National Institute for Health and Care Excellence

Preoperative tests (update)

Routine preoperative tests for elective surgery

NICE guideline NG45

Appendix H: Clinical evidence tables

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Contents

Appendix H: Clinical evidence tables

H.1 Resting electrocardiography

H.1.1 Prognostic review

Table 1: Biteker 2012[7]

Reference	Biteker 2012
Study type and analysis	Single prospective cohort Multivariate logistic regression
Number of participants and characteristics	n=660 Patients aged >18 years scheduled for non-cardiac, non-vascular surgery Mean age: 65.3 ± 14 Male sex: 348 (52.8%) Mean BMI: 28.4 ± 12.4
Prognostic variable(s)	Resting electrocardiography (ECG)
Confounders OR stratification strategy	Age, gender, comorbidity, pharmacological treatment, QRS duration, clinical risk indicators.
Outcomes and effect sizes	Perioperative cardiovascular event: adjusted OR [95% CI]: 1.04 (1.03–1.06)
Comments	Short follow-up period. High risk surgery not included in analysis. Only patients with a preoperative cardiovascular work-up were included.

Table 2: Fritsch 2012[15]

Reference	Fritsch 2012

Reference	Fritsch 2012
Study type and analysis	Single centre prospective cohort Multivariate forward likelihood ratio
Number of participants and characteristics	n=1363 Patients scheduled for elective surgery Mean age: 50.2 ± 19.9 Female sex: 764 (56.1%)
Prognostic variable(s)	Resting ECG
Confounders OR stratification strategy	Age, gender, invasiveness of procedure, comorbidity, preoperative tests
Outcomes and effect sizes	Cardiac, cerebrovascular, respiratory and bleeding complications: adjusted OR [95% CI]: 2.81 (1.36–5.82)
Comments	Length of follow up not standardised Assessor blinding not clear.

Table 3: Koike 1999 [29]

Reference	Koike 1999
Study type and analysis	Single centre prospective cohort Multivariate Cox proportional hazard analysis
Number of participants and characteristics	n=114 Patients scheduled for hip fracture surgery Mean age: 81 (range 65 to 98)
Prognostic variable(s)	Resting ECG
Confounders OR stratification strategy	Age, gender, type of fracture, preoperative interval, intercurrent illness, type of housing, Goldman's cardiac risk index, preoperative dependence, mental function, anaemia, blood urea, ECG abnormality, malignancy, malnutrition.
Outcomes and	One year mortality: adjusted RR [95% CI]:

Reference	Koike 1999
effect sizes	1.54 (0.95–2.49)
Comments	Inter-rater reliability unknown. Assessor blinding not clear.

Table 4: Kyo 1993[30]

Reference	Kyo 1993
Study type and analysis	Single centre retrospective cohort Multivariate Cox proportional hazard analysis
Number of participants and characteristics	n=427 Patients scheduled for hip fracture surgery Mean age: Female 76.6 (range 48 to 99) Male 80.7 (range 36 to 95) Female sex: 333
Prognostic variable(s)	Resting ECG
Confounders OR stratification strategy	Age, gender, prefracture ADL, ECG, EEG, Hasewaga's score, haemoglobin, total protein, type of fracture.
Outcomes and effect sizes	Survival rate: adjusted HR [95% CI]: 2.66 (1.54–4.59)
Comments	Assessor blinding not clear.

Table 5: Landesberg 2007 [31]

Reference	Landesberg 2007
Study type and analysis	Single centre retrospective cohort Multivariate Cox proportional hazard analysis
Number of participants	n=624 Patients scheduled for major vascular surgery

Reference	Landesberg 2007
and characteristics	Mean age: 65.8 ± 11.0 Female: 155 (24.8%) Male: 469 (75.2%)
Prognostic variable(s)	Resting ECG
Confounders OR stratification strategy	Age, diabetes mellitus, cerebrovascular disease, IHD, congestive heart failure, kidney disease, preoperative CR, calcium blockers, hypolipidaemic agents
Outcomes and effect sizes	Long-term survival: adjusted HR [95% CI]: 1.94 (1.48–2.54)
Comments	Retrospective. No external validation.

Table 6: Liu 2002 [33]

Reference	Liu 2002
Study type and analysis	Single centre prospective cohort Multivariate stepwise logistic regression
Number of participants and characteristics	n=513 Patients scheduled for non-cardiac surgery Mean age: 78 ± 6.1 Female: 282 (55%) Male: 231 (45%)
Prognostic variable(s)	Resting ECG
Confounders OR stratification strategy	Confounding variables not clearly described
Outcomes and effect sizes	Post-operative cardiac complications: adjusted OR [95% CI]: 0.63 (0.28–1.42)

Reference	Liu 2002
Comments	Lack of clarity regarding confounding variables. Potential for systematic error as ECG findings were considered in unison with general health.

Table 7: Vanklei 2007 [42]

Reference	Vanklei 2007
Study type and analysis	Multicentre prospective cohort Multivariate logistic regression
Number of participants and characteristics	n=2967 Patients scheduled for non-cardiac surgery Male gender: 1661 (56.0%) Age: 64.9 SD ± 9.2
Prognostic variable(s)	Resting ECG
Confounders OR stratification strategy	Age, gender, high risk surgery, ischaemic heart disease, right bundle branch block, left bundle branch block
Outcomes and effect sizes	Post-operative myocardial infarction: Left bundle branch block: adjusted OR [95% CI] 3.1 (1.0–9.61) Right bundle branch block: adjusted OR [95% CI] 2.1 (1.0–4.41) Death during admission: Left bundle branch block: adjusted OR [95% CI] 3.5 (1.3–9.42)
Comments	Multiple raters not adjusted for. Retrospective. Length of follow up not standardised.

H.2 Resting echocardiography

H.2.1 Intervention review

Table 8: Poso 2014 [36]

Study	Poso 2014[36]
Study type	Non-randomised comparative study
Number of studies (number of participants)	n=46
Countries and setting	Conducted in Sweden; setting: Department of Cardiothoracic Anaesthesia, Heart Centre, Umea University, Sweden
Line of therapy	1st line
Duration of study	Not clear
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: transthoracic echocardiography
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Morbidly obese subjects scheduled for bariatric surgery by laparoscopic Roux-en-Y gastric bypass surgery
Exclusion criteria	Subjects with untreated systemic or pulmonary hypertension, atrial fibrillation, pacemaker, unstable angina pectoris, and significant failure of heart valves
Recruitment/selection of patients	Consecutive patients
Age, gender and ethnicity	Age – mean (SD): intervention 43 (14); control 46 (11). Gender (M:F): 9/37. Ethnicity: not reported.
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Resting Echocardiography. Transthoracic echocardiography in supine position. Sequoia-512, Acuson-Siemens, Mountain View, CA or Vivid 6, GE Vingmed, Horten, Norway ultrasound devices were used. Duration: echocardiography completed 45 minutes preoperatively and followed up 30 days post-operatively. Concurrent medication/care: not stated. (n=20) Intervention 2: Control – no echocardiography. Duration: 30 days post-operative. Concurrent medication/care: not stated.
Funding	Academic or government funding (Norrbotten County Council)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RESTING ECHOCARDIOGRAPHY versus CONTROL	

Study	Poso 2014[36]
Length of stay: - Group 1: mean 2.4 days (SD 2); n=26, Group 2: mean 1.7 days (SD 0.7); n=20; risk of bias: high; indirectness of outcome: no indirectness All-cause mortality: Group 1: 0/26, Group 2: 0/20; risk of bias: very high; indirectness of outcome: no indirectness – could not be meta-analysed.	
Protocol outcomes not reported by the study	Quality of life; complications related to surgery or anaesthesia; adverse events caused by testing; composite outcomes (for example MACE); optimisation of medical therapy; operative delay at up to surgery; change in management at prior to surgery; hospital readmission

Table 9: Wijeysundera 2011[47]

Study	Wijeysundera 2011[46]
Study type	Non-randomised comparative study
Number of studies (number of participants)	1 (n=70996)
Countries and setting	Conducted in Canada; setting: acute care hospitals in Ontario Canada (1 April 1999–31 March 2008)
Line of therapy	Not applicable
Duration of study	30 days follow up post-surgery.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: resting echocardiography
Stratum	Overall
Subgroup analysis within study	Post-hoc subgroup analysis
Inclusion criteria	Preoperative adult population undergoing non-cardiac surgery. Echocardiography group versus control group.
Exclusion criteria	None
Recruitment/selection of patients	Retrospective, propensity scores for matching
Age, gender and ethnicity	Age–mean (SD): echocardiography group=70.7, no echocardiography group=67.0. Gender (M:F): 127964/136859. Ethnicity: not reported.
Further population details	Cardiovascular: Coronary artery disease: Entire cohort (echocardiography group=9374/40084, no echocardiography group=20712/224739). Matched cohort (echocardiography group=8011/35498, no echocardiography group=8021/35498).

	Congestive heart disease: Entire cohort (echocardiography group=2174/40084, no echocardiography group=3950/224739). Matched cohort (echocardiography group=1860/35498, no echocardiography group=1866/35498). Atrial fibrillation: Entire cohort (echocardiography group=2398/40084, no echocardiography group=4830/224739). Matched cohort (echocardiography group=2012/35498, no echocardiography group=2084/35498). Cardiac valvular disease: Entire cohort (echocardiography group=692/40084, no echocardiography group=604/224739). Matched cohort (echocardiography group=446/35498, no echocardiography group=425/35498). Mechanical cardiac valve: Entire cohort (echocardiography group=305/40084, no echocardiography group=340/224739). Matched cohort (echocardiography group=255/35498, no echocardiography group=225/35498). Hypertension: Entire cohort (echocardiography group=30964/40084, no echocardiography group=138374/224739). Matched cohort (echocardiography group=27185/35498, no echocardiography group=27361/35498). Thromboembolic disease: Entire cohort (echocardiography group=273/40084, no echocardiography group=1160/224739). Matched cohort (echocardiography group=241/35498, no echocardiography group=244/35498). Pulmonary disease: Entire cohort (echocardiography group=4604/40084, no echocardiography group=15873/224739). Matched cohort (echocardiography group=3920/35498, no echocardiography group=3987/35498). Cerebrovascular: Entire cohort (echocardiography group=2126/40084, no echocardiography group=5443/224739). Matched cohort (echocardiography group=1877/35498, no echocardiography group=1917/35498). Cholesterol: not applicable/not stated/unclear Diabetes: Entire cohort (echocardiography group=10741/40084, no echocardiography group=43159/224739). Matched cohort (echocardiography group=9451/35498, no echocardiography group=9562/35498).

