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Systematic Review

Risk Factors for Readmission After Knee Arthroplasty Based on Predictive Models: A Systematic Review

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ABSTRACT

Background: An increase in the aging yet active US population will continue to make total knee arthroplasty (TKA) procedures routine in the coming decades. For such joint procedures, the Centers for Medicare and Medicaid Services introduced programs such as the Comprehensive Care for Joint Replacement to emphasize accountable and efficient transitions of care. Accordingly, many studies have proposed models using risk factors for predicting readmissions after the procedure. We performed a systematic review of TKA literature to identify such models and risk factors therein using a reliable appraisal tool for their quality assessment.

Methods: Five databases were searched to identify studies that examined correlations between post-TKA readmission and risk factors using multivariate models. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis methodology and Transparent Reporting of a multivariate prediction model for Individual Prognosis Or Diagnosis criteria established for quality assessment of prognostic studies.

Results: Of 29 models in the final selection, 6 models reported performance using a C-statistic, ranging from 0.51 to 0.76, and 2 studies used a validation cohort for assessment. The average 30-day and 90-day readmission rates across the studies were 5.33% and 7.12%, respectively. Three new significant risk factors were discovered.

Conclusions: Current models for TKA readmissions lack in performance measurement and reporting when assessed with established criteria. In addition to using new techniques for better performance, work is needed to build models that follow the systematic process of calibration, external validation, and reporting for pursuing their deployment in clinical settings.

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Introduction

The Affordable Care Act of 2010 aimed to universally increase patient access to care, reduce overall health-care spending, and improve the quality of medical services throughout the United States. To address this goal of reduced spending for effective and efficient medical care, the Hospital Readmission Reduction Program within the Affordable Care Act altered the existing landscape of hospital-based medicine, with its emphasis on incentivizing quantifiable, inpatient health outcomes [1]. Specifically, Section 3205 enables hospitals to receive financial incentives for minimizing all-cause 30-day patient readmissions [2]. This integration of financial incentives with overall practice quality has had a great effect on a variety of procedures, with one of the most noticeable impacts being in the field of orthopaedics through total knee arthroplasties (TKAs) and total hip arthroplasties [3].

The combined cost for hospital readmissions after primary total hip arthroplasty and TKA is exorbitant, amounting to roughly 1.1

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billion USD [4]. By the year 2030, more than 3.5 million TKAs will have been performed, with potential for an exponential increase, given Medicaid's expansion qualifying more individuals for elective procedures [1,5,6]. This amounts to a greater than 600% projected increase for TKA, most of which is already covered by Medicare [3]. Thus, the Centers for Medicare and Medicaid Services (CMS) introduced the Comprehensive Care for Joint Replacement model in 2016 for total knee and hip replacements in many metropolitan areas. This model represents a departure from the typical fee-for-service model and makes hospitals responsible for a bundle of care, starting from admission to 90 days after discharge; if hospitals spend more than the precalculated cost of care determined by the CMS for hip or knee replacements, they are responsible for covering the rest of the cost, but if they spend less, they receive a financial bonus [7]. This system imposes caps on repayment and bonuses depending on the sequential year of implementation, with an ultimate goal of promoting regional competition among hospitals to implement low-cost but highly effective ways to increase quality of care and decrease readmissions. Decreasing cost associated with readmissions concurrently improves transition of care at and after discharge, thereby decreasing the likelihood of further readmissions [8,9] and increasing value for patients.

In response to the changing care landscape, many studies have proposed predictive models for readmissions after TKA to better assess risk and costs and to facilitate transitions of care. For instance, a predictive model developed in 2019 by Ali et al [10] delineated specific predictors of 30-day TKA readmissions based on an analysis of 566,273 procedures in the United Kingdom over a 10-year period. Specific predictors found to significantly increase 30-day readmissions included obesity, coagulopathy, psychosis, arrhythmias, chronic obstructive pulmonary disease, advanced age, and emergency hospital admission in the previous 12 months. Another large study by Urish et al [11] noted that the greatest predictors for TKA 30-day readmissions include congestive heart failure, hospital length of stay (LOS) greater than 4 days, and chronic renal disease, with a median cost of approximately $6753 USD per readmission. Despite these valuable findings, both studies fall short when appraised against gold-standard criteria and use of a validation cohort. These studies are representative of paucity in the literature delineating evidence-based and critically appraised risk factors contributing to 30-day TKA readmissions. Accordingly, the purpose of this study was threefold: (i) to identify validated and clinically usable statistical models predicting readmissions for patients undergoing TKA; (ii) to assess the quality of the models with a reliable appraisal tool; and (iii) to leverage the identified models to elucidate new evidence-based factors contributing to 30-day TKA readmission. We hypothesize that the majority of current studies outlining predictors for 30-day TKA readmissions lack appraisal against standard gold criteria and inclusion of held-out or external validation cohorts.

Material and methods

Search strategy and criteria

This study followed criteria set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement [12]. The article heading, use of the PRISMA

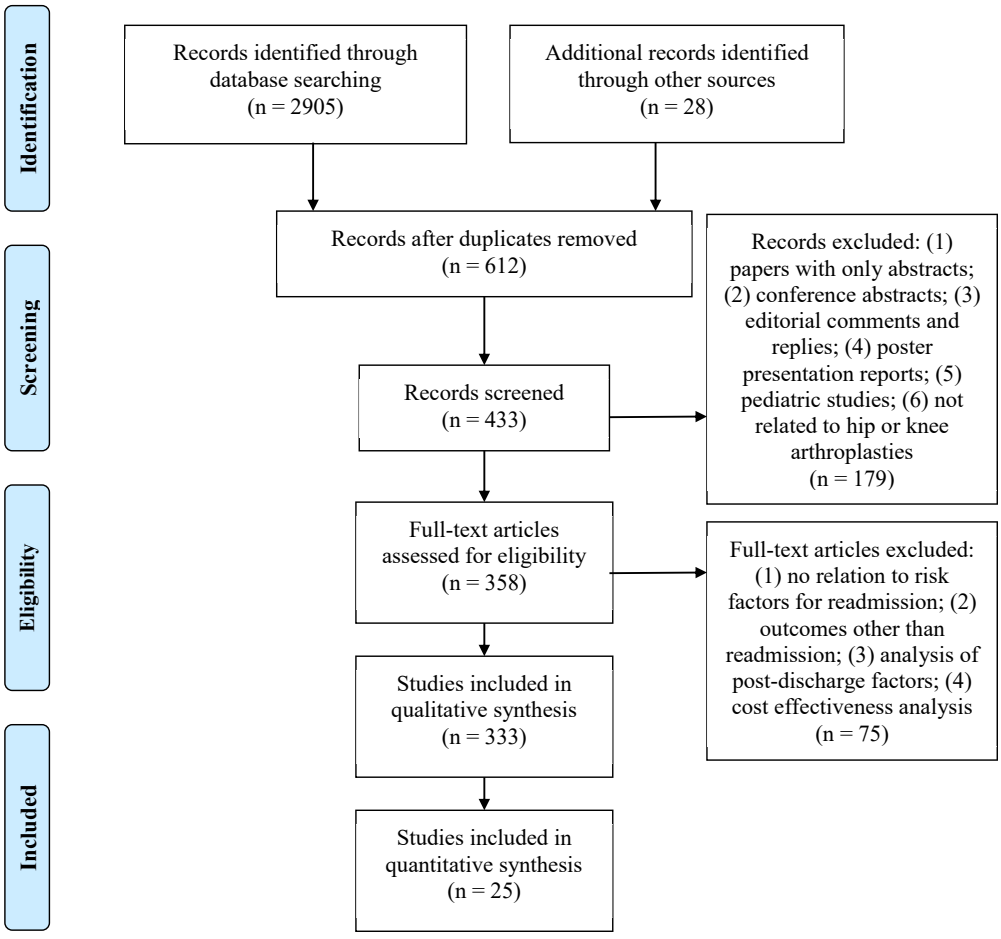

Figure 1. PRISMA flow diagram for systematic review of predictive models for TKA readmissions.

flow diagram shown in Figure 1 for study selection [13], and use of the PRISMA-P checklist in Electronic Supplementary Table 1 reflect adherence to the PRISMA-P criteria [14]. In addition, a priori protocol registration and description were performed at the PROSPERO registry site (Registration number: CRD42018108571) [15].

The initial search began with a manual exploration of printed articles in the hospital medical library and an electronic search on Google Scholar. Important and relevant reference articles from the initial search were additionally obtained, ultimately accounting for 28 articles during manual search. Analysis of these articles helped establish an automated strategy for searching electronic databases. This systematic review describes readmission prediction models for only knee arthroplasty; however, the search criteria were formulated for both hip and knee arthroplasty procedures. This strategy was adopted for completeness because our initial search revealed 3 paradigms for cohort selection: (i) some studies had used combined cohorts of patients undergoing hip and knee arthroplasties; (ii) some others had created separate subgroups for hip and knee arthroplasties from a common cohort; and (iii) the remaining had used only patients who underwent knee arthroplasty. A medical librarian and one author (B.T.A. and S.M.M.) designed and implemented all the searches in the following databases: (1) PubMed; (2) Embase; (3) Ovid MEDLINE; (4) Cochrane Database of Systematic Reviews; and (5) Web of Science. If the database did not take the exact date for search, it was approximated to the nearest month and/or year. We searched for articles between the date of inception of each database and February 2019. Each database had slightly different search methodology; nonetheless, the search was first started with *hospital readmission* as the exploded Medical Subject Headings (MeSH) term, and the key words *readmi**, *rehosp**, where * was used as the truncation character. Second, we searched for *risk* as the exploded MeSH term, and the key words were *model**, *predict**, *use**, *util**, and *risk**. Third, we performed a search that used the exploded MeSH terms *arthroplasty*, *replacement*, *total*, *partial*, *prosthesis*, and *knee*. Fourth, we performed a search that used the exploded MeSH terms *arthroplasty*, *replacement*, *total*, *partial*, *hemiarthroplasty*, *prosthesis*, and *hip*. Finally, we combined all the search criteria that identified our final reference set in each database.

