PRE-OPERATIVE RISK ASSESSMENT TOOLS FOR MORBIDITY AFTER CARDIAC SURGERY: A SYSTEMATIC REVIEW

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ABSTRACT

BACKGROUND

Post-operative morbidity places considerable burden on health and resources. Thus, strategies to identify, predict and reduce post-operative morbidity are needed.

AIMS

To identify and explore existing pre-operative risk assessment tools for morbidity after cardiac surgery.

METHODS

Electronic databases (including MEDLINE, CINAHL, Embase) were searched to December 2020 for pre-operative risk assessment models for morbidity after adult cardiac surgery. Models exploring one isolated post-operative morbidity and those in patients having heart transplantation or congenital surgery were excluded. Data extraction and quality assessments were undertaken by two authors.

RESULTS

From 2,251 identified papers, 22 models were found. The majority (54.5%) were developed in USA or Canada, defined morbidity outcome within the in-hospital period (90.9%), and focused on major morbidity. Considerable variation in morbidity definition was identified, with morbidity incidence between 4.3% and 52%. The majority (45.5%) defined morbidity and mortality separately but combined them to develop one model, while seven studies (33.3%) constructed a morbidity-specific model. Models contained between five to 50 variables. Commonly included variables were age,

emergency surgery, left ventricular dysfunction and reoperation/previous cardiac surgery, although definition differences across studies were observed. All models demonstrated at least reasonable discriminatory power (area under receiver operating curve (0.61-0.82).

CONCLUSION

Despite the methodological heterogeneity across models, all demonstrated at least reasonable discriminatory power and could be implemented depending on local preferences. Future strategies to identify, predict and reduce morbidity after cardiac surgery should consider the aging population and those with minor and/or multiple complex morbidities.

KEYWORDS: post-operative morbidity; cardiac surgery; pre-operative risk; risk prediction models; morbidity outcome

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INTRODUCTION

It is widely recognised that mortality alone provides only a crude representation of surgical quality and that high quality surgical care should include mortality, morbidity and patient-reported outcomes[1]. In particular, post-operative complications are a serious global concern affecting up to 16.8% of patients[2]. In cardiac surgery, where over one million cardiac surgeries are performed worldwide each year[3], up to 48% of patients experience at least one complication[4]. Those experiencing post-operative complications experience increased intensive care length of stay (LOS)[4], hospital LOS[4, 5, 6,] substantial morbidity at 6-weeks after surgery (between 28%[7] and 38.9%[8], and readmission requirement (between 6%[7] and 15.3%[8]). Moreover, almost a quarter of cardiac surgery patients require community health service support in the initial period after discharge[7] and those who suffer post-operative complications also experience worse quality of life[9] lasting up to three years after surgery[10] and report increased anxiety and fear of dying[11].

In addition to the patient and societal health burden, this poses a huge financial and organisational load on health care systems. Data from the Society of Thoracic Surgeons (STS) suggests the total cost of complications after isolated coronary artery bypass graft surgery (CABG) over the last 10 years was $78.6million in the USA alone[12]. More specifically, the average in-hospital incremental cost of experiencing any complication after CABG is approximately $15,000 per patient[13], higher in those undergoing combined CABG and valve surgery[5], with additional morbidities exponentially increasing costs[12]. Such costs, and the associated challenges imposed on healthcare delivery services, will only continue to increase as surgical complexity, increasing patient age and associated co-morbid conditions also increase[12].

Despite this increasing burden, few countries reliably record post-operative morbidity outcomes after cardiac surgery [14] due to its considered subjective and imprecise nature[15]. That said, greater emphasis has been placed on morbidity outcome in recent years with both the STS National Database (USA) and the National Institute of Cardiovascular Outcomes Research Adult Cardiac Surgery (UK) reporting some morbidity outcomes at national level (for example, reoperation for bleeding or wound infection, post-operative stroke or post-operative renal failure). However, there lacks an international consensus or standardised definition for post-operative morbidity and clinical endpoints in cardiac surgery trials are measured and reported inconsistently[16, 17]. This poses considerable challenges as there is a specific need to be able to identify, measure and then accurately predict complications after cardiac surgery[12]. If strategies to identify, predict and then subsequently reduce post-operative morbidity after cardiac surgery can be found this will improve patient well-being, reduce healthcare costs and increase healthcare service efficiency.