	Obesity: not applicable/not stated/unclear Peripheral vascular disease: Entire cohort (echocardiography group=7647/40084, no echocardiography group=15243/224739). Matched cohort (echocardiography group=5921/35498, no echocardiography group=5811/35498). Renal disease: Entire cohort (echocardiography group=1731/40084, no echocardiography group=4363/224739). Matched cohort (echocardiography group=1438/35498, no echocardiography group=1478/35498). Respiratory disease: not applicable/not stated/unclear
Surgery types	Abdominal aortic aneurysm repair: Entire cohort (echocardiography group=4288/40084, no echocardiography group=6115/224739). Matched cohort (echocardiography group=3128/35498, no echocardiography group=3062/35498). Carotid endarterectomy: Entire cohort (echocardiography group=3172/40084, no echocardiography group=5710/224739). Matched cohort (echocardiography group=2800/35498, no echocardiography group=2794/35498). Peripheral vascular bypass: Entire cohort (echocardiography group=2684/40084, no echocardiography group=7802/224739). Matched cohort (echocardiography group=2206/35498, no echocardiography group=2180/35498). Total hip replacement: Entire cohort (echocardiography group=7143/40084, no echocardiography group=52667/224739). Matched cohort (echocardiography group=6571/35498, no echocardiography group=6639/35498). Total knee replacement: Entire cohort (echocardiography group=11277/40084, no echocardiography group=79998/224739). Matched cohort (echocardiography group=10480/35498, no echocardiography group=10554/35498).

	Large bowel surgery: Entire cohort (echocardiography group=5807/40084, no echocardiography group=47153/224739). Matched cohort (echocardiography group=5271/35498, no echocardiography group=5230/35498). Liver resection: Entire cohort (echocardiography group=216/40084, no echocardiography group=1539/224739). Matched cohort (echocardiography group=189/35498, no echocardiography group=172/35498). Whipple procedure: Entire cohort (echocardiography group=171/40084, no echocardiography group=1358/224739). Matched cohort (echocardiography group=158/35498, no echocardiography group=139/35498). Pneumonectomy or lobectomy: Entire cohort (echocardiography group=2400/40084, no echocardiography group=6560/224739). Matched cohort (echocardiography group=2100/35498, no echocardiography group=2148/35498). Gastrectomy or oesophagectomy: Entire cohort (echocardiography group=1116/40084, no echocardiography group=4547/224739). Matched cohort (echocardiography group=1005/35498, no echocardiography group=985/35498). Nephrectomy: Entire cohort (echocardiography group=1459/40084, no echocardiography group=8921/224739). Matched cohort (echocardiography group=1300/35498, no echocardiography group=1296/35498). Cystectomy: Entire cohort (echocardiography group=351/40084, no echocardiography group=2369/224739). Matched cohort (echocardiography group=290/35498, no echocardiography group=299/35498).
Indirectness of population	No indirectness: Preoperative adult population undergoing non-cardiac surgery
Interventions	(n=35498) Intervention 1: Resting echocardiography. Preoperative resting echocardiography. Duration: preoperative resting echocardiography.

	Concurrent medication/care: perioperative care Epidural anaesthesia: echocardiography group=9932/35498, no echocardiography group=9906/35498 Arterial line: echocardiography group=15751/35498, no echocardiography group=15718/35498 Central venous line: echocardiography group=5939/35498, no echocardiography group=5836/35498 Pulmonary artery catheter: echocardiography group=1914/35498, no echocardiography group=1894/35498 (n=35498) Intervention 2: Control – no echocardiography. Preoperative resting echocardiography. Duration: preoperative testing. Concurrent medication/care: preoperative resting echocardiography. Comments: retrospective, propensity scores for matching
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RESTING ECHOCARDIOGRAPHY versus NO ECHOCARDIOGRAPHY Length of stay: MD 0.31 (95%CI 0.17 to 0.44); risk of bias: high; indirectness of outcome: no indirectness All-cause mortality at 30 days: Group 1: 693/35498, Group 2: 609/35498; risk of bias: high; indirectness of outcome: no indirectness Complications related to surgery or anaesthesia: Surgical site infection at 30 days; Group 1: 4690/35498, Group 2: 4570/35498; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Quality of life; adverse events caused by testing; composite outcomes (for example MACE); optimisation of medical therapy; operative delay at up to surgery; change in management at prior to surgery; hospital readmission

H.3 Cardiopulmonary exercise testing (CPET)

H.3.1 Intervention review

Table 10: Goodyear 2013[17]

Study	Goodyear 2013 [17]
Study type	Retrospective non-randomised observational study with matched historical control. Patients undergoing abdominal aortic aneurysms (AAA) repair at the University Hospitals Coventry and Warwickshire NHS Trust
Number of studies (number of participants)	1 (n=316): CPET=188, historical control=128
Countries and setting	UK, University Hospitals Coventry and Warwickshire NHS Trust
Line of therapy	Not applicable
Duration of study	Follow-up 30 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Post-operative CPET
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients elective to undergo infra-renal AAA (AAA≥5.5 cm)
Exclusion criteria	Patients diagnosed with thoracoabdominal or suprarenal aneurysms, repairs of ruptured or urgent (symptomatic, non-ruptured) AAA.
Recruitment/selection of patients	Consecutive cohort infra-renal AAA patients (2007-2011) / Consecutive historical control infra-renal AAA patients (2003-2007 pre-CPET era)
Age, gender and ethnicity	Age (years, median [95% CI]): Historical control: 74 (71.9 to 74.4) CPET: CPET-pass (n=131): 74 (72.1 to 74.7) CPET-fail (n=35): 75 (73.1 to 78.3) CPET-submaximal (n=22): 80.5 (76.7 to 81.4) BMI (kg/m^2, median [95% CI]): Historical control: pre-CPET era (n=128): N/A

Study	Goodyear 2013 [17]
	CPET: CPET-pass (n=131): 27.3 (26.8 to 28.2) CPET-fail (n=35): 30 (27.6 to 31.4) CPET-submaximal (n=22): 27.6 (25.7 to 31.3)
Further population details	Aneurysm size (cm, median [95% CI]): Historical control: (n=128): 6.3 (6.5 to 6.9) CPET-pass: (n=131): 6.1 (6.2 to 6.6) CPET-fail: (n=35): 6.1 (6 to 6.7) CPET-submaximal: (n=22): 6.3 (6 to 6.9)
Surgery types	Open AAA repair performed by consultant vascular surgeon or a consultant-supervised higher surgical trainee using a transperitoneal inlay repair with knitted Dacron graft prostheses. EVAR AAA repairs were planned and performed by a consultant vascular surgeon and consultant interventional radiologist. The EVAR devices used were the Cook Zenith (Cook, Brisbane, Australia) endovascular system, Medtronic Endurant (Medtronic, Minneapolis, MN, USA) and Lombard Aorfix (Lombard Medical, Oxfordshire, UK).
Indirectness of population	No indirectness
Interventions	CPET
Funding	Academic or government funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Preoperative CPET versus NO preoperative CPET

Length of inpatient stay:

- EVAR:

Median length of inpatient stay at days: 4.0 (95% CI 4.6 to 6.7) versus 6.0 (95% CI 5.3 to 8.6); risk of bias: very high; indirectness of outcome: no indirectness

- Open surgery:

Median length of inpatient stay at days: 10.0 (95% CI 10.3 to 13.5) versus 13.0 (95% CI 13.9 to 19.0); risk of bias: very high; indirectness of outcome: no indirectness

30 day mortality:

- EVAR

Study	Goodyear 2013 [17]
Group 1: 0/25; Group 2:1/69; risk of bias: very high; indirectness of outcome: no indirectness - Open surgery Group 1: 4/100; Group 2: 13/103; risk of bias: very high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Quality of life; adverse events caused by testing; composite outcomes (for example MACE); optimisation of medical therapy; operative delay at up to surgery; change in management at prior to surgery; hospital readmission

H.3.2 Prognostic review

Table 11: Barakat 2015[4]

Reference	Barakat 2015
Study type and analysis	Prospectively gathered cohort data on consecutive patients (September 2011–September 2013) Multivariable logistic regression analysis CPET was not used to determine fitness for surgery or perioperative management
Number of participants and characteristics	n=130 selected for endovascular or open AAA repair (all successfully completed preoperative CPET) Needed to be able to perform an exercise test on a treadmill and provide informed consent Male=89.2% Age=mean 74.2 (SD: 6.9) BMI=27.8 (SD: 4.2) 44.6% had ischaemic heart disease 16.2% chronic airway disease 17.7% cerebrovascular disease 12.3% diabetes
Prognostic variable(s)	Peak VO_2 VE/VCO_2 AT
Confounders OR	Age, sex, method of repair, and CPET parameters (peak VO_2, V_E/VCO_2 and AT).