Inclusion and exclusion

Study eligibility was determined using 3 stages of title review, abstract review, and full-article review. In addition, studies were considered eligible if they (a) used readmission as an independent or composite outcome; (b) measured readmission after index hospitalization for TKA; (c) examined the association between readmission and predictors using a multivariate statistical model; and (d) were published in the English language. Finally, if a study reported multiple models, one of which used readmission as an outcome, that model was included in this analysis.

Assessment of study quality

Figure 1 shows the steps of article selection in the PRISMA flow diagram. It also shows exclusion criteria at each step of the selection process, starting with 2933 articles and ending with 358 articles for full review.

In the final step, we excluded studies (n = 85) that (1) analyzed readmissions after generic index admission and did not have TKA as the discharge diagnosis and (2) created cohorts based on explicit subgroups such as revision arthroplasty or knee fracture. Each article selected for detailed review was appraised for risk of bias using the Transparent Reporting of a multivariate prediction model for Individual Prognosis Or Diagnosis (TRIPOD) assessment tool [16]. The TRIPOD standard is used specifically for transparent reporting of studies developing, validating, or updating a multivariate prediction model for prognostic purposes. It is implemented as a 22-item checklist that provides comprehensive criteria for ensuring that authors report the necessary information to compare, contrast, and assess the predictive capabilities of various models. Electronic Supplementary Table 2 shows the checklist applied to all the models in the final selection of studies. The TRIPOD tool factored out studies that did not analyze multivariate models (n = 213), and thus, it reduced the risk of bias in the final selection of studies. During this step, we also found other reviews (n = 10); 6 of these were related to the postoperative management and interventions after joint or knee surgery discharge and hence were excluded from our analysis. Of the remaining 4 reviews [17-20], one review considered only postoperative factors after hip arthroplasties [17]. The 2 reviews focused on total joint arthroplasties but did not adhere to formal systematic review standards; they are literature reviews and described modifiable and nonmodifiable risk factors for patients undergoing joint arthroplasties [19,20]. One of the two studies also considered perioperative risk factors including administrative and systemic factors after the discharge and hence did not describe predictive factors for readmissions [20]. Podmore et al. (2018) [18] considered short- and long-term impacts of comorbidities in patients undergoing joint arthroplasty on many outcome variables, with readmission as one of the outcomes in their systematic review and meta-analysis. Risk factors other than comorbidities, however, were not considered in their review. Thus, none of the reviews have aimed to carry out a systematic review adhering to the specific reporting standards to understand the quantitative impact of all the risk factors on readmission after TKA.

Data collection and abstraction

Our detailed review entailed 25 studies that described 29 risk models (7 combined hip and knee arthroplasty cohort models and 22 TKA models). Cram et al. (2012) [21], Mnatzaganian et al. (2014) [22], and Swenson et al. (2018) [23] created 2, 3, and 2 models, respectively, in the same study, with subgroups based on specific predictors or outcome criteria. This analysis was carried out by at least 2 authors separately (E.K. and S.M.M.; C.N. and S.M.M.; J.B. and S.M.M.), and results of the selection process were verified for selection bias and resolution of low-confidence selections by each author. A predictive model was considered to be a statistical construct for this review, created to understand the combined effect of predictors derived from known data sources on readmission as the outcome, using a specific study design. Predictive models may also be referred to as risk stratification models—both here and in other literature—in that a predictive model is used to stratify population of patients based on their membership of specific risk categories such as high, medium, or low risk of readmission. In addition, we extracted the following data items from each study in a tabulated format in 3 separate documents: (1) the research study design, the country where the study was conducted, data source and timeframe of the data cohort, derivation and validation cohort sizes, statistical model used, and whether the risk score was created (items summarized as research study characteristics and shown in Table 1); (2) readmission as a single or composite outcome measure, whether the outcome was TKA specific or all-cause or surrogate readmission measure, timeframe used for readmission, observed readmission rate, and C-statistic or area under the curve for validation cohort (items summarized as outcome characteristics and shown in Table 2); (3) significant risk factors in each final model (items summarized as risk factor characteristics and shown in Table 3).

Table 1
Study design characteristics for studies for readmissions for TKA.

Study	Research study design	Data source	Year(s) of data	Derivation cohort	Validation cohort	Statistical model	Country/risk score creation
(Solomon, Chibnik et al., 2006) [24]	Retrospective	CMS files and EHR system	2000	9073	NR	HMLR	USA/Yes
(Higuera, Elsharkawy et al., 2011) [25] (TKA subgroup)	Prospective	Single-center EHR system	2008	352	NR	HMLR	USA/No
(Cram, Lu et al., 2012-a) [21] (Primary TKA only)	Retrospective	CMS files	1991-2010	915,562	NR	MLR	USA/No
(Cram, Lu et al., 2012-b) [21] (Revision TKA only)	Retrospective	CMS files	1991-2010	74,935	NR	MLR	USA/No
(Pugely, Callaghan et al., 2013) [26] (TKA subgroup)	Retrospective	ACS-NSQIP	2011	11,814	NR	MLR	USA/No
(Pugely, Martin et al., 2013) [27]	Retrospective	ACS-NSQIP	2005-2010	14,052	NR	MLR	USA/No
(Mnatzaganian, Ryan et al., 2014-a) [22] (Subset1 predictors)	Retrospective	Single-center EHR system	1996-1999	819	NR	CPHR	Australia/No
(Mnatzaganian, Ryan et al., 2014-b) [22] (Subset2 predictors)	Retrospective	Single-center EHR system	1996-1999	819	NR	CPHR	Australia/No
(Mnatzaganian, Ryan et al., 2014-c) [22] (Subset3 predictors)	Retrospective	Single-center EHR system	1996-1999	819	NR	CPHR	Australia/No
(Schairer, Vail et al., 2014) [28]	Retrospective	Single-center EHR system	2005-2011	1408	NR	CPHR	USA/No
(Belmont, Goodman et al., 2016) [29]	Retrospective	ACS-NSQIP	2011-2012	1754	NR	MLR	USA/No
(Feng, Lin et al., 2017) [30]	Retrospective	Single-center knee arthroplasty registry	2008-2013	1542	NR	MLR	China/No
(Lee, Kumar et al., 2017) [31]	Retrospective	Single-center EHR system	2004-2013	3049	NR	MLR	Korea/No
(Siracuse, Ippolito et al., 2017) [32]	Retrospective	HCUP for 4 states	2006-2011	433,638	269,934	MLR	USA/Yes
(Kimball, Nichols et al., 2018) [33] (TKA subgroup)	Retrospective	CMS files	2014-2015	58,064	NR	CPHR	USA/No
(Lehtonen, Hess et al., 2018) [34]	Retrospective	ACS-NSQIP	2012-2015	137,209	NR	MLR	USA/No
(Saku, Madanat et al., 2018) [35]	Retrospective	Finnish Hospital Discharge Register	2015	894	NR	MLR	Finland/No
(Urish, Qin et al., 2018) [11]	Retrospective	HCUP	2014	224,465	NR	MLR	USA/No
(Yohe, Funk et al., 2018) [36]	Retrospective	ACS-NSQIP	2008-2014	12,026	NR	MLR	USA/No
(Ali, Louffler et al., 2019) [10]	Retrospective	NHS ES	2006-2016	566,323	NR	MLR	UK/No
(Zmistowski, Restrepo et al., 2013) [37]	Retrospective	Single-center EHR system	2004-2008	5426	NR	MLR	USA/No
(Mesko, Bachmann et al., 2014) [38]	Retrospective	Single-center EHR system	2010-2011	1291 THKA combined	1291 (with bootstrapping of 1000 samples)	MLR	USA/Yes
(Tiberi, Hansen et al., 2014) [39] (Only for cirrhosis patients undergoing THKA)	Retrospective – 1:2 matched case control	Single-center EHR system	2000-2012	230 THKA combined	NR	MLR	USA/Yes
(Ricciardi, Oi et al., 2017) [40]	Retrospective – 1:2 matched case control	Single-center EHR system	2010-2014	21,864 THKA combined	NR	MLR	USA/No
(Sher, Keswani et al., 2017) [41]	Retrospective	ACS-NSQIP	2011-2014	7474 THKA combined	NR	MLR	USA/No
(Yao, Keswani et al., 2017) [42] (TKA subgroup)	Retrospective	ACS-NSQIP	2011-2014	71,293	NR	MLR	USA/No
(Schroer, Diesfield et al., 2018) [43]	Retrospective	Multicenter (5) EHR system	2014-2015	6968 THKA combined	NR	DS	USA/No
(Swenson, Bastian et al., 2018-a) [23] (30 day readmission)	Retrospective	Single-center EHR system	2013-2015	622 THKA combined	NR	MLR	USA/No
(Swenson, Bastian et al., 2018-b) [23] (90 day readmission)	Retrospective	Single-center EHR system	2013-2015	622 THKA combined	NR	MLR	USA/No

CPHR, Cox proportional hazards regression; DS, descriptive study; HCUP, Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality; HMLR, Hierarchical Logistic Regression Model using Generalized Estimating Equations; MLR, multivariate logistic regression; NHS ES, National Health Service Hospital Episode Statistics database; NR, not reported; Subset1, subset predictors of age and the number of comorbidities; Subset2, subset predictors of age and Charlson Comorbidity Index; Subset3, Subset predictors of age and Elixhauser Comorbidity Index; THKA, total hip or knee arthroplasty.