Thus, we sought to undertake a systematic review of pre-operative risk assessment tools of post-operative morbidity after cardiac surgery to identify and examine the existing tools used to define, measure and assess pre-operative risk of post-operative morbidity after cardiac surgery.

METHODS

This review was registered on PROSPERO, an international prospective register of systematic review (February 2019, reference CRD42019120080).

Protocol and registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines[18].

Eligibility criteria

All studies that develop (with or without validation) a pre-operative risk assessment tool of post-operative morbidity after cardiac surgery were eligible for inclusion. Studies were included if they met the following inclusion and exclusion criteria: *Population*: adults (≥18 years of age) undergoing any form of cardiac surgery (including coronary artery bypass grafts and/or valve surgery in isolation or combination) but excluding those undergoing heart transplant, cardiology procedures (for example, percutaneous coronary intervention or Transcatheter Aortic Valve Implantation); *Outcome:* morbidity after cardiac surgery, excluding those that assess one isolated post-operative morbidity outcome (for example, stroke or bleeding only). Studies were not excluded on the basis of publication date or quality assessment outcome, but were required to be available in English language.

Information sources

A search of MEDLINE, Cumulated Index of Nursing and Allied Health Literature, Embase, British Nursing Index, the Cochrane Library and ClinicalTrials.gov (www.clinicaltrials.gov) was undertaken for relevant papers published up to and including December 2020 (last search date 14th December 2020). Identified systematic reviews were reviewed to identify any additional tools.

Search strategy

The above data sources were searched using a strategy comprised of title/abstract text terms paired with (majored) exploded Medical Subject Heading (MeSH) terms, or equivalent, in the following combinations, as per the Cochrane Library search: (*MeSH descriptor:* [Thoracic Surgery] *explode all trees* OR *MeSH descriptor:* [Cardiovascular Surgical Procedures] *explode all trees* OR (((cardiac OR heart*) NEXT (surge* OR surgical*)) OR CABG OR "coronary artery bypass"):ti,ab,kw) AND (*MeSH descriptor:* [Morbidity] *explode all trees* OR (Morbidit*):ti,ab,kw) AND (*MeSH descriptor:* [Risk Assessment] *explode all trees* OR (risk* NEXT (assess* OR scor* OR tool*)):ti,ab,kw). Clinicaltrials.gov

(www.clinicaltrials.gov) was also searched for trials-in-progress, and citation searches were performed on relevant papers.

Study selection

Two rounds of screening occurred. First, a title and abstract review was undertaken followed by a full paper review of those included from the first screening. All screening was undertaken independently by two authors, in accordance with the inclusion and exclusion criteria, with a third author reviewing any discrepancies between authors. The full-text paper of potential studies identified through systematic reviews were obtained and were also screened as per the above process.

Data collection and syntheses (data items and data collection process)

Data extraction included primary author, date of publication, country of study, study design, type of surgery, sample size (in development and validation datasets, where appropriate), definition of morbidity use, morbidity rate, variables (and attributed scores) included in the final tool, and reliability and validity assessment outcome. All data were extracted and collated into a standardised proforma by two authors, with differences resolved through discussion until consensus achieved.

Risk of bias and quality assessment

All included papers were reviewed for quality by two authors using the Critical Appraisal Skills Programme template for clinical prediction rule[19]. A risk of bias graph was generated[20] and studies were not excluded on the basis of the quality assessment.

Analysis

Meta-analysis was not possible due to the heterogeneity of studies. Thus, results were summarised using descriptive statistics, tables and narrative synthesis, as appropriate. Interpretation of the

discriminatory power of the models followed that described by Hosmer and Lemeshow[21]. MedCalc® version 19.7.4 was used to generate a forest plot to compare the discriminatory power of each the models. Interpretation of the analysis was discussed and agreed by all members of the authorship team.

RESULTS

Study selection

A total of 2251 non-duplicate papers were identified for possible inclusion (Figure 1) with 105 papers undergoing independent full-text assessment. This resulted in 22 papers being included for data analysis that described the development of a pre-operative risk assessment tool for post-operative morbidity after cardiac surgery. A complete reference list of all included studies is presented in Supplementary Table 1.