Reference	Barakat 2015
stratification strategy	
Outcomes and effect sizes	• Complications during post-operative hospital stay • Cardiac complications: ischaemic complications (MI presenting as chest pain with ECG changes and elevation of cardiac enzymes, or new-onset unstable angina); new-onset arrhythmia requiring management or lasting >1 hour; need for inotropic support for at least 12 hours; and occurrence of congestive cardiac failure defined by clinical and radiological changes. • Pulmonary complications: occurrence of pneumonia by clinical features with either a positive sputum culture or radiographic changes; need for mechanical ventilation for >48 hours in post-operative course; unplanned tracheal re-intubation; pulmonary embolism determined by positive CT pulmonary angiogram. Cardiac complications: OR (95%CI): Peak VO_2 (ml/O_2/kg/minute): 1.03 (0.81–1.31) V_E/VCO_2: 0.96 (0.86–1.09) AT (ml O_2/kg/minute): 0.55 (0.37–0.82) Pulmonary complications: OR (95%CI): Peak VO_2 (ml/O_2/kg/minute): 0.89 (0.69–1.15) V_E/VCO_2: 1.18 (1.05–1.33) AT (ml O_2/kg/minute): 0.85 (0.62–1.17)
Comments	Symptom-limited, treadmill exercise test, performed within 8 weeks of AAA repair in all but two cases

Table 12: Brunelli 2009 [9]

Reference	Brunelli 2009
Study type and analysis	Prospective consecutive cohort Stepwise logistic regression
Number of participants and characteristics	n=287 Consecutive patients who underwent lung resection for lung cancer from January 2006 to June 2008. 24/287 did not undergo the CPET Patients fit for major resection (n=204); age (years) 66.5 (9.6); BMI 26.3 (4.2)

Reference	Brunelli 2009
	Patients unfit for major resection (n=59); age (years) 68.1 (9.6); BMI 27.1 (4.4)
Prognostic variable(s)	0_2 pulse (VO_2/peak heart rate ratio)
Confounders OR stratification strategy	Multivariate analyses adjusted by: age, BMI, gender, heart rate reserve, expired ventilation, breathing reserve, physiologic dead space ventilation, 0_2 pulse (VO_2/peak heart rate ratio), anaerobic threshold (AT), coronary artery disease, type of operation (lobectomy versus pneumonectomy) and neoadjuvant chemotherapy
Outcomes and effect sizes	30-day pulmonary complications: OR (95% CI): Peak VO_2 in ml/kg/minute: 0.87 (0.77–0.99)
Comments	Consecutive patients/prospective study/multivariate analysis A symptom-limited incremental cardiopulmonary exercise test on an electronically braked cycle ergometer using a ramp-pattern increase in work rate and exercise duration of between 8 and 12 minutes. Recordings of heart rate were made using a 12-lead ECG every minute. The test was stopped when on or more of the following criteria were present: fatigue, dyspnoea, excessive systemic BP increase, a ≥2mm ST depression in at least two adjacent leads and/or angina. The peak VO_2 was the average VO_2 during the last 15 seconds of exercise. Abnormal test was defined as FEV1<30% predicted and a predicted post-operative diffusing capacity of the lung for the CO<30% predicted in association with a peak of VO_2<10 ml/kg/minute. Patients would be considered unfit for major resection (and would have minor resections).

Table 13: Brunelli 2012 [8]

Reference	Brunelli 2012
Study type and analysis	Prospective observational Single centre Multivariate and univariate analysis
Number of participants and characteristics	n=225 consecutive 197/225 lobectomy 28/225 pneumonectomy
Prognostic variable(s)	VE/VCO_2 slope
Confounders OR stratification	Multivariate analysis adjusted for those <0.05 in univariate analysis (FEV1, ppoFEV1, induction chemotherapy, COPD and VE/VCO_2 slope)

Reference	Brunelli 2012
strategy	
Outcomes and effect sizes	30-day pulmonary complications: OR (95% CI): VE/VCO_2 slope: 1.09 (1.03–1.16)
Comments	Peak VO_2 cut-off: 10 Multivariate and univariate analysis Symptom-limited CPET on electronically braked cycle ergometer using a ramp-pattern increase in work rate to reach exhaustion. Inoperability criteria determined as peak VO_2 <10 ml/kg/minute with ppoFEV <30% and ppoDLCO <30%

Table 14: Carlisle 2007 [10]

Reference	Carlisle 2007
Study type and analysis	Repair of an unruptured abdominal aortic aneurysm Prospective between 1999–2006
Number of participants and characteristics	Total n=167 CPET=130
Prognostic variable(s)	AT VE/VCO_2 (42 cut-off) VE/VO_2 Peak VO_2 (<15 ml/kg/minute)
Confounders OR stratification strategy	Unclear whether all variables from univariate analysis were included in the multivariate analysis
Outcomes and effect sizes	Mid-term survival (35 months) (HR, 95% CI): Anaerobic threshold (ml O_2/kg/minute): 0.84 (0.73 to 0.96) VE/VCO_2: 1.13 (1.07 to 1.19)
Comments	Unclear whether patients were consecutive. No patient characteristic details. CPET measured using either MedGraphics CardioO2 or Sensor Medics Vmax equipment to measure ventilatory minute volume, oxygen

Reference	Carlisle 2007
	consumption and carbon dioxide production by pedalling an exercise bicycle (no further details on how test was carried out was provided). Grant from Torbay Hospital Special medical projects charity.

Table 15: Grant 2015 [18]

Reference	Grant 2015
Study type and analysis	Prospective Elective open and endovascular abdominal aortic aneurysm repair Multivariable Cox proportional hazards model
Number of participants and characteristics	Open n=179 EVAR=327 n=506, all had CPET Cohort significantly overlaps with Hartley 2012 Two vascular centres: • Central Manchester University Hospital Trust • University Hospital of South Manchester Mean age years 73.4 (range: 44–90) Women n=88 Diabetes n=48 Ischaemic heart disease n=44.9 Treated hypertension n=46.6 Median time between CPET and surgery 56 days
Prognostic variable(s)	VE/VCO_2 at AT

Reference	Grant 2015
	Peak VO_2 (<15 ml/kg/minute)
Confounders OR stratification strategy	Stratified on operation type (open, EVAR), and adjusted for sex, age, diabetes, inducible cardiac ischemia, statin, elevated urea, creatinine haemoglobin, VE/VCO_2 at AT<42, peak VO_2<15 ml/kg/minute
Outcomes and effect sizes	Survival after elective AAA repair: HR (95% CI) – 3 years VE/VCO_2 >42 at AT: 1.63 (1.01–2.63) Peak VO_2 <15 ml/kg per/minute): 1.68 (1.01–2.80)
Comments	All variables missing for more than 15% of subjects were excluded from analysis. Symptom-limited, maximal exercise CPET, performed on a cycle ergometer using a ramped test protocol with Ultima CardiO2 MedGraphics equipment linked into BreezeSuite software. Baseline recorded, 3 minutes cycling without resistance at 60rpm, resistance was applied using a ramped protocol 5–20 W/minute. Test until maximal patient effort achieved, defined as HR 80%>predicted HR, respiratory exchange>1.15 or ventilation limitation (breathing reserve<15%). All CPETs performed and interpreted by anaesthetist. CPET discriminatory variables based on published literature: • AT<10.2 ml/kg/minute • Peak VO_2 (<15 ml/kg/minute) • VE/VCO_2>42 If AT could not be determined at CPET, it was assumed to be <10.2 ml/kg/minute Cohort significantly overlaps with Hartley 2012 Funding: no specific funding

Table 16: Hartley 2012 [23]

Reference	Hartley 2012
Study type and analysis	Prospective Open and endovascular abdominal aortic aneurysm Multivariate analysis
Number of participants and characteristics	n=415, all had CPET Includes 17 patients from a Pilot study 2005–2007, the remaining 398 patients were consecutive (2007–2011) Open repair:

Reference	Hartley 2012
	Age ≥80 years n=12 Women n=31 Diabetes n=10 Ischaemic heart disease n=49 Treated hypertension n=49 Creatinine ≥120 µmol/l n=28 AAA diameter>65 mm n=51 EVAR: Age ≥80 years n=82 Women n=35 Diabetes n=33 Ischaemic heart disease n=130 Treated hypertension n=55 Creatinine≥120 µmol/l n=55 AAA diameter>65 mm n=77
Prognostic variable(s)	HR 80% >predicted HR, respiratory exchange >1.15 or ventilation limitation (breathing reserve <15%). All CPETs performed and interpreted by anaesthetist. CPET discriminatory variables based on published literature: - AT <10.2 ml/kg/minute - Peak VO_2 (<15 ml/kg/minute) - VE/VCO_2 >42 If AT could not be determined at CPET, it was assumed to be <10.2 ml/kg/minute
Confounders OR stratification strategy	Type of repair (open, EVAR), sex, age, diabetes, ischaemic heart disease, treated hypertension, antiplatelet medications, statin, anaemia, urea (> or <7.5 mmol/litre), creatinine (> or <120 mmol/litre), AAA location and diameter (> or <65 mm), inducible cardiac ischaemia, AT <10.2 ml/kg/minute, VE/VCO_2, peak VO_2 <15 ml/kg/minute,≥ 2 abnormal CPET values
Outcomes and	30-day mortality (OR, 95% CI):

Reference	Hartley 2012
effect sizes	Anaerobic threshold: 6.35 (1.84 to 21.92) 90-day mortality: (OR, 95% CI): Peak VO_2 (<15 ml per kg per min): 8.59 (2.33 to 31.67)
Comments	All variables missing for more than 15% of subjects were excluded from analysis. Very high risk of bias due to inaccurate outcome reporting.