Results

The earliest predictive model for TKA readmissions was published in 2006 with the majority published between 2011 and 2019 (Table 1). Of the total, 22 of 29, or 76%, were built in the United States [11,21,23–29,32–34,36–43]. Three models were built in Australia [22], and one each in China [30], Finland [35], Korea [31], and the United Kingdom [10]. One model was based on the prospective design [25], and the remaining (97%) were retrospective designs with 2 models applying additional case control [39,40].

Table 2
Outcome characteristics for studies for readmissions for TKA.

Study	Outcome: readmission—single measure or composite readmission/mortality or other complications requiring readmission	Readmission days	Observed readmission rate (%)	C-statistics or AUC for validation cohort
(Solomon, Chibnik et al., 2006) [24]	Composite	90	3.6	0.62
(Higuera, Elsharkawy et al., 2011) [25]	Composite–complications	90	9.4	NR
(Cram, Lu et al., 2012-a) [21]	Single	30	5.0	NR
(Cram, Lu et al., 2012-b) [21]	Single	30	8.9	NR
(Pugely, Callaghan et al., 2013) [26]	Composite–complications	30	4.6	NR
(Pugely, Martin et al., 2013) [27]	Composite–complications	30	10.7 & 12.3[a]	NR
(Mnatzaganian, Ryan et al., 2014-a) [22]	Single	90	NR	0.51
(Mnatzaganian, Ryan et al., 2014-b) [22]	Single	90	NR	0.54
(Mnatzaganian, Ryan et al., 2014-c) [22]	Single	90	NR	0.61
(Schairer, Vail et al., 2014) [28]	Composite–complications	30 & 90	4.0 & 8.0	NR
(Belmont, Goodman et al., 2016) [29]	Single	30	6.2	0.75
(Feng, Lin et al., 2017) [30]	Composite–complications	30	8.9	NR
(Lee, Kumar et al., 2017) [31]	Single	30 and 90[b]	1.9 and 3.3	NR
(Siracuse, Ippolito et al., 2017) [32]	Single	30	5.1	NR
(Kimball, Nichols et al., 2018) [33]	Single	30	5.4	NR
(Lehtonen, Hess et al., 2018) [34]	Single	30	3.4	NR
(Saku, Madanat et al., 2018) [35]	Single	90	8.0	NR
(Urish, Qin et al., 2018) [11]	Composite–complications	30	4.0	NR
(Yohe, Funk et al., 2018) [36]	Composite–complications	30	4.7	NR
(Ali, Louffler et al., 2019) [10]	Single	30	6.0	NR
(Zmistowski, Restrepo et al., 2013) [37]	Composite–complications	30 & 90	3.1 & 5.3	NR
(Mesko, Bachmann et al., 2014) [38]	Single	30	3.6	0.76
(Tiberi, Hansen et al., 2014) [39]	Single	90	10.0	NR
(Ricciardi, Oi et al., 2017) [40]	Single	30	NR	NR
(Sher, Keswani et al., 2017) [41]	Composite–complications	30	1.9	NR
(Yao, Keswani et al., 2017) [42]	Composite–complications	30	3.5	NR
(Schroer, Diesfield et al., 2018) [43]	Composite–complications	90	8.4	NR
(Swenson, Bastian et al., 2017-a) [23]	Composite–complications	30	3.4	NR
(Swenson, Bastian et al., 2017-b) [23]	Composite–complications	90	8.1	NR

AUC, area under the curve; NR, not reported.
[a] : For spinal and general anesthesia, respectively.
[b] Not reported which outcome was used for modeling.

Most studies used either the Electronic Health Record (EHR) database at the facility (13 of 29, or 44%) [22,23,25,28,31,37,38,39,40,43] or the American College of Surgeons–National Surgical Quality Improvement Program (ACS NSQIP) database (7 of 29, or 24%) [26,27,29,34,36,41,42] for building models. The other data sources used were insurance files, health databases, and surgical procedure registers at a national level (7 of 29, or 24%) [10,21,24,30,33,35] and health databases at a state level (2 of 29, or 7%) [11,32]. The models were built with a minimum of 230 patients and a maximum of 566,323 patients. Most researchers used multiple logistic regression (23 of 29, or 79%) [10,11,21,23–27,29,30–32,34–42], with 2 studies [24,25] using its hierarchical version. Five of 29 models (17%) [22,28,33] used Cox proportional hazards regression, whereas one study [43] provided descriptive statistics with frequency percentages for various risk factors in the sample cohort.

All the studies determined any- or all-cause readmission after TKA in accordance with the CMS definition of 30-day readmission, as opposed to only TKA-related readmissions (Table 2). 13 of 29 models (45%) [11,23,25–27,30,36,37,41–44] used various types of postsurgical complications as surrogate outcomes for readmission. Most models focused on 30-day readmission (17 of 29, or 59%) [10,11,21,23,26,27,29,30,32–34,36,38,40–42]. Nine models (31%) [22–25,35,39,43] used 90-day readmission as an outcome measure, whereas 3 models (10%) [28,31,37] used both 30-day and 90-day outcome measures for readmissions. The cohort-specific empirical readmission rates varied across the studies, and 2 studies, one with 3 models [22] and the other with one model [40], did not report readmission rates in their cohorts. In the remaining studies, 20 models built with 30-day readmission as an outcome had an average readmission rate of 5.33% (min: 1.90%; max: 12.30%; standard deviation: 2.82). The remaining 9 models built on 90-day readmission as an outcome variable had an average readmission rate of 7.12% (min: 3.30%; max: 10.00%; standard deviation: 2.45). Thus, in the pooled sample, the average 90-day readmission rate is 34% higher than the average 30-day readmission rate. All the models presented adjusted odds ratios (ORs) for significant predictors where applicable; however, only 6 of 29 models across 4 studies [22,24,29,38] presented an aggregate performance C-statistic that ranged from a minimum of 0.51 to a maximum of 0.76.

We classified the risk factors into overarching categories to understand their impact on post-TKA readmissions (Table 3). Accepting only risk factors in the 75th percentile of the number of references predicting readmission, the following factors were found to be significant: age, sex, discharge disposition, LOS, hypertension, heart disease, American Society of Anesthesiologists (ASA) physical status class, coagulopathy, diabetes, smoking, and pulmonary disease (Fig. 2). The 75th percentile cutoff was chosen for what was considered substantial support because of the right-skewed distribution: selecting those above average 50th percentile would have included many risk factors with weak support from merely one or 2 studies (Fig. 3). Note that Figure 3 depicts only significant factors of readmission found across the reviewed publications. Meta-analysis on the risk factors across the studies was not attempted because of inconsistencies in the factor and outcome definitions. For example, some studies used age as continuous variable [22,42], whereas others created bins for age as a categorical variable as per differing cutoff points [24–27,32]. Similarly, some studies presented ORs for 30-day readmission as an outcome [10,11,21,26,30,32,33,34,36], whereas others for 90-day readmission as an outcome [23–25,35,43].

Table 3
Risk factor characteristics for studies for readmissions for TKA.