Study characteristics

The study characteristics of the 22 included studies are detailed in Tables 1 and 2. The majority of studies were conducted in USA or Canada (n=12 (54.5%)) (Table 1), with just over a quarter (n=6 (27.3%)) published in the last 10 years. Equal proportions of tools were developed in mixed cohorts of cardiac surgery patients and those specifically undergoing CABG (n=9 (40.9%)), four (18.2%) were developed specifically in valve surgery patients[22, 23, 24, 25] and two focused on risk assessment in the elderly (>70 years[26]; >80 years[27]. More recently, focus has been on adapting existing models, for example, combining tools[26], and adding biomarkers[28, 29] and echo parameters[23]. Overall, development set sample sizes ranged from 152[26] to 670,830[25], while almost all defined outcome within the in-hospital post-operative period (n=20 (90.9%)). Only one study included morbidity outcome up to six months after surgery[30].

Risk of bias

Figure 2 demonstrates the risk of bias across studies. While the vast majority conducted the development of the models in an appropriate cohort of patients, just under half did not validate the model in a different group of patients. Furthermore, in almost three-quarters of studies performance or detection bias was detected or unclear, although the clinical prediction rule was clearly defined in over 75% of studies. Considering studies individually (Figure 3), only three studies demonstrated no bias in any category[31,32, 25,] one study demonstrated bias in all categories and another was unclear in all but the sample population bias category[33].

Definition of post-operative morbidity

Across studies four broad types of definition of morbidity were used (Table 2). Two studies defined morbidity using a surrogate marker (LOS >12 days[34], LOS >10 days[22], while the majority (n=10), and all studies pre-1996, defined morbidity and mortality separately but combined them to develop one model. Similarly, three further studies included death within the morbidity definition[31, 32, 35]. The construction of separate models for mortality and morbidity was first reported in 2000[36] with seven of 12 studies (58.3%) from this time defining and constructing a separate model for post-operative morbidity. However, within these models only two studies used the same definition of morbidity (Hsieh et al 2007[27] used that of Dupuis etc al 2001[37]) (Supplementary Table 1), highlighting the variation of morbidity definitions. The majority defined morbidity as severe morbidity, including a range of variables of varying definitions/criteria, while only Magovern and colleagues defined morbidity as either a major or minor complication[31].

Incidence of post-operative operative morbidity

Overall, the majority of studies (n=9, 40.9%) reported post-operative morbidity incidence between 20% to 30%, although the range across studies was 4.3%[35] to 52%[31, 27]. However, it is important to note that Hsieh et al only included those >80 years old[27], and is considerably higher than that

reported by Dupuis et al using the same morbidity definition but in a younger cohort[37]. Equally, as highlighted previously, Magovern et al was the only study to include both major and minor complications (36% minor complication, 16% major complication)[31]. The reverse is true for Fortescue et al where only five serious adverse events were included in the morbidity definition (death, renal failure, myocardial infarction, cardiac arrest, stroke and coma)[35], which are uncommonly experienced after cardiac surgery[38].

Pre-operative risk assessment model

Six models either used statements or categories to assess risk[37,22] or, as detailed previously, combined or modified existing scores[26,28,29,23.] Of the newly developed models, including those using EuroSCORE, the number of variables included in a model ranged from six[32] to 50[25]. Overall, 94 variables were included across studies with the highly common variables identified as age (n=16), emergency surgery (n=14), left ventricular dysfunction/ejection function (n=14), reoperation/previous cardiac surgery (n=13), renal dysfunction/failure (including creatinine level categories) (n=11) and gender (n=10), where female gender was consistently identified as higher risk (n=8) (Supplementary Table 1). However, despite some variables being commonly included in the models, considerable variations in the definitions of the variables existed. For example, where categorised, eight different age, seven different left ventricular dysfunction/ejection function and eight different renal function definitions were identified. Considering those models defining and measuring post-operative morbidity only (n=7) the common variables were similar and included age (n=7), left ventricular dysfunction/ejection function (n=6), renal dysfunction/failure (including creatinine level categories) (n=4), combined surgery (n=4), lung disease (n=4) and gender (n=4). The discriminatory power of each model is shown in Figure 4, excluding three early models that did not report the area under the receiver operating characteristic curve (area under ROC) or C-statistic [39, 40, 41]. Four studies demonstrated poor discriminatory power (0.6-0.7) while fair (0.7-0.8) or good

(0.8-0.9) discriminatory power was demonstrated in two-thirds of the models (fair n=12 (54.5%); good n=3 (13.6%). No models demonstrated excellent discriminatory power (0.9-1.0).