Table 17: Junejo 2012 [28]

Reference	Junejo 2012
Study type and analysis	Prospective cohort, consecutive Multivariate regression
Number of participants and characteristics	108/244 had CPET 94/108 underwent surgery 44/94=minor hepatic resection 50/94=major hepatic resection All undergoing liver resection. Risk stratification: >65 all patients. <65 with a comorbidity. CPET indicated based on predefined inclusion criteria=131, 117 underwent resection. 108/131 had CPET. 23 'high risk' patients didn't have CPET because of clinical decision not to delay surgery. Age (median)=71 (24–85)
Prognostic variable(s)	AT VE/VCO_2

Reference	Junejo 2012
Confounders OR stratification strategy	Unclear, said to be including preoperative variables that were significant in simple analyses (p≤0.1)
Outcomes and effect sizes	Cardiopulmonary complications: (OR, 95% CI): VE/VCO_2: 3.45 (1.31–9.09) All complications: (OR, 95% CI): VE/VCO_2: 3.97 (1.44–10.96)
Comments	AT:9.9 CPET carried out by two observers, clinical scientists and anaesthetist; 12-lead ECG and cycle ergometer and face mask. Risk stratified

Table 18: Junejo 2014 [27]

Reference	Junejo 2014
Study type and analysis	Prospective cohort Simple logistic regression
Number of participants and characteristics	n=143 consecutive patients undergoing pancreaticoduodenectomy 93/143 high risk. High risk were those who were >65 or <65 with a comorbidity. 89/93 underwent CPET. 4/93 pancreatic resection without CPET. 50/143 were deemed low risk and underwent operation without CPET. Age=64 (45–80) Sex=38:26 BMI=26 (15–44) ASA score=3 (1–3) Revised cardiac risk index=1 (1–3)

Reference	Junejo 2014
	Whipple surgery=89% Subtotal pancreatectomy (extended whipple)=3% Whipple+liver+gallbladder resection=2% Whipple+portal vein resection=2%
Prognostic variable(s)	AT VE/VCO_2 VO_2 max
Confounders OR stratification strategy	Simple logistical regression Obstructive jaundice
Outcomes and effect sizes	In-hospital mortality: (OR, 95% CI): AT: 0.90(0.52-1.53), VE/VCO_2: 1.26(1.05-1.52) VO_2 max: 1.03(0.77-1.37), 30 day mortality: (OR, 95% CI): AT: 1.23(0.72-2.11) VE/VCO_2: 1.35(1.03-1.77) VO_2 max: 1.32(0.91-1.93) Cardiopulmonary complications: (OR, 95% CI): AT: 1.05 (0.82-1.24) VE/VCO_2: 0.98 (0.9-1.07) VO_2 max: 1.00 (0.86-1.17) Any complications: (OR, 95% CI): AT: 1.07(0.83-1.39) VE/VCO_2: 0.97(0.89-1.07)

Reference	Junejo 2014
	VO_2 max: 1.00(0.86-1.18)
Comments	41 VE/VCO_2 cut-off Risk stratified

Table 19: Licker 2011 [32]

Reference	Licker 2011
Study type and analysis	Prospective cohort Multivariate logistic regression
Number of participants and characteristics	n=210/243 consecutive lung cancer patients between 2001–2009 underwent CPET Underwent CPET if FEV1<80% predicted
Prognostic variable(s)	Peak VO_2
Confounders OR stratification strategy	Surgery type Age Duration of anaesthesia Tidal volume predicted body weight
Outcomes and effect sizes	All complications (OR, 95% CI): 0.79 (0.71–0.88) Cardiovascular complications: (OR, 95% CI): 0.80(0.68–0.92) Pulmonary complications: (OR, 95% CI): 0.84 (0.75–0.94)
Comments	Study methods and outcomes well reported Risk stratified

Table 20: McCullough 2006 [35]

Reference	McCullough 2006
Study type and analysis	Prospective (no controlled) study, bariatric surgery (laparoscopic Roux-en-Y gastric bypass). Multivariate analysis.
Number of participants and characteristics	n=109 consecutive, morbidly obese patients November 2001–December 2003 consecutive patients in single centre Inclusion criteria: BMI>35 kg/m^2 and >40 kg/m^2 in patients with and without diabetes respectively, absence of limiting cardiopulmonary disease, ability to perform CPET to exhaustion. Exclusion criteria: patients with severe lung disease requiring long-term oxygen therapy Mean age: 46 (10.4) years Female: 75.2% Mean BMI: 48.1 (range 36 to 90 kg/m^2) Baseline characteristics were stratified by tertile of peak VO_2; first tertile (peak VO_2: 14.2 ml/kg/minute [6.8-15.8]), second tertile (peak VO_2: 17.1 ml/kg/minute [15.9-18.4]) and third tertile (peak VO_2: 20.8 ml/kg/minute [18.5-27.7]).
Prognostic variable(s)	Peak VO_2
Confounders OR stratification strategy	Adjusted by age, gender, BMI, eGFR
Outcomes and effect sizes	Complications (myocardial infarction, unstable angina, DVT, PE, renal failure, stroke and death): (OR, 95% CI): Peak VO_2 <15.8 ml/kg/minute: 12.89 (1.14–145.76) Peak VO_2 continuous: 1.61 (1.19–2.18)
Comments	Patients underwent peak or symptom-limited CPX using Bruce or modified Bruce treadmill protocols that increased workload by approximately 2 METS every 3 minutes. Heart rate (HR) and blood pressure (BP) (standard cut-off method) were measured at rest in supine and standing positions during each 3 minute stage of exercise and throughout a 6 minute recovery.

Reference	McCullough 2006
	Termination criteria included: patient request, volitional fatigue, increasing chest or leg pain, ECG abnormalities, and a hypertensive or hypotensive BP response.

Table 21: Prentis 2012 [37]

Reference	Prentis 2012
Study type and analysis	Prospective single-centre blinded study of unselected cohort of patients scheduled for aortic aneurysm repair at the Freeman Hospital, Newcastle upon Tyne, UK. Multivariate analysis
Number of participants and characteristics	n=212; 101 patients underwent EVAR, 84 had an open repair, 27 had indeterminate AT values. The clinicians involved in the perioperative management of these patients had no a priori knowledge of the CPET results.
Prognostic variable(s)	AT, peak VO_2, VO_2/heart rate, VE/VCO_2, maximum heart rate, watts
Confounders OR stratification strategy	Adjusted by demographic characteristics, exercise testing variables (peak VO_2, VO_2/heart rate, VE/VCO_2, maximum heart rate, watts), preoperative blood tests, medications and aneurysm size
Outcomes and effect sizes	Open surgery: Complications: (OR, 95% CI): 0.71 (0.57–0.88)
Comments	All patients underwent a symptom-limited, progressive ramped exercise test on an electronically braked cycle ergometer. Cardiac function was measured by 12-lead electrocardiography. The test was stopped on voluntary termination (fatigue, pain, light-headedness), failure to maintain >40 rpm for >30 seconds despite encouragement, or presentation of clinical indications. By the Medical Research Council Newcastle Centre for Brain Ageing and Vitality; the UK National Institute for Health Research Biomedical Research Centre on Ageing and Age Related Diseases. The study reported hazard ratios for length of hospital stay and length of critical care by surgery type: open or EVAR. However, these were not included in the report and it is unclear how the hazard ratios were calculated (for example whether they have compared those with a higher AT to those with a lower AT or compared those with a lower AT to those with a higher AT as a means of calculating the HR), therefore we have not extracted these as a forest plot.

Table 22: Prentis 2013 [38]

Reference	Prentis 2013
Study type and analysis	Prospective cohort multivariable logistic regression
Number of participants and characteristics	n=69/82 CPET and radical cystectomy Elderly population Consecutive, single centre Patients excluded from analysis: 5=unable to obtain AT at CPET 8=did not undergo RC due to fitness, refusal or advanced malignancy
Prognostic variable(s)	AT VO_2/HR VE/VCO_2 QUES Peak VO_2
Confounders OR stratification strategy	AT VO_2/HR VE/VCO_2 QUES Peak VO_2
Outcomes and effect sizes	Post-operative morbidity (OR, 95% CI): AT: 0.74 (0.57–0.97) Length of hospital stay (HR, 95% CI): AT <12: HR=0.47(0.28–0.79)
Comments	Optimal AT determined to be 12 CPET results blinded from clinicians

Reference	Prentis 2013
	Other outcomes: ROC curve showed AT had good accuracy for major complications: 0.72 (0.60–0.82) Elderly population

Table 23: Snowden 2010 [39]

Reference	Snowden 2010
Study type and analysis	Prospective cohort Multivariate analysis
Number of participants and characteristics	n=171 123/171 underwent both CPET and surgery Consecutive patients, single centre, January 2006–February 2008 Patients were selected for CPET on the basis of metabolic equivalent (MET) score of 7 or below. 48=did not undergo surgery 6/43=died on waitlist 20/48=unfit at preoperative assessment 7/48=refused 15/48=inoperable No significance difference found in baseline characteristics
Prognostic variable(s)	AT
Confounders OR stratification strategy	Factors significant in univariate analysis adjusted for in multivariate analysis: Veterans activity score index (VASI) AT Peak VO_2 Early emergency surgical intervention
Outcomes and effect sizes	Any complication (OR, 95% CI): AT=0.44 (0.30–0.64)
Comments	AT cut-off of 10.1/kg/minute Patients did not have surgery refused based on CPET result

Reference	Snowden 2010
	Univariate analysis also separated by complication type POMS Risk stratified according to METS and VASI included as confounder

Table 24: Torchio 2010 [41]

Reference	Torchio 2010
Study type and analysis	Retrospective cohort Multivariate analysis
Number of participants and characteristics	n=145/250 consecutive (2005–2007) COPD patients with lung cancer who underwent CPET Male=128 Females=17 Age=64 (41–82) BMI=25.6 36% had mild COPD, 58% moderate COPD, 6% severe COPD 93% history of smoking 6.2% chemotherapy
Prognostic variable(s)	VE/VCO_2 slope Peak VO_2
Confounders OR stratification strategy	Age, BMI, spirometry and CPET parameters
Outcomes and effect sizes	30-day mortality (OR, 95% CI): VE/VCO_2 slope: OR 1.24 (1.06–1.44) Cardiopulmonary complications (OR, 95% CI):

Reference	Torchio 2010
	VE/VCO_2 slope: 0.05 (0.01–0.58)
Comments	AT not reported Multivariate analysis All patients had COPD Symptom-limited CPET with a respiratory gas exchange measurement using a treadmill with Balke protocol. 12-lead ECG, heart rate and arterial blood pressure taken at rest and at each minute during exercise. Breath-by-breath gas exchange measurement using Sensor Medics Vmax 29C. Minute ventilation, peak oxygen uptake, and carbon dioxide output calculated breath-by-breath.

