19]	4856 patients (15 studies)	meta-analysis (7 studies mixed noncardiac surgery, 1 orthopedic, 7 vascular)	NT-proBNP (6 studies) BNP (9 studies)	**Cardiac mortality:** **No. events/Total** Positive NT-proBNP/BNP*: 45/482 (9.3%) Negative NT-proBNP/BNP*: 3/1905 (0.2%) OR 23.88 (95% CI, 9.43-60.43) I^2=0%	*positivity threshold varied across studies cardiac death required evidence of MI, cardiac arrhythmia, or congestive cardiac failure
ALL-CAUSE MORTALITY					
Rodseth 2011[18]	850 patients (6 studies)	see above	see above	**All-cause mortality at 30 days**: aOR for NT-proBNP/BNP higher than the threshold: aOR 3.1 (95% CI, 1.4-6.7)*	*no measure of heterogeneity reported General optimal test threshold: BNP =116 pg/ml and NT-proBNP= 277.5 pg/ml
Ryding 2009[19]	4856 patients (15 studies)	see above	see above	**Short-term all-cause mortality:** **No. events/Total** Positive NT-proBNP/BNP*: 22/216 (10.2%) Negative NT-proBNP/BNP*: 4/484 (0.8%) OR 7.81 (95% CI, 2.83-21.58) I^2=0%	short term = within 48 days *positivity threshold varied across studies

aOR = adjusted odds ratio, BNP = brain natriuretic peptide, CI = confidence interval, MI = myocardial infarction, NP = natriuretic peptide, NT-proBNP = N-terminal pro-brain natriuretic peptide, OR = odds ratio, RCRI = Revised Cardiac Risk Index

Supplemental Table 9. GRADE quality assessment for preoperative NT-proBNP/BNP

Quality Assessment						Summary of evidence			
No of patients (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated incidence with positive NT-proBNP or BNP result (95% CI)**	**Anticipated incidence with negative NT-proBNP or BNP result (95% CI)**	**Pooled Estimate (95% CI)**	**Quality of evidence**
RODSETH 2014[17]									
COMPOSITE OF DEATH AND MYOCARDIAL INFARCTION at 30 days									
2179 patients (18 studies)	No serious limitation	No serious limitation	No serious limitation	No serious limitation	Potential limitation(1)	21.8% (19.0%-24.8%)	4.9% (3.9%-6.1%)	aOR 3.40 (2.57-4.47)	Moderate
RODSETH 2011[18]									
ALL-CAUSE MORTALITY									
850 patients (6 studies)	No serious limitation	Undetermined	No serious limitation	Serious limitation(2)	Potential limitation(3)	N/A	N/A	aOR 3.1 (1.4-6.7)	Low
MYOCARDIAL INFARCTION at 30 days									
850 patients (6 studies)	No serious limitation	Undetermined	No serious limitation	Serious limitation(2)	Potential limitation(3)	N/A	N/A	aOR 7.5 (4.1-13.6	Low

CARDIAC MORTALITY									
850 patients (6 studies)	No serious limitation	Undetermined	No serious limitation	Serious limitation[2]	Potential limitation[3]	N/A	N/A	aOR 4.3 (1.7-11.3)	Low
RYDING 2009[19]									
ALL-CAUSE MORTALITY within 48 days									
4856 patients (15 studies)	Serious limitation[4]	No serious limitation	No serious limitation	Serious limitation[5]	Undetected	10.2%	0.8%	OR 7.81 (2.83-21.58)	Low
CARDIAC MORTALITY									
4856 patients (15 studies)	Serious limitation[4]	No serious limitation	No serious limitation	Serious limitation[5]	Undetected	9.3%	0.2%	OR 23.88 (9.43-60.43)	Low

aOR = adjusted odds ratio, BNP = brain natriuretic peptide, CI = confidence interval, N/A = not available, NT-proBNP = N-terminal pro-brain natriuretic peptide, OR = odds ratio.

1. Since dataset were only given by willing investigator, negative dataset could have not been shared
2. Large confidence interval and small number of events (not mentioned)
3. Only 6 out of 10 datasets obtained for individual patient meta-analysis
4. No adjustment for potential confounders. All studies were conducted in a blinded fashion, except one in which the BNP values were known to the clinicians treating the patients. Furthermore, systematic screening for asymptomatic postoperative cardiac events was not carried out, which may have led to bias in this study. Otherwise, there was no evidence of selective reporting of data or systematic bias in the other studies
5. Very wide confidence interval and very few events

Supplemental Table 10. Summary of findings for preoperative resting echocardiography

Author Year	Population	Total no. patients	Design	Echocardiography Parameters	Systematic outcome monitoring	Outcome Results	Comments
Park 2011[7]	consecutive patients with cardiac consult and echo-cardiography before elective noncardiac surgery	1923	prospective cohort study with 30 days of follow-up	TTE within 2 weeks before surgery LVEF, RWMI, LA volume index, E/E'	troponin was measured at the end of the surgical day and 24 hours later	**Major CV events** Events/Total: 280/1923 (14.6%) **Major CV events** **LVEF <50%** aRR 2.2 (95% CI, 1.6-2.9) **E/E' ≥13** aRR 1.6 (95% CI, 1.2-2.1) **LA volume index ≥33** aRR 1.4 (95% CI, 1.1-1.9) **RWMI ≥1.04** aRR 1.7 (95% CI, 1.3-2.2) **RCRI score ≥2** aRR 1.3 (95% CI, 1.0-1.8) **NTproBNP ≥301 ng/L** aRR 3.9 (95% CI, 3.1-4.9)	major CV events: MI, pulmonary edema, cardiac death all TTE parameters were inferior to NT-proBNP for predicting major CV events p<0.001
Rohde 2001[20]	non-emergency, noncardiac surgery, expected LOS ≥2 days	570	prospective cohort	TTE < 3 months before surgery -LV systolic function -LVH -MR and AS	CKMB and ECG were measured for the first few days after surgery	**Major CV events** Events/total: 44/570 (8%) **Systolic dysfunction** aOR 2.0 (95% CI, 1.0-4.5) **Mod-severe LVH** aOR 2.3 (95% CI, 1.0-4.5) **Peak instantaneous aortic gradients of ≥40 mm Hg** aOR 6.8 (95% CI, 1.3-31) Other variables in the model : CHF, diabetes with insulin, high-risk surgery, CVD, CAD, CKD	blinded outcome assessment major CV events: MI, cardiogenic pulmonary edema, VF or primary cardiac arrest, sustained complete heart block models using echocardiographic variables were better able to predict major CV events compared to models that used clinical variables only (c statistic 0.73 v 0.68, p<0.05)

Halm 1996[21]	elective major noncardiac surgery; patients with known CAD, PVD or high-risk of CAD	339	prospective cohort	EF, wall motion, LVH	yes	**<u>Major CV events</u>** **EF <40%** aOR 2.5 (95% CI, 1.2-5.0) no echocardiographic variables were predictive of post-operative ischemic events (i.e., cardiac death, nonfatal MI, unstable angina) <u>Other variables in the model</u>: vascular surgery, history of dysrhythmia, history of CAD, use of digoxin	blinded outcome assessment major CV events: cardiac death, nonfatal MI, unstable angina, CHF, VT interobserver agreement rate: 90% incremental value of adding echocardiographic information over clinical risk factors was minimal, with minimal change in c-statistic

aOR = adjusted odds ratio, aRR = adjusted relative risk, AS = aortic stenosis, AUC = area under the receiver operator curve, CHF = congestive heart failure, CKMB = creatine kinase MB isoenzyme, CV = cardiovascular, ECG = electrocardiogram, E/E' = transmitral early diastolic velocity/tissue Doppler mitral annular early diastolic velocity, LA= left atrial, LVEF = left ventricular ejection fraction, LV = left ventricular, LVH = left ventricular hypertrophy, MI = myocardial infarction, MACE = major adverse cardiac events, MR = mitral regurgitation, NT-proBNP = N-terminal pro-brain natriuretic peptide, RWMI = regional wall motion index, TTE = transthoracic echocardiography, VT = ventricular tachycardia.

Supplemental Table 11. GRADE quality assessment for preoperative resting echocardiography

Quality Assessment						Summary of evidence	
No of Participants (No. of studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled estimate of effect**	**Quality of evidence**
MAJOR CARDIOVASCULAR COMPLICATIONS							
2832 (3 studies)[7, 20, 21]	Serious limitation(1)	Serious limitation(2)	No serious limitation	Serious limitation(3)	Potential(4)	N/A	Very low

1. Risk of interrater variability in echocardiographic readings
2. Inconsistent association between echocardiographic findings and ischemic events in the 3 studies
3. Large confidence intervals and small number of events
4. Only 3 studies found on the topic

Supplemental Table 12. Summary of findings for preoperative coronary CT angiography

Author Year	Population	Total no. patients	Design	Threshold for CT angiogram	Systematic outcome monitoring	Outcome Results	Comments
Sheth 2015[16]	in-hospital noncardiac surgery, patients age ≥45 and history of, or risk factors for, athero-sclerotic disease, or a history of CHF	955	prospective cohort study	1) normal: no evidence of coronary atherosclerosis; 2) non-obstructive CAD: evidence of ≥1 coronary artery plaque with a <50% stenosis; 3) obstructive CAD: ≥1 coronary artery plaque with a ≥50% stenosis; 4) extensive obstructive disease: ≥50% stenosis in 2 coronary arteries including the proximal LAD artery, ≥50% stenosis in three coronary arteries, or ≥50% stenosis in the left main coronary artery	troponin was measured daily for 3 days after surgery, an ECG was obtained if a troponin elevation was detected	**Non-fatal MI and CV death:** Events/Total: 74/955 patients (8%) **RCRI + CCTA** AUC 0.66 (95% CI, 0.60-0.73) **Extensive obstructive CAD** aHR 3.76 (95% CI, 1.12-12.62) Overall absolute net reclassification in a sample of 1000 patients is that CCTA will result in an inappropriate estimate of risk in 81 patients (based on risk categories of <5%, 5-15%, and >15% for the primary outcome)	blinded outcome assessment
Hwang 2015[22]	non-cardiac surgery patients with >1 clinical CV risk factors or taking CV medication, and no contra-indication for CT	844	prospective cohort study	Segment Involvement score: no. of coronary artery segments with stenosis irrespective of the severity (0–16). Duke Jeopardy score: presence of luminal diameter stenosis (DS) ≥50% in left main, or DS ≥70% in LAD artery,	No	**Major CV events:** Events/Total: 25/844 (3%) **RCRI + Segment Involvement score>3** AUC 0.72 (95% CI, 0.62–0.83) **RCRI + Duke Jeopardy>0** AUC 0.70 (95% CI, 0.59–0.82) **RCRI + Duke Jeopardy>0 + Segment Involvement score>3** AUC 0.76 (95% CI, 0.65–0.87)	major CV events: MI, pulmonary edema, cardiac death no blinded outcome assessment

				diagonal branch, left circumflex coronary artery, obtuse marginal branch, or posterior descending artery. Each segment is assigned 2 points, maximum score = 12		NRI 0.92 (95% CI, 0.55–1.29)*	
Kong 2015[23]	liver transplantation	443	retrospective cohort study	positive CCTA: coronary calcium score>400 432 (97.5%) had a coronary calcium score of ≤400	yes* *patients were excluded if they did not have troponin monitoring after surgery (n=60)	**<u>Major CV events:</u>** Events/Total: 38/443 (8.6%) **Coronary calcium score>400** aOR 4.62 (95% CI, 1.14-18.72)* <u>other variables in the model</u>: gender, statin	major CV events: non-fatal MI, serious arrhythmia (VT, VF, or heart block requiring treatment), and cardiac death (because of fatal MI or CHF). no blinded outcome assessment
Ahn 2013[24]	intermediate risk intra-thoracic, intraperitoneal, orthopedic, head and neck, and prostate disease	239	prospective cohort study	1) angiographically significant disease was categorized into 4 groups ranging from no significant stenosis to 3-vessel disease 2) coronary calcium score (CACS) ≥113	no	**<u>Major CV events:</u>** Events/Total: 19/239 (8%) **CACS ≥113** aOR 4.21 (95% CI, 1.25–14.18)* **Multivessel disease (2-3 vessels)** aOR 7.31 (95% CI, 2.25–23.69)* <u>*other variables in the model</u>: ischemic heart disease, CHF, CKD	major CV events: cardiac death, ACS, pulmonary edema, VF, VT with hemodynamic compromise, and complete heart block. no blinded outcome assessment

ACS = acute coronary syndrome, CAD = coronary artery disease, CCTA = coronary CT angiogram, CKD = chronic kidney disease, CHF = congestive heart failure, CV = cardiovascular, CT = computed tomography, DS = diameter stenosis, ECG = electrocardiogram, LAD = left anterior descending, MI = myocardial infarction, RCRI = Revised Cardiac Risk Index, ULN = upper limit of normal, VF = ventricular fibrillation, VT = ventricular tachycardia.