DISCUSSION

The impact of post-operative morbidity after cardiac surgery, on in-hospital[4], post-discharge[8] physical health and quality of life [9], and the associated financial burden [12], means that strategies to identify, predict and reduce morbidity after cardiac surgery are needed. Our systematic review identified 22 models of pre-operative risk assessment of morbidity after cardiac surgery. There are several findings of note from these studies. Firstly, there is a recognition of a shift over time in how post-operative morbidity has been defined and measured as the relevance, impact and importance of post-operative morbidity has heightened. Secondly, there remains ongoing challenges relating to varying morbidity definitions resulting in a multitude of prediction models using different outcomes;. Thirdly, there is still an overwhelming focus on in-hospital morbidity outcome despite the evidence supporting impact beyond discharge and potentially for several years and finally, only three models demonstrated 'good' discriminatory power while only one of the 22 models considered both major and minor complications. However, it is also interesting to note that morbidity outcome for those undergoing valve surgery is beginning to be considered separately from CABG with four models now available focusing on this patient group.

Increasing age and risk profile

Cardiac surgery is experiencing an increasing age and risk profile of patients although mortality has continued to fall[42]. Despite this, considerable post-operative morbidity was reported in those over 70 years old (24.3%)[26] and 80 years old (51.6%)[27]. Clearly, the differences in definition influence interpretation of these figures but there are two noteworthy points. Firstly, Hsieh and colleagues used the same morbidity definition as the Cardiac Anaesthesia Risk Evaluation Score model[37], which included all cardiac surgery patients and identified a morbidity rate of 20.7% in the development and

22.2% in the validation dataset. Secondly, Afilalo and colleagues added frailty and disability scales to known mortality prediction tools and reported improved model discrimination (compared to mortality prediction alone) for post-operative morbidity[26]. This suggests that elderly patients experience greater post-operative morbidity and that consideration of pre-operative frailty and disability may be useful in predicting post-operative morbidity risk. As it is expected that any life expectancy gains over the next 20 years will be spent living with multiple complex morbidities, efforts on prevention and efficient service provision is needed[43].

Utility in practice

A fundamental challenge of clinical risk prediction scores is their utility in practice [44]. Since operative mortality has been found to be associated with both the number and severity of complications after cardiac surgery[45], and operative mortality risk tools are routinely used in practice, it is not unreasonable to consider whether existing mortality risk prediction tools may also have value in morbidity prediction. Certainly, EuroSCORE, developed to predict operative mortality risk and used widely across Europe, has been applied to explore post-operative morbidity risk prediction. Indeed, two tools identified in this review[28,29] added biomarkers to the EuroSCORE to create new models. Unsurprisingly, due to its discriminatory power in predicting operative mortality, EuroSCORE appears to perform reasonably well in predicting overall in-hospital major morbidity incidence[36,46]. However, EuroSCORE only predicts some, but not all, major (for example, stroke, acute renal failure, respiratory infection, bleeding, myocardial infarction) post-operative complications[47, 46, 48, 49] and these results are also inconsistent across studies. Equally, previous work has highlighted that different risk factors are associated with morbidity outcome as time from surgery progresses. Thus, accepted risk factors and models for operative mortality may only be useful for predicting morbidity risk in the first few critical days of recovery[50]. This principle may also be applied to the vast majority of models in this review, since almost all only considered in-hospital morbidity and major morbidities.

The ‘holy grail’ of prognostic factor research is to improve patient outcomes by providing a personalised approach to healthcare and risk prediction[51] and how these factors can be used to improve patient or treatment outcomes[52]. Clinical risk prediction scores are an important driver for person-centred care[44], at a time when shared decision-making to meaningfully improve outcomes that are important to patients[53] is advocated. Specifically, in the UK these currently include improving the outcomes of frail heart surgery patients and those with chronic conditions, including long-term outcomes [54]. Enhanced Recovery After Surgery cardiac programmes recognise the culture-shift to a person-centred system of care and the importance of the multidisciplinary team in this to optimise patient outcomes and experience[55]. Certainly, nurses and allied professionals working in primary care, optimisation or pre-operative clinics are ideally placed to use clinical risk prediction scores to provide this level of personalised care prior to surgery[56].