Table 25: West 2014 [45]

Reference	West 2014
Study type and analysis	Prospective cohort Forward stepwise selection
Number of participants and characteristics	n=136 Patients aged >18 years scheduled for major colonic surgery Male: 89 (65%) Female: 47 (35%) Age: 71 (62–77) BMI: 27 (7)
Prognostic variable(s)	Preoperative CPET
Confounders OR stratification strategy	VO_2 and gender
Outcomes and effect sizes	Any complications: (OR, 95% CI): VO_2 increase of 1.0 ml/minute/kg: 0.77 [0.66, 0.90] VO_2 increase of 2.0 ml/minute/kg: 0.60 [0.45, 0.80]
Comments	High risk of bias CPET results did not alter perioperative management

H.4 Polysomnography

H.4.1 Clinical evidence tables for review question 1: Intervention review

Table 26: Chung 2008 [12]

Study	Chung 2008[12]
Study type	Non-randomised comparative study
Number of studies (number of participants)	n=416
Countries and setting	Conducted in Canada; setting: preoperative clinics of Toronto Western Hospital and Mount Sinai Hospital, Toronto, Canada
Line of therapy	1st line
Duration of study	Intervention + follow up: 30 days post hospital discharge
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: overnight in-laboratory polysomnography
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients aged 18 years or older who had an ASA physical status of I-IV and were scheduled to undergo elective procedures in general surgery, gynaecology, orthopaedics, urology, plastic surgery, ophthalmology, or neurosurgery.
Exclusion criteria	Patients who were unwilling or unable to give informed consent, patients previously diagnosed with OSA or any other sleep breathing disorder, or patients who were expected to have abnormal electroencephalographic findings (for example brain tumour, epilepsy surgery, patients with deep brain stimulator) were excluded.
Recruitment/selection of patients	All patients who visited the preoperative clinics for their scheduled surgery and met the inclusion criteria were approached by the research staff.
Age, gender and ethnicity	Age – mean (SD): 56 (13). Gender (M:F): 212/204. Ethnicity: not reported.
Further population details	
Indirectness of population	Serious indirectness: study included ASA 1 patients and patients undergoing neurosurgery
Interventions	(n=211) Intervention 1: Polysomnography. Collection of continuous sleep architectural data was obtained using a standard electroencephalographic montage consisting of an electroencephalogram, electrooculogram, submental electromyogram, and electrocardiogram. Ancillary channels were used to specifically record respiratory parameters, including respiratory effort by thoracoabdominal excursion, respiratory inductive plethysmography and oronasal airflow by nasal airflow pressure. Oxygen saturation was measured with a pulse oximeter. Duration: overnight.

Study	Chung 2008[12]
	Concurrent medication/care: not stated Comments: not applicable (n=205) Intervention 2: No polysomnography Duration: not applicable Concurrent medication/care: not stated
Funding	Academic or government funding (Physician Services Incorporated Foundation, Toronto; University Health Network Foundation, Toronto; University of Toronto, Toronto)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: POLYSOMNOGRAPHY versus NO POLYSOMNOGRAPHY Hospitalisation: - Respiratory complication at post-operative; Group 1: 39/211, Group 2: 25/205; risk of bias: very high; indirectness of outcome: no indirectness - Cardiac complication at post-operative; Group 1: 12/211, Group 2: 6/205; risk of bias: very high; indirectness of outcome: no indirectness - Neurologic complication at post-operative; Group 1: 2/211, Group 2: 3/205; risk of bias: very high; indirectness of outcome: no indirectness - Readmission within 30 days at 30 days after surgery; Group 1: 4/211, Group 2: 5/205; risk of bias: very high; indirectness of outcome: no indirectness ITU admissions: - Unplanned ICU admission at post-operative; Group 1: 4/211, Group 2: 1/205; risk of bias: very high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Quality of life

H.4.2 Clinical evidence tables for review question 2: Prognostic review

Table 27: Weingarten 2011 [44]

Reference	Weingarten 2011
Study type and analysis	Retrospective cohort Single centre Logistic regression adjusted by covariates
Number of	n=797

Reference	Weingarten 2011
participants and characteristics	Inclusion: patients over 18 years old who had first time bariatric surgery who were referred from preoperative testing clinic to have polysomnography at one attached centre only
Prognostic variable(s)	AHI >5 defined as significant polysomnography result Compared with group AHI <5
Confounders OR stratification strategy	Age, sex, operative approach (laparoscopic or open), BMI
Outcomes and effect sizes	Pulmonary complications (aspiration, pneumonia, new requirement for CPAP or biPAP, use of naloxone, post-operative tracheal intubation, mechanical ventilator support, respiratory arrest): Adjusted OR [95% CI]: 1.0 [0.44, 2.27] Surgical complications (bleeding, wound dehiscence, anastomotic leak, wound infection or the need for reoperation): Adjusted OR [95% CI]: 1.33 [0.79, 2.24] Other post-operative complications (myocardial infarction, dysrhythmia, stroke, thromboembolic events, sepsis, liver failure, acute kidney injury, hospital readmission, or death within 30 post-operative days): Adjusted OR [95% CI]: 0.79 [0.49, 1.27] All post-operative complications: Adjusted OR [95% CI]: 0.86 [0.59, 1.25]
Comments	At least one post-operative complication occurred in 259 patients. Study ranked AHI scores as significant, moderate, mild and no obstructive sleep apnoea. It found no association between pulmonary, operative and total complications. It found that the frequency of other complications decreased with increasing AHI (OR 0.97 per five unit AHI increase, 95% confidence interval 0.94–1.00 p=0.44).

H.5 Health technology assessment update

H.5.1 Lung function tests (also including blood gas analysis)

Table 28: Hamoui et al., (2006)[21]

Reference	Hamoui 2006
Study type and analysis	Prospective cohort Multivariate logistic regression analysis
Number of participants and characteristics	n=146 consecutive, morbidly obese patients who had duodenal switch operation surgery (bariatric surgery) during a 12-month period. Inclusion criteria: not explicitly stated Exclusion criteria: not explicitly stated Consecutive patients in single centre (USA) Complications (n=27) No complications (n=119)
Prognostic variable(s)	Vital capacity (VC), Functional residual capacity (FRC) and total lung capacity (TLC), forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1), maximal voluntary ventilation (MVV), and pO_2.
Confounders OR stratification strategy	Adjusting for age, sex and BMI as well as variables identified as statistically significant on univariate analysis.
Outcomes and effect sizes	Post-operative complications (composite outcomes including failed extubation, reintubation, pneumonia, wound infection/dehiscence, pulmonary embolism, deep venous thrombosis, cardiac arrhythmia, intra-abdominal abscess, renal failure, ileus, urinary tract infection, bacteraemia) Vital capacity – RR (95% CI): RR 2.29 for every 10% decrease in percent of predicted value (2.2–2.35)
Comments	None

Table 29: Jeong 2013[26]

Reference	Jeong 2013
Study type and analysis	Retrospective cohort study Multivariate analysis was carried out using variables that were significant at p≤0.05 as covariates
Number of participants and characteristics	n=538 patients who underwent elective gastric cancer surgery and who underwent pulmonary function tests using lung spirometry prior to surgery. Other inclusion criteria: not explicitly stated Exclusion criteria: patients who underwent an operation under an emergency condition, such as for bleeding or perforation; patients who underwent exploratory or bypass surgery for unresectable disease; or patients who received preoperative systemic chemotherapy. Baseline characteristics were divided by normal or abnormal spirometry results (see definition in prognostic factor column).
Prognostic variable(s)	Normal/abnormal pulmonary function test: defined based on FEV1/FVC ratios and FEV1 values with FEV1/FVC ≥0.7 classified as normal; FEV1/FVC <0.7, FEV1 ≥80% predicted classified as mild; FEV1/FVC <0.7, FEV1 50%–80% predicted classified as moderate; FEV1/FVC <0.7, FEV1 30%–50% predicted classified as severe; FEV1/FVC <0.7, FEV1 <30% predicted classified as very severe.
Confounders OR stratification strategy	For post-operative surgical complications confounders in the model were: age resection type, operative approach and tumour node metastasis stage. Post-operative systemic complications: age, history of pulmonary disease.
Outcomes and effect sizes	Post-operative surgical complications and post-operative systemic complications (a complication near the operation filed was surgical whereas a complication not associated with the operation site classed as systemic): <u>Abnormal pulmonary function tests result(for surgical complications):</u> (OR 1.75 95% CI: 1.03 to 2.97) <u>Systemic complications</u>: (OR 1.11 95% CI: 0.32 to 3.86)
Comments	None

H.5.2 Full blood count (haemoglobin, white blood cell count and platelet count)

Table 30: Amaranto 2011[3]

Reference	Amaranto 2011
Study type and analysis	Retrospective study: endovascular and open repair of carotid stenosis, aortic aneurysm and peripheral arterial disease Single centre Multivariable analysis – logistic regression
Number of participants and characteristics	n=1773 endovascular patients in the Division of Vascular Surgery at Northwestern Memorial Hospital from1 April 1999 to 31 May 2009 Inclusion criteria: adults with normal preoperative WBC (3.5-10.5 K/microlitre) who underwent carotid endarterectomy (CEA), carotid artery stenting (CAS), open repair of abdominal aortic aneurysm (AAA), endovascular repair of abdominal aortic aneurysm (EVAR), open repair of thoracoabdominal aortic aneurysm (TAAA), endovascular repair of thoracoabdominal aneurysm (TEVAR), lower extremity bypass grafting (LEB), or lower extremity stenting (LES). Exclusion criteria: patients without preoperative WBC or with preoperative WBC outside the normal range (3.5–10.5 K/microlitre) determined by Northwestern Memorial Hospital; patients who received major surgical intervention within 30 days before or after their index vascular procedure. 1024 patients from the initial 2807 sample had to be excluded on these grounds. Patients were divided into an endovascular surgery cohort (CAS, EVAR, TEVAR and LES) and an open cohort (CEA, AAA, TAAA and LEB): Endovascular (n=804) Open (n=969)
Prognostic variable(s)	White blood cell count (WBC) within normal range – most recent WBC taken before the procedure was recorded
Confounders OR stratification strategy	Age, gender, diabetes, congestive heart failure, myocardial infarction, renal insufficiency, hypertension, hyperlipidaemia, emergent presentation
Outcomes and effect sizes	Adjusted odds ratio from logistic regression with WBC as a linear variable OR (95% CI) Complications:

Reference	Amaranto 2011
	Endovascular: 1.32 (1.11–1.58) Open: 0.97 (0.86–1.08) Major adverse event: Endovascular: 1.67 (1.23–2.27) Open: 1.07 (0.98–1.17) Death: Endovascular: 1.82 (1.12–2.96) Open: 1.17 (1.05–1.30)
Comments	Univariate logistic regression revealed that for every 1 K/microlitre increase in preoperative WBC, endovascular patients had a 31.4%, 66.8%, and 128.1% increase in their relative odds of developing post-operative complications, MAE, and death, respectively.