Supplemental Table 13: GRADE quality assessment for preoperative coronary CT angiography

Quality Assessment						Summary of Evidence	
No. of participants (No. of studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Estimate of effect**	**Quality of evidence**
MAJOR CARDIOVASCULAR COMPLICATIONS – 30 days							
2481 (4 studies) [16, 22-24]	No serious limitation[(1)]	No serious limitation	No serious limitation	Serious limitation[(2)]	Not detected	Overall absolute net reclassification in a sample of 1000 patients is that CCTA will result in an inappropriate estimate of risk in 81 patients (based on risk categories of <5%, 5-15%, and >15% for the primary outcome)	Moderate

CT = computed tomography, CCTA = coronary computed tomography angiography.

1. 3 of 4 studies were not blinded to CCTA results and 2 of 4 did not systematically assess for primary outcome. However, one study[16] was high quality (i.e. blinded outcome assessment, systematic outcome monitoring, adjusted analysis) and was given the most weight in the recommendation.
2. Small number of events and large confidence intervals.

Supplemental Table 14: Summary of findings for preoperative exercise stress testing

Author Year	Population	Total no. patients	Design	Exercise testing results	Systematic monitoring of outcome	Outcome Results	Comments
Kaaja[25] 1993	vascular surgery	58	prospective cohort study	ECG monitoring with bicycle pedaling; unclear assessment for test positivity and no formal protocol Test positive/Total: 14/58 (24.1%)	no	**Myocardial infarction** positive stress test: 2/14 (14.3%) negative stress test: 0/44 (0%)	no risk-adjusted analysis performed
McPhail 1987[26]	vascular surgery	101	prospective cohort study	61 patients with treadmill exercise testing with ECG monitoring (Bruce protocol) 40 patients with arm crank ergometry (Schwade protocol)	no	**Major cardiac events** **Predicted max heart rate (PMHR)** PMHR <85%: 17/70 (24.3%) PMHR >85%: 2/30 (6.6%) (p=0.04) **ST depression with exercise** no significant association with cardiac events *no risk-adjusted analysis for clinical risk factors	major cardiac events: MI, acute CHF, VT, VF, cardiac death MI definition: ST elevation and CKMB elevation
Carliner 1985[27]	elective major non-cardiac surgery with general anesthesia	200	prospective cohort study	treadmill exercise testing with ECG monitoring	CK and CKMB monitoring after surgery	**Death and MI** no independent association between ECG exercise change and outcome	MI definition: new Q waves or persistent deep T-wave inversion with elevated CK and CK-MB
Sgura 2000[28]	vascular surgery	149	prospective cohort study	supine bicycle with ECG monitoring; patients categorized as	unclear	**Death and MI** low capacity: 9 /73 (12%) intermediate: 2/70 (3%)	

				low (<4 METs), intermediate (4-7 METs), or high-functional (>7 METs) capacity		high capacity: 0/6 (p=0.03) no significant association between exercise induced ST depression, or any clinical variable (other than age)	

CHF = congestive heart failure, CKMB = creatine kinase MB isoenzyme, ECG = electrocardiogram, METSs = metabolic equivalents, MI = myocardial infarction, VF = ventricular fibrillation, VT = ventricular tachycardia.

Supplemental Table 15: GRADE quality assessment for preoperative exercise stress testing

Quality Assessment						Summary of findings	
No. of participants (No. of studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled estimate of effect**	**Quality of evidence**
MAJOR CARDIOVASCULAR EVENTS							
508 patients (4 studies)[25-28]	Very serious limitation[(1)]	Serious limitation[(2)]	No serious limitation	Serious limitation[(3)]	Unclear	N/A	Very low

N/A = not available.

1. Lack of risk-adjusted analysis, systematic monitoring of outcome, and outcome adjudication
2. Inconsistent association between exercise testing results and cardiovascular outcomes between studies
3. Very small number of events

Supplemental Table 16: Summary of findings for preoperative cardiopulmonary exercise testing (CPET)

Author Year	Population	Total No. Patients	Design	CPET results	Systematic monitoring of outcome	Outcome Results	Comments
Grant 2014[29]	elective endo-vascular AAA repair	506	prospective cohort study	threshold determined a priori, analyzed as dichotomous 1) VO_2 at AT<10.2 ml*kg^{1}min: 241/506 (47.6%) 2) peak VO_2<15 ml*kg^{-1}min: 255/506 (50.4%) 3) V_E/VCO_2 at AT>42: 79/506 (15.6%)	yes (mortality)	**All-cause mortality at 5 years**: Events/Total: 90/506 (17.8%) **V_E/VCO_2 at AT>42** aHR 1.63 (95% CI, 1.01–2.63) **peak VO_2<15 ml*kg^{-1}min** aHR 1.68 (95% CI, 1.00–2.80) other variables in the model: age, sex, diabetes, cardiac ischemia, statin, creatinine, urea, hemoglobin	potential selection bias number of loss to follow-up not reported; no multivariable analysis for 30-day outcomes reported
Dunne 2014[30]	hepa-tectomy	197	retrospective cohort study	analyzed as continuous variables 1) mean AT: 11.5 ml kg^{-1} min^{-1} (SD 2.5) 2) peak VO_2: 17.7 ml kg^{-1} min^{-1} (SD 4.5) 3) mean V_E/VCO_2 at the AT: 31.8 (SD 5.2)	no	**Cardiopulmonary complications 30 days**: Events/Total: 24/197 (12%). CPET variables were not associated with outcome in univariable or multivariable analysis (data not reported)	cardiorespiratory complications included all chest infections, cardiac arrhythmias, and ischemic cardiac events
Junejo 2012[31]	hepa-tectomy	94	prospective cohort study	analyzed as dichotomous, threshold determined by AUC analysis in univariable analysis: V_E/VCO_2 at AT ≥34.5	no	**Cardiovascular events (30-day):** Events/Total: 11/94 (11%) no analysis reported **Cardiopulmonary events (up to 4 years)**: 39/94 (41%) **V_E/VCO_2 at AT ≥34.5** aOR 3.45 (95% CI, 1.31-9.14)	pulmonary: *de novo* requirement for supplemental O2 or other respiratory support, cardiovascular: MI, myocardial

						<u>other variables in the model</u>: age only	ischemia, hypotension requiring treatment, atrial or ventricular arrhythmias, or pulmonary edema
Colson 2012[32]	elective major abdominal or thoracic surgery	1725	prospective cohort study	analyzed as <u>continuous</u> variables, AT-P_{EO2} AT-V_{O2}/HR AT-RER AT-$V_{O2*}kg^{-1}$	yes	**<u>All-cause mortality at 5 years:</u>** 616/1725 (36%) <u>weak evidence of effect for:</u> **AT-P_{EO2},** [P(B≠0)=70%] **AT-V_{O2}/HR,** [P(B≠0)=65%] **AT-RER**, [P(B≠0)=57%] **AT-$V_{O2*}kg^{-1}$** [P(B≠0)=54%] <u>other variables in the model</u> (very strong predictors: [P(B≠0)=100%]): gender, surgery type, forced vital capacity ratio	no multivariable analysis for 30-day outcomes reported estimate of effect not reported (e.g. odds ratio or hazard ratio). The authors provided the following explanation for the results: interpretation of P(B≠0) : 50%: against an effect 50–75%:weak 75–95%:positive 95–99%:strong >99%:very strong evidence of an effect

Lai 2013[33]	elective major colorectal surgery	269	prospective cohort study	dichotomous, threshold determined a priori: 1) Fit: AT ≥ 11.0 - 174/269 (64.7%) 2) Unfit: AT < 11.0 ml - 69/269 (25.7%) 3) Unable: failed to pedal the cycle or demonstrate an AT - 26/269 (9.7%)	yes (mortality)	**All-cause mortality at 2 yrs:** Events/Total: 19/174 (fit), 14/69 (unfit), 14/26 (unable) **Unable to perform CPET (compared to Fit)** aOR 3.98 (95% CI, 1.04-11.73) other variables in the model: age, gender, Dukes staging of malignancy	no multivariable analysis for short term outcomes reported no loss to follow-up
Hartley 2012[34]	elective AAA repair	415	prospective cohort study	dichotomous, threshold determined a priori: 1) VO_2 at AT <10.2: 191/415 (46.0%) 2) peak VO_2 <15: 221/415 (53.3%) 3) V_E/VCO_2 at AT >42: 176/415 (42.4%)	yes	**All-cause mortality at 30 days:** Events/Total: 14/415 (3.4%) **1) VO_2 at AT <10.2** aOR 6.35 (95% CI, 1.84-29.80) other variables in the model: open surgery, inducible cardiac ischemia, anemia **2) ≥2 subthreshold CPET values** aOR 11.39 (95% CI, 2.89-76.46) other variables in the model: inducible cardiac ischemia, open surgery, juxta/suprarenal AAA, anemia **All-cause mortality at 90 days:** Events/Total: 19/415 (4.6%) **1) peak VO_2 <15** aOR 8.59 (95% CI, 2.33-55.75) other variables in the model: open surgery, inducible cardiac ischemia, anemia	

						2) ≥2 subthreshold CPET values aOR 5.40 (95% CI, 1.86-19.67) other variables in the model: inducible cardiac ischemia, open surgery, juxta/suprarenal AAA, anemia	
Carlisle 2007[35]	AAA repair	130	prospective cohort study	analyzed as continuous in multivariable analysis	yes	**All-cause mortality at 30 days** Events/Total: 14/130 (10.8%) reported in the text that "Multivariable analyses indicated that survival, to both 30 days and for the total observation period, correlated best with V_E/VCO_2" but no estimate of effect reported **All-cause mortality at median 35 months**: Events/Total: 29/130 (22.3%) **1) V_E/VCO_2** aHR 1.13 (95% CI, 1.07-1.19) p<0.001 other variables in the model: RCRI, AT **2) AT** aHR 0.84 (95% CI, 0.72-0.98) p=0.033 other variables in the model: RCRI, VE/VCO_2 Sequential log rank tests to determine fit vs unfit definition based on survival times	low risk of selection bias but only AAA patients no multivariable analysis result reported for short term outcomes

						Unfit: RCRI >1 and V_E/VCO_2 >42, 55% survival at 2 years **Fit**: RCRI =1 and $V_E/VCO_2 \leq 42$, 97% survival at 2 years	

AAA = aortic abdominal aneurysm, aHR = adjusted hazard ratio, aOR = adjusted odds ratio, ASA = American Society of Anesthesiologists, AT = anaerobic threshold, AUC = area under the receiver operate curve, CI = confidence interval, CPET = cardiopulmonary exercise testing, HR = heart rate, MI = myocardial infarction, P_{EO2} = end-tidal oxygen concentration, RCRI = Revised Cardiac Risk Index, RER = respiratory exchange ratio of carbon dioxide production to oxygen consumption, SD = standard deviation, VCO_2 = carbon dioxide production rate, V_E = pulmonary minute ventilation, VO_2 = oxygen consumption rate.