Although few countries to date have reliably recorded post-operative morbidity after cardiac surgery[14], efforts to do so are being progressed[57, 42]. This provides the opportunity for more detailed and accurate identification, prediction and subsequent reduction of post-operative morbidity in the future.

Study limitations

This review has three main limitations. Firstly, no studies were excluded on the basis of the quality assessment. This was to enable full exploration of all the models available, although as the results detail, the studies were of varying quality. Secondly, we purposefully only included pre-operative risk assessment tools, excluding those that included intra-operative (and post-operative) variables. If strategies to predict, and then subsequently reduce, post-operative morbidity after cardiac surgery are to be implemented, then pre-operative risk assessment is necessary. Thirdly, due to the heterogeneity of the outcome definition and variations in methodological detail direct comparisons

or undertaking a meta-analysis are not feasible. Despite this, our review, conducted with considerable methodological rigor (for example, not employing any date restrictions, undertaking double independent searching, data extraction and quality assessments), is valuable in describing and summarising the current evidence in this area to enable subsequent work to be undertaken to improve morbidity burden after cardiac surgery.

In conclusion, this review identified 22 pre-operative risk prediction tools for morbidity outcome after cardiac surgery. Those including minor morbidities, focusing on the elderly and including Growth Differentiation Factor 15 biomarker performed well. However, due to the methodological heterogeneity of studies, the lack of ability to undertake direct comparisons or a meta-analysis does limit the scope of conclusion that can be made as they all measure and predict different factors. Certainly, obtaining consensus, both nationally and internationally, would be beneficial for future work. Despite this current lack of standardisation, the review has highlighted that strategies to identify, predict and reduce morbidity after cardiac surgery should consider minor, as well as major morbidities, the impact of in-hospital complications on longer-term recovery and the increasing age, with accompanying multiple complex morbidities, of the current and future cardiac surgery population.

IMPLICATIONS FOR PRACTICE

- Clinical risk prediction models are important for person-centred care and can provide a basis for shared decision making
- Three models exhibit good discrimination and could be used in pre-operative clinics to optimise patient outcome and experience
- Age, frailty and multiple complex morbidities are important factors to consider
- New models that include minor morbidities and consider longer-term recovery are needed

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DECLARATION OF CONFLICTING INTERESTS

The author(s) declare that there are no conflict of interest.

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TABLES AND FIGURES

Table 1: **The study characteristics of each included model (n=22): model name, year of publication, country, design, data collection period and population.**

Study (author, reference and *model name* (where stated*).*	**Year published**	**Country**	**Design** *(includes validation design where conducted)*	**Data collection period**	**Population (surgery type)**
Parsonnet[39]	1989	USA	Retrospective	1982-1987	Open heart surgery
Higgins[58] *Cleveland Clinic score*	1992	USA	Development: Retrospective Validation: Prospective	1986-1988	CABG
Tuman[40]	1992	Canada	Prospective	Not stated	Isolated cardiac surgery
Geraci[59]	1993	USA	Retrospective	1985-1986	CABG
Hattler[41]	1994	USA	Prospective	1991-1993	CABG
Roques[33] *Ontario Province Risk Score (French score)*	1995	France	Prospective	1993	Cardiac surgery
Kurki and Kataja[34]	1996	Finland	Retrospective	1990-1991	CABG

CABDEAL score					
Magovern[31]	1996	USA	Retrospective	Development 1991-1992 Validation: 1993-1994	CABG
Staat[32]	1999	France	Retrospective	1996	CABG
Pitkanen[36]	2000	Finland	Development: Retrospective Validation: Prospective	Development 1992-1996 Validation: 1998-1999	Cardiac surgery
Dupuis[37] *Cardiac Anaesthesia Risk Evaluation Score (CARE)*	2001	Canada	Prospective	Development: 1996-1998 Validation: 1998-1999	Cardiac surgery
Fortescue[35] *Quality Measurement and Management Initiative (QMMI) score*	2001	USA	Prospective	1993-1995	CABG
Wouters[30] *CORRAD score*	2002	Netherlands	Retrospective	Development: 1998 Validation: 1999-2000	CABG