Table 31: Bedke 2012[6]

Reference	Bedke 2012
Study type and analysis	Retrospective observational study; single centre Multivariable Cox model
Number of participants and characteristics	327 patients who underwent partial or radical nephrectomy for clear cell RCC between 1993 and 2007. Inclusion criteria: as above Exclusion criteria: not stated Mean age: 63.5 years Female: 67% Surgical technique: evaluated by axial imaging at the time of surgery and post-operatively every 3–4 months for the first year, semi-annually for the second and third years and annually by chest X-ray or thoracic CT, abdominal sonography, CT or MRI, and serum chemistry
Prognostic variable(s)	White blood cell count measured 1–2 days before surgery with an automated cell counter

Reference	Bedke 2012
Confounders OR stratification strategy	Adjusted by well-known prognostic factors such as TNM stage, tumour size, Fuhrman grade and Karnofsky index (unclear if other variables were also used), as well as CRP and leucocytes
Outcomes and effect sizes	Hazard ratio for different breakpoints – HR (95%): WBC ≤9.5 versus >9.5: 1.91 (1.1–3.32) WBC ≤10.0 versus >10.0: 1.56 (0.86–2.83) WBC ≤11.0 versus >11.0: 1.97 (1.00–3.88)
Comments	None

Table 32: Beattie 2009[5]

Reference	Beattie 2009
Study type and analysis	Retrospective cohort study: non-cardiac surgery Single centre Multivariable analysis – logistic regression using variables identified as significant on the univariate analysis and propensity score analyses (matching anaemic and non-anaemic patients to balance confounding variables)
Number of participants and characteristics	n=7679 consecutive non-cardiac surgery patients at the Toronto General Hospital from March 2003 to June 2006. Included vascular and oncology surgery in head and neck, urology, and thoracic, hepatobiliary, general, and gynaecologic procedures. Inclusion criteria: adults (age >18 years) who underwent non-cardiac surgery, receiving patient-controlled analgesia, patient-controlled epidural anaesthesia, epidural or intravenous pain management. Exclusion criteria: transplantation and cardiac surgery cases.

Reference	Beattie 2009
	Mean age: not stated Female: 37%
Prognostic variable(s)	Preoperative anaemia: haemoglobin concentration threshold of WHO gender-based definition (12.0 g/dl in women and 13.0 g/dl in men)
Confounders OR stratification strategy	The variables assessed included height, weight, age, sex, history of coronary disease, congestive heart failure, cerebrovascular disease, diabetes, renal disease, chronic obstructive pulmonary disease, preoperative platelet count, time in hospital before surgery, type of surgery, perioperative transfusion, and medications including -blockers, lipid-lowering agents, angiotensin-converting enzyme inhibitors, and calcium channel blockers. Specifically, transfusions were categorized as 0, 1–2 units, 3–4 units, 4–9 units, and 10 or more units. The variables included were: • Age >70 years • In-hospital status • History of CHF • Preoperative renal dysfunction • Perioperative medications: ○ No beta-blockers ○ Metoprolol ○ Atenolol or bisoprolol ○ ACE inhibitors ○ Calcium channel blockers • Post-operative NSAID • Transfusion: ○ No blood products ○ 1–2 units ○ 3–4 units ○ 5–10 units ○ >10 units
Outcomes and effect sizes	Adjusted odds ratio from logistic regression – OR (95% CI): Full model – all anaemic patients:

Reference	Beattie 2009
	2.36 (1.57–3.55) Excluding severe anaemia (Hb <9.5 g/dl): 1.79 (1.17–2.74) Excluding those with RBC transfusions: 3.04 (1.80–5.13)
Comments	None

Table 33: Dunkelgrun et al. (2008) [14]

Reference	Dunkelgrun 2009
Study type and analysis	Retrospective study of patients who were referred for elective non-cardiac open vascular surgery Multivariable analysis was carried out using Cox proportional hazard regression.
Number of participants and characteristics	n=1211 patients who were scheduled for elective non-cardiac open vascular surgery and who were referred for preoperative testing from February 1990 to August 2006 to one medical centre in Rotterdam, The Netherlands. Inclusion criteria: not explicitly stated Exclusion criteria: patients who were tested at another centre for their surgery Mean age: 68 (11) years Male: 77%
Prognostic variable(s)	Preoperative anaemia: defined as the haemoglobin measured during a patient's last preoperative outpatient screening before surgery according to the WHO criteria (serum haemoglobin level <13 g/dl for men a level < 12 g/dl for women)
Confounders OR stratification strategy	Adjustments for anaemia, renal dysfunction, heart failure, age, gender type of vascular surgery (central or peripheral open procedure), diabetes mellitus, chronic obstructive pulmonary disease, hypertension, ischemic heart disease and stroke.
Outcomes and effect sizes	After adjusting for confounders, preoperative mild anaemia was not, but moderate and severe anaemia were, independently predictive of 30-day major adverse cardiac event: OR (95% CI):

Reference	Dunkelgrun 2009
	Mild: 1.80 (0.80 to 4.05) Moderate: 2.30 (1.10 to 4.81) Severe: 4.70 (2.6 to 8.50)
Comments	None

Table 34: Glance 2014[16]

Reference	Glance 2014
Study type and analysis	Retrospective observational study American College of Surgeons National Surgical Quality improvement database (NSQIP) with >200 participating hospitals (systematic sampling strategy used to avoid bias in case selection and to ensure a diverse surgical case mix) Multivariable analysis with multiple imputation for missing values of preoperative serum creatinine
Number of participants and characteristics	n=316,644 consecutive patients without clinical indications for preoperative platelet (coagulation) testing Inclusion criteria: surgical patients without indications for coagulation testing Exclusion criteria: no platelet counts (71,276), no haematoocrits (838), procedures with work relative value units equal to zero (7790), missing demographic information (7780), missing ASA Physical Status (428) and missing information on blood transfusion (547) Note: stratified analyses were performed in (1) low-risk patients (defined as having an ROM ≤0.5%); intermediate risk patients (ROM: >0.5 to 3.5%); and high-risk patients (ROM: >3.5%).
Prognostic variable(s)	Platelet count Stratified a priori into:

Reference	Glance 2014
	(1) moderate-to-severe thrombocytopenia (<100,000 µl−1); (2) mild thrombocytopenia (101,000–150,000 µl−1); (3) low-normal (151,000–200,000 µl−1); (4) normal (201,000–450,000 µl−1); and (5) thrombocytosis (≥450,000 µl−1).
Confounders OR stratification strategy	Haematocrit, age, sex, BMI (underweight, overweight, obesity, morbid obesity, and super obesity), admission source (home, transfer from other hospital, chronic care facility), race, inpatient status (versus outpatient), emergency status, surgical complexity (work relative value units), previous operation within 30 days, and comorbidities: diabetes (oral hypoglycaemics, insulin treatment), pulmonary (chronic obstructive pulmonary disease, pneumonia, mechanical ventilation before surgery, dyspnoea at rest, dyspnoea on exertion), cardiac (congestive heart failure, myocardial infarction, angina, percutaneous coronary intervention, open heart surgery), hypertension, peripheral vascular disease, renal disease (stage 2 chronic kidney disease: glomerular filtration rate, 60–89 ml/minute/1.73 m^2; stage 3 chronic kidney disease: glomerular filtration rate, 30–59 ml/minute/1.73 m^2; stage 4 chronic kidney disease: glomerular filtration rate, 15–29 ml/minute/1.73 m^2), central nervous system (stroke with neurologic deficit, stroke without neurologic deficit, transient ischemic attack, impaired sensorium, coma, hemiplegia, paraplegia, quadriplegia, tumour involving the central nervous system). Blood transfusion was added as a covariate in a separate analysis as a categorical variable: unit erythrocytes (reference category, 1 unit erythrocytes, 2 units erythrocytes, 3 units erythrocytes, 4 units erythrocytes, and >4 units erythrocytes).
Outcomes and effect sizes	Multivariable analysis for the outcomes of: • Receipt of any erythrocyte transfusion • 30-day mortality and the following 30-day complications: (1) cardiac (acute myocardial infarction or cardiac arrest); (2) pulmonary (pneumonia, ventilatory support for >48 hours); (3) renal (progressive renal insufficiency or acute renal failure); (4) central nervous system (cerebrovascular accident or coma lasting >24 hours); (5) sepsis (sepsis or septic shock); (6) wound infection (deep incisional surgical site infection, organ or space surgical site infection, or wound dehiscence); (7) thromboembolic (deep venous thrombosis or pulmonary embolism); and (8) graft failure.
Comments	Limitations include 18% of original sample being excluded because no coagulation testing was performed (may over-estimate prognostic relevance).