Supplemental Table 17: GRADE quality assessment for preoperative cardiopulmonary exercise testing (CPET)

Quality Assessment						Summary of evidence	
No. of participants (No. of studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled estimate of effect (95% CI)**	**Quality of evidence**
ALL-CAUSE MORTALITY at long term (90 days-5 years)							
3139 patients (6 studies)[29, 31-35]	Serious limitation(1)	Serious limitation(2)	No serious limitation	Serious limitation(3)	Not detected	N/A	Low
ALL-CAUSE MORTALITY at 30 days							
706 patients (3 studies)[30, 31, 34]	Serious limitation(1)	No serious limitation	Serious limitation(4)	Serious limitation(3)	Suspected(5)	N/A	Very low
MAJOR CARDIOPULMONARY COMPLICATIONS							
291 patients (2 studies)[30, 31]	Serious limitation(1)	Serious limitation(1)	Serious limitation(4)	Serious limitation(3)	Suspected(6)	N/A	Very low

CI = confidence interval.

1. Failure to adequately control for known prognostic factors in multivariable analysis in certain studies, risk of selection bias
2. Wide variation in strength of association between CPET results and long-term mortality
3. Large confidence intervals in most studies
4. Cardiovascular complications not directly reported, combined with pulmonary complications
5. Most studies on CPET collected information on short-term mortality but the majority did not report estimate of effect (i.e., no analysis performed)

Supplemental Table 18: Summary of findings for preoperative pharmacological stress echocardiography and radionuclide imaging

Author Year	Population	Total no. patients	Design	Cardiac stress test	Systematic outcome monitoring	Outcome results	Comments
STRESS ECHOCARDIOGRAPHY							
Ballal 1999[36]	vascular surgery	233	prospective cohort study	dobutamine stress echo-cardiography	yes	**Major CV events – in hospital:** Events/Total: 30/233 **Ischemia on DSE** : aRR 3.3 (95%CI, 1.6-6.82) p<0.01 other variables in the model: age, sex, Eagle criteria, LV function	major CV events: cardiac death, MI, and unstable or progressive angina requiring revascularization
Torres 2002[37]	noncardiac mixed surgery	105	prospective cohort study	dobutamine stress echo-cardiography	troponin and CKMB obtained daily in the recovery and intensive care wards	**Major CV events - in-hospital:** Events/Total: 10/105 **Abnormal DSE**: aOR 40.5, p=0.002* other variables in the model: not specified	major cardiac events: acute coronary syndrome, MI or cardiac death potential risk of selection bias *no 95% CI provided
Day 2000[38]	vascular and thoracic surgery	300	retrospective cohort study	dobutamine stress echo-cardiography	no	**Major CV events – in hospital:** Events/Total: 48/300 **Resting wall motion abnormality:** aOR 4.7, p=0.005* **Hypotension during DSE:** aOR 4.1. p=0.002* other variables in the model: age, gender, hypotensive response during stress test, arrhythmia induced by stress test	major CV events: in-hospital cardiac death, nonfatal MI, and myocardial ischemia. potential risk of selection bias *no 95%CI provided

Das 2000[39]	non-vascular surgery	530	prospective cohort	dobutamine stress echo-cardiogram	post-operative serial cardiac enzyme values (frequency and duration not specified)	**<u>Major CV events*</u>:** Events/Total: 32/530 **Ischemic threshold < 60%**: aOR 7.002 (95%CI, 2.79-17.61) p=0.0001 <u>other variable in the model</u>: CHF	*unclear duration of follow-up for outcome assessment major CV events: cardiac death or acute MI ischemic threshold was defined as the heart rate at which new echo-cardiographic wall motion abnormalities first occurred divided by the age-predicted maximal heart rate(220-age)
Lalka 1992[40]	vascular surgery	60	prospective cohort	dobutamine stress echo-cardiography	yes	**<u>Major CV events – 30 days:</u>** Events/Total: 12/60 **Inability to achieve target heart rate >120 BPM during dobutamine infusion**: significant increased risk of major CV events (p=0.004)* **More severely abnormal DSE result**: significant increased risk of with major CV events (p=0.012)* <u>other variables in the model:</u> age >70 years, prior MI, CHF, cardiac symptoms, events during DSE (i.e., angina, abnormal ECG, heart rate ≤ 120)	*no estimate of effect reported for multivariable analysis, only p-value major CV events: cardiac death, nonfatal MI, unstable angina, or asymptomatic elevation of cardiac isoenzymes without ECG changes.

							potential risk of selection bias risk of model overfitting (i.e. small no. of events and large no. of predictors)
RADIONUCLIDE IMAGING							
Hendel 1995[41]	vascular surgery	567	prospective cohort study	dipyridamole thallium	no	**Major CV events – 30 days:** Events/Total: 46/567 **Transient defect in Men:** aRR 3.9 (95%CI, 1.5-10.2) other variables in the model: diabetes, angina, Q wave, CHF, ST segment change **Transient defect in Women:** aRR 5.5 (95%CI, 1.4-22.0) other variable in the model: angina	major CV events: nonfatal MI and cardiac death potential risk of selection bias risk of model overfitting (i.e. small no. of events and large no. of predictors)
Stratmann 1996[42]	elective vascular surgery	197	prospective cohort study	dipyridamole technetium-99m sestamibi tomography	no	**Major CV events after discharge or ≥30 days after surgery**: Events/Total: 26/172 **Reversible defect**: aRR 2.7 (95% CI, 1.2-6.1) other variables in the model CHF, diabetes, past coronary revascularization, CAD, Q wave on ECG, chest pain during dipyridamole	major CV events: unstable angina, acute ischemic pulmonary edema, nonfatal MI, and cardiac death. risk of model overfitting (i.e. small no. of events and large no. of predictors)

Younis 1990[43]	vascular surgery	111	prospective cohort study	dipyridamole thallium	no	**Nonfatal MI and cardiac death - in hospital:** Events/Total: 8/111 **Perfusion defect** perfusion defect was associated with an increased risk of MI/CV death (p=0.003)* other variables in the model: angina, chest pain, reversible thallium defect	potential risk of selection bias risk of model overfitting (i.e. small no. of events and large no. of predictors) *no estimate of effect provided
Vanzetto 1995[44]	elective AAA surgery	134	prospective cohort study	dipyridamole thallium	CKMB twice daily for 3 days	**Any cardiac events - in-hospital:** Events/Total: 30/134 **No. segments with reversible defect:** significant increased risk of any cardiac events (p<0.001)* other variables in the model: history of myocardial infarction **Major CV events:** Events/Total: 12/134 **No. segments with reversible defect:** significant increased risk of major CV events p<0.001* other variables in the model: history of MI, anterior Q wave on the ECG, anterior ischemia on the ECG	any cardiac events: cardiac death or nonfatal MI, unstable angina, CHF, severe ventricular arrhythmias major cardiac events: cardiac death, nonfatal MI potential risk of selection bias *no estimate of effect provided
Marshall 1995[45]	vascular surgery	122	prospective cohort study	adenosine radionuclide	no	**Non-fatal MI or death:** Events/Total: 27/122 **No. of reversible defects**:	*no estimate of effect provided

				perfusion imaging		significant increased risk of nonfatal MI and death (p=0.017)* <u>other variables in the model</u>: not specified	duration of follow-up not reported but all events occurred within first 2 days after surgery
Coley 1992[46]	non-vascular surgery	100	retrospective cohort study	dipyridamole thallium scan	no	**<u>Major CV events*:</u>** Events/Total: 9/100 **Thallium redistribution:** aOR 14.6 (95%CI, 1.3-160.5) <u>other variables in the model</u>: age, CHF	*duration of follow-up not reported cardiac death, nonfatal MI, unstable angina, pulmonary edema potential risk of selection bias risk of model overfitting (i.e. small no. of events and large no. of predictors)
Levinson 1990[47]	vascular surgery	62	retrospective cohort study	dipyridamole thallium	no	**<u>Major CV events*</u>:** Events/Total: 17/62 **Redistribution in >1 view** significant increased risk of major CV events (p<0.001)** **2 coronary zones with redistribution**: significant increased risk of major CV events (p=0.02)** <u>other variables in the model</u>: not specified	*duration of follow-up not reported major CV events: unstable angina pectoris, ischemic pulmonary edema, MI and cardiac death. **no estimate of effect provided

Chen 2002[48]	vascular surgery	180	prospective cohort study	dipyridamole thallium	no	**Major CV events*:** Events/Total: 9/180 **Reversible defect:** aOR 7.0 (95%CI, 1.7-28) p=0.0071* **Reversible defect (low risk patient)**: aOR 11.6 (95%CI, 2.3-57.4) p=0.004 other variables in the model: age, type of ASO, smoking, hyperlipidemia, HTN, diabetes, MI, history of angina, Goldman index, Detsky index, Intermediate-high risk	*duration of follow-up not reported major CV events: cardiac death, non-fatal MI, unstable angina, CHF risk of model overfitting (i.e. small no. of events and large no. of predictors)
Zarich 1995[49]	peripheral vascular surgery in patients with diabetes	93	prospective cohort study	dipyridamole thallium	no	**Nonfatal MI or death:** Events/Total: 9/93 **Total number of defects per scan** Significant increased risk of nonfatal MI or death (p< 0.004)* other variables in the model: age, sex, number of thallium defects per scan, presence of reversible defects in the left anterior descending artery territory, prior MI, history of angina, history of CHF, hypertension, insulin use, and presence of pathological Q waves.	*no estimate of effect provided risk of model overfitting (i.e. small no. of events and large no. of predictors)
Hashimoto 2003[50]	noncardiac surgery	481	retrospective cohort study	dipyridamole with ECG gating	yes	**Major CV events – 30 days:** Events/Total: 39/481 significant increased risk of with major CV events.* other variables in the model: age, diabetes mellitus	*no estimate of effect or p-value reported major CV events:

							cardiac death, nonfatal MI, unstable angina, CHF, and performance of revascularization
Baron 1994[51]	AAA repair	457	prospective cohort	dipyridamole thallium and gated radionuclide angiogram	yes	**Major CV events – 30 days**: Events/Total: 86/457 no independent association for EF < 50%, fixed thallium defect, and thallium redistribution other variables in the model: age, CAD	major CV events: prolonged myocardial ischemia patients, MI, CHF, and severe ventricular tachyarrhythmia blinded outcome assessment
Kontos 1996[52]	mixed non-cardiac surgery	87	prospective cohort	dipyridamole thallium	CKMB and ECG for 4 days	**Major CV events – 30 days:** Events/Total: 14/87 after adjusting for other variables, stress test findings were not associated with outcome other variables in the model : adjusted for HTN, heart failure, class I Goldman, class 2-3 Goldman, and results on imaging (redistribution, abnormal dipyridamole, normal dipyridamole, abnormal LVEF)	major CV events : acute MI, cardiac death, or need for revascularization before surgery potential risk of selection bias risk of model overfitting (i.e. small no. of events and large no. of predictors)

Only studies which performed risk adjusted analysis were included.

AAA = abdominal aortic aneurysm, BPM = beats per minute, CAD = coronary artery disease, CI = confidence interval, CHF = congestive heart failure, CKMB = creatine kinase MB isoenzyme, CV = cardiovascular, DSE = dobutamine stress echocardiography, ECG = electrocardiogram, HTN = hypertension, LVEF = left ventricular ejection fraction, MI = myocardial infarction.

Supplemental Table 19. GRADE quality assessment for preoperative pharmacological stress echocardiography and radionuclide imaging

Quality Assessment						Summary of evidence	
No of patients (No. of studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled AUC (95% CI)**	**Quality of evidence**
PHARMACOLOGICAL STRESS ECHOCARDIOGRAPHY							
MAJOR CARDIOVASCULAR COMPLICATIONS							
1228 (5 studies) [36-40]	Very serious limitation[(1)]	No serious limitation	No serious limitation	Serious limitation[(2)]	Not detected	AUC 0.80 (0.76–0.84)	Low
PHARMACOLOGICAL STRESS RADIONUCLIDE IMAGING							
DEATH AND NONFATAL MYOCARDIAL INFARCTION							
326 (3 studies) [43, 45, 49]	Serious limitation[(1)]	No serious limitation	No serious limitation	Serious limitation[(3)]	Not detected	N/A	Low
MAJOR CARDIOVASCULAR COMPLICATIONS							
2265 (9 studies) [41, 42, 44, 46-48]	Serious limitation[(1)]	No serious limitation	No serious limitation	No serious limitation	Not detected	AUC 0.75 (0.70–0.80)	Moderate

AUC = area under the receiver operator curve, CI = confidence interval, N/A = not available.