Huijskes[60] *Amphibia score*	2003	Netherlands	Retrospective	1997-2001	CABG +/- valve surgery
Hsieh[27]	2007	Taiwan	Retrospective	2004-2006	Cardiac surgery (>80 years old)
Grinberg[22] *Valve, Myocardial function, Coronary artery disease and Pulmonary artery pressure (VMCP) score*	2009	Brazil	Retrospective	Not stated	Heart valve surgery
Afilalo[26]	2012	USA and Canada	Prospective	2008-2010	CABG +/- valve replacement or repair (>70 years old)
Heringlake[28]	2013	Germany	Prospective	Development: 2009 Validation: 2008	Cardiac surgery
Schoe[29]	2014	Netherlands	Prospective	2006-2010	Elective cardiac surgery

Tan[23]	2015	USA and Canada	Retrospective	USA: 2008-2010 Canada: 2010-2012	Surgical AVR +/- CABG. Also included aortic surgery
LaPar[24]	2018	USA	Retrospective	2002-2014	Isolated tricuspid valve operations
O'Brien[25] *STS Adult Cardiac Surgery Risk Model*	2018	USA and Canada	Retrospective	Development: 2011-2014 Validation: 2014-2016	Considered separately: CABG, Valve, and CABG and Valve

Table 2: **The model characteristics of each included model (n=22): sample size, morbidity definition, timing of morbidity outcome, number of variables in the score and morbidity rate.**

Study *(author and reference)*	**Sample size** *(development and validation)*	[a]**Morbidity definition for model development**	**Timing of morbidity outcome** *(eg in-hospital, 1 week)*	[d]**Number of variables in score** *(taken from text, where stated, otherwise counted from results table)*	**Morbidity rate (%)**
Parsonnet[39]	Development: 3,500 Validation: 300	2	In-hospital[b]	15	23.5
Higgins[58]	Development: 5,051 Validation: 4,069	2	In-hospital	13	13.5
Tuman[40]	Development: 3,156 Validation: 394	2	In-hospital[b]	12	22.2 development 19.8 validation

Geraci[59]	Development: 2,213 (split in half for development and validation)	2	Post-operative	11	33
Hattler[41]	Development: 728 No validation	2	Unclear – some done post-discharge	17	Not stated
Roques[33]	Development: 7,181 No validation	2	In-hospital[b]	8	Not stated
Kurki[34]	Development: 386 No validation	1	In-hospital	7	Not stated
Magovern[31]	Development: 1,567 Validation: 1,235	3	In-hospital[b]	20	16 (major) 36 (minor)
Staat[32]	Development: 679 Validation: 226	3	Post-operative	6	23
Pitkanen[36]	Development: 4,592	4	Post-operative	14	22.0 development

	Validation: 821				18.4 validation
Dupuis[37]	Development: 2,000 Validation: 1,548	1 and 2	In-hospital	6 (statements)	20.7 development 22.2 validation
Fortescue[35]	Development: 6,237 Validation: 3,261	3	Post-operative	16	4.3
Wouters[30]	Development: 653 Validation: 969	4 and 3	Up to 6 months after surgery	20	19.1 development 21 validation
Huijskes[60]	7,282 (split 2/3 for development and 1/3 for validation)	4 and 3	In-hospital	8	17
Hsieh[27]	Development: 199 Validation: 423	4	In-hospital[b]	13	51.6
Grinberg[22]	Development: 768 No validation	1	In-hospital[b]	4 categories each with 4 categories/statements in each	Not stated

Afilalo[26]	Development: 152 No validation	2	In-hospital	Not stated specifically but combines 5 meter-gait speed, STS-PROMM and Nagi scales	24.3
Heringlake[28]	Pooled datasets due to some loss of samples, and low event rate (3.4% mortality): 1452	4	In-hospital[b]	16[c]	14.4
Schoe[29]	Development: 679 No validation	4 and 3 and 1	In-hospital[b]	16[c]	27.5
Tan[23]	Development: 432 No validation	2	In-hospital[b]	STS model (version or number of variables not stated) and echo parameters (3)	20.4
LaPar[24]	Development: 2,050	4	Post-operative	9	42%

	No validation				
O'Brien[25]	Development: 670,830 Validation: 579,335	2	In-hospital[b]	CABG: 50 Valve: 45 CABG and Valve: 47	All: 17.4 CABG: 15.0 Valve: 18.4 CABG and Valve: 28.3

[a] Morbidity definition codes: 1: morbidity defined using surrogate marker (all were hospital LOS); 2. Specifically defined morbidity and mortality separately but included all outcomes in developing one model; 3. Included death in the morbidity definition; 4. Defined mortality and morbidity separately and constructed separate models for each. [b] In-hospital outcome only inferred but not explicitly stated. [c]EuroSCORE used was additive/model 1[61] containing 15 variables; [d]The specific variables included for each model are available in Supplementary Table 1