Table 35: Greenky et al. (2012)[19]

Reference	Greenky 2012
Study type and analysis	Retrospective cohort study using data from 15,722 in one centre collected between 2000 and 2007. Both a multivariable logistic regression analysis and a propensity score analysis generated through a regression model were carried out.
Number of participants	n=15,222 retrospectively collected data from patients in a prospective institutional database Inclusion criteria: patients undergoing total hip arthroplasty or total knee arthroplasty

Reference	Greenky 2012
and characteristics	Exclusion criteria: patients with acute trauma or admitted with post-operative/periprosthetic joint infection (PJI); n=500 Consecutive patients in single centre Mean age: 65 (range 15–100) years Male: 42.7% Baseline characteristics were stratified by reference and anaemia groups. People with anaemia were more often female, of black race, slightly older, with a lower BMI.
Prognostic variable(s)	Anaemia as defined by the guidelines of the World Health Organisation (Hb <12 g/dl in women and <13 g/dl in men).
Confounders OR stratification strategy	Analysis adjusted for all demographic and comorbidity variables with p< 0.05 in the univariate analysis. In a second analysis a propensity score was generated through a regression model which was then included as an independent covariate in the model.
Outcomes and effect sizes	Periprosthetic joint infections: (OR 95% CI): Propensity-adjusted OR 1.95 (95% CI 1.41–2.70) Mortality – 30 day: Propensity-adjusted OR 0.59 (95% CI 0.10–3.53) Mortality – 90 day: Propensity-adjusted OR 1.54 (95% CI 0.50– 4.73) Mortality – 1 year: Propensity-adjusted OR 1.81 (95% CI 1.00–3.29)
Comments	None

Table 36: Jamsen et al. (2015)[24]

Reference	Jamsen 2015
Study type and analysis	Prospective cohort study using data from one centre collected between 2009 and 2011. Multivariable binary logistic regression analysis
Number of participants and characteristics	n=191 (74 hip and 117 knee replacements) prospectively collected data Inclusion criteria: patients of all ages undergoing primary hip or knee replacement for osteoarthritis. Patients with and without diabetes were included. Exclusion criteria: regular corticosteroid treatment Median age: 66 (range 43–89) years Male: 35% Median BMI: 30 (range 21–50) years ASA risk score: I – 8%, II – 48%, III – 43%, IV – 1% Cemented fixation was used in the majority of knee replacements (87 of 117, 74%) whereas 55 of the 74 hip replacements (74%) were cementless. Spinal anaesthesia was used in all operations. A single 3.0 g bolus of cefuroxime was used as antibiotic prophylaxis (but when contraindicated, clindamycin was used instead). Antibiotic-impregnated cement was used in all cemented joint replacements.
Prognostic variable(s)	Anaemia as defined by local laboratory reference values (Hb <117 g/l in women and <136 g/l in men
Confounders OR stratification strategy	Binary logistic regression with adjustment for age, sex, operated joint (hip, knee), and ASA risk score
Outcomes and effect sizes	Hyperglycaemia - adjusted OR (95%): 3.9 (0.91–16.71) <u>Severe hyperglycaemia - adjusted OR (95%):</u>

Reference	Jamsen 2015
	Adjusted OR: 2.0 (0.5–8.00)
Comments	None

Table 37: Jans 2014[25]

Reference	Jans 2014
Study type and analysis	Prospective observational cohort study Multivariate logistic regression used for the confounders listed A separate multivariate analysis was undertaken to account for both preoperative risk factors (including anaemia) and the occurrence of RBC transfusion during primary admission.
Number of participants and characteristics	n=5165 episodes, or 4940 unique patients. Inclusion: all unilateral primary total hip arthroplasty (n=2702, 52.3%) or total knee arthroplasty (n=2463, 47.7%) taking place in centres participating in the study. Exclusion: emergency procedures (hip or knee fracture), fracture or prior surgery on the same hip or knee less than 3 months previously, preceding elective hip or knee arthroplasty during the study period less than 45 days before index procedure, or surgery due to malignancy or severe congenital deformity. Mean age was 67 +/- 11 years. 2936 (56.8%) were female.
Prognostic variable(s)	Preoperative anaemia (n=662) • <13 g/litre for males • <12 g/litre for women
Confounders OR stratification strategy	Age, procedure (THA versus TKA), female, hypertension, cardiac disease, pulmonary disease, cerebrovascular disease, preoperative walking aid

Reference	Jans 2014
Outcomes and effect sizes	Risk of RBC transfusion during primary admission: OR (95% CI): 4.70 (3.8–5.1) Length of stay >5 days: OR (95% CI): 2.5 (1.9–3.29) All-cause readmission within 90 days after surgery: OR (95 %CI): 1.4 (1.1–7.8)
Comments	Preoperative demographics and Hb were prospectively collected within 30 days prior to surgery. No information on whether these were acted on or whether the anaesthetist/surgeon were aware of Hb level. Data on a number of blood transfusions received was obtained from regional blood banks, and data on morbidity from the Danish national health registry was collected retrospectively. The assessors extracting the information from computer databases were blinded to the patient's preoperative anaemic status. Other findings from the study included that perioperative transfusion of red blood cells had a clinically significantly raised risk of readmission and length of stay over 5 days. The study also reports that when the coded reasons for length of stay or readmission possibly connected with anaemia were removed from the analysis, comparable results to the total analysis were found (although not displayed in the report and unable to extract).

Table 38: Yoshihara (2014)[47]

Reference	Yoshihara 2014
Study type and analysis	Retrospective cohort study using data from the Nationwide Inpatient Sample (NIS) collected between 2000 and 2009. Multivariable logistic regression analysis.
Number of participants and characteristics	n=1,786,373 hip and 4,270,282 knee Inclusion criteria: patients who underwent primary total hip or knee arthroplasty (THA or TKA) according to ICD-9-CM codes

Reference	Yoshihara 2014
	Exclusion criteria: emergency surgery for hip fracture; simultaneous bilateral procedures Baseline data were separated for THA and TKA, and allogenic blood transfusion (ALBT) and non-ALBT groups. THA ALBT group: Age: ≤17 – 0.1% 18-44 – 4.5% 45-64 – 27.2% 65-84 – 60.2% ≥85 – 8.1% Male: 28.9% Autologous-related blood transfusion: 9.3% THA non-ALBT group: Age: ≤17 – 0.1% 18-44 – 6.7% 45-64 – 40.1% 65-84 – 49.9% ≥85 – 3.2% Male: 46.5% Autologous-related blood transfusion: 10.6% TKA ALBT group: Age: ≤17 – 0.1% 18-44 – 1.3% 45-64 – 24.3% 65-84 – 67.4%

Reference	Yoshihara 2014
	≥85 – 6.8% Male: 24.5% Autologous-related blood transfusion: 8.5% TKA non-ALBT group: Age: ≤17 – 0.0% 18-44 – 2.1% 45-64 – 38.9% 65-84 – 56.3% ≥85 – 2.6% Male: 37.1% Autologous-related blood transfusion: 7.6%
Prognostic variable(s)	Anaemia, unclear definition
Confounders OR stratification strategy	Logistic regression with adjustment for age, sex, race, comorbidity, Elixhauser Comorbidity Score, autologous-related blood transfusion, hospital size, hospital caseload, hospital region and payer information
Outcomes and effect sizes	Allogenic blood transfusion – total hip arthroplasty: – OR (95% CI): 2.03 (1.86–2.22) Allogenic blood transfusion – total knee arthroplasty: – OR (95% CI): 2.70 (2.52–2.91)
Comments	

Table 39: Wang et al (2015)[43]

Reference	Wang 2015

Reference	Wang 2015
Study type and analysis	Retrospective cohort study using data collected between 2006 and 2012. Multivariable Cox hazards analysis.
Number of participants and characteristics	n=223 hepatobiliary surgery patients Inclusion criteria: (1) gall bladder cancer (GBC) diagnosis confirmed by histopathology; and (2) gallbladder resection was neither preceded nor followed by adjuvant chemotherapy and/or radiotherapy. Exclusion criteria: (1) coexisting or previous cancers other than GBC; (2) concomitant diseases suspected of increasing the serum platelet concentration, including severe hypertension, splenic disease and blood coagulation disorders; and (3) the use of aspirin or other acetylsalicylic acid drugs one month before the surgery. Mean age: 59.1 (8.1) years M/F (%): 30/70%
Prognostic variable(s)	Platelet count (3 days before surgery), threshold defined using optimum threshold in study sample (>178 x 109 l)
Confounders OR stratification strategy	Cox regression with adjustment for lymph node metastasis, TNM stage, tumour location
Outcomes and effect sizes	Overall survival platelet count ≤178 : OR (95% CI): 1.54 (1.04-2.29)
Comments	None

H.5.3 Kidney function tests (urea, estimated glomerular filtration rate and electrolyte tests) (U&Es)

Table 40: AbuRahma 2013 [1]

Reference	AbuRahma 2013

Reference	AbuRahma 2013
Study type and analysis	Retrospective observational study of prospectively gathered data from 2010–2011 West Virginia Multivariable logistic regression analysis using variables identified as significant on the univariate analysis
Number of participants and characteristics	n=881 (940 operations) patients who underwent carotid endarterectomy during 2010 and 2011 Inclusion criteria: as above Exclusion criteria: redo carotid endarterectomy, combined carotid endarterectomy with coronary artery bypass grafting, complex brachiocephalic reconstruction with carotid endarterectomy, acute renal failure. Female: 45% Mean BMI: not stated Surgical technique: carotid endarterectomies performed under general anaesthesia using routine shunting and intravenous heparin. Patients were divided into 3 groups: • Normal renal function: GFR ≥60 ml/minute/1.73m^2 • Moderate chronic renal insufficiency: GFR ≥60 to 59 ml/minute/1.73m^2 • Severe chronic renal insufficiency: GFR <30 ml/minute/1.73m^2
Prognostic variable(s)	eGFR
Confounders OR stratification strategy	Unclear what variables multivariable analysis included (only GFR was significant on univariate analysis)
Outcomes and effect sizes	30-day stroke and/or death: adjusted OR (95% CI): 3.7 (1.3–10.53)
Comments	No GFR data available in 15/940 operations Patients with moderate and severe renal insufficiency had more comorbidities