Predictors (level)	Unit of measure and comparison	Effect size [CI] (wrt reference)[a,b]	Study
Demographics			
Age (patient)	65-70/71-80/81-95 years	OR: 1.3 [1.0-1.6] (71-80 wrt 65-70) OR: 1.6 [1.1-2.4] (81-95 wrt 65-70)	(Solomon, Chibnik et al., 2006) [24]
Age (patient)	65-74/75-84/85+ years	RR: 1.43 [1.14-1.80] (75-84 wrt 65-74) RR: 1.25 [0.79-1.98] (85 + wrt 65-74)	(Higuera, Elsharkawy et al., 2011) [25]
Age (patient)	65-74/75-84/85+ years	OR: 1.4 [1.4-1.4] (75-84 wrt 65-74) OR: 1.8 [1.8-1.9] (85 + wrt 65-74)	(Cram, Lu et al., 2012-a) [21]
Age (patient)	65-74/75-84/85+ years	OR: 1.2 [1.1-1.2] (75-84 wrt 65-74) OR: 1.4 [1.3-1.5] (85 + wrt 65-74)	(Cram, Lu et al., 2012-b) [21]
Age (patient)	<45/46-55/56-65/66-75/76-85/>85 years	OR: 2.59 [1.44-4.67] (<45 wrt 56-65) OR: 1.42 [1.08-1.85] (76-85 wrt 56-65) OR: 1.79 [1.09-2.97] (>85 wrt 56-65)	(Pugely, Callaghan et al., 2013) [26]
Age (patient)	50-59/60-69/70-79/>=80 years	OR: 1.53 [1.26-1.87] (70-79 wrt 50-59) OR: 2.17 [1.73-2.74] (>=80 wrt 50-59)	(Pugely, Martin et al., 2013) [27]
Age (patient)	Continuous years	HR: 1.02 [0.98-1.06]	(Mnatzaganian, Ryan et al., 2014-b) [22]
Age (patient)	41-50/51-60/61-70/71-80/81-90 years	OR: 1.13 [1.05-1.22] (41-50 wrt 51-60) OR: 1.01 [0.97-1.06] (61-70 wrt 51-60) OR: 1.21 [1.15-1.28] (71-80 wrt 51-60) OR: 1.70 [1.61-1.81] (81-90 wrt 51-60)	(Siracuse, Ippolito et al., 2017) [32]
Age (patient)	50-59/60-69/70-79/>80	OR: 1.40 [0.72-2.69] (50-59 wrt <50) OR: 1.66 [0.87-3.16] (60-69 wrt <50) OR: 2.33 [1.18-4.59] (70-79 wrt <50) OR: 4.17 [1.18-4.59] (>80 wrt <50)	(Sher, Keswani et al., 2017) [41]
Age (patient)	Continuous years	OR: 1.01 [1.01-1.02]	(Yao, Keswani et al., 2017) [42]
Race (patient)	White/African/Hispanic-Asian-Native (other)	OR: 1.2 [1.2-1.3] (African wrt white) OR: 0.9 [0.9-1.0] (Other wrt white)	(Cram, Lu et al., 2012-a) [21]
Race (patient)	White/African/Hispanic-Asian-Native (Other)	OR: 1.1 [1.0-1.2] (African wrt white) OR: 0.9 [0.8-1.1] (Other wrt white)	(Cram, Lu et al., 2012-b) [21]
Race (patient)	African/white	OR: 1.68 [1.35-2.09] (African wrt white)	(Pugely, Martin et al., 2013) [27]
Race (patient)	White/African/Hispanic-Asian-Native (other)	OR: 1.37 [1.30-1.44] (African wrt white) OR: 1.08 [1.04-1.13] (Other wrt white)	(Siracuse, Ippolito et al., 2017) [32]
Sex (patient)	Male/female	OR: 1.6 [1.3-2.1] (Male wrt female)	(Solomon, Chibnik et al., 2006) [24]
Sex (patient)	Male/female	OR: 1.3 [1.2-1.3] (Male wrt female)	(Cram, Lu et al., 2012-a) [21]
Sex (patient)	Male/female	OR: 1.1 [1.0-1.2] (Male wrt female)	(Cram, Lu et al., 2012-b) [21]
Sex (patient)	Male/female	OR: 1.25 [1.03-1.53] (Male wrt female)	(Pugely, Callaghan et al., 2013) [26]
Sex (patient)	Male/female	OR: 1.18 [1.35-2.09] (Female wrt male)	(Pugely, Martin et al., 2013) [27]
Sex (patient)	Male/female	OR: 1.75 [1.15-2.68] (Female wrt male)	(Belmont, Goodman et al., 2016) [29]
Sex (patient)	Male/female	OR: 1.19 [1.16-1.23] (Male wrt female)	(Siracuse, Ippolito et al., 2017) [32]
Sex (patient)	Male/female	OR: 1.31 [1.21-1.42] (Male wrt female)	(Yao, Keswani et al., 2017) [42]
Sex (patient)	Male/female	OR: 3.44 [2.838-4.042] (Male wrt female)	(Swensen, Bastian et al., 2018-a) [23]
Sex (patient)	Male/female	OR: 10.6 [9.67-11.53] (Male wrt female)	(Swensen, Bastian et al., 2018-b) [23]
BMI (patient)	BMI >40 kg/m^2	OR: 1.25 [0.73-2.16] (BMI >40 wrt no)	(Sher, Keswani et al., 2017) [41]
BMI (patient)	BMI >40 kg/m^2	OR: 1.09 [0.96-1.23] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Obesity (patient)	BMI >45 kg/m^2	DS: 11.3%	(Schroer, Diesfield et al., 2018) [43]
Administrative			
Cluster 5 (patient)	Age 59.17/BMI 41.25/LOS 59.33/pain 33.47/symptoms 34.91/function daily life 33.3/function sports and leisure 7.89/QOL 10.43	OR: 4.52 [3.779-5.261]	(Swensen, Bastian et al., 2018-a) [23]
Discharge HHC (system)	Yes/no	OR: 23.5 [22.06-24.94] (Yes wrt no)	(Swensen, Bastian et al., 2018-b) [23]
Discharge other location (system)	Other than HHC, SNF, and IRF: Yes/no	OR: 31.3 [30.183-32.417] (Yes wrt no)	(Swensen, Bastian et al., 2018-a) [23]
Discharge other location (system)	Other than HHC, SNF, and IRF: Yes/no	OR: 48.1 [46.45-49.75] (Yes wrt no)	(Swensen, Bastian et al., 2018-b) [23]
Disposition (system)	Home/IRF	OR: 1.99 [1.50-2.64] (IRF wrt home)	(Zmistowski, Restrepo et al., 2013) [37]
Disposition (system)	Home or IRF/SNF	HR: 1.62 [1.11-1.24] (SNF wrt home or IRF)	(Schairer, Vail et al., 2014) [28]
Dedicated orthopaedic operating room for >75% time (system)	Yes/no	OR: 1.3 [1.0-1.7] (No wrt yes)	(Solomon, Chibnik et al., 2006) [24]
Hospital teaching status (system)	Major/minor/nonteaching	OR: 0.9 [0.9-1.0] (Minor wrt major) OR: 0.9 [0.9-0.9] (Nonteaching wrt major)	(Cram, Lu et al., 2012-a) [21]
Hospital teaching status (system)	Major/minor/nonteaching	OR: 0.9 [0.9-1.0] (Minor wrt major) OR: 0.9 [0.9-1.0] (Nonteaching wrt major)	(Cram, Lu et al., 2012-b) [21]
Hospital volume for primary TKA (system)	Quartile1/ Quartile2/ Quartile3/ Quartile4	OR: 0.9 [0.8-0.9] (Quartile2 wrt Quartile1) OR: 0.8 [0.8-0.9] (Quartile3 wrt Quartile1)	(Cram, Lu et al., 2012-a) [21]

(*continued on next page*)

Table 3 (*continued*)