1. Most studies were at risk of selection bias, multivariable analysis failed to adjust for clinical risk factors and majority of multivariable models were at risk of being overfitted (i.e. very small number or events and high number of variables in the model which can result in inaccurate prediction[53])
2. Very small number of events in most studies and wide confidence intervals.
3. Studies did not report estimate of effect in publication and very small number of events

Supplemental Table 20: Summary of findings for perioperative ASA initiation and continuation

Author year	Total no. patients	Population	Intervention and comparator	Systematic outcome monitoring	Results	Comments
DEATH AND NONFATAL MYOCARDIAL INFARCTION						
Devereaux 2014[54]	10,010	noncardiac surgery	ASA 200 mg preoperatively and starting the day after surgery 100 mg daily versus placebo for 7 days (continuation stratum) or 30 days (initiation stratum)	troponin or CKMB were measured daily for first 3 days after surgery	**Death and Nonfatal MI at 30 days** Events/Total: ASA: 351/4998 (7.0%) Placebo: 355/5012 (7.1%) HR 0.99 (95% CI, 0.86–1.15) p=0.92	MI definition: Third universal definition of MI
ALL-CAUSE MORTALITY						
Devereaux 2014[54]	10,010	noncardiac surgery	see above	yes	**Death at 30 days** Events/Total: ASA: 65/4998 (1.3%) Placebo: 62/5012 (1.2%) HR 1.05 (95% CI, 0.74–1.49) p=0.78	POISE-2 included 5628 patients who were not previously taking aspirin and 4382 patients who were taking aspirin chronically but had stopped taking aspirin a median of 7 days before surgery
PEP Trial 2000[55]	13,356	hip fracture surgery	ASA 160 mg daily for 35 days started immediately after randomization before surgery	yes	**Death at 35 days** Events/Total: ASA: 447/6679 (6.7%) Placebo: 461/6677 (6.9%) HR 0.97 (95% CI, 0.85–1.10)	some patients were taking aspirin chronically but the number of patients was not reported

CARDIAC DEATH						
Devereaux 2014[54]	10,010	noncardiac surgery	see above	yes	**Cardiac death at 30 days** Events/Total: ASA: 35/4998 (0.7%) Placebo: 35/5012 (0.7%) HR 1.00 (95% CI, 0.63–1.60) p=0.99	any death with a vascular cause and included those deaths following a MI, cardiac arrest, stroke, cardiac revasc. procedure (i.e., PCI or CABG), PE, hemorrhage, or deaths due to an unknown cause
PEP Trial 2000[55]	13,356	hip fracture surgery	see above	yes	**Cardiac death at 30 days*** Events/Total: ASA: 235/6679 (3.5%) Placebo: 252/6677 (3.8%) HR 0.93 (95% CI, 0.78–1.11)	* vascular death
MYOCARDIAL INFARCTION						
Devereaux 2014[54]	10,010	noncardiac surgery	see above	troponin or CKMB were measured daily for first 3 days after surgery	**MI at 30 days** Events/Total: ASA: 309/4998 (6.2%) Placebo: 315/5012 (6.3%) HR 0.98 (95% CI, 0.84–1.15) p=0.85	MI definition: Third universal definition of MI
PEP Trial 2000[55]	13,356	hip fracture surgery	see above	no there was no systematic monitoring of cardiac	**MI at 35 days*** Events/Total: ASA: 105/6679 (1.6%) Placebo: 79/6677 (1.2%) HR 1.33 (95% CI, 1.00–1.78) p=0.05	* nonfatal MI and fatal ischemic heart disease

				biomarkers after surgery		
BLEEDING						
Devereaux 2014[54]	10 010	Noncardiac surgery	see above	yes	**<u>Major bleeding</u>** Events/Total: ASA: 230/4998 (4.6%) Placebo: 188/5012 (3.8%) HR 1.23 (95% CI, 1.01–1.49) p=0.04 **<u>Life-threatening bleeding</u>** Events/Total: ASA: 87/4998 (1.7%) Placebo: 73/5012 (1.5%) HR 1.19 (95% CI, 0.88–1.63) p=0.26	Bleeding predicted MI (HR 1.82, p<0.001) ASA increased risk of life threatening or major bleeding until day 8 after surgery
PEP Trial 2000[55]	13,356	hip fracture surgery	see above	yes	**<u>Bleeding resulting in a transfusion</u>** Events/Total: ASA: 197/6679 (2.9%) Placebo: 157/6677 (2.4%) HR 1.24 (95% CI, 1.01–1.53) p=0.04	

ASA = acetylsalicylic acid, HR = hazard ratio, CABG = coronary artery bypass grafting, CKMB = creatine kinase MB isoenzyme, MI = myocardial infarction, PCI = percutaneous coronary intervention, PE = pulmonary embolism.

Supplemental Table 21: GRADE quality assessment for perioperative ASA initiation and continuation*

Quality Assessment						Summary of evidence			
No. of participants (No. of studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with ASA**	**Anticipated absolute effects without ASA**	**Estimate of effect HR (95% CI)**	**Quality of evidence**
DEATH AND NONFATAL MI – 30 days									
10,010 (1 study)[54]	No serious limitation[(1)]	No serious limitation	No serious limitation	No serious limitation	Not detected	7.0%	7.1%	HR 0.99 (0.86–1.15)	High
MAJOR BLEEDING									
10,010 (1 study)[54]	No serious limitation[(1)]	No serious limitation	No serious limitation	No serious limitation	Not detected	4.6%	3.8%	HR 1.23 (1.01–1.49)	High

ASA = acid acetylsalicylic, CI = confidence interval, HR = hazard ratio.

1. Adequate allocation concealment and blinding, performed systematic outcome monitoring, blinded outcome adjudication, intention-to-treat analysis, and minimal loss to follow-ups (11 patients).

* GRADE quality assessment table based on POISE-2 results because more reflective of noncardiac surgery and systematically monitored for MI.

Supplemental Table 22: Summary of findings for perioperative β-blocker initiation

Author Year	Design	Total No. Patients (No. of studies)	Eligibility criteria	Results	Comments
ALL-CAUSE MORTALITY					
Wijeysundera 2014[56]	systematic review and meta-analysis of RCTs	10,785 (14 trials)	- comparison: perioperative β-blockade against placebo or standard care - adults undergoing noncardiac surgery - sample size >100 - β-blocker started at any point between 45 days prior to surgery and 24h after surgery. - treatment had to be continued until hospital discharged or second day after surgery	**All-cause mortality** Events/Total: β-blocker: 161/5394 (3.0%) No β-blocker: 126/5391 (2.3%) RR 1.30 (95% CI, 1.03-1.63) heterogeneity: I^2=0%, p=0.63	results excluding trials by Poldermans
CARDIAC MORTALITY					
Wijeysundera 2014[56]	see above	10,648 (12 trials)	see above	**Cardiac mortality** Events/Total β-blocker: 88/5327 (1.7%) No β-blocker: 70/5321 (1.3%) RR 1.25 (95%CI, 0.92-1.71) heterogeneity not reported	results excluding trials by Poldermans
MYOCARDIAL INFARCTION					

Wijeysundera 2014[56]	see above	10,785 (14 trials)	see above	**Non-fatal MI** Events/Total : β-blocker: 181/5394 (3.4%) No β-blocker: 256/5391 (4.7%) RR 0.72 (95%CI, 0.59 – 0.86) heterogeneity: I^2=0% p=0.837	non-fatal MI in-hospital or 30-day results excluding trials by Poldermans
STROKE					
Wijeysundera 2014[56]	see above	10,545 (9 trials)	see above	**Non-fatal Stroke** Events/Total : β-blocker: 40/5274 (0.8%) No β-blocker: 21/5271 (0.4%) RR 1.86 (95%CI, 1.09–3.16) heterogeneity: not reported	non-fatal stoke in-hospital or 30-day results excluding trials by Poldermans heterogeneity I^2=0%

CI = confidence interval, MI = myocardial infarction, RCT = randomized controlled trial, RR = relative risk.

Supplemental Table 23: GRADE quality assessment for perioperative β-blocker initiation

Quality Assessment						Summary of Evidence			
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with β-blocker**	**Anticipated absolute effects without β-blocker**	**Pooled Estimate RR (95% CI)**	**Quality of evidence**
ALL CAUSE MORTALITY									
10,785 (14 trials)[56]	No serious limitation	No serious limitation	No serious limitation	No serious limitation	Less likely	3.0%	2.3%	RR 1.30 (1.03-1.63)	High
CARDIAC MORTALITY									
10,648 (12 trials)[56]	No serious limitation	Unclear(1)	No serious limitation	No serious limitation	Less likely	1.7%	1.3%	RR 1.25 (0.92-1.71)	Moderate
MYOCARDIAL INFARCTION									
10,785 (14 trials)[56]	No serious limitation	No serious limitation	No serious limitation	No serious limitation	Less likely	3.4%	4.7%	RR 0.72 (0.59-0.86)	High
STROKE									
10,545 (9 trials)[56]	No serious limitation	No serious limitation	No serious limitation	Serious limitation(2)	Less likely	0.8%	0.4%	RR 1.86 (1.09-3.16)	Moderate

CI = confidence interval, RR = relative risk.

1. Heterogeneity not reported
2. Wide Confidence Interval

Supplemental Table 24: Summary of findings for perioperative β-blocker continuation

Author year	Design	Population	Total no. patients	Intervention	Systematic outcome monitoring	Results	Comments
Kwon 2012[57]	retrospective cohort study	patients with history of taking a BB who were undergoing elective colon/rectal or bariatric procedures	1975	BB continued: preoperatively within 24 hours of surgery or before leaving the post-anesthesia care unit n=1302 BB missed on the day of surgery n=673	yes	**In-hospital Mortality** Continuation: 1.1% Missed: 1.6% p=0.29 no risk-adjusted analysis **30-day Mortality** Continuation: 1.2% Missed: 2.2% p=0.09 no risk-adjusted analysis	
Wallace 2010[58]	retrospective cohort	noncardiac surgery; patients with cardiac risk, or CAD, or PVD, who had inpatient surgery	12,105	BB withdrawal: BB preoperatively, no BB postoperatively BB continued: BB preoperatively and BB postoperatively	yes	**All-cause mortality at 30 days** **BB addition:** aOR 0.58 (95% CI, 0.37-0.92) p=0.02 **BB continued:** aOR 0.74 (95% CI, 0.51-1.05) p=0.09 **BB withdrawal:** aOR 3.57 (95% CI, 2.31-5.52) p<0.0001 other variables in the model: CAD, PVD	propensity score matched analysis for noncardiac surgery only

aOR = adjusted odds ratio, BB = β-blocker, CI = confidence interval, CAD = coronary artery disease, CI = confidence interval, PVD = peripheral vascular disease, OR = odds ratio.

Supplemental Table 25: GRADE quality assessment for perioperative β-blocker continuation

Quality Assessment						Summary of Evidence			
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with β-blocker**	**Anticipated absolute effects without β-blocker**	**Estimate aOR (95% CI)**	**Quality of evidence**
30 DAY MORTALITY									
12,105 (1 study)[58]	Serious limitation(1)	No serious limitation	No serious limitation	No serious limitation	Possible(2)	1.2%	2.2%	BB continued: aOR 0.74 (0.51-1.05) BB withdrawal: aOR 3.57 (2.31-5.52)	Very Low

aOR = adjusted odds ratio, BB = β-blocker, CI = confidence interval.

1. High risk of bias. Patients who had β-blocker withdrawn preoperatively may have had worse medical conditions that warrant β-blocker discontinuation (e.g., infection leading to hypotension). Retrospective cohort study. Database review. No systematic monitoring of perioperative β-blocker administration and postoperative outcomes. Small events numbers.
2. Very few articles published on this topic.