Figure 1: Preferred Reporting Items for Systematic reviews and Meta-Analyses flow chart

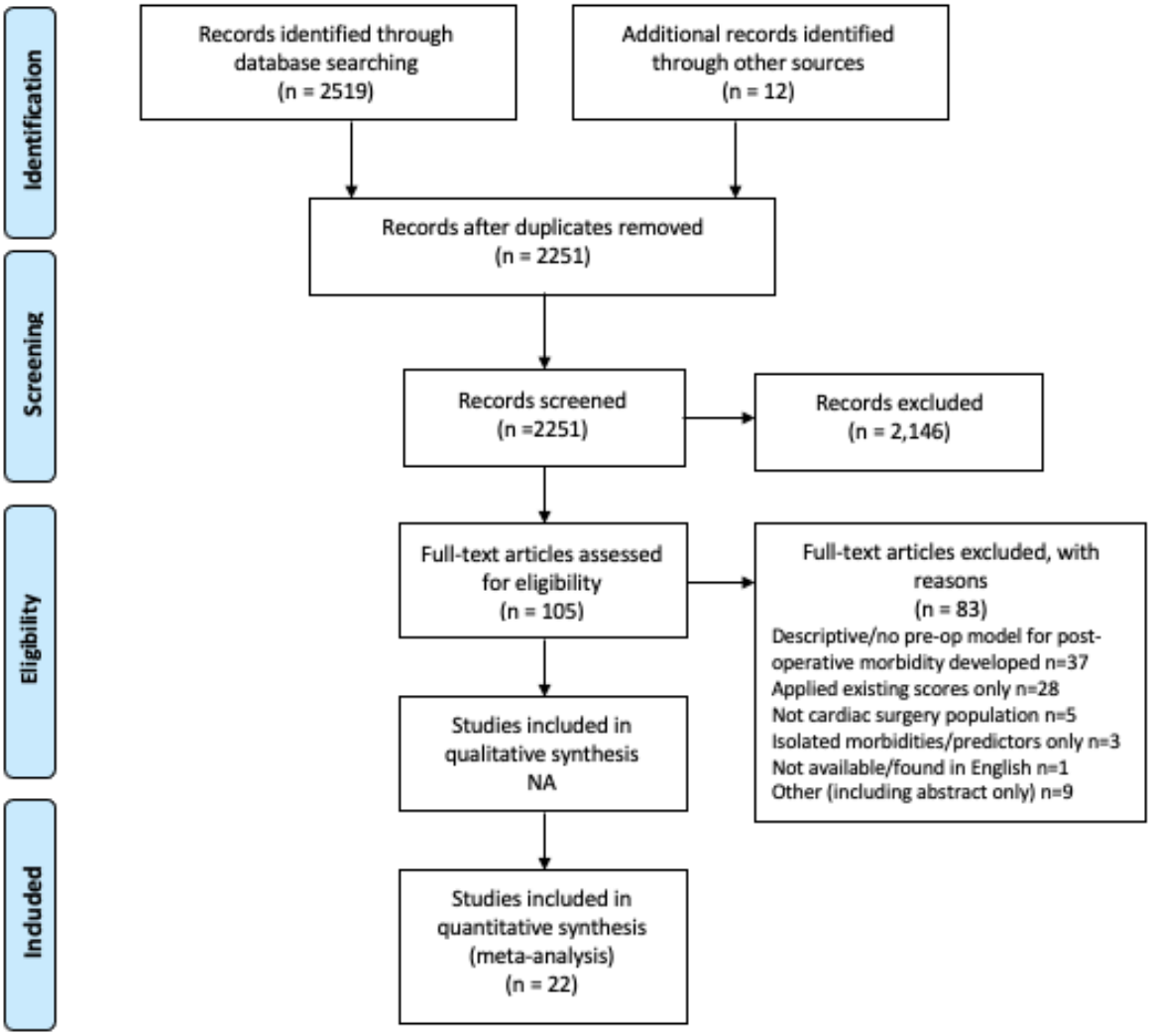

Figure 2: Risk of bias summary

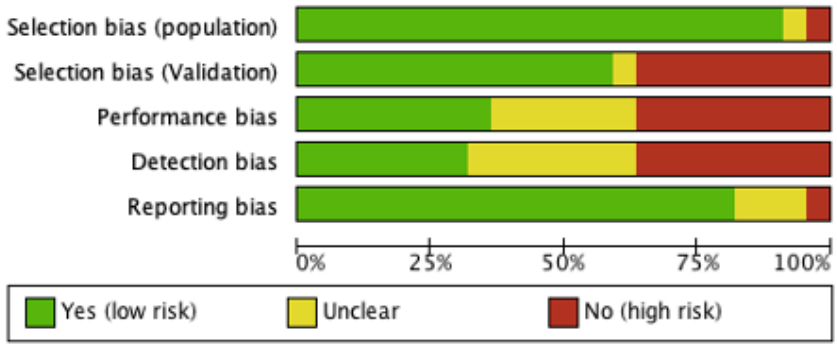

Figure 3: Risk of bias of individual studies

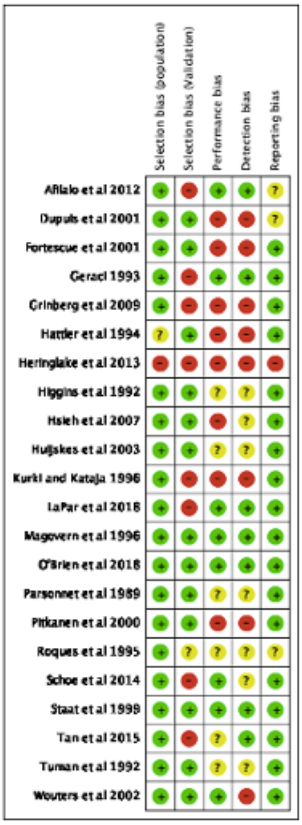

Figure 4: The discriminatory power of each model

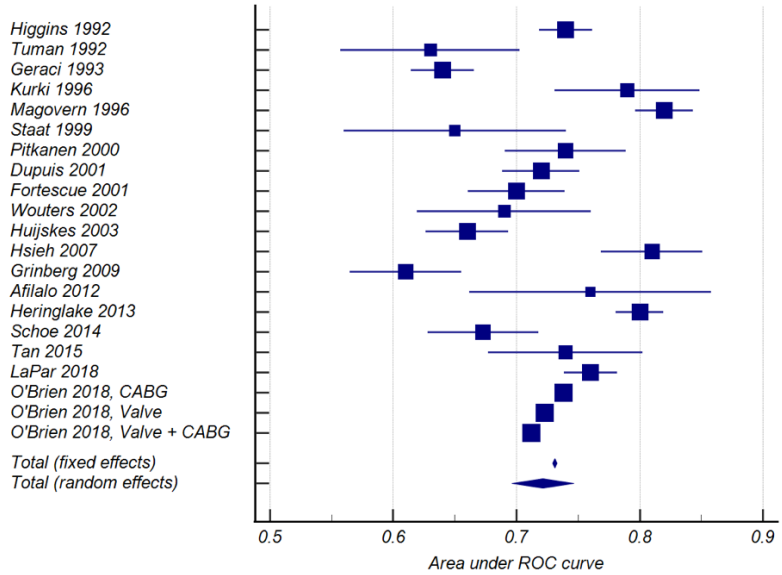

FIGURE LEGENDS

Figure 1: Preferred Reporting Items for Systematic reviews and Meta-Analyses flow chart.

Abbreviations: NA - Not applicable; Pre-op – pre-operative.

Figure 2: A summary of the overall risk of bias across all 22 studies included in Tables 1 and 2. Red = high risk of bias; Yellow = unknown risk of bias; Green = low risk of bias.

Figure 3: The risk of bias of the 22 individual studies included in Tables 1 and 2. Red (-) = high risk of bias; Yellow (?) = unknown risk of bias; Green (+) = low risk of bias.

Figure 4: For the models listed in Tables 1 and 2 (excluding three that studies that did not report the area under the receiver operating characteristic curve (area under ROC) or C-statistic), the individual effect sizes (squares) and their confidence intervals (95%) are shown. The size of the square reflects the random effect weight assigned to each study. There is significant heterogeneity between the studies so the random effects estimate for the overall effect is 0.72 (0.69-0.75) (diamond).

Abbreviations: ROC - receiver operating characteristic curve