Predictors (level)	Unit of measure and comparison	Effect size [CI] (wrt reference)[a,b]	Study
		OR: 0.8 [0.7-0.8] (Quartile4 wrt Quartile1)	
Hospital volume for revision TKA (system)	Quartile1/ Quartile2/ Quartile3/ Quartile4	OR: 1.0 [0.8-1.1] (Quartile2 wrt Quartile1) OR: 1.0 [0.8-1.1] (Quartile3 wrt Quartile1) OR: 0.9 [0.8-1.1] (Quartile4 wrt Quartile1)	(Cram, Lu et al., 2012-b) [21]
Hospital volume for TKR (system)	High (≥23)/low (<23)	OR: 1.6 [1.1-2.5] (Low wrt high)	(Solomon, Chibnik et al., 2006) [24]
Income (patient)	First/second/third/fourth quartile	OR: 0.99 [0.95-1.04] (First wrt fourth) OR: 0.98 [0.94-1.02] (Second wrt fourth) OR: 0.97 [0.94-1.01] (Third wrt fourth)	(Siracuse, Ippolito et al., 2017) [32]
Insurance (patient)	Private/Medicare/Medicaid/ self-pay	OR: 1.27 [1.22-1.32] (Medicare wrt private) OR: 1.43 [1.33-1.54] (Medicaid wrt private) OR: 0.70 [0.52-0.93] (Self-pay wrt private)	(Siracuse, Ippolito et al., 2017) [32]
LOS - log (patient)	Continuous days	OR: 1.9 [1.9-2.0]	(Cram, Lu et al., 2012-a) [21]
LOS - log (patient)	Continuous days	OR: 2.1 [2.0-2.2]	(Cram, Lu et al., 2012-b) [21]
LOS (patient)	≤5/>5 days	HR: 1.94 [1.3-2.9] (>5 wrt <=5)	(Schairer, Vail et al., 2014) [28]
LOS (patient)	Continuous days	OR 1.19 [1.00-1.40]	(Saku, Madanat et al. 2018) [35]
Preoperative teaching program (system)	Yes/no	OR: 1.8 [1.2-2.6] (No wrt yes)	(Solomon, Chibnik et al., 2006) [24]
Type of anesthesia (provider)	Spinal/other	RR: 0.65 [0.51-0.81] (Spinal wrt other)	(Higuera, Elsharkawy et al., 2011) [25]
Type of anesthesia (provider)	General/spinal	OR: 1.13 [1.00-1.27] (General wrt spinal)	(Pugely, Martin et al., 2013) [27]
Type of anesthesia (provider)	General/other (spinal-epidural-regional)	OR: 1.74 [1.09-2.79] (General wrt other)	(Belmont, Goodman et al., 2016) [29]
Type of surgery - revision (provider)	Primary/revision/AS TKA	HR: 2.0 [1.3-3.0] (Revision wrt primary) HR: 1.79 [1.0-3.1] (ACS wrt primary)	(Schairer, Vail et al., 2014) [28]
Type of surgery - unilateral or bilateral (provider)	Unilateral/bilateral TKA	RR: 1.66 [1.18-2.35] (Bilateral wrt unilateral)	(Higuera, Elsharkawy et al., 2011) [25]
Comorbidities			
Anemia (patient)	Yes/no	OR: 1.19 [1.14-1.23] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
Anemia (patient)	Hemoglobin <10 g/dL	DS: 20%	(Schroer, Diesfield et al., 2018) [43]
Ischemic heart disease/arrhythmia (patient)	Yes/no	RR: 1.73 [1.36-2.21] (Yes wrt no)	(Higuera, Elsharkawy et al., 2011) [25]
Arrhythmia (patient)	Yes/no	OR: 11.3 [10.25-12.35] (Yes wrt no)	(Swensen, Bastian et al., 2018-b) [23]
ASA level (patient)	Class 4/class 1-2	OR: 1.42 [1.15-1.74] (4 wrt 1-2)	(Pugely, Callaghan et al., 2013) [26]
ASA level (patient)	Class 3-4/not 3-4	OR: 1.20 [1.06-1.37] (3-4 wrt not 3-4)	(Pugely, Martin et al., 2013) [27]
ASA class (patient)	Class 3-4/1-2	OR: 1.42 [1.01-2.00] (Class 3-4 wrt 1-2)	(Sher, Keswani et al., 2017) [41]
ASA class (patient)	Class 3 or 4: Yes/no	OR: 1.37 [1.25-1.50] (Yes wrt no)	(Yao, Keswani et al. 2017) [42]
Asthma (patient)	Yes/no	OR: 2.60 [1.30-5.21] (Yes wrt no)	(Saku, Madanat et al., 2018) [35]
COPD (patient)	Yes/no	OR: 1.29 [1.24-1.34] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
Avascular necrosis etiology (patient)	Yes/no	OR: 0.69 [0.22-2.19] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Bleeding disorder (patient)	Yes/no	OR: 2.01 [1.34-3.01] (Yes wrt no)	(Pugely, Callaghan et al., 2013) [26]
Bleeding disorder (patient)	Yes/no	OR: 1.22 [1.11-1.34] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
Bleeding disorders (patient)	Current bleeding-causing disorder (Yes/no)	OR: 2.56 [1.22-5.38] (Yes wrt no)	(Sher, Keswani et al., 2017) [41]
Bleeding disorders (patient)	Yes/no	OR: 1.63 [1.33-2.01] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Cancer (patient)	Yes/no	OR: 11.73 [1.93-71.30] (Yes wrt no)	(Pugely, Callaghan et al. 2013) [26]
Lymphoma (patient)	Yes/no	OR: 23.6 [22.25-24.95] (Yes wrt no)	(Swensen, Bastian et al., 2018-b) [23]
CCI (patient)	0.8	RR: 1.18 [1.11-1.26] (Per index point)	(Higuera, Elsharkawy et al., 2011) [25]
CCI (patient)	Continuous	HR: 1.09 [0.98-1.19]	(Mnatzaganian, Ryan et al., 2014-b) [22]
Number of comorbidities (patient)	Continuous	OR: 2.20 [1.94-2.46]	(Swensen, Bastian et al., 2018-a) [23]
Cardiac disease (patient)	Chronic heart failure in 30 days before surgery, myocardial infarction within 6 months of surgery, previous percutaneous coronary intervention, or history of angina within 1 month of surgery: Yes/no	OR: 1.44 [0.73-2.84] (Yes wrt no)	(Sher, Keswani et al., 2017) [41]
Congestive heart failure (patient)	Yes/no	OR: 1.64 [1.53-1.76] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
Chronic heart failure (patient)	Yes/no	OR: 1.14 [0.56-2.35] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Deep venous thrombosis (patient)	Yes/no	OR: 8.59 [2.36-31.24] (Yes wrt no)	(Belmont, Goodman et al., 2016) [29]
Diabetes (patient)	Yes/no	OR: 1.19 [1.15-1.23] (Yes wrt no)	(Siracuse, Ippolito et al. 2017) [32]
Diabetes (patient)	Yes/no	OR: 1.28 [0.82-2.01] (Yes wrt no)	(Sher, Keswani et al., 2017) [41]
Diabetes (patient)	Yes/no	DS: 11%	(Schroer, Diesfield et al., 2018) [43]
Diabetes (patient)	Yes/no	OR: 1.03 [0.92-1.15] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
ECI (patient)	0/1-2/3-4/>4		(Cram, Lu et al., 2012-a) [21]

Table 3 (*continued*)

Predictors (level)	Unit of measure and comparison	Effect size [CI] (wrt reference)[a,b]	Study
		OR: 1.3 [1.2-1.3] (1-2 wrt 0) OR: 1.8 [1.7-1.8] (3-4 wrt 0) OR: 2.3 [2.2-2.5] (>4 wrt 0)	
ECI (patient)	0/1-2/3-4/>4	OR: 1.2 [1.0-1.3] (1-2 wrt 0) OR: 1.4 [1.3-1.6] (3-4 wrt 0) OR: 1.8 [1.6-2.1] (>4 wrt 0)	(Cram, Lu et al., 2012-b) [21]
Epilepsy (patient)	Yes/no	OR: 5.36 [1.17-24.62] (Yes wrt no)	(Saku, Madanat et al., 2018) [35]
Fluid and electrolyte disorders (patient)	Yes/no	HR: 1.80 [1.12-1.27] (Yes wrt no)	(Schairer, Vail et al., 2014) [28]
Fluid and electrolyte disorders (patient)	Yes/no	OR: 1.25 [1.19-1.32] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
High number of drugs (patient)	Yes/no	OR: 1.11 [1.04-1.19] (Yes wrt no)	(Saku, Madanat et al., 2018) [35]
Hypertension (patient)	Yes/no	OR: 1.10 [1.07-1.14] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
Hypertension (patient)	Yes/no	OR: 2.10 [1.14-3.87] (Yes wrt no)	(Saku, Madanat et al., 2018) [35]
Hypertension-managed (patient)	Yes/no	OR: 0.61 [0.31-0.96] (Yes wrt no)	(Belmont, Goodman et al., 2016) [29]
Hypertension (patient)	Yes/no	OR: 1.28 [0.91-1.79] (Yes wrt no)	(Sher, Keswani et al., 2017) [41]
Hypertension (patient)	Yes/no	OR: 23.6 [22.4-24.8] (Yes wrt no)	(Swensen, Bastian et al., 2018-b) [23]
Hypertension (patient)	Yes/no	OR: 1.18 [1.08-1.30] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Liver disease (patient)	Yes/no	OR: 1.27 [1.13-1.43] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
Malnutrition (patient)	Albumin <3.4 g/dL	DS: 8.8%	(Schroer, Diesfield et al., 2018) [43]
Narcotic use (patient)	Narcotic prescription filled within 3 months of surgery	DS: 10.7%	(Schroer, Diesfield et al., 2018) [43]
Preoperative knee flexion (patient)	<110 degrees (Yes/no)	OR: 1.86 [1.03-3.36] (Yes wrt no)	(Saku, Madanat et al., 2018) [35]
Preoperative tibiofemoral angle (patient)	Angle <0/0-4 /11-15/>15	OR: 1.16 [0.51-2.65] (Angle <0 wrt 5-10) OR: 1.18 [0.46-3.04] (Angle 0-4 wrt 5-10) OR: 2.94 [1.19-7.27] (Angle 11-15 wrt 5-10) OR: 1.27 [0.39-4.12] (Angle >15 wrt 5-10)	(Saku, Madanat et al., 2018) [35]
Preoperative serum BUN level (patient)	Continuous mg/dL	OR: 1.02 [1.01-1.03]	(Pugely, Callaghan et al., 2013) [26]
Preoperative serum creatinine level (patient)	Continuous mg/dL	OR: 1.48 [1.24-1.75]	(Pugely, Martin et al., 2013) [27]
Psychiatric disease (patient)	Yes/no	OR: 2.97 [1.30-6.81] (Yes wrt no)	(Saku, Madanat et al., 2018) [35]
Walking aid (patient)	Yes/no	OR: 2.26: [1.03-4.94] (Yes wrt no)	(Saku, Madanat et al., 2018) [35]
Pulmonary disease (patient)	Yes/no	OR: 1.36 [0.65-2.86] (Yes wrt no)	(Sher, Keswani et al. 2017) [41]
Pulmonary disease (patient)	Yes/no	OR: 1.43 [0.56-2.35] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Smoking (patient)	Yes/no	DS: 7.6%	(Schroer, Diesfield et al., 2018) [43]
Smoking (patient)	Yes/no	OR: 1.62 [1.06-2.46] (Yes wrt no)	(Sher, Keswani et al., 2017) [41]
Smoking (patient)	Yes/no	OR: 1.43 [1.25-1.63] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Steroid use (patient)	Yes/no	OR: 1.79 [0.86-3.74] (Yes wrt no)	(Sher, Keswani et al., 2017) [41]
Steroids for chronic disease (patient)	Yes/no	OR: 1.35 [1.11-1.65] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Operative variables			
Severe adverse event before discharge (patient)	Yes/no	OR: 13.13 [5.1-33.79] (Yes wrt no)	(Sher, Keswani et al., 2017) [41]
Severe adverse event before discharge (patient)	Yes/no	OR: 3.69 [2.79-4.86] (Yes wrt no)	(Yao, Keswani et al., 2017) [42]
Postoperative medical complications			
MELD score (patient)	<10/≥10	OR: 3.16 [1.35-7.39] (≥10 wrt <10)	(Tiberi, Hansen et al., 2014) [39]
Number of significant risk factors (patient)	0/1/2/3/≥4	OR: 1.43 [1.09-1.88] (1 wrt 0) OR: 2.08 [1.61-2.69] (2 wrt 0) OR: 2.82 [2.18-3.64] (3 wrt 0) OR: 4.36 [3.37-5.66] (>4 wrt 0)	(Yao, Keswani et al., 2017) [42]
Postoperative surgical complications			
RCI (patient)	0/1/2+	OR: 1.5 [1.2-1.9] (1 wrt 0) OR: 1.7 [1.2-2.3] (2 + wrt 0)	(Solomon, Chibnik et al., 2006) [24]
MELD score (patient)	<10/≥10	OR: 4.75 [1.45-15.56] (≥10 wrt <10)	(Tiberi, Hansen et al., 2014) [39]
Renal disease (patient)	Yes/no	OR: 1.33 [1.25-1.42] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
Rheumatoid arthritis (patient)	Yes/no	OR: 1.14 [1.06-1.23] (Yes wrt no)	(Siracuse, Ippolito et al., 2017) [32]
Stroke or cerebrovascular accident (patient)	Yes/no	OR: 3.47 [1.30-9.25] (Yes wrt no)	(Belmont, Goodman et al., 2016) [29]
Superficial surgical site infection (patient)	Yes/no	OR: 16.57 [5.82-47.22] (Yes wrt no)	(Belmont, Goodman et al., 2016) [29]
Deep or incisional or organ space surgical site infection (patient)	Yes/no	OR: 15.09 [5.57-40.91] (Yes wrt no)	(Belmont, Goodman et al., 2016) [29]
Urinary tract infection (patient)	Yes/no	OR: 3.41 [1.04-11.22] (Yes wrt no)	(Belmont, Goodman et al., 2016) [29]