Supplemental Table 26: Summary of findings for preoperative initiation of α_2-agonist

Author year	Design	No. patients (no. studies)	Population / type of surgery	Intervention and comparator	Systematic outcome monitoring	Results	Comments
ALL-CAUSE MORTALITY							
Devereaux 2014[59]	RCT	10,010 (1 RCT) 5009 clonidine 5001 placebo	noncardiac surgery, known vascular disease or risk factors >45 years	clonidine orally 1 hour before surgery and transdermal for 72 hours	yes (mortality)	**All-cause mortality at 30 days** Events/Total: Clonidine: 64/5009 (1.3%) Placebo: 63/5001 (1.3%) HR 1.01 (95% CI, 0.72–1.44) p=0.94	
Wijeysundera 2009[60]	systematic review and meta-analysis of RCTs	2851 (9 trials)	noncardiac surgery	different α_2-agonists	unclear	**All-cause mortality** Events/Total : α_2-agonists: 30/1514 (2.0%) Control: 45/1337 (3.4%) RR 0.61 (95% CI, 0.39-0.96) p=0.03	incidence dominated by one trial of mivazerol
MORTALITY AND NONFATAL MYOCARDIAL INFARCTION							
Devereaux 2014[59]	RCT	see above	see above	see above	troponin or CKMB were measured daily for first 3 days after surgery	**Death or nonfatal MI at 30 days** Clonidine: 367/5009 (7.3%) Placebo: 339/5001 (6.8%) HR 1.08 (95% CI, 0.93–1.26) p=0.29	composite of death or nonfatal MI ≤30 days postoperatively MI definition: Universal definition of MI
VASCULAR MORTALITY							
Devereaux 2014[59]	RCT	see above	see above	see above	yes	**Vascular death at 30 days** Events/Total:	death following cardiac or vascular event

						Clonidine: 38/5,009 (0.8%) Placebo: 32/5,001 (0.6%) HR 1.08 (95% CI, 0.74–1.90) p=0.48	
Wijeysundera 2009[60]	see above	2,515 (4 RCTs)	see above	see above	unclear	**Cardiac mortality** Events/Total Alpha-2: 15/1,308 (1.1%) Control: 29/1,207 (2.4%) RR 0.51 (95% CI, 0.27-0.93) p=0.03 no measurable heterogeneity	incidence dominated by one trial of mivazerol
NONFATAL MYOCARDIAL INFARCTION							
Devereaux 2014[59]	see above	see above	see above	see above	yes	**Non-fatal MI at 30 days** Events/Total: Clonidine: 329/5,009 (6.6%) Placebo : 295/5,001 (5.9%) HR 1.11 (95% CI, 0.95-1.30) p=0.18	see above
Wijeysundera 2009[60]	see above	2,817 (8 RCTs)	see above	see above	unclear	**Non-fatal MI** Events/Total: Alpha-2: 178/1,490 (11.9%) Control: 95/1,327 (7.2%) RR 0.49 (95% CI, 0.22-1.09) p=0.08 moderate heterogeneity	incidence dominated by one study of mivazerol
SIDE EFFECTS							
Devereaux 2014[59]	RCT	see above	see above	see above	yes	**Hypotension** Events/Total:	clinically important hypotension (SBP<90)

						Clonidine: 2385/5009 (47.6%) Placebo: 1854/5001 (37.1%) HR 1.32 (95% CI 1.24-1.40) p<0.001 **<u>Bradycardia</u>** Events/Total: Clonidine: 600/5009 (12.0%) Placebo: 403/5001 (8.1%) HR 1.49 (95% CI, 1.32–1.69) p<0.001 **<u>Nonfatal cardiac arrest</u>** Events/Total: Clonidine: 16/5009 (0.3%) Placebo: 5/5001 (0.1%) HR 3.20 (95% CI, 1.17–8.73) p=0.02	or bradycardia (heart rate<55) requiring treatment or study drug discontinuation
Wijeysundera 2009[60]	see above	2845 (10 RCTs)	see above	see above	unclear	**<u>Hypotension</u>** RR 1.32 (95% CI, 1.07-1.62) p=0.009 Moderate heterogeneity **<u>Bradycardia</u>** RR 1.44 (95% CI, 0.89-2.31)	

BP = blood pressure, ECG = electrocardiogram, HR = hazard ratio, MI = myocardial infarction, SBP = systolic blood pressure, RCT = randomized controlled trial, RR = risk ratio.

Supplemental Table 27: GRADE quality assessment for preoperative α_2-agonist initiation*

Quality Assessment						Summary of Evidence			
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with α_2-agonist**	**Anticipated absolute effects without α_2-agonist**	**Estimate HR (95% CI)**	**Quality of evidence**
ALL-CAUSE MORTALITY									
10,010 (1 study)[59]	No serious limitation	No serious limitation	No serious limitation	No serious limitation	Not detected	1.3%	1.3%	HR 1.01 (0.72–1.44)	High
MYOCARDIAL INFARCTION									
10,010 (1 study)[59]	No serious limitation	No serious limitation	No serious limitation	No serious limitation	Not detected	7.3%	6.8%	HR 1.11 (0.95–1.30)	High
CARDIAC/VASCULAR MORTALITY									
10,010 (1 study)[59]	No serious limitation	No serious limitation	No serious limitation	No serious limitation	Not detected	0.8%	0.6%	HR 1.08 (0.74–1.90)	High
HYPOTENSION									
10,010 (1 study)[59]	No serious limitation	No serious limitation	No serious limitation	No serious limitation	Not detected	47.6%	37.1%	HR 1.31 (1.24–1.40)	High

CI = confidence interval, HR = hazard ratio.

* GRADE quality assessment table based on POISE-2 results because more reflective of noncardiac surgery and systematically monitored for MI.

Supplemental Table 28: Summary of findings for perioperative calcium channel blocker initiation

Author	Design	Eligibility Criteria	No. of studies for each type of surgery (no. patients)	Total No. Patients (No. studies)	Results	Comments
ALL-CAUSE MORTALITY						
Wijeysundera 2003[61]	Systematic review of RCTs	published RCTs evaluating CCBs administered immediately before, during or after surgery within 48hrs and reported on death, MI, ischemia and supraventricular tachyarrythmia	2 mixed or major general (n=126) 1 orthopedic (n=50) 5 thoracic (n=682) 1 urologic (n=58) 1 vascular (n=30) (no. type of surgery and patients in overall systematic review)	692 patients (5 trials reporting on all-cause mortality)	**Death** Events/Total: CCB: 5/358 (1.4%) No CCB: 12/334 (3.6%) RR 0.40 (95% CI, 0.14-1.16) heterogeneity p=0.54	prevalence of pre-operative β-blocker use was 13% (62/493) in 3 trials, β-blockers were specific exclusion criterion no relationship between β-blocker use and assignment to CCB arm overall
DEATH AND NON-FATAL MYOCARDIAL INFARCTION COMPOSITE						
Wijeysundera 2003[61]	see above	see above	see above	692 patients (5 trials reporting on death and nonfatal MI)	**Death and MI** RR 0.35 (95% CI, 0.15-0.86) p=0.02 heterogeneity p=0.90	no standard definition for peri-operative MI number of events not reported for this composite outcome
MYOCARDIAL INFARCTION						

Wijeysundera 2003[61]	see above	see above	see above	486 patients (6 trials reporting on MI)	**MI (6 trials)**: Events/Total: CCB: 0/252 (0%) No CCB: 5/234 (2.1%) RR 0.25 (95% CI, 0.05-1.18) p=0.08 heterogeneity p=0.99	no standard definition for peri-operative MI
ISCHEMIA						
Wijeysundera 2003[61]	see above	see above	see above	263 patients (6 trials reporting on ischemia)	**Ischemia (6 trials)**: Events/Total: CCB: 18/133 (13.5%) No CCB: 36/130 (27.7%) RR 0.49 (95% CI, 0.30-0.80) p=0.004 heterogeneity p=0.10 **Ischemia – Diltiazem only** RR 0.34 (95% CI, 0.18-0.63) p=0.0005 heterogeneity p=0.39 **Ischemia – Nifedipine only (1 trial)** RR 1.85 (95% CI, 0.64-5.35) p=0.26 **Ischemia – Verapamil only (1 trial)** RR 0.15 (95% CI, 0.01-2.70) p=0.20	one study reporting on ischemia alone required withholding of all antianginals for at least 24 hours pre-op. No effect on estimate of effect.

HYPOTENSION						
Wijeysundera 2003[61]	see above	see above	see above	341 patients (4 trials reporting on hypotension)	**Hypotension (4 trials)**: Events/Total: 28/341 (8%) RR 1.74 (95% CI, 0.28-10.81) p=0.55 heterogeneity p=0.05	in subgroup analysis, only verapamil was not associated with hypotension
BRADYCARDIA						
Wijeysundera 2003[61]	see above	see above	see above	605 patients (4 trials reporting on bradycardia)	**Bradycardia (4 trials)**: Events/Total: 35/605 (8%) RR 3.32 (95% CI, 0.70-15.66) p=0.13 heterogeneity p=0.07	in subgroup analysis, only verapamil was not associated with bradycardia

CI = confidence interval, CCB = calcium channel blocker, CHF = congestive heart failure, MI = myocardial infarction, RCT = randomized controlled trial, RR = relative risk.

Supplemental Table 29: GRADE quality assessment for preoperative calcium channel blocker initiation

Quality Assessment						Summary of Evidence			
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with CCB**	**Anticipated absolute effects without CCB**	**Pooled Estimate RR (95% CI)**	**Quality of evidence**
ALL CAUSE MORTALITY									
692 patients (5 trials)[61]	Serious limitation (1)	No serious limitation	No serious limitation	Very serious limitation(2)	Likely(3)	1.4%	3.6%	RR 0.40 (0.14-1.16)	Very low
DEATH AND NON-FATAL MYOCARDIAL INFARCTION COMPOSITE									
692 patients (5 trials)[61]	Serious limitation (1)	No serious limitation	No serious limitation	Very serious limitation(2)	Likely(3)	N/A	N/A	RR 0.35 (0.15-0.86)	Very low
MYOCARDIAL INFARCTION									
486 patients (6 trials)[61]	Serious limitation (1)	No serious limitation	No serious limitation	Very serious limitation(2)	Likely(3)	0%	2.1%	RR 0.25 (0.05-1.18)	Very low
HYPOTENSION									
341 patients (4 trials)[61]	Serious limitation (1)	No serious limitation	No serious limitation	Very serious limitation(2)	Likely(3)	N/A	N/A	RR 1.74 (0.28-10.81)	Very low

CCB = calcium channel blocker, CI = confidence interval, N/A = not available, RR = relative risk.

1. Only half the studies double blinded, and only one performed allocation concealment

2. All studies were small with very few events (17 deaths total)
3. Marked geographic variation in studies suggesting possible publication bias
4. Heterogeneity partially accounted for by effect of diltiazem

Supplemental Table 30: Summary of findings for withholding ACEI/ARB in the noncardiac surgery setting