Table 41: Mases 2014 [34]

Reference	Mases 2014
Study type and analysis	Retrospective/post-hoc analysis of prospectively collected data from 23 hospitals in Spain States logistic regression analysis but not well reported/documented
Number of participants and characteristics	n=2323 patients who underwent scheduled (93%) or emergency (7%) non-cardiac surgery from October 2007 to June 2008. Inclusion criteria: middle-aged to elderly patients (≥40 years of age) undergoing scheduled or emergency non-cardiac operations of intermediate-to-high surgery-specific risk according to the guidelines of the American College of Cardiology (ACC) and American Heart Association (AHA). Exclusion criteria: age <40 years, childbirth or any obstetrical procedure related to pregnancy, exclusive use of local or peripheral nerve anaesthesia, procedures outside the operating theatre, surgical procedures related to a previous post-operative complication, and ambulatory surgery. Median (IQR) age: 67 (57–76) years Female: 50.1% Median (IQR) BMI: 27.2 (24.2–30.5) ASA grade: I – 7.4%; II – 52.9%; III – 34.7%; IV – 5.0% Surgical technique: all patients received general or spinal/epidural anaesthesia Patients were divided into 6 groups according to eGFR: • Stage 1: eGFR >90 • Stage 2: eGFR 60–89.9 • Stage 3a: eGFR 45–59.9 • Stage 3b: eGFR 30–44.9 • Stage 4: eGFR 15–29.9 • Stage 5: eGFR <15
Prognostic variable(s)	eGFR calculated from routine serum creatinine measurements preoperatively

Reference	Mases 2014
Confounders OR stratification strategy	The eGFR formula (MDRD equation) itself modifies GFR according to race, age, sex, serum albumin and serum urea nitrogen
Outcomes and effect sizes	All-cause mortality: adjusted OR (95% CI): • Stage 1: ref • Stage 2: 0.8 (0.3–1.8) • Stage 3a: 2.2 (0.9–5.38) • Stage 3b: 2.8 (0.9–7.1) • Stage 4: 11.3 (4.3–70.1) • Stage 5: 5.8 (1.5–22.43) MAACE: Adjusted OR (95% CI): • Stage 1: ref • Stage 2: 1.5 (0.9–2.5) • Stage 3a: 1.8 (0.9–3.60) • Stage 3b: 3.9 (1.90–8.01) • Stage 4: 4.8 (1.90–12.03) • Stage 5: 3.9 (1.3–11.70)
Comments	132 of the original 3519 sample lost to follow-up and 1064 had missing data (34% total missing data)

Table 42: Soong 2008 [40]

Reference	Soong 2008
Study type and analysis	Retrospective observational study of consecutive patients from the Belfast City Hospital database States multiple regression analysis but not well reported/documented
Number of participants	n=155 patients who underwent elective endovascular aneurysm repair from November 1998 to June 2005.

Reference	Soong 2008
and characteristics	Inclusion criteria: diagnosis of elective endovascular repair of abdominal aortic aneurysm (AAA), with or without iliac involvement Exclusion criteria: isolated iliac aneurysm, thoraco-abdominal aneurysm Mean age: 74.9 years Female: 21% Mean BMI: not stated Mean follow-up: 997 days Surgical technique: all patients received non-ionic radiocontrast Note: nine patients had severe renal failure (including 3 haemodialysis-dependent patients) Patients were divided into four groups: • Group I: SCr ≤1.5 mg/dl • Group II: SCr >1.5 mg/dl • Group III: eGFR ≥60 ml/minute • Group IV: eGFR <60 ml/minute
Prognostic variable(s)	eGFR (Serum creatinine measured preoperatively and post-operatively on day 1, 3 and 5, and 1, 3 and 12 months, then annual follow-up. eGFR calculated from above timepoints)
Confounders OR stratification strategy	The eGFR formula (MDRD equation) itself modifies GFR according to race, age, sex, serum albumin and serum urea nitrogen
Outcomes and effect sizes	Perioperative mortality: adjusted RR (95% CI): 0.25 (0.03–2.32) Post-operative renal failure: adjusted OR (95% CI): 0.07 (0.03–0.21)
Comments	132 of original 3519 sample lost to follow-up and 1064 had missing data (34% total missing data)

H.6 Glycated haemoglobin test

H.6.1 HbA1c in diabetes

Table 43: Afsar 2012 [2]

Reference	Afsar 2012
Study type and analysis	Retrospective cohort Single centre Multivariate logistic regression analysis
Number of participants and characteristics	n=73/233 patients with diabetes and stage 5 chronic kidney disease undergoing arteriovenous fistula surgery Mean age=59 Mean BMI=25.5 Smokers=16
Prognostic variable(s)	HbA1c
Confounders OR stratification strategy	• Age • Gender • Smoking status • Fistula location • BMI • Presence of coronary artery disease • Peripheral artery disease • Fasting glucose • HbA1c • Use of antiplatelet drugs
Outcomes and	Primary arteriovenous fistula failure: adjusted OR (95% CI):

Reference	Afsar 2012
effect sizes	2.78 (1.30–5.94)
Comments	Less than 10 events per variable included in the multivariate analysis High risk of attrition bias 15.2% Not stratified by ASA grade

Table 44: Chrastil 2015 [11]

Reference	Chrastil 2015
Study type and analysis	Retrospective cohort Multicentre Multivariable Cox proportional hazards model
Number of participants and characteristics	n=328/13272 patients with diabetes undergoing either primary total knee arthroplasty or primary total hip arthroplasty. Median age=64 Median BMI=35
Prognostic variable(s)	HbA1c
Confounders OR stratification strategy	• HbA1c • Preoperative glucose • Age • Gender • BMI • Charlson comorbidity index • Smoking status • Diabetic complications
Outcomes and effect sizes	Periprosthetic joint infection: HR (95% CI): 0.86 (0.68–1.101)

Reference	Chrastil 2015
	Death: HR (95% CI): 1.30 (1.08–1.56)
Comments	Retrospective Unclear which variables adjusted for Not stratified by ASA grade

Table 45: Dronge 2006 [13]

Reference	Dronge 2006
Study type and analysis	Retrospective cohort Single centre Logistic regression
Number of participants and characteristics	n=490/647 diabetics patients undergoing major non-cardiac surgery Age (median)=71.3 Race (black)=60 Race (other)=430 ASA 1–3=404 ASA 4–5=86 ADL assessment (independent)=401 ADL assessment (not independent)=89 Case status (elective)=382 Case status (urgent)=108 Diabetic therapy (oral treatment)=289 Diabetic therapy (insulin)=201 Wound classification (clean)=273 Wound classification (unclean)=217 Operation length, min (median)=115 HbA1c (median)=7.3

Reference	Dronge 2006
Prognostic variable(s)	HbA1c
Confounders OR stratification strategy	Age, ASA grade, ADL assessment, case status, operation length, wound class, HbA1c
Outcomes and effect sizes	Post-operative infectious complications: OR (95% CI): 2.13 (1.23–3.69)
Comments	Multivariate analysis performed only on factors significant in the univariate analysis HbA1c level of 7

Table 46: Harris 2013 [22]

Reference	Harris 2013
Study type and analysis	Retrospective cohort Single centre Propensity score analysis using boosted regression methods
Number of participants and characteristics	n=6088 diabetics patients undergoing joint arthroplasty
Prognostic variable(s)	HbA1c
Confounders OR stratification strategy	38 variables including: age at time of surgery, gender, race, BMI, ASA physical score status, alcohol consumption, smoking status, comorbidities, VASQIP functional health status score, anaesthesia technique, total operation time, postgraduate year of surgeon and other preoperative lab values
Outcomes and effect sizes	Any complications: OR (95% CI): 1.22 (1.01–1.47) Number of complications: OR (95% CI):

Reference	Harris 2013
	1.18 (0.97–1.43) 90-day mortality: OR (95% CI): 1.37 (0.82–2.29)
Comments	Large sample Analysis is quite clear Retrospective analysis

H.6.2 HbA1c in undiagnosed diabetes

Table 47: Gustafsson 2009 [20]

Reference	Gustafsson 2009
Study type and analysis	Prospective cohort in a single centre in Sweden Univariate and multivariate logistic regression analysis
Number of participants and characteristics	n=120/141 patients undergoing major colorectal surgery Patient characteristics stratified by preoperative HbA1c. Patients with a high HbA1c level were older and had higher BMI. HbA1c >6% mean age (range): 70 (46–84) HbA1c ≤6% mean age (range): 64 (31–90) *p* = 0.013 HbA1c >6% mean BMI (SD): 27.7 (5.2) HbA1c ≤6% mean BMI (SD): 25.3 (4.2) *p* = 0.015 ASA I 14% ASA II 70% ASA III 14% ASA IV 2%

Reference	Gustafsson 2009
	Surgical procedures: 30% anterior resection, 16% abdominal-perineal resection, 6% total colectomy, 24% right hemicolectomy, 8% left hemicolectomy, 16% other resection.
Prognostic variable(s)	HbA1c measured in two categories: >6% and within normal range (defined as 4.5–6%) measured on the day before surgery.
Confounders OR stratification strategy	Age, sex, BMI, ASA grade, preoperative bleeding and duration of surgery
Outcomes and effect sizes	Post-operative surgical complications: OR (95% CI): 2.51 (1.07 to 5.90) Infection: OR (95% CI): 2.02 (0.78 to 5.24)
Comments	The outcome of post-operative complications included a diverse range of complications and although the authors stated there was high heterogeneity across the different types based on HbA1c groupings, this was not further explored. Unclear whether the presented ORs come from univariate or multivariate analysis.

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