wrt, with respect to; AS, antibiotic spacer; ASA, American Society of Anesthesiologists patient fitness level before surgery; BMI, body mass index; CCI, Charlson Comorbidity Index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; DS, descriptive statistics; HHC home health care; IRF, Inpatient Rehabilitation Facility; MELD, Model for End-stage Liver Disease; QOL quality of life; RCI, Replacement Composite Index; SNF, Skilled Nursing Facility; TKR, total knee replacement.

[a] Effect size reported as adjusted odds ratio (OR) or hazards ratio (HR) or relative risks ratio (RR) typically at $P < .05$ (some ratios significant at higher P values are reported by some authors).

[b] Odds ratio for continuous variables is reported as change in readmission odds for unit change in continuous variable.

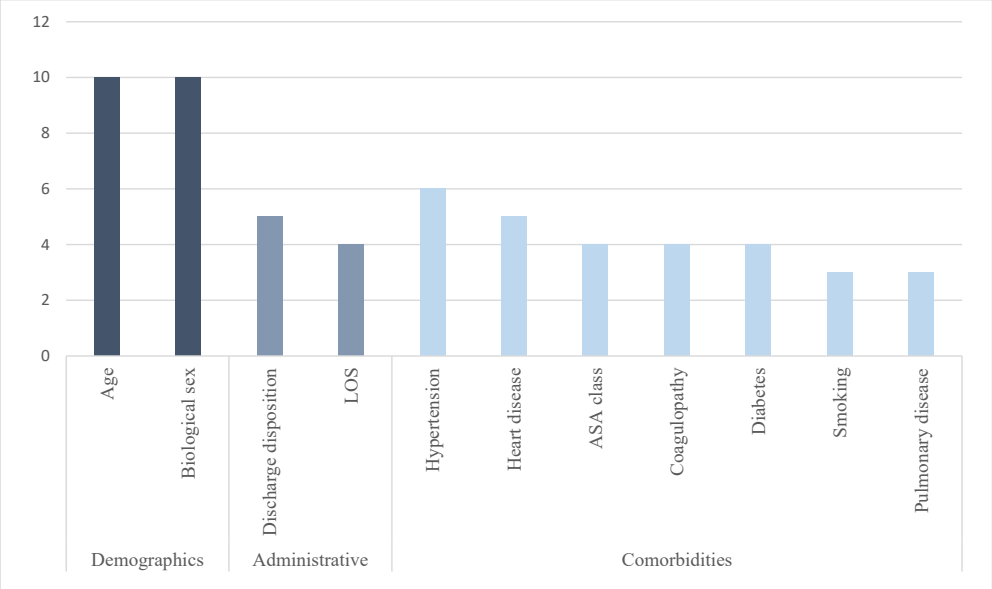

Figure 2. Number of references associated with each significant risk factor.

Discussion

Study design characteristics

All the studies except one in the final selection of the review used single-arm, retrospective, and observational design for cohort selection. This is expected because no interventions were considered in any study while quantifying and predicting the risk of future readmission, and given that the main objective of all selected studies was to understand factors associated with the risk of post-TKA readmission. Many studies used ACS-NSQIP data sets to take advantage of the large sample size and diverse geographic representation of patients across multiple years. This cohort setup is useful for deriving statistical models; however, only 2 models [32,38] of 29 used it to create separate test data sets for validation of the derived models. A large percentage of studies used data sets derived from the facility EHR systems. This preference for building models and understanding the risk factors based on the local data sets represents an interesting divergence from using national data sources. Nonetheless, support for significant risk factors for post-TKA readmission appears to be impervious to specific data origin. Finally, none of the models used newer and more advanced methods—such as machine learning and deep learning methods—for building predictive models. This lack of use of new tools might represent a scarcity of professionals with advanced computational and statistical backgrounds and signifies a missed opportunity to implement better-performing predictive models for eventual deployment in clinical practice.

Outcome characteristics

The studies in our review used differing outcome measures, perhaps because the Readmission Reduction Program uses a 30-day readmission measure, whereas the bundled payment model uses a 90-day readmission measure. Another finding is that a majority of studies have not reported any predictive performance measures. This is concerning in terms of incomplete reporting, but more importantly, the absence of any reportable performance measure makes it hard to compare and understand the influence of the combined risk factors on the predicted outcome. This is a requirement if one wants to deploy the models in clinical practice for assessing risk of future events.

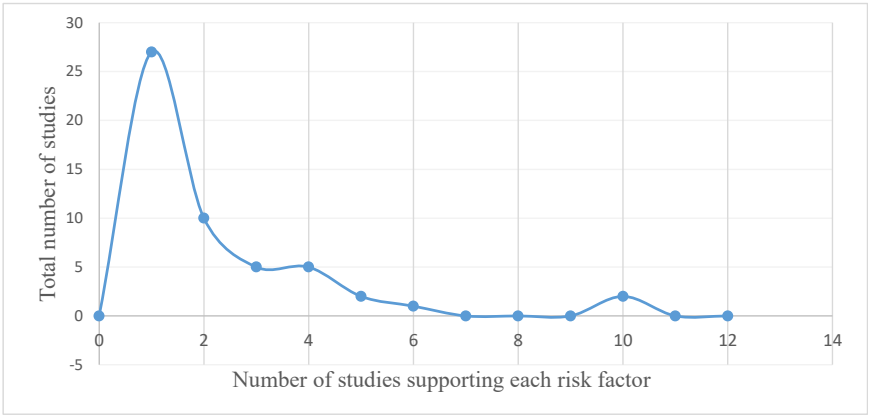

Figure 3. Right-skewed distribution in the number of references associated with each risk factor.

Previously established risk factors for readmission after TKA

A risk factor was deemed previously established if it was referenced by reviews before the beginning of our analysis. Of the factors in the 75th percentile of the number of supporting references, 8 of 11 factors had been previously established as risk factors for readmission after TKA: age, sex, LOS, hypertension, heart disease, diabetes, smoking, and pulmonary disease.

Sveom et al. [20] previously referenced age and found that there were moderate increases in readmission in older patients. We found that among new studies included in our review (Table 3), older age was a risk factor for readmission after TKA. However, there were 2 studies that also showed a slight uptick in readmission in a younger population group. Pugely et al. found that patients younger than 45 years had a significantly increased risk of readmission after TKA (OR: 2.59 [1.44, 4.67]) [26]. Siracuse et al. backed this finding with a slightly higher risk in patients aged 41-50 years (OR: 1.13 [1.05, 1.22]) [32]. Both used 50-60 years of age as a reference range. However, the remaining 8 studies that referenced age as a risk factor indicated that increased age was associated with increased risk [21,22,24,25,27,41,42]. Increased age has also been shown to be associated with an increased number of comorbidities, which can result in poorer wound healing, poorer rehabilitation potential, and increased recovery time after a major joint replacement [45].

Sveom et al. also referenced sex as a risk factor previously [20], finding that males were at higher risk for readmission. Among the 10 studies in our review that referenced sex as a risk factor for readmission (Table 3), 8 studies found male sex as a significant risk factor for readmission. Pugely et al. and Belmont et al. both found that female sex was associated with a higher risk for readmission [29,27]. However, a second study by Pugely et al. found that male sex was associated with a higher risk for readmission [26]. Despite these conflicting data, the vast majority of studies indicated male sex as a risk factor for readmission after TKA [21,23,24,26,32,42]. Many studies have previously documented the variable manifestations of common diseases between male and female patients based on hormone composition, such as the influence of testosterone and the protective benefits of estrogen in bone health and joint recovery [46]. Thus, it is plausible that a lack of estrogen might contribute to the slightly increased risk for readmission among male patients.

Sveom et al. [20] found that an increased LOS was associated with a higher risk of readmission. Three other studies in our review also identified LOS as a risk factor for readmission (Table 3) [21,28,35]. Similar to the effects of age and sex, a longer LOS has been previously correlated with a higher number of comorbidities, such as chronic obstructive pulmonary disease, congestive heart failure, and diabetes [47,48]. The downstream manifestations of these chronic medical conditions lead to less-robust postsurgical recovery, thereby causing higher readmission risks for patients with longer LOS, given a higher likelihood of complications including hospital-acquired infections.