Author	Total no. patients	Design; population	Intervention and comparator	Outcome definition	Systematic outcome monitoring	Results	Comments
HYPOTENSION							
Coriat 1994[62]	51	RCT vascular surgery patients chronically treated for HTN with enalapril or captopril	captopril continued (n=17), enalapril continued (n=9), captopril withdrawn 12h preop (n=19), enalapril withdrawn 24h preop (n=11)	lowest BP within 10 min after induction and before surgical intervention lowest mean BP SBP < 90 at induction	yes	**lowest SBP (mmHg)** – Mean±SD Enalapril: 71±10 (cont) vs 100±15 (stop) Captopril: 86±11 (cont) vs 101±21 (stop) **Lowest mean BP (mmHg)** – Mean±SD Enalapril: 48±8 (cont) vs 69±15 (stop) Captopril: 58±9 (cont) vs 69±17 (stop) **SBP < 90 at induction** ACEI or ARB : 16/21 (cont) vs 6/30 (stop) p<0.001 RR 3.81 (95%CI 1.79-8.10)	risk of co-intervention bias as care givers were probably not blinded to intervention. However, no difference in mean dose of ephedrine between groups. unclear risk of outcome detection bias, frequency and method of BP recording not mentioned unclear allocation concealment and blinding not intention to treat analysis
Betrand 2001[63]	37	RCT vascular surgery patients chronically	ARB given 1h before anesthesia (n=19) vs ARB discontinued	Hypotension SBP <80 lasting >1 min Refractory hypotension	yes	**Hypotension** At least one episode (no.): 19/19 (cont) vs 12/18 (stop) p<0.01 RR 1.50 (95% CI 1.08-2.08)	unclear risk of co-intervention bias unclear allocation concealment and blinding

		treated with ARB	1 day before surgery (n=18)	SBP<100 despite vasopressor (up to 24 mg ephedrine or 100 ug phenylephrine) and requiring terlipressine		Episode of hypotension (no.) - mean±SD 2±1 (cont) vs 1±1 (stop) p<0.01 Duration of episode (min) - mean±SD 8±7 (cont) vs 3±4 (stop) p<0.01 **Refractory hypotension** 6/19 (cont) vs 0/18 (stop) p<0.01	
Schirmer 2007[64]	100	RCT; elective ENT surgery chronically treated with enalapril or captopril for HTN	ACEI given on morning of surgery versus ACEI last dose day before surgery	Hypotension Mean arterial BP <60	yes	**Hypotension** 17/50 (cont) vs 5/50 (stop) p=0.007 RR 3.40 (95%CI 1.36-8.50)	publication in German unclear allocation concealment
COMPOSITE CARDIAC COMPLICATIONS							
Betrand 2001[63]	37	RCT; Vascular surgery patient chronically treated with ARB	ARB given 1h before anesthesia (n=19) versus ARB discontinued 1 day before surgery (n=18)	Composite of cardiac complications	yes	**Cardiac events**: 1/19 (cont) vs 1/18 (stop) one unstable angina and one myocardial ischemia	very low number of events unclear allocation concealment and blinding
MYOCARDIAL INFARCTION							
Kheterpal 2008[65]	17,758	retrospective cohort, registry database	Chronic ACEI-ARB therapy versus no	serum TnI ≥ x5 ULN within the first 4 post-operative days	no	**MI at 7 days** ACEI: 36/5,073 (0.7%) No ACEI: 44/6,828 (0.6%) OR 1.10 (95% CI 0.71-1.71)	propensity score matching but no further covariate adjustment performed

		adult general surgery requiring general anesthesia	chronic ACEI/ARB therapy	with associated cardio-pulmonary symptoms			high troponin elevation threshold to define MI

ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker, BP = blood pressure, cont = medication continued on the day of surgery, ENT = ears, nose and throat, HTN = hypertension, MI = myocardial infarction, preop = preoperatively, OR = odds ratio, RCT = randomized controlled trial, RR = relative risk, SBP = systolic blood pressure, SD = standard deviation, stop = medication interrupted on the day of surgery, TnI = troponin I, ULN = upper limit of normal.

Supplemental Table 31: GRADE quality assessment for withholding ACEI/ARB in the noncardiac surgery setting

Quality Assessment						Summary of Evidence			
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with ACEI/ ARB**	**Anticipated absolute effects without ACEI/ ARB**	**Estimate RR (95% CI)**	**Quality of evidence**
MYOCARDIAL INFARCTION									
17,758 (1 study)[65]	Serious limitation[(1)]	No serious limitation	No serious limitation	No serious limitation	Not detected	0.7%	0.6%	OR 1.10 (0.71-1.71)	Very Low
HYPOTENSION									
188 (3 studies)[62-64]	Serious limitation[(2)]	No serious limitation	No serious limitation	Serious limitation[(3)]	Potential[(4)]	57.8%	23.5%	RR 2.53 (1.08-5.93)	Low

ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker, CI = confidence interval, RR = Relative Risk, OR = odds ratio.

1. High risk of bias: risk of selection bias (i.e., patients treated with ACEI systematically different than patients not on ACEI on other aspects than just medication, potentially not captured by propensity score matching); no data on medication intake on the morning of surgery in the treated group, outcome detection bias due to definition of MI.
2. 3 trials with unclear allocation concealment and unclear blinding, 1 trial did not performed analysis with intention-to-treat principle, risk of co-intervention bias with hypotensive therapy
3. Very low number of events
4. Very few published trials

Supplemental Table 32. Summary of findings for preoperative statin initiation

Author year	Design	Eligibility criteria	Total No. patients (no studies)	Exposure of interest vs comparator	Results	Comments
MORTALITY						
Sanders 2013[66]	systematic review and meta-analysis of RCTs	adult who were scheduled for elective or emergency noncardiac arterial vascular surgery, including both open and endovascular procedures	178 patients (3 trials)	studies that have prescribed statins of any type, dose, commenced de novo or with existing users randomly assigned to different dosages	**<u>All-cause mortality</u>** Events/Total: Statin: 7/105 (6.7%) No statin: 10/73 (13.7%) RR 0.73 (95% CI, 0.31-1.75) heterogeneity: not applicable	only 1 trial had events, other 2 trials had no events in both groups excluded trials from Poldermans' group
NONFATAL MYOCARDIAL INFARCTION						
Sanders 2013[66]	see above	see above	178 patients (3 trials)	see above	**<u>Nonfatal MI</u>** Events/Total Statin: 4/105 (3.8%) No statin: 8/73 (11.0%) RR 0.47 (95% CI, 0.15-1.52) heterogeneity: I^2=0%	excluded trials from Poldermans' group

CI = confidence interval, MI = myocardial infarction, RCT = randomized controlled trial, RR = relative risk.

Supplemental Table 33: GRADE quality assessment for preoperative statin initiation

Quality Assessment						Summary of Evidence			
No of patients (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with statin**	**Anticipated absolute effects without statin**	**RR (95% CI)**	**Quality of evidence**
ALL-CAUSE MORTALITY									
178 (3 trials)[66]	No serious limitation	Unclear[(1)]	No serious limitation	Serious limitation[(2)]	Unlikely	6.7%	13.7%	RR 0.73 (0.31-1.75)	Low
MYOCARDIAL INFARCTION									
178 (3 trials)[66]	No serious limitation	No serious limitation	No serious limitation	Serious limitation[(2)]	Unlikely	3.8%	11.0%	RR 0.47 (0.15-1.52)	Moderate

CI = confidence interval, RR = relative risk.

1. Estimate of effect based on only one study (all 17 events occurred in the same study)
2. Very small number of events and confidence intervals cross the point of no effect

Supplemental Table 34: Summary of findings for perioperative statin continuation

Author year	Design	Population	Total no. patients	Exposure of interest vs comparator	Systematic outcome monitoring	Results	Comments
Xia 2015[67]	RCT	noncardiac surgery patients with stable CAD on long-term statin therapy	550	rosuvastatin (20 mg loading) or placebo 2 h prior to their surgery	CK, CK-MB, and troponin T were collected at 6, 12, and 24h after surgery	**Myocardial infarction at 30 days** Events/Total: Statin: 10/275 (3.6%) Placebo: 22/275 (8.0%) RR 0.45 (95% CI, 0.22-0.94) p=0.02	MI was defined as ischemia due to a primary coronary event, such as plaque erosion and/or rupture, fissuring, or dissection

CAD = coronary artery disease, CI = confidence interval, RCT = randomized controlled trial, RR = relative risk.

Supplemental Table 35: GRADE quality assessment for perioperative statin continuation

Quality Assessment						Summary of Evidence			
No of patients (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with statin**	**Anticipated absolute effects without statin**	**RR (95% CI)**	**Quality of evidence**
MYOCARDIAL INFARCTION									
550 (1 study)[67]	Serious limitation[(1)]	No serious limitation	No serious limitation	No serious limitation	Unlikely	3.6%	8.0%	RR 0.45 (0.22-0.94)	Moderate

CI = confidence interval, RR = relative risk.

1. Randomization using sealed envelope at risk of unblinding of allocation concealment, unclear randomization method, risk of outcome detection bias due to unclear definition of MI

Supplemental Table 36: Summary of findings for preoperative coronary revascularization

Author year	No. patients	Population/ type of surgery	Intervention and comparator	Outcome definition	Systematic outcome monitoring	Results	Comments
ALL-CAUSE MORTALITY							
McFalls 2004[68] (CARP Trial)	510	vascular surgery (AAA vs PAD)	revascularization (PCI or CABG) (n=258) vs. medical therapy (n=252)	all-cause mortality at median follow-up of 2.8 years (IQR, 1.7-3.9)	yes	**Death BEFORE vascular surgery** Intervention: 10/225 (4.4%) Control: 1/237 (0.4%) **All-cause mortality at 30 days** Intervention: 7/225 (3.1%) Control: 8/237 (3.4%) p=0.87 **Long term mortality** Intervention: 70/225 (31%) Control: 67/237 (28.3%) RR 0.98 (95% CI, 0.70-1.37) p=0.92	no difference in mortality but significant delay in surgery – 54 vs. 18 days **exclusion of left main disease 50% or greater blinded outcome assessment no, but stopped early for slow recruitment and reduced length of follow-up
Illuminati 2015[69]	426	patients undergoing CEA with no apparent evidence of CAD, normal ECG, and a normal echo-cardiography	coronary angiography before CEA (n=216) vs. CEA performed without coronary angiography (n=210)	myocardial infarction and all-cause mortality	yes median length of follow-up was 6.2 years.	**All-cause mortality at 30 days** Intervention: 0/216 (0%) Control: 2/210 (1.0%) p=0.24	among 216 patients assigned to coronary angiography before CEA, 68 (31%) had significant CAD on angiography, and 66 of these patients had PCI and then while still taking aspirin and clopidogrel underwent CEA a mean of 4 days

							later and 2 had CABG and CEA combined
MYOCARDIAL INFARCTION							
McFalls 2004[68] (CARP Trial)	510	vascular surgery (AAA vs PAD)	revascularization (PCI or CABG) (n=258) vs. medical therapy (n=252)	all-cause mortality at median f/u 2.8y (IQR, 1.7-3.9)	yes	**MI at 30 days** Intervention: 19/225 (8.4%) Control: 20/237 (8.4%) p=0.99	**exclusion of left main disease 50% or greater blinded outcome adjudication no, but stopped early for slow recruitment and reduced f/u
Illuminati 2015[69]	426	patients undergoing CEA without a previous CAD, normal ECG, normal echocardiography	preoperative coronary angiography (n=216) vs. no preoperative coronary angiography (n=210)	Third universal definition of MI	Yes, trop measured ad 24h after surgery	**MI at 30 days** Intervention: 0/216 (0%) Control: 9/210 (4.3%) OR 0.22 (95% CI, 0.06-0.81) p=0.01	****In the coronary angiogram group:** 68 (31.5%) had significant CAD stenosis; 66 had PCI and 2 had CABG
STROKE							
Illuminati 2015[69]	426	patients undergoing CEA without a previous CAD, normal ECG, normal echocardiography	preoperative coronary angiography (n=216) vs. no preoperative coronary angiography (n=210)		Unclear	**Stroke at 30 days** Intervention: 1/216 (0.5%) Control: 2/210 (1.0%) p=0.62	

AAA = aortic abdominal aneurysm, CABG = coronary artery bypass graft, CAD = coronary artery disease, CEA = carotid endarterectomy, CI = confidence interval, ECG = electrocardiogram, HR = hazard ratio, MI = myocardial infarction, PAD = peripheral artery disease, PCI = percutaneous coronary intervention.

Supplemental Table 37: GRADE quality assessment for preoperative coronary revascularization

Quality Assessment						Summary of Evidence			
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with intervention**	**Anticipated absolute effects without intervention**	**Pooled Estimate RR (95% CI)**	**Quality of evidence**
ALL CAUSE MORTALITY at 30 days									
888 patients (2 studies)[68, 69]	No serious limitation	No serious limitation	Serious limitation(1)	Serious limitation(2)	Unlikely	1.6% (7/441)	2.2% (10/447)	RR 0.79 (0.31-2.04)	Low
MYOCARDIAL INFARCTION at 30 days									
888 patients (2 studies)[68, 69]	No serious limitation	Serious limitation(3)	No serious limitation	Serious limitation(2)	Unlikely	4.3% (19/441)	6.5% (29/447)	RR 0.30 (0.01-6.65)	Low

CI = confidence interval, N/A = not available, RR = relative risk.

1. Only includes vascular surgery patients
2. Very large CI, small number of events
3. One study showed no effect and the other a large magnitude of effect.

Supplemental Table 38: Summary of findings for preoperative smoking cessation

Author year	No. patients	Population/ type of surgery	Design	Intervention and comparator	Systematic outcome monitoring	Results	Comments
CARDIOVASCULAR EVENTS							
Lindstrom 2008[70]	117	general and orthopedic, daily smokers >2 cigarettes daily for ≥ 1year	RCT	weekly smoking cessation counselling with nicotine replacement therapy, 4 weeks before surgery and 4 weeks after surgery versus standard of care	unclear	**Cardiovascular complications** Intervention: 1/48 (2.1%) Control: 1/54 (1.9%) p=1.00	15 post-randomization exclusion CV complications included MI, stroke, TIA, DVT and PE stopped early for slow recruitment
Moller 2002[71]	120	orthopedic, daily smoker	RCT	weekly smoking cessation counselling and nicotine replacement therapy 6–8 weeks before and 10 days after surgery, vs standard of care	unclear	**MI or CHF at 1 month*** Intervention: 0/56 (0%) Control: 5/52 (9.6%) no analysis	12 post-randomization exclusion not intention-to-treat analysis *MI and CHF definition not reported

Thomsen 2010[72]	130	patients scheduled for breast cancer surgery, daily smokers	RCT	smoking cessation counselling therapy with nicotine replacement 3-7 days before surgery, versus standard therapy	unclear	**Major CV events at 30 days** Events/Total Intervention: 2/57 (3.5%) Control: 1/62 (1.6%) no analysis	major CV events definition not reported
Wong 2012[73]	286	adults undergoing elective mixed noncardiac surgery seen in preoperative clininc, smokers ≥10 cigarettes per day during the previous year, and had no period of smoking abstinence longer than 3 months	RCT	varenicline versus placebo, started 1 week before surgery and continued for a total of 12 weeks	yes	**Major CV events in hospital** Events/Total Intervention: 2/151 (1.3%) Control: 4/135 (3.0%) p=0.43	definition of major CV events non reported
SMOKING CESSATION							
Thomsen 2014[74]	Systematic review meta-analysis of RCTs	RCTs of smokers undergoing elective surgery who were	1251 (9 trials)	intervention groups received smoking		**Smoking cessation at time of surgery** Events/Total (%)	treatment effects demonstrated heterogeneity that was mainly explained by the

		randomized to a smoking cessation intervention at least 48 hours before surgery or control		cessation counselling and nicotine replacement treatment Control groups received standard care with little or no information on smoking cessation .	Intensive intervention: 55/104 (52.9%) Control: 5/106 (4.7%) RR 10.76 (95% CI: 4.55-25.46) heterogeneity: I^2=0% Brief intervention: 307/615 (50%) Control: 202/526 (38.4%) RR 1.30 (95% CI, 1.16-1.46) Heterogeneity: I^2=75% **<u>Smoking cessation at 12 month follow-up</u>** Intensive intervention: 31/104 (29.8%) Control: 11/105 (10.5%) RR 2.96 (95% CI, 1.57-5.55) heterogeneity: I^2=38% Brief intervention: 29/166 (17.5%) Control: 28/175 (16.0%) RR 1.09 (95% CI, 0.68-1.76) heterogeneity: I^2=0%	intensity of the intervention. intense interventions included weekly face-to-face or telephone counselling at least 4 weeks before surgery and used nicotine replacement therapy brief interventions included one counselling session and some trials also offered nicotine replacement therapy to some patients

CHF = congestive heart failure, CI = confidence interval, CV = cardiovascular, DVT = deep vein thrombosis, MI = myocardial infarction, PE = pulmonary embolism, ppm = parts per million, RR = relative risk, TIA = transient ischemic attack,

Supplemental Table 39: GRADE quality assessment for preoperative smoking cessation

Quality Assessment						Summary of Evidence			
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Anticipated absolute effects with intervention**	**Anticipated absolute effects without intervention**	**Pooled Estimate RR (95% CI)**	**Quality of evidence**
CARDIOVASCULAR EVENTS									
615 (4 studies)[74]	Serious limitation[(1)]	No serious limitation	No serious limitation	Very serious limitation[(2)]	Potential[(3)]	1.6%	3.6%	RR 0.58 (0.17 – 1.96) I^2=11%	Very low
SMOKING CESSATION at time of surgery									
1867 (12 studies)[74]	Serious limitation[(4)]	Serious limitation[(5)]	No serious limitation	No serious limitation	Unlikely	Intensive intervention 52.9%	Control 4.7%	Intensive intervention RR 10.76 (4.55-25.46) I^2=0%	Low
						Brief intervention 50.0%	Control 38.4%	Brief intervention RR 1.30 (1.16-1.46) I^2=75%	
SMOKING CESSATION up to 12-month follow-up									
836 (5 studies)[74]	Serious limitation[(4)]	No serious limitation[(6)]	No serious limitation	No serious limitation	Potential[(6)]	Intensive intervention 29.8%	Control 10.5%	Intensive intervention RR 2.96 (1.57-5.55) I^2=38%	Low
						Brief intervention 17.5%	Control 16.0%	Brief intervention RR 1.09 (0.68-1.75) I^2=0%	

CI = confidence interval, RR = risk ratio

1. High number of post-randomization inclusion in most studies, small sample size in most studies with potential imbalance in risk factors, unclear definition of cardiovascular events, no systematic outcome monitoring
2. Very small number of events and large confidence interval
3. Several studies did not report on cardiovascular outcomes
4. High number of post-randomization drop outs in most studies, small sample size in most studies with potential imbalance in risk factors
5. High heterogeneity I^2=75% with brief intervention
6. Several studies did not report on long term smoking cessation

Supplemental Table 40: Summary of findings for postoperative troponin monitoring

Author	Design	Total No. Patients (no. studies)	Population	Type of Troponin	Results	Comments
ALL-CAUSE MORTALITY						
Levy 2011[75]	systematic review and meta-analysis of observational studies	3318 patients (14 studies)	12 vascular 7 orthopedic 4 general surgery 3 gynecology/ urology	TnI (10 studies) TnT (3 studies) TnI&TnT (2 studies)	ORs for an elevated Tn after surgery: **All-cause mortality at 12 months**: aOR 6.7 (95% CI 4.1-10.9) I^2=0	individual patient data meta-analysis wide variation across studies in threshold used for an increased Tn
Redfern 2011[76]	systematic review and meta-analysis of observational studies	1873 patients (9 studies)	vascular surgery	TnI (8 studies) TnT (1 study)	**All-cause mortality at 30 days:** Events/Total (%): Tn positive: 25/210 (11.9%) Tn negative: 38/1663 (2.3%) OR 5.03 (95% CI, 2.88-8.79) I^2=24.7% insufficient data to evaluate risk of intermediate-term mortality (>180 days)	focused on isolated Tn elevation in vascular patients who did not fulfill criteria for perioperative MI.
Botto 2014[77]	prospective cohort study	15,065 patients	noncardiac surgery includes emergent/ urgent and elective 20.4% orthopedic 20.3% general, 39.4% low-risk	TnT 4th generation (Roche)	**30 Day Mortality** Events/Total (%): MINS: 117 / 1,194 (9.8%) Controls: 147 / 13,822 (1.1%) aOR 3.90 (95% CI, 2.90–5.27) MINS Population Attributable Risk for Death in the population = 34.0%	MINS Criteria = peak TnT ≥ 0.03 ng/ml due to myocardial ischemia. MINS does not require the presence of an ischemic feature

						84.2% suffering MINS did not experience ischemic symptom 34.9% of patients with MINS had ischemic ECG finding 58.2% of MINS patients did not fulfill universal definition of MI
MAJOR CARDIOVASCULAR EVENTS						
Levy 2011[75]	systematic review and meta-analysis of observational studies	1436 patients (5 studies)	12 vascular 7 orthopedic 4 general 3 gynecology/ urology	TnI (4 studies) TnT (1 study)	**<u>Major Cardiovascular Events</u>:** Events/Total (%): Events among Tn positive patients 162/1436 (11.3%) aOR/aHR ranged from 3.9 - 17.4 for each of the studies*	wide variation across studies in threshold used for an increased Tn * definition of major cardiovascular events varied widely between studies but all 5 studies demonstrated increased Tn was an independent predictor of major cardiovascular event
Botto 2014[77]	prospective cohort study	15,065 patients	noncardiac surgery includes emergent/ urgent (20.4% orthopedic, 20.3% general, 39.4% low-risk)	TnT 4th generation (Roche)	**<u>Major CV events</u>** Events/Total: MINS: 224/1,194 (18.8%) Controls: 325/13,822 (2.4%) OR, 9.59 (95% CI, 7.99–11.51)	major CV events: death, arrest, CHF, CVA

CHF = congestive heart failure, CV = cardiovascular, CVA = cardiovascular arrest, ECG = electrocardiogram, HR = hazard ratio, MI = myocardial infarction, MINS = myocardial injury after noncardiac injury, OR = odds ratio, Tn = troponin

Supplemental Table 41: GRADE quality assessment for postoperative troponin monitoring

Quality Assessment						Summary of Evidence	
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled Estimate aOR (95% CI)**	**Quality of evidence**
ALL-CAUSE MORTALITY AT 30 DAYS							
15,065 (1 study)[77]	Potential limitation	No serious limitation[1]	No serious limitation	No serious limitation	Undetected	aOR 3.90 (2.90–5.27)	Moderate
MAJOR CARDIOVASCULAR EVENTS							
15,065 (1 study)[77]	No serious limitation	No serious limitation[1]	No serious limitation	No serious limitation	Undetected	aOR 9.59 (7.99–11.51)	Moderate

aOR = adjusted odds ratio, CI = confidence interval, N/A = not available.

1. Results based on largest highest quality study

Supplemental Table 42: Summary of findings for postoperative electrocardiography (ECG) monitoring

Author year	Design	Type of surgery	Total no. patients	ECG monitoring and ischemia definition	Systematic outcome monitoring	Results	Comments
Rinfret 2004[78]	prospective cohort study	major noncardiac surgery, age ≥50 years old	3564	ECG in recovery room and on the first, third and fifth postoperative days ischemia definition: new ST-segment depression (≥1 mm in ≥2 leads), ST segment elevation (≥1 mm in ≥2 leads), or other changes consistent with ischemia or strain (including T wave inversion)	CK-MB immediately after surgery, on the evening after surgery and on the next 2 mornings*	**Major CV events**** Events/Total: Ischemia on ECG: 18/268 (6.7%) No ischemia on ECG: 62/3296 (1.9%) **Ischemia on ECG** aOR 2.0 (95% CI, 1.1-3.7) Other variables in the model: RCRI, SBP<80mmHg during surgery, duration of surgery, estimated blood loss, heart rate>120 BPM during surgery, β-blocker therapy, pre-operative ECG abnormalities, initial SBP before surgery, age, hypertension, peripheral vascular disease, and American Society of Anesthesia class **Unclear duration of follow-up, presumed "in-hospital"	major CV events: MI, pulmonary edema, VF or primary cardiac arrest, and complete heart block MI definition: (1) peak CK-MB >5% of high total CK, (2) peak CK-MB >3% of high total CK in the presence of ECG changes consistent with ischemia or infarction, 3) peak CK-MB levels exceeded the normal range and the ratio of CK-MB to total CK was >0.0278 or, in the setting of ECG changes >0.0167 risk of selection bias since only patients who had ECG performed were included in the study (82.7% inclusion) *14.4% of patients did not get systematic CKMB monitoring blinded outcome assessment

Hietala 2014[79]	prospective cohort study	hip fracture	200	12 lead ECG before surgery and daily x 2 after surgery ischemia definition: European Society of Cardiology definition	troponin-T before and after surgery daily x 2	**<u>Mortality at 30 days</u>** no difference detected in the prognosis between patients with no ischemic ECG and those with T-wave inversion or ST depression ST elevation (n=7) had 29% mortality at 30 day	high incidence of ischemia on ECG (52%)
Bottiger 2004[80]	prospective cohort study	vascular surgery	55	ECG at 15min, q4h x 24h, then q8h x 24h, and hten q12h x 24h holter 8h before surgery to 96h after surgery ischemia definition: new negative T wave, ST depression/ elevation > 0.2 mV in one or more leads	CKMB, troponin T and troponin I at 84 hours after surgery	**<u>Myocardial ischemia at 96 hours</u>** **ECG** Events/Total Ischemia on ECG: 17/24 No ischemia on ECG: 1/31 no risk-adjusted analysis reported	myocardial ischemia defined as elevated troponin postoperative concordance of ECG and TnT to detect ischemia = 85% concordance of Holter and TnT to detect ischemia = 72% 88% of patients developing evidence of ischemia began to show signs on ECG at 15 min after surgery
Landesberg 2001[81]	prospective cohort study	vascular surgery	185	continuous 12 lead ECG x 48-72h after surgery ischemia definition: ST depression/	troponin-I and CK-MB immediately after surgery and daily x 3	**<u>Myocardial infarction in-hospital</u>** **ECG** Events/Total Ischemia on ECG: 12/38 No ischemia on ECG: 0/147	no risk-adjusted analysis reported perioperative myocardial ischaemia detected by 12-lead ECG was identifiable in 88% of patients 15 min after surgery

				elevation ≥0.2 mV in one lead or ≥0.1 mV in two contiguous leads that lasted >10 minutes		no significant association between ischemia on ECG and MI in multivariable analysis <u>other variables in the model</u>: diabetes, LVH	

aOR = adjusted odds ratio, AAA = abdominal aortic aneurysm, BPM = beats per minute, CI = confidence interval, CKMB = creatine kinase MB isoenzyme, CV = cardiovascular, ECG = electrocardiogram, LVH = left ventricular hypertrophy, MI = myocardial infarction, mV = millivolt, RCRI = revised cardiac risk index, SBP = systolic blood pressure, TnT = troponin T, VF = ventricular fibrillation.