Hypertension has been previously indicated as a risk factor by Podmore et al. for contributing to increased risk of TKA readmissions [18]. Furthermore, Belmont et al. found that hypertension treated with medication decreased the risk of readmission after TKA (OR: 0.61 [0.39, 0.96]) [29], making it a tractable and modifiable risk factor. Overall, hypertension has been indicated as a risk factor for readmission by 6 studies (Table 3) [23,29,32,35,41,42]. Hypertension is associated with numerous complications as it is often secondary to atherosclerosis, especially in elderly patients. In such situations, patients may experience decreased overall perfusion, leading to diminished oxygen transport and blood flow to recovering tissues after joint replacement surgery.

Diabetes has been extensively indicated as a risk factor for readmission after TKA [18-20,49]. Four studies in our review indicated diabetes as a risk factor (Table 3) [32,41–43]. Diabetes has been well characterized as leading to delayed wound healing because of the effect of glucose in hindering immune cell activation and transport through an osmotic effect [50]. Specifically, diabetes creates a proinflammatory state in the body, with cytokines further contributing to erroneous signaling during postsurgical recovery. Thus, delayed wound healing can lead to further complications, most notably wound infection, that lead to increased readmission risk.

Smoking has also been extensively indicated as a risk factor for readmission after TKA [19,20,49]. Three studies in our review also indicated smoking as a risk factor for readmission (Table 3) [41–43]. The combination of nicotine and carbon monoxide from cigarettes causes vasoconstriction and decreased oxygen saturation, both of which lead to decreased oxygen supply to healing tissue. Smoking also negatively affects lipid profiles by increasing low-density lipoprotein and decreasing high-density lipoprotein [51]. With this vasoconstriction and alteration in lipid profiling, decreased overall perfusion from smoking delays wound healing and increases risk of readmission.

Sveom et al. and Podmore et al. have characterized heart disease as a risk factor for readmission [18,20]. Five studies included in our review also characterized heart disease as a risk factor for readmission (Table 3) [23,25,32,41,42]. Sveom et al. and Podmore et al. [18,20] have also identified pulmonary disease as a risk factor for readmission. Four studies in our review characterized pulmonary disease as a risk factor for readmission (Table 3) [32,35,41,42]. Because heart disease and pulmonary disease are generic risk factors, it is difficult to pinpoint an exact mechanism by which they increase the risk of readmission. However, they are both likely related to decreased oxygen perfusion, longer recovery times, and increased risk of infection.

New risk factors for readmission after TKA

Among the factors in the 75th percentile of the number of references in our review, coagulopathy, ASA class, and discharge disposition have not yet been referenced as risk factors previously for post-TKA readmission.

Coagulopathies were referenced 4 times as risk factors for readmission after TKA (Table 3). Patients with a coagulopathy were indicated to be at a higher risk for readmission [26,32,41,42]. Coagulopathies are comorbidities that predispose patients to bleeding, which could lead to postoperative complications requiring readmission. Because TKA disrupts well-vascularized tissue, bleeding is common. Rosenburg describes 3 complications from bleeding: hemarthrosis, hematoma, and wound drainage [52]. All 3 complications need careful observation if mild but severe bleeding could lead to clinical symptoms that require treatment [52]. By predisposing patients to bleeding, coagulopathies increase the risk for severe complications requiring treatment.

The ASA class was referenced 4 times as a risk factor for readmission after TKA (Table 3). ASA class 1 is indicative of a normal, healthy patient, and ASA class 2 is indicative of a patient with mild systemic disease [53]. Patients are classified as ASA class 3 if they have a severe systemic disease that is not life-threatening and class 4 if they have a severe systemic disease that is a constant threat to life. The studies in our review identified ASA classes 3 and 4 as significant risk factors for readmission when compared with ASA classes 1 and 2 [26,27,41,42]. Patients categorized as ASA class 5 require surgery to survive, such as in cases of ruptured abdominal aortic aneurysm or intracranial hemorrhage with mass effect; similarly, patients categorized as ASA class 6 are brain dead and undergoing surgery for organ donation [53]. TKA, being an elective surgery with the goal of improving quality of life, is not typically performed on patients considered ASA class 5 or 6, so these were

likely not included for the analysis. ASA classes 3 and 4 are risk factors for readmission after TKA when compared with classes 1 and 2 because patients with severe systemic disease have a higher likelihood of presenting with exacerbations of their systemic disease or further complications.

Discharge disposition was cited as a risk factor for readmission by 3 studies. However, the studies in our review had differing results when it came to which discharge dispositions were considered as risk factors (Table 3) [23,28,37]. Swenson et al. found that discharge to nonrehabilitation centers, including discharge on home health support, was associated with an increased risk of readmission when compared with not being discharged on home health [23]. In contrast, Zmistowski et al. and Schairer et al. found that discharge to home was associated with a decreased risk of readmission when compared with discharge to an inpatient rehabilitation facility or skilled nursing facility [28,37]. One hypothesis is that these differences in outcomes could be attributed to the individualized circumstances related to discharge disposition. Some patients are discharged to an inpatient rehabilitation facility if they have multiple comorbidities that need to be comanaged in the presence of insufficient familial support, in which case these patients have a higher baseline risk of readmission. Some patients operate best in the familiarity of their homes, so having a structured routine could improve outcomes.

Clinical implications

There are several risk factors highlighted in our analysis that can be addressed to improve future clinical outcomes: age, diabetes, hypertension, ASA class, and coagulopathy. Age is a nonmodifiable risk factor for readmission that could still have clinical importance through the lens of decreasing readmission rates. Although elderly patients between the age of 65 and 84 years are the primary age group for elective TKA [54], risk for readmission after TKA increases with increasing age. Surgeons have been and should continue to be wary of age when discussing eligibility for surgery. Diabetes is a modifiable risk factor that could be managed with diet and medication. Previous studies have shown that well-managed diabetes decreases the risk for readmission after noncritical care admissions [55]. We expect that extrapolating this result to TKA would have similar results. Similarly, hypertension is also a modifiable risk factor that could be managed with diet and medication. Belmont et al. found that adequate management of hypertension decreased the risk for readmission after TKA [29]. Adequate management of hypertension by collaborating with primary care before surgery should help alleviate this risk factor. Similarly, well-managed comorbidities by the primary care team would result in lower ASA class assignment before surgery, thereby reducing the likelihood of post-TKA readmission. Coagulopathy is a modifiable risk factor that can predispose patients to postoperative complications such as hemarthrosis, hematoma, or wound drainage [52]. Adequate control of coagulopathy in patients before and after TKA may improve patient outcomes and reduce risk of readmission.

Limitations

Despite adhering to a rigorous process and applying multiauthor vetting for the article selection process, there is a possibility of selection bias in our review. We may have missed some studies written in languages other than English without known available translations. Because we focused on primary TKA cohort studies in our review, some additional nuances related to revision arthroplasties and knee fracture cohorts are missing in our analyses. As all the studies in our review are single-arm retrospective observational cohorts, there is inherent systemic bias in their results, despite the evidence for many new and motivating risk factors. Our review is also limited by the poor adherence to standard TRIPOD development and reporting criteria and a lack of use of widely accepted procedures such as testing the models with external or bootstrapped validation cohorts. Indeed, even with partial credit being awarded to several criteria during evaluation, the average TRIPOD score was 69% (Electronic Supplementary Table 3). Because the TRIPOD statement is intended to be a checklist for the essential components for transparent reporting, studies should ideally have a TRIPOD score closer to 100%. However, the studies in our review scored from 56% to 83%, with a median of 71%. The interquartile range of 65% to 74% indicates that most studies either failed the TRIPOD evaluation or were borderline passing. It is also worth noting that the TRIPOD standard was published in 2015—therefore, it is possible that authors publishing studies before the 2015-2016 timeframe did not have access to the checklist when reporting study results. Nonetheless, certain aspects of the TRIPOD standard were widely espoused before its publication by precedent standards such as the CHecklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies checklist [56] and Critical Appraisal Skills Programme tool [57]. For example, discriminative statistics reporting (C-statistics or area under the curve) was widely promoted by earlier guidelines but was found to be lacking in many of the models covered by this analysis. Authors of predictive model studies should be mindful to conduct reporting based on whatever prevalent standard is available at the time of publication.

Conclusions

Our review of predictive models for the risk of readmission after TKA entailed 29 models from detailed analyses of 25 studies using the TRIPOD quality assessment criteria. Most models were built over the last decade in the United States, either using a facility EHR system or the ACS-NSQIP data sets. Despite 2 validated models showing moderate predictive capabilities, most studies did not use new statistical techniques for building models. Most studies neither measured nor validated the model performance using an external, held-out, or bootstrapped cohort. This review emphasizes that authors of future studies must be mindful of adhering to accepted reporting practices to maximize clinical utility of predictive models, especially given that clinical applicability is not recommended until these steps have been taken into account. Some comorbidities—coagulopathies, hypertension, heart disease, and diabetes—were found to be risk factors with strong support for the risk of post-TKA readmission. In particular, coagulopathy, ASA class, and discharge disposition were not only mentioned in previous systematic reviews but also found to be strong risk factors for readmission. The clinical ramifications of these findings should be noted and acted upon by care teams in practice.

Conflict of interest

The authors declare there are no conflicts of interest.

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Electronic Supplementary Table 1
PRISMA-P checklist for systematic review of studies for readmissions for TKA.