Supplemental Table 43: GRADE quality assessment for postoperative ECG monitoring*

Quality Assessment						Summary of Evidence	
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled Estimate aOR (95% CI)**	**Quality of evidence**
MAJOR CARDIOVASCULAR EVENTS							
3564 patients (1 study)[78]	Serious limitation(1)	No serious limitation	No serious limitation	Serious limitation(2)	Potential limitation(3)	aOR 2.19 (1.22-3.93)	Low

aOR = adjusted odds ratio, CI = confidence interval, ECG = electrocardiogram.

1. Risk of selection bias since only patients who had ECG performed were included in the study (82.7% inclusion) and risk of outcome detection bias since 14.4% of patients did not get systematic CKMB monitoring
2. Very small number of events
3. Other small studies did not report on major cardiovascular outcomes.

*GRADE quality assessment only on largest study by Rinfret 2004 since had the most weight in grading recommendation.

Supplemental Table 44: Summary of findings for postoperative telemetry monitoring

Author year	Design	Type of surgery	Total no. patients	Telemetry monitoring	Ischemia definition	Systematic outcome monitoring	Results	Comments
Landesberg 1993[82]	prospective cohort study	vascular surgery	151	telemetry (3 bipolar leads) 1 day before, during and 1 day after surgery	downsloping or horizontal ST segment depression ≥0.1mV lasting 60s and separated from a previous episode >60s or ST elevation ≥0.2mV. if baseline ST depression, need J point and ST segment fall at least 0.1mV below baseline	CKMB q6h x 24h, then postoperative day 3 and 5	**Major CV events in hospital** **Postoperative ischemia** aRR = 2.1* (p=0.43) **Cumulative postoperative ischemic duration > 2 h** aOR = 21.7* (p=0.001) other variable in the model: Detsky risk score	incidence ischemia on telemetry 13/151 (8.6%) blinded outcome assessment major CV events: MI, CHF, UA *95% CI not reported
Raby 1992[83]	prospective cohort study	peripheral vascular surgery	115	telemetry (bipolar inferior/lateral leads) at least 24 hours prior, during and up to 72 hours after surgery	downsloping or horizontal ST depression ≥ 1mm, present at 60ms from J point, present for at least 60 seconds	CKMB every 8 to 12 hours on post-operative days 1 and 2	**Major CV events in hospital** **Postoperative ischemia** aOR 24.8* (p<0.001) *95% CI not reported other variable in the model: hypertension, history of MI, CHF, CAD, preop ischemia.	major CV events: death from cardiac cause, MI, UA and ischemic pulmonary edema. blinded outcome assessment 96% monitored for at least 24 hours post op, 70% monitored

								for 48 hours post op
Mangano 1990[84]	prospective cohort study	non cardiac surgery with general anesthesia	474 (only men)	2 Channel Holter Monitor for up to 2 days preoperative, intra-operative and ad post-operative day 2	downsloping or horizontal ≥ 1mm ST depression or ≥ 2mm ST elevation for at least 1 minute	CK and CKMB at day 1 and day 5	**Major CV events in hospital** **Ischemia on Holter** Events/Total: 83/474 (18%) aOR 2.8 (95% CI, 1.3-4.9) other variables in the model: history of dysrhythmia, preoperative use of digoxin for CHF, vascular surgery	major CV events: Cardiac death, MI, UA blinded outcome assessment

aOR = adjusted odds ratio, aHR = adjusted hazard ratio, CAD = coronary artery disease, CHF = congestive heart failure, CKD = chronic kidney disease, CKMB = creatine kinase MB isoenzyme, CV = cardiovascular, MI = myocardial infarction, mm = millimeter, mV = millivolt, OR = odds ratio, Tn = troponin, UA = unstable angina.

Supplemental Table 45: GRADE quality assessment for postoperative telemetry monitoring

Quality Assessment						Summary of Evidence	
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Estimate aOR (95% CI)**	**Quality of evidence**
MAJOR POST OPERATIVE CARDIAC EVENTS (IN-HOSPITAL)							
740 (3 studies)[82-84]	Serious limitation[(1)]	No serious limitation	No serious limitation	Serious limitation[(2)]	Potential	aOR 2.8 (1.3-4.9)[84]	Low

aOR = adjusted odds ratio, CI = confidence interval.

1. Potential selection bias
2. Small number of events and large confidence interval

Supplemental Table 46: Summary of findings for postoperative pulmonary artery catheter monitoring

Author	Design	Total No. Patients (no. studies)	Population	Intervention/Comparator	Results	Comments
ALL-CAUSE MORTALITY						
Shah 2005[85]	systematic review and meta-analysis of RCTs	2667 (8 trials)	1 RCT hip fracture 2 RCTs high risk surgery 5 RCTs vascular surgery	2 RCTs: PAC vs no PAC 6 RCT: PAC with hemodynamic targets vs no PAC	**Mortality** Events/Total: PAC: 92/1389 (6.6%) No PAC: 101/1318 (7.7%) OR 0.84 (95%CI, 0.63-1.13)* I^2 = 57% (p=0.03)	*Pooled analysis only including RCTs in noncardiac surgery patients
PULMONARY EMBOLISM						
Shah 2005[85]	systematic review and meta-analysis of RCTs	1994 (1 trial)	1 RCT high risk surgery	PAC with hemodynamic targets vs no PAC	**Pulmonary embolism** Events/Total: PAC: 8/997 (0.8%) No PAC: 0/997 p=0.004	only one study reported on pulmonary embolism

PAC = pulmonary artery catheter, OR = odds ratio, RCT = randomized controlled trial.

Supplemental Table 47: GRADE quality assessment for postoperative pulmonary artery catheter monitoring

Quality Assessment						Summary of Evidence	
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled Estimate OR (95% CI)**	**Quality of evidence**
ALL CAUSE MORTALITY							
2667 (13 studies)[85]	No serious Limitation[(1)]	Serious limitation[(2)]	No serious limitation	Serious limitation[(3)]	Unlikely	OR 0.84 (0.63-1.13)	Moderate

CI = confidence interval, PAC = pulmonary artery catheter, OR = odds ratio, RCT = randomized controlled trial.

1. RCTs on use of pulmonary artery catheters cannot be blinded
2. Moderate heterogeneity (I^2 = 57%)
3. 6 studies were small with 38 deaths in 673 patients and wide confidence intervals; however large Sandham study consistent with overall point estimate

Supplemental Table 48: Summary of findings for postoperative shared care models

Author Year	Design	Intervention/Control	No. of patients (no. studies)	Total No. Patients for each study type	Results	Comments
ALL-CAUSE MORTALITY						
Grigoryan 2013[86]	systematic review and meta-analysis of RCTs or observational studies	intervention: inpatient systematic multidisciplinary approach to hip fracture management involving an orthopedic surgeon and a geriatrician control: standard care group which consisted of a surgeon requesting a consult from a medical specialist or geriatrician as needed.	9096 patients (18 studies)	8 RCTs (1552 patients) 4 prospective cohort studies with retrospective controls (2362 patients) 6 retrospective chart reviews (5182 patients)	**In-hospital Death** Events/Total: 240/3609 (7%) RR 0.60 (95% CI, 0.43-0.84) I^2 = 28.4% **Long-term mortality** Events/Total: 1051/6325 (16.6%) RR 0.83 (95% CI, 0.74-0.94) I^2 = 0%	no assessment to explain heterogeneity long-term mortality = 12 months after surgery

CI = confidence interval, RCT = randomized controlled trial, RR = relative risk.

Supplemental Table 49: GRADE quality assessment for postoperative shared care models

Quality Assessment						Summary of Evidence	
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Pooled Estimate RR (95% CI)**	**Quality of evidence**
ALL CAUSE MORTALITY – SHORT TERM							
3609 patients (9 studies)[86]	Serious limitation(1)	No serious limitation	Serious limitation(2)	No serious limitation	Likely(2)	RR 0.60 (0.43-0.84)	Very low
ALL CAUSE MORTALITY – LONG TERM							
6325 patients (11 studies)[86]	Serious limitation(1)	No serious limitation	Serious limitation(2)	No serious limitation	Likely(2)	RR 0.83 (0.74-0.94)	Very low

CI = confidence interval, RR = relative risk.

1. All studies rated as good to fair with based on United States Preventative Services Task Force criteria; however, matched observational studies also included
2. Meta-analysis only for orthopedic elderly population, no studies for mixed noncardiac surgery population.

Supplemental Table 50: Summary of findings for ASA and statin in patient who suffer myocardial injury after noncardiac surgery

Author year	Type of study	Population	Total no. patients	Intervention/ Control	Results	Outcome definition	Comments
Foucrier 2014[87]	retrospective case-control study	major vascular surgery, patients who suffered a MINS	66	cardio-vascular medication intensification vs no intensification	**Cardiac events at 1 year** with cardiovascular medication intensification HR 0.63 (95% CI, 0.10–1.19) without cardiovascular medication intensification HR 1.77 (95% CI, 1.13–2.42)	death, MI, myocardial revascularization, or pulmonary edema requiring hospitalization	cardiovascular medication : antiplatelet, statin, β-blocker, ACEI no analysis for individual medication
Devereaux 2011[88]	prospective cohort	noncardiac surgery, patients who suffered an MI after noncardiac surgery	415	ASA at discharge Statin at discharge	**30-day mortality** statin vs no statin aOR 0.26 (95% CI, 0.13-0.54) ASA vs no ASA aOR 0.54 (95% CI, 0.29-0.99)	all-cause mortality	

ACEI = angiotensin-converting enzyme inhibitor, aOR = adjusted odds ratio, ASA = acetylsalicylic acid, CI = confidence interval, HR = hazard ratio, MI = myocardial infarction, MINS = myocardial injury after noncardiac surgery.

Supplemental Table 51: GRADE quality assessment for postoperative ASA and statin after cardiac complications

Quality Assessment						Summary of Evidence	
No of participants (No studies)	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Estimate aOR (95% CI)**	**Quality of evidence**
ALL-CAUSE MORTALITY							
481 (2 studies)[87, 88]	Serious limitation(1)	No serious limitation	No serious limitation(2)	Serious limitation(3)	Not detected	ASA: aOR 0.54 (0.29-0.99) Statin: aOR 0.26 (0.13-0.54)	Moderate

aOR = adjusted odds ratio, ASA = acetylsalicylic acid, CI = confidence interval.

1. Potential selection bias in physicians' decision to prescribe postoperative statin or inability of patients to take oral statin due to illness. Postoperative troponin blinded might have resulted in missed MIs.
2. Due to the large body of literature of ASA and statin benefit after MI in nonsurgical settings, the panel felt it represented a factor to consider to upgrade the quality of evidence
3. Relatively large confidence interval

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