Section and topic	Item No	Checklist item	(Page no.#)
Administrative information			
Title			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	5
Authors			
Contact	3a	Provide the name, institutional affiliation, e-mail address of all protocol authors; provide the physical mailing address of the corresponding author	Title page
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	N/A
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state the plan for documenting important protocol amendments	N/A
Support			
Sources	5a	Indicate sources of financial or other support for the review	Title page
Sponsor	5b	Provide name for the review funder and/or sponsor	
Role of the sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	3-4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	3-4
Methods			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers, or other gray literature sources) with planned dates of coverage	5-6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	5-6
Study records			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	8-9
Selection process	11b	State the process that will be used for selecting studies (such as 2 independent reviewers) through each phase of the review (ie, screening, eligibility, and inclusion in meta-analysis)	8-9
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	8-9
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any preplanned data assumptions and simplifications	8-9
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Tables 1–3
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be performed at the outcome or study level, or both; state how this information will be used in data synthesis	ESM 2
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	ESM 3
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	N/A
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	ESM 2

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol [14].

Electronic Supplementary Table 2
TRIPOD checklist for readmission risk models for TKA.

Section/Topic	Item		Checklist item	Page
Title and abstract				
Title	1	D;V	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	D;V	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3-4
Introduction				
Background and objectives	3a	D;V	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5-6
	3b	D;V	Specify the objectives, including whether the study describes the development or validation of the model or both.	6-7
Methods				
Source of data	4a	D;V	Describe the study design or source of data (eg, randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	7-8
	4b	D;V	Specify the key study dates, including the start of accrual; the end of accrual; and, if applicable, end of the follow-up.	7
Participants	5a	D;V	Specify key elements of the study setting (eg, primary care, secondary care, general population) including number and location of centers.	7
	5b	D;V	Describe eligibility criteria for participants.	7-8
	5c	D;V	Give details of treatments received, if relevant.	n/a
Outcome	6a	D;V	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	9
	6b	D;V	Report any actions to blind assessment of the outcome to be predicted.	8
Predictors	7a	D;V	Clearly define all predictors used in developing the multivariable prediction model, including how and when they were measured.	8
	7b	D;V	Report any actions to blind assessment of predictors for the outcome and other predictors.	8
Sample size	8	D;V	Explain how the study size was arrived at.	9
Missing data	9	D;V	Describe how missing data were handled (eg, complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	11
Statistical analysis methods	10a	D	Describe how predictors were handled in the analyses.	10
	10b	D	Specify type of model, all model-building procedures (including any predictor selection), and the method for internal validation.	10-12
	10c	V	For validation, describe how the predictions were calculated.	n/a
	10d	D;V	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	12-13
	10e	V	Describe any model updating (eg, recalibration) arising from the validation, if performed.	n/a
Risk groups	11	D;V	Provide details on how risk groups were created, if performed.	12-13
Development vs validation	12	V	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	n/a
Results				
Participants	13a	D;V	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	13
	13b	D;V	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	13-14
	13c	V	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors, and outcome).	n/a
Model development	14a	D	Specify the number of participants and outcome events in each analysis.	14
	14b	D	If performed, report the unadjusted association between each candidate predictor and outcome.	Table 2 (15)
Model specification	15a	D	Present the full prediction model to allow predictions for individuals (ie, all regression coefficients, and model intercept or baseline survival at a given time point).	16-17 (Table 3)
	15b	D	Explain how to use the prediction model.	16-18
Model performance	16	D;V	Report performance measures (with CIs) for the prediction model.	18-19
Model updating	17	V	If performed, report the results from any model updating (ie, model specification, model performance).	n/a
Discussion				
Limitations	18	D;V	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	22-23
Interpretation	19a	V	For validation, discuss the results with reference to performance in the development data and any other validation data.	n/a
	19b	D;V	Give an overall interpretation of the results, consider objectives, limitations, results from similar studies, and other relevant evidence.	19-22
Implications	20	D;V	Discuss the potential clinical use of the model and implications for future research.	20-22
Other information				
Supplementary information	21	D;V	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	10
Funding	22	D;V	Give the source of funding and the role of the funders for the present study.	7, 24

TRIPOD checklist: Prediction model development and validation.
Items relevant only to the development of a prediction model are denoted by D, items relating solely to a validation of a prediction model are denoted by V, and items relating to both are denoted D;V. We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

Electronic Supplementary Table 3
TRIPOD scoring with partial scores.

Study	Title	Abstract	Background and objectives	Source of data	Participants	Outcome	Predictors	Sample size	Missing data	Statistical analysis methods	Risk groups	Development vs validation	Participants	Model development	Model specification	Model performance	Model updating	Limitations	Interpretation	Implications	Supplementary information	Funding	Average score	
"Solomon, Chibnik et al. 2006" [24]	0	0.9	1	1	1	0.5	0.5	0	0	0.75	1	0	0.66	0.5	0.9	1	n/a	1	1	1	0	1	0.65	
"Higuera, Elsharkawy et al. 2011" [25]	1	1	1	1	1	0.5	0	1	0	0.75	0	0	0.67	0.5	0	0	n/a	1	1	1	1	1	0.64	
"Cram, Lu et al. 2012"		0.67	1	1	1	1	0.5	0.5	1	0.5	0.9	0	0	0.66	1	0.9	0	n/a	1	1	1	1	1	0.74
"Pugely, Callaghan et al. 2013" [26]	0.67	1	1	1	1	0.5	0.5	1	1	0.6	0	1	0.67	0.5	0.9	0	n/a	1	1	1	0	1	0.73	
"Pugely, Martin et al. 2013" [27]		0.33	1	1	1	1	0.5	1	1	1	0.75	0	0	0	0.5	0.9	0	n/a	1	1	1	1	1	0.71
"Mnatzaganian, Ryan et al. 2014"	0	1	1	1	1	0.5	0.33	1	0	1	0	0	0.66	0.5	1	0	n/a	1	1	1	1	1	0.67	
"Schairer, Vail et al. 2014" [28]		0	1	1	1	1	0.5	0.5	1	0	0.75	0	0	0.66	0.5	0.9	0	n/a	1	1	1	0	0	0.56
"Belmont, Goodman et al. 2016" [29]	0.67	1	1	1	1	0.5	0.5	1	1	0.75	0	0	0.66	0.5	0	0	n/a	1	1	1	1	0	0.65	
"Feng, Lin et al. 2017" [30]		0.33	1	0.84	1	0.67	0.5	0.5	1	1	1	n/a	n/a	1	0.5	0.5	1	n/a	1	1	1	n/a	1	0.82
"Lee, Lumar, & Kim. 2017" [31]		0.67	0.9	1	1	0.67	0.5	0.5	1	0	1	n/a	n/a	1	0.5	0.5	1	n/a	1	1	1	n/a	0	0.74
"Siracuse, Ippolito et al. 2017" [32]	0	1	1	1	1	0.5	0.5	1	0	0.75	1	1	1	0.5	0.9	0	n/a	1	1	1	0	1	0.72	
"Kimball, Nicholas et al. 2018" [33]	0.33	1	1	1	0.67	0.5	0.5	1	1	1	n/a	n/a	1	0.5	0.5	1	n/a	1	1	1	n/a	1	0.83	
"Lehtonen, Hess et al. 2018" [34]		0.33	1	1	1	0.67	0.5	0.5	1	1	0.75	n/a	n/a	1	0.5	0.5	1	n/a	1	1	1	n/a	0	0.76
"Saku, Madanat et al., 2018" [35]		0.67	1	1	1	1	1	0.5	1	0	0.75	0	0	1	0.5	0.5	1	n/a	1	1	1	0	1	0.71
"Urish, Qin, et al., 2018" [11]		0.33	1	1	1	1	0.5	0.5	1	0	0.75	n/a	0	1	0.5	0.5	1	n/a	1	1	1	0	1	0.70
"Yohe, Funk et al. 2018" [36]		0.67	1	1	1	1	0.5	0.5	1	0	0.75	0	0	1	0.5	0.5	1	n/a	1	1	1	0	1	0.69
"Ali, Loeffler et al. 2019" [10]		0.33	0.9	1	1	0.67	0.5	0.5	1	0	1	n/a	n/a	1	1	1	1	n/a	1	1	1	n/a	0	0.77
"Zmistowski, Retrepo et al. 2013" [37]	0	0.8	1	1	1	0.5	0.5	1	1	0.75	0	0	0	0.5	0.9	0	n/a	1	1	1	0	1	0.62	
"Mesko, Bachmann et al. 2014" [38]	1	0.9	1	1	1	0.5	0.5	1	0	0.75	0	1	1	0.5	1	0	n/a	1	1	1	0	1	0.72	
"Tiberi, Hansen et al. 2014" [39]		0.33	1	1	1	0.5	0.5	0.5	1	0	0.75	0	0	0.67	0.5	0.9	0	n/a	1	1	1	0	1	0.60
"Ricciardi, Oi et al. 2017" [40]		0.33	1	1	1	1	0.5	0.5	1	0	0.75	0	0	0.67	0.5	0.9	0	n/a	1	1	1	0	0	0.58
"Sher, Keswani et al. 2017" [41]		0.33	1	1	1	1	0.5	0.5	1	0	1	0	0	1	0.5	0.5	1	n/a	1	1	1	0	1	0.68
"Swensen, Bastian et al. 2018"	0.33	0.8	1	1	1	1	0.5	1	1	0.75	0	0	1	0.5	1	1	n/a	1	1	1	1	0	0.76	
"Yao, Keswani et al. 2017" [42]		0.67	1	1	1	1	0.5	0.5	1	1	0.75	1	0	1	0.5	0.5	1	n/a	1	1	1	0	0	0.73
"Schroer, Diesfield et al. 2018" [43]	0.33	0.9	1	1	1	0.5	0.5	1	0	0.33	1	0	1	0.5	0	0	n/a	1	1	1	0	0	0.57	